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Effectiveness of a brief positive skills intervention to improve psychological adjustment in patients with end-stage kidney disease newly initiated on haemodialysis: protocol for a randomised controlled trial (HED-Start)

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ABSTRACT

Introduction Initiation onto haemodialysis is a critical transition that entails multiple psychosocial and behavioural demands that can compound mental health burden. Interventions guided by self-management and cognitive–behavioural therapy to improve distress have been variably effective yet are resource-intensive or delivered reactively. Interventions with a focus on positive affect for patients with end-stage kidney disease are lacking. This study will seek (1) to develop a positive life skills intervention (HED-Start) combining evidence and stakeholder/user involvement and (2) evaluate the effectiveness of HED-Start to facilitate positive life skills acquisition and improve symptoms of distress and adjustment in incident haemodialysis patients.

Methods and analysis This is a single/assessor-blinded randomised controlled trial (RCT) to compare HED-Start to usual care. In designing HED-Start, semistructured interviews, a codesign workshop and an internal pilot will be undertaken, followed by a two-arm parallel RCT to evaluate the effectiveness of HED-Start. A total of 148 incident HD patients will be randomised using a 1:2 ratio into usual care versus HED-Start to be delivered in groups by trained facilitators between January 2021 and September 2022. Anxiety and depression will be the primary outcomes; secondary outcomes will be positive and negative affect, quality of life, illness perceptions, self-efficacy, self-management skills, benefit finding and resilience. Assessments will be taken at 2 weeks prerandomisation (baseline) and 3 months postrandomisation (2 weeks post-HED-Start completion). Primary analyses will use an intention-to-treat approach and compare changes in outcomes from baseline to follow-up relative to the control group using mixed-effect models.

Ethics and dissemination Ethics approval was obtained from Nanyang Technological University Institutional Review Board (IRB-2019-01-010). Written informed consent will be obtained before any research activities. Trial results will be disseminated via publications in peer-reviewed journals and conference presentations and will inform revision(s) in renal health services to support the transition of new patients to haemodialysis.

Trial registration number NCT04774770.

Strengths and limitations of this study

- This randomised controlled trial (RCT) will be the first study to test the effectiveness of a positive skills intervention in end-stage kidney disease.
- RCT will recruit a large sample using outcome assessor-blinded study design.
- HED-Start is fully manualised and accompanied by structured training making replication in other settings easier.
- Only short-term outcomes will be evaluated, hence sustainability of effects (if any) will not be known.
- Implementation of intervention may be challenging due to the COVID-19 pandemic.

INTRODUCTION

Chronic kidney disease (CKD) is progressive disorder characterised by diminishing renal function lasting for more than 3 months.[1] It is categorised into stages that are determined by filtering capacity of kidneys most commonly quantified by estimated glomerular filtration rate. In the most advanced stages, that is, end-stage CKD, renal replacement therapy, dialysis or renal transplantation are required to sustain life. Patients with end-stage kidney disease (ESKD) suffer a high disease burden, including the illness causing CKD, comorbid conditions and complications of the dialysis treatment. Dialysis is a life-sustaining, chronic procedure for patients with ESKD that involves substituting the function of the kidneys in the removal of waste products using dialysers.[1] Globally, ESKD prevalence

has been steadily increasing, especially in Southeast Asia.[2] In Singapore, the age-standardised incidence rate of dialysis reached 187 per million population in 2018[3] and expected to rise further with ageing and increased rates of diabetes. Haemodialysis (HD), the most common dialysis modality, typically requires 4 hours of dialysis treatment three times a week in dedicated facilities. The pathway towards dialysis initiation is often stressful and fraught with challenges and adaptive demands for patients and their families alike.[4]

Patients with ESKD often express reluctance toward dialysis and may at times feel obligated to accept dialysis due to social pressure or demands, without thoughtful or adequate preparation for this critical treatment transition.[4] As per 2018 US Renal Data System, 35.4% of incident ESKD patients received little to no predialysis care, with over 80% of new HD patients starting with a temporary access.[5] Prior work in Singapore indicate that even among those already known to renal care, 51% reported that they intend to delay dialysis preparation and 59.5% fail to initiate on HD with access in place.[6] Unplanned initiation onto HD, defined as the initiation onto dialysis with a central venous catheter or as an inpatient,[7] often leads to heightened feelings of fear, depression and frustration in patients.

Depression is common in ESKD with an estimated prevalence of 39.3% among people established on dialysis compared with a prevalence of 27% in patients with CKD (stages 1–5).[8] Comorbid depression and ESKD are associated with poor quality of life (QOL), higher risk of death, morbidity and hospitalisations and increased healthcare costs.[9 10]

Prospective studies showed that 25% of incident HD patients experience depressive symptoms in the first year of dialysis with symptoms being higher among those with unplanned start.[11] Most importantly distress symptoms do not resolve but persist over time,[12] compounding risk for poor prognosis.[13 14]

Despite their clinical significance, early recognition and treatment in context of routine renal care remains a challenge.[15] Cognitive–behavioural therapy (CBT) is a psychological treatment that has shown to be effective in treating depression and anxiety, and is considered a treatment of choice by the National Institute for Health and Care Excellence.[16] Programmes based on CBT have been the most frequently evaluated interventions, with evidence to support their effectiveness to reduce distress in CKD.[17 18] CBT involves modifying or counteracting unhelpful thoughts or beliefs which can lead to changes in emotion and behaviour. Patients and families often report exaggerated, overcatastrophising beliefs about dialysis,[19 20] equating treatment to end of meaningful life and imminent death.[21 22] CBT supports individuals in developing skills and strategies to challenge such thoughts and better manage emotions, yet the reach or accessibility of these interventions is limited as typically delivered only to those patients with targeted risk, such as screened with depression/subthreshold depression. They are also constrained by high costs, intensity, considerable dropout rates and shortage of mental health professionals in routine renal care,[23 24] making their translation to clinical practice challenging.

'Prevention' programmes offered proactively and universally to all patients to support transition to renal replacement therapy may mitigate the risk for depression and need to escalate to more intensive step-up programmes. Most of the non-targeted/universally offered interventions, however, focus predominantly on education and self-management skills. The RightStart programme,[25] a structured programme of education and health counselling for newly initiated HD patients, yielded improvement in terms of first year morbidity and mortality but impact of on depression was not examined. The Haemodialysis Self-Management Randomised Trial interventions focused on behavioural change[26 27] improved clinical markers, self-management skills as well as symptoms of distress, indicating that skill-imparting interventions may have broader benefits. This is particularly pertinent in Asian cultures in which the stigma attached to mental health services may hinder the acceptability, participation or retention in CBT programmes.[28–30]

Other approaches may also have value but have not yet been applied in CKD. Positive psychological states are associated a range of adaptive outcomes from psychological well-being, health behaviours and physical health and even lower risk of mortality, independent of both distress and other traditional risk factors.[31] Guided by theories such as the broaden-and-build theory of positive emotion,[32] positive psychology interventions focus on strategies to increase optimism, positive experiences and positive affect as means to mitigate stress and depression as improve adjustment. These interventions have been shown to be effective in reducing symptoms of depression and improving psychological well-being in various populations, that is, diabetes,[33] hypertension,[34] cancer,[35] HIV[36] and dementia caregivers.[37 38] Meta-analyses indicate medium effects sizes for this work that are sustained over time.[37 39–43] Such positive skills interventions may represent another pathway to support emotional adjustment for patients new to HD. Furthermore, as these interventions are resource efficient that is, no specialist required, low costs and time commitment for patients, they can be offered to all new patients without a stratification for depression or other clinical psychiatric conditions, thereby expanding reach and access of psychosocial care within renal health services. The potential of such intervention to be delivered proactively to all patients may also help to reduce the stigma often associated with mental health interventions. Leveraging on the burgeoning field of evidence of positive emotion and positive skills interventions, the present study ('HED-Start') has been designed to address the limited evidence in CKD. A two-arm, parallel randomised controlled trial (RCT) will be conducted to test whether a positive skills intervention can improve adjustment outcomes in patients newly established onto HD.

Study aims

This RCT will seek to evaluate the effectiveness of HED-Start intervention against usual care in reducing anxiety and depression symptoms in incident HD patients and in improving the following secondary outcomes, QOL, positive and negative affect, illness perceptions, resilience, self-efficacy, self-management skills and benefit finding.

The primary hypothesis is that participants allocated to the intervention arm will show a reduction in anxious and depressive symptoms post intervention relative to those in usual care. Secondary outcomes are also expected to be higher in the intervention arm relative to the control.

Concurrently with the effectiveness evaluation, an additional aim is to undertake a process evaluation to explore the acceptability and implementation of HED-Start and help in the interpretation of the outcome results. The process evaluation will seek to document the implementation of HED-Start, to describe the processes in HED-Start delivery and to collect information from study participants and facilitators about the experience with HED-Start.

METHODS AND ANALYSIS

This protocol describes a two-arm parallel RCT to evaluate the effectiveness of HED-Start on patient-reported outcomes. This protocol is in accord with the Standard Protocol Items: Recommendations for Interventional Trials 2013 statement,[44] and the intervention is described according to the Consolidated Standards of Reporting Trials checklist.

The RCT will run from January 2021 to September 2022. Recruitment began in January 2021 (suspended for 2 months due to pandemic measures) and is now in progress. Data collection will continue to Q2 of 2022.

Developing HED-Start

We will use a systematic process combining theory and existing evidence and, stakeholder involvement to develop the intervention. A scoping review of interventions for HD patients and qualitative interviews with incident HD patients and family members will be conducted first to establish their needs/challenges and available support and care pathways on renal replacement therapy initiation. The interview will comprise open-ended questions about the patients and family members' concerns, difficulties, and challenges in managing their dialysis. Recruitment for the qualitative interviews is determined to be completed once thematic saturation is reached (ie, no new themes in two consecutive interviews).

Using a codesign approach, input from renal healthcare professionals (HCPs), patients and research teams will be sought so as to ensure HED-Start is meaningful, feasible and pertinent to patients and renal HCPs. This phase will include (1) multiple codesign meetings among investigators, researchers and renal HCPs/facilitators and one patient advocate to develop the preliminary content and materials for HED-Start and (2) one codesign workshop with HD patients to explore acceptability of procedures/materials and refinement/ adjustments (if any) for the programme. A total of 10–12 patients will be invited to the codesign workshop to allow good size for meaning discussions and some representation of gender, age and ethnicity (Chinese, Malay, Indian). National Kidney Foundation (NKF) staff will identify eligible participants among those enrolled in patient advocate scheme in NKF, who will then be approached and consented by independent research staff. During the codesign workshop, feedback and suggestions garnered will be used to refine and finalise programme content and study procedures.

Internal pilot

Before the RCT, an internal pilot involving 25–30 participants and 2 full runs of HED-Start (1 delivered in Mandarin and 1 in English) will be conducted to assess whether recruitment and randomisation procedures and the intervention will run as planned. The exact procedures as those planned for the main RCT will be applied. If no changes are required, data from the internal pilot will be included in the main trial. If major changes to the procedures are required, the protocol will be revised, and approval will be sought from the ethics committee before starting the RCT. The main trial may be stopped if deemed unfeasible.

Progression criteria

Progression criteria to RCT are set as follows: minimum recruitment target of 30 patients in 2 months to ensure that sufficient recruitment will be achievable during main trial; retention of 70% of participants from baseline to follow-up assessments (no more than 30% attrition rate); 70% of intervention participants completing at least two sessions in HED-Start and no adverse effects (ie, hospitalisation, injury and deaths) related to HED-Start during the follow-up. Adverse events noted from participants' medical records or reported by participants during follow-up will be classified as related, unrelated or possibly related to HED-Start. The detailed progression criteria based on recommendations[45] are described (see figure 1).

Patient and public involvement

Patients are involved in several stages of the research process. Prior to study design, qualitative interviews conducted with patients and their family members will seek to determine key needs and existing resources on renal replacement therapy initiation. Development of intervention content will be informed by several codesign meetings with a patient advocate, and from a group of patients via a codesign workshop to explore the acceptability of procedures and materials. Feedback received will be used to refine and finalise programme content and study procedures. An internal pilot will be conducted to test run the full HED-Start programme to obtain patient feedback on the intervention delivery.

	Green (Proceed with HED-Start)	Amber (Proceed, with amendments required)	Red (Do not proceed, review protocol and resolve issue)
Recruitment	At least 30 patients in 2 months recruited for study	At least 30 patients recruited within 2-4 months	Target of 30 patients not reached by 4 months
Retention	Retention of 70% of participants through follow up (no more than 30% attrition rate)	50% of retention rate through follow up	More than 50% of participants attrition through follow up
Intervention completion	At least 70% of participants completing at least 2 sessions	Only 50-70% of participants completed at least 2 sessions	Less than 50% of participants completed at least 2 sessions
Adverse events	No adverse intervention-related events during follow-up	Less than 5 adverse intervention-related events during follow-up	Five or more serious adverse intervention-related events during follow-up

Figure 1 Progression criteria for HED-Start.

Sample size

Sample size calculation was performed using G*Power V.3.19.7. The selected medium effect size (standardised effect size=−0.6) was based on the pooled effect estimate obtained from most recent systematic reviews and meta-analyses on psychosocial interventions on reducing depression and anxiety symptoms in those with CKD ranging from d=−0.48 to −0.60.[41–43] Assuming a medium effect size of 0.6 and adopting a 1:2 allocation ratio, 34 and 68 participants will be allocated to control and intervention arm, respectively for a (two-tailed) significance level of 5% and a power of 80%. An unequal allocation ratio is to be adopted to account for the potential higher attrition rates in the intervention arm than those of the usual care. Assuming an attrition rate of 30%, a sample size of 148 participants will be sought for the RCT (50 and 98 participants for control and intervention, respectively).

Participants

A two-arm RCT design will be used to recruit participants from the NKF Singapore dialysis centres. Dialysis centres will be randomly chosen and all eligible patients in the centre will be invited to participate in the study.

Inclusion and exclusion criteria

In order to be eligible, participants have to be (1) 21 years of age or older, (2) diagnosed with ESKD, (3) no more than 6 months since HD placement at NKF Singapore and (4) able to speak and read English or Mandarin. Exclusion criteria will be as follows: (1) unwilling or unable to give consent or refuse to be randomised, (2) have cognitive impairments or psychiatric conditions that preclude consent as noted in medical records or evidenced in the screening visit, (3) currently involved in other intervention trials or (4) failing on dialysis and approaching end of life (palliative care pathway). We will also exclude participants with social/living circumstances that would preclude attendance of intervention sessions such as living in nursing homes or institutionalised care settings.

Recruitment

Recruitment location will be at NKF dialysis centres. Research staff independent to patients' renal care teams will approach eligible patients at the NKF dialysis centres to solicit participation and administer study questionnaire following informed consent.

A token participation (S$20) will be offered for each questionnaire administration (both trial arms). Those randomised to HED-Start will be provided a travel reimbursement of S$10 for each intervention session attended (intervention arm only).

Randomisation and blinding

A computer-generated randomisation will be carried out by an independent statistician, not connected to the trial or involved in patients' management. To minimise contamination between participants in different study arms, the dialysis centres will be the unit of randomisation. Centres will be randomised to usual care or HED-Start using a 1:2 ratio. The allocation sequence will remain concealed from intervention facilitators and study participants until the baseline data collection is completed. Care providers in dialysis centres (ie, dialysis nurses) and outcome assessors (ie, research staff involved in taking baseline and follow-up measurements) will also be blinded to allocation.

HED-Start intervention

Usual care and intervention groups

All participants (both in usual care and HED-Start) will receive usual renal care including dialysis sessions, medical/laboratory tests or routine check-ups in accordance with established care protocols, and consultations with renal HCPs or referrals to other care services or other support programmes. Usual care participants will be invited to HED-Start programme at completion of the trial. Intervention participants will receive HED-Start plus usual care.

HED-Start programme

The HED-Start programme will be developed specifically to be facilitated by existing frontline HCPs (ie, medical social workers) who are already employed in the organisation to ensure delivery, engagement and subsequent scaling up if proven effective. HED-Start will combine elements of CBT (eg, psychoeducation on mood and interplay of thoughts emotions and actions, cognitive reframing), and positive psychology (eg, strength-based activities (affirmations, social resources), positive coping strategies, gratitude, acceptance) and self-management (ie, emphasis on own agency/self-responsibility, skill(s) acquisition (eg, making sense of blood assays) and goal-setting).

To support engagement, motivational interviewing principles will be weaved into the delivery of the programme including Elicit-Provide-Elicit Framework for offering advice/feedback as opposed to didactic delivery, and

Table 1 HED-Start session outline

Session and theme	Outline of session
Session 1—Self-management/self-care skills, and setting goals related to treatment	Introduce HED-Start programme outline and key principles; provide information and facilitate activity on self-management and symptom experience; goal setting of a short-term, specific and realistic behavioural goal (using confidence rulers and considering its benefits, barriers and importance) to practice before the next session.
Session 2—Cognitive reframing and acceptance/mindfulness	Review goal setting progress and problem solve any barriers; revise goal(s) set in session 1 or set goal (if none set at session 1); recap on session 1 content; psychoeducation on the CBT model; activity on cognitive reframing; psychoeducation on acceptance and mindfulness practice; and homework practice on cognitive reframing.
Session 3—Recognise positive events and social resources	Review goal setting progress and problem solve any barriers; revise goal set in session 2; review homework practice; recap on session 2 content; activity to construct a map of participants' social resources and activities; psychoeducation on positive moments and gratitude; homework practice to identify positive moments and gratitude diary.
Session 4—Personal strengths and goal setting for the future	Review goal setting progress; review homework practice; recap on session 3 content; activity to appreciate dialysis as just another part of life; identifying personal strengths activity; setting longer-term goals for the future (beyond HED-Start); review of topics and key learning points in sessions 1–3.

CBT, cognitive–behavioural therapy.

supporting patients' autonomy in (any) goals (including their choice not to set goals).

HED-Start will focus on the following key skills, shown to support emotional adjustment: goal setting and working towards attainable goals[27 46]; cognitive reframing[47]; acceptance, gratitude and mindfulness[48]; personal strengths and affirmations.[49]

HED-Start will comprise four sessions to be delivered every 2 weeks in groups of 5–8 participants (as per safe management procedures). Sessions, lasting 120 min each, are to be cofacilitated by two renal HCPs (ie, medical social workers) following training and an internal pilot to ensure consistency. The content of sessions is briefly outlined in table 1. Each session focuses on two skills and includes up to two homework exercises to be completed between sessions.

All intervention participants will receive a booklet that includes session handouts/materials; key learning points for each session and the activity worksheets to be used both in-session and for homework. The compiled information and completed activity sheets may also serve to solidify learning beyond HED-Start.

To minimise attrition and boost engagement with the intervention, facilitators will send out reminders on locations/dates for subsequent sessions and to complete assigned homework exercises. To facilitate intervention scheduling, participants will also be asked to indicate their preferred language (English, Chinese); availability for sessions scheduled on non-dialysis days, and/or over weekends, transport requirements and mobility issues (ie, wheelchair use, etc).

Facilitator training

The facilitators will be provided with a comprehensive manual containing an overview of key principles underpinning HED-Start, all required materials (ie, handouts, goal-setting sheets, activity charts/props) and detailed step-by-step instructions for each of the four sessions (eg, script for didactic content and instructions for the activities/homework, learning points, sample prompts for the debrief, etc).

In addition to the manual, facilitators will attend a training programme developed by the research team on key principles of Motivational Interviewing, CBT and Group facilitation. The training will be delivered by KG (study principal investigator (PI) and motivational interviewing trainer). The training sessions (6× half days) will cover Motivational Interviewing Fundamental Skills and Coaching on how to embed Motivational Interviewing in the delivery of HED-Start content. Core techniques taught will include: the use of effective open-ended questions, reflective listening, agenda-setting/mapping, the Elicit-Provide-Elicit to exchange information (as opposed to didactic advice giving), the use of questions and reflection to soften resistance, positive reframing and setting/reviewing goals. Guided by the manual, each session will first be discussed, demonstrated by trainer and then practiced by trainees under supervision and feedback.

To further support competency and consistency, facilitators will be required to deliver at least n=1 intervention session to patients not enrolled in the internal pilot or RCT that will be reviewed by KG. The facilitators are experienced medical social workers and generally expected to require only minimal supervision on intervention procedures. Additional optional support and feedback however will be offered as per facilitators' request/preference.

Fidelity will be monitored through observation or audio-recording of approximately 10% of the intervention sessions. A template will be used to record use of core techniques, adherence to the recommended session workflow, use of HED-Start materials and the occurrence

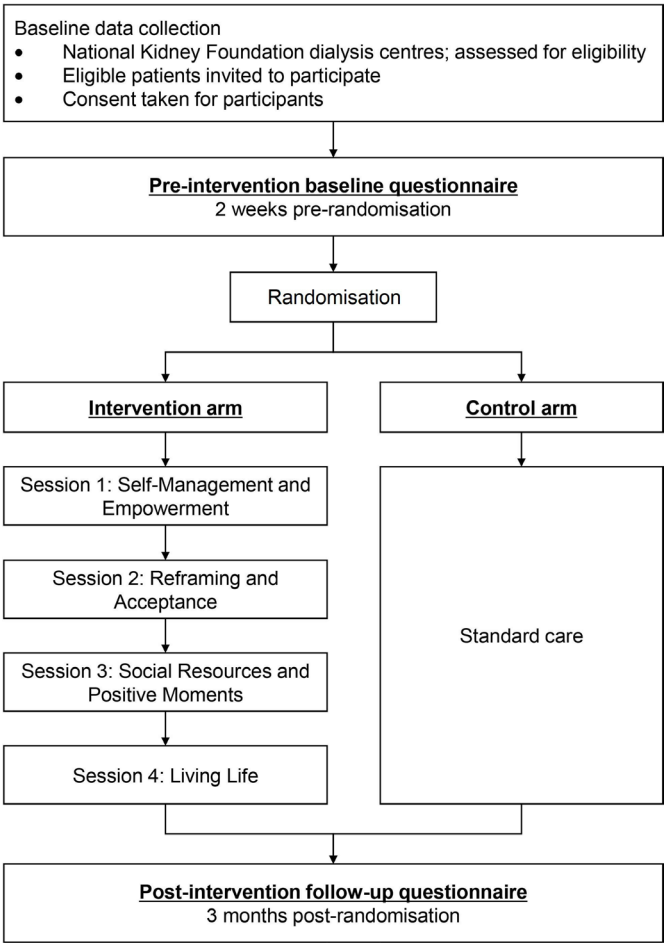

Figure 2 Study flow and randomisation.

any unhelpful delivery techniques (eg, confrontation, didactic advice giving, 'forced' goal setting).

Outcome assessments

Assessments will be conducted at baseline (prerandomisation) and 3 months postrandomisation (ie, 2 weeks following completion of the intervention; see figure 2). Informed by the relevant evidence in ESKD and the Standardised Outcomes in Nephrology Guidelines,[50] we will collect the following data: (A) patient-reported outcomes, (B) sociodemographic and clinical information and (C) qualitative interviews. Most of the chosen questionnaires have been used in prior renal research or in local context.[26 51–55] The instruments chosen have also been linguistically validated in Mandarin,[56–59] a key consideration for use in local context.

Patient-reported outcomes

The following validated measures of patient-reported outcomes (mood, QOL, self-management skills) will be used.

Primary outcomes will be symptoms of anxiety and depression to be measured with the Hospital Anxiety and Depression Scale (HADS).[60] HADS comprises 14 items, with seven items measuring depressive symptoms and seven other measuring anxious symptoms. Both English and Chinese versions of HADS have shown good psychometric properties in terms of internal consistency and factor structure.[61 62] Higher scores indicate worse anxiety and depression symptoms with a clinical cut-off of 8 and above in each subscale to signify caseness.[61]

Secondary outcomes will be:

- Health-related and generic QOL measured respectively using the burden of disease subscale from the Kidney Disease Quality of Life Short Form (KDQOL-SF), and the following subscales from the WHO Quality of Life instrument (WHOQOL-BREF): overall QOL, general health, psychological health and social relationships. All raw scores will be transformed to range from 0 to 100. Higher scores signify better QOL. Both English and Chinese versions of the KDQOL-SF and WHOQOL-BREF have demonstrated good reliability and validity for use in Singapore.[63–66]
- The Brief Illness Perception Questionnaire (BIPQ) to assess illness perceptions of CKD.[67] The eight-item BIPQ comprises eight subscales (ie, consequences, timeline, personal control, treatment control, identity, concern, coherence and emotional representation). Consistent with prior applications with renal populations, the term *kidney disease* will be used in place of illness.[68] Subscale scores range from 0 to 10, with higher scores reflective of more negative illness perceptions. The BIPQ has been extensively used and both English and Chinese versions have shown good psychometric properties in terms of good reliability and acceptable construct validity.[68 69]
- The Scale of Positive and Negative Experience (SPANE) which comprises six items (eg, positive, good, pleasant) assessing positive affect and six items (eg, negative, bad, unpleasant) assessing negative affect.[70] The SPANE has been validated in several cultures and languages including Mandarin and has demonstrated good reliability and validity.[62 70] Items are rated on a 5-point scale from 1 (very rarely or never) to 5 (very often or always). Higher scores in the Positive and Negative affect subscale indicate greater positive and negative affect, respectively.
- Self-efficacy to be measured with Self-Efficacy for Managing Chronic Disease six-item Scale.[71] Items are rated from 1 (not at all confident) to 10 (totally confident) with higher scores indicating greater self-efficacy. The English and Chinese versions of the scale have good internal consistency and a unidimensional structure.[72 73]
- Resilience measured by the two-item Connor-Davidson Resilience Scale (CD-RISC-2).[74] Each item ranges from 0 (not true at all) to 4 (true nearly all the time). Higher scores indicate greater resilience. Both English and Chinese CD-RISC-2 scales have demonstrated acceptable reliability and validity.[74 75]
- To measure experience of meaning and personal growth, two subscales (personal growth; acceptance)

from the Benefit Finding Scale will be used.[76] Originally developed for cancer, the instructions will be modified so that each item is rated in response to having started on HD, using a 5-point scale from 1 (not at all) to 5 (extremely). Higher scores indicate a greater extent of benefit finding. English and Chinese versions of the scale have shown good reliability and construct validity.[56 77]

- Other self-management skills will be measured using six subscales from the Health Education Impact Questionnaire (heiQ): Positive and Active Engagement in Life, Skill and Technique Acquisition, Constructive Attitudes and Approaches, Self-Monitoring and Insight, Health Services Navigation and Social Integration and Support.[78] All items are rated on a 4-point scale from 1 (strongly disagree) to 4 (strongly agree). Higher scores indicate greater proficiency with the relevant skill domain. The heiQ has been reported to have good reliability and validity.[79]

Sociodemographic and clinical information

Socialdemographic data, that is, age, gender, ethnicity, marital status, employment status, education, household type and living arrangement will be collected. Relevant clinical data including comorbidities/complications, primary kidney diagnosis, details about renal replacement therapy initiation and lab assays indicative of patients' clinical status and adherence (eg, haemoglobin, albumin, phosphate, potassium, interdialytic weight gains) will be extracted from medical records. Data on mortality, and hospitalisation will also be recorded from patients' medical records. Participants will also self-report adverse events since entry into study in the follow- up assessment.

Process evaluation

The process evaluation of trial will adopt a mixed-method approach[80] combining (1) interviews with the facilitators and participants and (2) data on implementation and engagement (feedback ratings, number of sessions delivered, duration/intervals, attendance, retention and completion of homework).

In-depth semistructured interviews will be conducted by research staff independent to intervention delivery to examine issues related to acceptability and implementation of programme to guide refinements if necessary. All facilitators (N=8) and a subset of intervention attendees (N=20 including those who have completed all sessions and those who have not completed all sessions) will be invited to share with on their experiences following programme completion. The exact numbers of participants recruited for the interview will depend on when thematic saturation has been achieved that is, when no new themes have emerged after two consecutive interviews. Facilitators will be asked about issues such as their experiences of the training, the programme, how they felt the participants responded to HED-Start and perceived facilitators and barriers to implementation. Intervention participants will be asked about their expectations and experiences of sessions, facilitators and barriers to their participation, their feedback on homework and if they had completed assigned homework, reasons for adherence/non-adherence to sessions (and homework) and suggested improvements.

Data on engagement will include number of participants who attended each session, number of participants who dropped out and completion of homework. Facilitators will review homework in session to assess participants' engagement with the assigned practice and to discuss their key takeaways or learning points.

Meshing quantitative and qualitative methods will allow a more in-depth understanding of the effectiveness of HED-Start. Qualitative data will be used both to contextualise and expand on the quantitative data (ie, ratings on aspects of programme, homework completion), generating insights on the most valuable elements, and those less helpful elements that may need fine-tuning and the overall experience of patients in the programme. The four criteria of trustworthiness will be examined.[81] Credibility will be established by ensuring that interviewers are trained with the required qualitative research skills. Dependability and confirmability will be established by keeping an audit trail of project workflow and investigator triangulation.

Statistical analyses

Statistical analyses will be performed at the 5% significance level using SPSS (V.25). All intervention evaluations will be performed on the principle of intention-to-treat, using the observed data collected from all randomised participants. A per-protocol analysis may be conducted on the subset of participants who completed all sessions of the programme. Demographics and baseline characteristics will be summarised using descriptive statistics. Continuous variables will be summarised as numbers of observed values, mean, SD, median, minimum and maximum. Categorical variables will be described as frequency and percentage. Information collected on primary and secondary outcomes will be first summarised using descriptive statistics at baseline and at 6 months. Differences between study arms in baseline will be assessed using univariable analyses such as χ^2 test for categorical variables and independent samples t-test or analysis of variance for continuous variables, where appropriate. Linear regression models will be used to examine the effect of HED-Start on primary and secondary study outcomes adjusting for baseline outcome value, and (any) casemix if significant with outcomes in question. Logistic regression models will be applied to categorical outcomes (eg, depression caseness). Both single and multiple imputation methods may be considered based on different assumptions on the missing data to assess the robustness of intervention evaluation. Adverse events, that is, hospitalisation and mortality will be analysed using negative binomial regression and the Kaplan-Meier estimation method,

respectively.[82 83] Clustering effect will be adjusted for in sensitivity analyses.

Qualitative analyses

Interviews with facilitators and patients will be transcribed verbatim in English. Interviews conducted in Mandarin will be directly translated into English. Data will be analysed using thematic analysis following six steps: familiarisation with data, generation of initial codes, searching for themes, reviewing of themes, naming themes and lastly report writing.[84] An iterative process will be used to identify and revise codes and themes that emerge from the interviews. Qualitative data will help elaborate on the context in which the quantitative findings are situated that is, patients' experiences in HED-Start and how these may have shaped the effectiveness outcomes measured in the trial or other (if any) effects of HED-Start (not directly measured in trial but emerging in the interviews).

ETHICS AND DISSEMINATION

Ethics approval for this trial was obtained from the Nanyang Technological University Singapore Institutional Review Board (Reference number: IRB-2019-01-010). Written informed consent will be obtained from all participants before data collection. Data will be deidentified by assigning each participant a unique code. Hardcopy consent forms and questionnaires will be kept in locked cabinets in the PI's office. Qualitative interviews will be audiorecorded for transcription purposes and audiorecordings will be deleted following completion of transcription. Electronic transcripts and questionnaire data will be kept securely on a password-protected computer at the PI's lab, and only research team members will have access to electronic files. All data will be safely stored/archived for a period of 10 years after the completion of the study after which time all hard copies of research data will be discarded by shredding and all softcopy research data will be deleted. Dissemination will include study progress report to funding agency (NKF Singapore), publications in peer-reviewed journals, conference presentations and feedback about study results which will be shared with patients through outreach efforts by collaborating with relevant organisations such as NKF Singapore.

DISCUSSION

HD incurs considerable costs for both healthcare systems and patients. Patients receiving HD are often plagued with psychological distress and can benefit from psychological interventions to support emotional adjustment. While CBT interventions can be effective in improving symptoms of distress, they are also resource/labour intensive and are constrained by shortage of mental health professionals and low retention and acceptability by patients. These considerations make their translation into routine renal care practice difficult.

Another important consideration is that CBT programmes are often only offered to the subset of patients on positive screen for distress or clinical depression. Minor or subclinical depression despite being highly prevalent in general and patient populations remains unrecognised and untreated.[85] Proactive interventions[86] offered to all new patients have the potential to support adjustment by imparting broader positive skills for patients to navigate transition and adaptation to renal replacement therapy but these have not yet evaluated in the context of CKD.

HED-Start was conceptualised in response to the scarcity of such programmes. The HED-Start programme is based on principles of self-management, motivational interviewing and CBT, used in prior HD work.[27 87] It comprises four group sessions delivered by front-line facilitators aimed to teach skills shown to enhance emotional management and adjustment: goal setting, psychoeducation on thoughts, feelings and behaviour, cognitive reframing, acceptance and gratitude, personal strengths. The focus on broader skills is also expected to enhance engagement and retention. The chosen approach of up-skilling clinical teams and universal offering to all patients provides opportunity for wider delivery and reach in this population. The trial will include a process evaluation to assess qualitatively and quantitatively the engagement and delivery of HED-Start, and to collect information about the experiences of the trial facilitators and participants.

Limitations should be acknowledged. The trial sample will be derived from an organisation that serves socioeconomically disadvantaged groups (lower to middle socioeconomic status) in Singapore, hence replication in other settings is warranted. Sample size calculation is based on depression and not both the coprimary outcomes, that is, depression and anxiety, due to scarcity of evidence on anxiety in ESKD. Although depression and anxiety often coexist, future studies intending to replicate this protocol should consider adjusting for two primary outcomes.[88] Planned follow-up will be relatively short. Study outcomes will only be assessed at end of programme hence the long-term effects of HED-Start (if any) or stability/maintenance of short-term effects cannot be established. We also anticipate several challenges in forming groups and the delivery of trial amid the COVID-19 pandemic. Safe management procedures implemented to curb the spread of COVID-19 are more pertinent for HD settings as patients on dialysis are considered a high-risk group. These measures include wearing of masks, physical distancing between individuals and limited group sizes, ranging from 5 to 8 (inclusive of facilitators), depending to National Phase-alertness guidelines. Guidelines and protocols are changing frequently depending on pandemic response, and number of active infections. For instance, guidelines prohibiting intermingling of patients from

difference dialysis centres were in place in Q4 of 2020, lifted in Q1 of 2021 and then reimposed in Q2 of 2021.

There are additional logistical considerations as the HED-Start is offered in both English and Chinese. Language preference (ie, having to form separate English-speaking or Mandarin-speaking groups in context of safe management measures) is an additional consideration when scheduling sessions. Furthermore, although new HD patients are typically allocated to dialysis centres based on residential proximity, final centre allocation is subject to dialysis station availability. Some dialysis centres operate at almost full capacity and are unable to admit new patients for a few months, which further complicate recruitment. To maximise the formation of single language groups in context of safe management procedures, we purposefully opted for 1:2 randomisation ratio for the control and intervention arms, respectively. We also extended trial recruitment window to allow for delays related to pandemic measures. We have also planned for an internal pilot with the first 25–30 patients that would allow us to test and refine procedures before launching the full RCT. With the shift of healthcare and health information online, it may useful to consider leveraging on technology to deliver these services online, especially when participants may have access to internet and/or smart devices.[89] E-health interventions can transcend the service barriers and potential disruptions due to pandemic, hence if HED-Start is proven effective, we will consider adaptations to allow for virtual delivery and wider dissemination across all dialysis centres in Singapore.

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