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A Pilot Randomized Controlled Trial of an Energy Management Program for Adults on Chronic Hemodialysis: The Fatigue-HD Study

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Trial Registration: NCT03825770; clinicaltrials.gov

Abstract

Background: Identifying interventions to reduce fatigue and improve life participation are top research priorities of patients on chronic hemodialysis. We aimed to determine the feasibility and value of conducting a randomized controlled trial of an energy management program for people on chronic hemodialysis.

Methods: We conducted a parallel-arm, 1:1, blinded, pilot randomized controlled trial. Participants were on chronic hemodialysis and reported fatigue on the Fatigue Severity Scale. Participants were randomized to an attention control (general disease self-management education) or the Personal Energy Planning (PEP) program, a tailored, web-supported 7-9 week energy management program. Eligibility, recruitment and attrition rates were recorded, and standardized intervention effects were calculated for several fatigue and life participation questionnaires at immediate post-intervention and 12 weeks post-intervention.

Results: 159 of 253 screened patients were eligible to be approached. 42 (26%) had fatigue, were interested and consented to participate, of whom 30 met eligibility criteria and were randomized (mean age 62.4 (±14.7), 60% male). Twenty-two enrolled participants (73%) completed all study procedures. Medium-sized intervention effects were observed on the COPM-Performance Scale, global life participation scale, and global life participation satisfaction scale at immediate post-intervention follow-up, compared to control. At 12-week follow-up, large and very large intervention effects were observed on the COPM Performance and Satisfaction Scales, respectively.

Conclusion: It is feasible to enroll and follow patients on hemodialysis in a randomized controlled trial of an energy management intervention. As the intervention was associated with improved life participation on some measures, a larger trial is justified.

Keywords: Fatigue, life participation, chronic kidney disease, dialysis, energy management

Article Summary:

- Fatigue and its impact on life participation have been identified as top concerns of patients on chronic hemodialysis
- Feasible and evidence-based interventions to address these outcomes in the chronic hemodialysis population are currently limited
- This study suggests it is feasible to enroll and follow patients on hemodialysis in a randomized controlled trial of an energy management intervention
- Results also suggest a potential impact of energy management education on life participation, which suggests a randomized trial would be of value

Strengths and Limitations:

- We developed the study protocol using the SPIRIT guidelines for a pilot RCT, and used a standardized intervention training protocol to maximize treatment fidelity across program administrators
- We used randomization, participant blinding and an active control group to control for bias
- Required proficiency in English means results might not be generalizable to non-English speaking populations

- Unequal attrition rates between the intervention and control groups limits the conclusions that can be drawn about program efficacy from this pilot study, underscoring the need for further research to confirm these preliminary findings

Introduction

Kidney failure is associated with a variety of symptoms, including pain, nausea, and insomnia, that can affect quality of life[1,2]. One of the most challenging symptoms, chronic fatigue[3], is experienced by an estimated 70% of the kidney failure population on chronic hemodialysis [1]. Fatigue can negatively affect various aspects of well-being in people with kidney failure, including mood, motivation, and quality of life[4,5]. However, its negative impact on their ability to participate in valued life activities (ie., life participation) has been identified as their top priority for research and intervention[5]. People on hemodialysis have described limitations in their ability to perform valued activities, such as work, socializing, and household management, because of fatigue [4–6]. They have indicated that the ability to participate in life activities should be a key indicator of treatment effectiveness[5]. However, evidence-based treatments to reduce fatigue or mitigate its impact on life participation are limited for this population. There are a complex and poorly-understood range of factors that contribute to kidney disease fatigue, including anemia, chronic inflammation, malnutrition, and depression[7], which limits efficacious treatments. Erythropoeitin stimulating agents (ESAs) and exercise training are currently the primary evidence-based approaches for treating fatigue in this population[8,9]; however, ESAs are already used in a large proportion of patients, and exercise training is challenging to promote in this patient group[10,11]. There is therefore a need to explore alternative approaches that can help people with kidney disease fatigue participate in valued life activities.

Energy management education (EME) aims to improve life participation in people with fatigue by providing strategies to conserve or reallocate energy during routine daily activities[12]. Energy management strategies can include prioritizing, changing body postures, organizing the home environment, or using assistive tools (eg. mobility aids, long-handled reachers)[13]. The Personal

Energy Planning (PEP) program is an energy management program designed to improve life participation in the kidney failure population, by helping patients identify energy management strategies that target individual life participation goals[14]. Proof-of-concept evidence suggests the Personal Energy Planning (PEP) program might be associated with improvements in life participation and/or fatigue in dialysis patients[15], justifying the need for further evaluation with a randomized controlled trial. However, recruitment for randomized trials can be challenging in the kidney failure population[16], in part due to a reluctance among dialysis patients to participate in research studies that require extra study-related activities or visits[17].

We designed a randomized controlled trial of the "PEP" program[18] that attempts to minimize study burden by using simple communication materials (eg. a brochure-style consent form); brief questionnaires; concise intervention sessions; and a flexibility around missed or delayed treatment sessions. However, the feasibility of recruiting and retaining participants for a trial remains unknown. More information is also needed about how the "PEP" program impacts various facets of life participation and fatigue, to inform the choice of a primary outcome measure and aid power calculations for a randomized controlled trial.

The primary objective of our pilot trial was to estimate the proportion of patients on chronic hemodialysis that met eligibility criteria, agreed to participate, and completed all study procedures for a randomized controlled trial of the "PEP" energy management education program. Our secondary objective was to estimate the effects of the program on various facets of fatigue and life participation, to ensure a trial will be adequately powered and will use the most appropriate primary outcome measure.

Methods

Study design

We conducted a multi-site, parallel group, 1:1, pilot randomized controlled trial (www.clinicaltrials.gov; NCT03825770). We randomized 30 participants on chronic hemodialysis to undergo the PEP energy management program, or an active control (general self-management support).

Ethics Approval

This pilot trial adhered to the principles of the Declaration of Helsinki and was approved by the Conjoined Health Research Ethics Board at the University of Calgary (#18-1657).

Participants

We recruited participants on chronic hemodialysis therapy at six hemodialysis units from February 1, 2019 to August 27, 2019. We sought patients aged ≥18 years who were undergoing hemodialysis for ≥3 months at time of recruitment; were clinically and cognitively stable (able to provide informed consent); and scored an avg. of ≥4 on items 5, 7 , 8 and 9 from the Fatigue Severity Scale[19] (ie., items that assess the impact of fatigue on life participation). We excluded patients if they had a plan in place to discontinue in-center hemodialysis within 6 months of recruitment; if they had inadequate written and verbal English comprehension for study activities; if they resided in a long-term care facility; or, if they had a visual impairment that would preclude them from engaging with study materials.

We approached patients identified by clinical staff as being clinically and cognitively stable and English-speaking, to assess their interest in the study. Interested patients provided written

informed consent before we conducted full eligibility screening. We then enrolled and randomized eligible and consenting patients into the study.

Randomization and blinding

We allocated participants equally (1:1) to intervention or control, using a computer-generated random number sequence. We used permuted blocked randomization, with block sizes of 2-6, stratified by dialysis unit. We concealed allocation by having a research manager not otherwise involved with the study, provide treatment allocation to study coordinators over the phone. Study participants were blinded to their treatment status (intervention or active control). It was not feasible to blind study coordinators, given the extensive training they received to learn to administer the intervention compared to the control.

Intervention: The "PEP" Program

Participants randomized to the treatment arm completed the tailored, 7-9 week PEP program (Table 1), teaching them how to use energy management strategies (e.g., simplifying tasks, pacing, using assistive devices, organizing home environments) to improve participation in three self-selected life activities. Study coordinators received in-person training in the treatment and control protocols from a trained occupational therapist prior to administering the intervention. They were also provided with a written guidebook for administering the treatment and control conditions. Study coordinators monitored and encouraged participant adherence to the treatment protocol during weekly visits. Missed or incomplete intervention sessions were documented and addressed as outlined in the study protocol[18].

Control: General information about kidney disease

Participants randomized to the control arm reviewed general information about kidney disease management (eg. blood pressure management; diet; communicating with healthcare team) from the Kidney School online learning modules during six to eight 1:1 sessions with a trained study nurse coordinator. Sessions took place while participants were undergoing hemodialysis.

Data collection

Trained study coordinators collected baseline demographic and clinical data on participants at the time of the first study visit, through chart review and/or participant interview. The study coordinators tracked the number of screened patients who met study eligibility criteria, consented to participate, and completed all study procedures (intervention and assessment sessions), using study logs. The study coordinators administered a series of self-reported questionnaires measuring life participation and fatigue (Table 2), at three timepoints:

1. Pre-intervention baseline;
2. One week after the PEP program was completed;
3. 12 weeks after the PEP program was completed

Participants completed study questionnaires during their hemodialysis sessions.

Statistical analyses

We calculated the proportion of patients on hemodialysis meeting each of the feasibility endpoints (study eligibility, enrolment and completion), with accompanying 95% confidence intervals. We reported participant demographic and clinical data as means and standard deviations for continuous parametric data; medians and interquartile ranges for continuous nonparametric data; and frequencies and percentages for categorical data. We then calculated simple and standardized treatment effect sizes for each life participation and fatigue outcome

measure, at both the immediate post-intervention and twelve weeks post-intervention timepoints. We used the Cohen's D statistic to calculate standardized effect sizes, and categorized effect size estimates as very small (0.01-0.20), small (0.2-0.49), medium (0.5-0.79), large (0.8-1.19), or very large (>1.20). Missing follow-up data were addressed using pairwise deletion.

Post-hoc sensitivity analyses were performed that assumed best-case scenario for missing data (ie. the median intervention effect was imputed for missing intervention values, and the median control effect was imputed for missing control values), and worst-case scenario (ie. the median intervention effect was imputed for missing control values, and the median control effect was imputed for missing intervention values).

Sample size

We originally chose a sample size of 40 patients for the pilot trial. This was based on recommendations for optimal pilot study sample sizes[20], an expected participant pool of 425 patients, and our anticipated eligibility and recruitment rates. The target sample size was subsequently reduced to 30 due to an inability of our study team to follow patients on evening dialysis shifts, which reduced our potential participant pool from 425 to 253 patients.

Patient and public involvement

The study intervention was developed based on results of patient engagement research which suggested a need to further investigate fatigue in kidney disease. Two patients were involved in the development of the intervention through a series of individual interviews that informed program refinement. Two patients were consulted about the acceptability of the active control used in this study. A patient partner reviewed the manuscript and provided feedback about the discussion and interpretation of results.

Results

Feasibility

We screened all patients (n=253) undergoing daytime chronic hemodialysis at six dialysis centers between February and August 2019 for preliminary eligibility ie. (no language barrier, clinically and cognitively stable) (Figure 1). All 159 patients who met preliminary eligibility (63% (95% CI 57, 69%)) were approached. 42 patients (26% (95% CI 20%, 34%)) reported fatigue, were interested in participating, and provided consent. Of those, 30 patients (71% (95% CI 55%, 84%)) met full study eligibility criteria and were enrolled and randomized. In total, 30 of 159 clinically stable and English-speaking patients (19%, 95% CI 13%, 25%) were enrolled in the study.

22 of 30 enrolled patients (73% (95% CI 54%, 88%)) completed all study procedures: 8 in the intervention group, and 14 in the control group. Reasons for study discontinuation in the intervention group included: hospitalization or illness due to nephrectomy (n=1), hypoxia (n=1), neurological symptoms (n=1), or unknown reason (n=1); low blood pressure during dialysis (n=1); switching dialysis modalities (n=1); and kidney transplantation (n=1). The reason for discontinuation in the control group was hospitalization due to unknown reason (n=1).

Participant characteristics

Baseline characteristics of participants are described in Table 3. The mean age of participants was 62.4 (SD = 14.7), 60% were male, and 50% had diabetes. Participants had been on dialysis for a median of 3.6 years (IQR 1.8, 7.3), and 77% were living independently at baseline. Thirty percent of participants screened positively for cognitive impairment, and 40% screened

positively for depression. Participant characteristics were similar across treatment and control groups (Table 3).

Effect size estimates

We observed a large standardized intervention effect at the immediate post-intervention follow-up assessment on the COPM-Performance Scale (Cohen's D = .64; moderate effect), compared to control. At immediate post-intervention, participants in the intervention group (n=10) reported a clinically meaningful improvement (≥2 points) in 40% of their life participation goals according to the COPM-Performance Scale, compared to 21% in the active control group (n=14) (Figure 2). We also observed moderate intervention effects on the Fatigue Management Questionnaire's Global Life Participation Scale (Cohen's D = .52), Global Life Participation Satisfaction Scale (Cohen's D = .52), and Self-Efficacy Scale (Cohen's D = .51). The remainder of fatigue and life participation measures detected either small intervention effects, or no effects, at immediate post-intervention follow-up compared to control (Table 4).

At 12-weeks post-intervention, we observed large and very large effects on the COPM-Performance Scale (Cohen's D = .94) and COPM-Satisfaction Scale (Cohen's D = 1.42) in the intervention group (n=8), respectively, compared to control (n=14) (Table 4). Participants in the intervention group reported a clinically meaningful improvement (≥2 points) in 64% of their life participation goals according to the COPM-Performance Scale at the 12 week post-intervention timepoint, compared to 24% in the active control group (Figure 2). We found minimal to no effects associated with the intervention on the remainder of fatigue or life participation measures at the 12-week post-intervention follow-up, compared to control. Results of the sensitivity analysis, assuming best-case and worst-case scenarios for missing data, are included in Appendix 1.

Discussion

In this pilot study, we assessed the feasibility of recruiting and retaining patients on chronic hemodialysis with fatigue for a randomized controlled trial of an energy management program, and the potential impact of such a program. Although previous proof-of-principle evidence[15] suggested a randomized controlled trial was warranted, the proportion of participants who would commit to completing study activities (eg. intervention sessions, outcome questionnaires) for a trial was unknown. Furthermore, the impact of the "PEP" program on various facets of life participation and fatigue compared to a control group remained unclear. We were able to recruit ~25% of clinically stable and English-speaking hemodialysis patients into this pilot randomized controlled trial, and retain 70% of enrolled participants for the duration of the trial, which met our pre-trial expectations for study participation[18]. Although fatigue did not appear to be affected by the PEP program, the program was associated with medium to large-sized effect on personalized life participation at both short-term and medium-term follow-up, compared to an attention control condition. Collectively, these results suggest that a randomized controlled trial of the PEP program would be feasible, and is warranted.

Our recruitment and retainment results suggest that, despite the added responsibilities of filling out study questionnaires and completing the intervention or control program, the study was acceptable to a substantial proportion of our target population. We note that although only 25% of all stable and English-speaking hemodialysis patients consented to participate, only 50-70% of them likely had fatigue, based on existing estimates of fatigue prevalence[1]; thus, we estimate that approximately half of eligible patients with fatigue in fact agreed to the study. This suggests that study burden was not an insurmountable barrier to recruitment. Although the dropout rate was

higher in the intervention arm than the control (43 vs. 13%), our documented reasons for study withdrawals were unrelated to the intervention, and were rather due to the general medical complexity of this patient population. We therefore assume that with a larger sample of patients, the attrition rate would balance between the two groups. Our overall attrition rate of 30% is not unexpected for the dialysis population over the course of a five-month study, given that they typically experience high rates of acute medical events and hospitalizations[21,22]. We attribute the general acceptability of the intervention to the use of study materials that were user-friendly (eg. a brochure-style consent form); brief questionnaires to assess target outcomes; and a flexible protocol for missed treatment sessions. Acceptability could be further increased in a full-scale trial by reducing the number of questionnaires used to assess life participation and fatigue, particularly now that the pilot trial has provided clarity about the best measures for assessing these outcomes.

The finding that the PEP program was associated with improvements in life participation, compared to control, is important because this outcome directly aligns with patient priorities[3,5]. Patients on hemodialysis with fatigue view life participation as "the fundamental goal of treatment, because it symbolizes some indicator of being able to live a life without being confined by the disease"[5]. Although fatigue was not directly impacted by the intervention, our results suggest that energy management strategies developed during the intervention might have helped participants to accomplish their day-to-day goals more effectively by working around fatigue. This improvement in personalized life participation we observed is relatively unique within the energy management literature[23]. Our intervention incorporated a number of novel features to more directly target life participation, compared to other energy management interventions, in accordance with the priorities of hemodialysis patients. For example, we used

personalized goal-setting to ensure interventions were tailored to specific patients' needs, and a problem-solving training approach to facilitate patient independence at solving their own life participation challenges. Our findings support the potential efficacy of these features, although it is important to note the potential impact of unequal attrition between the intervention and control groups on our pilot results. This further emphasizes the need for a full-scale trial to more conclusively establish program effectiveness.

With respect to outcome measures, we found that the Canadian Occupational Performance Measure[24] detected the strongest intervention effects compared to other life participation and fatigue measures. The COPM is the only measure we used that assesses life participation in three patient-chosen activities, rather than a generic set of life activities. Although the COPM has not been formally validated in the kidney failure population, it has strong validity, reliability and responsiveness data from multiple other clinical populations and age groups[25]. It also aligns with patient preferences for a measure of life participation that is individualized [5]. Collectively, these findings suggest the COPM is the best choice for a primary outcome for an RCT of the "PEP" program. Estimates based on our pilot results suggest data on 36 participants would be needed to detect a clinically meaningful change of >2 points on the COPM-performance scale in a randomized controlled trial, with significance set at 80% power and p=0.05. Based on our rates of screened-to-enrolled patients, the participant screening pool would need to include 415 patients on hemodialysis to achieve this sample size.

Study Limitations

We excluded non-English speaking patients from the study, limiting its generalizability to non-English-speaking kidney failure populations. Positive findings about the PEP program might,

however, justify developing program materials in the future that are accessible to a wider range of renal patients. We were also unable to blind study coordinators to participants' treatment allocation, which might have unduly affected their approach to treatment. The infeasibility of blinding is a well-recognized limitation of trials that study psychosocial or behavioural interventions, because of the challenges of identifying and implementing an appropriate control. Finally, unequal attrition rates between the intervention and control groups limits the conclusions that can be drawn about program efficacy from this pilot study, and underscores the need for further research using a larger sample of patients to confirm our preliminary results.

Conclusions

The PEP energy management program appears to be acceptable to patients, and might lead to improvements in life participation. Further investigation in an adequately powered randomized controlled trial is warranted.

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None.

Conflict of Interest Statement

The authors have no conflicts of interest to disclose. Results presented in this paper have not been published previously in whole or part, except in abstract format.

Data Sharing Statement

Data from the study can be made available upon reasonable request to the corresponding author.

Authors' Contributions

JF led the design, coordination, analysis and authorship of the study and manuscript. BH provided advice and mentorship on all aspects of the study. CT, BM and MD helped with the development of the participant identification plan, and provided advice on other key study issues. PR and ME contributed feedback on trial design. All authors assisted with the interpretation and presentation of results for publication. NV provided review and perspective from a patient's point of view.

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Table 1: Description of the Personal Energy Planning ("PEP") Program

Program Section	Description
Part 1: Computer modules	• Participants complete 3 computer modules over 3 sessions (~20-30 mins each) that explain the basic principles of energy management • Modules are completed on laptops during hemodialysis sessions, with support for module completion provided by study coordinators
Part 2: Individualized problem-solving	• Participants work 1:1 with a trained administrator over 4-6 sessions (~30 mins each) to develop energy management strategies for 3 life participation goals • Energy management strategies are developed using a metacognitive problem-solving process called "***Goal-Plan-Do-Check***": 1. Set a life participation ***goal*** 2. Analyze current energy expenditure patterns to come up with a ***plan*** to conserve energy for the goal; 3. ***Do*** the plan; 4. ***Check*** to see if it worked, and what aspects of the plan should be revised • This process continues until an effective plan is found for each goal, or the program maximum of 9 weekly treatment sessions is reached • Study coordinators use ***guided discovery teaching*** to encourage patient independence in working through the Goal-Plan-Do-Check process

Table 2: Life Participation and Fatigue Outcome Measures

Outcome	Measure	Description
Life participation	*Canadian Occupational Performance Measure*[24] *– Performance Subscale (COPM-P)*	Asks individuals to rate, on a 10-point Likert scale, his/her performance in three self-selected priority activities of everyday living. The COPM has been found to be a valid, reliable, clinically useful and responsive measure of occupational performance in multiple chronic disease populations[25].
	Canadian Occupational Performance Measure[24] *– Satisfaction Subscale (COPM-S)*	Asks individuals to rate, on a 10-point Likert scale, their satisfaction with their performance in three self-selected priority activities of everyday living.
	Reintegration to Normal Living Index[26] *(RNLI)*	Assesses the degree to which individuals who have experienced traumatic or incapacitating illness achieve reintegration into normal activities, using 11 declarative statements accompanied by a visual analogue scale. The RNLI has strong validity and reliability in multiple chronic disease populations[27].
	Fatigue Management Questionnaire (FMQ)	Asks individuals to rate various aspects of their fatigue management (e.g., overall impact on life participation; satisfaction; self-efficacy) on five Likert-scale questions. The FMQ was created for this study to assess life participation and self-efficacy pertaining specifically to fatigue management.
Fatigue	*Fatigue Severity Scale*[19] *(FSS)*	Includes 9 items that ask individuals to rate, on a Likert scale from 1-7, the severity of their fatigue and its impact on their life during the past week. The FSS is a valid, reliable and responsive measure[28] that has been used in the dialysis population.
	Modified Fatigue Impact Scale[29] *(MFIS)*	A 21-item Likert-based scale that assesses the effects of fatigue on physical, cognitive, and psychosocial functioning. The MFIS is frequently used as a primary outcome measure in energy management education studies.
	SONG-HD Fatigue[5]	Assesses the severity of fatigue, and its impact on daily living, in people on chronic hemodialysis using 3 Likert-style questions. The measure was developed in conjunction with kidney failure patients and other key informants, and is currently undergoing psychometric validation.

Table 3: Baseline Characteristics of Participants

	All Participants (n=30)	Control (n = 15)	Intervention (n = 15)
Age (yrs) (mean, SD)	62.4 (14.7)	64.8 (14.4)	60.0 (15.1)
Male	18 (60)	10 (67)	8 (53)
Residence			
Independent living	27 (90)	14 (93)	13 (86)
Retirement/supported living	3 (10)	1	2
Lives alone	20 (67)	6 (40)	4 (27)
Married	17 (57)	10 (67)	7 (46)
Employed	4 (27)	0 (0)	4 (27)
Education			
No high school diploma	3 (10)	2 (13)	1 (7)
High school diploma	12 (40)	6 (40)	6 (40)
College/trade school	10 (33)	5 (33)	5 (33)
University degree	4 (13)	2 (13)	2 (13)
Graduate/professional degree	1 (3)	0 (0)	1 (7)
Uses computer/tablet/phone	27 (3)	14 (93)	13 (86)
Dialysis vintage (yrs) (Median, IQR)	3.6 (1.8, 7.3)	2.6 (1.7, 6.0)	4.0 (1.7, 9.5)
Comorbidities			
Diabetes	15 (50)	9 (60)	6 (40)
Depression	9 (30)	3 (20)	6 (40)
Coronary artery disease	10 (33)	6 (40)	4 (27)
Congestive heart failure	8 (27)	3 (20)	5 (33)
Cerebrovascular disease	3 (10)	3 (12)	0 (0)
Alzheimer's disease	1 (3)	0 (0)	1 (7)
Multiple Sclerosis	1 (3)	0 (0)	1 (7)
Chronic Obstructive Pulmonary Disease	1 (3)	1 (7)	0 (0)
Cancer	7 (23)	5 (33)	2 (13)
Baseline serum hemoglobin (g/L) (Mean, SD)	101.6 (18.7)	107.7 (8.7)	95.0 (23.3)
Baseline serum albumin (g/L) (Mean, SD)	35.0 (10.8)	33.0 (3.9)	37.2 (15.0)
Activities of daily living dependence	7 (23)	2 (13)	5 (33)
MiniCog impaired	9 (30)	4 (27)	5 (33)
Personal Health Questionnaire-2 impaired	12 (40)	5 (33)	7 (47)

*Data are expressed as n(%) unless otherwise specified

Table 4: Changes in Fatigue and Life Participation Ratings in the Intervention versus Control Groups

Domain	Measure	Study Arm	Baseline	Immediate Post-Treatment Follow-up			12 Weeks Post-Treatment Follow-up		
			Median score IQR)	*Median score (IQR)*	*Median change from baseline (IQR)*	*Cohen's D effect size estimate*	*Median score (IQR)*	*Median change from baseline (IQR)*	*Cohen's D effect size estimate*
Life Participation	***COPM-P***	*Control*	4.3 (3.7, 7.7)	4.7 (2.5, 7.8)	-0.3 (-1.8, +1.0)	0.64 Medium	4.3 (1.7, 5.3)	+0.3 (-2.0, +1.3)	0.94 Large
		Treatment	4.7 (4.0, 6.7)	5.3 (4.7, 6.7)	+1.3 (+0.3, +1.7)		6.8 (5.4, 7.6)	+1.9 (0.0, +3.5)	
	COPM-S	*Control*	4.0 (2.3, 8.0)	6.0 (3.0, 8.0)	+0.3 (-0.8, +2.0)	0.13 Very small	4.0 (1.0, 5.0)	0.0 (-2.0, +0.7)	1.42 Very large
		Treatment	4.0 (3.3, 5.3)	5.3 (3.8, 6.5)	+0.7 (-0.3, +1.8)		6.7 (4.9, 7.5)	+1.8 (+1.4, +3.1)	
	FMQ-Global LP	*Control*	6.0 (4.7, 7.0)	6.5 (4.8, 8.1)	0.0 (-1.4, +2.4)	0.52 Medium	5.6 (3.0, 8.0)	-0.4 (-2.0, +1.0)	0.17 Very small
		Treatment	4.7 (3, 6.3)	6.3 (5.8, 7.4)	+1.8 (+.5, +2.1)		5 (2.25, 5.75)	+1.0 (-2.0, +4.0)	
	FMQ-Global LPS	*Control*	5.0 (4.0, 8)	7.5 (4.5, 9.0)	+1.0 (-1.3, +3.3)	0.52 Medium	6.0 (4.0, 7.5)	0.0 (-2.0, +1.0)	0.17 Very small
		Treatment	4.0 (2.0, 5.0)	7.0 (4.5, 8.3)	+4.0 (+.5, +5.3)		4.5 (2.25, 5.75)	0.0 (-2.0, +4.0)	
	RNLI	*Control*	78 (51, 88)	81.0 (58.0, 94.0)	-1.0 (-5.0, +15.0)	Favours control	83 (60, 101)	+5.5 (-7.5, +24.0)	Favours control
		Treatment	71 (56, 83)	61.5 (51.5, 78.8)	-3.0 (-10.0, +11.3)		61.5 (50.5, 78.5)	-1.0 (-20.0, +12.8)	
Fatigue	***FSS***	*Control*	5.0 (4.3, 6.1)	4.3 (3.8, 5.9)	-0.3 (-1.1, +1.0)	0.37 Small	4.0 (2.7, 4.9)	-1.1 (-1.8, -3.5)	Favours control
		Treatment	6.0 (5.6, 6.3)	5.3 (4.4, 6.0)	-0.6 (-1.9, +0.2)		5.2 (4.1, 6.0)	-0.8 (-1.0, 0.0)	
	MFIS	*Control*	50.0 (38, 55)	39.5 (29.5, 49.3)	-6.5 (-23, +.5)	Favours control	29 (22.5, 49.5)	-12.0 (-20.0, -6.5)	Favours control
		Treatment	52.0 (45, 59)	48 (38.5, 51.5)	-8.0 (-13, +1.5)		47.5 (39.0, 65.0)	-1.0 (-10.0, +12.0)	
	Song-HD Fatigue	*Control*	6.0 (4.0,7.0)	4.5 (3.3, 7.0)	0.0 (-2.0, 0.0)	0.16 Very small	5.0 (3.25, 6.0)	-1.0 (-2.0, +1.0)	Favours control
		Treatment	6.0 (3.8, 9)	5.0 (3.8, 6.0)	-1.0 (-4.5, +2.5)		6.0 (5.0, 6.0)	0.0 (-1.0, +3.0)	
	Self-Efficacy	*Control*	5.0 (5.0, 8.0)	6.2 (5.0, 9.0)	+0.2 (-1.0, +3.3)	0.51 Medium	8.0 (4.5, 9.0)	0.0 (-1.0, +3.0)	0.02 Very small
		Treatment	4.0 (2.0, 5.0)	6.5 (4.3, 7.3)	+3.0 (-0.0, +3.0)		5.0 (3.0, 5.0)	+0.5 (-1.5, +3.0)	

Legend: FSS = Fatigue Severity Scale; MFIS = Modified Fatigue Impact Scale; Global LP = Global Life participation; Global LP-S = Global Life Participation Satisfaction; RNLI = Reintegration to Normal Living Index; COPM-P = Canadian Occupational performance Measure – Performance Scale; COPM-S = Canadian Occupational Performance Measure – Satisfaction Scale; SONG-HD Fatigue = Standardized Outcomes in Nephrology - Hemodialysis Fatigue

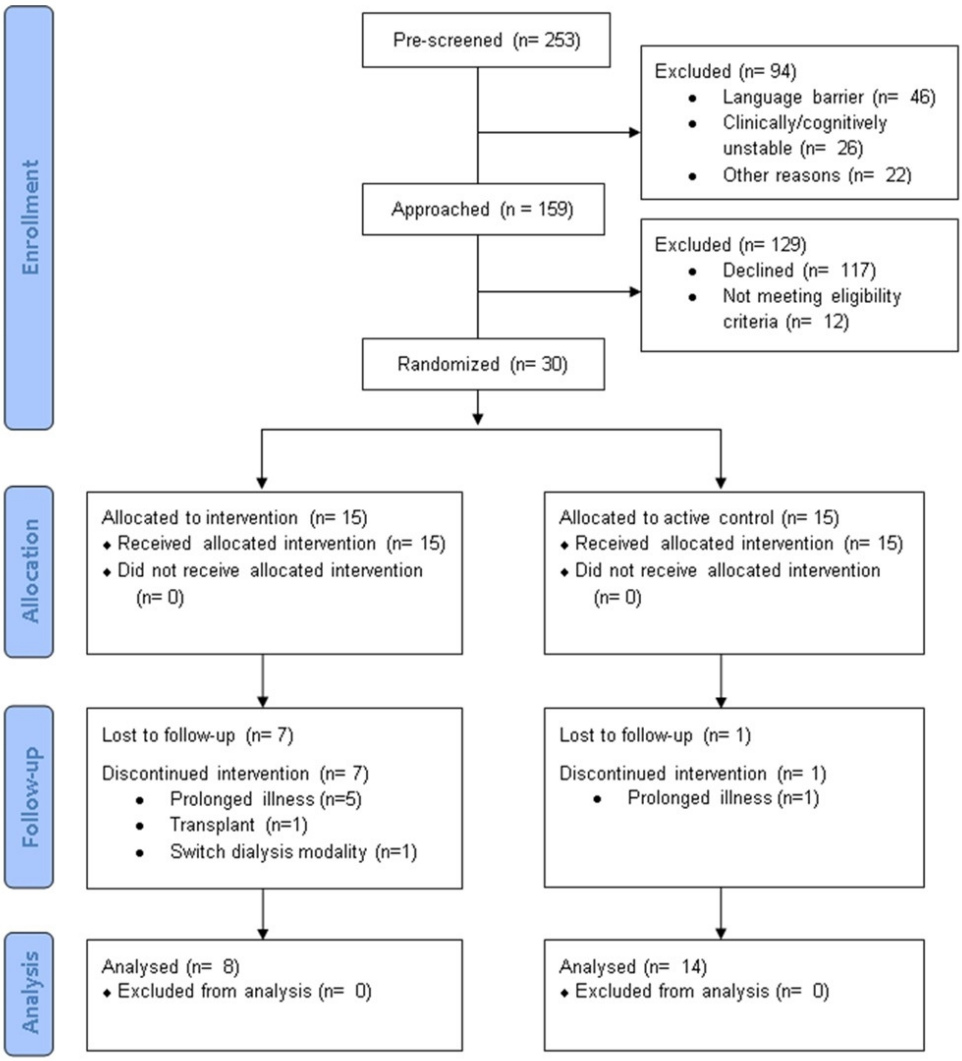
*Values expressed are medians (interquartile ranges)

Figure Legends

Figure 1: CONSORT Participant Flow Diagram

Figure 2: Proportion of Patients Achieving Life Participation Goals in Intervention vs. Control

Note: "Improved" means increase of ≥2 points (established MCID) on COPM performance subscale; "no change" means no clinically significant change; "declined" means decrease of ≥2 points on COPM performance subscale



CONSORT Participant Flow Diagram

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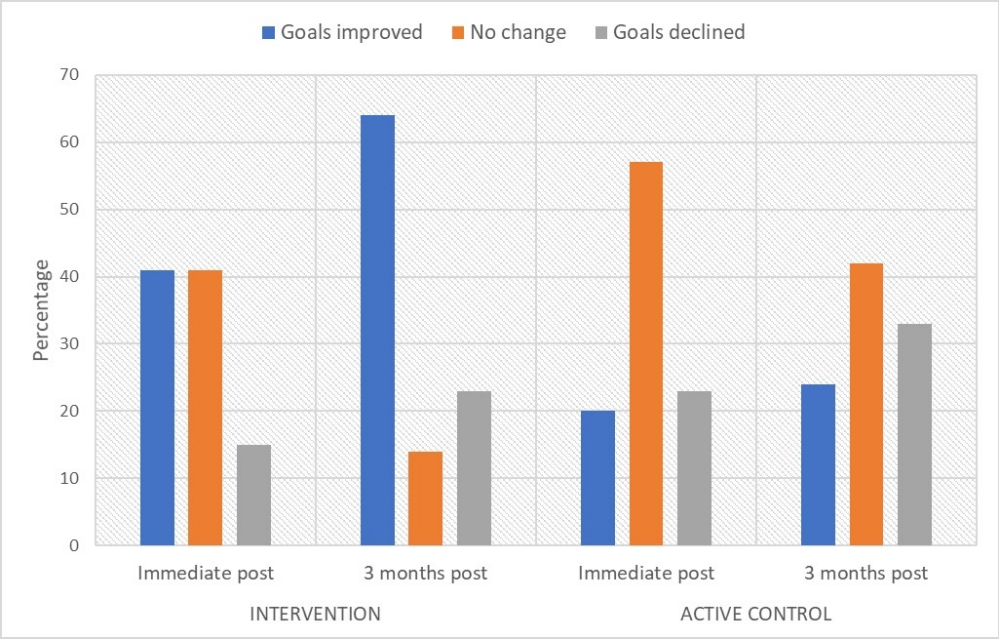

Proportion of Patients Achieving Life Participation Goals in Intervention vs. Control

173x110mm (150 x 150 DPI)

Appendix 1: Cohen's D Effect Size Estimates, Assuming Best-Case and Worst-Case Scenarios for Missing Data

	Immediate Post-Intervention		12 Weeks Post-Intervention	
	Worst-case scenario	**Best-case scenario**	**Worst-case scenario**	**Best-case scenario**
FSS	.28 Small	.36 Small	Favours control	Favours control
MFIS	Favours control	Favours control	Favours control	Favours control
Global LP	.30 Small	.74 Medium	.42 Small	.48 Small
Global LP-S	.32 Small	.67 Medium	.07 Very small	.08 Very small
Self-Efficacy	.43 Small	.71 Medium	Favours control	Favours control
RNLI	Favours control	Favours control	Favours control	Favours control
COPM-P	.25 Small	.83 Large	.30 Small	1.02 Large
COPM-S	.02 Very small	.14 Very small	.52 Medium	1.65 Very large
SONG-HD	No difference	.25 Small	Favours control	Favours control

Legend: FSS = Fatigue Severity Scale; MFIS = Modified Fatigue Impact Scale; Global LP = Global Life participation; Global LP-S = Global Life Participation Satisfaction; RNLI = Reintegration to Normal Living Index; COPM-P = Canadian Occupational performance Measure – Performance Scale; COPM-S = Canadian Occupational Performance Measure – Satisfaction Scale; SONG-HD Fatigue = Standardized Outcomes in Nephrology - Hemodialysis Fatigue

Adapted CONSORT Checklist for Clinical Trials

Section/Topic	Checklist Item	Response
Title	Identified as a randomized trial in the title.	Yes
Background	Specific objectives or hypotheses clearly stated.	Yes
Trial Design	Trial design *(such as parallel, factorial)* including allocation ratio.	Yes
	Important changes to methods after trial commencement *(such as eligibility criteria)*, with reasons.	NA
Participants	Eligibility criteria for participants.	Yes
	Settings and locations where the data were collected.	Yes
Interventions	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered.	Yes
Outcomes	Completely defined per-specified primary and secondary outcome measures, including how and when they were assessed.	Yes
	Any changes to trial outcomes after the trial commenced, with reasons.	NA
Sample Size	How sample size was determined.	Yes
	Explanation of any interim analyses and stopping guidelines.	NA
Randomization		
• ***Sequence generation***	Method used to generate the random allocation sequence.	Yes
	Type of randomization; details of any restriction *(such as blocking and block size)*.	Yes
• ***Allocation concealment mechanism***	Mechanism used to implement the random allocation sequence *(such as sequentially numbered containers)*, describing any steps taken to conceal the sequence until interventions were assigned.	Yes
• ***Implementation***	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions.	Yes
Blinding	If done, who was blinded after assignment to interventions *(for example, participants, care providers, those assessing outcomes)*.	Yes
	If relevant, description of the similarity of interventions.	Yes
Statistical Methods	Statistical methods used to compare groups for primary and secondary outcomes.	Yes
	Methods for additional analyses, such as subgroup analyses and adjusted analyses.	Yes
Participant Flow *(a diagram is strongly recommended)*	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analyzed for the primary outcome .	Yes
	For each group, losses and exclusions after randomization, together with reasons.	Yes
Recruitment	Dates defining the periods of recruitment and follow-up.	Yes
	Why the trial ended or was stopped.	NA
Baseline Data	A table showing baseline demographic and clinical characteristics for each group.	Yes
Numbers Analyzed	For each group, number of participants *(denominator)* included in each analysis and whether the analysis was by original assigned groups.	Yes
Outcomes and Estimation	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision *(such as 95% confidence interval)*.	Yes
	For binary outcomes, presentation of both absolute and relative effect sizes.	NA
Ancillary Analyses	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory.	Yes
Harms	All important harms or unintended effects in each group.	NA
Data Sharing	A data sharing statement is included.	Yes

Additional Details:

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A Pilot Randomized Controlled Trial of an Energy Management Program for Adults on Maintenance Hemodialysis: The Fatigue-HD Study

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Trial Registration: NCT03825770; clinicaltrials.gov

Abstract

Background: Identifying interventions to reduce fatigue and improve life participation are top research priorities of people on maintenance hemodialysis.

Objective: Our primary objective was to explore the feasibility of conducting a randomized controlled trial of an energy management program for people on maintenance hemodialysis.

Design: Parallel-arm, 1:1, blinded, pilot randomized controlled trial.

Participants: Participants were recruited from 6 dialysis units in Calgary, Canada. Eligible patients were on maintenance hemodialysis, clinically stable, and reported disabling fatigue on the Fatigue Severity Scale items 5, 7, 8 and 9.

Randomization: Participants were randomized using a computer-generated random number sequence according to permuted blocked randomization, stratified by dialysis unit.

Blinding: Participants were blinded to treatment allocation.

Interventions: Participants received an attention control (general disease self-management education) or the Personal Energy Planning (PEP) program, a tailored, web-supported 7-9 week energy management program.

Outcomes: Eligibility, recruitment and attrition rates were recorded, and standardized intervention effects (Hedge's G) were calculated for fatigue and life participation questionnaires at one week post-intervention and 12 weeks post-intervention.

Results: 159 of 253 screened patients were eligible to be approached. 42 (26%) had fatigue, were interested, and consented to participate, of whom 30 met eligibility criteria and were

randomized (mean age 62.4 (±14.7), 60% male). Twenty-two enrolled participants (73%) completed all study procedures. Medium-sized intervention effects were observed on the Canadian Occupational Performance Measure (COPM)--Performance Scale, global life participation scale, and global life participation satisfaction scale at one week post-intervention follow-up, compared to control. At 12-week follow-up, large and very large intervention effects were observed on the COPM Performance and Satisfaction Scales, respectively.

Conclusion: It is feasible to enroll and follow patients on hemodialysis in a randomized controlled trial of an energy management intervention. As the intervention was associated with improved life participation on some measures, a larger trial is justified.

Keywords: Fatigue, life participation, chronic kidney disease, dialysis, energy management maintenance hemodialysismaintenance hemodialysis

Strengths and Limitations:

- We referenced the SPIRIT guidelines for a pilot RCT throughout the development and writing of the trial protocol, and used a standardized intervention training protocol to maximize treatment fidelity across program administrators
- We used randomization, participant blinding and an active control group to control for bias
- Required proficiency in English means results might not be generalizable to non-English speaking populations
- Unequal attrition rates between the intervention and control groups limits the conclusions that can be drawn about program efficacy from this pilot study, underscoring the need for further research to confirm these preliminary findings

Introduction

Kidney failure is associated with a variety of symptoms, including pain, nausea, and insomnia, that can affect quality of life[1,2]. One of the most challenging symptoms, chronic fatigue[3], is experienced by an estimated 70% of the population with kidney failure on maintenance hemodialysis [1]. Fatigue can negatively affect various aspects of well-being in people with kidney failure, including mood, motivation, and quality of life[4,5]. However, its negative impact on their ability to participate in valued life activities (ie., life participation) has been identified as their top priority for research and intervention[5]. People on hemodialysis have described limitations in their ability to perform valued activities, such as work, socializing, and household management, because of fatigue [4–6]. They have indicated that the ability to participate in life activities should be a key indicator of treatment effectiveness[5]. However, evidence-based treatments to reduce fatigue or mitigate its impact on life participation are limited for this population. There are a complex and poorly-understood range of factors that contribute to kidney disease fatigue, including anemia, chronic inflammation, malnutrition, and depression[7], which limits efficacious treatments. Erythropoeitin stimulating agents (ESAs) and exercise training are currently the primary evidence-based approaches for treating fatigue in this population[8,9]; however, ESAs are already used in a large proportion of patients, and exercise training is challenging to promote in this patient group because of several factors including inadequate staff expertise, competing patient symptoms, and low motivation among patients to participate in exercise[10,11]. There is therefore a need to explore alternative approaches that can help people with kidney disease fatigue participate in valued life activities.

Energy management education (EME) aims to improve life participation in people with fatigue by providing strategies to conserve or reallocate energy during routine daily activities[12]. The

theory underlying energy management is that life participation can be improved in people with chronic fatigue by minimizing the exertional fatigue associated with performing daily activities[12,13]; this exertional fatigue could either be a casual or exacerbating factor in the underlying fatigue and disability experienced in many chronic diseases, including kidney disease. Energy management strategies can include prioritizing, changing body postures, organizing the home environment, or using assistive tools (eg. mobility aids, long-handled reachers)[14]. The Personal Energy Planning (PEP) program is an energy management program designed to improve life participation in people with kidney failure, by helping patients identify energy management strategies that can facilitate their individual life participation goals[15]. Proof-of-concept evidence has suggested the Personal Energy Planning (PEP) program might be associated with improvements in life participation and/or fatigue in dialysis patients[16], justifying the need for further evaluation with a randomized controlled trial. However, recruitment for randomized trials can be challenging in people with kidney failure[17], in part due to a reluctance among dialysis patients to participate in research studies that require extra study-related activities or visits[18]. Furthermore, the acceptability of, and interest in, the energy management approach has never been explored in people on maintenance hemodialysis.

We designed a randomized controlled trial of the "PEP" energy management program[19] that attempts to minimize study burden by using simple communication materials (eg. a brochure-style consent form); brief questionnaires; concise intervention sessions; and a flexibility around missed or delayed treatment sessions. However, the feasibility of recruiting and retaining participants for a trial of an energy management program remains unknown. More information is also needed about how the "PEP" program impacts various facets of life participation and

fatigue, to inform the choice of a primary outcome measure and aid power calculations for a randomized controlled trial.

The primary objective of our pilot trial was to estimate the proportion of patients on maintenance hemodialysis that met eligibility criteria, agreed to participate, and completed all study procedures for a randomized controlled trial of the "PEP" energy management education program. Our secondary objective was to estimate the effects of the program on various facets of fatigue and life participation, to ensure a trial will be adequately powered and will use the most appropriate primary outcome measure.

Methods

Study design

We conducted a multi-site, parallel group, 1:1, pilot randomized controlled trial[19] (www.clinicaltrials.gov; NCT03825770). We randomized 30 participants on maintenance hemodialysis to undergo the PEP energy management program, or an active control (general self-management support).

Ethics Approval

This pilot trial adhered to the principles of the Declaration of Helsinki and was approved by the Conjoined Health Research Ethics Board at the University of Calgary (#18-1657).

Participants

We recruited participants on maintenance hemodialysis therapy at six hemodialysis units from February 1, 2019 to August 27, 2019. We sought patients aged ≥18 years who were undergoing hemodialysis for ≥3 months at time of recruitment; were clinically and cognitively stable (able to provide informed consent); and scored an avg. of ≥4 on items 5, 7 , 8 and 9 from the Fatigue Severity Scale[20] (ie., items that assess the impact of fatigue on life participation). We excluded patients if they had a plan in place to discontinue in-center hemodialysis within 6 months of recruitment; if they had inadequate written and verbal English comprehension for study activities; if they resided in a long-term care facility; or, if they had a visual impairment that would preclude them from engaging with study materials. Original exclusion criteria also included a score of >3 on the PHQ-2 depression tool; however, this was subsequently removed due to interest from patients in participating in the study, and a lack of conclusive evidence that depression would impede study participation or outcomes. Instead, we measured and monitored depression at baseline in all enrolled participants.

We approached patients identified by clinical staff as being clinically and cognitively stable and English-speaking, to assess their interest in the study. Interested patients provided written informed consent before we conducted full eligibility screening. We then enrolled and randomized eligible and consenting patients into the study.

Randomization and blinding

We allocated participants equally (1:1) to intervention or control, using a computer-generated random number sequence. We used permuted blocked randomization, with block sizes of 2-6, stratified by dialysis unit. We concealed allocation by having a research manager not otherwise

involved with the study, provide treatment allocation to study coordinators over the phone. Study participants were blinded to their treatment status (intervention or active control). It was not feasible to blind study coordinators, given the extensive training they received to learn to administer the intervention compared to the control.

Intervention: The "PEP" Program

Participants randomized to the treatment arm completed the tailored, 7-9 week PEP program[14,18] (see Table 1 for further information). The PEP program is a two-part intervention that teaches participants how to use energy management strategies (e.g., simplifying tasks, pacing, using assistive devices, organizing home environments) to improve participation in three self-selected life activities. In the first part of the intervention, participants complete 3 web modules that define and explain the energy management approach, and describe a structured strategy for problem-solving around fatigue. In the second part of the intervention, participants work 1:1 with a study coordinator during 4-6 sessions to apply the principles and strategies from part one, and problem-solve around their fatigue problems to accomplish 3 life participation goals (eg. cook dinner twice per week; garden in the backyard more frequently). The number of individual sessions during this part was determined by individual patient needs and progress.

Study coordinators received in-person training in the treatment and control protocols from a trained occupational therapist prior to administering the intervention. Training consisted of three in-person training sessions, led by an occupational therapist (JF), on the core facilitation skills of the problem-solving method used in PEP (client-chosen goals, guided discovery, global problem-solving strategy, dynamic performance analysis, and energy management strategies). They were also provided with a written guidebook, including suggested scripts to introduce key concepts;

example dialogues between coach and patients; and analysis questions and suggested energy management suggestions for various possible life participation goals. Study coordinators monitored and encouraged participant adherence to the treatment protocol during weekly visits. Missed or incomplete intervention sessions were documented and addressed as outlined in the study protocol[19].

Control: General information about kidney disease

Participants randomized to the control arm reviewed general information about kidney disease management (eg. blood pressure management; diet; communicating with healthcare team) from the Kidney School online learning modules during six to eight 1:1 sessions with a trained study coordinator. Sessions took place while participants were undergoing hemodialysis.

Data collection

Trained study coordinators collected baseline demographic and clinical data on participants at the time of the first study visit, through chart review and/or participant interview. The study coordinators tracked the number of screened patients who met study eligibility criteria, consented to participate, and completed all study procedures (intervention and assessment sessions), using study logs. The study coordinators administered a series of self-reported questionnaires measuring life participation and fatigue (see Table 2 for list of measures and details), at three timepoints:

1. Pre-intervention baseline;
2. One week after the PEP program was completed;
3. 12 weeks after the PEP program was completed

Participants completed study questionnaires during their hemodialysis sessions.

Statistical analyses

We calculated the proportion of patients on hemodialysis meeting each of the feasibility endpoints (study eligibility, enrolment and completion), with accompanying 95% confidence intervals. We reported participant demographic and clinical data as means and standard deviations for continuous parametric data; medians and interquartile ranges for continuous nonparametric data; and frequencies and percentages for categorical data. We then calculated raw and standardized treatment effect sizes for each life participation and fatigue outcome measure, at both the one week post-intervention and twelve weeks post-intervention timepoints. We used the Hedge's G statistic to calculate standardized effect sizes, and categorized effect size estimates as very small (0.01-0.20), small (0.2-0.49), medium (0.5-0.79), large (0.8-1.19), or very large (>1.20)[21]. Missing follow-up data were addressed using pairwise deletion.

Post-hoc sensitivity analyses were performed that assumed best-case scenario for missing data (ie. the median intervention effect was imputed for missing intervention values, and the median control effect was imputed for missing control values), and worst-case scenario (ie. the median intervention effect was imputed for missing control values, and the median control effect was imputed for missing intervention values).

Sample size

We originally chose a sample size of 40 patients for the pilot trial. This was based on recommendations for optimal pilot study sample sizes[22], an expected participant pool of 425 patients, and our anticipated eligibility and recruitment rates. The target sample size was subsequently reduced to 30 due to an inability of our study team to follow patients on evening dialysis shifts, which reduced our potential participant pool from 425 to 253 patients.

Patient and public involvement

The study intervention was developed based on results of patient engagement research which suggested a need to further investigate fatigue in kidney disease. Two patients were involved in the development of the intervention through a series of individual interviews.. Two patients were consulted about the acceptability of the active control used in this study. A patient partner reviewed the manuscript and provided feedback about the discussion and interpretation of results. Patient involvement resulted in refinement and improvement of both the intervention and control conditions, to enhance their acceptability to patients. Our patient partner provided valuable insights about important qualitative information to collect from patients, which was subsequently incorporated into a sub-study involving a follow-up interviews with study participants.

Results

Feasibility

We screened all patients (n=253) undergoing daytime maintenance hemodialysis at six dialysis centers between February and August 2019 for preliminary eligibility ie. (no language barrier, clinically and cognitively stable) (Figure 1). All 159 patients who met preliminary criteria for the study (63% (95% CI 57, 69%)) were approached. 42 patients (26% (95% CI 20%, 34%)) reported fatigue, were interested in participating, and provided consent. Of those, 30 patients (71% (95% CI 55%, 84%)) met full study eligibility criteria and were enrolled and randomized. In total, 30 of 159 clinically stable and English-speaking patients (19%, 95% CI 13%, 25%) were enrolled in the study.

22 of 30 enrolled patients (73% (95% CI 54%, 88%)) completed all study procedures: 8 in the intervention group, and 14 in the control group. Reasons for study discontinuation in the intervention group included: hospitalization or illness due to nephrectomy (n=1), hypoxia (n=1), neurological symptoms (n=1), or unknown reason (n=1); low blood pressure during dialysis (n=1); switching dialysis modalities (n=1); and kidney transplantation (n=1). The reason for discontinuation in the control group was hospitalization due to unknown reason (n=1).

Participant characteristics

Baseline characteristics of participants are described in Table 3. The mean age of participants was 62.4 (SD = 14.7), 60% were male, and 50% had diabetes. Participants had been on dialysis for a median of 3.6 years (IQR 1.8, 7.3), and 77% were living independently at baseline. Thirty percent of participants screened positively for cognitive impairment, and 40% screened positively for depression. Participant characteristics were similar across treatment and control groups (Table 3).

Effect size estimates

We observed a large standardized intervention effect at the one week post-intervention follow-up assessment on the COPM-Performance Scale (Hedge's G = .62; moderate effect), compared to control. At one week post-intervention, participants in the intervention group (n=10) reported a clinically meaningful improvement (≥2 points) in 40% of their life participation goals according to the COPM-Performance Scale, compared to 21% in the active control group (n=14) (Figure 2). We also observed moderate intervention effects on the Fatigue Management Questionnaire's Global Life Participation Scale (Hedge's G = .50), Global Life Participation Satisfaction Scale (Hedge's G = .50), and Self-Efficacy Scale (Hedge's G = .50). The remainder of fatigue and life

participation measures detected either small intervention effects, or no effects, at one week post-intervention follow-up compared to control (Table 4).

At 12-weeks post-intervention, we observed large and very large effects on the COPM-Performance Scale (Hedge's G = .90) and COPM-Satisfaction Scale (Hedge's G = 1.36) in the intervention group (n=8), respectively, compared to control (n=14) (Table 4). Participants in the intervention group reported a clinically meaningful improvement (≥2 points) in 64% of their life participation goals according to the COPM-Performance Scale at the 12 week post-intervention timepoint, compared to 24% in the active control group (Figure 2). We found minimal to no effects associated with the intervention on the remainder of fatigue or life participation measures at the 12-week post-intervention follow-up, compared to control. Results of the sensitivity analysis, assuming best-case and worst-case scenarios for missing data, are included in Appendix 1.

Discussion

In this pilot study, we assessed the feasibility of recruiting and retaining patients on maintenance hemodialysis with fatigue for a randomized controlled trial of an energy management program, and the potential impact of such a program. Although previous proof-of-principle evidence[16] suggested a randomized controlled trial was warranted, the proportion of participants who would commit to completing study activities (eg. intervention sessions, outcome questionnaires) for a trial was unknown. Furthermore, the impact of the "PEP" program on various facets of life participation and fatigue compared to a control group remained unclear. We were able to recruit ~25% of clinically stable and English-speaking hemodialysis patients into this pilot randomized controlled trial, and retain 70% of enrolled participants for the duration of the trial, which met our pre-trial expectations for study participation[19]. Although fatigue did not appear to be affected

by the PEP program, the program was associated with medium to large-sized effect on personalized life participation at both short-term and medium-term follow-up, compared to an attention control condition. Collectively, these results suggest that a randomized controlled trial of the PEP program would be feasible, and is warranted.

Our recruitment and retainment results suggest that, despite the added responsibilities of filling out study questionnaires and completing the intervention or control program, the study was acceptable to a substantial proportion of our target population. We note that although only 25% of stable and English-speaking hemodialysis patients consented to participate, only 50-70% of them likely had fatigue, based on existing estimates of fatigue prevalence[1]; thus, we estimate that approximately half of eligible patients with fatigue in fact agreed to the study. This suggests that study burden was not an insurmountable barrier to recruitment. Although the dropout rate was higher in the intervention arm than the control (43 vs. 13%), our documented reasons for study withdrawals were unrelated to the intervention, and were rather due to the general medical complexity of this patient population. We therefore assume that with a larger sample of patients, the attrition rate would balance between the two groups. Our overall attrition rate of 30% is not unexpected for the dialysis population over the course of a five-month study, given that they typically experience high rates of acute medical events and hospitalizations[23,24]. We attribute the general acceptability of the intervention to the use of study materials that were user-friendly (eg. a brochure-style consent form); brief questionnaires to assess target outcomes; and a flexible protocol for missed treatment sessions. Acceptability could be further increased in a full-scale trial by reducing the number of questionnaires used to assess life participation and fatigue, particularly now that the pilot trial has provided clarity about the best measures for assessing these outcomes.

The finding that the PEP program was associated with improvements in life participation, compared to control, is important because this outcome directly aligns with patient priorities[3,5]. Patients on hemodialysis with fatigue view life participation as "the fundamental goal of treatment, because it symbolizes some indicator of being able to live a life without being confined by the disease"[5]. Although fatigue was not directly impacted by the intervention, our results suggest that energy management strategies developed during the intervention might have helped participants to accomplish their day-to-day goals more effectively by working around fatigue. In addition, the fatigue measures used in this study do not directly assess exertional fatigue (the type of fatigue targeted by the PEP program); as such, participants might have been reporting that their underlying "baseline" level of fatigue had not changed in response to the program, but still might have been experiencing a reduction in exertional fatigue during valued activities. The improvement in personalized life participation we observed in this study is, nonetheless, significant and relatively unique within the energy management literature[25]. Our intervention incorporated a number of novel features to more directly target life participation, compared to other energy management interventions, in accordance with the priorities of hemodialysis patients. For example, we used personalized goal-setting to ensure interventions were tailored to specific patients' needs, and a problem-solving training approach to facilitate patient independence at solving their own life participation challenges. Our findings support the potential efficacy of these features, although it is important to note the potential impact of unequal attrition between the intervention and control groups on our pilot results. This further emphasizes the need for a full-scale trial to more conclusively establish program effectiveness.

With respect to outcome measures, we found that the Canadian Occupational Performance Measure[26] detected the strongest intervention effects compared to other life participation and

fatigue measures. The validity and reliability of the life participation measures used have not been established in the chronic kidney disease population; as such, measures such as the Reintegration to Normal Living Index or Fatigue Management Questionnaire might not have detected intervention effects because, for example, they did not capture relevant areas or aspects of life participation among this population; were not worded in an understandable way, or were not responsive enough to capture changes in the outcomes, among other potential explanations. The COPM is also the only measure we used that assessed life participation in patient-chosen activities, rather than a generic set of life activities and/or areas which might not have been relevant to the study participants. This also might explain the enhanced performance of the COPM at detecting change associated with the intervention, compared to the other life participation measures. Although the COPM has similarly not been formally validated in people with kidney failure, it has strong validity, reliability and responsiveness data from multiple other clinical populations and age groups[27], and uniquely aligns with preferences of people with kidney disease for a measure of life participation that is individualized[5]. Collectively, these findings suggest the COPM is the best choice for a primary outcome for an RCT of the "PEP" program. Estimates based on our pilot results suggest data on 36 participants would be needed to detect a clinically meaningful change of >2 points on the COPM-performance scale in a randomized controlled trial, with significance set at 80% power and p=0.05. Based on our rates of screened-to-enrolled patients, the participant screening pool would need to include 415 patients on hemodialysis to achieve this sample size.

Study Limitations

We excluded non-English speaking patients from the study, limiting its generalizability to non-English-speaking people with kidney failure. Positive findings about the PEP program might,

however, justify developing program materials in the future that are accessible to a wider range of people with kidney disease. We were also unable to blind study coordinators to participants' treatment allocation, which might have unduly affected their approach to treatment. The infeasibility of blinding is a well-recognized limitation of trials that study psychosocial or behavioural interventions, because of the challenges of identifying and implementing an appropriate control. Finally, unequal attrition rates between the intervention and control groups limits the conclusions that can be drawn about program efficacy from this pilot study, and underscores the need for further research using a larger sample of patients to confirm our preliminary results.

Conclusions

The PEP energy management program appears to be acceptable to patients, and might lead to improvements in life participation. Further investigation in an adequately powered randomized controlled trial is warranted.

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None.

Conflict of Interest Statement

The authors have no conflicts of interest to disclose. Results presented in this paper have not been published previously in whole or part, except in abstract format.

Data Sharing Statement

Data from the study can be made available upon reasonable request to the corresponding author.

Authors' Contributions

JF led the design, coordination, analysis and authorship of the study and manuscript. BH provided advice and mentorship on all aspects of the study. CT, BM and MD helped with the development of the participant identification plan, and provided advice on other key study issues. PR and ME contributed feedback on trial design. All authors assisted with the interpretation and presentation of results for publication. NV provided review and perspective from a patient's point of view.

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Table 1: Description of the Personal Energy Planning ("PEP") Program

Program Section	Description
Part 1: Computer modules	• Participants complete 3 computer modules over 3 sessions (~20-30 mins each) that explain the basic principles of energy management • Modules are completed on laptops during hemodialysis sessions, with support for module completion provided by study coordinators
Part 2: Individualized problem-solving	• Participants work 1:1 with a trained administrator over 4-6 sessions (~30 mins each) to develop energy management strategies for 3 life participation goals • Energy management strategies are developed using a metacognitive problem-solving process called "***Goal-Plan-Do-Check***": 1. Set a life participation ***goal*** 2. Analyze current energy expenditure patterns to come up with a ***plan*** to conserve energy for the goal; 3. ***Do*** the plan; 4. ***Check*** to see if it worked, and what aspects of the plan should be revised • This process continues until an effective plan is found for each goal, or the program maximum of 9 weekly treatment sessions is reached • Study coordinators use ***guided discovery teaching*** to encourage patient independence in working through the Goal-Plan-Do-Check process

Table 2: Life Participation and Fatigue Outcome Measures

Outcome	Measure	Description
Life participation	*Canadian Occupational Performance Measure*[26] *– Performance Subscale (COPM-P)*	Asks individuals to rate, on a 10-point Likert scale, his/her performance in each of three self-selected priority activities of everyday living. Higher scores out of 10 indicate better performance. The COPM has been found to be a valid, reliable, clinically useful and responsive measure of occupational performance in multiple chronic disease populations[27].
	COPM[26] *– Satisfaction Subscale (COPM-S)*	Asks individuals to rate, on a 10-point Likert scale, their satisfaction with their performance in three self-selected priority activities of everyday living Higher scores out of 10 indicate better satisfaction with performance.
	Reintegration to Normal Living Index[28] *(RNLI)*	Assesses the degree to which individuals who have experienced traumatic or incapacitating illness achieve reintegration into normal activities, using 11 declarative statements each accompanied by a 10-point visual analogue scale. Scores are then added to produce an overall score out of 110, with higher scores indicating better reintegration to normal living. The RNLI has strong validity and reliability in multiple chronic disease populations[29].
	Fatigue Management Questionnaire (FMQ)	Asks individuals to rate various aspects of their fatigue management (e.g., overall impact on life participation; satisfaction; self-efficacy), out of 10, on five Likert-scale questions. Scores are then summed and averaged for each of two subscales (Performance subscale, or FMQ-P, and Satisfaction subscale, or FMQ-S), with higher scores out of 10 indicating better fatigue management. The FMQ was created for this study to assess life participation and self-efficacy pertaining to fatigue management.
Fatigue	*Fatigue Severity Scale*[20] *(FSS)*	Includes 9 items that ask individuals to rate, on a Likert scale from 1-7, the severity of their fatigue and its impact on their life during the past week. Scores are then summed and averaged to create a total score out of 7, with higher scores indicating worse fatigue. The FSS is a valid, reliable and responsive measure[30] that has been used in the dialysis population.
	Modified Fatigue Impact Scale[31] *(MFIS)*	A 21-item Likert-based scale that assesses the effects of fatigue on physical, cognitive, and psychosocial functioning. Scores are summed to produce an overall score out of 84, with higher scores indicating worse fatigue impact. The MFIS is frequently used as an outcome measure in energy management studies.
	**SONG-HD Fatigue*[32]	Assesses the severity of fatigue, and its impact on daily living, in people on maintenance hemodialysis using 3 Likert-style questions. Scores are summed to produce a total score out of 9, with higher scores indicating worse fatigue. The measure was developed in conjunction with kidney failure patients and other key informants, and is currently undergoing psychometric validation.

*Measure was finalized and added after trial registration, upon consultation with the measure developers

Table 3: Baseline Characteristics of Participants

	All Participants (n=30)	Control (n = 15)	Intervention (n = 15)
Age (yrs) (mean, SD)	62.4 (14.7)	64.8 (14.4)	60.0 (15.1)
Male	18 (60)	10 (67)	8 (53)
Residence			
Independent living	27 (90)	14 (93)	13 (86)
Retirement/supported living	3 (10)	1	2
Lives alone	20 (67)	6 (40)	4 (27)
Married	17 (57)	10 (67)	7 (46)
Employed	4 (27)	0 (0)	4 (27)
Education			
No high school diploma	3 (10)	2 (13)	1 (7)
High school diploma	12 (40)	6 (40)	6 (40)
College/trade school	10 (33)	5 (33)	5 (33)
University degree	4 (13)	2 (13)	2 (13)
Graduate/professional degree	1 (3)	0 (0)	1 (7)
Uses computer/tablet/phone	27 (3)	14 (93)	13 (86)
Dialysis vintage (yrs) (Median, IQR)	3.6 (1.8, 7.3)	2.6 (1.7, 6.0)	4.0 (1.7, 9.5)
Comorbidities			
Diabetes	15 (50)	9 (60)	6 (40)
Depression	9 (30)	3 (20)	6 (40)
Coronary artery disease	10 (33)	6 (40)	4 (27)
Congestive heart failure	8 (27)	3 (20)	5 (33)
Cerebrovascular disease	3 (10)	3 (12)	0 (0)
Alzheimer's disease	1 (3)	0 (0)	1 (7)
Multiple Sclerosis	1 (3)	0 (0)	1 (7)
Chronic Obstructive Pulmonary Disease	1 (3)	1 (7)	0 (0)
Cancer	7 (23)	5 (33)	2 (13)
Baseline serum hemoglobin (g/L) (Mean, SD)	101.6 (18.7)	107.7 (8.7)	95.0 (23.3)
Baseline serum albumin (g/L) (Mean, SD)	35.0 (10.8)	33.0 (3.9)	37.2 (15.0)
Activities of daily living dependence	7 (23)	2 (13)	5 (33)
MiniCog impaired	9 (30)	4 (27)	5 (33)
Personal Health Questionnaire-2 impaired	12 (40)	5 (33)	7 (47)

*Data are expressed as n(%) unless otherwise specified

Table 4: Changes in Fatigue and Life Participation Ratings in the Intervention versus Control Groups

Domain	Measure	Study Arm	Baseline	One Week Post-Treatment Follow-up			12 Weeks Post-Treatment Follow-up		
			Median score IQR)	*Median score (IQR)*	*Median change from baseline (IQR)*	*Hedge's G Hedge's Geffect size estimate*	*Median score (IQR)*	*Median change from baseline (IQR)*	*Hedge's G Hedge's G effect size estimate*
Life Participation	***COPM-P***	*Control*	4.3 (3.7, 7.7)	4.7 (2.5, 7.8)	-0.3 (-1.8, +1.0)	0.62 Medium	4.3 (1.7, 5.3)	+0.3 (-2.0, +1.3)	0.90 Large
		Treatment	4.7 (4.0, 6.7)	5.3 (4.7, 6.7)	+1.3 (+0.3, +1.7)		6.8 (5.4, 7.6)	+1.9 (0.0, +3.5)	
	COPM-S	*Control*	4.0 (2.3, 8.0)	6.0 (3.0, 8.0)	+0.3 (-0.8, +2.0)	0.13 Very small	4.0 (1.0, 5.0)	0.0 (-2.0, +0.7)	1.36 Very large
		Treatment	4.0 (3.3, 5.3)	5.3 (3.8, 6.5)	+0.7 (-0.3, +1.8)		6.7 (4.9, 7.5)	+1.8 (+1.4, +3.1)	
	FMQ-Global LP	*Control*	6.0 (4.7, 7.0)	6.5 (4.8, 8.1)	0.0 (-1.4, +2.4)	0.50 Medium	5.6 (3.0, 8.0)	-0.4 (-2.0, +1.0)	0.16 Very small
		Treatment	4.7 (3, 6.3)	6.3 (5.8, 7.4)	+1.8 (+.5, +2.1)		5 (2.25, 5.75)	+1.0 (-2.0, +4.0)	
	FMQ-Global LPS	*Control*	5.0 (4.0, 8)	7.5 (4.5, 9.0)	+1.0 (-1.3, +3.3)	0.50 Medium	6.0 (4.0, 7.5)	0.0 (-2.0, +1.0)	0.16 Very small
		Treatment	4.0 (2.0, 5.0)	7.0 (4.5, 8.3)	+4.0 (+.5, +5.3)		4.5 (2.25, 5.75)	0.0 (-2.0, +4.0)	
	RNLI	*Control*	78 (51, 88)	81.0 (58.0, 94.0)	-1.0 (-5.0, +15.0)	Favours control	83 (60, 101)	+5.5 (-7.5, +24.0)	Favours control
		Treatment	71 (56, 83)	61.5 (51.5, 78.8)	-3.0 (-10.0, +11.3)		61.5 (50.5, 78.5)	-1.0 (-20.0, +12.8)	
Fatigue	***FSS***	*Control*	5.0 (4.3, 6.1)	4.3 (3.8, 5.9)	-0.3 (-1.1, +1.0)	0.36 Small	4.0 (2.7, 4.9)	-1.1 (-1.8, -3.5)	Favours control
		Treatment	6.0 (5.6, 6.3)	5.3 (4.4, 6.0)	-0.6 (-1.9, +0.2)		5.2 (4.1, 6.0)	-0.8 (-1.0, 0.0)	
	MFIS	*Control*	50.0 (38, 55)	39.5 (29.5, 49.3)	-6.5 (-23, +.5)	Favours control	29 (22.5, 49.5)	-12.0 (-20.0, -6.5)	Favours control
		Treatment	52.0 (45, 59)	48 (38.5, 51.5)	-8.0 (-13, +1.5)		47.5 (39.0, 65.0)	-1.0 (-10.0, +12.0)	
	Song-HD Fatigue	*Control*	6.0 (4.0,7.0)	4.5 (3.3, 7.0)	0.0 (-2.0, 0.0)	0.15 Very small	5.0 (3.25, 6.0)	-1.0 (-2.0, +1.0)	Favours control
		Treatment	6.0 (3.8, 9)	5.0 (3.8, 6.0)	-1.0 (-4.5, +2.5)		6.0 (5.0, 6.0)	0.0 (-1.0, +3.0)	
	Self-Efficacy	*Control*	5.0 (5.0, 8.0)	6.2 (5.0, 9.0)	+0.2 (-1.0, +3.3)	0.50 Medium	8.0 (4.5, 9.0)	0.0 (-1.0, +3.0)	0.02 Very small
		Treatment	4.0 (2.0, 5.0)	6.5 (4.3, 7.3)	+3.0 (-0.0, +3.0)		5.0 (3.0, 5.0)	+0.5 (-1.5, +3.0)	

Legend: FSS = Fatigue Severity Scale; MFIS = Modified Fatigue Impact Scale; Global LP = Global Life participation; Global LP-S = Global Life Participation Satisfaction; RNLI = Reintegration to Normal Living Index; COPM-P = Canadian Occupational performance Measure – Performance Scale; COPM-S = Canadian Occupational Performance Measure – Satisfaction Scale; SONG-HD Fatigue = Standardized Outcomes in Nephrology - Hemodialysis Fatigue

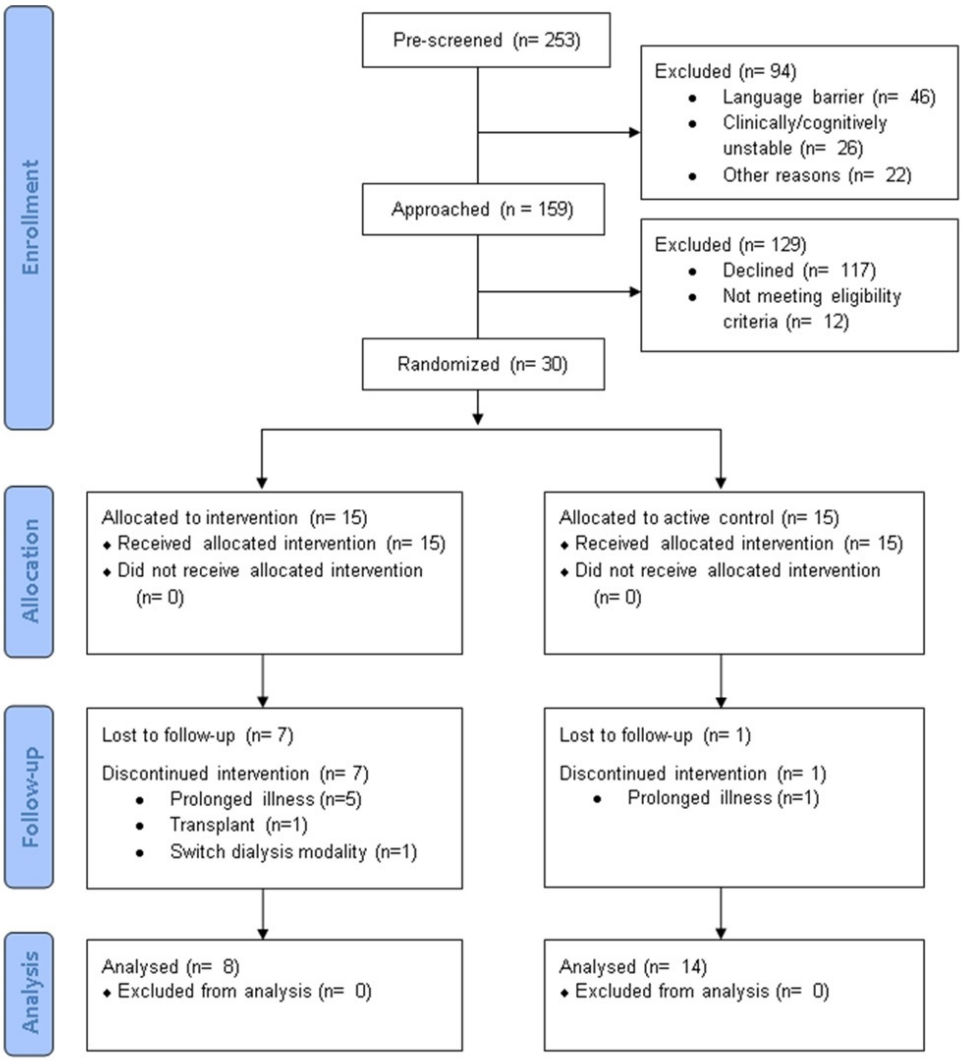
*Values expressed are medians (interquartile ranges)

Figure Legends

Figure 1: CONSORT Participant Flow Diagram

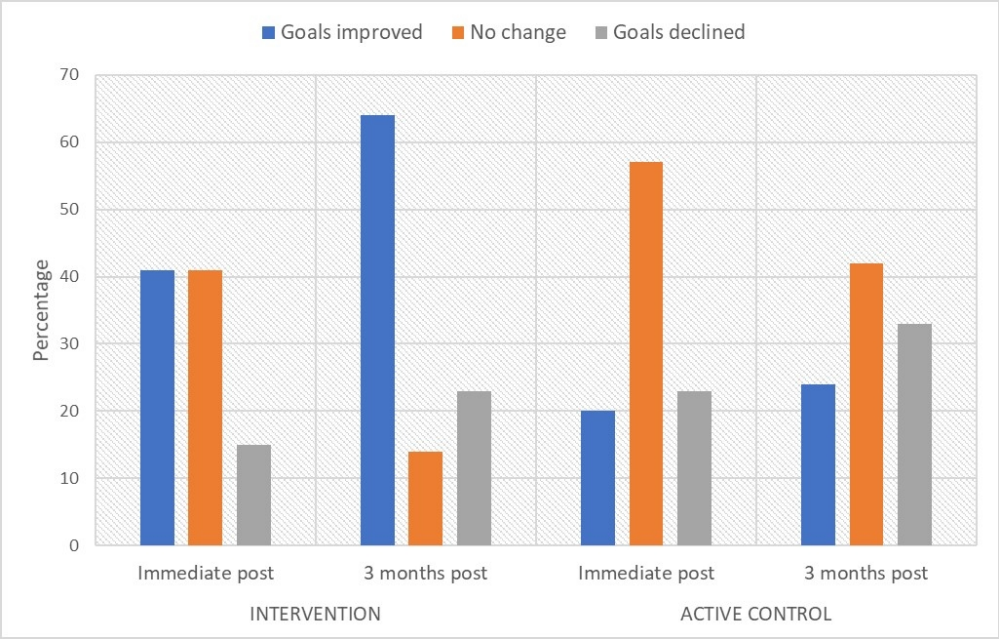
Figure 2: Proportion of Patients Achieving Life Participation Goals in Intervention vs. Control

Note: "Improved" means increase of ≥2 points (established MCID) on COPM performance subscale; "no change" means no clinically significant change; "declined" means decrease of ≥2 points on COPM performance subscale



CONSORT Participant Flow Diagram

172x193mm (150 x 150 DPI)



Proportion of Patients Achieving Life Participation Goals in Intervention vs. Control

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Appendix 1: Hedge's G Effect Size Estimates, Assuming Best-Case and Worst-Case Scenarios for Missing Data

	Immediate Post-Intervention		12 Weeks Post-Intervention	
	Worst-case scenario	**Best-case scenario**	**Worst-case scenario**	**Best-case scenario**
FSS	.27 Small	.35 Small	Favours control	Favours control
MFIS	Favours control	Favours control	Favours control	Favours control
Global LP	.29 Small	.71 Medium	.40 Small	.46 Small
Global LP-S	.31 Small	.65 Medium	.07 Very small	.08 Very small
Self-Efficacy	.41 Small	.68 Medium	Favours control	Favours control
RNLI	Favours control	Favours control	Favours control	Favours control
COPM-P	.24 Small	.80 Large	.29 Small	0.98 Large
COPM-S	.02 Very small	.13 Very small	.50 Medium	1.59 Very large
SONG-HD	No difference	.24 Small	Favours control	Favours control

Legend: FSS = Fatigue Severity Scale; MFIS = Modified Fatigue Impact Scale; Global LP = Global Life participation; Global LP-S = Global Life Participation Satisfaction; RNLI = Reintegration to Normal Living Index; COPM-P = Canadian Occupational performance Measure – Performance Scale; COPM-S = Canadian Occupational Performance Measure – Satisfaction Scale; SONG-HD Fatigue = Standardized Outcomes in Nephrology - Hemodialysis Fatigue

CONSORT 2010 checklist of information to include when reporting a pilot or feasibility trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a pilot or feasibility randomised trial in the title	1
	1b	Structured summary of pilot trial design, methods, results, and conclusions (for specific guidance see CONSORT abstract extension for pilot trials)	2
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale for future definitive trial, and reasons for randomised pilot trial	6-7
	2b	Specific objectives or research questions for pilot trial	7
Methods			
Trial design	3a	Description of pilot trial design (such as parallel, factorial) including allocation ratio	7
	3b	Important changes to methods after pilot trial commencement (such as eligibility criteria), with reasons	8
Participants	4a	Eligibility criteria for participants	8
	4b	Settings and locations where the data were collected	8
	4c	How participants were identified and consented	8
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	9; Table 1
Outcomes	6a	Completely defined prespecified assessments or measurements to address each pilot trial objective specified in 2b, including how and when they were assessed	10; Table 2
	6b	Any changes to pilot trial assessments or measurements after the pilot trial commenced, with reasons	Table 2
	6c	If applicable, prespecified criteria used to judge whether, or how, to proceed with future definitive trial	14-15
Sample size	7a	Rationale for numbers in the pilot trial	11
	7b	When applicable, explanation of any interim analyses and stopping guidelines	N/A
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	8
	8b	Type of randomisation(s); details of any restriction (such as blocking and block size)	8
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	8

Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	8
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	8
	11b	If relevant, description of the similarity of interventions	8-9
Statistical methods	12	Methods used to address each pilot trial objective whether qualitative or quantitative	11
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were approached and/or assessed for eligibility, randomly assigned, received intended treatment, and were assessed for each objective	Figure 1
	13b	For each group, losses and exclusions after randomisation, together with reasons	Figure 1
Recruitment	14a	Dates defining the periods of recruitment and follow-up	8
	14b	Why the pilot trial ended or was stopped	N/A
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	Table 1
Numbers analysed	16	For each objective, number of participants (denominator) included in each analysis. If relevant, these numbers should be by randomised group	12
Outcomes and estimation	17	For each objective, results including expressions of uncertainty (such as 95% confidence interval) for any estimates. If relevant, these results should be by randomised group	12-14; Appendix 1
Ancillary analyses	18	Results of any other analyses performed that could be used to inform the future definitive trial	N/A
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	
	19a	If relevant, other important unintended consequences	N/A
Discussion			
Limitations	20	Pilot trial limitations, addressing sources of potential bias and remaining uncertainty about feasibility	18
Generalisability	21	Generalisability (applicability) of pilot trial methods and findings to future definitive trial and other studies	14-17
Interpretation	22	Interpretation consistent with pilot trial objectives and findings, balancing potential benefits and harms, and considering other relevant evidence	14-17
	22a	Implications for progression from pilot to future definitive trial, including any proposed amendments	14-17
Other information			
Registration	23	Registration number for pilot trial and name of trial registry	7
Protocol	24	Where the pilot trial protocol can be accessed, if available	7 (reference)
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	19
	26	Ethical approval or approval by research review committee, confirmed with reference number	7

Citation: Eldridge SM, Chan CL, Campbell MJ, Bond CM, Hopewell S, Thabane L, et al. CONSORT 2010 statement: extension to randomised pilot and feasibility trials. BMJ. 2016;355.

*We strongly recommend reading this statement in conjunction with the CONSORT 2010, extension to randomised pilot and feasibility trials, Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.