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Improving Distress in Dialysis (iDiD): A feasibility two arm parallel randomised controlled trial of an online cognitive behavioural therapy intervention with and without telephone support for psychological distress in haemodialysis patients

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4 **Improving Distress in Dialysis (iDiD): A feasibility two arm parallel**
5 **randomised controlled trial of an online cognitive behavioural**
6 **therapy intervention with and without telephone support for**
7 **psychological distress in haemodialysis patients**
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Abstract

Introduction: Psychological distress is common in End-Stage Renal Disease (ESRD) and is associated with poorer health outcomes. Cognitive-behavioural therapy (CBT) is recommended in UK clinical guidelines for the management of depression in people with long-term conditions (LTCs). Online CBT based treatments offer a pragmatic solution for under-resourced renal services. However the application CBT treatment principles to the psychosocial needs of ESRD patients requires a degree of tailoring to ensure appropriate application. This study seeks to explore the feasibility and acceptability of implementing a two-arm parallel randomised controlled trial (RCT) of online CBT with (intervention arm) and without (control arm) therapist support to improve psychological distress in haemodialysis patients.

Methods: Patients will be screened for depression and anxiety whilst attending for their haemodialysis treatments. We aim to recruit sixty adult haemodialysis patients who meet criteria for mild to moderately severe symptoms of depression and/or anxiety will be individually randomised using a computer generated 1:1 sequence ratio with allocation concealment by automated email to patients on completion of their online baseline questionnaire. Patients will be randomised to either online CBT with telephone support from a therapist (intervention arm) or online CBT with no telephone support (control arm). Outcomes include feasibility and acceptability data on rates of recruitment, randomisation, retention, and treatment adherence. We will also explore change in self-report measures of depression (Patient Health Questionnaire-9), anxiety (Generalised Anxiety Disorder-7), quality of life (Euro-QoL), service use (client service receipt inventory), and illness cognitions (brief illness perception questionnaire). A qualitative process evaluation will also be conducted.

Ethics and dissemination: An NHS research ethics committee approved the study. Data from this study will provide essential information for the design and testing of further interventions to ameliorate distress in dialysis patients and will be of interest to patients the renal multi-disciplinary team.

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Keywords: End-stage renal disease, haemodialysis, cognitive-behavioural therapy, psychological distress, online therapy, online treatment, computerised therapy

Introduction

End-stage renal disease (ESRD) is a chronic condition that permanently affects kidney function (1). Without treatment with renal replacement therapy (e.g. dialysis or transplantation) a person's physical health would rapidly deteriorate because of the build-up of toxins and waste products in the body (2). In 2013, 56,940 adults in the UK were receiving renal replacement therapy (3) accumulating direct physical health care costs of £27,000 per patient, per year (4). The treatment of ESRD is not only costly but burdensome for patients, requiring adherence to dialysis regimens, prescribed medications, diet and fluid restrictions, and regular attendance at health care appointments (5).

Psychological distress is common in ESRD, with an estimated prevalence of 39% among people in receipt of dialysis (6). When psychological distress co-occurs alongside ESRD higher rates of mortality (7) and health care utilisation (8) are observed. The application of UK clinical guidelines for psychological distress management in chronic physical health problems specifically to people with ESRD is fraught with difficulties (9). First, the safety and efficacy of pharmacotherapy in managing psychological distress among people with ESRD remains unclear, because of a lack of robust randomised controlled trials (10). Second, whilst talking therapies likely offer a safer alternative to pharmacotherapy because they target non-biological causal pathways, reducing the potential for contraindicated treatments, their efficacy in the ESRD population is largely unknown. Only two small scale, non-UK based, randomised controlled trials (RCTs) have examined the efficacy of cognitive behavioural therapy (CBT) relative to usual care among haemodialysis patients (11, 12). Both trials found CBT was effective in reducing psychological distress. These findings are consistent with larger scale RCTs of CBT treatments for depression in people with coronary heart disease (13).

However the NHS has limited resources to allow the demand for CBT therapist time to be met adequately. A practical approach to address this problem is to implement a stepped care health service delivery model (14). Within this model a person suffering from psychological distress is initially offered the "least restrictive" evidence based treatment

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3 available, for example, guided self-help treatment materials in the form of treatment
4 manuals or computer therapy packages. Individuals begin their treatment with low-intensity
5 interventions unless their distress is deemed too severe to benefit from the type of minimal
6 intervention offered. The concept “least restrictive” means that there is decreased
7 treatment burden for patients, but equally health services can treat a larger volume of
8 patients, by offering less intensive treatment interventions. If necessary a patient is
9 “stepped up” to receive more intensive treatments to manage their distress after the initial
10 low-intensity treatment.
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18 Guided self-help CBT treatments are effective in the management of psychological distress
19 in people with (15) and without co-morbid physical health conditions (16). Furthermore, on-
20 line/computerised self-help resources offer a greater degree of personalisation, presenting
21 only information that is relevant to the needs of the patient based on their responses to
22 specific questions. This allows better management of informational needs and encourages
23 active engagement, thus fostering a sense of personal control from the patient (17). Indeed,
24 in people without physical health conditions, online/computerised guided self-help
25 treatments have largely demonstrated equivalence with face-to-face psychological
26 interventions in terms of their clinical effectiveness (depression and anxiety) (18) and
27 degree of adherence to treatment sessions (19). The degree of efficacy of online self-help
28 interventions for improving symptoms of distress among people with chronic physical
29 health conditions remains mixed (20). Overall, self-help interventions that included a CBT
30 treatment model effectively reduced distress (20).
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42 However there are a number of factors that determine the efficacy of online/computerised
43 self-help treatments. One moderating factor is whether support is provided by a health care
44 professional. Dovetailing online/computerised self-help treatments with support from
45 health care professionals improves outcomes and prevents treatment drop-out (21, 22). The
46 type of support provided is also important. Studies that provided technical/administrative
47 support to overcome practical barriers with online/computerised self-help treatments have
48 demonstrated poorer clinical outcomes compared with studies that used qualified
49 therapists or health care professionals trained to deliver psychological treatments (22).
50 However, the difference of effect was statistically non-significant but this was likely because
51 of an absence of statistical power not an absence of effect per se. A recent RCT explored the
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3 efficacy of online CBT with weekly technical/motivational support telephone calls from a
4 non-clinician for the management of depression and compared it with usual GP care (23). Its
5 findings confirmed that providing patients with access to online CBT with only technical
6 support had no added benefit on depression outcomes compared with GP usual care.
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11 It seems likely that access to a skilled therapist is especially important in the context of co-
12 morbid mental and physical health conditions because of the potential for treatment
13 antagonisms, whereby the effective management of a person's mental health has the
14 potential to dysregulate the management of physical health or vice versa (24). However,
15 individual differences can also determine a person's perceived need for support from a
16 health care professional. A qualitative meta-synthesis of online/computerised therapies for
17 depression and anxiety identified conflicting user experiences (25). Positive experiences
18 included feelings of empowerment, independence, and anonymity, whilst negative
19 experiences included perceived treatment burden from the online/computerised
20 treatments and feelings of isolation because of a lack of human interaction.
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30 Given that the evidence points to the efficacy of online/computerised treatments with
31 therapeutic support for the management of psychological distress in people with and
32 without physical LTCs; it remains uncertain whether these findings apply to the
33 management of psychological distress in UK NHS haemodialysis treatment settings. An
34 online CBT treatment intervention designed to manage psychological distress in people on
35 haemodialysis has the potential to offer both a pragmatic and effective treatment for the
36 management of psychological distress in ESRD. This study seeks to explore the feasibility
37 and acceptability of implementing a two arm parallel RCT of online CBT with (intervention
38 arm) and without (control arm) therapist support to improve psychological distress in
39 people receiving haemodialysis treatments within a stepped care health service delivery
40 framework.
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49 *Background to the study*

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51 The development of the improving distress in dialysis (iDiD) online CBT treatment involved a
52 multi-disciplinary team of health psychologists, clinical psychologists, psychiatrists,
53 nephrologists, and six patient and public involvement representatives. The preliminary
54 content of the website was initially determined by self-help resources used to manage
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3 adjustment outcomes in LTCs implemented in previous trials by one of our authors (RMM)
4 (26-28). In addition, a literature review of the correlates of distress in dialysis was used to
5 develop an ESRD specific CBT treatment model (29). The content of each online treatment
6 session was first drafted on paper and reviewed by the research team. Once approved by
7 the research team, patient representatives provided feedback on the relevance and ease of
8 understanding of the information and CBT intervention techniques described in each of the
9 treatment sessions. Any issues raised within each session were incorporated into the
10 development of subsequent sessions. The informational and CBT content was then
11 uploaded onto an online platform using LifeGuide software (30). Advice was given from (LY)
12 regarding how to tailor information and CBT intervention techniques shown to individuals
13 based on their responses to specific questions/options on the website. This allowed the
14 generation of an interactive online therapy tool that was responsive to the needs of
15 patients. The presentation and navigation through the website was tested using patient
16 representatives and “think-aloud” techniques. This process occurred iteratively so that
17 comments on early sessions could be incorporated into the design of subsequent sessions.

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The website includes a total of seven sessions. The content of each session is summarised in
Table 1. For more detailed information about the cognitive-behavioural content of the
sessions see our distress in dialysis CBT treatment model (29). Patients are encouraged to
complete one session per week and each session was designed to last approximately one
hour in duration. In brief, the first two sessions are psycho-educational providing specific
information about ESRD, its management and the potential for this to impact on mood.
Patients generate their own personal model of distress consisting of ESRD specific triggers,
feelings, thoughts, behaviours, and physical symptoms. The remaining four sessions target
components from the patients self-generated personal model of distress including:
implementing positive coping strategies for dealing with emotions (e.g. acceptance,
exposure, expression), thought challenge techniques, problem solving, behavioural
activation, sleep, and assertiveness skills training for managing difficult social relationships.
At the end of each online session, patients are encouraged to set a goal to complete over
the next week. A variety of goals are displayed relevant to the content shown in the online
session the patient is working on. After selecting a goal, the patient is encouraged to make
an action plan. All goals are stored to a specific “My tasks” area on the website. Each time

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3 the patient logs onto the website they are asked to review their progress with their goals.
4 The “My tasks” function allows patients to track their progress as they work through the
5 website and store any information they have found particularly useful. The final session
6 concentrates on relapse prevention where patients reflect on the skills they have learnt
7 over the six sessions and generate action plans to sustain these behaviours moving forward.
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10 11 12 **Objectives**

13 The following aims will be addressed as part of the feasibility and acceptability study of a
14 parallel RCT of online CBT with therapist led telephone support vs online CBT without
15 telephone support, delivered within a stepped care framework among outpatient
16 haemodialysis patients with co-morbid psychological distress.
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- 22 1. To assess the feasibility and acceptability of screening all patients who attend for
23 haemodialysis. Patients will be screened for depression and anxiety using
24 standardised measures presented on iPads. The presence of psychological distress is
25 often not identified by non-mental health trained clinicians (31). Implementing
26 screening questionnaires for psychological distress in medical settings can promote
27 its detection (32) and ultimately the provision of mental health care. We will
28 quantify number of people who agree to be screened.
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- 30 2. To explore rates of recruitment and retention into the trial.
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- 32 3. To examine willingness to be randomised to either the intervention arm (with
33 telephone support) or control arm (with no telephone support) by recording
34 participant reasons for non-consent into the study (if disclosed).
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- 36 4. To explore the level of adherence to online treatment sessions and telephone
37 support calls (intervention arm only).
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- 39 5. To explore the potential efficacy of an on-line intervention with therapist led
40 telephone support in reducing psychological distress when compared with website
41 alone to inform the planning of a future full-scale trial to detect clinically meaningful
42 change in psychological distress outcomes.
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6. To examine if change in quality of life differs between the intervention group (online intervention plus therapist led telephone support) and control group (online intervention only)
7. To provide a preliminary assessment of the cost-effectiveness of the intervention.
8. To examine the pre-post difference in ESRD illness cognitions and whether their effect differs between the intervention and control arm (online intervention only).
9. To qualitatively explore patient perceptions of the acceptability and usability of the website and telephone support calls and identify areas of improvement for future interventions.

Methods

Design

A two parallel armed randomised controlled trial (RCT) with participants randomised using a 1:1 ratio computerised algorithm at the level of the individual and a nested qualitative study.

Setting and participants

Participants will be recruited from haemodialysis units at Guy's and St Thomas' hospital (London, UK). Participants will be eligible for inclusion if:

- 1) Aged 18 years or over and receive hospital haemodialysis three-times weekly.
- 2) They have mild to moderately severe depressive symptoms (based on PHQ-9 (33) scores of 5 to 19; a self-report measure of depression) and/or presence of mild to moderate anxiety symptoms (based on GAD-7 (34) scores of 5-14).
- 3) They speak English sufficiently well to engage with screening tools.
- 4) They have a basic understanding of how to use the Internet and an email address.

Participants will be ineligible if:

- 1) They currently receive active treatment for depression and/or anxiety. We consider active treatment, as any current psychological treatments (talking therapies) or receipt of a new anti-depressant and/or anti-anxiety medication. A medication is considered new if commenced three months prior to the completion of the depression and anxiety screening questionnaire. A participant will become eligible

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3 for the study once three months has elapsed from commencing their anti-depressant
4 and/or anti-anxiety medication.

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7 2) They have a severe mental health disorder, for example, psychosis, bi-polar disorder.
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9 3) They have active suicidal thoughts, as indicated by a score of greater than one on the
10 depression PHQ-9 item "Thoughts that you would be better off dead, or of hurting
11 yourself".
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13 4) They have evidence of addiction to alcohol or drugs.
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16 A participant will be withdrawn from the study if:

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19 1) There are safety concerns in relation to their physical or mental health.
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21 2) The participant chooses to withdraw from the study.
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23 3) A patient's level of psychological distress deteriorates.
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25 **Flow of recruitment and participant timeline**

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27 Participants will be identified for inclusion using web-based screening questionnaires
28 routinely used as part of the Integrating Mental and Physical healthcare: research, training
29 and services (IMPARTS) initiative at Guy's and St Thomas' hospital (35). Face-to face
30 screening will occur by a renal dialysis nurse or a member of the research team. Participants
31 consenting to the screen will be assessed for depression and anxiety using the PHQ-9 (36)
32 and GAD-7 (34) respectively. The PHQ-9 is a nine item self-report questionnaire deemed
33 acceptable for the identification of depression in medical care settings, including specialist
34 settings (32). Likewise, the GAD-7, is a self-report seven item questionnaire with evidenced
35 criterion validity for the detection of generalized anxiety disorder (34). The patient will
36 complete the web-based questionnaires either alone or with the assistance of a renal
37 nurse/researcher. Whilst completing the screening questionnaire, patients will be asked to
38 give their permission (yes/no) for a member of the research team to contact them about the
39 present study.
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51 Results from the screening questionnaires are uploaded onto the patient's electronic
52 medical record, which will be checked by the nursing team/researcher for immediate risk.
53 Risk is defined as a score of greater than one on the depression PHQ-9 item "Thoughts that
54 you would be better off dead, or of hurting yourself". If suicidal ideation is detected then a
55 risk assessment will be performed to determine the immediacy of referral to either liaison
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3 psychiatry or renal clinical psychology. Level of risk will be assessed in line with the IMPARTS
4 risk assessment protocol. This includes enquiring about degree of suicidal ideation and level
5 of hopelessness, whether active plans are present, enquiring about the patient's history of
6 suicidal attempts, recent life stressors, protective factors, and degree of social support. The
7 outcome of the risk assessment will be immediately discussed with either the renal clinical
8 psychologist or liaison psychiatrist and a management plan will be put into place.
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12 All anonymised screening results will be securely emailed from the IMPARTS database to the
13 iDiD research team, on a weekly basis. A stratified stepped care model, according to the
14 criteria outlined in Figure 1 will be applied to the anonymised data to identify potentially
15 eligible participants for the study. The stratified stepped-care approach assigns individuals
16 to treatments of varying intensity based on the severity of their symptoms (37). PHQ-9
17 scores within the range of 5-19, are considered indicative of mild to moderately severe
18 symptoms of depression (36). Likewise, GAD-7 scores within the range of 5 to 14 indicate
19 the presence of mild to moderately severe anxiety (34). Individuals with mild to moderately
20 severe symptoms of depression and/or anxiety will be considered appropriate for treatment
21 with the iDiD online CBT treatment and for inclusion in this study. Individuals with moderate
22 to severe depression (PHQ-9 score ≥ 20) and/or anxiety (GAD7 score ≥ 15) or individuals with
23 evidence of current suicidal ideation are considered inappropriate for the iDiD online CBT
24 intervention. These patients will be referred and managed by either the renal clinical
25 psychology team or liaison psychiatry. Finally, any individuals who are identified as having
26 current suicidal ideation and severe depression (PHQ-9 score ≥ 20) will receive an urgent
27 referral to liaison psychiatry.
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32 Individuals who meet the criteria for mild to moderately severe symptoms of depression
33 and/or anxiety will have their data de-anonymised providing they give us consent to contact
34 them about the study. These potential participants will be screened against the remaining
35 inclusion/exclusion criteria during weekly referral meetings with the research and clinical
36 team. If they remain eligible then a researcher will approach the participant whilst they
37 attend for dialysis to explain the study with the participant information sheet. Participants
38 will be given a minimum of 24 hours to establish if they would like to take part.
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3 All patients with mild to moderately severe symptoms of depression and/or anxiety who
4 either: i) do not meet our remaining study inclusion criteria, ii) choose not to consent into
5 the study, or iii) do not provide consent for us to approach them about the study, will be
6 provided with the option of receiving usual care follow-up from the renal clinical psychology
7 team. Usual care includes a face-to-face clinical assessment followed by a tailored
8 psychological treatment intervention. Patients who decline psychological treatment will be
9 issued with the renal clinical psychology service contact details and will be provided with
10 advice on how to contact the team should they become concerned about their emotional
11 health in the future.
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20 As discussed above, patients who screen positive for moderate to severe symptoms of
21 depression and/or anxiety (PHQ-9 score ≥ 20 and/or GAD7 score ≥ 15) will receive an
22 automatic referral to the renal clinical psychology team. If upon clinical assessment by the
23 renal clinical psychologist a moderate to severely depressed and/or anxious patient is
24 deemed appropriate for the iDiD self-help study, then they will be “stepped down” for
25 approach by the iDiD research team. Likewise, the research team will be informed by the
26 renal clinical psychology team of any patients who meet the iDiD study inclusion criteria and
27 declare an interest in the study despite initially stating during screening that they did not
28 want to be contacted by the study team.
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Participants who consent to take part in the study will be issued with an iDiD study
identification number. A researcher will attend the dialysis unit and help the patient to sign-
up to the iDiD online CBT treatment using an iPad. At sign-up participants will be asked to
enter their personal email address and select a password for use each time they logon. At
the point of sign-up participants will also be asked to enter their NHS number (supplied to
them by the researcher) to ensure that multiple iDiD accounts are not registered by the
same participant. Participants will then receive a confirmatory email with a link to the iDiD
website. After signing up, participants will complete the baseline questionnaires online. If
baseline questionnaires are not completed, then participants will receive two reminder
emails and an assistance based telephone call/visit at the dialysis unit. Participants will be
informed of their randomisation process outcome immediately after completing the online
baseline questionnaire. Participants will also receive an email confirming their treatment
allocation. We anticipate the participant’s journey through the study will last approximately

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3 six months as summarised in Figure 2. We expect a period of one month to elapse from the
4 point of screening to randomisation. Once participants are randomised, both groups will be
5 able to access the iDiD website for a period of 12 weeks before being prompted to complete
6 the follow-up questionnaires via email. The email will also advise participants that their
7 access to the iDiD website is ending within a few weeks and to print off any information
8 they have found helpful from the “My tasks” tab of the website. Two reminder emails and
9 an assistance based telephone call/visit will occur over a period of three weeks if the follow-
10 up questionnaires remain incomplete. After 20 weeks participants will receive an email
11 thanking them for their participation in iDiD study. Access to the iDiD website will no longer
12 be available after this time. On completion of the three months follow-up questionnaires a
13 subsample of participants will be asked to complete a qualitative interview. We will follow-
14 up participants for a period of approximately six months post their randomisation date to
15 complete the interview.
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26 27 **Randomisation, allocation concealment, and blinding**

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29 Participants will be randomised to iDiD online CBT plus telephone support or iDiD online CBT
30 only condition using Lifeguide software (a computerised random number generator with a
31 1:1 ratio). Because the randomisation sequence is automated by Lifeguide in real-time the
32 allocation sequence is concealed from researchers. All baseline questionnaires will be
33 completed online prior to randomisation. Participants will be randomised at the individual
34 level. The trial co-ordinator will also receive an automated email informing them of the
35 outcome of the randomisation procedure to identify participants who require telephone
36 support calls during the trial. The researcher conducting the qualitative interviews will also
37 be unblinded at follow-up to ensure that appropriate questions are asked in relation to
38 telephone support calls. The statistician will remain blinded to treatment allocation.
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47 *Trial Intervention*

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49 All participants have access to the iDiD online CBT website (treatment content outlined in
50 Table 1 and described in detail in our ESRD CBT Treatment Model (29)). Participants will be
51 advised in the participant information sheet to logon to the website once a week.
52 Participants will also receive weekly reminder emails to encourage engagement with the
53 website. iPADs will be available for participants to use during their dialysis sessions.
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iDiD online CBT website plus therapist led telephone support (Intervention arm)

Participants in the intervention arm of the trial will receive three 30 minute telephone support calls at weeks two, four, and six from a psychological wellbeing practitioner and a member of the research team (JH) who has a PhD in health psychology and has trained and worked as a psychological wellbeing practitioner (PWP). Psychological wellbeing practitioners typically work in primary care mental health service teams as part of the UK IAPT initiative (38). PWPs are trained to deliver low-intensity CBT based treatments including: cognitive restructuring, behavioural activation, problem solving, medication management, exposure therapy, and sleep management. The purpose of the telephone support calls are to promote engagement with the website and support the patient in collaboratively developing goals to work on using the resources and information available to them on the website. At the start of each telephone call the PWP will set an agenda with the participant and end the telephone call with a summary of the telephone support call and a shared goal for the participant to work towards. The first telephone support call is scheduled for when the participant should have completed online their own personal model of distress. The PWP will develop a shared understanding of the participants source of distress, provide empathy, reinforce with the participant the relationships between thoughts, feelings, and behaviours, and inform participants of the content the website which is likely most applicable to them as they continue to move forward with the website. The PWP and patient will develop a goal to work towards prior to their next telephone call.

The second telephone support call will provide an opportunity for the PWP to review with the participant their progress on their self-generated goals, work through a particular cognitive-behavioural intervention technique selected by the patient, and close the session with a shared goal to work towards with the help of the website in advance of the final telephone support call. The final telephone support call will follow a similar format to that of the second call except the telephone session will end with a relapse prevention plan. The plan will be generated collaboratively with the patient. All telephone support calls will be audio-recorded to provide intervention fidelity checks and for self-reflection during clinical supervision.

Clinical supervision

JH was trained to deliver the telephone support calls using role played sessions with feedback from RMM. Ongoing supervision will be provided by a renal clinical psychologist (AC). During supervision audio-recorded sessions will be listened to. Shared reflection on the PWP's telephone session will be discussed in line with the core competency framework for delivering psychological therapies in long-term conditions (39). Shared goals will be identified for the PWP to work towards over the course of the study. Supervision will also be an opportunity for case management. The PWP will discuss their proposed treatment plan in response to the first telephone support call and degree of patient progress at each supervision session. If a patient needs to be stepped up to receive more intensive psychological treatments then this will be initiated by the research team and managed by the renal clinical psychologist.

iDiD online CBT website with no telephone support (control arm)

Participants allocated to the control arm of the study will receive their usual renal care in addition to having access to the website. Usual care for individuals with ESRD managed with haemodialysis includes attending for dialysis three times per week for up to five hours at a time. Participants can be referred or self-refer into the renal clinical psychology service or primary care mental health service if their symptoms of depression and/or anxiety increase. We will ask participants in the three-month follow-up questionnaire whether they have commenced any new treatments for mental health since starting the study and this will be statistically accounted for.

Outcomes

Data collection and feasibility outcomes

Because this is a feasibility study our primary focus is to collect data on the feasibility and acceptability of the trial design and intervention by collecting descriptive data on *recruitment and retention rates and willingness to be randomised* according to CONSORT trial guidelines (40). We will also examine *adherence* to the online intervention and telephone support calls (intervention arm only). The degree of adherence to the online intervention will be automatically recorded by the Lifeguide software. We will calculate descriptive values for the mean number of sessions completed, the number of participants

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3 who complete all sessions, the number of participants who complete 80% or more sessions,
4 and the number of participants who complete each session (e.g. session 1, 2, 3 etc). Degree
5 of adherence to the telephone call (intervention arm only) will be recorded by the
6 psychological wellbeing practitioner. The following values will be calculated: mean number
7 of telephone calls completed, number of participants who complete all telephone calls,
8 number who complete 1 or more telephone call, number of participants who complete
9 telephone sessions 1, 2, and 3 respectively, and mean duration of telephone calls across all
10 three telephone support calls. In addition to a qualitative interview (described below)
11 patients will be asked to self-report their experience of using the iDiD website at three
12 months follow-up. The open-ended questions will enquire about: i) how useful they found
13 the iDiD website and ii) whether they found the website easy to use. Participants will also be
14 given the option to add any further comments.
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25 Self-reported patient outcomes will also be collected via the iDiD website at baseline and
26 three months follow-up. The assessment schedule completed by patients is summarised in
27 Table 2 and described below.
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31 • Continuous self-report measure of depression: PHQ-9(36) (described in detail above,
32 scale range from 0 to 27, high scores indicate greater depressive symptoms)
- 33
34 • Continuous self-report measure of anxiety: (GAD-7) (34) (described in detail above,
35 scale 0 to 21, high scores indicate greater anxiety symptoms).
- 36
37 • The five item EuroQoL (EQ-5D) (41) includes a five item measure of health status
38 across the following domains: mobility, ability to self-care, ability to continue with
39 activities (i.e. work, social life), pain, and anxiety and depression. In addition it has a
40 visual analogue scale ranging from 0 to 100 where a person is asked to rate their
41 overall health. The EQ-5D is recommended by NICE for use in cost-effectiveness
42 evaluations (42).
- 43
44 • The Client Service Receipt Inventory (CSRI) (43) collects retrospective data on service
45 use across the following five domains: i) background and client information (i.e.
46 hospital admissions and discharge, frequency of GP visits, medications), ii)
47 accommodation and living situation, iii) employment history, earnings, and other
48 personal resources, iv) service receipt (i.e. hospital appointments, home help), and v)
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3 receipt of informal care from caregivers. This information will be used in our cost-
4 effectiveness evaluations.
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7 • The brief illness perception questionnaire (BIPQ) (44) will assess participants self-
8 reported beliefs about their ESRD and will provide an indication of whether
9 participants beliefs about their ESRD change in response to clinical intervention. This
10 information will be assessed at baseline and follow-up.
11
- 12 • Satisfaction with care will be evaluated using a 2-item scale that asks participants to
13 rate their degree of satisfaction with the care they receive for their physical and
14 mental health on a five-item Likert response scale. This information will be assessed
15 at baseline and follow-up.
16
- 17 • Serious adverse events will be directly enquired about using self-report at follow-up
18 only according to good clinical practice guidelines. Participants will be asked whether
19 they have experienced any adverse events since starting the study choosing from a
20 list of five options. If participants indicate they have experienced adverse events
21 then they will be asked for details. In addition participants will be asked if they have
22 experienced any adverse health effects since starting the study and encouraged to
23 elaborate where needed.
24
- 25 • Treatments for depression and/or anxiety: Two brief self-report questions at follow-
26 up will ask participants if they have received any pharmacological or psychological
27 treatments for their depression and/or anxiety in addition to the iDiD website since
28 starting the study.
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33 *Socio-demographic and clinical characteristics*

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35 Socio-demographic characteristics including: gender, age, ethnicity, home environment
36 (marital status, housing situation, number of dependents) and level of education will be
37 collected at baseline only via self-report. Likewise, clinical characteristics including: dialysis
38 vintage and treatment history for depression and anxiety will be self-reported by patients at
39 baseline.
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43 Number and type of co-morbidities will be extracted from notes at baseline only. The
44 following clinical outcomes and covariates will be extracted from notes at baseline and
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3 follow-up: Kt/V (dialysis treatment adequacy), haemoglobin, serum albumin, C reactive
4 protein, serum potassium levels, interdialytic weight gain, serum phosphate levels.
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7 8 **Qualitative interviews**

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10 Qualitative interviews with a sub-group of participants over the phone will be conducted
11 post-intervention (three months) by a researcher who has not been involved in their
12 treatment. These interviews will explore whether the intervention met patient expectations,
13 positive and negative opinions about the website, whether patients felt they gained any
14 benefit from using website, its personal relevance to them, and its acceptability as a
15 treatment. A minimum of ten participants will be purposively sampled across a range of
16 socio-demographic and clinical characteristics (e.g. treatment group, age, gender, ethnicity,
17 dialysis vintage, degree of adherence to the intervention, degree of improvements in
18 outcomes from the intervention). Interviews will continue until data saturation occurs. The
19 outcomes of these qualitative interviews will help to revise our theoretical understanding of
20 distress in dialysis and update the content of the intervention accordingly, in line with
21 current medical research guidelines for process evaluations (45). Interviews will be
22 transcribed verbatim and an inductive thematic analysis will be performed.
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33 **Sample size**

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35 The aim of this study is to explore the feasibility of implementing our trial procedures and to
36 inform a power calculation for a future randomised controlled trial. We have calculated the
37 sample size required based on the margins of error associated with the recruitment. The
38 approximate size of the Guy's and St Thomas' dialysis population is 600 patients, in which
39 we expect to be able approach 400. Assuming a conservative uptake rate of 50%, 200
40 patients will be screened with approximately 40% meeting the inclusion criteria (the
41 estimated prevalence of depression symptoms in HD patients; see Palmer et al, 2013). If we
42 assume 50% of those eligible will consent to be randomised a sample size of approximately
43 66 would allow us to estimate the true population consent rate with a 5% margin of error
44 and a 95% confidence level.
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53 **Analysis plan**

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55 To examine the feasibility and acceptability of our screening, recruitment, retention, and
56 randomisation process (objectives 1-3), we will quantify the flow of participants through the
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3 study using frequencies and percentages in accordance with the consort flow diagram (40)
4 shown in Figure 2. We will also record and quantify reasons for non-consent, exclusion, and
5 drop-out for each stage of the study. We will examine degree of adherence to the
6 intervention and telephone support calls (where applicable) using descriptive statistics
7 (objective 4).
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12 We will also perform an *exploratory* intention to treat mixed models analysis blind to
13 treatment group on the following self-report outcomes at three months follow-up:
14 depression, anxiety, and quality of life (objective 5 & 6). Variability in these patient
15 outcomes will help to inform a future power calculation for a full-scale trial.
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20 Service costs will be calculated by combining service use data with appropriate unit costs
21 (46). These will be added to the costs of the intervention which will be based on
22 development costs and the time spent providing telephone support. Costs will be compared
23 between the two groups and cost-effectiveness assessed by combining the costs with the
24 primary outcome measures and quality adjusted life years (QALYs) in the form of
25 incremental cost-effectiveness ratios (ICERs). Uncertainty around the ICERs will be
26 addressed using cost-effectiveness planes and acceptability curves (objective 7). We will
27 also perform an exploratory process analysis using intention to treat mixed models to
28 establish whether illness cognitions changed in response to the online intervention and
29 whether differences occurred between the intervention and control group (objective 8).
30 Qualitative interviews will be transcribed verbatim and analysed using thematic analysis to
31 allow the feasibility and acceptability of the online intervention and telephone support calls
32 to be explored (objective 9).
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44 **Ethics**

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47 This study has ethical approval from the NHS research ethics committee (14/LO/1934) and is
48 sponsored by King's College London.
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50 **Data collection and management**

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52 The IMPARTS screening interface, developed by Teleologic Ltd, is web-based and installed
53 on the server configuration already in use at King's College Hospital NHS Foundation Trust
54 (KCH) for Teleologic specialty systems and has been extended to Guy's & St Thomas'
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3 Hospitals NHS Foundation Trust. The patient logs on to the system with their unique
4 Hospital Number. Their screening results are outputted to the documents folder of the
5 Electronic Patient Record via the most secure wifi network within each NHS Trust. In
6 addition, the system writes to a SQL Server database with documented table schema that is
7 available for reporting and interrogation within the acute trusts' firewalls.
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12 All quantitative outcomes are measured via online questionnaires that participants will
13 access via iDiD website. The information is stored on a secure server associated with the
14 Lifeguide program at the University of Southampton. The website prompts the participant
15 when data is missing. Study data can only be downloaded from the server by members of
16 the research team who are granted password access. All data will be confidentially stored in
17 accordance with the data protection act (47) and King's College London data management
18 procedures.
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25 26 **Formal committee**

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28 A trial management team will meet regularly to discuss the overall running of the study
29 including: rates of recruitment, adherence to the protocol, safety and confidentiality of
30 patients. All serious adverse events related to the study will be reported to the study
31 sponsor, ethics committee, and, Guy's and St Thomas' research and development
32 department.
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37 38 **Discussion**

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40 Psychological distress is common in people with ESRD. However, studies examining the
41 efficacy of either pharmacological or psychological interventions for the management of
42 distress in dialysis are limited. Likewise, access to psychological treatment interventions
43 tailored to the specific psycho-social stresses associated with ESRD is problematic. An online
44 CBT treatment designed specifically to manage distress in dialysis, offers a pragmatic
45 solution to under-resourced health services, which are advised to offer integrated mental
46 and physical health care treatments.
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54 This is the first study to examine whether it is feasible to implement a RCT of online CBT
55 with telephone support vs online CBT without telephone support within a stepped care
56 framework, to secondary care haemodialysis patients with co-morbid distress. Indeed, it will
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3 identify unique challenges that occur in the dialysis population in the recruitment and
4 retention of patients for a treatment intervention designed to manage their distress
5 alongside an already burdensome ESRD treatment regimen. Likewise, the study will be able
6 to simultaneously examine the acceptability of this treatment to patients in terms of
7 whether its content was relevant and useful. In addition, the utility of the online mode of
8 delivery with or without telephone support will be examined. We anticipate that the results
9 of this trial will substantially inform the design of a future large scale trial powered to detect
10 the efficacy of online CBT treatments for the management of distress in dialysis.
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17 **Trial Status**

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19 The study commenced recruitment in February 2015. Recruitment will continue until
20 February 2016 with the last patient's follow-up in May 2016.
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24 **Funding:** This work was funded by Guy's and St Thomas' charity (GSTT, grant number:
25 EFT130206).
26
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28 **List of abbreviations**

29
30 CBT, Cognitive behavioural therapy; ESRD, End-stage renal disease; ICERS, incremental cost-
31 effectiveness ratios; iDiD, Improving distress in dialysis; QALYs, Quality Adjusted Life Years;
32 RCT, Randomised Controlled Trial
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37 **Competing Interests:** None to declare
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40 **Authors Contributions:**

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42 Study design: All authors
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46 Intervention development: JH, RMM, DG, AC, LY, JC:
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50 Statistical analysis plan: PM, JC.
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53 All authors contributed to writing the protocol.
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Proposed referral pathway Stepped Care model for distress in ESRD

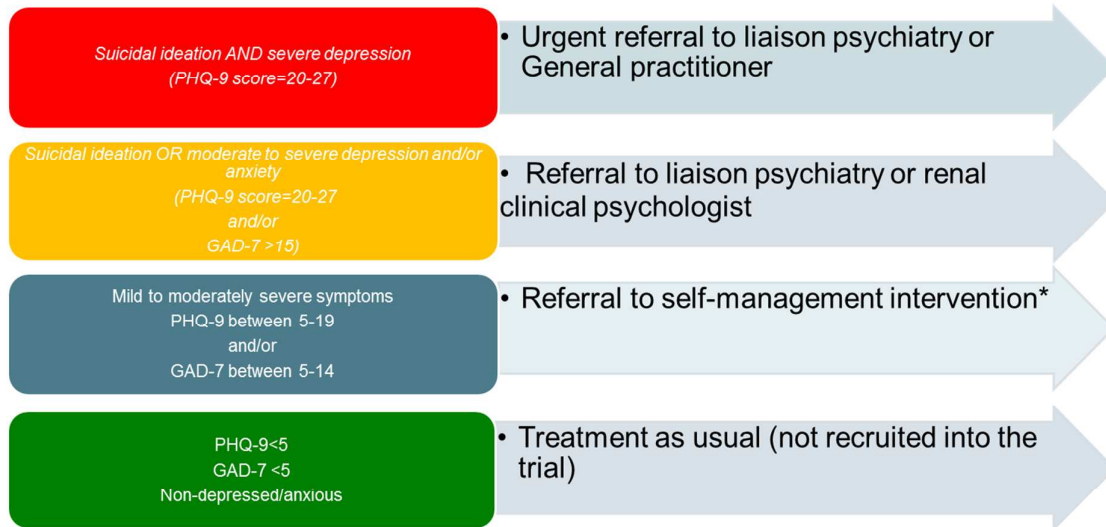


Figure 1: Stratified stepped care referral pathway for managing psychological distress among individuals attending for haemodialysis

Figure 2: Flow of participants through the study

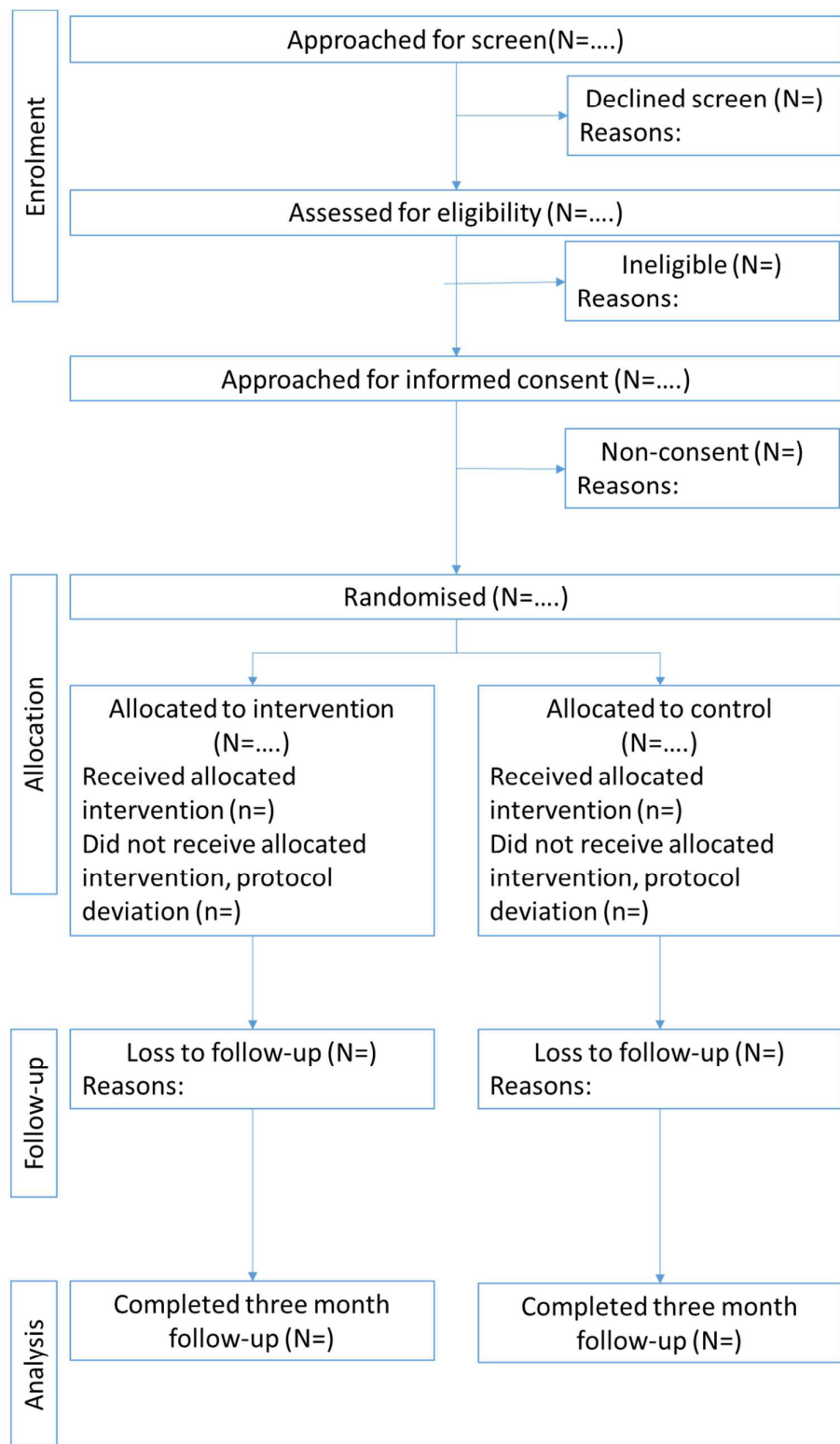


Table 1: Summary of iDiD online treatment sessions

Session	Content
1. What is end-stage renal failure?	<p>-Psycho-education including information about:</p> <ul style="list-style-type: none"> -ESRD and its treatment -Expectation management about the effectiveness of dialysis treatments and its psycho-social consequences. -Explaining the rationale for specific ESRD treatments (i.e. improving physical health) and psychological interventions (i.e. improving emotional health)
2. Why do I feel distressed?	<p>-Recap on information learnt about in session 1</p> <p>-Self-generation of a personal model of distress. Patients self-identify their own vicious cycle to improve their understanding of the inter-relationships between ESRD specific stressors (triggers), feelings, thoughts, behaviours, and physical symptoms.</p> <p><i>Between session task:</i> Recap on the content of session 2 by re-reading the session.</p>
3. Dealing with my negative feelings	<p>-Recap on information learnt about in session 2</p> <p>-Recap on the reinforcing relationship between unhelpful coping behaviours and the maintenance of psychological distress.</p> <p>-Examples provided of positive emotion regulation strategies including: acceptance, relaxation, expression, exercise, behavioural activation, behavioural experiments, graded exposure, tips for improving the quality of sleep.</p> <p><i>Between session task:</i> Selection of a helpful coping</p>

	strategies for managing negative emotions before completion of next online session.
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<p>1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21</p> <p>4. Tackling unhelpful thoughts about end-stage renal disease</p>	<p>-Recap on information learnt about in session 3</p> <p>-Provide examples of unhelpful thoughts typical in people with ESRD, information about the identification of unhelpful thoughts using thought records, and provide examples of how to challenge and gradually alter unhelpful thinking styles.</p> <p><i>Between session task:</i> Encourage patients to continue working on their goals from session three and complete a thought record sheet if relevant to their personal needs.</p>
<p>22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45</p> <p>5. Goal setting and problem solving</p>	<p>-Recap on information learnt about in session 4.</p> <p>-Explain the rationale for “SMART” goals and how to use the technique. Link with activity monitoring and action planning.</p> <p>-Explain the seven steps to problem solving technique. Use to foster confidence that participants are implementing the best possible solution to challenging situations.</p> <p><i>Between session task:</i> Encourage participants to continue working on their goals from previous sessions that they find useful and relevant and if feasible implement: i) “SMART” goal techniques, ii) action planning, or iii) seven steps to problem solving approach.</p>
<p>46 47 48 49 50 51 52 53 54 55 56 57 58 59 60</p> <p>6. Managing difficult social relationships</p>	<p>-Recap on information learnt about session 5</p> <p>-Provide case examples of social situations people with ESRD find challenging (i.e. dealing with medical professionals).</p> <p>-Describe what assertiveness is and how behaving assertively can improve how you feel in social situations</p>

	<p>that are perceived as stressful. Provide case examples of how others have behaved assertively in ESRD specific social contexts to allow participants to adapt for their own use.</p> <p>-Encourage patients to think about their social support network and whether they are making ideal use of their social networks or is there scope to improve their social networks.</p> <p><i>Between session tasks:</i> Prepare potential assertive responses to stressful social situations and/or consider social support networks and how to optimise them.</p>
<p>7. Progress recap and preparing for the future</p>	<p>-Recap on the progress made over the previous six sessions by encouraging patients to reflect on their new skills and achieved goals.</p> <p>-Generation of action plans to continue using skills and thinking about what skills they can implement when an acute stressful situations arises.</p>

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Table 2: Schedule of assessments

Assessment	Time		
	Screening	Baseline	3 months
PHQ-9	x	x	x
GAD-7	x	x	x
EQ-5D		x	x
Client Service Receipt Inventory		x	x
Socio-demographics		x	
Clinical characteristics		x	
Biological clinical outcomes		x	x
Self-reported adverse events			x
Self-reported treatments for depression and anxiety during the study			x
Brief illness perception questionnaire		x	x
Satisfaction with care		x	x
Experience of using the iDiD website			x

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Improving Distress in Dialysis (iDiD): A feasibility two arm parallel randomised controlled trial of an online cognitive behavioural therapy intervention with and without therapist led telephone support for psychological distress in haemodialysis patients

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4 **1 Improving Distress in Dialysis (iDiD): A feasibility two arm parallel**
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6 **2 randomised controlled trial of an online cognitive behavioural**
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8 **3 therapy intervention with and without therapist led telephone**
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10 **4 support for psychological distress in haemodialysis patients**
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3 25 **Abstract**
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5 26 **Introduction:** Psychological distress is common in End-Stage Renal Disease (ESRD) and is
6 associated with poorer health outcomes. Cognitive-behavioural therapy (CBT) is
7 recommended in UK clinical guidelines for the management of depression in people with
8 long-term conditions (LTCs). Access to skilled therapists competent in managing the
9 competing mental and physical health demands of ESRD is limited. Online CBT treatments
10 tailored to the needs of the ESRD population offers a pragmatic solution for under-
11 resourced services. This study examines the feasibility and acceptability of implementing a
12 two-arm parallel randomised controlled trial (RCT) of online CBT with (intervention arm) and
13 without (control arm) therapist support to improve psychological distress in haemodialysis
14 patients.
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24 36 **Methods:** Patients will be screened for depression and anxiety whilst attending for their
25 haemodialysis treatments. We aim to recruit sixty adult haemodialysis patients who meet
26 criteria for mild to moderately severe symptoms of depression and/or anxiety. Patients will
27 be randomised individually (using a 1:1 computerised sequence ratio) to either online CBT
28 with therapist telephone support (intervention arm) or online CBT with no therapist (control
29 arm). Outcomes include feasibility and acceptability descriptive data on rates of
30 recruitment, randomisation, retention, and treatment adherence. Self-report outcomes
31 include measures of depression (Patient Health Questionnaire-9), anxiety (Generalised
32 Anxiety Disorder-7), quality of life (Euro-QoL), service use (client service receipt inventory),
33 and illness cognitions (brief illness perception questionnaire). A qualitative process
34 evaluation will also be conducted. The statistician will be blinded to treatment allocation.
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44 47 **Ethics and dissemination:** An NHS research ethics committee approved the study. Data
45 from this study will provide essential information for the design and testing of further
46 interventions to ameliorate distress in dialysis patients. Any amendments to the protocol
47 will be submitted to the NHS committee and study sponsor.
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51 51 **Keywords:** End-stage renal disease, haemodialysis, cognitive-behavioural therapy,
52 psychological distress, online therapy, online treatment, computerised therapy
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5 55 **Trial registration:** ClinicalTrials.gov Identifier-NCT0235287026
7 56 **Funder:** This work was funded by Guy's and St Thomas' charity (GSTT, grant number:
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9 57 EFT130206).10
11 58 **Strengths and limitations of this study**

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- 14 59 • This protocol provides a framework for the design and evaluation of an online
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- 15 60 cognitive-behavioural therapy treatment for the management of co-morbid distress
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- 16 61 and end-stage renal disease.
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- 18 62 • First feasibility study to evaluate cognitive-behavioural therapy using online
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- 19 63 pragmatic delivery methods in a UK NHS haemodialysis setting.
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- 21 64 • Recruitment from a single UK NHS site may hinder generalisability of feasibility
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- 22 65 outcomes.
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- 24 66 • Patient treatment preferences are not accounted for.
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29 67 **Introduction**30
31 68 End-stage renal disease (ESRD) is a chronic condition that permanently affects kidney
32 69 function (1). Without renal replacement therapy (e.g. dialysis or transplantation) a person's
33 70 physical health would rapidly deteriorate because of the build-up of toxins and waste
34 71 products in the body (2). In addition to renal replacement therapy patients are required to
35 72 attend regular clinical appointments, take multiple medications and adhere to rigid dietary
36 73 and fluid restrictions (3).37
38 74 Psychological distress is common in ESRD with an estimated prevalence of 39% among
39 75 people in receipt of dialysis compared with a prevalence of 27% in patients with chronic
40 76 kidney disease (stages 1-5) (4). Co-morbid psychological distress and ESRD is associated with
41 77 higher rates of mortality (5) and health care utilisation (6). The safety and efficacy of
42 78 pharmacotherapy in managing psychological distress among people with ESRD remains
43 79 unclear because of a lack of robust randomised controlled trials (7). Whilst talking therapies
44 80 likely offer a safer alternative to pharmacotherapy, their efficacy in the ESRD population is
45 81 largely unknown. Only two small scale, non-UK based, randomised controlled trials (RCTs)
46 82 have examined the efficacy of cognitive behavioural therapy (CBT) relative to usual care
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3 83 among haemodialysis patients (8, 9). Both trials found CBT was effective in reducing
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5 84 psychological distress. These findings are consistent with larger scale RCTs of CBT
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7 85 treatments for depression in people with coronary heart disease (10).
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10 86 The NHS has limited resources to allow the demand for CBT therapist time to be met
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12 87 adequately. A practical approach to address this problem is to implement a stepped care
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14 88 health service delivery model (11). Within this model individuals begin with low-intensity
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16 89 interventions unless their distress is deemed too severe to benefit from the type of minimal
17
18 90 intervention offered. Providing low-intensity treatments means that there is decreased
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20 91 treatment burden for patients, but equally health services can treat a larger volume of
21
22 92 patients. If necessary a patient is “stepped up” to receive more intensive intervention if the
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24 93 initial low-intensity treatment did not improve outcomes.

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26 94 Guided self-help CBT treatments are considered low-intensity interventions (12) and are
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28 95 effective in the management of psychological distress in people with (13) and without co-
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30 96 morbid physical health conditions (14). On-line/computerised self-help resources allow
31
32 97 better management of the informational needs of patients and encourage active
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34 98 engagement with treatment by interacting with the online interface (15). Indeed, in people
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36 99 without physical health conditions, online/computerised guided self-help treatments have
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38 100 largely demonstrated equivalence with face-to-face psychological interventions in terms of
39
40 101 their clinical effectiveness (depression and anxiety) (16) and degree of adherence to
41
42 102 treatment sessions (17).

43
44 103 However there are a number of factors that determine the efficacy of online and
45
46 104 computerised self-help treatments. One moderating factor is whether support is provided
47
48 105 by a health care professional. Online/computerised self-help treatments with support from
49
50 106 health care professionals improves outcomes and prevents treatment drop-out (18, 19). The
51
52 107 type of support provided is also important. A recent RCT explored the efficacy of online CBT
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54 108 with weekly technical/motivational support telephone calls from a non-clinician for the
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56 109 management of depression and compared it with usual GP care (20). Its findings confirmed
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58 110 that providing patients with access to online CBT with only technical support had no added
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60 111 benefit on depression outcomes compared with GP usual care. Access to a skilled therapist
112 is especially important in the context of co-morbid mental and physical health conditions

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3 113 because of the potential for treatment antagonisms, whereby the effective management of
4 114 a person's mental health has the potential to dysregulate the management of physical
5 115 health or vice versa (21).
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9 116 Given that the evidence points to the efficacy of online/computerised treatments with
10 117 therapeutic support for the management of psychological distress in people with and
11 118 without physical LTCs; it remains uncertain whether these findings apply to the
12 119 management of psychological distress in UK NHS haemodialysis treatment settings. This
13 120 study seeks to explore the feasibility and acceptability of implementing a two arm parallel
14 121 RCT of online CBT with (intervention arm) and without (control arm) therapist support to
15 122 improve psychological distress in people receiving haemodialysis treatments within a
16 123 stepped care health service delivery framework.
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24 124 *Background to the study*

25 125 The development of the improving distress in dialysis (iDiD) online CBT treatment involved a
26 126 multi-disciplinary team of health psychologists, clinical psychologists, psychiatrists,
27 127 nephrologists, and six patient and public involvement representatives. The preliminary
28 128 content of the website was initially determined by self-help resources used to manage
29 129 adjustment outcomes in LTCs implemented in previous trials by one of our authors (RMM)
30 130 (22-24). In addition, a literature review of the correlates of distress in dialysis was used to
31 131 develop an ESRD specific CBT treatment formulation and seven session protocol (25). In
32 132 brief our CBT formulation recognises the unique acute and chronic stressors that occur in
33 133 the dialysis population including: ESRD diagnosis, surgical procedures needed for vascular
34 134 access site generation, loss of independence, changes in body and self-image, uncertainty
35 135 about health and future, the unseen burden of kidney disease, and chronic illness self-
36 136 management challenges-specifically managing thirst and food cravings, and dealing with
37 137 health professionals. CBT intervention techniques for managing these illness specific
38 138 stressors are then introduced in subsequent online treatment sessions. The content of each
39 139 treatment session was first drafted on paper and reviewed by the research team. Patient
40 140 representatives then provided feedback on the relevance and ease of understanding of the
41 141 information and CBT intervention techniques described. Next the intervention content was
42 142 uploaded onto an online platform using LifeGuide software (26). The presentation and
43 143 navigation through the website was tested using patient representatives and "think-aloud"
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3 144 techniques. This process occurred iteratively so that comments on early sessions could be
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5 145 incorporated into the design of subsequent sessions.
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7 146 The intervention includes a total of seven sessions. The content of each session is
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9 147 summarised in Table 1. For more detailed information see our distress in dialysis CBT
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11 148 treatment formulation model (25). Patients are encouraged to complete one session per
12
13 149 week and each session was designed to last approximately one hour in duration.
14

150 Objectives

151 The following aims will be addressed as part of the feasibility and acceptability study of a
152 feasibility parallel RCT of online CBT with therapist led telephone support vs online CBT
153 without therapist support, delivered within a stepped care framework among outpatient
154 haemodialysis patients with co-morbid psychological distress.

- 155 1. To assess the feasibility and acceptability of screening all patients who attend for
156 haemodialysis. Patients will be screened for depression and anxiety using
157 standardised measures presented on iPads. The presence of psychological distress is
158 often not identified by non-mental health trained clinicians (27). Implementing
159 screening questionnaires for psychological distress in medical settings can promote
160 its detection (28) and ultimately the provision of mental health care. We will
161 quantify the number of people who agree to be screened.
- 162 2. To explore rates of recruitment and retention into the trial.
- 163 3. To examine willingness to be randomised to either the intervention arm (with
164 telephone support) or control arm (no telephone support) by recording participant
165 reasons for non-consent into the study (if disclosed).
- 166 4. To explore the level of adherence to online treatment sessions and telephone
167 support calls (intervention arm only).
- 168 5. To explore the potential efficacy of an online intervention with therapist led
169 telephone support in reducing psychological distress when compared with website
170 alone. This will inform the planning of a future full-scale trial to detect clinically
171 meaningful change in psychological distress outcomes.
- 172 6. To examine if change in quality of life differs between the intervention arm and
173 control arm

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3 174 7. To provide a preliminary assessment of the cost-effectiveness of the intervention.
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5 175 8. To examine change in ESRD illness cognitions and whether their effect differs
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7 176 between the intervention and control arm.
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9 177 9. To qualitatively explore patient perceptions of the acceptability and usability of the
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11 178 website and telephone support calls and identify areas of improvement for future
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13 179 interventions.

14 180 **Methods**

15 16 17 181 *Design*

18 182 A two parallel armed randomised controlled feasibility trial (RCT). Participants will be
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20 183 randomised, individually, using a 1:1 ratio computerised algorithm. A nested qualitative
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22 184 study will evaluate patient experience.

23 24 25 185 *Setting and participants*

26 186 Participants will be recruited from haemodialysis units at Guy's and St Thomas' hospital
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28 187 (London, UK).

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31 188 Participants will be eligible for inclusion if:

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34 189 1) Aged 18 years or over and receive hospital haemodialysis three-times weekly.
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36 190 2) They have mild to moderately severe depressive symptoms (based on PHQ-9 (29)
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38 191 scores of 5 to 19; a self-report measure of depression) and/or presence of mild to
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40 192 moderately severe anxiety symptoms (based on self-report GAD-7 (30) scores of 5-
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42 193 14).
43
44 194 3) They speak English sufficiently well to engage with screening tools.
45
46 195 4) They have a basic understanding of how to use the Internet and an email address.

47 196 Participants will be ineligible if:

- 48
49 197 1) Currently receiving active treatment for depression and/or anxiety. Active treatment
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51 198 is defined as any current psychological treatment (talking therapies) or receipt of a
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53 199 new anti-depressant and/or anti-anxiety medication. A medication is considered new
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55 200 if commenced three months prior to the completion of the depression and anxiety
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57 201 screening questionnaire.
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- 202 2) They have a severe mental health disorder, for example, psychosis, bi-polar disorder.
- 203 3) They have active suicidal thoughts, as indicated by a score of greater than one on the
- 204 depression PHQ-9 item “Thoughts that you would be better off dead, or of hurting
- 205 yourself”.
- 206 4) They have evidence of addiction to alcohol or drugs.

207 A participant will be withdrawn from the study if:

- 208 1) There are safety concerns in relation to their physical or mental health.
- 209 2) The participant chooses to withdraw from the study.
- 210 3) A patient’s level of psychological distress deteriorates.

211 **Flow of recruitment and participant timeline**

212 Participants will be identified for inclusion using web-based screening questionnaires
213 routinely used as part of the Integrating Mental and Physical healthcare: research, training
214 and services (IMPARTS) initiative at Guy’s and St Thomas’ hospital (31). Participants
215 consenting to the screen will be assessed for depression and anxiety using the PHQ-9 (32)
216 and GAD-7 (30) respectively. The PHQ-9 is a nine item self-report questionnaire deemed
217 acceptable for the identification of depression in medical care settings, including specialist
218 settings (28). Likewise, the GAD-7, is a self-report seven item questionnaire with evidenced
219 criterion validity for the detection of generalized anxiety disorder (30). Both the PHQ-9 and
220 GAD-7 are routinely used in UK primary care Improving Access to Psychological Therapy
221 (IAPT) sites (33) to monitor patient outcomes. The patient will complete the web-based
222 questionnaires either alone or with the assistance of a renal nurse/researcher. Whilst
223 completing the screening questionnaire, patients will be asked to give their permission
224 (yes/no) for a member of the research team to contact them about the present study.

225 Results from the screening questionnaires are uploaded onto the patient’s electronic
226 medical record. Results will be checked by the nursing team/researcher for immediate risk.
227 Risk is defined as a score of greater than one on the depression PHQ-9 item “Thoughts that
228 you would be better off dead, or of hurting yourself”. If suicidal ideation is detected then a
229 risk assessment will be performed to determine the immediacy of referral to either liaison
230 psychiatry or renal clinical psychology. Level of risk will be assessed in line with the IMPARTS
231 risk assessment protocol. This includes enquiring about degree of suicidal ideation and level

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3 232 of hopelessness, whether active plans are present, enquiring about the patient's history of
4 233 suicidal attempts, recent life stressors, protective factors, and degree of social support. The
5 234 outcome of the risk assessment will be immediately discussed with either the renal clinical
6 235 psychologist or liaison psychiatrist and a management plan will be put into place.

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10 236 Anonymised screening results will be securely emailed from the IMPARTS database to the
11 237 iDiD research team on a weekly basis. A stratified stepped care model, according to the
12 238 criteria outlined in Figure 1 will be applied to the anonymised data to identify potentially
13 239 eligible participants for the study. The stratified stepped-care approach assigns individuals
14 240 to treatments of varying intensity based on the severity of their symptoms (34). PHQ-9
15 241 scores within the range of 5-19, are considered indicative of mild to moderately severe
16 242 symptoms of depression (32). Likewise, GAD-7 scores within the range of 5 to 14 indicate
17 243 the presence of mild to moderately severe anxiety (30). Individuals with mild to moderately
18 244 severe symptoms of depression and/or anxiety will be considered appropriate for treatment
19 245 with the iDiD online CBT program and for inclusion in this study. Individuals with severe
20 246 depression (PHQ-9 score ≥ 20) and/or anxiety (GAD7 score ≥ 15) or individuals with evidence
21 247 of current suicidal ideation are considered inappropriate for iDiD online CBT. These patients
22 248 will be referred and managed by either the renal clinical psychology team or liaison
23 249 psychiatry (when detected at the point of screen).

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27 250 Individuals who meet the criteria for mild to moderately severe symptoms of depression
28 251 and/or anxiety will have their data de-anonymised providing they give us consent to contact
29 252 them about the study. These potential participants will be screened against the remaining
30 253 inclusion/exclusion criteria during weekly referral meetings with the research and clinical
31 254 team. If they remain eligible then a researcher will approach the participant whilst they
32 255 attend for dialysis to explain the study with the participant information sheet. Participants
33 256 will be given a minimum of 24 hours to establish if they would like to take part.

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37 257 All patients with mild to moderately severe symptoms of depression and/or anxiety who
38 258 either: i) do not meet our remaining study inclusion criteria, ii) choose not to consent into
39 259 the study, or iii) do not provide consent for us to approach them about the study will be
40 260 provided with the option of receiving usual care follow-up from the renal clinical psychology

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3 261 team. Usual care includes a face-to-face clinical assessment followed by a tailored
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5 262 psychological treatment intervention or referral to an IAPT service.
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7 263 As discussed above, patients who screen positive for severe symptoms of depression and/or
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9 264 anxiety (PHQ-9 score ≥ 20 and/or GAD7 score ≥ 15) will receive an automatic referral to the
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11 265 renal clinical psychology team. If upon clinical assessment by the renal clinical psychologist a
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13 266 severely depressed and/or anxious patient is deemed appropriate for the iDiD self-help
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15 267 study, then they will be “stepped down” for approach by the iDiD research team. Likewise,
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17 268 the research team will be informed by the renal clinical psychology team of any patients
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19 269 who meet the iDiD study inclusion criteria and declare an interest in the study despite
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21 270 initially stating during screening that they did not want to be contacted by the study team.

22 271 Participants who consent to take part in the study will be issued with an iDiD study
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24 272 identification number. A researcher will attend the dialysis unit and help the patient to sign-
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26 273 up to the iDiD online CBT treatment using an iPad. At sign-up participants will be asked to
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28 274 enter their personal email address and select a password for use each time they logon. At
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30 275 the point of sign-up participants will also be asked to enter their NHS number (supplied to
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32 276 them by the researcher) to ensure that multiple iDiD accounts are not registered by the
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34 277 same participant. Participants will then receive a confirmatory email with a link to the iDiD
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36 278 website. After signing up, participants will complete the baseline questionnaires online. If
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38 279 baseline questionnaires are not completed, then participants will receive two reminder
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40 280 emails and an assistance based telephone call/visit at the dialysis unit. Participants will be
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42 281 informed of their randomisation process outcome immediately after completing the online
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44 282 baseline questionnaire. Participants will also receive an email confirming their treatment
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46 283 allocation. We anticipate the participant’s journey through the study will last approximately
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48 284 six months as summarised in Figure 2. We expect a period of one month to elapse from the
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50 285 point of screening to randomisation. Once participants are randomised, both groups will be
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52 286 able to access the iDiD website for a period of 12 weeks before being prompted to complete
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54 287 the follow-up questionnaires via email. The email will also advise participants that their
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56 288 access to the iDiD website is ending within a few weeks and to print off any information
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58 289 they have found helpful from the “My tasks” tab of the website. Two reminder emails and
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60 290 an assistance based telephone call/visit will occur over a period of three weeks if the follow-
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up questionnaires remain incomplete. After 20 weeks participants will receive an email

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3 292 thanking them for their participation in iDiD study. Access to the iDiD website will no longer
4 293 be available after this time. On completion of the three month follow-up questionnaires a
5 294 subsample of participants will be asked to complete a qualitative interview. We will follow-
6 295 up participants for a period of approximately six months post their randomisation date to
7 296 complete the interview.

297 **Randomisation, allocation concealment, and blinding**

298 Participants will be randomised to iDiD online CBT plus therapist led telephone support or
299 iDiD online CBT only condition using Lifeguide software (a computerised random number
300 generator with a 1:1 ratio). Because the randomisation sequence is automated by Lifeguide
301 in real-time the allocation sequence is concealed from researchers. All baseline
302 questionnaires will be completed online prior to randomisation. Participants will be
303 randomised at the individual level. The trial co-ordinator will also receive an automated
304 email informing them of the outcome of the randomisation procedure to identify
305 participants who require telephone support calls during the trial. The researcher conducting
306 the qualitative interviews will also be unblinded at follow-up to ensure that appropriate
307 questions are asked in relation to telephone support calls. Because of the nature of the
308 intervention patients will not be blind to their treatment allocation. Follow-up outcomes will
309 be completed independently by participants when prompted by email unless the participant
310 requires assistance. The statistician will remain blinded to treatment allocation.

311 *Trial Intervention*

312 All participants have access to the iDiD online CBT treatment (summarised in Table 1 and
313 described in detail in our ESRD CBT formulation model (25)). Participants will be advised in
314 the participant information sheet to logon to the website once a week. Participants will also
315 receive weekly reminder emails to encourage engagement with the website. iPADs will be
316 available for participants to use during their dialysis sessions.

317 *iDiD online CBT website plus therapist led telephone support (Intervention arm)*

318 Participants in the intervention arm of the trial will receive three 30 minute telephone
319 support calls at weeks two, four, and six from JH who has a PhD in health psychology and is
320 a trained psychological wellbeing practitioner (PWP). PWPs typically work in primary care
321 mental health teams as part of the UK Improving Access to Psychological Therapies (IAPT)

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3 322 initiative (33). PWPs deliver low-intensity CBT treatments including: cognitive restructuring,
4 323 behavioural activation, problem solving, medication management, exposure therapy, and
5 324 sleep management. The purpose of the telephone support calls are to promote engagement
6 325 with the website and to support the patient in collaboratively developing goals to work on
7 326 using the resources and information available to them on the website. At the start of each
8 327 telephone call the PWP will set an agenda with the participant. The first telephone support
9 328 call is scheduled for when the participant will have completed session two online. During
10 329 session two the participant will have completed a self-assessment and developed their own
11 330 personal model of distress. Thus during the first call the PWP will develop a shared
12 331 understanding of the participants source of distress, provide empathy, reinforce with the
13 332 participant the relationships between thoughts, feelings, and behaviours, and inform
14 333 participants of the content the website which is likely most applicable to them as they
15 334 continue to move forward with the website. The PWP and patient will develop a goal to
16 335 work towards prior to their next telephone call.

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19 336 The second telephone support call will provide an opportunity for the PWP to review with
20 337 the participant their progress on their self-generated goals, work through a particular
21 338 cognitive-behavioural intervention technique selected by the participant, and close the
22 339 session with a shared goal to work towards with the help of the website in advance of the
23 340 final telephone support call. The final telephone support call will follow a similar format
24 341 except the telephone session will end with a relapse prevention plan. The plan will be
25 342 generated collaboratively with the patient. All telephone support calls will be audio-
26 343 recorded to provide intervention fidelity checks and for self-reflection during clinical
27 344 supervision.

28 29 30 345 *Clinical supervision*

31 346 JH was trained to deliver the telephone support calls using role played sessions with
32 347 feedback from RMM. Ongoing supervision will be provided by a renal clinical psychologist
33 348 (AC). Shared reflection on audio-recorded sessions will be discussed in line with the core
34 349 competency framework for delivering psychological therapies in long-term conditions (35).
35 350 Shared goals will be identified for the PWP to work towards over the course of the study.
36 351 Supervision will also be an opportunity for case management. The PWP will discuss their
37 352 proposed treatment plan in response to the first telephone support call and degree of

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3 353 patient progress at each supervision session. If a patient needs to be stepped up to receive
4 354 more intensive psychological treatments then this will be initiated by the research team and
5 355 managed by the renal clinical psychologist.
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9 356 *iDiD online CBT website with no telephone support (control arm)*

10 357 Participants allocated to the control arm of the study will receive their usual renal care in
11 358 addition to having access to the website. Usual care for individuals with ESRD managed with
12 359 haemodialysis includes attending for dialysis three times per week for up to five hours at a
13 360 time. Participants can be referred or self-refer into the renal clinical psychology service or
14 361 primary care mental health service if their symptoms of depression and/or anxiety increase.
15 362 We will ask participants in the three-month follow-up questionnaire whether they have
16 363 commenced any new treatments for mental health since starting the study.
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24 364 **Outcomes**

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27 365 *Data collection and feasibility outcomes*

28 366 Because this is a feasibility study our primary focus is to collect data on the feasibility and
29 367 acceptability of the trial design and intervention by collecting descriptive data on
30 368 *recruitment and retention rates and willingness to be randomised* according to CONSORT
31 369 trial guidelines (36). We will also examine *adherence* to the online intervention and
32 370 telephone support calls (intervention arm only). The degree of adherence to the online
33 371 intervention will be automatically recorded by the Lifeguide software. We will calculate
34 372 descriptive values for the mean number of sessions completed, the number of participants
35 373 who complete all sessions, the number of participants who complete 50% or more sessions,
36 374 and the number of participants who complete each session. Degree of adherence to the
37 375 telephone call (intervention arm only) will be recorded by the psychological wellbeing
38 376 practitioner. The following values will be calculated: mean number of telephone calls
39 377 completed, number of participants who complete all telephone calls, number who complete
40 378 one or more telephone call, number of participants who complete telephone sessions one,
41 379 two, and three respectively, and mean duration of telephone calls across all three telephone
42 380 support calls. In addition to a qualitative interview (described below) patients will be asked
43 381 to self-report their experience of using the iDiD website at three months follow-up. The
44 382 open-ended questions will enquire about: i) how useful they found the iDiD website and ii)
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3 383 whether they found the website easy to use. Participants will also be given the option to
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5 384 add any further comments.
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8 385 Self-reported patient outcomes will also be collected via the iDiD website at baseline and
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10 386 three months follow-up. The assessment schedule completed by patients is summarised in
11
12 387 Table 2 and described below.

- 13 388 • Continuous self-report measure of depression: PHQ-9 (32) (described in detail
14 389 above, scale range from 0 to 27, high scores indicate greater depressive symptoms)
- 15
16 390 • Continuous self-report measure of anxiety: (GAD-7) (30) (described in detail above,
17 391 scale range from 0 to 21, high scores indicate greater anxiety symptoms).
- 18
19 392 • The five item EuroQoL (EQ-5D) (37) includes a five item measure of health status
20 393 across the following domains: mobility, ability to self-care, ability to continue with
21 394 activities (i.e. work, social life), pain, and anxiety and depression. In addition it has a
22 395 visual analogue scale ranging from 0 to 100 where a person is asked to rate their
23 396 overall health. The EQ-5D is recommended by NICE for use in cost-effectiveness
24 397 evaluations (38).
- 25 398 • The Client Service Receipt Inventory (CSRI) (39) collects retrospective data on service
26 399 use across the following five domains: i) background and client information (i.e.
27 400 hospital admissions and discharge, frequency of GP visits, medications), ii)
28 401 accommodation and living situation, iii) employment history, earnings, and other
29 402 personal resources, iv) service receipt (i.e. hospital appointments, home help), and v)
30 403 receipt of informal care from caregivers. The CSRI was amended to make its content
31 404 relevant to the needs of the dialysis population in collaboration with the trial health
32 405 economist (PM) and Renal Consultant (DG).
- 33 406 • The brief illness perception questionnaire (BIPQ) (40) will assess participants self-
34 407 reported beliefs about their ESRD. The BIPQ was developed and validated among
35 408 patients with long-term conditions, including renal disease. This information will be
36 409 assessed at baseline and follow-up. It will provide an indication of whether
37 410 participants beliefs about their ESRD change in response to clinical intervention.
- 38 411 • Satisfaction with care will be evaluated using a 2-item scale that asks participants to
39 412 rate their degree of satisfaction with the care they receive for their physical and

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3 413 mental health on a five-item Likert response scale. This information will be assessed
4 414 at baseline and follow-up.
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6 415 • Serious adverse events will be directly enquired about using self-report at follow-up
7 only, according to good clinical practice guidelines. Participants will be asked
8 416 whether they have experienced any adverse events since starting the study choosing
9 417 from a list of five options. If participants indicate they have experienced adverse
10 418 events then they will be asked for details. In addition participants will be asked if
11 419 they have experienced any adverse health effects since starting the study and
12 420 encouraged to elaborate where needed.
13 421
14 422 • Treatments for depression and/or anxiety: Two brief self-report questions at follow-
15 423 up will ask participants if they have received any pharmacological or psychological
16 424 treatments for their depression and/or anxiety in addition to the iDiD website since
17 425 starting the study.

426 *Socio-demographic and clinical characteristics*

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28 427 Socio-demographic characteristics including: gender, age, ethnicity, home environment
29 428 (marital status, housing situation, number of dependents) and level of education will be
30 429 collected at baseline only via self-report. Clinical characteristics including: dialysis vintage
31 430 and treatment history for depression and anxiety will be self-reported by patients at
32 431 baseline.

33
34 432 Number and type of co-morbidities will be extracted from notes at baseline only. The
35 433 following clinical outcomes and covariates will be extracted from notes at baseline and
36 434 follow-up: Kt/V (dialysis treatment adequacy), haemoglobin, serum albumin, C reactive
37 435 protein, serum potassium levels, interdialytic weight gain, and serum phosphate levels.

436 **Qualitative interviews**

38
39 437 Qualitative interviews with a sub-group of participants over the phone will be conducted
40 438 post-intervention (three months) by a researcher who has not been involved in their
41 439 treatment. These interviews will explore whether the intervention met patient expectations,
42 440 positive and negative opinions about the website, whether patients felt they gained any
43 441 benefit from using website, its personal relevance to them, and its acceptability as a
44 442 treatment. A minimum of ten participants will be purposively sampled across a range of

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3 443 socio-demographic and clinical characteristics (e.g. treatment group, age, gender, ethnicity,
4 444 dialysis vintage, degree of adherence to the intervention, degree of improvements in
5 445 outcomes from the intervention). Interviews will continue until data saturation occurs. The
6 446 outcomes of these qualitative interviews will help to revise our theoretical understanding of
7 447 distress in dialysis and update the content of the intervention accordingly, in line with
8 448 current medical research guidelines for process evaluations (41). Interviews will be
9 449 transcribed verbatim and an inductive thematic analysis will be performed.

16 450 **Sample size**

17 451 The aim of this study is to explore the feasibility of implementing our trial procedures and to
18 452 inform a power calculation for a future randomised controlled trial. We have calculated the
19 453 sample size required based on the margins of error associated with recruitment. The
20 454 approximate size of the Guy's and St Thomas' dialysis population is 600 patients, in which
21 455 we expect to be able approach 400. Assuming a conservative uptake rate of 50%, 200
22 456 patients will be screened with approximately 40% meeting the inclusion criteria (the
23 457 estimated prevalence of depression symptoms in HD patients; see (4)). If we assume 50% of
24 458 those eligible will consent to be randomised a sample size of approximately 66 would allow
25 459 us to estimate the true population consent rate with a 5% margin of error and a 95%
26 460 confidence level.

37 461 **Analysis plan**

38 462 To examine the feasibility and acceptability of our screening, recruitment, retention, and
39 463 randomisation process (objectives 1-3), we will quantify the flow of participants through the
40 464 study using frequencies and percentages in accordance with the consort flow diagram (36)
41 465 shown in Figure 2. We will also record and quantify reasons for non-consent, exclusion, and
42 466 drop-out for each stage of the study. We will examine degree of adherence to the
43 467 intervention and telephone support calls (where applicable) using descriptive statistics
44 468 (objective 4).

45 469 We will also perform an *exploratory* intention to treat mixed model analysis blind to
46 470 treatment group on the following self-report outcomes at three months follow-up:
47 471 depression, anxiety, and quality of life (objective 5 & 6). Variability in these patient
48 472 outcomes will help to inform a future power calculation for a full-scale trial.

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3 473 Service costs will be calculated by combining service use data with appropriate unit costs
4 474 (42). These will be added to the costs of the intervention which will be based on
5 475 development costs and the time spent providing telephone support. Costs will be compared
6 476 between the two groups and cost-effectiveness assessed by combining the costs with the
7 477 primary outcome measures and quality adjusted life years (QALYs) in the form of
8 478 incremental cost-effectiveness ratios (ICERs). Uncertainty around the ICERs will be
9 479 addressed using cost-effectiveness planes and acceptability curves (objective 7). We will
10 480 also perform an exploratory process analysis using intention to treat mixed models to
11 481 establish whether illness cognitions changed in response to the online intervention and
12 482 whether differences occurred between the intervention and control group (objective 8).
13 483 Qualitative interviews will be transcribed verbatim and analysed using thematic analysis to
14 484 allow the feasibility and acceptability of the online intervention and telephone support calls
15 485 to be explored (objective 9).

26 486 **Ethics**

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28
29 487 This study has ethical approval from the NHS research ethics committee (14/LO/1934) and is
30 488 sponsored by King's College London.

33 489 **Data collection and management**

34 490 The IMPARTS screening interface, developed by Teleologic Ltd, is web-based and installed
35 491 on the server configuration at Guy's & St Thomas' Hospitals NHS Foundation Trust. The
36 492 patient logs on to the system with their unique Hospital Number. Their screening results are
37 493 outputted to the documents folder of the Electronic Patient Record via the most secure wifi
38 494 network within each NHS Trust.

39 495 All quantitative outcomes are measured via online questionnaires that participants will
40 496 access via iDiD website. The information is stored on a secure server associated with the
41 497 Lifeguide program at the University of Southampton. The website prompts the participant
42 498 when data is missing. Study data can only be downloaded from the server by members of
43 499 the research team who are granted password access. All data will be confidentially stored in
44 500 accordance with the data protection act (43) and King's College London data management
45 501 procedures.

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3 502 **Formal committee**
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5 503 A trial management team will meet regularly to discuss the overall running of the study
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7 504 including: rates of recruitment, adherence to the protocol, safety and confidentiality of
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9 505 patients. All serious adverse events related to the study will be reported to the study
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11 506 sponsor, ethics committee and Guy's and St Thomas' research and development
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13 507 department.

14
15 508 **Discussion**
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17 509 Psychological distress is common in people with ESRD. However, studies examining the
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19 510 efficacy of either pharmacological or psychological interventions for the management of
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21 511 distress in dialysis are limited. Likewise, access to psychological treatment interventions
22
23 512 tailored to the specific psycho-social stresses associated with ESRD is problematic. An online
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25 513 CBT treatment designed specifically to manage distress in dialysis offers a pragmatic
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27 514 solution to under-resourced health services, which are advised to offer integrated mental
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29 515 and physical health care treatments.

30 516 This is the first study to examine whether it is feasible to implement a RCT of online CBT
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32 517 with telephone support vs online CBT without telephone support within a stepped care
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34 518 framework to secondary care haemodialysis patients with co-morbid distress. Indeed, it will
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36 519 identify unique challenges that occur in the dialysis population in the recruitment and
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38 520 retention of patients. Likewise, the study will be able to simultaneously examine the
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40 521 acceptability of this treatment to patients in terms of whether its content was relevant and
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42 522 useful. In addition, the utility of the online mode of delivery with or without telephone
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44 523 support will be examined. We anticipate that the results of this trial will substantially
45
46 524 inform the design of a future large scale trial powered to detect the efficacy of online CBT
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48 525 treatments for the management of distress in dialysis.

49 526 **Trial Status**
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51 527 The study commenced recruitment in February 2015. Recruitment will continue until
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53 528 February 2016 with the last patient's follow-up in May 2016. Outcomes will be disseminated
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55 529 at national and international conferences and in journal articles.

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3 531 **List of abbreviations**
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5 532 CBT, Cognitive behavioural therapy; ESRD, End-stage renal disease; ICERS, incremental cost-
6 effectiveness ratios; iDiD, Improving distress in dialysis; QALYs, Quality Adjusted Life Years;
7 533
8 RCT, Randomised Controlled Trial
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11 535 **Authors Contributions:**
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14 536 Study design: All authors
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17 537 Intervention development: JH, RMM, DG, AC, LY, JC:
18

19 538 Statistical analysis plan: PM, JC.
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21
22 539 All authors contributed to writing the protocol.
23

24 540 **Sponsor:** King's College London, Mr Keith Brennan (Keith.brennan@kcl.ac.uk)
25

26 541 **Protocol version:** Version 3: Date 11.05.15
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30 543 **Role of sponsor and funder**
31

32 544 The funder and sponsor had no role in the design and conduct of the study; the collection,
33 545 management, analysis, and interpretation of the data; and the preparation, review, or
34 approval of the manuscript. The views expressed in this article are those of the authors.
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37 547 **Conflicts of interest:**
38

39 548 None
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41 549 **Access to data:** Data will be confidentially and securely stored for 7 years as per University
42 550 policy. Anonymised aggregated data will be made available upon request to the
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44 551 corresponding author.
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674 **Table 1: Summary of iDiD online treatment sessions**

Session	Content
1. What is end-stage renal failure?	-Psycho-education including information about: -ESRD and its treatment. -Expectation management concerning the effectiveness of dialysis treatments and its psycho-social consequences. -The rationale for specific ESRD treatments (i.e. improving physical health) and psychological interventions (i.e. improving emotional

	<p>health).</p> <p>-Normalising the experience of distress in the context of dialysis.</p>
2. Why do I feel distressed?	<p>-Recaps on information learnt about in session 1.</p> <p>-Self-generation of a personal model of distress. Patients self-identify their own vicious cycle to improve their understanding of the inter-relationships between ESRD specific stressors (triggers), feelings, thoughts, behaviours, and physical symptoms.</p> <p><i>Between session task:</i> Recap on the content of session 2 by re-reading the session.</p>
3. Dealing with my negative feelings	<p>-Recaps on information learnt about in session 2.</p> <p>-Revision of reinforcing relationship between unhelpful coping behaviours and the maintenance of psychological distress.</p> <p>-Explanation of positive emotion regulation strategies including: behavioural activation, emotional expression, graded exposure, and tips for improving the quality of sleep. Patients are also informed of the value of acceptance, relaxation, and physical exercise.</p> <p><i>Between session task:</i> Selection of a helpful coping strategy for managing negative emotions before completion of next online session.</p>

<p>1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24</p> <p>4. Tackling unhelpful thoughts about end-stage renal disease</p>	<p>-Recaps on information learnt about in session 3.</p> <p>-Examples of unhelpful thoughts typical in people with ESRD provided.</p> <p>-Information and skill development on the identification of unhelpful thoughts using thought records.</p> <p>-Explanation of how to challenge and gradually alter unhelpful thinking styles by generating alternatives.</p> <p><i>Between session task:</i> Continue working on goals from session three (if useful) and complete a thought record if relevant to their personal needs.</p>
<p>25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51</p> <p>5. Goal setting and problem solving</p>	<p>-Recaps on information learnt about in session 4.</p> <p>-The rationale for “SMART” goals and how to use the technique is explained in depth.</p> <p>-Information about the value of activity monitoring, behavioural activation, and action planning.</p> <p>-Explanation of the seven steps to problem solving technique is introduced. Use to foster confidence in illness self-management.</p> <p><i>Between session task:</i> Continue working on goals from previous sessions that remain useful and relevant. If applicable implement one of the following: i) “SMART” goal techniques, ii) activity monitoring/behavioural activation, or iii) seven steps to problem solving approach.</p>
<p>52 53 54 55 56 57 58 59 60</p> <p>6. Managing difficult social relationships</p>	<p>-Recaps on information learnt about session 5</p> <p>-Case examples of social situations people with ESRD find challenging (i.e. dealing with medical professionals)</p>

	<p>provided.</p> <ul style="list-style-type: none"> -Introduction to assertiveness concept and its effects on physical and psychological health. -Case examples provided of how others behave assertively in ESRD specific social contexts to allow participants to adapt for their own use. -Reflection on social support network and whether there is scope to improve it to meet physical, emotional, and informational needs. <p><i>Between session tasks:</i> Continue working on goals from previous sessions that remain useful and relevant. If feasible/applicable implement: a potential assertive responses to a stressful social situation or reflect on social support networks and how to optimise them.</p>
7. Progress recap and preparing for the future	<ul style="list-style-type: none"> -Recaps on the progress made over the previous six sessions by encouraging patients to reflect on their new skills and achieved goals. -Generation of action plans to continue using skills moving forward. Identification of a specific action plan to implement when an acute stressful situations arises.

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Table 2: Schedule of assessments

Assessment	Time		
	Screening	Baseline	3 months
PHQ-9	x	x	x
GAD-7	x	x	x
EQ-5D		x	x
Client Service Receipt Inventory		x	x
Socio-demographics		x	
Clinical characteristics		x	
Biological clinical outcomes		x	x
Self-reported adverse events			x
Self-reported treatments for depression and anxiety during the study			x
Brief illness perception questionnaire		x	x
Satisfaction with care		x	x
Experience of using the iDiD website			x

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Figure titles:

Figure 1: Stratified stepped care referral pathway for managing psychological distress among individuals attending for haemodialysis

Figure 2: Flow of participants through the study

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Figure 1: Stratified stepped care referral pathway for managing psychological distress among individuals attending for haemodialysis

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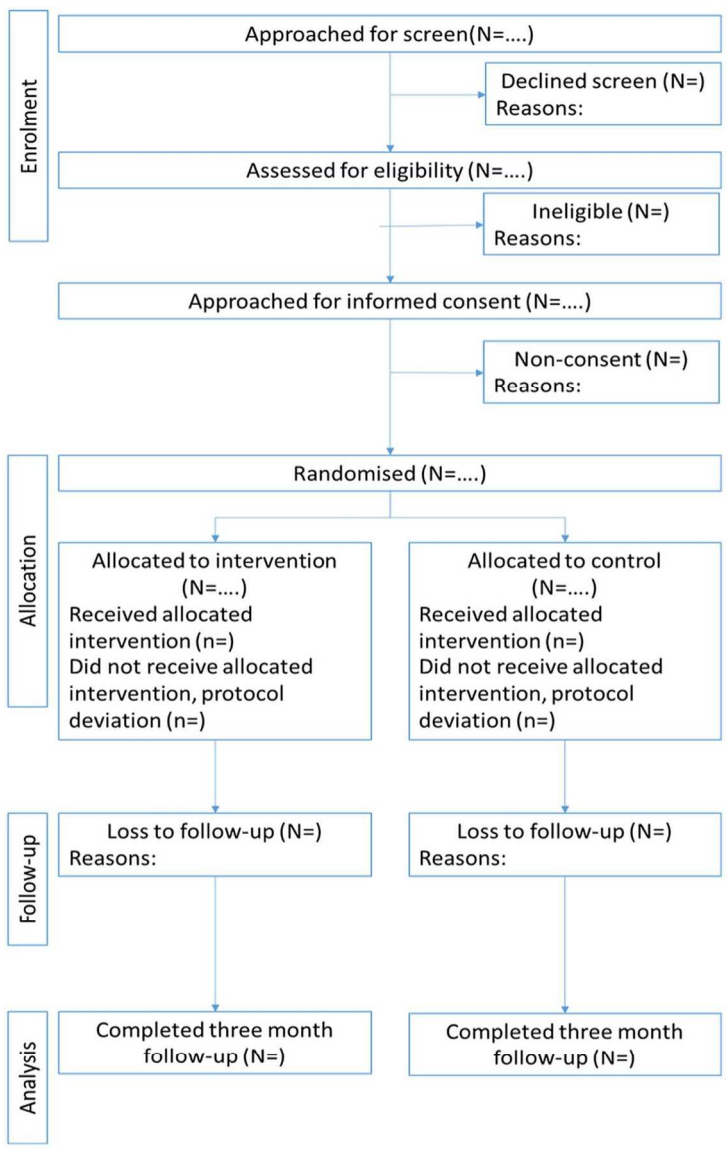


Figure 2: Flow of participants through the study
99x153mm (300 x 300 DPI)



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

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	_1_____
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	_2_____
	2b	All items from the World Health Organization Trial Registration Data Set	Documented in trial registry (2a) & page 1_____
Protocol version	3	Date and version identifier	_3_____
Funding	4	Sources and types of financial, material, and other support	_3_____
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	_1_____
	5b	Name and contact information for the trial sponsor	_3_____
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	_3_____

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	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	_NA for feasibility study_____
			-

Introduction

Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	4 to 6_____
	6b	Explanation for choice of comparators	5 to 6_____
Objectives	7	Specific objectives or hypotheses	7_____
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	7_____

Methods: Participants, interventions, and outcomes

Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	8_____
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	8 to 9_____
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	12 to 14_____
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	9_____
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	11 and 13_____
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	14_____

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3	Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	15 and 16 _____
4				
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8	Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	9 to 13 _____
9				
10				
11	Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	17 _____
12				
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14	Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	17 _____
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17 **Methods: Assignment of interventions (for controlled trials)**

18 Allocation:

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21	Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions ¹²	12 _____
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26	Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	12 _____
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30	Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	9 to 12 _____
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34	Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	12 _____
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37		17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	NA as trial co-ordinator is not blind. _____
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Methods: Data collection, management, and analysis

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5	Data collection	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related	9 to 11_____
6	methods		processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of	
7			study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known.	
8			Reference to where data collection forms can be found, if not in the protocol	
9				
10				
11		18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be	9 to 11_____
12			collected for participants who discontinue or deviate from intervention protocols	
13				
14	Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality	18_____
15			(eg, double data entry; range checks for data values). Reference to where details of data management	
16			procedures can be found, if not in the protocol	
17				
18	Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the	17 to 18_____
19			statistical analysis plan can be found, if not in the protocol	
20				
21		20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	17 to 18_____
22				
23		20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any	
24			statistical methods to handle missing data (eg, multiple imputation)	17 to 18_____
25				
26				
27	Methods: Monitoring			
28				
29	Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of	NA for feasibility
30			whether it is independent from the sponsor and competing interests; and reference to where further details	study_____
31			about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not	
32			needed	
33				
34		21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim	NA for feasibility
35			results and make the final decision to terminate the trial	study_____
36				
37	Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse	16_____
38			events and other unintended effects of trial interventions or trial conduct	
39				
40	Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent	NA for feasibility
41			from investigators and the sponsor	study_____
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3 **Ethics and dissemination**
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5	Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	18_____
8	Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	2 and 16_____
12	Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	9 and 10_____
16		26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	NA_____
19	Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	18_____
22	Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	3_____
25	Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	3_____
28	Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	NA harms addressed according to King's indemnity insurance_____
35	Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	19_____
39		31b	Authorship eligibility guidelines and any intended use of professional writers	20_____
41		31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	1_____

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Appendices

Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	Adheres to NHS consent form _____
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	_____

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

Peer review only

BMJ Open

Improving Distress in Dialysis (iDiD): A feasibility two arm parallel randomised controlled trial of an online cognitive behavioural therapy intervention with and without therapist led telephone support for psychological distress in haemodialysis patients

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2016-011286.R2
Article Type:	Protocol
Date Submitted by the Author:	14-Mar-2016
Complete List of Authors:	Hudson, Joanna; King's College London (Institute of Psychiatry) Moss-Morris, Rona; King's College London (Institute of Psychiatry) Game, David; Guy's and Saint Thomas' NHS Foundation Trust, Renal medicine Carroll, Amy; Guy's and Saint Thomas' NHS Foundation Trust, Renal medicine McCrone, Paul; King's College London (Institute of Psychiatry) Hotopf, Matthew; King's College London (Institute of Psychiatry), Yardley, Lucy; University of Southampton, Academic Unit of Psychology Chilcot, Joseph; King's College London, Psychology
Primary Subject Heading:	Mental health
Secondary Subject Heading:	Patient-centred medicine
Keywords:	Nephrology < INTERNAL MEDICINE, Depression & mood disorders < PSYCHIATRY, STATISTICS & RESEARCH METHODS

SCHOLARONE™
Manuscripts

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4 **1 Improving Distress in Dialysis (iDiD): A feasibility two arm parallel**
5
6 **2 randomised controlled trial of an online cognitive behavioural**
7
8 **3 therapy intervention with and without therapist led telephone**
9
10 **4 support for psychological distress in haemodialysis patients**

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16 Matthew Hotopf⁴, Lucy Yardley⁵, Joseph Chilcot^{1*}

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1
2
3 25 **Abstract**
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5 26 **Introduction:** Psychological distress is common in End-Stage Kidney Disease (ESKD) and is
6 associated with poorer health outcomes. Cognitive-behavioural therapy (CBT) is
7 recommended in UK clinical guidelines for the management of depression in people with
8 long-term conditions (LTCs). Access to skilled therapists competent in managing the
9 competing mental and physical health demands of ESKD is limited. Online CBT treatments
10 tailored to the needs of the ESKD population offers a pragmatic solution for under-
11 resourced services. This study examines the feasibility and acceptability of implementing a
12 two-arm parallel randomised controlled trial (RCT) of online CBT with (intervention arm) and
13 without (control arm) therapist support to improve psychological distress in haemodialysis
14 patients.
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24 36 **Methods:** Patients will be screened for depression and anxiety whilst attending for their
25 haemodialysis treatments. We aim to recruit sixty adult haemodialysis patients who meet
26 criteria for mild to moderately severe symptoms of depression and/or anxiety. Patients will
27 be randomised individually (using a 1:1 computerised sequence ratio) to either online CBT
28 with therapist telephone support (intervention arm) or online CBT with no therapist (control
29 arm). Outcomes include feasibility and acceptability descriptive data on rates of
30 recruitment, randomisation, retention, and treatment adherence. Self-report outcomes
31 include measures of depression (Patient Health Questionnaire-9), anxiety (Generalised
32 Anxiety Disorder-7), quality of life (Euro-QoL), service use (client service receipt inventory),
33 and illness cognitions (brief illness perception questionnaire). A qualitative process
34 evaluation will also be conducted. The statistician will be blinded to treatment allocation.
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44 47 **Ethics and dissemination:** An NHS research ethics committee approved the study. Data
45 from this study will provide essential information for the design and testing of further
46 interventions to ameliorate distress in dialysis patients. Any amendments to the protocol
47 will be submitted to the NHS committee and study sponsor.
48
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51 51 **Keywords:** End-stage kidney disease, haemodialysis, cognitive-behavioural therapy,
52 psychological distress, online therapy, online treatment, computerised therapy
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55 **Trial registration:** ClinicalTrials.gov Identifier-NCT023528702

56 **Funder:** This work was funded by Guy's and St Thomas' charity (GSTT, grant number:
57 EFT130206).

58 **Sponsor:** King's College London, Mr Keith Brennan (Keith.brennan@kcl.ac.uk)

59 **Protocol version:** Version 3: Date 11.05.15

60

61 **Role of sponsor and funder**

62 The funder and sponsor had no role in the design and conduct of the study; the collection,
63 management, analysis, and interpretation of the data; and the preparation, review, or
64 approval of the manuscript. The views expressed in this article are those of the authors.

65 **Conflicts of interest:**

66 None

67 **Access to data:** Data will be confidentially and securely stored for 7 years as per University
68 policy. Anonymised aggregated data will be made available upon request to the
69 corresponding author.

70 **Strengths and limitations of this study**

- 71 • This protocol provides a framework for the design and evaluation of an online
72 cognitive-behavioural therapy treatment for the management of co-morbid distress
73 and end-stage renal disease.
- 74 • First feasibility study to evaluate cognitive-behavioural therapy using online
75 pragmatic delivery methods in a UK NHS haemodialysis setting.
- 76 • Recruitment from a single UK NHS site may hinder generalisability of feasibility
77 outcomes.
- 78 • Patient treatment preferences are not accounted for. However such designs would
79 be associated with increased costs, a prohibitive factor in the current study, and
80 increase the potential for confounding factors.

81 **Introduction**

82 End-stage kidney disease (ESKD) is a chronic condition that permanently affects kidney
83 function (1). Without renal replacement therapy (e.g. dialysis or transplantation) a person's
84 physical health would rapidly deteriorate because of the build-up of toxins and waste
85 products in the body (2). In addition to renal replacement therapy patients are required to
86 attend regular clinical appointments, take multiple medications and adhere to rigid dietary
87 and fluid restrictions (3).

88 Psychological distress is common in ESKD with an estimated prevalence of 39% among
89 people in receipt of dialysis compared with a prevalence of 27% in patients with chronic
90 kidney disease (stages 1-5) (4). Co-morbid psychological distress and ESKD is associated with
91 higher rates of mortality (5) and health care utilisation (6). The safety and efficacy of
92 pharmacotherapy in managing psychological distress among people with ESKD remains
93 unclear because of a lack of robust randomised controlled trials (7). Whilst talking therapies
94 likely offer a safer alternative to pharmacotherapy, their efficacy in the ESKD population is
95 largely unknown. Only two small scale, non-UK based, randomised controlled trials (RCTs)
96 have examined the efficacy of cognitive behavioural therapy (CBT) relative to usual care
97 among haemodialysis patients (8, 9). Both trials found CBT was effective in reducing
98 psychological distress. These findings are consistent with larger scale RCTs of CBT
99 treatments for depression in people with coronary heart disease (10).

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2
3 100 The NHS has limited resources to allow the demand for CBT therapist time to be met
4 101 adequately. A practical approach to address this problem is to implement a stepped care
5 102 health service delivery model (11). Within this model individuals begin with low-intensity
6 103 interventions unless their distress is deemed too severe to benefit from the type of minimal
7 104 intervention offered. Providing low-intensity treatments means that there is decreased
8 105 treatment burden for patients, but equally health services can treat a larger volume of
9 106 patients. If necessary a patient is “stepped up” to receive more intensive intervention if the
10 107 initial low-intensity treatment did not improve outcomes.

11 108 Guided self-help CBT treatments are considered low-intensity interventions (12) and are
12 109 effective in the management of psychological distress in people with (13) and without co-
13 110 morbid physical health conditions (14). On-line/computerised self-help resources allow
14 111 better management of the informational needs of patients and encourage active
15 112 engagement with treatment by interacting with the online interface (15). Indeed, in people
16 113 without physical health conditions, online/computerised guided self-help treatments have
17 114 largely demonstrated equivalence with face-to-face psychological interventions in terms of
18 115 their clinical effectiveness (depression and anxiety) (16) and degree of adherence to
19 116 treatment sessions (17).

20 117 However there are a number of factors that determine the efficacy of online and
21 118 computerised self-help treatments. One moderating factor is whether support is provided
22 119 by a health care professional. Online/computerised self-help treatments with support from
23 120 health care professionals improves outcomes and prevents treatment drop-out (18, 19). The
24 121 type of support provided is also important. A recent RCT explored the efficacy of online CBT
25 122 with weekly technical/motivational support telephone calls from a non-clinician for the
26 123 management of depression and compared it with usual GP care (20). Its findings confirmed
27 124 that providing patients with access to online CBT with only technical support had no added
28 125 benefit on depression outcomes compared with GP usual care. Access to a skilled therapist
29 126 is especially important in the context of co-morbid mental and physical health conditions
30 127 because of the potential for treatment antagonisms, whereby the effective management of
31 128 a person’s mental health has the potential to dysregulate the management of physical
32 129 health or vice versa (21).

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3 130 Given that the evidence points to the efficacy of online/computerised treatments with
4
5 131 therapeutic support for the management of psychological distress in people with and
6
7 132 without physical LTCs; it remains uncertain whether these findings apply to the
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9 133 management of psychological distress in UK NHS haemodialysis treatment settings. This
10
11 134 study seeks to explore the feasibility and acceptability of implementing a two arm parallel
12
13 135 RCT of online CBT with (intervention arm) and without (control arm) therapist support to
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15 136 improve psychological distress in people receiving haemodialysis treatments within a
16
17 137 stepped care health service delivery framework.

138 *Background to the study*

139 The development of the improving distress in dialysis (iDiD) online CBT treatment involved a
140
141 multi-disciplinary team of health psychologists, clinical psychologists, psychiatrists,
142
143 nephrologists, and six patient and public involvement representatives. The preliminary
144
145 content of the website was initially determined by self-help resources used to manage
146
147 adjustment outcomes in LTCs implemented in previous trials by one of our authors (RMM)
148
149 (22-24). In addition, a literature review of the correlates of distress in dialysis was used to
150
151 develop an ESKD specific CBT treatment formulation and seven session protocol (25). In
152
153 brief our CBT formulation recognises the unique acute and chronic stressors that occur in
154
155 the dialysis population including: ESKD diagnosis, surgical procedures needed for vascular
156
157 access site generation, loss of independence, changes in body and self-image, uncertainty
158
159 about health and future, the unseen burden of kidney disease, and chronic illness self-
management challenges-specifically managing thirst and food cravings, and dealing with
health professionals. CBT intervention techniques for managing these illness specific
stressors are then introduced in subsequent online treatment sessions. The content of each
treatment session was first drafted on paper and reviewed by the research team. Patient
representatives then provided feedback on the relevance and ease of understanding of the
information and CBT intervention techniques described. Next the intervention content was
uploaded onto an online platform using LifeGuide software (26). The presentation and
navigation through the website was tested using patient representatives and “think-aloud”
techniques. This process occurred iteratively so that comments on early sessions could be
incorporated into the design of subsequent sessions.

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3 160 The intervention includes a total of seven sessions. The content of each session is
4
5 161 summarised in supplementary table 1. For more detailed information see our distress in
6
7 162 dialysis CBT treatment formulation model (25). Patients are encouraged to complete one
8
9 163 session per week and each session was designed to last approximately one hour in duration.

10 11 164 **Objectives**

12
13 165 The following aims will be addressed as part of the feasibility and acceptability study of a
14
15 166 feasibility parallel RCT of online CBT with therapist led telephone support vs online CBT
16
17 167 without therapist support, delivered within a stepped care framework among outpatient
18
19 168 haemodialysis patients with co-morbid psychological distress.

- 20
21 169 1. To assess the feasibility and acceptability of screening all patients who attend for
22
23 170 haemodialysis. Patients will be screened for depression and anxiety using
24
25 171 standardised measures presented on iPads. The presence of psychological distress is
26
27 172 often not identified by non-mental health trained clinicians (27). Implementing
28
29 173 screening questionnaires for psychological distress in medical settings can promote
30
31 174 its detection (28) and ultimately the provision of mental health care. We will
32
33 175 quantify the number of people who agree to be screened.
- 34
35 176 2. To explore rates of recruitment and retention into the trial.
- 36
37 177 3. To examine willingness to be randomised to either the intervention arm (with
38
39 178 telephone support) or control arm (no telephone support) by recording participant
40
41 179 reasons for non-consent into the study (if disclosed).
- 42
43 180 4. To explore the level of adherence to online treatment sessions and telephone
44
45 181 support calls (intervention arm only).
- 46
47 182 5. To explore the potential efficacy of an online intervention with therapist led
48
49 183 telephone support in reducing psychological distress when compared with website
50
51 184 alone. This will inform the planning of a future full-scale trial to detect clinically
52
53 185 meaningful change in psychological distress outcomes.
- 54
55 186 6. To examine if change in quality of life differs between the intervention arm and
56
57 187 control arm
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59 188 7. To provide a preliminary assessment of the cost-effectiveness of the intervention.
- 60

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2
3 189 8. To examine change in ESKD illness cognitions and whether their effect differs
4 190 between the intervention and control arm.
5
6 191 9. To qualitatively explore patient perceptions of the acceptability and usability of the
7 192 website and telephone support calls and identify areas of improvement for future
8 193 interventions.
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13 194 **Methods**

14 195 *Design*

15
16 196 A two parallel armed randomised controlled feasibility trial (RCT). Participants will be
17 197 randomised, individually, using a 1:1 ratio computerised algorithm. A nested qualitative
18 198 study will evaluate patient experience.
19

20 199 *Setting and participants*

21 200 Participants will be recruited from haemodialysis units at Guy's and St Thomas' hospital
22 201 (London, UK).
23

24 202 Participants will be eligible for inclusion if:

- 25 203 1) Aged 18 years or over and receive hospital haemodialysis three-times weekly.
26 204 2) They have mild to moderately severe depressive symptoms (based on PHQ-9 (29)
27 205 scores of 5 to 19; a self-report measure of depression) and/or presence of mild to
28 206 moderately severe anxiety symptoms (based on self-report GAD-7 (30) scores of 5-
29 207 14).
30 208 3) They speak English sufficiently well to engage with screening tools.
31 209 4) They have a basic understanding of how to use the Internet and an email address.
32

33 210 Participants will be ineligible if:

- 34 211 1) Currently receiving active treatment for depression and/or anxiety. Active treatment
35 212 is defined as any current psychological treatment (talking therapies) or receipt of a
36 213 new anti-depressant and/or anti-anxiety medication. A medication is considered new
37 214 if commenced three months prior to the completion of the depression and anxiety
38 215 screening questionnaire.
39 216 2) They have a severe mental health disorder, for example, psychosis, bi-polar disorder.
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3 217 3) They have active suicidal thoughts, as indicated by a score of greater than one on the
4 218 depression PHQ-9 item “Thoughts that you would be better off dead, or of hurting
5 219 yourself”.
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8 220 4) They have evidence of addiction to alcohol or drugs.

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11 221 A participant will be withdrawn from the study if:

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13 222 1) There are safety concerns in relation to their physical or mental health.
14 223 2) The participant chooses to withdraw from the study.
15 224 3) A patient’s level of psychological distress deteriorates.

16
17 225 **Flow of recruitment and participant timeline**

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20 226 Participants will be identified for inclusion using web-based screening questionnaires
21 227 routinely used as part of the Integrating Mental and Physical healthcare: research, training
22 228 and services (IMPARTS) initiative at Guy’s and St Thomas’ hospital (31). Participants
23 229 consenting to the screen will be assessed for depression and anxiety using the PHQ-9 (32)
24 230 and GAD-7 (30) respectively. The PHQ-9 is a nine item self-report questionnaire deemed
25 231 acceptable for the identification of depression in medical care settings, including specialist
26 232 settings (28). Likewise, the GAD-7, is a self-report seven item questionnaire with evidenced
27 233 criterion validity for the detection of generalized anxiety disorder (30). Both the PHQ-9 and
28 234 GAD-7 are routinely used in UK primary care Improving Access to Psychological Therapy
29 235 (IAPT) sites (33) to monitor patient outcomes. The patient will complete the web-based
30 236 questionnaires either alone or with the assistance of a renal nurse/researcher. Whilst
31 237 completing the screening questionnaire, patients will be asked to give their permission
32 238 (yes/no) for a member of the research team to contact them about the present study.

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37 239 Results from the screening questionnaires are uploaded onto the patient’s electronic
38 240 medical record. Results will be checked by the nursing team/researcher for immediate risk.
39 241 Risk is defined as a score of greater than one on the depression PHQ-9 item “Thoughts that
40 242 you would be better off dead, or of hurting yourself”. If suicidal ideation is detected then a
41 243 risk assessment will be performed to determine the immediacy of referral to either liaison
42 244 psychiatry or renal clinical psychology. Level of risk will be assessed in line with the IMPARTS
43 245 risk assessment protocol. This includes enquiring about degree of suicidal ideation and level
44 246 of hopelessness, whether active plans are present, enquiring about the patient’s history of

247 suicidal attempts, recent life stressors, protective factors, and degree of social support. The
248 outcome of the risk assessment will be immediately discussed with either the renal clinical
249 psychologist or liaison psychiatrist and a management plan will be put into place.

250 Anonymised screening results will be securely emailed from the IMPARTS database to the
251 iDiD research team on a weekly basis. A stratified stepped care model, according to the
252 criteria outlined in Figure 1 will be applied to the anonymised data to identify potentially
253 eligible participants for the study. The stratified stepped-care approach assigns individuals
254 to treatments of varying intensity based on the severity of their symptoms (34). PHQ-9
255 scores within the range of 5-19, are considered indicative of mild to moderately severe
256 symptoms of depression (32). Likewise, GAD-7 scores within the range of 5 to 14 indicate
257 the presence of mild to moderately severe anxiety (30). Individuals with mild to moderately
258 severe symptoms of depression and/or anxiety will be considered appropriate for treatment
259 with the iDiD online CBT program and for inclusion in this study. Individuals with severe
260 depression (PHQ-9 score ≥ 20) and/or anxiety (GAD7 score ≥ 15) or individuals with evidence
261 of current suicidal ideation are considered inappropriate for iDiD online CBT. These patients
262 will be referred and managed by either the renal clinical psychology team or liaison
263 psychiatry (when detected at the point of screen).

264 Individuals who meet the criteria for mild to moderately severe symptoms of depression
265 and/or anxiety will have their data de-anonymised providing they give us consent to contact
266 them about the study. These potential participants will be screened against the remaining
267 inclusion/exclusion criteria during weekly referral meetings with the research and clinical
268 team. If they remain eligible then a researcher will approach the participant whilst they
269 attend for dialysis to explain the study with the participant information sheet. Participants
270 will be given a minimum of 24 hours to establish if they would like to take part.

271 All patients with mild to moderately severe symptoms of depression and/or anxiety who
272 either: i) do not meet our remaining study inclusion criteria, ii) choose not to consent into
273 the study, or iii) do not provide consent for us to approach them about the study will be
274 provided with the option of receiving usual care follow-up from the renal clinical psychology
275 team. Usual care includes a face-to-face clinical assessment followed by a tailored
276 psychological treatment intervention or referral to an IAPT service.

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3 277 As discussed above, patients who screen positive for severe symptoms of depression and/or
4 278 anxiety (PHQ-9 score ≥ 20 and/or GAD7 score ≥ 15) will receive an automatic referral to the
5 279 renal clinical psychology team. If upon clinical assessment by the renal clinical psychologist a
6 280 severely depressed and/or anxious patient is deemed appropriate for the iDiD self-help
7 281 study, then they will be “stepped down” for approach by the iDiD research team. Likewise,
8 282 the research team will be informed by the renal clinical psychology team of any patients
9 283 who meet the iDiD study inclusion criteria and declare an interest in the study despite
10 284 initially stating during screening that they did not want to be contacted by the study team.

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18 285 Participants who consent to take part in the study will be issued with an iDiD study
19 286 identification number. A researcher will attend the dialysis unit and help the patient to sign-
20 287 up to the iDiD online CBT treatment using an iPad. At sign-up participants will be asked to
21 288 enter their personal email address and select a password for use each time they logon. At
22 289 the point of sign-up participants will also be asked to enter their NHS number (supplied to
23 290 them by the researcher) to ensure that multiple iDiD accounts are not registered by the
24 291 same participant. Participants will then receive a confirmatory email with a link to the iDiD
25 292 website. After signing up, participants will complete the baseline questionnaires online. If
26 293 baseline questionnaires are not completed, then participants will receive two reminder
27 294 emails and an assistance based telephone call/visit at the dialysis unit. Participants will be
28 295 informed of their randomisation process outcome immediately after completing the online
29 296 baseline questionnaire. Participants will also receive an email confirming their treatment
30 297 allocation. We anticipate the participant’s journey through the study will last approximately
31 298 six months as summarised in Figure 2. We expect a period of one month to elapse from the
32 299 point of screening to randomisation. Once participants are randomised, both groups will be
33 300 able to access the iDiD website for a period of 12 weeks before being prompted to complete
34 301 the follow-up questionnaires via email. The email will also advise participants that their
35 302 access to the iDiD website is ending within a few weeks and to print off any information
36 303 they have found helpful from the “My tasks” tab of the website. Two reminder emails and
37 304 an assistance based telephone call/visit will occur over a period of three weeks if the follow-
38 305 up questionnaires remain incomplete. After 20 weeks participants will receive an email
39 306 thanking them for their participation in iDiD study. Access to the iDiD website will no longer
40 307 be available after this time. On completion of the three month follow-up questionnaires a

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3 308 subsample of participants will be asked to complete a qualitative interview. We will follow-
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5 309 up participants for a period of approximately six months post their randomisation date to
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7 310 complete the interview.

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9 311 **Randomisation, allocation concealment, and blinding**

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11 312 Participants will be randomised to iDiD online CBT plus therapist led telephone support or
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13 313 iDiD online CBT only condition using Lifeguide software (a computerised random number
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15 314 generator with a 1:1 ratio). Because the randomisation sequence is automated by Lifeguide
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17 315 in real-time the allocation sequence is concealed from researchers. All baseline
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19 316 questionnaires will be completed online prior to randomisation. Participants will be
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21 317 randomised at the individual level. The trial co-ordinator will also receive an automated
22
23 318 email informing them of the outcome of the randomisation procedure to identify
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25 319 participants who require telephone support calls during the trial. The researcher conducting
26
27 320 the qualitative interviews will also be unblinded at follow-up to ensure that appropriate
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29 321 questions are asked in relation to telephone support calls. Because of the nature of the
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31 322 intervention patients will not be blind to their treatment allocation. Follow-up outcomes will
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33 323 be completed independently by participants when prompted by email unless the participant
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35 324 requires assistance. The statistician will remain blinded to treatment allocation.

36
37 325 *Trial Intervention*

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39 326 All participants have access to the iDiD online CBT treatment (summarised in supplementary
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41 327 table 1 and described in detail in our ESKD CBT formulation model (25)). Participants will be
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43 328 advised in the participant information sheet to logon to the website once a week.
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45 329 Participants will also receive weekly reminder emails to encourage engagement with the
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47 330 website. iPADs will be available for participants to use during their dialysis sessions.

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49 331 *iDiD online CBT website plus therapist led telephone support (Intervention arm)*

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51 332 Participants in the intervention arm of the trial will receive three 30 minute telephone
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53 333 support calls at weeks two, four, and six from JH who has a PhD in health psychology and is
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55 334 a trained psychological wellbeing practitioner (PWP). PWPs typically work in primary care
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57 335 mental health teams as part of the UK Improving Access to Psychological Therapies (IAPT)
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59 336 initiative (33). PWPs deliver low-intensity CBT treatments including: cognitive restructuring,
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337 behavioural activation, problem solving, medication management, exposure therapy, and

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3 338 sleep management. The purpose of the telephone support calls are to promote engagement
4 339 with the website and to support the patient in collaboratively developing goals to work on
5 340 using the resources and information available to them on the website. At the start of each
6 341 telephone call the PWP will set an agenda with the participant. The first telephone support
7 342 call is scheduled for when the participant will have completed session two online. During
8 343 session two the participant will have completed a self-assessment and developed their own
9 344 personal model of distress. Thus during the first call the PWP will develop a shared
10 345 understanding of the participants source of distress, provide empathy, reinforce with the
11 346 participant the relationships between thoughts, feelings, and behaviours, and inform
12 347 participants of the content the website which is likely most applicable to them as they
13 348 continue to move forward with the website. The PWP and patient will develop a goal to
14 349 work towards prior to their next telephone call.

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25 350 The second telephone support call will provide an opportunity for the PWP to review with
26 351 the participant their progress on their self-generated goals, work through a particular
27 352 cognitive-behavioural intervention technique selected by the participant, and close the
28 353 session with a shared goal to work towards with the help of the website in advance of the
29 354 final telephone support call. The final telephone support call will follow a similar format
30 355 except the telephone session will end with a relapse prevention plan. The plan will be
31 356 generated collaboratively with the patient. All telephone support calls will be audio-
32 357 recorded to provide intervention fidelity checks and for self-reflection during clinical
33 358 supervision.

359 *Clinical supervision*

360 JH was trained to deliver the telephone support calls using role played sessions with
361 feedback from RMM. Ongoing supervision will be provided by a renal clinical psychologist
362 (AC). Shared reflection on audio-recorded sessions will be discussed in line with the core
363 competency framework for delivering psychological therapies in long-term conditions (35).
364 Shared goals will be identified for the PWP to work towards over the course of the study.
365 Supervision will also be an opportunity for case management. The PWP will discuss their
366 proposed treatment plan in response to the first telephone support call and degree of
367 patient progress at each supervision session. If a patient needs to be stepped up to receive

368 more intensive psychological treatments then this will be initiated by the research team and
369 managed by the renal clinical psychologist.

370 *iDiD online CBT website with no telephone support (control arm)*

371 Participants allocated to the control arm of the study will receive their usual renal care in
372 addition to having access to the website. Usual care for individuals with ESKD managed with
373 haemodialysis includes attending for dialysis three times per week for up to five hours at a
374 time. Participants can be referred or self-refer into the renal clinical psychology service or
375 primary care mental health service if their symptoms of depression and/or anxiety increase.
376 We will ask participants in the three-month follow-up questionnaire whether they have
377 commenced any new treatments for mental health since starting the study.

378 **Outcomes**

379 *Data collection and feasibility outcomes*

380 Because this is a feasibility study our primary focus is to collect data on the feasibility and
381 acceptability of the trial design and intervention by collecting descriptive data on
382 *recruitment and retention rates and willingness to be randomised* according to CONSORT
383 trial guidelines (36). We will also examine *adherence* to the online intervention and
384 telephone support calls (intervention arm only). The degree of adherence to the online
385 intervention will be automatically recorded by the Lifeguide software. We will calculate
386 descriptive values for the mean number of sessions completed, the number of participants
387 who complete all sessions, the number of participants who complete 50% or more sessions,
388 and the number of participants who complete each session. Degree of adherence to the
389 telephone call (intervention arm only) will be recorded by the psychological wellbeing
390 practitioner. The following values will be calculated: mean number of telephone calls
391 completed, number of participants who complete all telephone calls, number who complete
392 one or more telephone call, number of participants who complete telephone sessions one,
393 two, and three respectively, and mean duration of telephone calls across all three telephone
394 support calls. In addition to a qualitative interview (described below) patients will be asked
395 to self-report their experience of using the iDiD website at three months follow-up. The
396 open-ended questions will enquire about: i) how useful they found the iDiD website and ii)
397 whether they found the website easy to use. Participants will also be given the option to

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3 398 add any further comments.
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5 399 Self-reported patient outcomes will also be collected via the iDiD website at baseline and
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7 400 three months follow-up. The assessment schedule completed by patients is summarised in
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9 401 Table 1 and described below.

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11 402 • Continuous self-report measure of depression: PHQ-9 (32) (described in detail
12 above, scale range from 0 to 27, high scores indicate greater depressive symptoms)
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14 403
15 404 • Continuous self-report measure of anxiety: (GAD-7) (30) (described in detail above,
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17 405 scale range from 0 to 21, high scores indicate greater anxiety symptoms).
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19 406 • The five item EuroQoL (EQ-5D) (37) includes a five item measure of health status
20 across the following domains: mobility, ability to self-care, ability to continue with
21 407 activities (i.e. work, social life), pain, and anxiety and depression. In addition it has a
22 408 visual analogue scale ranging from 0 to 100 where a person is asked to rate their
23 409 overall health. The EQ-5D is recommended by NICE for use in cost-effectiveness
24 410 evaluations (38).
25 411
26 412 • The Client Service Receipt Inventory (CSRI) (39) collects retrospective data on service
27 413 use across the following five domains: i) background and client information (i.e.
28 414 hospital admissions and discharge, frequency of GP visits, medications), ii)
29 415 accommodation and living situation, iii) employment history, earnings, and other
30 416 personal resources, iv) service receipt (i.e. hospital appointments, home help), and v)
31 417 receipt of informal care from caregivers. The CSRI was amended to make its content
32 418 relevant to the needs of the dialysis population in collaboration with the trial health
33 419 economist (PM) and Renal Consultant (DG).
34
35 420 • The brief illness perception questionnaire (BIPQ) (40) will assess participants self-
36 421 reported beliefs about their ESKD. The BIPQ was developed and validated among
37 422 patients with long-term conditions, including renal disease. This information will be
38 423 assessed at baseline and follow-up. It will provide an indication of whether
39 424 participants beliefs about their ESKD change in response to clinical intervention.
40
41 425 • Satisfaction with care will be evaluated using a 2-item scale that asks participants to
42 426 rate their degree of satisfaction with the care they receive for their physical and
43 427 mental health on a five-item Likert response scale. This information will be assessed
44 428 at baseline and follow-up.
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3 429 • Serious adverse events will be directly enquired about using self-report at follow-up
4 430 only, according to good clinical practice guidelines. Participants will be asked
5 431 whether they have experienced any adverse events since starting the study choosing
6 432 from a list of five options. If participants indicate they have experienced adverse
7 433 events then they will be asked for details. In addition participants will be asked if
8 434 they have experienced any adverse health effects since starting the study and
9 435 encouraged to elaborate where needed.
- 10 436 • Treatments for depression and/or anxiety: Two brief self-report questions at follow-
11 437 up will ask participants if they have received any pharmacological or psychological
12 438 treatments for their depression and/or anxiety in addition to the iDiD website since
13 439 starting the study.

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22 440 *Socio-demographic and clinical characteristics*

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25 441 Socio-demographic characteristics including: gender, age, ethnicity, home environment
26 442 (marital status, housing situation, number of dependents) and level of education will be
27 443 collected at baseline only via self-report. Clinical characteristics including: dialysis vintage
28 444 and treatment history for depression and anxiety will be self-reported by patients at
29 445 baseline.

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31
32 446 Number and type of co-morbidities will be extracted from notes at baseline only. The
33 447 following clinical outcomes and covariates will be extracted from notes at baseline and
34 448 follow-up: Kt/V (dialysis treatment adequacy), haemoglobin, serum albumin, C reactive
35 449 protein, serum potassium levels, interdialytic weight gain, and serum phosphate levels.

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38 450 **Qualitative interviews**

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41 451 Qualitative interviews with a sub-group of participants over the phone will be conducted
42 452 post-intervention (three months) by a researcher who has not been involved in their
43 453 treatment. These interviews will explore whether the intervention met patient expectations,
44 454 positive and negative opinions about the website, whether patients felt they gained any
45 455 benefit from using website, its personal relevance to them, and its acceptability as a
46 456 treatment. A minimum of ten participants will be purposively sampled across a range of
47 457 socio-demographic and clinical characteristics (e.g. treatment group, age, gender, ethnicity,
48 458 dialysis vintage, degree of adherence to the intervention, degree of improvements in

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3 459 outcomes from the intervention). Interviews will continue until data saturation occurs. The
4 460 outcomes of these qualitative interviews will help to revise our theoretical understanding of
5 461 distress in dialysis and update the content of the intervention accordingly, in line with
6 462 current medical research guidelines for process evaluations (41). Interviews will be
7 463 transcribed verbatim and an inductive thematic analysis will be performed.

12 13 464 **Sample size**

14 465 The aim of this study is to explore the feasibility of implementing our trial procedures and to
15 466 inform a power calculation for a future randomised controlled trial. We have calculated the
16 467 sample size required based on the margins of error associated with recruitment. The
17 468 approximate size of the Guy's and St Thomas' dialysis population is 600 patients, in which
18 469 we expect to be able approach 400. Assuming a conservative uptake rate of 50%, 200
19 470 patients will be screened with approximately 40% meeting the inclusion criteria (the
20 471 estimated prevalence of depression symptoms in HD patients; see (4)). If we assume 50% of
21 472 those eligible will consent to be randomised a sample size of approximately 66 would allow
22 473 us to estimate the true population consent rate with a 5% margin of error and a 95%
23 474 confidence level.

24 475 **Analysis plan**

25 476 To examine the feasibility and acceptability of our screening, recruitment, retention, and
26 477 randomisation process (objectives 1-3), we will quantify the flow of participants through the
27 478 study using frequencies and percentages in accordance with the consort flow diagram (36)
28 479 shown in Figure 2. We will also record and quantify reasons for non-consent, exclusion, and
29 480 drop-out for each stage of the study. We will examine degree of adherence to the
30 481 intervention and telephone support calls (where applicable) using descriptive statistics
31 482 (objective 4).

32 483 We will also perform an *exploratory* intention to treat mixed model analysis blind to
33 484 treatment group on the following self-report outcomes at three months follow-up:
34 485 depression, anxiety, and quality of life (objective 5 & 6). Variability in these patient
35 486 outcomes will help to inform a future power calculation for a full-scale trial.

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3 487 Service costs will be calculated by combining service use data with appropriate unit costs
4 488 (42). These will be added to the costs of the intervention which will be based on
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6 489 development costs and the time spent providing telephone support. Costs will be compared
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8 490 between the two groups and cost-effectiveness assessed by combining the costs with the
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10 491 primary outcome measures and quality adjusted life years (QALYs) in the form of
11
12 492 incremental cost-effectiveness ratios (ICERs). Uncertainty around the ICERs will be
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14 493 addressed using cost-effectiveness planes and acceptability curves (objective 7). We will
15
16 494 also perform an exploratory process analysis using intention to treat mixed models to
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18 495 establish whether illness cognitions changed in response to the online intervention and
19
20 496 whether differences occurred between the intervention and control group (objective 8).
21
22 497 Qualitative interviews will be transcribed verbatim and analysed using thematic analysis to
23
24 498 allow the feasibility and acceptability of the online intervention and telephone support calls
25
26 499 to be explored (objective 9).

27 500 **Ethics**

28
29 501 This study has ethical approval from the NHS research ethics committee (14/LO/1934) and is
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31 502 sponsored by King's College London.

32 33 503 **Data collection and management**

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35 504 The IMPARTS screening interface, developed by Teleologic Ltd, is web-based and installed
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37 505 on the server configuration at Guy's & St Thomas' Hospitals NHS Foundation Trust. The
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39 506 patient logs on to the system with their unique Hospital Number. Their screening results are
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41 507 outputted to the documents folder of the Electronic Patient Record via the most secure wifi
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43 508 network within each NHS Trust.

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45 509 All quantitative outcomes are measured via online questionnaires that participants will
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47 510 access via iDiD website. The information is stored on a secure server associated with the
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49 511 Lifeguide program at the University of Southampton. The website prompts the participant
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51 512 when data is missing. Study data can only be downloaded from the server by members of
52
53 513 the research team who are granted password access. All data will be confidentially stored in
54
55 514 accordance with the data protection act (43) and King's College London data management
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57 515 procedures.

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3 516 **Formal committee**

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5 517 A trial management team will meet regularly to discuss the overall running of the study
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7 518 including: rates of recruitment, adherence to the protocol, safety and confidentiality of
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9 519 patients. All serious adverse events related to the study will be reported to the study
10
11 520 sponsor, ethics committee and Guy's and St Thomas' research and development
12
13 521 department.

14
15 522 **Discussion**

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17 523 Psychological distress is common in people with ESKD. However, studies examining the
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19 524 efficacy of either pharmacological or psychological interventions for the management of
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21 525 distress in dialysis are limited. Likewise, access to psychological treatment interventions
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23 526 tailored to the specific psycho-social stresses associated with ESKD is problematic. An online
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25 527 CBT treatment designed specifically to manage distress in dialysis offers a pragmatic
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27 528 solution to under-resourced health services, which are advised to offer integrated mental
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29 529 and physical health care treatments.

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31 530 This is the first study to examine whether it is feasible to implement a RCT of online CBT
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33 531 with telephone support vs online CBT without telephone support within a stepped care
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35 532 framework to secondary care haemodialysis patients with co-morbid distress. Indeed, it will
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37 533 identify unique challenges that occur in the dialysis population in the recruitment and
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39 534 retention of patients. Likewise, the study will be able to simultaneously examine the
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41 535 acceptability of this treatment to patients in terms of whether its content was relevant and
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43 536 useful. In addition, the utility of the online mode of delivery with or without telephone
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45 537 support will be examined. We anticipate that the results of this trial will substantially
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47 538 inform the design of a future large scale trial powered to detect the efficacy of online CBT
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49 539 treatments for the management of distress in dialysis.

50
51 540 **Trial Status**

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53 541 The study commenced recruitment in February 2015. Recruitment will continue until
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55 542 February 2016 with the last patient's follow-up in May 2016. Outcomes will be disseminated
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57 543 at national and international conferences and in journal articles.

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3 545 **List of abbreviations**
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5 546 CBT, Cognitive behavioural therapy; ESKD, End-stage renal disease; ICERS, incremental cost-
6 effectiveness ratios; iDiD, Improving distress in dialysis; QALYs, Quality Adjusted Life Years;
7 547
8 RCT, Randomised Controlled Trial
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10
11 549 **Authors Contributions:**
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14 550 Study design: All authors
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17 551 Intervention development: JH, RMM, DG, AC, LY, JC:
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19 552 Statistical analysis plan: PM, JC.
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21 553 All authors contributed to writing the protocol.
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23

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Table 1: Schedule of assessments

Assessment	Time		
	Screening	Baseline	3 months
PHQ-9	x	x	x
GAD-7	x	x	x
EQ-5D		x	x
Client Service Receipt Inventory		x	x
Socio-demographics		x	
Clinical characteristics		x	
Biological clinical outcomes		x	x
Self-reported adverse events			x
Self-reported treatments for depression and anxiety during the study			x
Brief illness perception questionnaire		x	x
Satisfaction with care		x	x
Experience of using the iDiD website			x

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6 677 Figure titles:
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8 678 **Figure 1: Stratified stepped care referral pathway for managing psychological distress**
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10 679 **among individuals attending for haemodialysis**
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13 681 **Figure 2: Flow of participants through the study**
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For peer review only



Figure 1: Stratified stepped care referral pathway for managing psychological distress among individuals attending for haemodialysis

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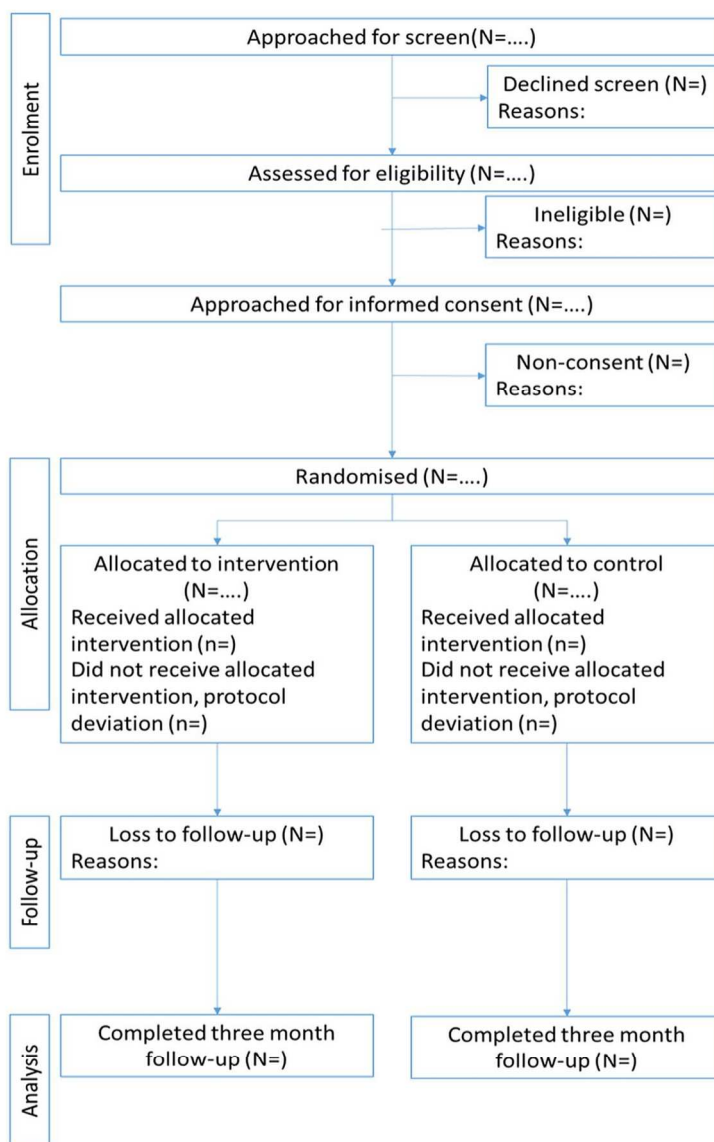


Figure 2: Flow of participants through the study
99x153mm (300 x 300 DPI)

Supplementary table 1: Summary of iDiD online treatment sessions

Session	Content
1. What is end-stage renal failure?	<p>-Psycho-education including information about:</p> <ul style="list-style-type: none"> -ESKD and its treatment. -Expectation management concerning the effectiveness of dialysis treatments and its psycho-social consequences. -The rationale for specific ESKD treatments (i.e. improving physical health) and psychological interventions (i.e. improving emotional health). -Normalising the experience of distress in the context of dialysis.
2. Why do I feel distressed?	<p>-Recaps on information learnt about in session 1.</p> <p>-Self-generation of a personal model of distress. Patients self-identify their own vicious cycle to improve their understanding of the inter-relationships between ESKD specific stressors (triggers), feelings, thoughts, behaviours, and physical symptoms.</p> <p><i>Between session task:</i> Recap on the content of session 2 by re-reading the session.</p>
3. Dealing with my negative feelings	<p>-Recaps on information learnt about in session 2.</p> <p>-Revision of reinforcing relationship between unhelpful coping behaviours and the maintenance of psychological distress.</p> <p>-Explanation of positive emotion regulation strategies including: behavioural activation, emotional expression, graded exposure, and tips for improving the quality of sleep. Patients are also informed of the value of acceptance, relaxation, and physical exercise.</p> <p><i>Between session task:</i> Selection of a helpful coping strategy for managing negative emotions before completion of next online session.</p>

<p>1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26</p> <p>4. Tackling unhelpful thoughts about end-stage renal disease</p>	<p>-Recaps on information learnt about in session 3.</p> <p>-Examples of unhelpful thoughts typical in people with ESKD provided.</p> <p>-Information and skill development on the identification of unhelpful thoughts using thought records.</p> <p>-Explanation of how to challenge and gradually alter unhelpful thinking styles by generating alternatives.</p> <p><i>Between session task:</i> Continue working on goals from session three (if useful) and complete a thought record if relevant to their personal needs.</p>
<p>27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55</p> <p>5. Goal setting and problem solving</p>	<p>-Recaps on information learnt about in session 4.</p> <p>-The rationale for “SMART” goals and how to use the technique is explained in depth.</p> <p>-Information about the value of activity monitoring, behavioural activation, and action planning.</p> <p>-Explanation of the seven steps to problem solving technique is introduced. Use to foster confidence in illness self-management.</p> <p><i>Between session task:</i> Continue working on goals from previous sessions that remain useful and relevant. If applicable implement one of the following: i) “SMART” goal techniques, ii) activity monitoring/behavioural activation, or iii) seven steps to problem solving approach.</p>
<p>56 57 58 59 60</p> <p>6. Managing difficult social relationships</p>	<p>-Recaps on information learnt about session 5</p> <p>-Case examples of social situations people with ESKD find challenging (i.e. dealing with medical</p>

	<p>professionals) provided.</p> <ul style="list-style-type: none"> -Introduction to assertiveness concept and its effects on physical and psychological health. -Case examples provided of how others behave assertively in ESKD specific social contexts to allow participants to adapt for their own use. -Reflection on social support network and whether there is scope to improve it to meet physical, emotional, and informational needs. <p><i>Between session tasks:</i> Continue working on goals from previous sessions that remain useful and relevant. If feasible/applicable implement: a potential assertive responses to a stressful social situation or reflect on social support networks and how to optimise them.</p>
7. Progress recap and preparing for the future	<ul style="list-style-type: none"> -Recaps on the progress made over the previous six sessions by encouraging patients to reflect on their new skills and achieved goals. -Generation of action plans to continue using skills moving forward. Identification of a specific action plan to implement when an acute stressful situations arises.



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

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	_1_____
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	_2_____
	2b	All items from the World Health Organization Trial Registration Data Set	Documented in trial registry (2a) & page 1_____
Protocol version	3	Date and version identifier	_3_____
Funding	4	Sources and types of financial, material, and other support	_3_____
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	_1_____
	5b	Name and contact information for the trial sponsor	_3_____
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	_3_____

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	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	_NA for feasibility study_____
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Introduction

Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	4 to 6_____
	6b	Explanation for choice of comparators	5 to 6_____
Objectives	7	Specific objectives or hypotheses	7_____
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	7_____

Methods: Participants, interventions, and outcomes

Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	8_____
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	8 to 9_____
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	12 to 14_____
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	9_____
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	11 and 13_____
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	14_____

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3	Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	15 and 16 _____
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8	Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	9 to 13 _____
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11	Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	17 _____
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14	Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	17 _____
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17 **Methods: Assignment of interventions (for controlled trials)**

18 Allocation:

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21	Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions ¹²	12 _____
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26	Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	12 _____
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30	Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	9 to 12 _____
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34	Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	12 _____
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37		17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	NA as trial co-ordinator is not blind. _____
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Methods: Data collection, management, and analysis

Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	9 to 11_____
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	9 to 11_____
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	18_____
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	17 to 18_____
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	17 to 18_____
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	17 to 18_____

Methods: Monitoring

Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	NA for feasibility study_____
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	NA for feasibility study_____
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	16_____
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	NA for feasibility study_____

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3 **Ethics and dissemination**
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5	Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	18_____
8	Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	2 and 16_____
12	Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	9 and 10_____
16		26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	NA_____
19	Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	18_____
22	Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	3_____
25	Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	3_____
28	Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	NA harms addressed according to King's indemnity insurance_____
35	Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	19_____
39		31b	Authorship eligibility guidelines and any intended use of professional writers	20_____
41		31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	1_____

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Appendices

Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	Adheres to NHS consent form _____
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	_____

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

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