Tailored online cognitive behavioural therapy with or without therapist support calls to target psychological distress in adults receiving haemodialysis: a feasibility randomised controlled trial

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Abstract

Background: Psychological distress is prevalent in haemodialysis (HD) patients yet access to psychotherapy remains limited. This study assessed the feasibility and acceptability of online cognitive-behavioural therapy (CBT) tailored for HD patients, with or without therapist support, for managing psychological distress.

Methods: This feasibility randomised controlled trial recruited patients from a UK HD centre. Following psychological distress screens, patients with mild-moderate psychological distress (Patient Health Questionnaire PHQ-9; score: 5-19 and/or Generalised Anxiety Disorder; GAD-7 score: 5-14) who met remaining inclusion criteria were approached for consent. Consenters were individually randomised (1:1) to online-CBT or online-CBT plus three therapist support calls. Outcomes included recruitment, retention, and adherence rates. Exploratory change analyses were performed for: psychological distress, quality of life (QoL), illness perceptions, and costs. The statistician was blinded to allocation.

Results: 182 (44%) out of 410 patients approached completed psychological distress screens. 26% found screening unacceptable; a further 30% found it unfeasible. Psychological distress was detected in 101 (55%) patients, 60 of these met remaining inclusion criteria. The primary reason for ineligibility was poor computer literacy (N=17, 53%). Twenty-five patients were randomised to the supported (N=18) or unsupported arm (N=7); 92% were retained at follow-up. No differences in psychological distress or cost-effectiveness were observed. No trial adverse events occurred.

Conclusion: Online CBT appears feasible but only for computer literate patients who identify with the label *psychological distress*. A definitive trial using the current methods for psychological distress screening and online care delivery is unfeasible.

Introduction

Self-reported psychological distress, including symptoms of depression (1) and anxiety (2), affects approximately 39% of people living with end-stage renal disease (ESRD) treated with dialysis (1) and is associated with increased morbidity (3), mortality (4-6), and health care utilisation rates (7). Identifying and treating psychological distress in haemodialysis (HD) patients remains a challenge (8) because effective and pragmatic ways of delivering integrated mental and physical care are yet to be established in this setting.

Identifying psychological distress in HD patients is the first challenge. Implementing thorough psychological assessment interviews is unfeasible with scarce resource (9). Specific self-report screens for psychological distress are validated for use in physical long-term conditions (LTCs) (10) and offer a practical solution for routine assessment. However, screening alone is insufficient. Integrated support with evidence-based treatment pathways are required to ensure patients' in need of support are effectively managed at the appropriate level of care (11).

Cognitive behavioural therapy (CBT) is an effective psychotherapy for the treatment of psychological distress (12-14). Three relatively small studies found CBT improved psychological distress outcomes in HD patients (15-17). However, meta-analyses report small effect sizes for CBT in people with LTCs (18, 19). One reason for these small effects may be because CBT treatments were originally developed to treat primary mental health conditions (19, 20). The application of CBT to people with physical LTCs may require tailoring to ensure that factors unique to chronic illness, including maladaptive and/or erroneous perceptions of illness (21) and poor coping skills in response to illness (9) are targeted. NHS England pathfinder work conducted within existing Improving Access to Psychological

Therapy (IAPT) services suggested that integrating LTC self-management needs alongside more traditional methods of treating anxiety and depression obtained larger treatment effects (22). The *improving Distress in Dialysis* (iDiD) treatment is a tailored CBT protocol designed to manage psychological distress by providing patients with CBT skills which address the psychological mechanisms that perpetuate distress in response to haemodialysis specific symptom and self-management challenges (23). However, access to skilled psychotherapists to support the implementation of CBT in physical health contexts is limited (24).

One method of increasing access to CBT is via tailored online self-help programmes. Therapist supported online CBT demonstrates equivalent efficacy to face-to-face CBT for the management of psychological distress (25). In addition, online CBT has comparable adherence rates to psychotherapy treatment sessions when compared with face-to-face CBT (26). Online CBT can be delivered using a stepped-care health service delivery model (27). According to this model, individuals identified as having psychological distress are offered the least restrictive, yet most effective treatment first. The term least restrictive applies to the intensity of support provided. Thus type, duration, and frequency of patient-psychotherapist contact is titrated to individual need.

HD patients face a considerable treatment burden, thus offering online CBT as a first-line treatment is a pragmatic solution for resource limited patients and health services. Systematic reviews suggest that providing therapist support alongside online CBT improves outcomes, thus a degree of therapist input is likely required (28, 29). To inform a future full-scale randomised controlled trial (RCT), this feasibility study evaluated if HD specific online CBT (iDiD), with or without telephone therapist support, is a feasible and acceptable

treatment for mild to moderate psychological distress in HD patients. This feasibility RCT addressed the below quantitative objectives to determine the appropriateness of the study design for a definitive RCT:

i) Assess the feasibility and acceptability of online screening for symptoms of psychological distress in all patients attending for HD.

ii) Explore trial recruitment and retention rates.

iii) Explore adherence to online CBT sessions and therapist support calls (for the purpose of this feasibility study adherence is defined as engagement with scheduled psychotherapy treatments sessions and does not refer to adherence to dialysis or other treatment schedules).

iv) Examine the potential efficacy of therapist supported online CBT in lowering symptoms of psychological distress and improving quality of life when compared with online CBT only. This will allow an estimate of the standard deviation of outcomes to inform a future power calculation for a definitive trial.

v) Study whether illness perceptions differ post-intervention between the supported and unsupported online CBT arms. This will allow an estimate of the standard deviation of illness perceptions to inform a future power calculation for a definitive trial.

vi) Examine preliminary cost-effectiveness of therapist supported online CBT compared with online CBT only.

Subjects and Methods

Study Design and Participants

This two-arm parallel group feasibility RCT was conducted at Guy's and St Thomas NHS Trust (GSTT; London, UK) HD units which treat approximately 600 HD patients. NHS ethical approval for this feasibility study was granted in December 2014 (reference: 14/LO/1934). Our full study protocol is published elsewhere (30). Patients were recruited and individually randomised to therapist supported online CBT or online CBT only (no therapist support) between February 2015 and January 2016.

Patients were eligible for inclusion if they were ≥ 18 years old, received in-centre HD, and had co-morbid psychological distress, defined as mild to moderately severe symptoms of depression and/or anxiety. This included a score ranging from 5-19 on the Patient Health Questionnaire (PHQ-9)(31) and/or a score ranging from 5-14 on the Generalised Anxiety Disorder questionnaire (GAD-7)(32). Patients needed to speak English well and have a basic understanding of the internet and email address to remain eligible. Patients were ineligible if they were receiving treatment for psychological distress (active psychotherapy or commenced pharmacotherapy within the last three months), had a severe mental health disorder (e.g. psychosis), or had current suicidal ideation.

Inclusion criteria were modified after three months of recruitment. Incident HD patients were found to have greater motivation to participate. Our original protocol (ClinicalTrials.gov Identifier-NCT02352870[a]) had the following two exclusion criteria: i) dialysis vintage of ≤ three months and ii) hospitalised one month prior to completing self-

[a] Please note: Owing to a clerical error the study was originally registered as an interventional trial in clinicaltrials.gov. The correct option should have been to list this trial as *'other'* to match the content of the registration document that fully indicates that the design of the study is a feasibility trial.

report screen. These criteria were removed to increase recruitment, which is acceptable given the nature of the study is to assess feasibility.

Potential patients completed online self-report psychological distress screens (31, 32) whilst attending for HD. This occurred as part of the Integrating Mental and Physical healthcare: research, training, and services initiative (IMPARTS) (33). Online screens were completed, either alone or with nurse/researcher, using iPads. The screening process asked potential patients for permission to contact them about study participation. Patients who: i) had mild-moderately severe psychological distress symptoms, ii) gave permission for research contact, and iii) met remaining inclusion criteria were approached for consent. If severe psychological distress was detected during screening, then the appropriate health care professional was informed. Figure 1 details the stepped-care model with psychological distress thresholds applied in this study for onward referral.

Randomisation, allocation concealment, and blinding

Consenting patients were individually randomised after completing the online baseline questionnaire. Simple randomisation occurred via Lifeguide (34) which is a software used to program online interventions. An automated random number generator with a 1:1 ratio was used to randomise patients to either therapist supported online CBT or online CBT only. The patient was informed of their group allocation via the online CBT program. The patient and trial coordinator also received an automated email. Because randomisation was automated by Lifeguide the allocation sequence remained concealed from the trial coordinator (JLH) and psychological therapists/supervisors (JLH, AC). The nature of the trial meant patients were unblinded to allocated treatments. Follow-up outcomes were completed by patients when prompted via an automated email. It was necessary for the research team to

111 complete follow-up measures with some patients (N=16). The statistician (SN) remained
112 blind to treatment allocation until after the analyses were conducted.

113 *Improving Distress in Dialysis (iDiD) Intervention*

114 All patients had access to the iDiD online intervention. iDiD includes a seven session CBT
115 protocol presented in detail elsewhere (23). In brief, iDiD targets specific cognitive,
116 emotional, and behavioural mechanisms associated with psychological distress in HD.
117 Patients were encouraged to complete online sessions weekly with automated email
118 reminders. Sessions were designed to last approximately 60 minutes in duration. iPads were
119 available at dialysis units for on-dialysis completion.

120 *Supported arm: online CBT with therapist telephone support calls*

121 Patients in the supported arm received three 30-minute telephone calls scheduled at weeks
122 two, four, and six (post-randomisation). Telephone support was delivered by a trained
123 psychological wellbeing practitioner (PWP) with a PhD in Health Psychology (JLH). PWPs are
124 competent in the delivery of brief CBT interventions according to UK Improving Access to
125 Psychological Therapies curriculum (35). Support calls aimed to promote engagement with
126 the website and CBT skills through a collaborative and empathic patient-therapist
127 relationship. The PWP guided the patient to the most relevant components of iDiD CBT
128 whilst also reviewing and problem-solving progress collaboratively. Support calls were audio
129 recorded for clinical supervision and fidelity checks.

130 The PWP received training and fortnightly supervision from psychologists (RMM or AC).
131 Supervision involved feedback on recorded therapy sessions and case-management (36).
132 Patients identified as requiring more intensive clinical input were stepped up.

Unsupported arm: online CBT with no therapist support calls

The unsupported arm had access to iDiD CBT and usual renal care. Usual renal care includes attending for HD three times per week. Whilst attending for dialysis patients may encounter multidisciplinary renal team members. Contact with the renal psychologist only occurs if a patient is referred or self-refers for treatment. None of the patients allocated to the unsupported arm had contact with the renal psychologist prior to follow-up.

Outcomes

Feasibility studies are not powered to detect change in a primary outcome, such as symptoms of psychological distress. The focus was to collect outcome data related to trial design and intervention procedures. Descriptive statistics on recruitment and retention rates were collected, consistent with CONSORT guidance (37, 38). Adherence to online psychotherapy sessions and therapist support calls, including number of completed calls and duration were recorded.

Patients completed self-report outcomes at baseline and 12 weeks post-randomisation. The proposed primary outcomes for the full-scale clinical trial are depression measured using the PHQ-9 (31) and anxiety measured using the GAD-7 (32). The PHQ-9 has a scale range of 0-27; high scores indicate increased depressive symptoms. It has comparable diagnostic accuracy with longer clinician administered depression measures (10). The GAD-7 has a scale range of 0-21 (32). High scores indicate higher anxiety. The GAD-7 has evidence of diagnostic accuracy for detecting the presence of generalised anxiety disorder (39) Quality of life (QoL) was measured using EuroQoL scale (40)(EQ-5D) and is a proposed secondary outcome for the full-scale trial. It includes five items (range, 1-5) to assess mobility, self-care, usual activities, pain/discomfort, and anxiety and depression. High item scores indicate

poorer QoL. The EQ-5D also includes a visual analogue global health rating (range, 0-100), high scores indicate better global health ratings. Intended mediators for the full-scale clinical trial are ESRD illness perceptions. Illness perceptions were assessed using the eight item Brief Illness Perception Questionnaire (41). Each item uses a 10 point likert scale. Item scores can be summed to generate a total illness perception score. High total scores indicate a more negative perception of ESRD. For the health economic analyses the Client Service Receipt Inventory (CSRI) (42) was used to collect data on health service utilisation combined with appropriate unit cost information(43-45).

Demographic and Clinical data

At baseline, patients self-reported the following demographic and clinical data: gender, age, ethnicity, living arrangements, education, dialysis vintage (time on dialysis), and self-reported history of depression and/or anxiety. Number and type of co-morbidities according to UK renal registry criteria - Appendix B (46) were extracted from clinical notes. Data on diagnosis of depression and/or anxiety was also extracted (if recorded). At follow-up, patients were asked whether they had experienced any adverse events during the trial period (12 weeks) and whether they had received mental health treatments in addition to the trial.

Sample size

The precision of the estimated screening to consent rate was used to calculate the target sample size because statistical power calculations are not required for feasibility studies (47). GSTT treat approximately 600 HD patients. It was anticipated that 400 patients would be approached during recruitment because screening was facilitated via IMPARTS (33) online software and not all HD units were compatible with this software (e.g. privately

managed HD units). A conservative 50% (N=200) uptake rate for psychological distress screening was assumed. With these forecasted proportions, it allows us to assess the *consent to screen* rate (200/400) to within a standard error of ± 5%, based on 95% confidence intervals. From the population of patients screened (N=200) a further 40% (N=80) were estimated to meet criteria for psychological distress (based on previous prevalence estimates) (1)). A conservative 50% *consent to trial rate* (N=40) from the eligible pool of participants was assumed (40/80). With these forecasted values we are able to estimate a 50% *consent to trial rate* (from those meeting all eligibility criteria) to within a standard error of ± 11%, based on 95% confidence intervals. Likewise, our total *population trial consent rate* of 10% (e.g. 40/400) can be estimated to within a standard error of ± 3%, based on 95% confidence intervals. However, we aimed to achieve a higher sample size within the region of 66 given that our previous research in the dialysis achieved a *consent to study rate* within the region of 80% when assessing depression on dialysis (48).

Analysis

Descriptive statistics were used to quantify screening, recruitment, retention and adherence rates. Adherence to psychotherapy was conservatively defined whereby everyone was included in the analysis based on their condition assigned, unless a patient became deceased during the trial (26). Linear regression analysis controlling for baseline scores were used to compare depression, anxiety, QoL, and illness perception outcomes between the supported and unsupported arm at 12 weeks follow-up. Because this is a feasibility study and consistent with latest CONSORT guidelines for feasibility studies, we report effect sizes and their precision only (e.g. standard error and 95% confidence intervals)(38, 47). Cost-effectiveness analyses used a healthcare perspective. The cost of the intervention was

calculated as the cost of developing and maintaining the iDiD online CBT programme (assumed to be £1000 if rolled out) plus telephone and email support costs (therapist supported arm). The email and telephone support was provided by a PWP, with a PhD, thus unit costs were based on £86 per hour of direct contact, equivalent to a CBT therapist (43). Other service use was measured with the CSRI. The main outcome measure for the economic analysis was quality-adjusted life years (QALYs) derived from an EQ-5D value set for England (49). Incremental cost effectiveness ratios (ICERs) and QALYs were calculated using regression models with follow-up costs and QALYs as dependent variables, controlling for treatment group, baseline costs and EQ-5D score.

Results

Feasibility of screening, recruitment rates, and baseline sample characteristics

A total of 410 HD patients were approached to complete psychological distress screens, of which 182 (44.4%; 95% CI 39.5% to 49.3%) agreed (Figure 2). Many patients (N=115, 63.2%; 95% CI 55.7% to 70.2%) required assistance to complete the screen. Reasons for screen non-completion included either pragmatic/external barriers (e.g. language, illness) or internal/patient generated barriers (e.g. non-disclosure of decline reason, lack of perceived need for distress screen). Pragmatic/external barriers prevented screening in 121 patients (29.5%; 95% CI 25.1% to 34.2%) whilst patient generated barriers prevented screening in 107 patients (26.1%; 95% CI 21.9% to 30.6%).

Among the 182 patients who completed the screen, a total of 101 patients (55.5%; 95% CI 47.9% to 62.8%) had mild-moderately severe symptoms of psychological distress. Of these 101 patients, a further 60 (59.4%; 95% CI 49.2% to 69.1%) met remaining inclusion criteria.

Poor computer literacy (N=17, 59.4%; 95% CI 49.2% to 69.1%) was the main reason for study ineligibility. Figure 2 provides further ineligibility details.

Of the 60 patients meeting the eligibility criteria that were approached for consent, 35 (58.3%; 95% CI 44.9% to 70.9%) declined. The main reason for non-consent was a perceived lack of treatment need (N=15; 42.8%; 95% CI 26.3% to 60.6%; See Figure 2 for details). A total of 25 patients consented and were randomised to either online CBT with therapist support calls (N=18; 72%) or online CBT only (N=7; 28%). It was necessary to approach 16 patients for screening for every one patient randomised (410/25=16.4; 95% CI 11.1 to 25.3). The *consent to trial rate* was 41.7% among those meeting all trial inclusion criteria (25/60; 95% CI 29.1 to 55.1).

Patients who consented to be randomised (N=25) had a mean age of 48 (SD 12.01) years and were predominantly male (60%) of non-white ethnicity (60%). The sample had a mean dialysis vintage of 26.52 (SD = 1.16) months and a mean of 1.16 (SD 1.21) comorbidities. Depression scores at baseline indicated the presence of mild depressive symptoms (Median = 7; Interquartile range IQR= 4-10). Median anxiety scores at baseline were considered sub-threshold for symptoms of anxiety (< 5) (median = 4, IQR = 1-5). See tables one and two for baseline sociodemographic, clinical, and self-report descriptive statistics.

Adherence to online intervention and telephone support calls

Adherence to online CBT sessions were lower for patients randomised to the supported arm (Median=3, IQR=1-5) compared with the unsupported arm (Median=6; IQR range=2-6). Table A – online appendix summarises adherence to each of the seven sessions. On-dialysis completion was the preferred location for engaging with iDiD CBT in both trial arms. Table B – online appendix summarises the degree of adherence to the telephone support calls and

reasons for non-completion; 53% of patients completed two or more scheduled support calls.

Protocol deviations occurred in both trial arms. It was necessary to generate an email address and provide brief internet education for six patients (24% of consented sample; supported arm N=5, unsupported arm N=1), thus these patients received a higher degree of technical support and face to face contact. One patient in the supported arm was unable to receive therapist calls because of their intensive home-care program (e.g. carers present) and associated multimorbidity. On-dialysis support was provided for this patient.

Comparison of self-report outcomes between the supported and unsupported arms at 12 weeks follow-up

In terms of trial retention rates, 23 (92.0%; 95% CI 73.5% to 99.0%) patients completed depression and anxiety outcomes at follow-up. Follow-up data was collected between June 2015 and May 2016.

Table three summarises preliminary analyses exploring trends in treatment effects comparing therapist supported online CBT with online CBT only. Given the study was not powered to detect differences, significance testing was not performed and the treatment effect estimates are provided for descriptive reasons only and to guide the design of a future definitive trial. Cohen's d effect size estimates indicate that the difference between the supported and unsupported arm on measures of depression and anxiety were minimal with large confidence intervals, highlighting the uncertainty around this effect size estimate. Pre-post mean change analysis across the whole sample indicated that mean depression scores increased by 0.39 (SD = 3.99; scale range 0-27) and mean anxiety scores decreased by -0.61 (SD 4.97; scale range 0-21)

Effect sizes for QoL showed greater improvements in the supported arm when compared with the unsupported arm across the five QoL items (see table three) and the visual analogue overall health rating. The largest effects (Cohen's d ≥ 0.80) were observed for mobility, pain, and usual daily activities items. However, confidence intervals for these estimates were large demonstrating uncertainty around these findings.

Compared with the unsupported arm, patients in the supported arm showed an improved illness related appraisal of ESRD in 4 out of 8 of the illness perception subscales, with moderate effect sizes (Cohen's d within the region of 0.50; see table three). This included personal control, illness coherence, illness concerns, and identity domains. However, patients in the supported arm also reported having a more negative emotional response to ESRD compared with the unsupported arm. Confidence intervals for these estimates were large highlighting uncertainty.

Adverse events and other potential harms

A total of 10 adverse events were detected. None were deemed related to the study. An additional two events occurred that the study team were unaware of and were self-reported by patients. Both included a hospital admission related to a routine renal procedure (e.g. fistulaplasty). Two patients scores indicated the presence of suicidal ideation in response to questions concerning "Thoughts you would be better off dead or harming yourself." at follow-up. These patients were immediately contacted and a risk assessment was performed. These responses occurred because patients completed questionnaires whilst attending for dialysis, which acted as a trigger for their low mood and feelings of exasperation. Excluding the two patients in which suicidal ideation was detected no patients met criteria for onward referral for a step three or four intervention at follow-up

as outlined in Figure 1. One patient expressed an interest in seeking to continue their treatment gains in response to iDiD with further face-to-face input from clinical psychology and an onward referral was made. A fourth patient also expressed an interest in receiving face-to-face input after finding it difficult to logon and use the iDiD online treatment – this patient also received an onward referral to renal clinical psychology.

Cost-effective analysis

Service use at baseline was different between the two groups (Table C online appendix). The mean cost of the intervention was £40 for the unsupported arm, and £244 for the supported arm. The follow-up healthcare costs adjusted for baseline were £2,271 higher for the supported arm, but with the small numbers (n = 16) this was not significant (95% C.I. £-2,766 to £7,307). At follow-up, the unsupported arm gained 0.144 QALYs, and the supported arm gained 0.192 QALYs. Adjusting for baseline utility the supported arm had 0.0276 more QALYs than the unsupported group (95% C.I., 0.0107 to 0.0444). The ICER was £2271 divided by 0.0276, i.e. £82,283 per QALY albeit with wide confidence intervals (95% CI £51, 149 – £212, 243).

Discussion

This study reports on the feasibility and acceptability of implementing tailored online CBT for psychological distress, with or without therapist support, in HD patients. The study's methods for proactively identifying and subsequently managing psychological distress in HD identified a disproportionately large screen to trial consent rate ratio (16:1), when compared with previous CBT feasibility studies in HD (15-17). Challenges to recruitment were accounted for by three factors: i) low levels of patient acceptability of screening for psychological distress, ii) low levels of computer literacy, and iii) lack of perceived treatment

need for psychological support. As such, this study did not recruit to its intended target of 66 patients. The study was terminated once it had exhausted all of its intended recruitment sampling frames within Guy's and St Thomas' HD units. Furthermore, adherence to online treatment sessions was low. In addition, exploratory effect size estimates for the intended primary outcomes for a full-scale trial did not suggest a trend for improved psychological distress outcomes or cost-effectiveness for patients randomised to the supported arm compared with the unsupported arm. These findings suggest the need for revisions to current trial design before a future definitive trial is implemented. The suggested revisions are discussed below.

Recruitment

A 56% psychological distress screen refusal rate was observed. This refusal rate is much higher than the 3% refusal rate observed by Duarte et al's small CBT trial for depression (15) and is high compared with screen refusal rates observed in other secondary care LTC contexts using similar screening methods (33). Nonetheless, the observed refusal rate is marginally higher than the forecasted 50% screen refusal rate. A quarter of all patients approached for screening found it unacceptable in HD settings. It is likely that the perceived acceptability/normalisation of screening is influenced by the context in which it is introduced to the patient. An alternative approach to detecting psychological distress may seek to embed screening procedures early on in a patients HD care pathway so that parity of esteem is achieved between mental and physical health outcomes, in effect normalising the process (24).

Whilst the trial identified a higher than anticipated prevalence of psychological distress (55% compared with an estimated 40%), once the remaining inclusion criteria were applied a

smaller than anticipated number of participants were eligible for approach for consent into the trial. The main reason for study ineligibility among patients meeting psychological distress thresholds was poor computer literacy. Recruitment rates may be improved if alternative forms of the iDiD CBT intervention are made available (e.g. written manuals).

Among patients meeting *all* study inclusion criteria, over a third found online CBT inappropriate for their needs, thus resulting in a lower than expected *consent to trial* rate. One main contributor to this low perceived need was the low symptom thresholds used to define the presence of psychological distress resulting in false-positive screens. A future trial may consider implementing a second screen for psychological distress after a fortnightly interval has elapsed. This will allow patients with persistent symptoms of distress to be identified (50). This likewise may be a useful strategy to apply in secondary care physical health setting with limited mental health resources. Nonetheless, the study's *consent to trial* rate from patients meeting *all* study inclusion criteria is comparable with a median uptake rate of 38% identified from a meta-analysis of online depression and anxiety interventions (51). Thus, barriers to online CBT are not unique to HD patients.

Treatment Adherence

Adherence to online treatment sessions across both arms were lower than those reported in other studies of online CBT for depression (26). Sustaining adherence to psychotherapy in multimorbid populations is identified as a key challenge but precisely what constitutes an active "dose" of psychotherapy remains unanswered (52-54). A greater time interval between scheduled therapy sessions may benefit patients with multimorbidty because their competing treatment demands may become more dispersed over time. This study also observed higher adherence rates in the unsupported arm. This conflicts with meta-analytic

findings which report the benefit of therapist supported online interventions for sustaining adherence (29). However, the meta-analysis also demonstrated that type of support provided (therapeutic vs administrative) had no impact on online adherence rates (29). The majority of patients in this study were provided with iPads by the study team whilst receiving HD, which is comparable to administrative support. Indeed, a quarter of all randomised patients required brief training in the use of iPads/Internet. A future definitive trial needs to take steps to ensure the amount of support provided to patients is standardised within and across each arm if on-dialysis access to self-help CBT is provided.

Preliminary effects size estimates

This study found no differences between the supported and unsupported arm on psychological distress outcomes which contradicts previous small scale CBT studies in HD (15-17). However, two of these past trials (15, 16) recruited patients with higher baseline depression scores compared with the thresholds used here, overcoming the potential for floor effects. Whilst the third study used clinical thresholds for depression and anxiety that were comparable to this study, its sample had higher baseline scores for depression and anxiety, likewise overcoming the potential for floor effects (17). A future definitive trial and likewise secondary care treatment setting with limited resource for psychological care may consider using a higher baseline criteria for defining the presence of clinically significant symptoms of psychological distress. The findings from this study make a power calculation for a definitive randomised controlled trial challenging because of the absent treatment effect.

Exploratory statistical findings allude to the added benefit of therapeutic support for improving QoL outcomes. This finding is consistent with three previous studies of CBT in HD

(15-17). Observed improvements in QoL may relate to patients in the supported arm experiencing greater improvements in their ESRD illness perception (e.g. increased illness understanding and perceptions of control and a decreased ESRD symptom burden and illness related concerns). It should be noted however, that patients in the supported arm also reported that their ESRD affected them more emotionally (BIPQ – emotional response item). It may be that the telephone support calls prompted patients to recognise their emotional response to HD more readily. These effect size estimates need to be interpreted cautiously because of the small sample size, unevenly distributed groups, absence of statistical power, and aggregate level data analysis. However, it may be the case that iDiD CBT is more suited to addressing illness self-management challenges and improving QoL as opposed to treating diagnosable depression and anxiety disorders.

Exploratory cost-effectiveness analyses showed the supported arm had higher costs and more QALYs than the unsupported arm (online CBT only). The cost per QALY (£82,283) was beyond the £20,000-£30,000 NICE threshold which is applied to recommend new interventions (55). The inflated costs in the supported arm are accounted for by an increased rate of inpatient hospital admissions compared with the unsupported arm, which was likely an artefact of the unevenly distributed sample size. Nonetheless, the findings highlight that it is feasible to collect health service costs within this patient population.

Strengths and limitations

This is the first feasibility RCT of online CBT for the management of psychological distress in UK HD patients. An ethnically diverse sample was recruited which represented the ethnic profile of patients who attend London HD treatment centres (46). Our detailed descriptive recording of reasons for study non-consent permits us to comprehensively inform the

planning of the future full-scale trial to increase recruitment rates. Indeed, once a patient consented into the study we were able to achieve a robust retention rate. Limitations include a sample mean age that is lower than the national mean age of individuals who commence HD (46). However, this is likely because of the web-based nature of the intervention. Second, simple randomisation was used; because the recruited sample size was smaller than planned an uneven distribution of patients occurred across the two study arms. Randomisation procedures for our full-scale trial need amending to include block randomisation procedures to minimise the risk of unevenly distributed groups (56). Third, interpretation of our statistical analyses requires a high level of caution. Because this is a feasibility study our analyses were not statistically powered to detect clinically meaningful change in outcomes. In addition, our small sample size means that our effect size estimates lack precision. Findings identified in our study may not translate to a fullscale trial. Fourth, our feasibility study did not include a measure of cognitive impairment which is prevalent in the HD population (57). Whilst we excluded patients with severe mental health disorders (including dementia), we did not proactively examine the role of cognitive function and its potential to impact on adherence to the online intervention. This is likely an important moderator for inclusion in a future full-scale trial.

Implications for future trials and clinical practice

This study has identified that the current trial design is unfeasible and a number of necessary revisions are needed. First, there is a need to negotiate an acceptable illness label to define psychological distress in HD which mirrors the patients lived experience (58, 59) whilst also considering the contextual introduction of proactive psychological distress management strategies to promote normalisation (60). Second, whilst online self-help

treatments provide increased opportunities for tailoring treatment content to individual need (61), it is a barrier to accessing care among those with low computer literacy. Thus different self-help treatment modalities including written bibliotherapy resources are needed to promote access to care and improve recruitment to guided self-help trials. Third, consideration of the entry criteria into psychological distress trials and likewise entry and progression through psychological care pathways in LTC settings is needed. In the trial context, if entry criteria are too low the capacity to demonstrate change in psychological distress outcomes is hampered. In the haemodialysis care context, if low clinical thresholds are used, then limited resource may be diverted away from those with the highest degree of clinical need (11, 62). Fourth, low adherence to the online sessions ma have occurred because online treatments sessions were too intense for patients whom are simultaneously negotiating HD symptoms and self-management tasks. Shortening the content of the online sessions and/or increasing the post-intervention follow-up period will provide increased opportunities to engage with the treatment. The above revisions may be incorporated within a nested pilot study with strict "go no-go" criteria to monitor progress before a definitive multicentre trial is implemented.

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Table 1: Baseline sociodemographic and clinical characteristics and scores on self-report questionnaires for patients who consented into the study (N=25)

Variable	Supported Arm (N=18)	Unsupported Arm (N=7)
	Mean/Frequency (Standard Deviation/%)	Mean/Frequency (Standard Deviation)/%)
Gender/proportion of males	10 (56)	5 (71)
Age/years	49 (11.44)	47 (14.25)
Ethnicity/proportion of white ethnicity	6 (33)	4 (57)
Living arrangements/proportion living alone	5 (27)	1 (14)
Education status/proportion with no higher/university education	14 (78)	3 (43)
Mean number of comorbidities[2]	1.06 (1.16)	1.43 (1.39)
Dialysis vintage/months	23.72 (30.14)	33.70 (26.80)
Prior depression treatment	5 (26)	1 (14)
Prior anxiety treatment	2 (11)	1 (14)
Primary renal diagnosis (self-report)		
Diabetes	3 (16)	1 (14)
Hypertension	6 (34)	2 (29)
Other	9 (50)	4 (57)

[2] Includes sum of the following related conditions: coronary heart disease, cerebrovascular disease, diabetes, lung/chronic obstructive pulmonary disease, liver disease, cancer, peripheral vascular disease, depression and/or anxiety: range 0 – 8 long-term conditions.

Table 2: Descriptive statistics for primary and secondary outcomes at baseline and 12 weeks follow-up for the supported and unsupported therapy arms

	Supported arm				**Unsupported arm**			
	Baseline (N=18)		***Follow-up (N=See key)***		***Baseline (N=7)***		***Follow-up (N=See key)***	
Self-report questionnaires	Mean/ Frequency (SD/%)	Median (Interquartile range)	Follow-up Mean/Frequency (SD/%)	Median (Interquartile range)	Baseline Mean/ Frequency (SD/%)	Median (Interquartile range)	Follow-up Mean/Frequency (SD/%)	Median (Interquartile range)
Point of screen								
Depression (PHQ-9)	8.89 (4.17)	8.5 (6-12)	NA		8.57 (4.08)	8 (5-12)	NA	
Anxiety (GAD-7)	5.33 (3.88)	4.5 (3-7)	NA		3.86 (2.54)	4 (2-5)	NA	
Illness perceptions (BIPQ-Total)	48.89 (7.75)	48.5 (3-7)			39.86 (11.48)	39 (31-50)		
Psychological Distress								
Depression (PHQ-9)	7.11 (4.74)	6.5 (4-8)	7.5 (5.4)[$]	7 (3-11.5)	7.86 (4.06)	7 (4-10)	7.6 (4.7)[$]	8 (4-12)
Anxiety (GAD-7)	4.78 (3.81)	4 (1-7)	4.4 (4.1)[$]	3.5 (1.5-6)	4.86 (4.30)	3 (1-8)	3.9 (3.6)[$]	3 (1-5)
QoL Visual Analogue Scale	58.94 (25.11)	60 (50-77)	61.1 (16.2)[¶]	50 (50-71)	56.29 (22.73)	58 (42-81)	56.2 (14.3)[¶]	55 (48-60)
EQ5D – mood	1.78 (0.88)	2 (1-2)	1.5 (0.8)[¶]	1 (1-2)	1.71 (1.11)	1 (1-2)	2.0 (1.0)[¶]	2 (1-3)
EQ5D – mobility	2.28 (1.23)	2 (1-3)	1.5 (0.8)[¶]	1 (1-2	2.14 (1.68)	1 (1-4)	2.4 (1.5)[¶]	2 (1-4)
EQ5D – pain	1.94 (1.35)	1.5 (1-2)	1.6 (0.8)[¶]	1 (1-2	1.86 (1.21)	1 (1-3)	2.6 (1.3)[¶]	2 (2-4)
EQ5D - self-care	1.44 (0.70)	1 (1-2)	1.2 (0.6)[¶]	1 (1-2	1.57 (0.79)	1 (1-2)	1.4 (0.9)[¶]	1 (1-1)
EQ5D - usual activities	2.39 (1.24)	2.5 (1-3)	1.5 (0.8)[¶]	1 (1-2	2.14 (1.07)	2 (1-3)	2.8 (1.3)[¶]	3 (2-4)
Illness perceptions								
BIPQ-Total	45.33 (8.83)	46 (42-51)	44.2 (12.09)[¥]	46 (38-53)	41.86 (11.13)	40 (29-50)	41.2 (10.28)[¶]	39 (36-46)
BIPQ1. Consequences	8.94 (1.26)	9.5 (8-10)	7.9 (2.1)[¥]	8 (6-10)	7.85 (1.57)	8 (6-9)	7.2 (2.2)[¶]	8 (5-8)
BIPQ2. Timeline	6.67 (2.77)	6.5 (5-9)	6.6 (3.6)[¥]	8 (5-10)	6.71 (3.35)	8 (3-10)	6.2 (4.8)[¶]	9 (2-10)
BIPQ3. Personal control	4.56 (2.79)	4.5 (3-5)	4.9 (3.1)[¥]	4 (3-7)	4.43 (2.99)	4 (2-6)	3.2 (2.4)[¶]	3 (2-5)
BIPQ4. Treatment control	1.44 (1.65)	1 (0-2)	2.3 (2.4)[¥]	2 (0-5)	1.57 (1.27)	2 (0-3)	2.0 (2.4)[¶]	1 (0-4)
BIPQ5. Identity	5.78 (2.60)	5.5 (4-8)	5.6 (2.4)[¥]	5 (4-8)	6.29 (1.80)	6 (3-8)	8.0 (2.0)[¶]	9 (7-9)
BIPQ6. Concern	8.50 (1.86)	10 (7-10)	7.4 (2.4)[¥]	7 (5-10)	6.42 (3.21)	5 (4-10)	8.0 (2.8)[¶]	10 (6-10)
BIPQ7. Understanding	2.72 (2.65)	2 (1-5)	3.33 (2.4)[¥]	2 (2-5)	2.43 (1.72)	2 (1-4)	2.2 (2.6)[¶]	1(0-5)
BIPQ8. Emotional response	6.14 (2.27)	7.5 (5-10)	6.1 (2.8)[¥]	6 (5-8)	6.72 (3.30)	7 (3-7)	4.4 (4.0)[¶]	5 (1-6)

Key: BIPQ, Brief Illness Perception Questionnaire; EQ5D, EuroQoL scale, GAD-7, Generalised Anxiety Disorder; N, Number of patients; NA, Not applicable; PHQ- 9, Patient Health Questionnaire; $, N=16, supported arm and N=7, unsupported arm; ¶ N=13 supported arm and N= 5 unsupported arm; ¥= N= 15 supported arm.

Table 3: Effect size estimates for primary and secondary outcomes at 12 week follow-up

Self-report outcomes	Estimated group difference (Supported – Unsupported)[1]	Standard Error	Cohen's d[2]	95% lower limit	95% upper limit
Psychological Distress (N=23)					
Depression (PHQ-9)	0.70	1.81	0.14	-0.75	1.03
Anxiety (GAD-7)	0.58	1.78	0.15	-0.74	1.04
Quality of Life (N=18)					
EQ5D – visual analogue scale	7.50	8.47	0.47	-0.57	1.51
EQ5D - mood	-0.40	0.43	-0.47	-1.51	0.57
EQ5D – mobility	-0.72	0.42	-0.71	-1.76	0.35
EQ5D - pain	-0.87	0.48	-0.92	-1.99	0.16
EQ5D - self-care	-0.20	0.36	-0.24	-1.28	0.79
EQ5D - usual activities	-1.32	0.50	-1.38	-2.51	-0.26
Illness perceptions (N=20)					
BIPQ: Total score	2.22	3.73	0.19	-0.83	1.20
BIPQ1. Consequences	0.40	1.01	0.19	-0.85	1.22
BIPQ2. Timeline	1.35	1.47	0.34	-0.69	1.38
BIPQ3. Personal control	1.71	1.55	0.58	-0.47	1.63
BIPQ4. Treatment control	-0.14	1.20	-0.06	-1.09	0.97
BIPQ5. Identity	-1.85	1.06	-0.80	-1.82	0.26
BIPQ6. Concern	-1.75	0.90	-0.70	-1.75	0.36
BIPQ7. Understanding	1.12	1.24	0.46	-0.59	1.50
BIPQ8. Emotional response	1.62	1.48	0.51	-0.53	1.56

Key: BIPQ, Brief Illness Perception Questionnaire; EQ5D, EuroQoL scale, GAD-7, Generalised Anxiety Disorder; N, Number of patients included in complete case analysis; NA, Not applicable; PHQ- 9, Patient Health Questionnaire [1] Baseline level of the outcome variable is equal across groups; [2]Positive Cohen's d value indicates that the mean difference was higher in the supported arm compared with the unsupported arm

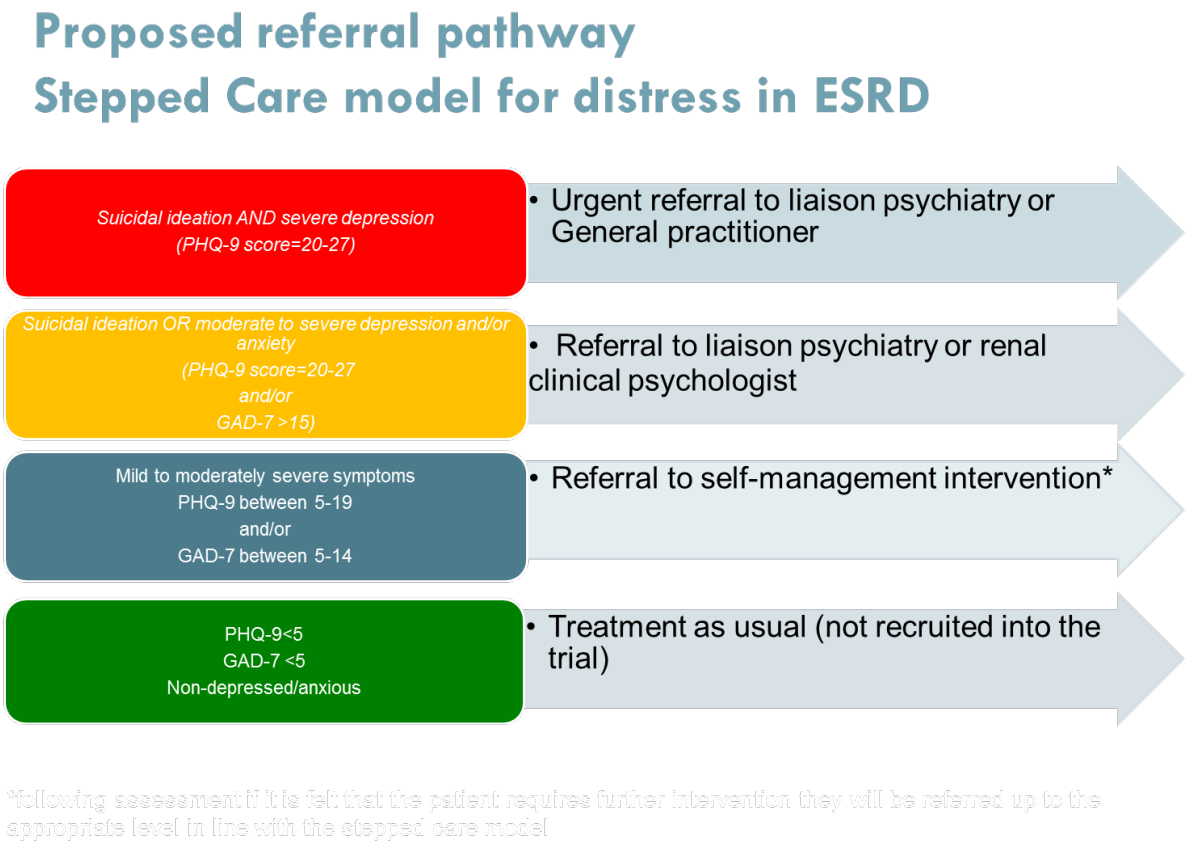

Figure 1: Stepped-care referral pathway with depression and anxiety thresholds used for onward referral to psychological care

*iDiD intervention with or without telephone support

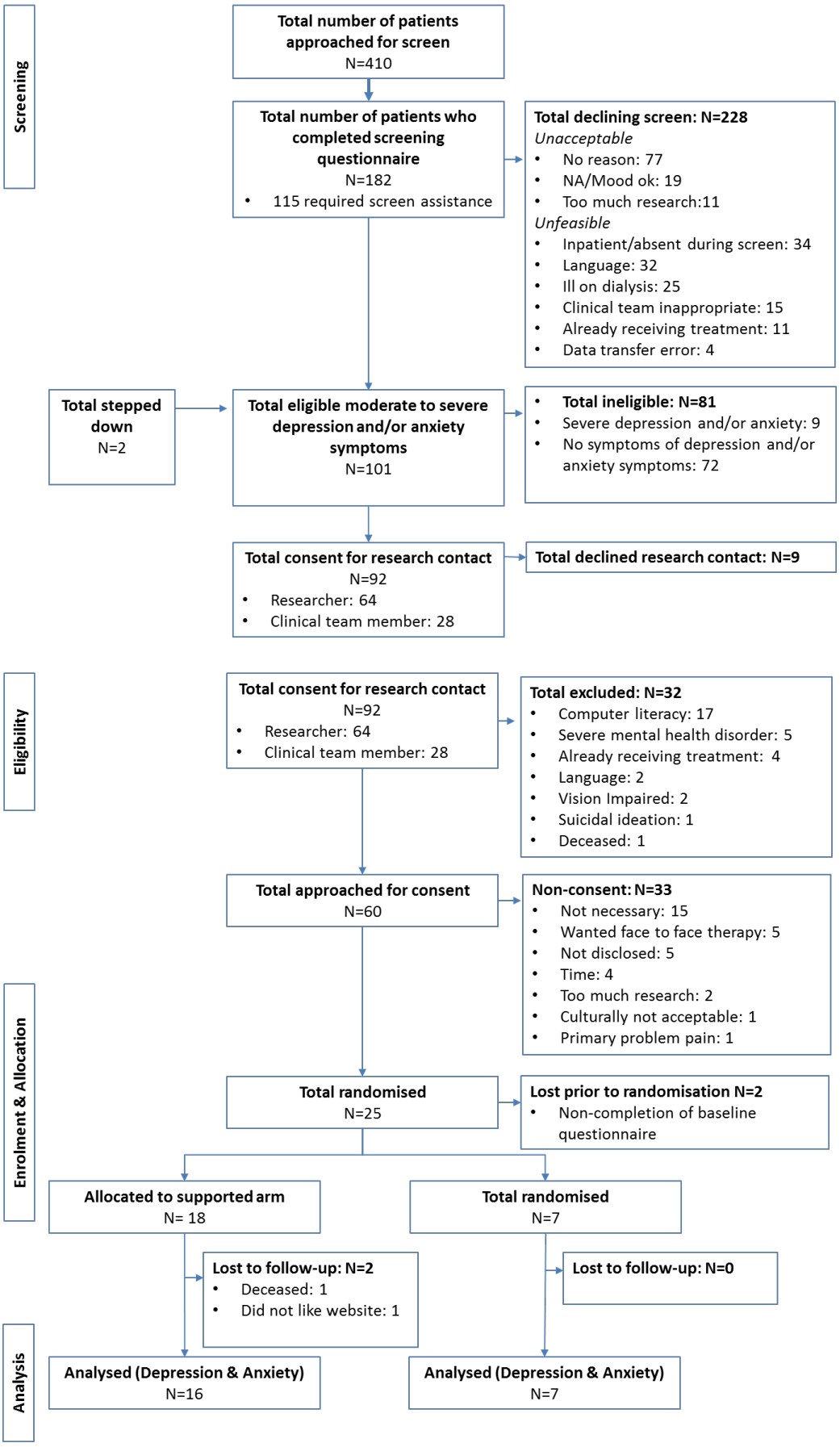

Figure 2: CONSORT flow diagram

Figure legends:

Figure 1: Stepped-care referral pathway with depression and anxiety thresholds used for onward referral to psychological care

Figure 2: Patient flow through each stage of the study