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A family-based intervention for prevention and self-management of disabilities due to leprosy, podoconiosis and lymphatic filariasis versus usual care in Ethiopia: study protocol for a cluster-randomised controlled trial

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Abstract

Introduction

Leprosy, podoconiosis and lymphatic filariasis (LF) are three skin-related neglected tropical diseases. All three conditions can lead to temporary and permanent impairments. These impairments progressively worsen and are major determinants of stigma, discrimination and participation restrictions. Self-care is essential to prevent disabilities and chronic disease complications. Many persons with leprosy-, LF- and podoconiosis-related disabilities need to practice self-management routines their entire life. This is difficult without support and encouragement of others. The objective of this study is to assess the effectiveness of a family-based intervention for prevention and self-management of disabilities due to leprosy, podoconiosis and LF compared to usual practice and care.

Methods and analysis

The study will use a cluster-randomised controlled trial design with two study arms. The project will be carried out in endemic districts in East and West Gojjam zones in the Amhara region in Ethiopia. A total of 630 participants will be included in the study, consisting of 420 persons affected (210 persons affected by leprosy and 210 persons affected by LF or podoconiosis; for each disease there will be one intervention and one control group) and 210 family members (in the intervention group). The family-based intervention comprises of an essential care package that consists of the following three main components: (1) self-management of disabilities; (2) economic empowerment; and (3) psychosocial support. Participants in the control areas will receive usual practice and care.

Ethics and dissemination

Ethical approval has been obtained from the Debre Markos University Health Sciences Institutional

Research Ethics Review Committee. Results will be disseminated through peer-reviewed publications, conference presentations and workshops.

Registration details

This study has been registered at the Pan African Clinical Trial Registry (PACTR202108907851342).

Article Summary

Strengths and limitations of this study

- This family-based intervention cluster-randomised controlled trial was preceded by a proof-of-concept study, in which the intervention was found feasible.
- While self-management of disabilities is the main component of the family-based intervention, the essential care package goes beyond self-care and also includes economic empowerment and a psychosocial care component.
- This study is led by and partly carried out by the Ethiopian National Association of Persons Affected by Leprosy (ENAPAL), a large Ethiopian leprosy disabled persons' organisation.
- Inclusion of family members in self-care activities ensures sustainability of the intervention.
- It is difficult to select study districts with a similar prevalence of persons with disease-related disabilities, that have geographical similarities and in which no previous or ongoing leprosy, podoconiosis or LF-related work of other organisations is or has been conducted.

Introduction

Leprosy, podoconiosis and lymphatic filariasis (LF) are Neglected Tropical Diseases (NTDs) [1]. NTDs are a group of communicable diseases that are among the most common conditions, particularly among the world's poorest populations [2,3]. These diseases predominate in rural and impoverished urban areas of low and middle-income countries [4]. Worldwide, over one billion people have one or more NTDs [5]. NTDs are "poverty promoting" conditions, they cause suffering through acute illness, pain, long-term disability, early death and through mental and social consequences [2,4].

Leprosy, podoconiosis and LF are three skin-related NTDs [1]. All three conditions have skin manifestations such as patches, ulcers, wounds, nodules or localized swelling [6–9]. They are caused by bacteria (leprosy), chronic exposure to red clay volcanic soil (podoconiosis) and nematode worms that are transmitted by mosquitoes (LF) [7,8,10]. Leprosy, podoconiosis and LF can lead to temporary and permanent impairments if not diagnosed and treated early [1,6,11]. These impairments progressively worsen and are major determinants of stigma and participation restrictions [12–14].

Social consequences of all three conditions may include reduced work and education opportunities, social isolation, exclusion and problems in interpersonal relationships, including marital problems [15–18]. Psychological consequences may include feelings of shame, low self-esteem, mental distress, depression, anxiety, and decreased individual and family quality of life [15–18]. In addition, these conditions may impose a social and economic burden on families [16,19]. Family members may also experience stigma [16,20–23]. Furthermore, costs for treatment and reduced ability to work may cause a financial burden for the entire family [16,19].

Most impairments, such as wounds, swelling and contractures, are largely preventable [1]. The most effective strategy for prevention of disabilities is early diagnosis and prompt treatment [24]. Self-care is also an essential component of prevention of disabilities, and for prevention of chronic disease complications [24–27]. Relatively simple methods exist for self-management of impairments, such as

daily washing of affected limbs, skin care, bandaging, exercises and the use of shoes [27]. Most of these methods can be practiced at home and are suitable for use across different skin-related NTDs [27–29]. These self-care interventions have been found effective in for example reducing the incidence of acute dermatolymphangioadenitis (ADLA) in persons affected by podoconiosis and LF [30,31] and in reducing ulcers among persons affected by leprosy [32]. Because physical impairments are an important determinant of stigma, disease management is also an indirect intervention to reduce stigma [33].

Many persons with leprosy-, podoconiosis- and LF-related disabilities need to practice self-management routines their entire life. This is difficult without support and encouragement of others. Family members can provide such support and encouragement. We recently conducted a proof-of-concept study in which we piloted a family-based intervention for prevention and self-management of disabilities due to leprosy, podoconiosis and LF in Ethiopia [34]. This family-based intervention consisted of self-management of disabilities, awareness raising and economic empowerment, and was delivered during several monthly group meetings. We found that the intervention had a positive effect on impairments and self-management of disabilities, family quality of life and stigma. However, sampling was not randomised, which means we couldn't determine the effectiveness of the intervention. To collect credible evidence for this new, previously piloted intervention, we aim to conduct a similar study using a randomised controlled design.

Objectives

The primary objective of this study is to assess the effectiveness of a family-based intervention for prevention and self-management of disabilities due to leprosy, podoconiosis or LF compared to usual practice and care. In addition to demonstrating the effectiveness of the family-based intervention in terms of management of disabilities, we also aim to assess the impact of the intervention on family quality of life, mental wellbeing, stigma, participation and economic empowerment of person affected and their families.

Methods and analysis

The protocol for this study is outlined below. This study protocol adheres to the SPIRIT statement [35].

Study design

The intervention consists of a cluster-randomised controlled trial, with two study arms. The two study arms consist of (1) the family-based intervention and (2) usual practice and care (control group).

Study setting

The project is carried out in endemic districts in East and West Gojjam zones in the Amhara region in Ethiopia (the proof-of-concept study was conducted in a different zone , the Awi zone). The Amhara region is the second largest state in population and is divided in 11 zones. All three conditions are endemic in the Amhara region. In 2019, Ethiopia had 3,201 new leprosy patients, 13% of the new patients had Grade 2 disabilities [36]. The prevalence of leprosy is highest in the Amhara, Afar and Oromiya regions [37,38]. LF is endemic in the Amhara, Beneshangul-Gumuz, SNNPR and Oromia regions. Thirty million people have been estimated to be at risk of LF in Ethiopia [37]. In addition, Ethiopia is estimated to have 25% (1 million cases) of the global burden of podoconiosis. Podoconiosis is spread out over one-fifth of the surface of Ethiopia, especially the Western part [37,39,40]. The regions with the high prevalence of podoconiosis are Amhara, SNNPR, Oromiya and Beneshangul-Gumuz [39,40].

West Gojjam zone and East Gojjam zone are subdivided into 16 and 20 districts (woredas) respectively. The three districts selected for this study are Dega Damot and Dembecha districts (West

Gojjam zone) and Enarge Enawga (East Gojjam zone). These districts have been selected based on their similarity in total population, sex ratio, number of urban/rural neighbourhoods (kebeles), number of hospitals, health centres and health posts, disease prevalence and lack of previous or ongoing leprosy, podoconiosis or LF-related work of other organisations (Table 1). The latter to avoid possible contamination of the study results. The study is being conducted in real-world settings and populations.

Table 1. Characteristics of the selected study areas. Data has been collected from field census, health office reports and [41,42].

	Dega Damot district	**Dembecha district**	**Enarge Enawga district**
Total population, *n* (%) Men, *n* (%) Women, *n* (%)	181,325 (100%) 89,756 (49.5%) 91,156 (50.5%)	218,257 (100%) 105,809 (48.48%) 112,448 (51.52%)	172,939 (100%) 86,297 (49.9%) 86,642 (49.1%)
Number of kebeles, *n* (%) Rural, *n* (%) Urban, *n* (%)	 36 (100%) 34 (94%) 2 (6%)	 31 (100%) 27 (87%) 4 (13%)	 35 (100%) 31 (89%) 4 (11%)
Number of health facilities Hospital, *n* Health centre, *n* Health post, *n*	 1 7 34	 1 7 28	 1 7 34
Number of health extension workers working in the area	88	60	76
Percentage of total population that has podoconiosis	>10%	1-5%	>10%
Estimated number of persons leprosy-, podoconiosis- or LF-related disabilities living in the area	Leprosy=132 Podoconiosis =352	Leprosy=135 Podoconiosis=1,042	Leprosy=213 Podoconiosis or LF=797
Geographic and background information	• Climate zones: 75% dega (cool temperate), 20% woina dega (subtropical) and 5% kolla (hot lowland). • Annual rainfall between 900-1,200 mm. • The district consists of 35% mountain, 30% hills, 20% valleys and 15% plains.	• Climate zones: 11% dega (cool temperature), 83% woina dega (subtropical) and 6% kolla (hot lowland) • Annual rainfall is between 1,221-1,602 mm. • The district consists of 60% plains, 30% mountain and 10% hills. • Elevation is between 1500-2995 meters above sea level.	• Climate zones: 30% dega (cool temperate), 50% woina dega (subtropical) and 20% kolla (hot lowland). • Annual rainfall is between 1,200-1,400 mm. • The district consists of 50% plains, 30% mountain and 20% hills. • Elevation is 1100-3200

		• Other: bordered by the Nile river.	meters above sea level.
Previous or ongoing work with the target group in the area?	No	Yes, with persons affected by podoconiosis (no persons affected by podoconiosis will be included from this district)	No

Participants

People with leprosy-related impairments and people with LF or podoconiosis-related lymphedema will be included in this study. Of each person affected, at least one adult family member will be included (e.g. people who have a family member such as sibling, child, parent or grandparent affected by leprosy, LF or podoconiosis living in the same household).

People 15 years and above will be included in the study. All participants need to have leprosy-, LF- or podoconiosis-related impairments and have to be eligible to participate in self-care activities. The focus is on skin and wound care of affected persons. All persons have to be residents of project areas of the study. People who are unable to coherently express themselves verbally (i.e. are unable to understand and participate in an interview) will be excluded. In addition, persons affected who live alone will excluded.

Intervention

This RCT was preceded by a proof-of-concept study in which a family-based intervention was developed and found feasible [34]. The family-based intervention consists of an essential care package that consists of the following three main components: (1) self-management of disabilities; (2) economic empowerment; and (3) psychosocial support. All components of the intervention are family-based and family focused. Although not mentioned as a separate component, awareness raising is an integral part of the intervention. The essential care package is described in more detail below:

- Training sessions/group meetings for self-management and prevention of disabilities. Based on the proof-of-concept study, at least five group meetings will be held in a location that is most convenient for the participants. These sessions will be delivered in group format (several families participate with one person affected and one family member present per family) to introduce the family-based methods for self-management and prevention of disabilities. In the first session basic training will be given to persons affected and their family members in using and giving psychosocial support, increasing prevention and self-management of disabilities skills, information on course and treatment of disease, identifying barriers and facilitators to self-care and creating strategies to overcome these barriers. In the following training sessions, the research assistants support and guide all participating families (repeating the basic training given in the first session) and are available to clarify questions. During these meetings, physical impairment outcomes will routinely (monthly) be collected. Family members are encouraged to help their affected family member with self-care at home. (Each group will have approximately 20 participants, therefore, training for participants in the intervention group will not all be given at the same day/time).
- Formation of self-help groups for economic empowerment. The project will facilitate the formation of self-help groups of affected persons, their family members are encouraged to join group meetings. Each self-help groups will collect a small contribution fee from its

participants, these fees are used to provide loans for the participants of the self-help groups (micro-finance). Self-help groups will also lobby for 'benefits', e.g. the use of land, from the government. In addition, each self-help group participant and at least one of their family members will receive (one) vocational training. Income generation is essential for sustainable self-management and prevention of disabilities: without income, self-care items such as Vaseline and shoes cannot be bought. Income generation will benefit the whole family.

- Psychosocial support will be part of the training sessions/group meetings for self-management and prevention of disabilities. Persons affected and their family members will be trained in using and giving psychosocial support.

The control group will receive treatment as usual. Participants in the control areas will receive the same basic training (one session) as the participants in the intervention group, but will have no family members present during the training. When the intervention group has their additional four meetings (at least five meetings will be held), the participants in the control group will receive usual practice and care. In addition, they will receive information about existing mechanisms for economic empowerment (such as "funeral saving groups" and other existing credit saving initiatives).

Procedures

This study has two main phases. Each phase is briefly described below.

Phase 1: Preparatory phase. In this phase, a literature review will be conducted to guide the development of the psychosocial support component that will be added to the family-based intervention. In addition, the Sari Stigma Scale (SSS), Beach Centre Family Quality of Life (FQoL) scale and Participation scale (P-scale) will be cross-culturally validated (the Patient Health Questionnaire (PHQ-9) has already been validated in Amharic [43–45]). We will assess conceptual, item, semantic, operational and measurement equivalence using a framework for cross-cultural equivalence testing based on the work of Herdman et al. [46], Terwee et al. [47] and Stevelink & van Brakel [48]. The Knowledge Attitudes and Practices (KAP) measure will be translated, and pilot tested. A training workshop will be organized to train community health extension workers, local area health workers and the research team in research methods and family-based intervention. A list of persons affected registered in the community level census that are eligible to participate in self-care activities will be prepared. Persons affected by leprosy, podoconiosis or LF and their family members will be recruited. A database will be established to monitor the routine intervention activities. Baseline data will be collected, and the results analysed.

Phase 2: Implementation and evaluation of the family-based intervention. In this phase, the intervention will be implemented: at least five training sessions and family meetings will be held. This training is done by the local researcher, with the research assistants and with at least one community health extension worker present at the meeting. Participants in the intervention and control area will receive basic tools to practice self-care (Vaseline, a bucket, shoes, and soda). In this phase, the effectiveness and acceptability of the intervention will be evaluated (feasibility has already been established [34]). This will be done by collecting the same information as in the baseline study (Table 2), a few weeks and one year after implementation of the intervention. In addition, interviews will be conducted to collect most significant change stories and to assess the impact qualitatively. All components of the study will be conducted in Amharic, the official language of Ethiopia and language spoken in the study areas.

Outcomes

Table 2 details the outcomes measured during this study, including the methods that will be used to measure the outcomes. Physical impairment outcomes are the primary outcome measures. Acceptability, family quality of life, stigma, social participation, mental wellbeing, disease knowledge, attitudes and economic empowerment are secondary outcomes.

Table 2. Outcomes measures

Type of outcome	Specific outcome	Outcome measures[a]
Implementation outcomes	Acceptability	Qualitative (IDI and FGD)
	Disability management practices	Observations (field notes), Qualitative (IDI and FGD)
Effectiveness (persons affected level)	Physical impairment outcomes	For persons affected by leprosy: • Eyes, Hands, Feet (EHF) score, wound count, registration of infection, observation For persons affected by podoconiosis and LF: • Lymphedema grading, measuring the largest point of swelling below the knee circumference, registering the frequency of acute attacks, wound count, registration of infection, observation.
	Family quality of life	Beach Centre Family Quality of Life scale (FQoL scale), IDI
	Perceived, experienced and self-stigma	SARI Stigma Scale (SSS)
	Social participation	Participation Scale (P-scale)
	Mental wellbeing [43–45]	Patient Health Questionnaire (PHQ-9)
	Disease knowledge [49,50]	Disease specific Knowledge Attitudes and Practices (KAP) measure
	Attitudes towards the disease and persons affected by the disease	Qualitative (IDI, FGD)
	Economic empowerment	Registration of attendance of persons affected organisation group meetings, monthly contribution, use of credit, qualitative (IDI)
Effectiveness (family member level)	Family quality of life	Beach Centre Family Quality of Life scale (FQoL scale), qualitative (IDI)
	Perceived, experienced and self-stigma	IDI
	Mental wellbeing [43–45]	Patient Health Questionnaire (PHQ-9)
	Disease knowledge [49,50]	Disease specific Knowledge Attitudes and Practices (KAP) measure
	Attitudes towards (persons affected by) the disease	Qualitative (IDI, FGD)
	Economic empowerment	Registration of attendance of persons affected organisation group meetings, monthly contribution, use of credit
		Qualitative (IDI)
Impact at community level	Most significant changes	Qualitative (IDI and FGD)
	Impact assessment (to evaluate the change in the target population and communities)	Qualitative (IDI and FGD)

[a] IDI = in-depth interview, FGD = focus group discussion.

Participant timeline

The participant timeline, in line with SPIRIT recommendations, can be found in Table 3.

Table 3. Participant timeline

	Study period[a]					
	Enrolment	Pre-allocation	Allocation	Post allocation		
Time point		**T0**		**Tx**	**T1**	**T2**
ENROLMENT:						
Eligibility screen	X					
Informed consent	X					
Allocation			X			
INTERVENTION:						
Group meetings				X		
ASSESSMENTS:						
Questionnaires[b]:						
SSS		X			X	X
FQoL		X			X	X
P-scale		X			X	X
PHQ-9		X			X	X
KAP		X			X	X
Routine data:						
Physical impairment outcomes		X		X	X	X
Group meeting attendance		X		X	X	X
In-depth interviews		X			X	X
Focus group discussions		X			X	X

[a] T0= before the intervention / baseline. Tx = monthly monitoring during the intervention (routine data collection). T1 = One-month post-intervention. T2 = One-year post-intervention.

[b] SSS = SARI Stigma Scale, FQoL = Beach Centre Family Quality of Life scale, P-scale = Participation Scale, PHQ-9 = Patient Health Questionnaire, KAP = Disease specific Knowledge Attitudes and Practices measure.

Sample size

A total of 630 participants will be included in the study. A total of 420 persons affected will be included: 210 persons affected by leprosy and 210 persons affected by LF or podoconiosis; for each disease there will be one intervention and one control group. In the intervention group, a total of 210 family members will also be included. The sample size calculation is based on data from the proof-of-concept study [34]. In the proof-of-concept study, 43% of the participants had leg impairments at intake. During the final assessment, the last session participants attended, the number of participants with leg impairments had dropped to 21%. A sample size calculation for two proportions (proportion 1: 43%; proportion 2: 21%) with a significance of 0.05 and a power of 90% would give a total sample size of 92 participants in each group. We expect that the loss to follow-up will be no more than 15% (we do not expect a higher loss to follow-up, as participants will be followed-up at home). Our sample size will therefore be 105 persons affected in each group.

Recruitment

Potential participants will be approached via community level enumeration, health care settings, persons affected organisations, community leaders, and by word of mouth. The recruitment period is six months, starting in October 2021. Once participants are enrolled, they will be followed up during

the study period up to 12 months in the nearby health centre or health posts. In the case of loss to follow up, participants will be visited in their home.

Allocation

The three districts will be randomly divided into clusters to implement either the family-based intervention or usual practice and care (control group). A complete enumeration of persons with the three diseases has been conducted in each district, kebeles (a lower administrative structure in the district) have been merged into "clusters" based on their geographical proximity and the number of cases in each kebele. In the three study districts a total of four clusters for leprosy and six clusters for podoconiosis and LF have been identified. The intervention and control areas will be randomly selected, by putting the cluster names in a cup or box and randomly drawing names. We will ensure that the number of intervention and control areas (clusters) in each district is equal. A list will be prepared with all patients (leprosy, podoconiosis/LF) living in the project areas, that are registered at community level enumeration and that are eligible to participate in self-care activities. Persons affected to be included in the study will be selected by stratified systematic sampling with a random start from a list of persons affected registered at the primary health care centre. This is done by selecting the first person affected on the list at random (by throwing dice), and then selecting every X-th patient on the list, based on the total number needed. Four separate lists will be created: two for persons affected by leprosy (one intervention and one control) and two for persons affected by LF or podoconiosis (one intervention and one control).

Blinding

Due to the nature of the intervention, participants cannot be blinded.

Data management

Confidentiality and anonymity of data will be ensured in data collection, data storage, analysis and publication. Research assistants who will collect the data will be fully trained in proper data management, maintenance of confidentiality and ensuring privacy during data collection. All data will be collected in Ethiopia. Only data that have been fully anonymised will be shared with the international research team. The project leader of this study will take full responsibility for ensuring the appropriate storage and security of data. Data will be kept for five years and will be destroyed after this timeframe when no longer required.

Data analysis

Quantitative data will be entered in a database created using EpiData software. Analyses will start once baseline data has been collected. Simple descriptive methods will be used to generate a demographic profile of the study sample. Differences between participants in the intervention and control groups will be evaluated using the Mann-Whitney U test or t-test for continuous variables and the chi-square statistic for categorical variables. In addition, the mean with standard deviation (or median with interquartile range, depending on the distribution of the data) of the total scores of the measures used will be calculated per participant group and per study area. The percentage change and corresponding 95%CI before and after the interventions are implemented and the statistical significance of this difference using a Z-test for differences between proportions will be calculated. Effect sizes will also be calculated. Stepwise multivariate regression with backward elimination will be done to examine what factors will have an independent effect on the outcomes. Data analysis will be done in the software packages Epi Info and SPSS Statistics. We will also use intention to treat (ITT) and difference in difference (DID) analysis to evaluate the effectiveness of the intervention.

Qualitative data -the recordings of the in-depth interviews and focus group discussions- will be transcribed, translated to English and analysed using open, inductive coding and content analysis.

Similar phrases with recurring themes will be coded in a qualitative software programme (MAXQDA) and clustered together in tables, to identify connections.

Patient and public involvement

This research will be led by and partly carried out by the Ethiopian National Association of Persons Affected by Leprosy (ENAPAL), a large Ethiopian leprosy disabled persons' organisation. Persons affected by leprosy, LF and podoconiosis will assist the researchers in analysis of the data by helping to put issues in perspective and context. We will seek to employ and train persons affected as research assistants or at least those who have a family member affected by an NTD or with a disability.

Ethics and dissemination

Ethics

Ethical approval has been obtained from the Debre Markos University Health Sciences Institutional Research Ethics Review Committee (approval number HSC/R/C/Ser/Co/11/13). All participants will be fully informed about the nature and objective of the study and of confidentiality of the data prior to data collection. Written informed consent will be obtained from each participant prior to data collection. All people who are participating in the research will be provided with a participant information sheet. No incentives will be paid to participants.

Dissemination

A publication plan has been developed, which lists several planned articles for publication in scientific journals. All articles will be published in peer-reviewed, open access journals. The results of the study will also be shared through international conferences and at (working) meetings with international researchers and local policy makers and health care staff. A meeting will be organised at the end of the study to disseminate the results in the communities in the study areas. In addition, we aim to share updates of the study through the International Federation of Anti-Leprosy Associations (ILEP) newsletter and the Sasakawa Health Foundation newsletter.

Authors' contributions

ATN, MWA, TT and APS designed the study and were responsible for funding acquisition. MWA is the principal investigator of the study. MWA, NAM and TT are responsible for the implementation of the study in Ethiopia. MWA will lead data analysis with support from ATN and NAM. ATN drafted the manuscript. All authors have read an approved the final version of the manuscript.

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Competing interests statement

The authors declare that they have no competing interests.

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SPIRIT

STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description
Administrative information		
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym The study design, population and intervention are mentioned in the title.
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry Mentioned in the abstract.
	2b	All items from the World Health Organization Trial Registration Data Set
Protocol version	3	Date and version identifier N/a
Funding	4	Sources and types of financial, material, and other support This has been mentioned in the funding statement.
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors Addressed under author contributions.
	5b	Name and contact information for the trial sponsor N/a
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities This has been mentioned in the funding statement.
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee) N/a
Introduction		

Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention Introduction
	6b	Explanation for choice of comparators Introduction, and methods > intervention
Objectives	7	Specific objectives or hypotheses Introduction > objectives
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory) Introduction, and methods > study design
Methods: Participants, interventions, and outcomes		
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained Methods > study setting
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists) Methods > participants
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered Methods > intervention, and methods > procedures
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease) N/a
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests) Methods > intervention
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial Methods > intervention

Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended Methods > outcomes, and Table 2.
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure) Methods > participant timeline and Table 3
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations Methods > sample size
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size Methods > recruitment

Methods: Assignment of interventions (for controlled trials)

Allocation:

Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions Methods > allocation
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned Methods > allocation
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions Methods > allocation
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how Methods > blinding

	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial N/a
Methods: Data collection, management, and analysis		
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol Methods > outcomes, and methods > data analysis plan
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols Methods > outcomes, and methods > sample size calculation
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol Methods > data management
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol Methods > data analysis
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses) Methods > data analysis
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation) Methods > data analysis
Methods: Monitoring		
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed N/a

	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial N/a
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct N/a
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor N/a
Ethics and dissemination		
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval Ethics and dissemination > ethics
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators) N/a
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32) Ethics and dissemination > ethics
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable N/a
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial Methods > data analysis plan
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site Competing interests statement
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators Methods > data analysis plan

Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation N/a
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions Ethics and dissemination > dissemination
	31b	Authorship eligibility guidelines and any intended use of professional writers Author's contributions
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code N/a
Appendices		
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.

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A family-based intervention for prevention and self-management of disabilities due to leprosy, podoconiosis and lymphatic filariasis versus usual care in Ethiopia: study protocol for a cluster-randomised controlled trial

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A family-based intervention for prevention and self-management of disabilities due to leprosy, podoconiosis and lymphatic filariasis versus usual care in Ethiopia: study protocol for a cluster-randomised controlled trial

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Abstract

Introduction

Leprosy, podoconiosis and lymphatic filariasis (LF) are three skin-related neglected tropical diseases. All three conditions can lead to temporary and permanent impairments. These impairments progressively worsen and are major determinants of stigma, discrimination and participation restrictions. Self-care is essential to prevent disabilities and chronic disease complications. Many persons with leprosy-, LF- and podoconiosis-related disabilities need to practice self-management routines their entire life. This is difficult without support and encouragement of others. The objective of this study is to assess the effectiveness of a family-based intervention in terms of physical outcomes related to prevention and self-management of disabilities due to leprosy, podoconiosis and LF and family quality of life and wellbeing compared to usual practice and care.

Methods and analysis

The study will use a cluster-randomised controlled trial design with two study arms. The project will be carried out in endemic districts in East and West Gojjam zones in the Amhara region in Ethiopia. Clusters consist of kebeles (lower administrative structures in the district) that have been merged, based on their geographical proximity and the number of cases in each kebele. A total of 630 participants will be included in the study. The intervention group will consist of 105 persons affected by leprosy, 105 persons affected by LF or podoconiosis, and 210 family members. The control group will consist of 105 persons affected by leprosy and 105 persons affected by LF or podoconiosis. The family-based intervention comprises of an essential care package that consists of the following three main components: (1) self-management of disabilities; (2) economic empowerment; and (3) psychosocial support. Participants in the control areas will receive usual practice and care. Data

analysis includes, but is not limited to, calculating the percentage of change and corresponding 95%CI of physical impairment outcomes in each group, before and after the intervention is implemented, effect sizes, intention to treat and difference in difference analysis.

Ethics and dissemination

Ethical approval has been obtained from the Debre Markos University Health Sciences Institutional Research Ethics Review Committee. Results will be disseminated through peer-reviewed publications, conference presentations and workshops.

Registration details

This study has been registered at the Pan African Clinical Trial Registry (PACTR202108907851342).

Article Summary

Strengths and limitations of this study

- This family-based intervention cluster-randomised controlled trial was preceded by a proof-of-concept study, in which the intervention was found feasible.
- While self-management of disabilities is the main component of the family-based intervention, the essential care package goes beyond self-care and also includes economic empowerment and a psychosocial care component.
- This study is led by and partly carried out by the Ethiopian National Association of Persons Affected by Leprosy (ENAPAL), a large Ethiopian leprosy disabled persons' organisation.
- Inclusion of family members in self-care activities ensures sustainability of the intervention.
- Because randomisation will be done at the level of kebeles, it will not be possible to conduct a blinded outcome assessment, because research staff will be aware of the area they are in. It is not considered feasible to find people from outside the study areas to conduct the outcome assessment.

Introduction

Leprosy, podoconiosis and lymphatic filariasis (LF) are Neglected Tropical Diseases (NTDs) [1]. NTDs are a group of communicable diseases that are among the most common conditions, particularly among the world's poorest populations [2,3]. These diseases predominate in rural and impoverished urban areas of low and middle-income countries [4]. Worldwide, over one billion people have one or more NTDs [5]. NTDs are "poverty promoting" conditions, they cause suffering through acute illness, pain, long-term disability, early death and through mental and social consequences [2,4].

Leprosy, podoconiosis and LF are three skin-related NTDs [1]. All three conditions have skin manifestations such as patches, ulcers, wounds, nodules or localized swelling [6–9]. They are caused by bacteria (leprosy), chronic exposure to red clay volcanic soil (podoconiosis) and nematode worms that are transmitted by mosquitoes (LF) [7,8,10]. Leprosy, podoconiosis and LF can lead to temporary and permanent impairments if not diagnosed and treated early [1,6,11]. These impairments progressively worsen and are major determinants of stigma and participation restrictions [12–14].

Social consequences of all three conditions may include reduced work and education opportunities, social isolation, exclusion and problems in interpersonal relationships, including marital problems [15–18]. Psychological consequences may include feelings of shame, low self-esteem, mental distress, depression, anxiety, and decreased individual and family quality of life [15–18]. In addition, these conditions may impose a social and economic burden on families [16,19]. Family members may also experience stigma [16,20–23]. Furthermore, costs for treatment and reduced ability to work

may cause a financial burden for the entire family [16,19].

Most impairments, such as wounds, swelling and contractures, are largely preventable [1]. The most effective strategy for prevention of disabilities is early diagnosis and prompt treatment [24]. Self-care is also an essential component of prevention of disabilities, and for prevention of chronic disease complications [24–27]. Relatively simple methods exist for self-management of impairments, such as daily washing of affected limbs, skin care, bandaging, exercises and the use of shoes [27]. Most of these methods can be practiced at home and are suitable for use across different skin-related NTDs [27–29]. These self-care interventions have been found effective in for example reducing the incidence of acute dermatolymphangioadenitis (ADLA) in persons affected by podoconiosis and LF [30,31] and in reducing ulcers among persons affected by leprosy [32]. Because physical impairments are an important determinant of stigma, disease management is also an indirect intervention to reduce stigma [33].

Many persons with leprosy-, podoconiosis- and LF-related disabilities need to practice self-management routines their entire life. This is difficult without support and encouragement of others. Family members can provide such support and encouragement. We recently conducted a proof-of-concept study in which we piloted a family-based intervention for prevention and self-management of disabilities due to leprosy, podoconiosis and LF in Ethiopia [34]. This family-based intervention consisted of self-management of disabilities, awareness raising and economic empowerment, and was delivered during several monthly group meetings. Economic empowerment was an important component of the intervention, as income generation is essential for sustainable self-management and prevention of disabilities: without income, self-care items such as Vaseline and shoes cannot be bought. We found that the intervention had a positive effect on impairments and self-management of disabilities, family quality of life and stigma. However, sampling was not randomised, which means we couldn't determine the effectiveness of the intervention. To collect credible evidence for this new, previously piloted intervention, we aim to conduct a similar study using a randomised controlled design.

Objectives

The primary objective of this study is to assess the effectiveness of a family-based intervention in terms of physical outcomes related to prevention and self-management of disabilities due to leprosy, podoconiosis or LF and family quality of life and wellbeing compared to usual practice and care. Secondary objectives include: (1) to reduce the number of people who have an episode of depression, as measured with the Patient Health Questionnaire (PHQ-9); (2) to reduce the level of stigma as measured with the SARI stigma scale (SSS), in-depth interviews and focus group discussions; (3) to improve social participation as measured with the Participation Scale (P-scale); (4) to increase the number of people who have adequate knowledge of leprosy, LF and podoconiosis as measures with disease specific Knowledge Attitudes and Practices (KAP) measures; (5) to empower people economically as measured by monthly household income, monthly financial contribution to the self-help group and in-depth interviews.

Methods and analysis

The protocol for this study is outlined below. This study protocol adheres to the SPIRIT statement [35].

Study design

The intervention consists of a cluster-randomised controlled trial, with two study arms. The two study arms consist of (1) the family-based intervention and (2) usual practice and care (control

group).

Study setting

The project is carried out in endemic districts in East and West Gojjam zones in the Amhara region in Ethiopia (the proof-of-concept study was conducted in a different zone, the Awi zone). The Amhara region is the second largest state in population and is divided in 11 zones. All three conditions are endemic in the Amhara region. In 2019, Ethiopia had 3,201 new leprosy patients, 13% of the new patients had Grade 2 disabilities [36]. The prevalence of leprosy is highest in the Amhara, Afar and Oromiya regions [37,38]. LF is endemic in the Amhara, Beneshangul-Gumuz, SNNPR and Oromia regions. Three million people are estimated to be at risk of LF in the Amhara region [39]. In addition, Ethiopia is estimated to have 25% (1 million cases) of the global burden of podoconiosis. Podoconiosis is spread out over one-fifth of the surface of Ethiopia, especially the Western part [37,40,41]. The regions with the high prevalence of podoconiosis are Amhara, SNNPR, Oromiya and Beneshangul-Gumuz [40,41].

East and West Gojjam zones are subdivided into 16 and 20 districts (woredas) respectively. The three districts selected for this study are Dega Damot and Dembecha districts (West Gojjam zone) and Enarge Enawga (East Gojjam zone). These districts have been selected based on their similarity in total population, sex ratio, number of urban/rural neighbourhoods (kebeles), number of hospitals, health centres and health posts, disease prevalence and lack of previous or ongoing leprosy, podoconiosis or LF-related work of other organisations (Table 1). The latter to avoid possible contamination of the study results. The study is being conducted in real-world settings and populations.

Table 1. Characteristics of the selected study areas. Data has been collected from field census, health office reports and [42,43].

	Dega Damot district	**Dembecha district**	**Enarge Enawga district**
Total population, *n* (%) Men, *n* (%) Women, *n* (%)	181,325 (100%) 89,756 (49.5%) 91,156 (50.5%)	218,257 (100%) 105,809 (48.48%) 112,448 (51.52%)	172,939 (100%) 86,297 (49.9%) 86,642 (49.1%)
Number of kebeles, *n* (%) Rural, *n* (%) Urban, *n* (%)	36 (100%) 34 (94%) 2 (6%)	31 (100%) 27 (87%) 4 (13%)	35 (100%) 31 (89%) 4 (11%)
Number of health facilities Hospital, *n* Health centre, *n* Health post, *n*	 1 7 34	 1 7 28	 1 7 34
Number of health extension workers working in the area	88	60	76
Percentage of total population that has podoconiosis	>10%	1-5%	>10%
Estimated number of persons leprosy-, podoconiosis- or LF-related disabilities living in the area	Leprosy=132 Podoconiosis =352	Leprosy=135 Podoconiosis=1,042	Leprosy=213 Podoconiosis or LF=797
Geographic and background information	• Climate zones: 75% dega (cool temperate), 20% woina dega (subtropical) and	• Climate zones: 11% dega (cool temperature), 83% woina dega (subtropical) and	• Climate zones: 30% dega (cool temperate), 50% woina dega

	5% kolla (hot lowland). • Annual rainfall between 900-1,200 mm. • The district consists of 35% mountain, 30% hills, 20% valleys and 15% plains.	6% kolla (hot lowland) • Annual rainfall is between 1,221-1,602 mm. • The district consists of 60% plains, 30% mountain and 10% hills. • Elevation is between 1500-2995 meters above sea level. • Other: bordered by the Nile river.	(subtropical) and 20% kolla (hot lowland). • Annual rainfall is between 1,200-1,400 mm. • The district consists of 50% plains, 30% mountain and 20% hills. • Elevation is 1100-3200 meters above sea level.
Previous or ongoing work with the target group in the area?	No	Yes, with persons affected by podoconiosis (no persons affected by podoconiosis will be included from this district)	No

Participants

People with leprosy-related impairments and people with LF or podoconiosis-related lymphedema ('persons affected') will be included in this study. In addition, of each person affected, at least one adult family member will be included (e.g. sibling, child, parent or grandparent of a person affected by leprosy, LF or podoconiosis).

People 15 years and above will be included in the study. All persons have to be residents of project areas of the study. All persons affected need to have leprosy-, LF- or podoconiosis-related impairments and have to be eligible to participate in self-care activities, as the focus is on skin and wound care of affected persons. Family members need to live in the same household as persons affected. People who are unable to coherently express themselves verbally (i.e. are unable to understand and participate in an interview) will be excluded. In addition, persons affected who live alone will excluded.

Intervention

This RCT was preceded by a proof-of-concept study in which a family-based intervention was developed and found feasible [34]. The family-based intervention consists of an essential care package that consists of the following three main components: (1) self-management of disabilities; (2) economic empowerment; and (3) psychosocial support. All components of the intervention are family-based and family focused. Although not mentioned as a separate component, awareness raising of leprosy, LF and podoconiosis in the family and the community is an integral part of the intervention. The essential care package is described in more detail below:

- Training sessions/group meetings for self-management and prevention of disabilities. Based on the proof-of-concept study, at least five group meetings will be held in a location that is most convenient for the participants. These sessions will be delivered in group format

(several families participate with one person affected and one family member present per family) to introduce the family-based methods for self-management and prevention of disabilities. In the first session basic training will be given to persons affected and their family members in using and giving psychosocial support, increasing prevention and self-management of disabilities skills, information on course and treatment of disease, identifying barriers and facilitators to self-care and creating strategies to overcome these barriers. In the following training sessions, the research assistants support and guide all participating families (repeating the basic training given in the first session) and are available to clarify questions. During these meetings, physical impairment outcomes will routinely (monthly) be collected. Family members are encouraged to help their affected family member with self-care at home. (Each group will have approximately 20 participants, therefore, training for participants in the intervention group will not all be given at the same day/time). We anticipate that the first group meeting will be held in January 2022. Group meetings will be conducted until September 2022.

- Formation of self-help groups for economic empowerment. The project will facilitate the formation of self-help groups of affected persons, their family members are encouraged to join group meetings. The Ethiopian National Association of Persons Affected by Leprosy (ENAPAL), a large Ethiopian leprosy disabled persons' organisation with a successful track record in establishing self-help groups, will coordinate and guide this part of the intervention. The facilitators of the project, trained by ENAPAL, will help to establish the self-help groups and will be present during the meetings but will not give guidance on the management of the groups. Management of the groups will be done by persons affected themselves, participants of the group will be asked to elect a 'committee' of persons affected. Each self-help group will collect a small contribution fee from its participants, these fees are used to provide loans for the participants of the self-help groups (micro-finance). Self-help groups will also lobby for 'benefits', e.g. the use of land, from the government. In addition, each self-help group participant and at least one of their family members will receive (one) vocational training. Income generation will benefit the whole family.
- Psychosocial support will be part of the training sessions/group meetings for self-management and prevention of disabilities. Persons affected and their family members will be trained in using and giving psychosocial support.

The control group will receive treatment as usual. Participants in the control areas will receive the same basic training (one session) as the participants in the intervention group, but will have no family members present during the training. When the intervention group has their additional four meetings (at least five meetings will be held), the participants in the control group will receive usual practice and care. In addition, they will receive information about existing mechanisms for economic empowerment (such as "funeral saving groups" and other existing credit saving initiatives).

Procedures

This study has two main phases. Each phase is briefly described below.

Phase 1: Preparatory phase. In this phase, a literature review will be conducted to guide the development of the psychosocial support component that will be added to the family-based intervention. In addition, the Sari Stigma Scale (SSS), Beach Centre Family Quality of Life (FQoL) scale and Participation scale (P-scale) will be cross-culturally validated (the Patient Health Questionnaire (PHQ-9) has already been validated in Amharic [44–46]). We will assess conceptual, item, semantic, operational and measurement equivalence using a framework for cross-cultural equivalence testing based on the work of Herdman et al. [47], Terwee et al. [48] and Stevelink & van Brakel [49]. The Knowledge Attitudes and Practices (KAP) measure will be translated, and pilot tested. A training workshop will be organized to train community health extension workers, local area health workers and the research team in research methods and family-based intervention. A list of persons affected registered in the community level census that are eligible to participate in self-care activities will be prepared. Persons affected by leprosy, podoconiosis or LF and their family members will be

recruited. A database will be established to monitor the routine intervention activities. Baseline data will be collected by the research assistants, and the results analysed by the researcher.

Phase 2: Implementation and evaluation of the family-based intervention. In this phase, the intervention will be implemented: at least five training sessions and family meetings will be held. This training is done by the researcher (who has extensive experience in providing training, self-care practices and the three conditions included in this study), with support from the research assistants and with at least one community health extension worker present at the meeting. Research assistants will receive a four-day training on how to implement the intervention, this training is facilitated by the researcher and project manager. In addition, each training session is carried out using standard operating procedures, that have been developed using the WHO's Integrated morbidity management for LF and podoconiosis [50], the Ethiopian Ministry of Health's LF and podoconiosis morbidity management and disability prevention guidelines and ILEP's guideline for prevention of disabilities in leprosy [51]. Participants in the intervention and control area will receive basic tools to practice self-care (Vaseline, a bucket, shoes, and soda). In this phase, the effectiveness and acceptability of the intervention will be evaluated (feasibility has already been established in the proof-of-concept study that was recently conducted [34]). This will be done by collecting the same information as in the baseline study (Table 2), a few weeks and one year after implementation of the intervention. In addition, interviews will be conducted to collect most significant change stories and to assess the impact qualitatively. Because randomisation will be done at the level of kebeles, it will not be possible to conduct a blinded outcome assessment, because research staff will be aware of the area they are in. It is not considered feasible to find people from outside the study areas to conduct the outcome assessment. All components of the study will be conducted in Amharic, the official language of Ethiopia and language spoken in the study areas.

Outcomes

Table 2 details the outcomes measured during this study, including the methods that will be used to measure the outcomes. Physical impairment outcomes are the primary outcome measures. Acceptability, family quality of life, stigma, social participation, mental wellbeing, disease knowledge, attitudes and economic empowerment are secondary outcomes.

Table 2. Outcomes measures

Type of outcome	Specific outcome	Outcome measures[a]
Implementation outcomes	Acceptability	Qualitative (IDI and FGD)
	Disability management practices	Observations (field notes), Qualitative (IDI and FGD)
	Economic empowerment	Registration of attendance of persons affected organisation group meetings, number of loans disbursed, total amount of money disbursed
Effectiveness (persons affected level)	Physical impairment outcomes	For persons affected by leprosy: • Eyes, Hands, Feet (EHF) score, total number of wounds present (wound count), registration of infection, observation (field notes) For persons affected by podoconiosis and LF: • Lymphedema grading, measuring the largest point of swelling below the knee circumference, registering the frequency of acute attacks, wound count, registration of infection, observation (field notes).

	Family quality of life	Beach Centre Family Quality of Life scale (FQoL scale), IDI
	Perceived, experienced and internalised stigma	(SSS
	Social participation	(P-scale
	Mental wellbeing [44–46]	(PHQ-9
	Disease knowledge [52,53]	Disease specific KAP measure
	Attitudes towards the disease and persons affected by the disease	Qualitative (IDI, FGD)
	Economic empowerment	Monthly household income, monthly financial contribution to the self-help group, qualitative (IDI)
Effectiveness (family member level)	Family quality of life	FQoL scale, qualitative (IDI)
	Perceived, experienced and internalised stigma	IDI
	Mental wellbeing [44–46]	(PHQ-9
	Disease knowledge [52,53]	Disease specific KAP measure
	Attitudes towards (persons affected by) the disease	Qualitative (IDI, FGD)
	Economic empowerment	monthly household income, monthly contribution to the self-help group, qualitative (IDI)
Impact at community level	Most significant changes	Qualitative (IDI and FGD)
	Impact assessment (to evaluate the change in the target population and communities)	Qualitative (IDI and FGD)

[a] IDI = in-depth interview, FGD = focus group discussion.

Participant timeline

The participant timeline, in line with SPIRIT recommendations, can be found in Table 3.

Table 3. Participant timeline

	Study period[a]					
	Enrolment	**Pre-allocation**	**Allocation**	**Post allocation**		
Time point		**T0**		**Tx**	**T1**	**T2**
ENROLMENT:						
Eligibility screen	X					
Informed consent	X					
Allocation			X			
INTERVENTION:						
Group meetings				X		
ASSESSMENTS:						

Questionnaires[b]:						
SSS		X			X	X
FQoL		X			X	X
P-scale		X			X	X
PHQ-9		X			X	X
KAP		X			X	X
Routine data:						
Physical impairment outcomes		X		X	X	X
Group meeting attendance		X		X	X	X
In-depth interviews		X			X	X
Focus group discussions		X			X	X

[a] T0= before the intervention / baseline. Tx = monthly monitoring during the intervention (routine data collection). T1 = One-month post-intervention. T2 = One-year post-intervention.
[b] SSS = SARI Stigma Scale, FQoL = Beach Centre Family Quality of Life scale, P-scale = Participation Scale, PHQ-9 = Patient Health Questionnaire, KAP = Disease specific Knowledge Attitudes and Practices measure.

Sample size

A total of 630 participants, consisting of 420 persons affected and 210 family members, will be included in the study. It is difficult to distinguish LF and podoconiosis based on clinical features under field conditions and the distinction between these conditions doesn't matter with regard to the outcomes of this study, therefore persons affected by both these conditions are treated as one group. There will be one intervention and one control group for persons affected by leprosy, and one for persons affected by LF or podoconiosis. Family members are only included in the intervention group. The intervention group will consist of 105 persons affected by leprosy, 105 persons affected by LF or podoconiosis, and 210 family members. The control group will consist of 105 persons affected by leprosy and 105 persons affected by LF or podoconiosis. The sample size calculation is based on data from the proof-of-concept study [34]. In the proof-of-concept study, 43% of the participants had leg impairments (wounds, nodules, and/or infections) at intake. During the final assessment, the last session participants attended, the number of participants with leg impairments had dropped to 21%. A sample size calculation for two proportions (proportion 1: 43%; proportion 2: 21%) with a significance of 0.05 and a power of 90% would give a total sample size of 92 participants in each group. We expect that the loss to follow-up will be no more than 15% (we do not expect a higher loss to follow-up, as participants will be followed-up at home). Our sample size will therefore be 105 persons affected in each group. The kebeles have been selected in such a way that they are similar to each other, we therefore do not anticipate a cluster effect in the current outcomes.

Recruitment

Potential participants will be approached via community level enumeration, health care settings, persons affected organisations, community leaders, and by word of mouth. The recruitment period is six months, starting in October 2021. Once participants are enrolled, they will be followed up during the study period up to 12 months in the nearby health centre or health posts. In the case of loss to follow up, participants will be visited in their home.

Allocation

The three districts will be randomly divided into clusters to implement either the family-based intervention or usual practice and care (control group). A complete enumeration of persons with the three diseases has been conducted in each district, kebeles (a lower administrative structure in the district) have been merged into “clusters” based on their geographical proximity and the number of cases in each kebele. In the three study districts a total of four clusters for leprosy and six clusters for podoconiosis and LF have been identified. The intervention and control areas will be randomly selected, by putting the cluster names in a cup or box and randomly drawing names. We will ensure

that the number of intervention and control areas (clusters) in each district is equal. A list will be prepared with all patients (leprosy, podoconiosis/LF) living in the project areas, that are registered at community level enumeration and that are eligible to participate in self-care activities. Persons affected to be included in the study will be selected by stratified systematic sampling with a random start from a list of persons affected registered at the primary health care centre. This is done by selecting the first person affected on the list at random (by throwing dice), and then selecting every X-th patient on the list, based on the total number needed. Four separate lists will be created: two for persons affected by leprosy (one intervention and one control) and two for persons affected by LF or podoconiosis (one intervention and one control).

Blinding

Due to the nature of the intervention, participants cannot be blinded.

Data management

Confidentiality and anonymity of data will be ensured in data collection, data storage, analysis and publication. Research assistants who will collect the data will be fully trained in proper data management, maintenance of confidentiality and ensuring privacy during data collection. All data will be collected in Ethiopia. Only data that have been fully anonymised will be shared with the international research team. The project leader of this study will take full responsibility for ensuring the appropriate storage and security of data. Data will be kept for five years and will be destroyed after this timeframe when no longer required.

Data analysis

Quantitative data will be entered in a database created using EpiData software. Analyses will start once baseline data has been collected. Simple descriptive methods will be used to generate a demographic profile of the study sample. Differences between participants in the intervention and control groups, including demographic information and physical impairment outcomes, will be evaluated using the Mann-Whitney U test or t-test for continuous variables and the chi-square statistic for categorical variables. In addition, the mean with standard deviation (or median with interquartile range, depending on the distribution of the data) of the total scores of the measures used will be calculated per participant group and per study area. The percentage change and corresponding 95%CI of physical impairment outcomes in each group, before and after the intervention is implemented and the statistical significance of this difference using a Z-test for differences between proportions will be calculated. Effect sizes will also be calculated. Stepwise multivariate regression with backward elimination will be done to examine what factors will have an independent effect on the outcomes. Data analysis will be done in the software packages Epi Info and SPSS Statistics. We will also use intention to treat (ITT) for categorical/nominal variables and difference in difference (DID) analysis for continues variables to evaluate the effectiveness of the intervention.

Qualitative data -the recordings of the in-depth interviews and focus group discussions- will be transcribed, translated to English and analysed using open, inductive coding and content analysis. Similar phrases with recurring themes will be coded in a qualitative software programme (MAXQDA) and clustered together in tables, to identify connections.

Patient and public involvement

This research will be led by and partly carried out by ENAPAL (a leprosy disabled persons' organisation). Persons affected by leprosy, LF and podoconiosis will assist the researchers in analysis of the data by helping to put issues in perspective and context. We will seek to employ and train persons affected as research assistants or at least those who have a family member affected by an NTD or with a disability.

Ethics and dissemination

Ethics

Ethical approval has been obtained from the Debre Markos University Health Sciences Institutional Research Ethics Review Committee (approval number HSC/R/C/Ser/Co/11/13). All participants will be fully informed about the nature and objective of the study and of confidentiality of the data prior to data collection. Written informed consent will be obtained from each participant prior to data collection. For participants who cannot read, an impartial witness will be present for the whole informed consent discussion. S/he will sign and date the consent form after the consent giver has done so. All people who are participating in the research will be provided with a participant information sheet. No incentives will be paid to participants.

Dissemination

A publication plan has been developed, which lists several planned articles for publication in scientific journals. All articles will be published in peer-reviewed, open access journals. The results of the study will also be shared through international conferences and at (working) meetings with international researchers and national policy makers and health care staff. A meeting will be organised at the end of the study to disseminate the results in the communities in the study areas. In addition, we aim to share updates of the study through the International Federation of Anti-Leprosy Associations (ILEP) newsletter and the Sasakawa Health Foundation newsletter.

Authors' contributions

ATN, MWA, TT and APS designed the study and were responsible for funding acquisition. MWA is the principal investigator of the study. MWA, NAM and TT are responsible for the implementation of the study in Ethiopia. MWA will lead data analysis with support from ATN and NAM. ATN drafted the manuscript. All authors have read an approved the final version of the manuscript.

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Competing interests statement

The authors declare that they have no competing interests.

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SPIRIT
STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description
Administrative information		
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym The study design, population and intervention are mentioned in the title.
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry Mentioned in the abstract.
	2b	All items from the World Health Organization Trial Registration Data Set
Protocol version	3	Date and version identifier N/a
Funding	4	Sources and types of financial, material, and other support This has been mentioned in the funding statement.
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors Addressed under author contributions.
	5b	Name and contact information for the trial sponsor N/a
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities This has been mentioned in the funding statement.
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee) N/a
Introduction		

Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention Introduction
	6b	Explanation for choice of comparators Introduction, and methods > intervention
Objectives	7	Specific objectives or hypotheses Introduction > objectives
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory) Introduction, and methods > study design
Methods: Participants, interventions, and outcomes		
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained Methods > study setting
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists) Methods > participants
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered Methods > intervention, and methods > procedures
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease) N/a
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests) Methods > intervention
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial Methods > intervention

Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended Methods > outcomes, and Table 2.
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure) Methods > participant timeline and Table 3
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations Methods > sample size
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size Methods > recruitment

Methods: Assignment of interventions (for controlled trials)

Allocation:

Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions Methods > allocation
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned Methods > allocation
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions Methods > allocation
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how Methods > blinding

	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial N/a
Methods: Data collection, management, and analysis		
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol Methods > outcomes, and methods > data analysis plan
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols Methods > outcomes, and methods > sample size calculation
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol Methods > data management
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol Methods > data analysis
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses) Methods > data analysis
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation) Methods > data analysis
Methods: Monitoring		
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed N/a

	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial N/a
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct N/a
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor N/a
Ethics and dissemination		
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval Ethics and dissemination > ethics
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators) N/a
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32) Ethics and dissemination > ethics
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable N/a
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial Methods > data analysis plan
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site Competing interests statement
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators Methods > data analysis plan

Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation N/a
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions Ethics and dissemination > dissemination
	31b	Authorship eligibility guidelines and any intended use of professional writers Author's contributions
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code N/a
Appendices		
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.

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A family-based intervention for prevention and self-management of disabilities due to leprosy, podoconiosis and lymphatic filariasis versus usual care in Ethiopia: study protocol for a cluster-randomised controlled trial

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A family-based intervention for prevention and self-management of disabilities due to leprosy, podoconiosis and lymphatic filariasis versus usual care in Ethiopia: study protocol for a cluster-randomised controlled trial

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Abstract

Introduction

Leprosy, podoconiosis and lymphatic filariasis (LF) are three skin-related neglected tropical diseases. All three conditions can lead to temporary and permanent impairments. These impairments progressively worsen and are major determinants of stigma, discrimination and participation restrictions. Self-care is essential to prevent disabilities and chronic disease complications. Many persons with leprosy-, LF- and podoconiosis-related disabilities need to practice self-management routines their entire life. This is difficult without support and encouragement of others. The objective of this study is to assess the effectiveness of a family-based intervention in terms of physical outcomes related to prevention and self-management of disabilities due to leprosy, podoconiosis and LF and family quality of life and wellbeing compared to usual practice and care.

Methods and analysis

The study will use a cluster-randomised controlled trial design with two study arms. The project will be carried out in endemic districts in East and West Gojjam zones in the Amhara region in Ethiopia. Clusters consist of kebeles (lower administrative structures in the district) that have been merged, based on their geographical proximity and the number of cases in each kebele. A total of 630 participants will be included in the study. The intervention group will consist of 105 persons affected by leprosy, 105 persons affected by LF or podoconiosis, and 210 family members. The control group will consist of 105 persons affected by leprosy and 105 persons affected by LF or podoconiosis. The

family-based intervention comprises of an essential care package that consists of the following three main components: (1) self-management of disabilities; (2) economic empowerment; and (3) psychosocial support. Participants in the control areas will receive usual practice and care. Data analysis includes, but is not limited to, calculating the percentage of change and corresponding 95%CI of physical impairment outcomes in each group, before and after the intervention is implemented, effect sizes, intention to treat and difference in difference analysis.

Ethics and dissemination
Ethical approval has been obtained from the Debre Markos University Health Sciences Institutional Research Ethics Review Committee. Results will be disseminated through peer-reviewed publications, conference presentations and workshops.

Registration details
This study has been registered at the Pan African Clinical Trial Registry (PACTR202108907851342).

Article Summary

Strengths and limitations of this study

- This family-based intervention cluster-randomised controlled trial was preceded by a proof-of-concept study, in which the intervention was found feasible.
- While self-management of disabilities is the main component of the family-based intervention, the essential care package goes beyond self-care and also includes economic empowerment and a psychosocial care component.
- This study is led by and partly carried out by the Ethiopian National Association of Persons Affected by Leprosy (ENAPAL), a large Ethiopian leprosy disabled persons' organisation.
- Inclusion of family members in self-care activities ensures sustainability of the intervention.
- Because randomisation will be done at the level of kebeles, it will not be possible to conduct a blinded outcome assessment, because research staff will be aware of the area they are in. It is not considered feasible to find people from outside the study areas to conduct the outcome assessment.

Introduction

Leprosy, podoconiosis and lymphatic filariasis (LF) are Neglected Tropical Diseases (NTDs) [1]. NTDs are a group of communicable diseases that are among the most common conditions, particularly among the world's poorest populations [2,3]. These diseases predominate in rural and impoverished urban areas of low and middle-income countries [4]. Worldwide, over one billion people have one or more NTDs [5]. NTDs are "poverty promoting" conditions, they cause suffering through acute illness, pain, long-term disability, early death and through mental and social consequences [2,4].

Leprosy, podoconiosis and LF are three skin-related NTDs [1]. All three conditions have skin manifestations such as patches, ulcers, wounds, nodules or localized swelling [6–9]. They are caused by bacteria (leprosy), chronic exposure to red clay volcanic soil (podoconiosis) and nematode worms that are transmitted by mosquitoes (LF) [7,8,10]. Leprosy, podoconiosis and LF can lead to temporary and permanent impairments if not diagnosed and treated early [1,6,11]. These impairments progressively worsen and are major determinants of stigma and participation restrictions [12–14].

Social consequences of all three conditions may include reduced work and education opportunities, social isolation, exclusion and problems in interpersonal relationships, including marital problems

[15–18]. Psychological consequences may include feelings of shame, low self-esteem, mental distress, depression, anxiety, and decreased individual and family quality of life [15–18]. In addition, these conditions may impose a social and economic burden on families [16,19]. Family members may also experience stigma [16,20–23]. Furthermore, costs for treatment and reduced ability to work may cause a financial burden for the entire family [16,19].

Most impairments, such as wounds, swelling and contractures, are largely preventable [1]. The most effective strategy for prevention of disabilities is early diagnosis and prompt treatment [24]. Self-care is also an essential component of prevention of disabilities, and for prevention of chronic disease complications [24–27]. Relatively simple methods exist for self-management of impairments, such as daily washing of affected limbs, skin care, bandaging, exercises and the use of shoes [27]. Most of these methods can be practiced at home and are suitable for use across different skin-related NTDs [27–29]. These self-care interventions have been found effective in for example reducing the incidence of acute dermatolymphangioadenitis (ADLA) in persons affected by podoconiosis and LF [30,31] and in reducing ulcers among persons affected by leprosy [32]. Because physical impairments are an important determinant of stigma, disease management is also an indirect intervention to reduce stigma [33].

Many persons with leprosy-, podoconiosis- and LF-related disabilities need to practice self-management routines their entire life. This is difficult without support and encouragement of others. Family members can provide such support and encouragement. We recently conducted a proof-of-concept study in which we piloted a family-based intervention for prevention and self-management of disabilities due to leprosy, podoconiosis and LF in Ethiopia [34]. This family-based intervention consisted of self-management of disabilities, awareness raising and economic empowerment, and was delivered during several monthly group meetings. Economic empowerment was an important component of the intervention, as income generation is essential for sustainable self-management and prevention of disabilities: without income, self-care items such as Vaseline and shoes cannot be bought. We found that the intervention had a positive effect on impairments and self-management of disabilities, family quality of life and stigma. However, sampling was not randomised, which means we couldn't determine the effectiveness of the intervention. To collect credible evidence for this new, previously piloted intervention, we aim to conduct a similar study using a randomised controlled design.

Objectives

The primary objective of this study is to assess the effectiveness of a family-based intervention in terms of physical outcomes related to prevention and self-management of disabilities due to leprosy, podoconiosis or LF and family quality of life and wellbeing compared to usual practice and care. Secondary objectives include: (1) to reduce the number of people who have an episode of depression, as measured with the Patient Health Questionnaire (PHQ-9); (2) to reduce the level of stigma as measured with the SARI stigma scale (SSS), in-depth interviews and focus group discussions; (3) to improve social participation as measured with the Participation Scale (P-scale); (4) to increase the number of people who have adequate knowledge of leprosy, LF and podoconiosis as measures with disease specific Knowledge Attitudes and Practices (KAP) measures; (5) to empower people economically as measured by monthly household income, monthly financial contribution to the self-help group and in-depth interviews.

Methods and analysis

The protocol for this study is outlined below. This study protocol adheres to the SPIRIT statement [35].

Study design

The intervention consists of a cluster-randomised controlled trial, with two study arms. The two study arms consist of (1) the family-based intervention and (2) usual practice and care (control group).

Study setting

The project is carried out in endemic districts in East and West Gojjam zones in the Amhara region in Ethiopia (the proof-of-concept study was conducted in a different zone, the Awi zone). The Amhara region is the second largest state in population and is divided in 11 zones. All three conditions are endemic in the Amhara region. In 2019, Ethiopia had 3,201 new leprosy patients, 13% of the new patients had Grade 2 disabilities [36]. The prevalence of leprosy is highest in the Amhara, Afar and Oromiya regions [37,38]. LF is endemic in the Amhara, Beneshangul-Gumuz, SNNPR and Oromia regions. Three million people are estimated to be at risk of LF in the Amhara region [39]. In addition, Ethiopia is estimated to have 25% (1 million cases) of the global burden of podoconiosis. Podoconiosis is spread out over one-fifth of the surface of Ethiopia, especially the Western part [37,40,41]. The regions with the high prevalence of podoconiosis are Amhara, SNNPR, Oromiya and Beneshangul-Gumuz [40,41].

East and West Gojjam zones are subdivided into 16 and 20 districts (woredas) respectively. The three districts selected for this study are Dega Damot and Dembecha districts (West Gojjam zone) and Enarge Enawga (East Gojjam zone). These districts have been selected based on their similarity in total population, sex ratio, number of urban/rural neighbourhoods (kebeles), number of hospitals, health centres and health posts, disease prevalence and lack of previous or ongoing leprosy, podoconiosis or LF-related work of other organisations (Table 1). The latter to avoid possible contamination of the study results. The study is being conducted in real-world settings and populations.

Table 1. Characteristics of the selected study areas. Data has been collected from field census, health office reports and [42,43].

	Dega Damot district	**Dembecha district**	**Enarge Enawga district**
Total population, *n* (%) Men, *n* (%) Women, *n* (%)	181,325 (100%) 89,756 (49.5%) 91,156 (50.5%)	218,257 (100%) 105,809 (48.48%) 112,448 (51.52%)	172,939 (100%) 86,297 (49.9%) 86,642 (49.1%)
Number of kebeles, *n* (%) Rural, *n* (%) Urban, *n* (%)	36 (100%) 34 (94%) 2 (6%)	31 (100%) 27 (87%) 4 (13%)	35 (100%) 31 (89%) 4 (11%)
Number of health facilities Hospital, *n* Health centre, *n* Health post, *n*	 1 7 34	 1 7 28	 1 7 34
Number of health extension workers working in the area	88	60	76
Percentage of total population that has podoconiosis	>10%	1-5%	>10%
Estimated number of persons leprosy-, podoconiosis- or LF-related disabilities living in the area	Leprosy=132 Podoconiosis =352	Leprosy=135 Podoconiosis=1,042	Leprosy=213 Podoconiosis or LF=797

Geographic and background information	• Climate zones: 75% dega (cool temperate), 20% woina dega (subtropical) and 5% kolla (hot lowland). • Annual rainfall between 900-1,200 mm. • The district consists of 35% mountain, 30% hills, 20% valleys and 15% plains.	• Climate zones: 11% dega (cool temperature), 83% woina dega (subtropical) and 6% kolla (hot lowland) • Annual rainfall is between 1,221-1,602 mm. • The district consists of 60% plains, 30% mountain and 10% hills. • Elevation is between 1500-2995 meters above sea level. • Other: bordered by the Nile river.	• Climate zones: 30% dega (cool temperate), 50% woina dega (subtropical) and 20% kolla (hot lowland). • Annual rainfall is between 1,200-1,400 mm. • The district consists of 50% plains, 30% mountain and 20% hills. • Elevation is 1100-3200 meters above sea level.
Previous or ongoing work with the target group in the area?	No	Yes, with persons affected by podoconiosis (no persons affected by podoconiosis will be included from this district)	No

Participants

People with leprosy-related impairments and people with LF or podoconiosis-related lymphedema ('persons affected') will be included in this study. In addition, of each person affected, at least one adult family member will be included (e.g. sibling, child, parent or grandparent of a person affected by leprosy, LF or podoconiosis).

People 15 years and above will be included in the study. All persons have to be residents of project areas of the study. All persons affected need to have leprosy-, LF- or podoconiosis-related impairments and have to be eligible to participate in self-care activities, as the focus is on skin and wound care of affected persons. Family members need to live in the same household as persons affected. People who are unable to coherently express themselves verbally (i.e. are unable to understand and participate in an interview) will be excluded. In addition, persons affected who live alone will excluded.

Intervention

This RCT was preceded by a proof-of-concept study in which a family-based intervention was developed and found feasible [34]. The family-based intervention consists of an essential care package that consists of the following three main components: (1) self-management of disabilities; (2) economic empowerment; and (3) psychosocial support. All components of the intervention are

family-based and family focused. Although not mentioned as a separate component, awareness raising of leprosy, LF and podoconiosis in the family and the community is an integral part of the intervention. The essential care package is described in more detail below:

- Training sessions/group meetings for self-management and prevention of disabilities. Based on the proof-of-concept study, at least five group meetings will be held in a location that is most convenient for the participants. These sessions will be delivered in group format (several families participate with one person affected and one family member present per family) to introduce the family-based methods for self-management and prevention of disabilities. In the first session basic training will be given to persons affected and their family members in using and giving psychosocial support, increasing prevention and self-management of disabilities skills, information about the disease, creating strategies to overcome barriers and facilitators to self-care. In the following training sessions, the research assistants support and guide all participating families (repeating the basic training given in the first session) and are available to clarify questions. During these meetings, physical impairment outcomes will routinely (monthly) be collected. Family members are encouraged to help their affected family member with self-care at home. (Each group will have approximately 20 participants, therefore, training for participants in the intervention group will not all be given at the same day/time). We anticipate that the first group meeting will be held in February 2022. Group meetings will be conducted until September 2022.
- Formation of self-help groups for economic empowerment. The project will facilitate the formation of self-help groups of affected persons, their family members are encouraged to join group meetings. The Ethiopian National Association of Persons Affected by Leprosy (ENAPAL), a large Ethiopian leprosy disabled persons' organisation with a successful track record in establishing self-help groups, will coordinate and guide this part of the intervention. The facilitators of the project, trained by ENAPAL, will help to establish the self-help groups and will be present during the meetings but will not give guidance on the management of the groups. Management of the groups will be done by persons affected themselves, participants of the group will be asked to elect a 'committee' of persons affected. Each self-help group will collect a small contribution fee from its participants, these fees are used to provide loans for the participants of the self-help groups (micro-finance). Self-help groups will also lobby for 'benefits', e.g. the use of land, from the government. In addition, each self-help group participant and at least one of their family members will receive (one) vocational training. Income generation will benefit the whole family.
- Psychosocial support will be part of the training sessions/group meetings for self-management and prevention of disabilities. Persons affected and their family members will be trained in using and giving psychosocial support.

The control group will receive treatment as usual. Participants in the control areas will receive the same basic training (one session) as the participants in the intervention group, but will have no family members present during the training. When the intervention group has their additional four meetings (at least five meetings will be held), the participants in the control group will receive usual practice and care. In addition, they will receive information about existing mechanisms for economic empowerment (such as "funeral saving groups" and other existing credit saving initiatives).

Procedures

This study has two main phases. Each phase is briefly described below.

Phase 1: Preparatory phase. In this phase, a literature review will be conducted to guide the development of the psychosocial support component that will be added to the family-based intervention. In addition, the Sari Stigma Scale (SSS), FQoL scale and Participation scale (P-scale) will be cross-culturally validated (the Patient Health Questionnaire (PHQ-9) has already been validated in Amharic [44–46]). We will assess conceptual, item, semantic, operational and measurement equivalence using a framework for cross-cultural equivalence testing based on the work of Herdman

et al. [47], Terwee et al. [48] and Stevelink & van Brakel [49]. The Knowledge Attitudes and Practices (KAP) measure will be translated, and pilot tested. A training workshop will be organized to train community health extension workers, local area health workers and the research team in research methods and family-based intervention. A list of persons affected registered in the community level census that are eligible to participate in self-care activities will be prepared. Persons affected by leprosy, podoconiosis or LF and their family members will be recruited. A database will be established to monitor the routine intervention activities. Baseline data will be collected by the research assistants, and the results analysed by the researcher.

Phase 2: Implementation and evaluation of the family-based intervention. In this phase, the intervention will be implemented: at least five training sessions and family meetings will be held. This training is done by the researcher (who has extensive experience in providing training, self-care practices and the three conditions included in this study), with support from the research assistants and with at least one community health extension worker present at the meeting. Research assistants will receive a four-day training on how to implement the intervention, this training is facilitated by the researcher and project manager. In addition, each training session is carried out using standard operating procedures, that have been developed using the WHO's Integrated morbidity management for LF and podoconiosis [50], the Ethiopian Ministry of Health's LF and podoconiosis morbidity management and disability prevention guidelines and ILEP's guideline for prevention of disabilities in leprosy [51]. As has been described in detail previously [34], participants in the intervention and control area will receive basic tools to practice self-care (Vaseline, a bucket, shoes, and soda). In this phase, the effectiveness and acceptability of the intervention will be evaluated (feasibility has already been established in the proof-of-concept study that was recently conducted [34]). This will be done by collecting the same information as in the baseline study (Table 2), a few weeks and one year after implementation of the intervention. In addition, interviews will be conducted to collect most significant change stories and to assess the impact qualitatively. Because randomisation will be done at the level of kebeles, it will not be possible to conduct a blinded outcome assessment, because research staff will be aware of the area they are in. It is not considered feasible to find people from outside the study areas to conduct the outcome assessment. All components of the study will be conducted in Amharic, the official language of Ethiopia and language spoken in the study areas.

Outcomes

Table 2 details the outcomes measured during this study, including the methods that will be used to measure the outcomes. Physical impairment outcomes are the primary outcome measures. Acceptability, family quality of life, stigma, social participation, mental wellbeing, disease knowledge, attitudes and economic empowerment are secondary outcomes.

Table 2. Outcomes measures

Type of outcome	Specific outcome	Outcome measures[a]
Implementation outcomes	Acceptability	Qualitative (IDI and FGD)
	Disability management practices	Observations (field notes), Qualitative (IDI and FGD)
	Economic empowerment	Registration of attendance of persons affected organisation group meetings, number of loans disbursed, total amount of money disbursed
Effectiveness (persons affected level)	Physical impairment outcomes	For persons affected by leprosy: • Eyes, Hands, Feet (EHF) score [52], total number of wounds present (wound count),

		registration of infection, observation (field notes) For persons affected by podoconiosis and LF: • Lymphedema grading, measuring the largest point of swelling below the knee circumference, registering the frequency of acute attacks, wound count, registration of infection, observation (field notes).
	Physical wellbeing	IDI
	Family quality of life	Beach Centre Family Quality of Life scale (FQoL scale), IDI
	Perceived, experienced and internalised stigma	SSS
	Social participation	P-scale
	Mental wellbeing [44–46]	PHQ-9
	Disease knowledge [53,54]	Disease specific KAP measure
	Attitudes towards the disease and persons affected by the disease	Qualitative (IDI, FGD)
	Economic empowerment	Monthly household income, monthly financial contribution to the self-help group, qualitative (IDI)
Effectiveness (family member level)	Family quality of life	FQoL scale, qualitative (IDI)
	Perceived, experienced and internalised stigma	IDI
	Mental wellbeing [44–46]	PHQ-9
	Disease knowledge [53,54]	Disease specific KAP measure
	Attitudes towards (persons affected by) the disease	Qualitative (IDI, FGD)
	Economic empowerment	Monthly household income, monthly contribution to the self-help group, qualitative (IDI)
Impact at community level	Most significant changes	Qualitative (IDI and FGD)
	Impact assessment (to evaluate the change in the target population and communities)	Qualitative (IDI and FGD)

[a] IDI = in-depth interview, FGD = focus group discussion.

Participant timeline

The participant timeline, in line with SPIRIT recommendations, can be found in Table 3.

Table 3. Participant timeline

	Study period[a]			
	Enrolment	**Pre-allocation**	**Allocation**	**Post allocation**

Time point		T0		Tx	T1	T2
ENROLMENT:						
Eligibility screen	X					
Informed consent	X					
Allocation			X			
INTERVENTION:						
Group meetings				X		
ASSESSMENTS:						
Questionnaires[b]:						
SSS		X			X	X
FQoL		X			X	X
P-scale		X			X	X
PHQ-9		X			X	X
KAP		X			X	X
Routine data:						
Physical impairment outcomes		X		X	X	X
Group meeting attendance		X		X	X	X
In-depth interviews		X			X	X
Focus group discussions		X			X	X

[a] T0= before the intervention / baseline. Tx = monthly monitoring during the intervention (routine data collection). T1 = One-month post-intervention. T2 = One-year post-intervention.
[b] SSS = SARI Stigma Scale, FQoL = Beach Centre Family Quality of Life scale, P-scale = Participation Scale, PHQ-9 = Patient Health Questionnaire, KAP = Disease specific Knowledge Attitudes and Practices measure.

Sample size

A total of 630 participants, consisting of 420 persons affected and 210 family members, will be included in the study. It is difficult to distinguish LF and podoconiosis based on clinical features under field conditions and the distinction between these conditions doesn't matter with regard to the outcomes of this study, therefore persons affected by both these conditions are treated as one group. There will be one intervention and one control group for persons affected by leprosy, and one for persons affected by LF or podoconiosis. Family members are only included in the intervention group. The intervention group will consist of 105 persons affected by leprosy, 105 persons affected by LF or podoconiosis, and 210 family members. The control group will consist of 105 persons affected by leprosy and 105 persons affected by LF or podoconiosis. The sample size calculation is based on data from the proof-of-concept study [34]. In the proof-of-concept study, 43% of the participants had leg impairments (wounds, nodules, and/or infections) at intake. During the final assessment, the last session participants attended, the number of participants with leg impairments had dropped to 21%. A sample size calculation for two proportions (proportion 1: 43%; proportion 2: 21%) with a significance of 0.05 and a power of 90% would give a total sample size of 92 participants in each group. We expect that the loss to follow-up will be no more than 15% (we do not expect a higher loss to follow-up, as participants will be followed-up at home). Our sample size will therefore be 105 persons affected in each group. The kebeles have been selected in such a way that they are similar to each other, we therefore do not anticipate a cluster effect in the current outcomes.

Recruitment

Potential participants will be approached via community level enumeration, health care settings, persons affected organisations, community leaders, and by word of mouth. The recruitment period is six months, starting in October 2021. Once participants are enrolled, they will be followed up during the study period up to 12 months in the nearby health centre or health posts. In the case of loss to

follow up, participants will be visited in their home.

Allocation

The three districts will be randomly divided into clusters to implement either the family-based intervention or usual practice and care (control group). A complete enumeration of persons with the three diseases has been conducted in each district, kebeles (a lower administrative structure in the district) have been merged into "clusters" based on their similarity, including their population characteristics, geographical proximity, the presence of a health centre and the number of cases in each kebele. Each cluster consists of 3-5 kebeles on average (ranging from 2-7) and all clusters have at least one health centre in the area. Sixteen clusters have been identified in the three study districts: Feresbet, Taeme, Dama Markos, Arefa, Damot Tsion, Sekela, Chat Warka (in Dega Damot district), Debre Work, Felege, Tenguma, Gedeb, Shifere, Metiya, Wonfit (in Enarge Enawga district), Dembecha town and Wad (in Dembecha district). Out of these sixteen clusters, a total of four clusters for leprosy and six clusters for podoconiosis and LF will be randomly selected. The intervention and control areas will be randomly selected, by putting the cluster names in a cup or box and randomly drawing names. We will ensure that the number of intervention and control areas (clusters) in each district is equal. A list will be prepared with all patients (leprosy, podoconiosis/LF) living in the project areas, that are registered at community level enumeration and that are eligible to participate in self-care activities. Persons affected to be included in the study will be selected by stratified systematic sampling with a random start from a list of persons affected registered at the primary health care centre. This is done by selecting the first person affected on the list at random (by throwing dice), and then selecting every X-th patient on the list, based on the total number needed. Four separate lists will be created: two for persons affected by leprosy (one intervention and one control) and two for persons affected by LF or podoconiosis (one intervention and one control).

Blinding

Due to the nature of the intervention, participants cannot be blinded.

Data management

Confidentiality and anonymity of data will be ensured in data collection, data storage, analysis and publication. Research assistants who will collect the data will be fully trained in proper data management, maintenance of confidentiality and ensuring privacy during data collection. All data will be collected in Ethiopia. Only data that have been fully anonymised will be shared with the international research team. The project leader of this study will take full responsibility for ensuring the appropriate storage and security of data. Data will be kept for five years and will be destroyed after this timeframe when no longer required.

Data analysis

Quantitative data will be entered in a database created using EpiData software. Analyses will start once baseline data has been collected. Simple descriptive methods will be used to generate a demographic profile of the study sample. Differences between participants in the intervention and control groups, including demographic information and physical impairment outcomes, will be evaluated using the Mann-Whitney U test or t-test for continuous variables and the chi-square statistic for categorical variables. In addition, the mean with standard deviation (or median with interquartile range, depending on the distribution of the data) of the total scores of the measures used will be calculated per participant group and per study area. The percentage change and corresponding 95%CI of physical impairment outcomes in each group, before and after the intervention is implemented and the statistical significance of this difference using a Z-test for differences between proportions will be calculated. Effect sizes will also be calculated. Stepwise multivariate regression with backward elimination will be done to examine what factors will have an independent effect on the outcomes. Data analysis will be done in the software packages Epi Info

and SPSS Statistics. We will also use intention to treat (ITT) for categorical/nominal variables and difference in difference (DID) analysis for continues variables to evaluate the effectiveness of the intervention.

Qualitative data -the recordings of the in-depth interviews and focus group discussions- will be transcribed, translated to English and analysed using open, inductive coding and content analysis. Similar phrases with recurring themes will be coded in a qualitative software programme (MAXQDA) and clustered together in tables, to identify connections.

Patient and public involvement

This research will be led by and partly carried out by ENAPAL (a leprosy disabled persons' organisation). Persons affected by leprosy, LF and podoconiosis will assist the researchers in analysis of the data by helping to put issues in perspective and context. We will seek to employ and train persons affected as research assistants or at least those who have a family member affected by an NTD or with a disability.

Ethics and dissemination

Ethics

Ethical approval has been obtained from the Debre Markos University Health Sciences Institutional Research Ethics Review Committee (approval number HSC/R/C/Ser/Co/11/13). All participants will be fully informed about the nature and objective of the study and of confidentiality of the data prior to data collection. Written informed consent will be obtained from each participant prior to data collection. For participants who cannot read, an impartial witness will be present for the whole informed consent discussion. S/he will sign and date the consent form after the consent giver has done so. All people who are participating in the research will be provided with a participant information sheet. No incentives will be paid to participants.

Dissemination

A publication plan has been developed, which lists several planned articles for publication in scientific journals. All articles will be published in peer-reviewed, open access journals. The results of the study will also be shared through international conferences and at (working) meetings with international researchers and national policy makers and health care staff. A meeting will be organised at the end of the study to disseminate the results in the communities in the study areas. In addition, we aim to share updates of the study through the International Federation of Anti-Leprosy Associations (ILEP) newsletter and the Sasakawa Health Foundation newsletter.

Contributorship statement

ATN, MWA, TT and APS designed the study and were responsible for funding acquisition. MWA is the principal investigator of the study. MWA, NAM and TT are responsible for the implementation of the study in Ethiopia. MWA will lead data analysis with support from ATN and NAM. ATN drafted the manuscript. All authors have read an approved the final version of the manuscript.

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Competing interests statement

The authors declare that they have no competing interests.

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SPIRIT
STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description
Administrative information		
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym The study design, population and intervention are mentioned in the title.
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry Mentioned in the abstract.
	2b	All items from the World Health Organization Trial Registration Data Set
Protocol version	3	Date and version identifier N/a
Funding	4	Sources and types of financial, material, and other support This has been mentioned in the funding statement.
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors Addressed under author contributions.
	5b	Name and contact information for the trial sponsor N/a
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities This has been mentioned in the funding statement.
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee) N/a
Introduction		

Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention Introduction
	6b	Explanation for choice of comparators Introduction, and methods > intervention
Objectives	7	Specific objectives or hypotheses Introduction > objectives
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory) Introduction, and methods > study design
Methods: Participants, interventions, and outcomes		
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained Methods > study setting
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists) Methods > participants
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered Methods > intervention, and methods > procedures
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease) N/a
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests) Methods > intervention
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial Methods > intervention

Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended Methods > outcomes, and Table 2.
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure) Methods > participant timeline and Table 3
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations Methods > sample size
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size Methods > recruitment

Methods: Assignment of interventions (for controlled trials)

Allocation:

Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions Methods > allocation
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned Methods > allocation
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions Methods > allocation
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how Methods > blinding

	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial N/a
Methods: Data collection, management, and analysis		
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol Methods > outcomes, and methods > data analysis plan
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols Methods > outcomes, and methods > sample size calculation
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol Methods > data management
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol Methods > data analysis
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses) Methods > data analysis
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation) Methods > data analysis
Methods: Monitoring		
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed N/a

	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial N/a
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct N/a
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor N/a
Ethics and dissemination		
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval Ethics and dissemination > ethics
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators) N/a
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32) Ethics and dissemination > ethics
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable N/a
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial Methods > data analysis plan
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site Competing interests statement
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators Methods > data analysis plan

Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation N/a
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions Ethics and dissemination > dissemination
	31b	Authorship eligibility guidelines and any intended use of professional writers Author's contributions
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code N/a
Appendices		
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.