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Energy Conservation Education Intervention for People with End-stage Kidney Disease Receiving Haemodialysis (EVEREST): protocol for a cluster randomised control trial

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TITLE PAGE

FULL TITLE: Energy Conservation Education Intervention for People with End-stage Kidney Disease Receiving Haemodialysis (EVEREST): protocol for a cluster randomised control trial

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Abstract

Introduction: Multiple symptoms occur in people with kidney failure receiving haemodialysis (HD) and these symptoms have a negative impact on health-related quality of life (HRQoL). Fatigue, the most common symptom, is debilitating and difficult to manage. Educational interventions involving energy conservation strategies are helpful in reducing fatigue, however the effectiveness of energy conservation has not been previously studied in those receiving HD. The aim of this study is to evaluate the effectiveness of an energy conservation education intervention for people with end-stage kidney disease receiving HD (EVEREST trial).

Methods and analysis: A pragmatic cluster randomised controlled trial with repeated measure will be used. One hundred and twenty-six participants from tertiary level dialysis centre will be cluster randomised to the intervention and control group according to HD treatment day. The intervention group will receive usual care along with a structured energy conservation intervention over 12 weeks comprising three individual face-to-face educational intervention sessions, one booster session, and a booklet. The control group will receive usual care from their healthcare providers and a booklet at the end of the study. The primary outcome is fatigue, and the secondary outcomes are other renal symptoms, occupational performance, and HRQoL. Intention-to-treat analysis will occur and will include a change in primary and secondary outcomes.

Ethics and dissemination: Ethical approval has obtained from the Human Research Committee of the Griffith University and Nepal Health Research Council. The results of this research will be published and presented in a variety of forums.

Trial registration number: NCT04360408; Pre-results

Strengths and limitations of this study

- This study will provide empirical evidence about the effectiveness of an education regarding energy conservation for fatigue management that can be integrated into the everyday life of people receiving HD.
- This study will be conducted in a developing country, and the educational material designed is simple and easily understood by people with limited education.
- This study includes the recruitment of participants from one dialysis centre in Nepal.
- The population of the study is limited to the people receiving HD, which limits the generalizability of the finding to people receiving conservative treatment and other forms of KRT.

Introduction

Chronic kidney disease (CKD) is both a major global public health problem and contributor to the overall burden of non-communicable disease [1], affecting about 13% of the global population.[2] It is defined as any degree of kidney damage or decline in kidney function or estimated glomerular filtration rate (eGFR) < 60.0ml/min/1.73m^2 for three months or longer irrespective of the cause.[3] The classification of CKD is based on cause of disease, level of GFR and level of albuminuria which is collectively called CGA classification.[4] If eGFR < 15 ml/min/1.73m^2 or treated by dialysis, then the term "kidney failure" is used to specify CKD stage G5.[4] There is no renal registry in Nepal; however, it was estimated that both the incidence and prevalence of kidney failure to be approximately 100 per million population (pmp). From this estimation, it is anticipated that approximately 2,900 people have kidney failure in Nepal.[5]

Haemodialysis is the most common modality of treatment for people with kidney failure and usually is prescribed three times per week, with a duration of 4-5 hours per session.[6] It can be performed either in-centre in a hospital or a satellite unit or at home.[7] This treatment impacts on most aspects of daily life leading to decreased health-related quality of life (HRQoL).[8] Being on HD also affects employment and being able to undertake routine social activities [9] as well as affecting family members.[10, 11]

Physical and psychological symptoms are common in this population and may be related to the underlying pathologies, presence of multiple co-morbidities, accumulation of uraemic toxins or fluids, medication side effects, and inadequacy of dialysis.[12] Several studies have described symptom burden in this population.[12-16] Almutary et al [13], who compared those not on dialysis with those receiving either HD or PD, reported that both symptom prevalence and severity was highest in those receiving HD, and that about 85% reported being fatigued.

Fatigue is an overwhelming subjective experience of discomfort associated with physical and mental exhaustion.[17] Fatigue in people with kidney failure negatively impacts individuals' day to day activities,[18, 19] HRQoL,[20] increases hospitalisations and mortality.[21] Various factors have been associated with fatigue in kidney failure such as demographic characteristics,[22] elevated urea levels, anaemia, depression, anxiety, and sleep disturbances.[22, 23] Medication side effects and HD treatment-related factors like dialysis inadequacy and excessive ultrafiltration have been associated with fatigue.[21, 24, 25]

Managing fatigue is essential in improving HRQoL for individuals on HD. It can be argued that adults receiving HD can benefit from self-symptom management techniques to reduce fatigue and other kidney failure symptoms.[26] Previous research has shown that exercise could reduce fatigue;[22, 27] however exercise may not be safe for all people.[28] Educational interventions are believed to improve cancer-related fatigue[29] and there is some evidence to support this in earlier stages of CKD.[30] Likewise, education about energy conservation is another approach to manage fatigue that has shown a significant reduction in fatigue in other chronic diseases, including multiple sclerosis[31] and cancer.[32, 33] However, its effectiveness has not yet been tested in the HD population.

In a systematic review, Blikman et al.[31] included six interventional studies which examined the effects of energy conservation management (ECM) for fatigue and HRQoL in people with multiple sclerosis (MS). Four studies included in this review used ECM intervention program based on Packers' "Managing Fatigue" course; two were guided by the MS fatigue guidelines. Interventions in these studies were delivered in group format and face-to-face except in the study by Finlayson et al[34] where the intervention was delivered via teleconference method. Meta-analysis of two studies[34, 35] included in this review showed that ECM intervention was more effective than no intervention in reducing the impact of fatigue on the cognitive subscale

(MD=-2.91; 95% CI –4.32 to –1.50), the physical subscale (MD = -2.99; 95% CI –4.47 to –1.52), and the psychological subscale (MD = -6.05; 95% CI –8.72 to –3.37).[31] The same study also revealed that ECM treatment improved three domains of HRQoL, namely role physical (MD= 17.26; 95% CI 9.69 to 24.84), social function (MD = 6.91; 95% CI 1.32 to 12.49), and mental health (MD = 5.55; 95% CI 2.27to 8.83). Another study evaluated the effect of energy conservation strategies in persons with breast cancer experiencing fatigue.[32] In this study, the intervention was delivered face-to-face in the form of small group discussion. Duration of each session was 90 mins and sessions were conducted weekly for the period of 5 weeks. The result of this study showed that application of energy conservation strategies significantly reduced the status of cancer-related fatigue in persons with breast cancer over the 8 weeks of follow-up period ($F = 69.8$, $p < 0.001$).[32]

Despite fatigue being highly prevalent in those receiving HD, a recent systematic review did not find any interventional studies that used an educational approach for self-management to reduce symptom and improve HRQoL in people undergoing HD.[36] Thus, this study aims to evaluate the effectiveness of an energy conservation education intervention for people with kidney failure receiving haemodialysis (EVEREST trial) in Nepal.

Research hypotheses

People with kidney failure on HD who receive EVEREST and usual care are more likely to:

H1: have reduced fatigue severity, frequency and interference compared to people undergoing HD who received usual care.

H2: have reduced number and severity of other renal symptom compared to people undergoing HD who received usual care.

H3 have improved occupational performance and satisfaction with that performance compared to people undergoing HD who received usual care.

H4: have improved HRQoL compared to people undergoing HD who received usual care

Methods and analysis

Study design

A pragmatic cluster randomised control trial (CRT [pCRT)]) design will be used. A pragmatic design attempts to find an answer to whether an intervention will work under usual conditions in a real clinical setting,[37] therefore a few exclusion criteria will be applied. To avoid possible treatment contamination because participants on the same dialysis day may interact with each other as they spend four hours in close proximity during dialysis, a cluster design will be used, with cluster cohorts based on the day of dialysis. The CONSORT flow diagram in Figure 1 presents the study design.

Setting

The study will be conducted at the National Kidney Centre (NKC), Kathmandu, Nepal. The NKC is the non-profit, non-governmental organisation with the largest HD treatment facility in Nepal. The NKC can serve around 240 people for HD treatment in a month. Currently, the centre has 42 dialysis machines. The NKC provides free HD service to all patients as mandated by the Ministry of Health and Population, Nepal.

Sample size

G power software™ was used to calculate the sample size by performing the priori power analysis for an independent group two-tailed t-test. A previous study[38] in which a large effect size (Cohen's *d* from 0.90 - 1.5) was demonstrated, was used for the calculation. To have resultant 80% power, a large effect size of 0.8 and a significance of 0.05, 52 participants will be needed (26 in each group). As this study is pCRT, and assuming a moderate intra-cluster

coefficient (ICC) of 0.03 to compensate for attrition and the possibility of non-normality of data, the calculation is further inflated by 20% and again 15% respectively. After adjusting for design effect, attrition, and a non-parametric statistic, a final sample size of 126 (63 in each group) is required.

Eligibility criteria

Participants diagnosed with ESKD and undergoing haemodialysis for ≥ 3 months, aged 18 years and above, able to speak and understand Nepali language and willing to participate will be included in this study. Participants who are in the early stage of CKD or not dependent on HD, those acutely ill, diagnosed with cognitive impairment and those who are not willing to participate will be excluded. Participants may be withdrawn from the study at any time due to a safety concern, if they became sick or if they are non-compliant with the trial procedure.

Study intervention

Intervention group

The intervention group will receive both the usual care from their healthcare providers and the 12 weeks of EVEREST intervention. The EVEREST uses education to teach individuals to recognise and modify their daily activities to reduce fatigue by analysing the daily work, home and leisure activities in all aspects of their life.[39] This intervention helps to develop a positive attitude towards decision-making and the maximum use of available energy.[31] It is designed to reduce the frequency, severity and impact of fatigue, increases a person's use of energy-conservation strategies and improves their confidence level and their ability to manage fatigue.[31] Seven energy conservation strategies will form the content EVEREST intervention (see table 1); each will be adapted to fit with the daily activities of Nepalese people. These energy conservation strategies were adopted from energy conservation course "Managing Fatigue" developed by Packer et al.[40]

Table 1 Summary of the content of the EVEREST

Session	Goal and objectives	Topics	Duration	Teaching methods
Session 1 (Week 1)	Goal: The goal of this session is to provide information about fatigue in kidney failure and, its causes, and energy conservation, strategies and its application in activities of daily livings. Objectives • To set a friendly environment and develop a trusting interpersonal relationship • To give information about fatigue, its causes • To give information about energy conservation, energy conservation strategy 1 and its application in activities of daily livings	• Fatigue in kidney failure • Causes of fatigue. • Introduction of energy conservation • Energy conservation strategies and its application in activities of daily livings ✓ Strategy 1: Organising daily routine and evaluating priorities • Summary	30-45 minutes	A face-face session with the help of PowerPoint on the laptop Question and answer Discussion
Session 2 (Week 3)	Goal: The goal of this session is to provide information about energy conservation strategies two, three, four and five and its application in activities of daily living Objectives	• Revision of previous session. • Energy conservation strategies and its application in activities of daily livings ✓ Strategy 2: Simplifying the everyday task	30 minutes	A face-face session with the help of PowerPoint on the laptop

	• To set a friendly environment and prepare participant for educational session. • To revise the content of session one. • To provide opportunity to ask question about previous session. • To give information about energy conservation 2,3,4, 5 and its application in activities of daily living	✓ Strategy 3: Organising station for activities and using the energy-efficient appliances ✓ Strategy 4: Pacing activities and avoid rushing ✓ Strategy 5: The value of rest and having rest periods during the day • Summary		Question and answer Discussion
Session 3 (Week 5)	Goal: The goal of this session is to provide information about energy conservation strategies 6,7 and its application in activities of daily living Objectives • To set a friendly environment and prepare participant for educational session • To revise session two • To identify any concern about previous session • To provide opportunity to ask question about previous session	• Revision of previous session • Energy conservation strategies and its application if activities of daily livings ✓ Strategy 6: Communicating personal needs to others ✓ Strategy 7: Using proper body mechanics and posture • Summary	30 minutes	A face-face session with the help of PowerPoint on the laptop Question and answer Discussion

	• To give information about energy conservation six, seven and its application in activities of daily livings.			
Session 4 Booster session (Week 10)	Goal: The goal of this session is to revise the content of all session with the help of educational booklet. Objectives • To set a friendly environment and prepare participant for educational session • To provide opportunity to ask question about previous session • To revise session 1, 2 and 3 • To reflect on progress in meeting the objectives of each session	• Revision of previous session • Summarise the content of the booklet ✓ Fatigue, energy conservation, its strategies and application in activities of daily livings	30-45 minutes	A face-face session with the help of booklet Question and answer Discussion

The EVEREST intervention will be guided by Symptom management theory (SMT) as the theoretical framework. This theory accounts for the person, health/illness, the environment, and includes the symptom experience, symptom management strategies and outcomes.[41] Symptom management theory is built on the premise that a symptom experience is based on how an individual perceives and responds to the symptom.[42] Symptom management strategies used by individuals to delay a negative outcome of the symptom experience can be targeted by appropriate intervention strategies. The theory also explains that outcomes (e.g., functional status, self-care, HRQoL) may be altered by the symptom experience and/or symptom management strategies. The dynamic interaction between each dimension of SMT provides explicit and testable relationships among these dimensions. In this study, the relationship between a person's fatigue experience and other renal symptoms, the EVEREST intervention , and outcomes including status of fatigue and other renal symptoms, HRQoL, and occupational performance will be tested using this theory.

Face-to-face education session

Four face-to-face educational sessions will be undertaken during participants' regular HD treatment. Sessions will be in weeks 1, 3, and 5, followed by a booster session in week 10. Each session will be 30-45 minutes in duration. Research assistants (RAs; nurses trained by the principal researcher) will deliver the entire intervention to avoid information bias. Recorded PowerPoint presentation with simple language will be displayed on a laptop. At the end of each session, RAs will identify the date of next session and inform the participants. This small strategy will promote participant retention in the study.

Educational booklet

Educational sessions will be supplemented by a booklet designed to be understood by an individual with minimal literacy to give a better understanding of fatigue in kidney failure, causes of fatigue, energy conservation strategies and their application in activities of daily

living. Simple text information, along with informative images, will be used to assist participants to understand and apply the energy conservation strategies.

Control group

Participants randomised to the control group will receive usual care (standard care with no formalised, structured, or tailored interventions to reduce symptom/s) from their healthcare providers. Participants in the control group will receive an EVEREST booklet once the study is completed.

Outcomes

Primary outcome

Fatigue

The primary outcome of the study is fatigue, which is measured at Time 0 = baseline, Time 1 = week 4, Time 2 = week 8 and Time 3 = week 12 using the Fatigue Symptom Inventory (FSI) [43]. This self-report instrument is comprised of 14 items assessing the frequency, severity, daily pattern of fatigue and its perceived interference with quality of life. Fatigue severity is measured by an 11 - point item scale (0 = not at all fatigue, 10 = as fatigued as I could be) that assesses least, average, and most fatigue in the past week and right now. A composite fatigue score (FSI composite) will be derived by calculating the average across the three severity items. Frequency is measured as the number of days in the past week (0 - 7) that participants felt fatigue, as well as the percentage of each day on average they felt fatigued (0% = none of the day; 100% = the entire day). Perceived interference**,** which assesses the degree to which fatigue in the past week was judged to interfere with the general level of activity, ability to bathe and dress, normal work activity, ability to concentrate, relations with others, enjoyment of life, and mood, is measured on separate 11-point scales (0 = no interference; 10 = extreme interference). These interference ratings can be summed (and averaged) to obtain a total

perceived interference score. The final item provides qualitative information about possible diurnal variation in the daily experience of fatigue. The FSI has been used previously in the study population of patients with kidney failure.[44] This instrument was translated into the Nepali language, and has a Cronbach's alpha was 0.79.[45]

Secondary outcomes

Secondary outcomes are other renal symptoms, occupational performance, and HRQoL, which will be measured at Time 0 (Baseline) and Time 1 (Week 12).

Other renal symptoms

Other renal symptoms will be measured using the Integrated Patient Outcome Scale Renal (IPOS-Renal); this is a short 11-item measure which combines the most common symptoms experienced by people with kidney disease; additional items such as information needs, practice issues; and anxiety of family.[46, 47] Question 2 of this instrument addresses 15 specific symptoms for each of these items, with responses rated 0 (no symptoms) – 4 (overwhelmingly) [48]. Questions 3-9 address the psychological, spiritual, communication, and practical problem or concern, for each of these, with responses also rated 0-4. Questions 1 and 11 are not scored. The overall IPOS-renal score can range from 0 to 92. The IPOS-Renal demonstrates good reliability and validity;[49] however, it is not yet available in the Nepali language. This instrument was translated into Nepali in the initial phase of this study. Translation process recommended by Sousa and Rojjanasrirat[50] was used to translate the instrument in English to the Nepali language. A content validity index will be calculated while reliability of the instrument will be tested in a representative sample of HD participants in this study.

Occupational performance

The occupational performance will be measured using the Nepali version of the Canadian occupational performance measure (COPM).[51] It is designed to identify changes in occupational performance over a period. Administration of COPM requires five steps. First, the individual identifies and prioritises everyday issues that restrict or impact the performance within the area of self-care, productivity, and leisure. Second, the individual has to rate the identified problem in terms of their importance on a scale of (not important at all) to 10 (extremely important). Third, the individual chose the five most urgent or important problem on which to focus during the intervention. Fourth, the individual rates their performance and satisfaction. Both scales range from 1-10, with higher values indicating better performance and greater satisfaction. After an appropriate interval, performance and satisfaction with performance are reassessed and calculated to measure changes in the individual's perceived occupational performance throughout an intervention. Cronbach's alpha of this instrument for performance score was 0.89, and for the satisfaction, the score was 0.88.[52]

Health-related quality of life

Health-related quality of life will be measured using the Nepali version of the SF-36 questionnaire.[53] The SF-36 contains 36 multidimensional questions and has eight sub-scales: physical functioning (PF), role physical (RP), bodily pain (BP), role emotional (RE), vitality (VT), general health (GH), social functioning (SF), and mental health (MH).[54] There are two distinct concepts measured by the SF-36, represented by the physical component summary (PCS) and mental component summary (MCS).[54] For each sub-scale, items are scored using a Likert scale, summed and transformed on to a scale from 0 (worst health) to 100 (best health).[54] This instrument had adequate reliability with Cronbach's alpha of 0.85.[53]

Additional measurements

Demographic and clinical information, except the blood test report, will be collected at baseline only. The demographic tool has been designed to collect information about participants age, gender, residence, marital status, ethnicity, type of family, educational status, occupation, duration of HD, family history of CKD, access to HD centre. Clinical information such as past medical and surgical history, cause of kidney failure, details of HD, medication prescription will be accumulated from hospital records, patient's records, and blood test report. In addition, eGFR, serum creatinine levels, serum albumin levels, blood urea nitrogen, electrolytes, iron studies and haemoglobin levels will be extracted from the individual's reports. The blood test report will be collected at week 4,8 and 12, which will be aligned with the fatigue assessment. Table 2 illustrates the timeline for measurement of outcome and intervention session.

Table 2: Timeline for outcome measurement and intervention sessions

Time point (Week)	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Enrolment												
Eligibility	×											
Informed consent	×											
Allocation	×											
Demographic Information	×											
Clinical Information	×											
Blood test report	×			×				×				×
Fatigue	×			×				×				×
Other renal symptoms	×											×
Occupational performance	×											×
HRQoL	×											×
Intervention												
Intervention: EVEREST	ES1		ES 2		ES 3					B		
Control: Usual care	×	×	×	×	×	×	×	×	×	×	×	×

¶ ES1: Educational session 1; ES2: Educational session 2; ES3: Educational session 3; B: Booster session

Randomisation

In this cluster randomised study, the unit of observation is at the level of the individual, and the unit of randomisation is at the level of dialysis day (cluster). Cluster randomisation will be done according to the HD day (Sunday/Tuesday/ Thursday or Monday/ Wednesday/ Friday). This method of randomisation will avoid possible treatment contamination. Instances of participants attending different dialysis day and being potentially exposed to the intervention will be documented. An equal number of participants will be recruited from each shift to ensure both intervention and control groups have an equal number. Randomisation will be used and documented by an independent person, not directly involved in the study.

Recruitment and data collection

The researcher will liaise with the dialysis nurse and medical doctor to identify eligible potential participants. A dialysis nurse who is taking care of the participant will seek approval from the participant and will ask if the member of the research team can introduce the study to them. Following confirmation, the research assistants (RAs) will approach potential participants to introduce herself, the purpose, and methods of the study. The RAs will then assess all inclusion/exclusion criteria and invite them to participate. Potential participants will be then given an opportunity to ask if any queries about the study and read the participants information sheet before giving written consent. After written consent, participants will then be invited to complete the self-reported instruments using the Redcap mobile application. Recruitment of the participants will occur until the required sample size is achieved. Training will be given to research assistants before data collection regarding all the procedure and administration of instruments.

Blinding

Blinding is an important aspect to minimise the bias in the study, where participants, data collector, investigators or healthcare providers remain unaware of the allocated intervention. It reduces the opportunity for clinicians or researchers to be influenced by knowledge of group allocation.[55] Due to the nature of the intervention and its pragmatic design, it will not be possible to blind the participants, researcher, dialysis nurse and nephrologist. However, to minimise the risk of bias, research assistant who will collect follow up data will be blinded to group allocation. Nephrologist and dialysis nurses who are responsible for caring for dialysis patients will not be involved in allocation, delivery of the intervention or data collection. They may be aware of the allocation, but this will not affect the outcome of the study.

Data management

All collected data will be be managed using an online research data management planning tool. Personal information will be anonymised by allocating an identification number for each participant. Paperwork, including questionnaires and consent forms, will be kept in a locked filing cabinet. Electronic data will be stored in the secure research storage service managed by the university. The stored data will be accessible only for the research team members. All identifiable information received from participants will be replaced with a unique code. A unique code that links identifying information will be stored separately in an electronic database only accessible by authorised members of the research team. Information used in the analyses will remain in the de-identified format, and other identifying information will not be disclosed in the document or any research publication. All the collected data will be retained for at least 15 years after the end of the study. After the 15 years of research data at the institution will be permanently deleted from the computer system, and any hard copies will be destroyed.

Data analysis

First, a coding manual for each outcome measurement variable will be developed. Responses obtained from the participants on the outcome measures will be scored prior to entering the IBM SPSS statistics software. After data entry, data will be cleaned and checked by the researcher to evaluate for missing data, any errors and invalid response code. Descriptive statistics will be used for all study variables. Baseline characteristics will be compared for the control and intervention group using independent *t*-test or Mann Whitney *U* tests for continuous variables while Chi-square or Fisher Exact tests for categorical variables. The differences between intervention and control groups in terms of changes in primary and secondary outcome variables will be analysed using generalised linear mixed model according to intention-to-treat principle. The model will be used to evaluate the effect of an intervention in different time point and the group-by-time interaction. This model is designed to adjust the clustered nature of the data and include all randomised participants in the analysis. For continuous variables, when the normality assumptions are not met, data will be transformed using log transformation to normalise the residual. Effectiveness of intervention will be reported using mean differences with 95% confidence intervals. Significance will be set at $p < 0.05$.

Ethics and dissemination

Ethical approval is obtained from the Human Research Committee of the university and Ethical Review Board of Nepal Health Research Council prior to the commencement of the study. Appropriate approval is also sought from the research site. Informed written consent will be obtained from each participant before study commencement. Participants will be informed about voluntary participation and that there is no foreseeable risk or harm in participating in the study. Participants will be assured that their confidentiality will always be maintained. Participants also have the liberty to discontinue participating in the study without any

clarification. All personal data will be deidentified before analysis and reported collectively. The trial has been accepted by and registered in ClinicalTrials.gov (Trial registration ID NCT04360408) on April 23, 2020.

The results of this research will be published and presented in a variety of forums. Manuscripts will be submitted to peer-reviewed journals and conference presentation will be prepared for both national and international conferences.

Discussion

There is growing evidence of a direct relationship between symptom burden and HRQoL in individuals with kidney failure;[56-58] however, the evidence to inform practice about improving HRQoL by targeting one or more symptoms is not apparent. Similarly, energy conservation management improves the ability of the participants to manage their fatigue by promoting the optimal use of available energy and thereby reducing the impact and severity of fatigue. This study is needed as it will provide empirical evidence about the effectiveness of an education regarding energy conservation for fatigue management that can be integrated into the everyday life of people receiving HD.

Major limitation of this study includes the recruitment of participants from one dialysis centre in Nepal. This limitation is somewhat mitigated because the selected setting is one of the largest dialysis centres with people from across Nepal referred for HD services. The population of the study is limited to the people receiving HD, which limits the generalizability of the finding to people receiving conservative treatment and other forms of KRT. This study will also use patient-reported outcome measure for the symptom, HRQoL and occupational performance; thus, it is difficult to identify whether participants will accurately report change in the

measurement over time. Moreover, participants in this study will not be followed up for a long period after the intervention.

In conclusion, this study will evaluate the effectiveness of energy conservation education interventions to reduce fatigue in people with kidney failure receiving HD. The evidence generated from this study is expected to positively influence patient outcomes by assessing symptoms and providing appropriate educational interventions during the HD session.

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Footnotes

Contributors: The study was conceived by SS, KA, TG, M-LW, and AB. SS led the literature review. All authors contributed to the preparation of the proposal, critical review, and final approval of the manuscript.

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Competing interests: The authors declare that they have no competing interest.

Ethics approval: Ethical approval is obtained from Human Research Ethics Committee, Griffith University (GU Ref. No. 2021/053), the Nepal Health Research Council (Reg No. 1520).

Provenance and peer review Not commissioned; externally peer reviewed.

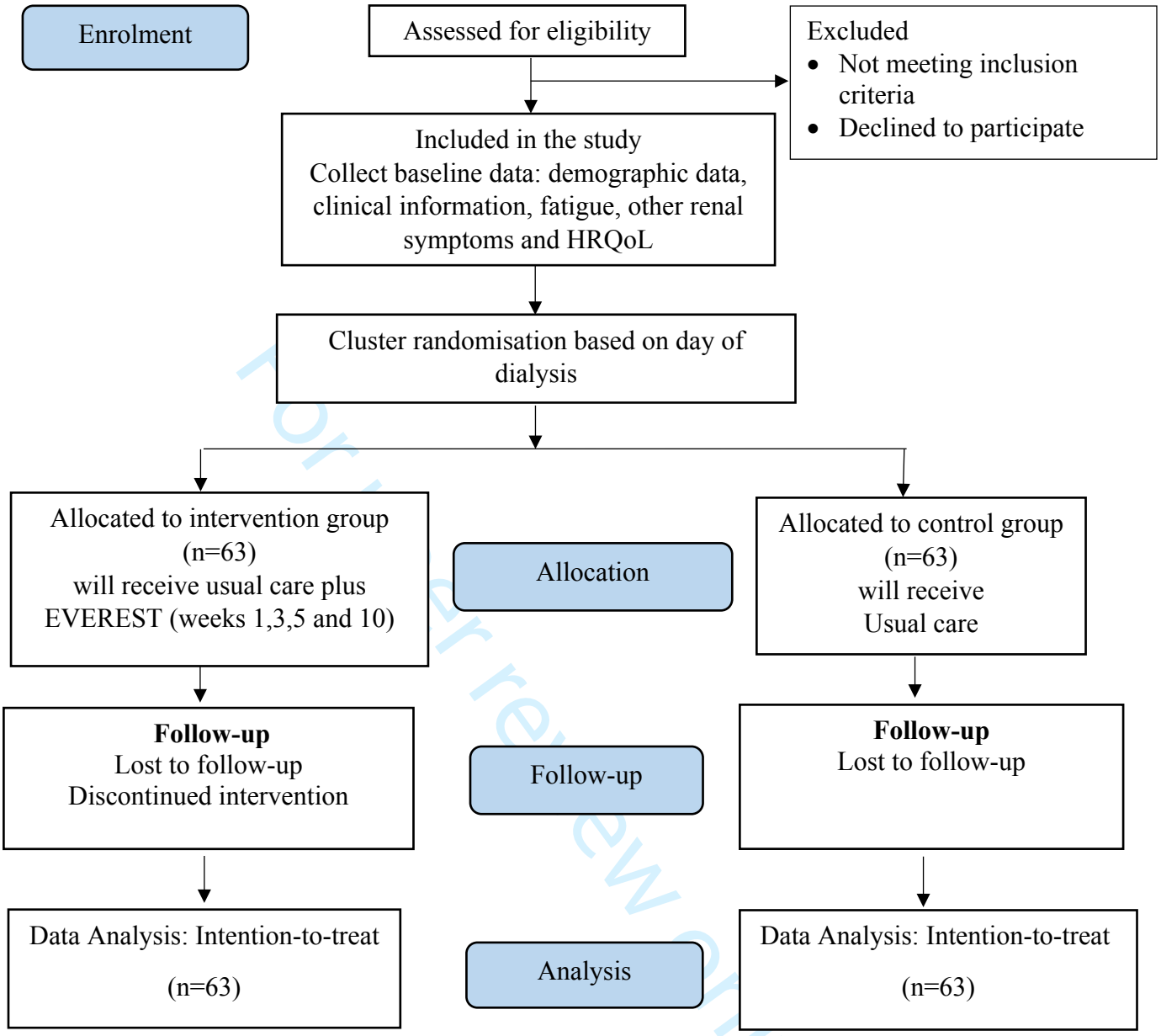

Figure 1: CONSORT Flow Diagram: Extension to Cluster

Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

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		Reporting Item	Page Number
Administrative information			
Title	#1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	Title page; full title, page no. 1
Trial registration	#2a	Trial identifier and registry name. If not yet registered, name of intended registry	Abstract; trial registration, page no. 2
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	N/A
Protocol version	#3	Date and version identifier	N/A
Funding	#4	Sources and types of financial, material, and other support	Page 29
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	Page 1 and 29

Roles and responsibilities: sponsor contact information	#5b	Name and contact information for the trial sponsor	N/A
Roles and responsibilities: sponsor and funder	#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	N/A
Roles and responsibilities: committees	#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	Page 4-6
Background and rationale: choice of comparators	#6b	Explanation for choice of comparators	Page 13
Objectives	#7	Specific objectives or hypotheses	Page 6-7
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, non-inferiority, exploratory)	Page 7
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	Page 7

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)	Page 8
Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	Page 8-13
Interventions: modifications	#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
Interventions: adherance	#11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests)	N/A
Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	N/A
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	Page 13-16
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)	Page 16
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	Page 7
Recruitment	#15	Strategies for achieving adequate participant enrolment to reach target size	Page 17
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	Page 17
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	Page 17
Allocation: implementation	#16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	Page 17
Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	Page 18
Blinding (masking): emergency unblinding	#17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	Page 18
Methods: Data collection, management, and analysis			
Data collection plan	#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	Page 17
Data collection plan: retention	#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	Page 17

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	Page 18
Statistics: outcomes	#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	Page 19
Statistics: additional analyses	#20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	N/A
Statistics: analysis population and missing data	#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)	Page 19
Methods: Monitoring			
Data monitoring: formal committee	#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
Data monitoring: interim analysis	#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	Page 19

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)	Page 19
Consent or assent: ancillary studies	#26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	Page 19
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	Page 19
Declaration of interests	#28	Financial and other competing interests for principal investigators for the overall trial and each study site	Page 29
Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	N/A
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: trial results	#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	Page 19
Dissemination policy: authorship	#31b	Authorship eligibility guidelines and any intended use of professional writers	N/A
Dissemination policy: reproducible research	#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	N/A

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	N/A

Notes:

- 1: Title page; full title, page no. 1
- 2a: Abstract; trial registration, page no. 2
- 5a: Page 1 and 29 The SPIRIT Explanation and Elaboration paper is distributed under the terms of the Creative Commons Attribution License CC-BY-NC. This checklist was completed on 17. August 2021 using https://www.goodreports.org/, a tool made by the EQUATOR Network in collaboration with Penelope.ai

PROJECT DESCRIPTION

Title

The Energy Conservation Education Intervention for People with End-stage Kidney Disease Receiving Haemodialysis (EVEREST)

Trial registration

Clinicaltrials.gov: NCT04360408

Project Team Roles & Responsibilities

1. Professor Ann Bonner (Principal supervisor): Principal investigator
   Head of School of Nursing and Midwifery, Griffith University
   Professor Ann Bonner (Principal supervisor) is the principal investigator of this research project. She is primarily responsible for providing supervision for the con-investigator in the conduct of this research project. She coordinates the supervisory team and student, provides academic leadership, and overall monitoring of the project.

2. Sita Sharma (PhD Student): Co-investigator
   School of Nursing and Midwifery, Griffith University
   Ms Sharma is responsible for overseeing all aspects of the project from protocol design, recruitment, data collection and data analyses. She is responsible for the ethical conduct of the project, protecting human participants' right, safety, welfare, protocol compliance, ensuring informed consent is appropriately obtained from each participant. She is also responsible for providing training to research assistants to ensure that they can commence their role in the study protocol.

3. Dr Winnie Wu (Associate Supervisor): Co-investigator
   Lecturer, School of Nursing and Midwifery, Griffith University
   Dr Wu is responsible for supervision in this project.

4. Professor Theresa Green (Associate Supervisor): Co-investigator, Conjoint Professor of Nursing, MNHHS/School of Nursing, Midwifery and Social Work,

University of Queensland. Professor Green is responsible for supervision in this project.

5. Associate Professor Kim Alexander (Associate Supervisor): Co-investigator
   Associate Professor, School of Nursing, Queensland University of Technology. A/Professor Alexander is responsible for overall supervision in this project.
6. Professor Rishi Kumar Kafle (Local Supervisor): Co-investigator
   Director at National Kidney Centre, Kathmandu, Nepal. Professor Kafle is responsible for supervising the conduct of the local researchers.

Funding

The conduct of this research will not require any external funding. Cost related to data collection and intervention will be drawn from student research allocation account.

1. Introduction

1.1 Background

Chronic kidney disease (CKD) is a major global public health problem and contributor to the overall global burden of non-communicable disease (Jha, 2013), affecting about 13% of the population (Hill et al., 2016). It is defined as any degree of kidney damage or decline in kidney function or glomerular filtration rate (GFR) < 60.0ml/min/1.73m^2 for three months or longer irrespective of the cause (Webster, Nagler, Morton, & Masson, 2017). The classification of CKD is based on cause of disease, level of GFR and level of albuminuria which is collectively called CGA classification (Levey et al., 2020). If GFR < 15 ml/min/1.73m^2 or treated by dialysis, then the term "kidney failure" is used to specify CKD stage G5 (Levey et al., 2020).

Worldwide, a concomitant rise in the incidence of kidney failure is anticipated due to diabetes and hypertension, resulting in a higher prevalence of CKD (Jha, 2013). Currently, the prevalence of kidney failure is estimated based on data about the people who have received KRT. However, that is likely an underestimation of people with kidney failure (Anand, Bitton, & Gaziano, 2013). Each year around 2.3 to 7.1 million progress to kidney failure and KRT globally, and those from low to

middle-income countries are disproportionally represented in these statistics (International Society of Nephrology (ISN), 2019).

Progression of CKD to kidney failure depends on many factors, such as underlying cause, disease-specific pathology, and predisposing factors (Ekart et al., 2013). Diabetes and hypertension are the two predominant causes for the development of kidney failure globally (Leonberg-Yoo & Weiner, 2016). Glomerulonephritis, polycystic kidney disease, obstruction of the urinary tract, recurrent pyelonephritis, medications such as Non-steroid anti-inflammatory drugs (NSAIDs), calcineurin inhibitors, and antiretroviral are other known causes kidney failure (Benjamin & Lappin, 2018).

People with kidney failure undergoing KRT experience a wide range of debilitating physical and psychological symptoms that may eventually have an impact on health-related quality of life (HRQoL). Impaired HRQoL may be associated with higher rates of hospitalisation and mortality (Chambers et al., 2016; Dąbrowska-Bender, Dykowska, Żuk, Milewska, & Staniszewska, 2018). Both kidney failure symptom burden and changes in HRQoL are often unrecognised by healthcare professionals (Cox, Parshall, Hernandez, Parvez, & Unruh, 2017; Senanayake et al., 2017).

1.2 Rationale/Justification

Individuals living with kidney failure receiving haemodialysis (HD) experience several symptoms that can affect their ability to do activities of daily livings. Symptom burden in this population may be related to the underlying pathology, presence of multiple co-morbidities, accumulation of uraemic toxins or fluids, side effects of medication, and inadequacy of dialysis (Moskovitch, Mount, & Davies, 2019). Many cross-sectional studies and systematic reviews report the symptom burden in people with kidney failure receiving HD (Almutary, Bonner, & Douglas, 2013, 2016; Bossola, Pepe, Picca, Calvani, & Marzetti, 2019; Dąbrowska-Bender, Dykowska, Żuk, Milewska, & Staniszewska, 2018; Davison, 2010; Moskovitch, Mount, & Davies, 2019). Almutary, Bonner, and Douglas (2016) in their study, reported that the mean number of symptoms and symptoms severity was highest

in people receiving HD than other groups. The same study also reported the most common symptoms experienced in this population as fatigue (84.8%), bone joint pain (68.7%), itching (65%), and decreased appetite (56.5%).

Fatigue is the most common physical symptom reported by 70% - 85% of people undergoing HD (Almutary, Bonner, & Douglas, 2013; Bossola et al., 2018). Fatigue is an overwhelming subjective feeling of physical and mental exhaustion, that affects an individual's everyday functioning (Bossola, Vulpio, & Tazza, 2011; Zalai & Bohra, 2016), HRQoL (Kraus et al., 2016). Fatigue is also associated with increase hospitalisation and mortality (Picariello, Moss-Morris, Macdougall, & Chilcot, 2016). Several factors have been associated with fatigue in people receiving HD including demographic (gender, age, educational status), physiological (BUN, anaemia, dialysis inadequacy), psychological factors (depression, anxiety and sleep disturbances), side effects of treatment, and treatment efficacy (Artom, Moss-Morris, Caskey, & Chilcot, 2014; Bonner, Wellard, & Caltabiano, 2008; Bonner, Wellard, & Caltabiano, 2010; Horigan, 2012; Picariello, Moss-Morris, Macdougall, & Chilcot, 2016). Physical inactivity has also been associated with fatigue in people undergoing HD (Bonner, Wellard, & Caltabiano, 2010).

Managing fatigue is an essential part of improving HRQoL for individuals on HD. Similar to patients with other chronic diseases, adults receiving HD may benefit from self-management strategies to reduce fatigue and other kidney failure symptoms (Horigan, Schneider, Docherty, & Barroso, 2013). Previous research has shown that interventions like exercise to increase physical activity can reduce fatigue. Interventions that have been successful in reducing fatigue also have limitations and may not be safe for all people. Educational interventions are believed to improve cancer-related fatigue and fatigue and depression in people with CKD, not on dialysis (Bennett et al., 2016; Kao, Huang, Chen, & Wang, 2012). Likewise, energy conservation education is another approach that has shown a significant reduction in fatigue in other chronic diseases, including multiple sclerosis and cancer. However, its effectiveness is not tested in people with kidney failure receiving HD.

Despite the growing documented burden of fatigue on those receiving HD, the diagnosis and treatment of fatigue has been paid minimal attention. A recent systematic review by Sharma, Green, Alexander, and Bonner (2020), also found that educational interventions targeting symptoms and self-management to improve HRQoL in people undergoing HD have yet to be evaluated. Thus, the aim of the proposed research is to test the effect of simple educational intervention about energy conservation strategies on fatigue and HRQOL in this population.

1.3 Research questions

1. Is there a difference in fatigue score from baseline to follow up within and between the intervention and control groups?
2. Is there a difference in other renal symptom scores from baseline to follow up within and between the intervention and control groups?
3. Is there a difference in occupational performance score from baseline to follow up within and between the intervention and control groups?
4. Is there a difference in HRQoL score from baseline to follow up within and between the intervention and control groups?

1.4 Research hypothesis

People with kidney failure receiving HD who receive EVEREST compared to usual care are more likely to:

H^1: have reduced fatigue frequency and severity.

H^1: have reduced number and severity of other renal symptoms.

H^1: have improved occupational performance.

H^1: have improved HRQoL.

1.5 Expected Outcomes

The outcome of the study will provide empirical evidence about the effectiveness of an educational intervention about energy conservation for symptom management in people with kidney failure receiving HD.

2. Project design

A pragmatic cluster randomised control trial (pCRT) will be used. A pragmatic design attempts to find an answer to whether an intervention will work under usual conditions in a real clinical setting (Yoong et al., 2014), so few exclusion criteria will be applied. To avoid possible treatment contamination because participants on the same dialysis day may interact with each other as they spend four hours in close proximity during dialysis necessitates, a cluster design will be used. Clusters will be based on the day of dialysis. The project protocol has been registered (Clinicaltrials.gov: NCT04360408).

2.1 Rationale of choice of methods/design

There are various study designs that can be considered while testing the effectiveness of an intervention. Randomised controlled trials (RCTs) are the best way to study the safety and efficacy of any new treatment or intervention (Hariton & Locascio, 2018). However, when the type of intervention carries a high risk of contamination that is, when the individuals randomised to different comparison groups are in contact with each other and may be influenced by contamination, cluster randomised control trial (CRT) are well suited in that case (Lorenz, Köpke, Pfaff, & Blettner, 2018). Thus, CRT was chosen as a design of this study.

2.2 Research project setting

The study will be conducted at National Kidney Centre (NKC), Kathmandu, Nepal. The NKC, is the non-profit, non-governmental organisation with the largest HD treatment facility in Nepal. The NKC can serve around 240 people for HD treatment in a month. Currently, the centre has 42 dialysis machines. The NKC provides free HD service to all patients as implemented by the Ministry of Health and Population, Nepal.

2.3 Participants

Inclusion criteria

Participants diagnosed with kidney failure (eGFR < 15 ml/min/1.73m^2) and undergoing haemodialysis for ≥ 3 months, aged 18 years and above, able to speak and understand Nepali language and willing to participate will be included in this study.

Exclusion criteria

Participants who are in the early stage of CKD or not dependent on HD, those acutely ill, diagnosed with cognitive impairment and those who are not willing to participate will be excluded.

2.4 Intervention

The intervention group will receive usual care from their healthcare providers and the 12 weeks of EVEREST intervention. The EVEREST uses education to teach individuals to recognise and modify their daily activities to reduce fatigue by analysing the daily work, home and leisure activities in all aspects of their life (Blikman et al., 2017). It is designed to reduce the frequency, severity and impact of fatigue, increases a person's use of energy-conservation strategies and improves their confidence level and their ability to manage fatigue (Blikman et al., 2013). Seven energy conservation strategies will form the content of the EVEREST intervention (see table 1); each will be adapted to fit with the daily activities of Nepalese people. These energy conservation strategies were adopted from energy conservation course "Managing Fatigue" developed by Packer, Brink, and Sauriol (1995). The Control group will receive usual care by their healthcare professionals. Both group will receive educational booklet at the end of the study.

Table 1 Summary of the content of the EVEREST

Session	Goal and objectives	Topics	Duration	Teaching methods
Session 1 (Week 1)	Goal: The goal of this session is to provide information about fatigue in kidney failure and, its causes, the fatigue cycle, and energy conservation and strategies. Objectives • To set a friendly environment and develop a trusting interpersonal relationship • To give information about fatigue, its causes • To give information about energy conservation, energy conservation strategy 1 and its application in activities of daily livings	• Introduction of fatigue in kidney failure • Causes of fatigue. • Introduction of energy conservation • Energy conservation strategies and its application in activities of daily livings ✓ Strategy 1: Organising daily routines and activities • Summary	30-45 minutes	A face-face session with the help of PowerPoint on the laptop Question and answer Discussion
Session 2 (Week 3)	Goal: The goal of this session is to provide information about energy conservation strategies two, three, four and five and its application in activities of daily living Objectives • To set a friendly environment and prepare participant for educational session. • To revise the content of session one. • To provide opportunity to ask question about previous session.	• Revision of previous session. • Energy conservation strategies and its application in activities of daily livings ✓ Strategy 2: Simplifying everyday task ✓ Strategy 3: Organising place for activities and using the energy-efficient appliances ✓ Strategy 4: Pacing activities and avoiding rush	30 minutes	A face-face session with the help of PowerPoint on the laptop Question and answer Discussion

	• To give information about energy conservation 2,3,4, 5 and its application in activities of daily living	✓ Strategy 5: The value of rest and having rest periods during the day • Summary		
Session 3 (Week 5)	Goal: The goal of this session is to provide information about energy conservation strategies 6,7 and its application in activities of daily living Objectives • To set a friendly environment and prepare participant for educational session • To revise session two • To identify any concern about previous session • To provide opportunity to ask question about previous session • To give information about energy conservation six, seven and its application in activities of daily livings.	• Revision of previous session • Energy conservation strategies and its application if activities of daily livings ✓ Strategy 6: Communicating personal needs to others ✓ Strategy 7: Using proper body mechanics and posture • Summary	30 minutes	A face-face session with the help of PowerPoint on the laptop Question and answer Discussion
Session 4 Booster session (Week 10)	Goal: The goal of this session is to revise the content of all session with the help of educational booklet. Objectives • To set a friendly environment and prepare participant for educational session • To provide opportunity to ask question about previous session • To revise session 1, 2 and 3 • To reflect on progress in meeting the objectives of each session	• Revision of previous session • Summarise the content of the booklet ✓ Fatigue, energy conservation, its strategies and application in activities of daily livings	30-45 minutes	A face-face session with the help of booklet Question and answer Discussion

Face-to-face education session

Four face-to-face educational sessions will be undertaken during their regular HD treatment. Sessions will be in weeks 1, 3, 5, followed by a booster session in week 10. Each session will be for 30-45 minutes duration. Trained research assistants will deliver the entire intervention to avoid information bias. The simple language will be used to explain each strategy as well as PowerPoint presentation displayed on a laptop.

Educational booklet

Educational sessions will be supplemented by a booklet based on the evidence and designed to be understood by an individual with minimal literacy to give a better understanding of fatigue in kidney failure, causes of fatigue, energy conservation strategies and its application in activities of daily living. The booklet consists of contents that align with each of the sessions. Simple text information, along with informative images, will be used to assist participants to understand and apply the energy conservation strategies.

2.5 Outcomes

2.5.1 Primary outcome

Fatigue

The primary outcome of the study is fatigue which is measured at Time 0 = baseline, Time 1 = week 4, Time 2 = week 8 and Time 3 = week 12 using the Fatigue Symptom Inventory (Hann et al., 1998). This self-report instrument is comprising 14 items that assess the frequency, severity, daily pattern of fatigue and its perceived interference with quality of life. Fatigue severity is measured by 11-point item (0= not at all fatigue, 10= as fatigued as I could be) that assesses least, average and most fatigue in the past week and right now. A composite fatigue score (FSI composite) was derived by calculating the average across the three severity items. Frequency is measured as the number of days in the past week (0-7) that participants felt fatigue as well as the percentage of each day on average they felt fatigued (0%= none of the day; 100%= the entire day). Perceived interference is measured on separate 11-point scales (0 = no interference; 10 = extreme interference) that assess the degree to which fatigue in the past week was judged to interfere with the general level of activity, ability

to bathe and dress, normal work activity, ability to concentrate, relations with others, enjoyment of life, and mood. These interference ratings can be summed (and averaged) to obtain a total perceived interference score. The final item provides qualitative information about possible diurnal variation in the daily experience of fatigue. The FSI has been used in the study population (Ju et al., 2018). This instrument was translated into the Nepali language, and has a Cronbach's alpha was 0.79 (Dahal & Meheta, 2018).

2.5.2 Secondary outcomes

Secondary outcomes are other renal symptoms, occupational performance and HRQoL, which will be measured at Time 0 = Baseline and Time 1 = Week 12.

Other renal symptoms

Other renal symptoms will be measured using the IPOS-Renal; a short 11-item measure which combines the most common symptoms experienced by people with kidney disease and additional items such as information needs, practice issues, and anxiety of family (Cicely Saunders Institute, 2016b; Murphy, Murtagh, Carey, & Sheerin, 2009). Question 2 of this instrument addresses 15 specific symptoms for each of these; five answer option is available (0-4; Cicely Saunders Institute, 2016a). Question 3-9 addresses the psychological, spiritual, communication and practical problem or concern, for each of these, five answer option is available (0-4). Question 1 and 11 are not scored. The overall IPOS-renal score can range from zero to 92. The IPOS-Renal demonstrates good reliability and validity (Raj, Ahuja, Frandsen, Murtagh, & Jose, 2018); however, it is not yet available in the Nepali language. This instrument was translated into Nepali in the initial phase of this study. Translation process recommended by Sousa and Rojjanasrirat (2011) was used to translate the instrument in English to the Nepali language. Content validity index will be calculated to ensure the content validity while reliability of the instrument will be tested in a representative sample of HD participants in this study.

Occupational performance

Occupational performance will be measured using the Nepali version of the Canadian occupational performance measure (Law et al., 1990). It is designed to identify changes in occupational performance over a period. Administration of

COPM requires five steps. First, the individual identifies and prioritises everyday issues that restrict or impact the performance within the area of self-care, productivity, and leisure. Second, the individual has to rate the identified problem in terms of their importance on a scale of (not important at all) to 10 (extremely important). Third, the individual chose the five most urgent or important problem on which to focus during the intervention. Fourth, the individual rates their performance and satisfaction. Both scales range from 1-10, with higher values indicating better performance and greater satisfaction. After an appropriate interval, performance and satisfaction with performance are reassessed and calculated to measure changes in the individual's perceived occupational performance throughout an intervention. Cronbach's alpha of this instrument for performance score was 0.89, and for the satisfaction, the score was 0.88 (Carswell et al., 2004).

Health-related quality of life

Health-related quality of life will be measured using the Nepali version of the SF-36 questionnaire (Kafle-Bhandari et al., 2018). SF-36 contain 36 multidimensional questions and have eight sub-scales, namely physical functioning (PF), role physical (RP), bodily pain (BP), role emotional (RE), vitality (VT), general health (GH), social functioning (SF), and mental health (MH) (Brazier et al., 1992). There are two distinct concepts measured by the SF-36 represented by the physical component summary (PCS) and mental component summary (MCS; Brazier et al., 1992). For each sub-scale, items are scored using a Likert scale, summed and transformed on to a scale from 0 (worst health) to 100 (best health; Brazier et al., 1992). This instrument had adequate reliability with Cronbach's alpha of 0.85 (Kafle-Bhandari et al., 2018).

2.5.3 Additional measurements

Demographic and clinical information except the blood test report will be collected at baseline only. The demographic tool has been designed to collect information about participants age, gender, residence, marital status, ethnicity, type of family, educational status, occupation, duration of HD, family history of CKD, access to HD centre. Clinical information like past medical and surgical history, cause of kidney failure, details of HD, medication prescription will be accumulated from hospital records and patient's record. In addition, eGFR, serum creatinine levels,

serum albumin levels, blood urea nitrogen, electrolytes, iron studies and haemoglobin levels will be extracted from the individual's blood test reports.

The blood test report will be collected at week 4,8 and 12, which will be aligned with the fatigue assessment. Table 2 illustrates the timeline for measurement of outcome and intervention session.

2.6 Sample size

G power software™ was used to calculate the sample size by performing the priori power analysis for an independent group two-tailed t-test. A previous study (Vadiraja et al., 2017) was which demonstrated a large effect size (Cohen's *d* from 0.90-1.5), was used for the calculation. To have resultant 80% power, a large effect size of 0.8 and a significance of 0.05, 52 participants will be needed (26 in each group). As this study is pragmatic cluster randomised controlled trial, and assuming a moderate intra-cluster coefficient (ICC) of 0.03 and to compensate for attrition and the possibility of non-normality of data, the calculation is further inflated by 20% and again 15% respectively. After adjusting for design effect, attrition and a non-parametric statistic a final sample size of 126 (63 in each group) is required.

2.7 Recruitment strategies and timeframe

Participants will be recruited from the National Kidney Centre. Recruitment of the participants will be done while they are receiving haemodialysis. Usually, each dialysis treatment lasts about four hours. The local researcher (Research Assistant [RA]) will liaise with dialysis nurses and medical doctor who will identify potential participants. The dialysis nurse who is taking care of the participant will seek approval from the participant and will ask if the member of research team can introduce the research to them. Then the RA will approach the participant and introduce herself, the purpose and the method of the research. The potential benefits and risks involved with this research will also be explained. The RA will then assess all inclusion/exclusion criteria and invite them to participate. Individual invited to participate in the research will be told about what they have

to do if they decide to be involved. Potential participants will be then given an opportunity to ask any questions about the research and read the participants information sheet before giving written consent. All participants have to complete the self-reported instruments (Socio-demographic at baseline, FSI at baseline, week 4, 8 and 12; IOPS-renal, SF-36 and COPM at baseline and week 12). It will take about 30-40 minutes to complete the questionnaires. Participants will also have routine blood test at week 4,8 and 12 and the results will be extracted from the medical records. Participants in the intervention group will have to complete the activity checklist at baseline and after the booster education session, which monitor any changes in ways of doing activities of daily livings.

2.8 Training to Research Assistants

Before starting the project, research assistants will be trained to ensure they are familiar with the background and aims of the study, the study protocol and processes, administration of instruments. The training will also include rehearsal of new or unfamiliar procedures. Research assistants involved in delivering an intervention will required to attend a day training course after completing the background reading. The training program will be focused on review of intervention and practice of the intervention techniques. The training will be provided by the co-investigator (PhD Student, Ms Sita Sharma) who was involved in preparing the content of the intervention. They will also have a training manual that will explain their roles and responsibility, ethical conduct of the research, step by step instruction to administer the questionnaire and to deliver the intervention.

Table 2: Timeframe for outcome measurement and intervention sessions

Time point (Week)	1	2	3	4	5	6	7	8	9	10	11	12
Enrolment												
Eligibility	×											
Informed consent	×											
Allocation												
Assessment												
Demographic Information	×											
Clinical Information	×											
Blood test report	×			×				×				×
Fatigue	×			×				×				×
Other renal symptoms	×											×
Occupational performance	×											×
HRQoL	×											×
Intervention												
Intervention: EVEREST	ES1		ES2		ES3					B		
Control: Usual care	×	×	×	×	×	×	×	×	×	×	×	×

¶ ES1: Educational session 1; ES2: Educational session 2; ES3: Educational session 3; B: Booster session

2.9 Allocation

In this cluster randomised study, the unit of observation is at the level of the individual, and the unit of randomisation is at the level of dialysis day (cluster). Cluster randomisation will be done according to the HD pattern (Sunday/Tuesday/ Thursday or Monday/ Wednesday/ Friday). This method of randomisation will avoid possible treatment contamination. Instances of participants attending different dialysis day and being potentially exposed to the intervention will be documented. An equal number of participants will be recruited from each shift to ensure both intervention and control groups have an equal number. Simple randomisation will be used and documented by an independent person, not directly involved in the study.

2.10 Blinding

Blinding is an important aspect to minimise the bias in the study, where participants, data collector, investigators or healthcare providers remain unaware of the allocated intervention. It reduces the opportunity for clinicians or researchers to be influenced by knowledge of group allocation (Bhide, Shah, & Acharya, 2018). Due to the nature of the intervention and its pragmatic design, it will not be possible to blind the participants, researcher, dialysis nurse and nephrologist. However, to minimise the risk of bias, research assistants who will collect follow up data will be blinded to group allocation. Nephrologist and dialysis nurses who are responsible for caring for dialysis patients will not be involved in allocation, delivery of the intervention or data collection. They may be aware of the allocation, but this will not affect the outcome of the study.

2.11 Data Collection methods

For this project, Redcap application will be used for collection, storage and maintenance of the research data. The Redcap application was chosen as it enables users to contribute via the internet to secure database and allow the investigator to overseeing all data entries. Data will be collected using patient-reported outcome measures via validated instruments and directly from the participant's medical record by the research assistants, who will have been trained

prior to commencing the study. All instruments have been used previously in people receiving HD.

2.12 Data Management

All collected data will be be managed using an online research data management planning tool. All paperwork will be stored in a secured box located at nursing station of National Dialysis Centre in Nepal. Paperwork will then be brought to Australia using secured courier service and will be kept in a locked filing cabinet at School of Nursing and Midwifery, Griffith University, Nathan Campus. Electronic files will be stored on a password-protected computer server. The stored data will be accessible only for the research team members. All identifiable information received from participants will be replaced with a unique code and converted to re-identifiable form. A unique code that links identifying information will be stored separately in an electronic database only accessible by authorised members of the research team. Information used in the analyses will remain in the de-identified format, and other identifying information will not be disclosed in the document or any research publication. All the collected data will be retained for at least 15 years after the end of the study. After the 15 years of research data at the institution will be permanently deleted from the computer system, and any hard copies will be destroyed.

2.13 Data Analysis:

First, a coding manual for each outcome measurement variable will be developed. Responses obtained from the participants on the outcome measures will be scored prior to entering the IBM SPSS statistics software. After data entry, data will be cleaned and checked by the researcher to evaluate for missing data, any errors and invalid response code. Descriptive statistics will be used for all study variables. Baseline characteristics will be compared for the control and intervention group using independent *t*-test or Mann Whitney *U* tests for continuous variables while Chi-square or Fisher Exact tests for categorical variables. The differences between intervention and control groups in terms of changes in primary and secondary

outcome variables will be analysed using generalised linear mixed model according to intention-to-treat principle. The model will be used to evaluate the effect of an intervention in different time point and the group-by-time interaction. This model is designed to adjust the clustered nature of the data and include all randomised participants in the analysis. For continuous variables, when the normality assumptions are not met, data will be transformed using log transformation to normalise the residual. Effectiveness of intervention will be reported using mean differences with 95% confidence intervals. Significance will be set at $p < 0.05$.

3. Ethical consideration

Ethical approval will be obtained from the Human Research Committee of the university prior to the commencement of the study. Approval was already sought from the research site. Informed written consent will be obtained from each participant before study commencement. Participants will be informed about voluntary participation and that there is no foreseeable risk or harm in participating in the study. Participants will be assured that their confidentiality will always be maintained. Participants will be given liberty to discontinue participating in the study without any clarification. All personal data will be coded before analysis and reported collectively.

3.1 Approach/es to provision of information to participants

A Participant information sheet and consent to participate will be provided to each participant. The information sheet include will include:

- Information that participation is voluntary
- Participants may withdraw from the study at any time
- Describe how to participate in the study and what to expect from the study
- Potential benefit and any risk involved with the study
- Information that participant's data will be treated with full confidentiality and if published will not be identifiable as theirs
- Contact detail of research team

3.1.1 Consent

The researcher will provide verbal overview of the project to ensure all detail have been understood and that participation in the study is voluntary. If participants are willing to participate, they will be asked to provide their consent in written form.

4. Results, Outcomes and Future Plans

4.1 Plan for return of results or findings of research to participants

At the end of the research, participants will be asked if they wish to receive the results of the research. Those who expressed their interest in receiving a copy will be asked to contact their attending nephrologist or member of research team to get a lay summary of the result. This report will contain aggregated data which will not identify individual participants.

4.2 Dissemination of and publication of Project Outcome

It is anticipated that the results of this research project will be published and presented in a variety of forums. Manuscripts will be submitted to peer-reviewed journals and conference presentation will be prepared for both national and international conferences. To protect the privacy of participants, no information will be published that could identify participant in this trial.

4.3 Other potential uses of the data at the end of the project

Data collected in this project will be solely use for the activities previously described.

4.4 Plan for sharing and/or future use of data

No future use of data involved.

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Energy Conservation Education Intervention for People with End-stage Kidney Disease Receiving Haemodialysis (EVEREST): protocol for a cluster randomised control trial

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TITLE PAGE

FULL TITLE: Energy Conservation Education Intervention for People with End-stage Kidney Disease Receiving Haemodialysis (EVEREST): protocol for a cluster randomised control trial

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Abstract

Introduction: Multiple symptoms occur in people with kidney failure receiving haemodialysis (HD) and these symptoms have a negative impact on health-related quality of life (HRQoL). Fatigue, the most common symptom, is debilitating and difficult to manage. Educational interventions involving energy conservation strategies are helpful in reducing fatigue, however the effectiveness of energy conservation has not been previously studied in those receiving HD. The aim of this study is to evaluate the effectiveness of an energy conservation education intervention for people with end-stage kidney disease receiving HD (EVEREST trial).

Methods and analysis: A pragmatic cluster randomised controlled trial with repeated measure will be used. One hundred and twenty-six participants from tertiary level dialysis centre will be cluster randomised to the intervention and control group according to HD treatment day. The intervention group will receive usual care along with a structured energy conservation education (ECE) program over 12 weeks comprising three individual face-to-face educational intervention sessions, one booster session, and a booklet. The control group will receive usual care from their healthcare providers and a booklet at the end of the study. The primary outcome is fatigue, and the secondary outcomes are other kidney symptoms, occupational performance, and health-related quality of life. Intention-to-treat analysis will occur and will include a change in primary and secondary outcomes.

Ethics and dissemination: Ethical approval has been obtained from the Human Research Committee of the Griffith University and Nepal Health Research Council. The results of this research will be published and presented in a variety of forums.

Trial registration number: NCT04360408; Pre-results

Strengths and limitations of this study

- This study used cluster randomisation according to the day of HD to prevent treatment contamination between groups.
- The intervention material was developed to be simple and easily understood by those with limited education.
- Participants are recruited from one haemodialysis centre in Nepal.
- This study is focused on those receiving haemodialysis limiting generalisability to this population.

Introduction

Chronic kidney disease (CKD) is both a major global public health problem and contributor to the overall burden of non-communicable disease,[1] affecting about 13% of the global population.[2] The internationally agreed definition of CKD is an estimated glomerular filtration rate (eGFR) < 60ml/min/1.73m^2 for three months or longer.[3] Chronic kidney disease is then classified into five grades based on eGFR.[4] When eGFR < 15ml/min/1.73m^2 then the term kidney failure (previously ESKD) is used.[4] While there is no kidney registry in Nepal, the prevalence of kidney failure is approximately 2,900.[5] Haemodialysis (HD) is the most common modality of treatment for those with kidney failure and usually prescribed three times per week, with a duration of 4 - 5 hours per session.[6] It can be performed either in-centre in a hospital or a satellite unit or at home.[7] This treatment impacts on almost all aspects of daily life leading to decreased health-related quality of life (HRQoL)[8] including maintaining employment and being able to undertake routine social activities[9] as well as affecting family members.[10, 11]

Physical and psychological symptoms are common in this population and may be related to the underlying pathologies, presence of multiple co-morbidities, accumulation of uraemic toxins or fluids, medication side effects, and inadequacy of dialysis.[12] Several studies have described symptom burden in this population.[12-16] Almutary et al, who compared those not on dialysis with those receiving either HD or peritoneal dialysis, reported that both symptom prevalence and severity was highest in those receiving HD, and that about 85% reported being fatigued.[13]

Fatigue is an overwhelming subjective experience of discomfort associated with physical and mental exhaustion.[17] Fatigue in people with kidney failure negatively impacts individuals' day to day activities,[18, 19] HRQoL,[20] increases hospitalisations and mortality. [21] Various factors have been associated with fatigue in kidney failure such as demographic characteristics,[22] elevated

urea levels, anaemia, depression, anxiety, and sleep disturbances.[22, 23] Medication side effects and HD treatment-related factors like dialysis inadequacy and excessive ultrafiltration have been associated with fatigue.[24-26]

Managing fatigue is essential in improving HRQoL for individuals on HD. It can be argued that adults receiving HD can benefit from symptom self-management techniques to reduce fatigue and other kidney failure symptoms.[27] Previous research has shown that exercise could reduce fatigue;[22, 28] however barriers such as having sufficient available expert staff, dialysis-related fatigue, comorbid conditions, and lack of motivation may limit the ability for some to be actively involved in exercise.[29] Educational interventions are believed to improve cancer-related fatigue [30] and there is some evidence to support this in earlier stages of CKD.[31] Likewise, education about energy conservation is another approach to manage fatigue that has shown a significant reduction in fatigue in other chronic diseases, including multiple sclerosis[32] and cancer.[33, 34] However, its effectiveness is yet to be tested in the HD population.

In a systematic review, Blikman et al.[32] included six interventional studies which examined the effects of energy conservation management (ECM) for fatigue and HRQoL in people with multiple sclerosis (MS). Four studies included in this review used an ECM intervention program based on Packers' "Managing Fatigue" course and two were guided by the MS fatigue guidelines. Interventions in these studies were delivered in group format and face-to-face except one study [35] where the intervention was delivered via teleconference. Meta-analysis of two studies[35, 36] included in this review showed that an ECM intervention was more effective than no intervention in reducing the impact of fatigue measured by fatigue impact scale (FIS).[32] There was a improvement in the FIS subscale significantly on the cognitive subscale (MD = -2.91; 95% CI -4.32 to -1.50), the physical subscale (MD = -2.99; 95% CI -4.47 to -1.52), and the psychological subscale (MD = -6.05; 95% CI -8.72 to -3.37).[32] The same study also

revealed that an ECM improved three domains of HRQoL, namely role physical (MD = 17.26; 95% CI 9.69 to 24.84), social functioning (MD = 6.91; 95% CI 1.32 to 12.49), and mental health (MD = 5.55; 95% CI 2.27 to 8.83). Another study evaluated the effect of energy conservation strategies in persons with breast cancer experiencing fatigue.[33] In this study, the intervention was delivered face-to-face in the form of small group discussion. Duration of each session was 90 minutes and sessions were conducted weekly for 5 weeks.[33] The result of this study showed that energy conservation strategies significantly reduced cancer-related fatigue in persons with breast cancer over an 8 week follow-up period ($F = 69.8$, $p < 0.001$).[33]

Despite fatigue being highly prevalent in those receiving HD, a recent systematic review did not find any interventional studies that used an educational approach for self-management to reduce symptoms and improve HRQoL in people undergoing HD.[37] Thus, this study aims to evaluate the effectiveness of an energy conservation education intervention for people with end-stage kidney disease receiving haemodialysis (EVEREST trial) in Nepal.

Research hypotheses

People with kidney failure on HD who receive energy conservation education (ECE) program and usual care are more likely to:

H1: have reduced fatigue severity, frequency and perceived interference compared to people undergoing HD who received only usual care.

H2: have reduced other kidney failure symptoms score compared to people undergoing HD who received only usual care.

H3: have improved occupational performance and satisfaction compared to people undergoing HD who received only usual care.

H4: have improved HRQoL compared to people undergoing HD who received only usual care.

Methods and analysis

Study design

A pragmatic cluster randomised controlled trial (CRT [pCRT)]) design with outcome assessor blinded, with 1:1 randomisation will be used. A pragmatic design attempts to find an answer to whether an intervention will work under usual conditions in a real clinical setting where few exclusion criteria are applied.[38] To avoid possible treatment contamination, because participants on the same HD day may interact with each other as they spend approximately four hours in close proximity to each other during dialysis, a cluster design is used with cluster cohorts based on the day of dialysis. The CONSORT flow diagram in Figure 1 presents the study design.

Study setting

The study will be conducted at the National Kidney Centre (NKC), Kathmandu, Nepal. The NKC is the non-profit, non-governmental organisation with the largest HD treatment facility in Nepal. The NKC provides HD treatment for around 240 people a month. Haemodialysis is free to all patients as mandated by the Ministry of Health and Population, Nepal although medications and routine blood tests require patients to fund.

Sample size

G power software™ was used to calculate the sample size by performing the priori power analysis for an independent group two-tailed t-test. The sample size was calculated based on a large effect size (Cohen's *d* from 0.90 - 1.5) taken from previous study in a breast-cancer patients on management of fatigue (measured with fatigue symptom inventory [FSI]) with yoga intervention.[39] To have resultant 80% power, an effect size of 0.8 and a significance of 0.05, 52 participants are needed (26 in each group). As this study uses a cluster design, and assuming

a moderate intra-cluster coefficient (ICC) of 0.03, the sample size is adjusted to compensate for design effect. To compensate for attrition and to avoid the possibility of non-normality of data, the calculation is further inflated by 20% and again 15% respectively. After adjusting for these, a final sample size of 126 (63 in each group) is required.

Eligibility criteria

Participants diagnosed with kidney failure and undergoing HD for ≥ 3 months, aged 18 years and above, able to speak and understand Nepali language, and willing to participate, will be included in this study. Participants who are in earlier grades of CKD or not dependent on HD, those acutely ill, diagnosed with cognitive impairment and those who are not willing to participate will be excluded. Participants may be withdrawn from the study at any time due to a safety concern, if they became sick or if unable to adhere with the trial procedure.

Study intervention

Intervention group

The intervention group will receive both usual care from their healthcare providers and the 12 weeks ECE program. The ECE program teaches individuals to recognise and modify their daily activities to reduce fatigue by analysing their daily work, home and leisure activities.[40] This program helps to develop a positive attitude towards decision-making and the maximum use of available energy.[32] It is designed to reduce the frequency, severity and impact of fatigue, increase a person's use of energy-conservation strategies and improve their confidence level and their ability to manage fatigue.[32] Seven energy conservation strategies adopted from the "Managing Fatigue" course developed by Packer et al.[41] form the content of the ECE program (see Table 1); each strategy is adapted to fit with the daily activities of Nepali people.

Table 1
Summary of the content of the ECE Program

Session	Goal and objectives	Topics	Duration	Teaching methods
Session 1 (Week 1)	Goal: The goal of this session is to provide information about fatigue in kidney failure, its causes, and energy conservation strategies and its application in daily activities. Objectives: • To set a friendly environment and develop a trusting interpersonal relationship • To give information about fatigue, its causes • To give information about energy conservation, energy conservation strategy 1 and its application in daily activities	• Fatigue in kidney failure • Causes of fatigue • Introduction of energy conservation • Energy conservation strategies and its application in daily activities ✓ Strategy 1: Organising daily routine and evaluating priorities • Summary	30-45 minutes	A face-to-face session with the help of recorded PowerPoint on the laptop Question and answer Discussion
Session 2 (Week 3)	Goal: The goal of this session is to provide information about energy conservation strategies 2, 3, 4 and 5, and there application in daily activities. Objectives: • To set a friendly environment and prepare participant for educational session • To revise the content of session 1 • To provide opportunity to ask question about previous session • To give information about energy conservation strategies 2, 3, 4, 5 and examples relevant to daily activities	• Revision of previous session • Energy conservation strategies and its application in daily activities ✓ Strategy 2: Simplifying the everyday task ✓ Strategy 3: Organising station for activities and using the energy-efficient appliances ✓ Strategy 4: Pacing activities and avoid rushing	30 minutes	A face-to-face session with the help of recorded PowerPoint on the laptop Question and answer

		✓ Strategy 5: The value of rest and having rest periods during the day • Summary		Discussion
Session 3 (Week 5)	Goal: The goal of this session is to provide information about energy conservation strategies 6 and 7 and there application to daily activities. Objectives: • To set a friendly environment and prepare participant for educational session • To revise session 2 • To identify any concern about previous session • To provide opportunity to ask question about previous sessions • To give information about energy conservation 6, 7 and its application in daily activities.	• Revision of previous session • Energy conservation strategies and its application in daily activities ✓ Strategy 6: Communicating personal needs to others ✓ Strategy 7: Using proper body mechanics and posture • Summary	30 minutes	A face-to-face session with the help of recorded PowerPoint on the laptop Question and answer Discussion
Session 4 Booster session (Week 10)	Goal: The goal of this session is to revise the content of all sessions with the help of educational booklet. Objectives: • To set a friendly environment and prepare participant for educational session • To provide opportunity to ask question about previous sessions • To revise session 1, 2 and 3 • To reflect on progress in meeting the objectives of each session	• Revision of previous session • Summarise the content of the booklet ✓ Introduction of fatigue, energy conservation, its strategies and application in daily activities	30-45 minutes	A face-to-face session with the help of booklet Question and answer Discussion

The ECE program is guided by Symptom management theory (SMT) as the theoretical framework. This theory accounts for the person, health/illness, the environment, and includes the symptom experience, symptom management strategies and outcomes.[42] Symptom management theory is built on the premise that a symptom experience is based on how an individual perceives and responds to the symptom.[43] Symptom management strategies used by individuals to delay a negative outcome of the symptom experience can be targeted by appropriate intervention strategies. The theory also explains that outcomes (e.g., functional status, self-care, HRQoL) may be altered by the symptom experience and/or symptom management strategies. The dynamic interaction between each dimension of SMT provides explicit and testable relationships among these dimensions. In this study, the relationship between a person's fatigue experience and other kidney symptoms, the ECE program, and outcomes including status of fatigue and other kidney symptoms, HRQoL, and occupational performance will be tested using this theory.

Face-to-face education session

Four face-to-face educational sessions will be undertaken during participants' regular HD treatment. Sessions will be in weeks 1, 3, and 5, followed by a booster session in week 10. Each session will be 30 - 45 minutes in duration. Research assistants (RAs; nurses trained by the principal researcher) will deliver the intervention to avoid information bias. Recorded PowerPoint presentations in simple Nepali language will be displayed on a laptop. At the end of each session, RAs will inform the participants of the date for the next session. This simple strategy will assist with participant retention in the study.

Educational booklet

Educational sessions will be supplemented by a booklet designed to be understood by an individual with minimal literacy to support a better understanding of fatigue in kidney failure,

causes of fatigue, energy conservation strategies and their application in daily activities. Simple text information, along with informative images, will be used to assist participants to understand and apply the energy conservation strategies.

Control group

Participants randomised to the control group will receive usual care (standard care with no formalised, structured, or tailored interventions to reduce symptom/s) from their healthcare providers. Participants in the control group will receive an ECE program booklet at week 12 once the study is completed.

Outcomes

Primary outcome

Fatigue

The primary outcome of the study is fatigue, which is measured at Time 0 = baseline, Time 1 = week 4, Time 2 = week 8 and Time 3 = week 12 using the Fatigue Symptom Inventory (FSI).[44] This self-report instrument is comprised of 14 items assessing the frequency, severity, daily pattern of fatigue and its perceived interference with quality of life. Fatigue severity is measured by an 11-point item scale (0 = not at all fatigue, 10 = as fatigued as I could be) that assesses least, average, and most fatigue in the past week and right now. A composite fatigue score (FSI composite) will be derived by calculating the average across the three severity items. Frequency is measured as the number of days in the past week (0 - 7) that participants felt fatigue, as well as the percentage of each day on average they felt fatigued (0% = none of the day; 100% = the entire day). Perceived interference**,** which assesses the degree to which fatigue in the past week was judged to interfere with the general level of activity, ability to bathe and dress, normal work activity, ability to concentrate, relations with others, enjoyment of life, and mood, is measured on separate 11-point scales (0 = no interference; 10 = extreme interference).

These interferences ratings can be summed (and averaged) to obtain a total perceived interference score. The final item provides qualitative information about possible diurnal variation in the daily experience of fatigue. The FSI has been used previously in the study kidney failure population.[45] This instrument was translated into the Nepali language, and has a Cronbach's alpha of 0.79.[46]

Secondary outcomes

Secondary outcomes are other kidney symptoms, occupational performance, and HRQoL, which will be measured at Time 0 (Baseline) and Time 3 (Week 12).

Other kidney symptoms

Other kidney symptoms will be measured using the Integrated Palliative Outcome Scale renal (IPOS-renal); designed to be used in chronic kidney disease population including those receiving HD. This self-report instrument is short (11-items) making it quick and easy to administer. It measures the most common symptoms experienced by people with kidney disease; additional items such as information needs, practice issues; and anxiety of family.[47, 48] Question 2 of this instrument assesses 15 specific symptoms for each of these items, with responses rated 0 (no symptoms) to 4 (overwhelmingly).[49] Questions 3-9 assess the psychological, spiritual, communication, and practical problem or concern, for each of these, with responses also rated 0 - 4. Questions 1 and 11 are not scored. The overall IPOS-renal score can range from 0 to 92. The IPOS-renal demonstrates good reliability and validity;[50] however, it is not available in Nepali language. Prior to starting the study, the instrument was translated into Nepali. The process recommended by Sousa and Rojjanasrirat was used to translate the instrument in English to the Nepali language.[51] A content validity index will be calculated while reliability of the instrument will be tested in a representative sample of HD participants in this study.

Occupational performance

Occupational performance is measured by the Nepali version of the Canadian occupational performance measure (COPM).[52] This instrument is designed to identify changes in occupational performance over a period of time. Administration of the COPM requires five steps. First, the individual identifies and prioritises everyday problems that restrict or impact the performance in the areas of self-care, productivity, and leisure. Second, the identified problems are rated in terms of their importance on a scale of 1 (not important at all) to 10 (extremely important). Third, the five most urgent or important problems are identified on which to focus during the intervention. Fourth, the individual rates their performance and satisfaction. Both scales range from 1-10, with higher values indicating better performance and greater satisfaction. After an appropriate interval (Week 12 in this study), performance and satisfaction are reassessed and calculated to measure changes overtime. Cronbach's alpha of this instrument for performance score was 0.89, and for the satisfaction, the score was 0.88.[53]

Health-related quality of life

Health-related quality of life is measured using the Nepali version of the SF-36 questionnaire.[54] The SF-36 contains 36 multidimensional questions and has eight sub-scales: physical functioning, role physical, role emotional, energy/fatigue, emotional wellbeing, social functioning, pain and general health.[55] There are two distinct concepts measured by the SF-36, represented by the physical component summary (PCS) and mental component summary (MCS).[55] For each sub-scale, items are scored using a likert scale, summed and transformed on to a scale from 0 (worst health) to 100 (best health).[55] This instrument has good reliability with Cronbach's alpha of 0.85.[54]

Additional measurements

Demographic and clinical information, except blood results, will be collected at baseline only. The demographic tool has been designed to collect information about participants age, gender, residence, marital status, ethnicity, religion, type of family, educational status, occupation, and income. Kidney characteristics such as CKD cause and duration, family history of CKD, duration and detail of HD treatment, past medical and surgical history, current medications will be extracted from hospital records. In addition, serum albumin, electrolytes, and haemoglobin levels as well as iron studies results will be extracted from the individual's reports. These results will be collected at baseline then weeks 4, 8 and 12; aligned with assessment of fatigue. The intervention group will record levels of activity while at home prior to starting the ECE program and then at week 12. Table 2 illustrates the timeline for measurement of outcomes and intervention sessions.

Table 2
Timeline for outcome measurement and intervention sessions

Time point (Week)	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Enrolment												
Eligibility	×											
Informed consent	×											
Allocation	×											
Measures												
Demographic Information	×											
Clinical Information	×											
Blood test results	×			×				×				×
Fatigue	×			×				×				×
Other kidney symptoms	×											×
Occupational performance	×											×
HRQoL	×											×
Activity checklist	×											×
Intervention												
Intervention: ECE Program	ES1		ES2		ES3					B		

Intervention: Usual care	×	×	×	×	×	×	×	×	×	×	×	×
Control: Usual care	×	×	×	×	×	×	×	×	×	×	×	×

Note. ¶ ES1: Educational session 1; ES2: Educational session 2; ES3: Educational session 3; B: Booster session

Randomisation

In this cluster randomised study, the unit of observation is at the level of the individual, and the unit of randomisation is at the level of dialysis day (cluster). Cluster randomisation will be done according to the HD day (Sunday/Tuesday/Thursday or Monday/Wednesday/Friday) determined by an independent person, not directly involved in the study. This method of randomisation will avoid possible treatment contamination. Instances of participants attending different dialysis days and being potentially exposed to the intervention will be documented. An equal number of participants will be recruited from each cluster to ensure both intervention and control groups have an equal number.

Recruitment and data collection

The research assistants (RAs) will liaise with the dialysis nurse and medical doctor to identify eligible potential participants. A dialysis nurse who is taking care of the participant will seek approval from the participant to introduce the RA. Following confirmation, the RAs will approach potential participants to introduce herself, the purpose, and methods of the study. The RAs will then assess all inclusion/exclusion criteria and invite them to participate. Potential participants will receive an information sheet and it will also be read out a loud (due to basic literacy concerns). Potential participants will also be given an opportunity to ask if there are any queries about the study before giving written consent. Baseline data will be collected by the RAs and entered into the Research Electronic Data Capture (REDCap) mobile application.

Recruitment will occur until the required sample size is achieved. Comprehensive training is provided to RAs prior to starting the study.

Blinding

Due to the nature of the intervention and its pragmatic design, it will not be possible to blind participants, researcher, dialysis nurses or nephrologists. However, to minimise the risk of bias, a different RA, who will collect follow up data, will be blinded to group allocation. Nephrologists and dialysis nurses who are responsible for caring for patients will not be involved in the allocation, delivery of the intervention or data collection. They may be aware of the allocation, but this will not affect the outcome of the study.

Data management

All data will be managed using the Research Electronic Data Capture (REDCap) tool. It is a secure web application designed to support data capture for studies[56], and it is suitable to use in Nepal. Hard copy material, including consent forms and activity checklist will be securely held in a locked filing cabinet. Electronic data will be stored in the secure research storage service managed by the university. The stored data will be accessible only by the research team. All identifiable information received from participants will be replaced with a unique code with the stored separately. Data used in the analyses will remain in the de-identified format. No identifying information will be published. All data will be retained for at least 15 years after the end of the study, and then permanently deleted from the computer system or shredded.

Data analysis

First, a coding manual for each outcome variable will be developed with responses scored prior to entering the IBM SPSS statistics software version 28. Data will then be cleaned and checked to evaluate for missing data, any errors or invalid responses. Descriptive statistics will

be used for all study variables. Baseline characteristics will be compared for the control and intervention group using independent *t*-test or Mann Whitney *U* tests for continuous variables while Chi-square or Fisher Exact tests for categorical variables. McNamar's test will be used to determine the difference in the activity before and after the intervention in the intervention group. Intention-to-treat principles using linear mixed models (LMM) will determine the differences between intervention and control groups between primary and secondary outcomes variables. This type of analysis is used to evaluate the effect of an intervention at different time points and also group-by-time interaction between groups. It is also possible to adjust the LMM due to the clustered nature of the data and include all randomised participants in the analysis. For continuous variables, when normality assumptions are not met, data will be transformed using log transformation. Effectiveness of intervention will be reported using mean differences with 95% confidence intervals (CI). Significance will be set at $p < 0.05$.

Trial Status

Trial is currently ongoing. Recruitment commenced in April 2021 and is expected to be completed in February 2021.

Patient and Public involvement

There is no active involvement of patients or public in the development of this study protocol.

Ethics and dissemination

Ethical approval was obtained from the Human Research Committee of Griffith University and also the Ethical Review Board of Nepal Health Research Council prior to the commencement of the study. Appropriate approval was also sought from the research site. Informed written consent will be obtained from each participant before study commencement. Participants will be informed about voluntary participation and that there is no foreseeable risk or harm in

participating in the study. Participants will be assured that their confidentiality will be maintained. Participants also have the liberty to discontinue participating in the study without any clarification. All personal data will be deidentified before analysis and reported collectively. The trial has been accepted by and registered in ClinicalTrials.gov (Trial registration ID NCT04360408) on April 23, 2020.

The results of this research will be published and presented in a variety of forums. Manuscripts will be submitted to peer-reviewed journals and conference abstracts will be prepared for national and international conferences.

Discussion

There is growing evidence of a direct relationship between symptom burden and HRQoL in individuals with kidney failure;[57-59] however, the evidence to inform practice about improving HRQoL by targeting the most prevalent and severe symptom, fatigue, is not apparent. Energy conservation management does seem to improve the self-management of fatigue in other chronic diseases although it's effectiveness for CKD-related fatigue is unknown. This study is needed as it will provide empirical evidence about the effectiveness of an ECE program for fatigue management that can be integrated into the everyday life of people receiving HD.

Major limitations of this study are that recruitment of participants is from one dialysis centre in Nepal. This limitation is somewhat mitigated because the selected setting is one of the largest centres in the country referred for HD services. In addition, the study's population is limited to those receiving HD, which limits the generalisability of the finding to other CKD groups such as those receiving conservative treatment or other forms of kidney replacement therapy. This study will also use patient-reported outcome measures for symptoms, HRQoL, and

occupational performance; thus, it is difficult to identify whether participants will accurately report change in outcomes over time. Moreover, participants in this study will not be followed up for a long period after the intervention.

In conclusion, this study will evaluate the effectiveness of an ECE program to reduce fatigue in people with kidney failure receiving HD. The evidence generated from this study is expected to positively influence patient outcomes by assessing symptoms and providing appropriate educational interventions during the HD session.

Figure Caption

Figure 1

CONSORT flow diagram: extension to cluster, reflecting the flow of participants in the study. CONSORT, Consolidated Standards of Reporting Trials; HRQoL, Health-related quality of life; ECE, Energy Conservation Education.

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Footnotes

Contributors: The study was conceived by SS, KA, TG, M-LW, and AB. SS led the literature review. All authors contributed to the preparation of the proposal, critical review, and final approval of the manuscript.

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Competing interests: The authors declare that they have no competing interest.

Ethics approval: Ethical approval is obtained from Human Research Ethics Committee, Griffith University (GU Ref. No. 2021/053), the Nepal Health Research Council (Reg No. 1520).

Provenance and peer review Not commissioned, externally peer reviewed.

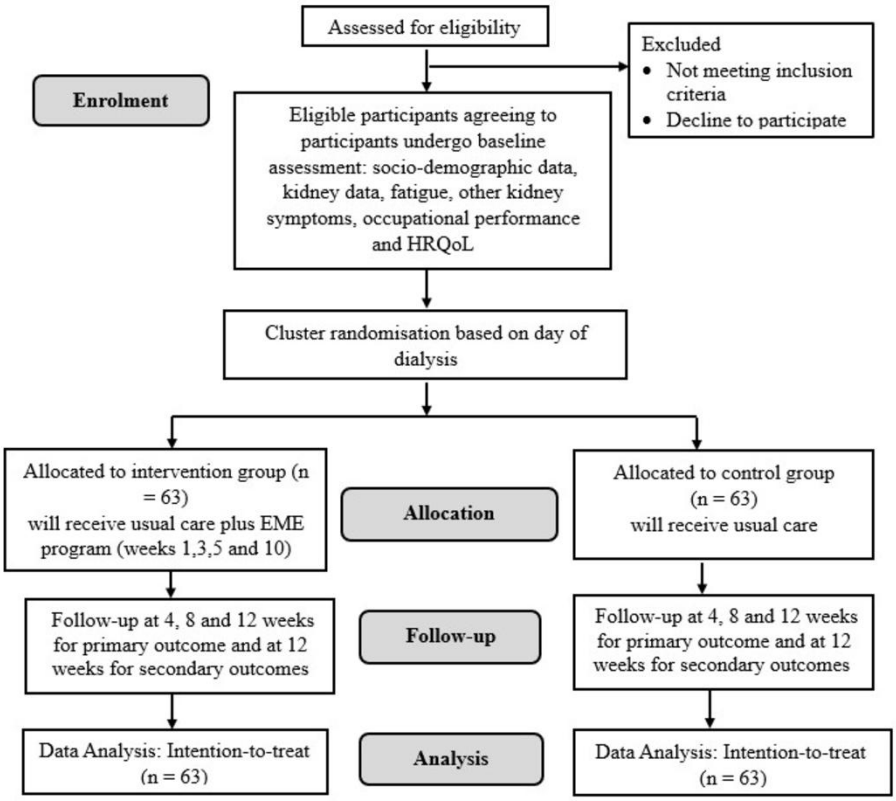

Figure 1
CONSORT flow diagram: extension to cluster, reflecting the flow of participants in the study. CONSORT, Consolidated Standards of Reporting Trials; HRQoL, Health-related quality of life; ECE, Energy Conservation Education.

96x89mm (300 x 300 DPI)

Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the SPIRITreporting guidelines, and cite them as:

Chan A-W, Tetzlaff JM, Gøtzsche PC, Altman DG, Mann H, Berlin J, Dickersin K, Hróbjartsson A, Schulz KF, Parulekar WR, Krleža-Jerić K, Laupacis A, Moher D. SPIRIT 2013 Explanation and Elaboration: Guidance for protocols of clinical trials. BMJ. 2013;346:e7586

		Reporting Item	Page Number
Administrative information			
Title	#1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	Title page; full title, page no. 1
Trial registration	#2a	Trial identifier and registry name. If not yet registered,	Abstract; trial

		name of intended registry	registration, page no. 2
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	N/A
Protocol version	#3	Date and version identifier	N/A
Funding	#4	Sources and types of financial, material, and other support	Page 29
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	Page 1 and 29
Roles and responsibilities: sponsor contact information	#5b	Name and contact information for the trial sponsor	N/A
Roles and responsibilities: sponsor and funder	#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	N/A
Roles and responsibilities: committees	#5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and	N/A

		other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	
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	Page 4-6
Background and rationale: choice of comparators	#6b	Explanation for choice of comparators	Page 12
Objectives	#7	Specific objectives or hypotheses	Page 6
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, non-inferiority, exploratory)	Page 7
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	Page 7

		can be obtained	
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)	Page 8
Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	Page 8-12
Interventions: modifications	#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
Interventions: adherance	#11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests)	N/A
Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	N/A
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	Page 12-15

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)	Page 15-16
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	Page 7
Recruitment	#15	Strategies for achieving adequate participant enrolment to reach target sample size	Page 16
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	Page 16
Allocation concealment mechanism	#16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to	Page 16

		conceal the sequence until interventions are assigned	
Allocation: implementation	#16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	Page 16
Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	Page 17
Blinding (masking): emergency unblinding	#17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	Page 17
Methods: Data collection, management, and analysis			
Data collection plan	#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	Page 17
Data collection plan: retention	#18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be	Page 16

		collected for participants who discontinue or deviate from intervention protocols	
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	Page 17
Statistics: outcomes	#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	Page 17-18
Statistics: additional analyses	#20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	N/A
Statistics: analysis population and missing data	#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)	Page 18
Methods: Monitoring			
Data monitoring: formal committee	#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	N/A

		protocol. Alternatively, an explanation of why a DMC is not needed	
Data monitoring: interim analysis	#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	Page 18
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	Page 18

		potential trial participants or authorised surrogates, and how (see Item 32)	
Consent or assent: ancillary studies	#26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	Page 18
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	Page 19
Declaration of interests	#28	Financial and other competing interests for principal investigators for the overall trial and each study site	Page 29
Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	N/A
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: trial results	#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	Page 18

Dissemination policy: authorship	#31b	Authorship eligibility guidelines and any intended use of professional writers	N/A
Dissemination policy: reproducible research	#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	N/A
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	N/A

Notes:

- 1: Title page; full title, page no. 1
- 2a: Abstract; trial registration, page no. 2
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