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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.

1 **Introduction**

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

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

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

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

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

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

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

- 50 i) Assess the feasibility and acceptability of online screening for symptoms of
51 psychological distress in all patients attending for HD.
- 52 ii) Explore trial recruitment and retention rates.
- 53 iii) Explore adherence to online CBT sessions and therapist support calls (for the
54 purpose of this feasibility study adherence is defined as engagement with
55 scheduled psychotherapy treatments sessions and does not refer to adherence
56 to dialysis or other treatment schedules).
- 57 iv) Examine the potential efficacy of therapist supported online CBT in lowering
58 symptoms of psychological distress and improving quality of life when compared
59 with online CBT only. This will allow an estimate of the standard deviation of
60 outcomes to inform a future power calculation for a definitive trial.
- 61 v) Study whether illness perceptions differ post-intervention between the
62 supported and unsupported online CBT arms. This will allow an estimate of the
63 standard deviation of illness perceptions to inform a future power calculation for
64 a definitive trial.
- 65 vi) Examine preliminary cost-effectiveness of therapist supported online CBT
66 compared with online CBT only.

67 **Subjects and Methods**

68 *Study Design and Participants*

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

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

84 Inclusion criteria were modified after three months of recruitment. Incident HD patients
85 were found to have greater motivation to participate. Our original protocol
86 (ClinicalTrials.gov Identifier-NCT02352870^a) had the following two exclusion criteria: i)
87 dialysis vintage of \leq 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.

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

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

100 *Randomisation, allocation concealment, and blinding*

101 Consenting patients were individually randomised after completing the online baseline
102 questionnaire. Simple randomisation occurred via Lifeguide (34) which is a software used to
103 program online interventions. An automated random number generator with a 1:1 ratio was
104 used to randomise patients to either therapist supported online CBT or online CBT only. The
105 patient was informed of their group allocation via the online CBT program. The patient and
106 trial coordinator also received an automated email. Because randomisation was automated
107 by Lifeguide the allocation sequence remained concealed from the trial coordinator (JLH)
108 and psychological therapists/supervisors (JLH, AC). The nature of the trial meant patients
109 were unblinded to allocated treatments. Follow-up outcomes were completed by patients
110 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.

133 *Unsupported arm: online CBT with no therapist support calls*

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

139 *Outcomes*

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

146 Patients completed self-report outcomes at baseline and 12 weeks post-randomisation. The
147 proposed primary outcomes for the full-scale clinical trial are depression measured using
148 the PHQ-9 (31) and anxiety measured using the GAD-7 (32). The PHQ-9 has a scale range of
149 0-27; high scores indicate increased depressive symptoms. It has comparable diagnostic
150 accuracy with longer clinician administered depression measures (10). The GAD-7 has a
151 scale range of 0-21 (32). High scores indicate higher anxiety. The GAD-7 has evidence of
152 diagnostic accuracy for detecting the presence of generalised anxiety disorder (39) Quality
153 of life (QoL) was measured using EuroQoL scale (40)(EQ-5D) and is a proposed secondary
154 outcome for the full-scale trial. It includes five items (range, 1-5) to assess mobility, self-
155 care, usual activities, pain/discomfort, and anxiety and depression. High item scores indicate

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

164 *Demographic and Clinical data*

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

173 *Sample size*

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

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

192 *Analysis*

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

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

211 **Results**

212 *Feasibility of screening, recruitment rates, and baseline sample characteristics*

213 A total of 410 HD patients were approached to complete psychological distress screens, of
214 which 182 (44.4%; 95% CI 39.5% to 49.3%) agreed (Figure 2). Many patients (N=115, 63.2%;
215 95% CI 55.7% to 70.2%) required assistance to complete the screen. Reasons for screen non-
216 completion included either pragmatic/external barriers (e.g. language, illness) or
217 internal/patient generated barriers (e.g. non-disclosure of decline reason, lack of perceived
218 need for distress screen). Pragmatic/external barriers prevented screening in 121 patients
219 (29.5%; 95% CI 25.1% to 34.2%) whilst patient generated barriers prevented screening in
220 107 patients (26.1%; 95% CI 21.9% to 30.6%).

221 Among the 182 patients who completed the screen, a total of 101 patients (55.5%; 95% CI
222 47.9% to 62.8%) had mild-moderately severe symptoms of psychological distress. Of these
223 101 patients, a further 60 (59.4%; 95% CI 49.2% to 69.1%) met remaining inclusion criteria.

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

226 Of the 60 patients meeting the eligibility criteria that were approached for consent, 35
227 (58.3%; 95% CI 44.9% to 70.9%) declined. The main reason for non-consent was a perceived
228 lack of treatment need (N=15; 42.8%; 95% CI 26.3% to 60.6%; See Figure 2 for details). A
229 total of 25 patients consented and were randomised to either online CBT with therapist
230 support calls (N=18; 72%) or online CBT only (N=7; 28%). It was necessary to approach 16
231 patients for screening for every one patient randomised (410/25=16.4; 95% CI 11.1 to 25.3).
232 The *consent to trial rate* was 41.7% among those meeting all trial inclusion criteria (25/60;
233 95% CI 29.1 to 55.1).

234 Patients who consented to be randomised (N=25) had a mean age of 48 (SD 12.01) years
235 and were predominantly male (60%) of non-white ethnicity (60%). The sample had a mean
236 dialysis vintage of 26.52 (SD = 1.16) months and a mean of 1.16 (SD 1.21) comorbidities.
237 Depression scores at baseline indicated the presence of mild depressive symptoms (Median
238 = 7; Interquartile range IQR= 4-10). Median anxiety scores at baseline were considered sub-
239 threshold for symptoms of anxiety (< 5) (median = 4, IQR = 1-5). See tables one and two for
240 baseline sociodemographic, clinical, and self-report descriptive statistics.

241 *Adherence to online intervention and telephone support calls*

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

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

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

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

257 In terms of trial retention rates, 23 (92.0%; 95% CI 73.5% to 99.0%) patients completed
258 depression and anxiety outcomes at follow-up. Follow-up data was collected between June
259 2015 and May 2016.

260 Table three summarises preliminary analyses exploring trends in treatment effects
261 comparing therapist supported online CBT with online CBT only. Given the study was not
262 powered to detect differences, significance testing was not performed and the treatment
263 effect estimates are provided for descriptive reasons only and to guide the design of a
264 future definitive trial. Cohen's d effect size estimates indicate that the difference between
265 the supported and unsupported arm on measures of depression and anxiety were minimal
266 with large confidence intervals, highlighting the uncertainty around this effect size estimate.
267 Pre-post mean change analysis across the whole sample indicated that mean depression
268 scores increased by 0.39 (SD = 3.99; scale range 0-27) and mean anxiety scores decreased by
269 -0.61 (SD 4.97; scale range 0-21)

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

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

282 *Adverse events and other potential harms*

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

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

298 *Cost-effective analysis*

299 Service use at baseline was different between the two groups (Table C online appendix). The
300 mean cost of the intervention was £40 for the unsupported arm, and £244 for the
301 supported arm. The follow-up healthcare costs adjusted for baseline were £2,271 higher for
302 the supported arm, but with the small numbers (n = 16) this was not significant (95% C.I. £-
303 2,766 to £7,307). At follow-up, the unsupported arm gained 0.144 QALYs, and the supported
304 arm gained 0.192 QALYs. Adjusting for baseline utility the supported arm had 0.0276 more
305 QALYs than the unsupported group (95% C.I., 0.0107 to 0.0444). The ICER was £2271 divided
306 by 0.0276, i.e. £82,283 per QALY albeit with wide confidence intervals (95% CI £51, 149 –
307 £212, 243).

308 **Discussion**

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

316 need for psychological support. As such, this study did not recruit to its intended target of
317 66 patients. The study was terminated once it had exhausted all of its intended recruitment
318 sampling frames within Guy's and St Thomas' HD units. Furthermore, adherence to online
319 treatment sessions was low. In addition, exploratory effect size estimates for the intended
320 primary outcomes for a full-scale trial did not suggest a trend for improved psychological
321 distress outcomes or cost-effectiveness for patients randomised to the supported arm
322 compared with the unsupported arm. These findings suggest the need for revisions to
323 current trial design before a future definitive trial is implemented. The suggested revisions
324 are discussed below.

325 *Recruitment*

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

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

339 smaller than anticipated number of participants were eligible for approach for consent into
340 the trial. The main reason for study ineligibility among patients meeting psychological
341 distress thresholds was poor computer literacy. Recruitment rates may be improved if
342 alternative forms of the iDiD CBT intervention are made available (e.g. written manuals).
343 Among patients meeting *all* study inclusion criteria, over a third found online CBT
344 inappropriate for their needs, thus resulting in a lower than expected *consent to trial* rate.
345 One main contributor to this low perceived need was the low symptom thresholds used to
346 define the presence of psychological distress resulting in false-positive screens. A future trial
347 may consider implementing a second screen for psychological distress after a fortnightly
348 interval has elapsed. This will allow patients with persistent symptoms of distress to be
349 identified (50). This likewise may be a useful strategy to apply in secondary care physical
350 health setting with limited mental health resources. Nonetheless, the study's *consent to*
351 *trial* rate from patients meeting *all* study inclusion criteria is comparable with a median
352 uptake rate of 38% identified from a meta-analysis of online depression and anxiety
353 interventions (51). Thus, barriers to online CBT are not unique to HD patients.

354 *Treatment Adherence*

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

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

370 *Preliminary effects size estimates*

371 This study found no differences between the supported and unsupported arm on
372 psychological distress outcomes which contradicts previous small scale CBT studies in HD
373 (15-17). However, two of these past trials (15, 16) recruited patients with higher baseline
374 depression scores compared with the thresholds used here, overcoming the potential for
375 floor effects. Whilst the third study used clinical thresholds for depression and anxiety that
376 were comparable to this study, its sample had higher baseline scores for depression and
377 anxiety, likewise overcoming the potential for floor effects (17). A future definitive trial and
378 likewise secondary care treatment setting with limited resource for psychological care may
379 consider using a higher baseline criteria for defining the presence of clinically significant
380 symptoms of psychological distress. The findings from this study make a power calculation
381 for a definitive randomised controlled trial challenging because of the absent treatment
382 effect.

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

385 (15-17). Observed improvements in QoL may relate to patients in the supported arm
386 experiencing greater improvements in their ESRD illness perception (e.g. increased illness
387 understanding and perceptions of control and a decreased ESRD symptom burden and
388 illness related concerns). It should be noted however, that patients in the supported arm
389 also reported that their ESRD affected them more emotionally (BIPQ – emotional response
390 item). It may be that the telephone support calls prompted patients to recognise their
391 emotional response to HD more readily. These effect size estimates need to be interpreted
392 cautiously because of the small sample size, unevenly distributed groups, absence of
393 statistical power, and aggregate level data analysis. However, it may be the case that iDiD
394 CBT is more suited to addressing illness self-management challenges and improving QoL as
395 opposed to treating diagnosable depression and anxiety disorders.

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

403 *Strengths and limitations*

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

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

425 *Implications for future trials and clinical practice*

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

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

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457

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612

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)
<i>Point of screen</i>								
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)		
<i>Psychological Distress</i>								
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)
<i>Illness perceptions</i>								
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

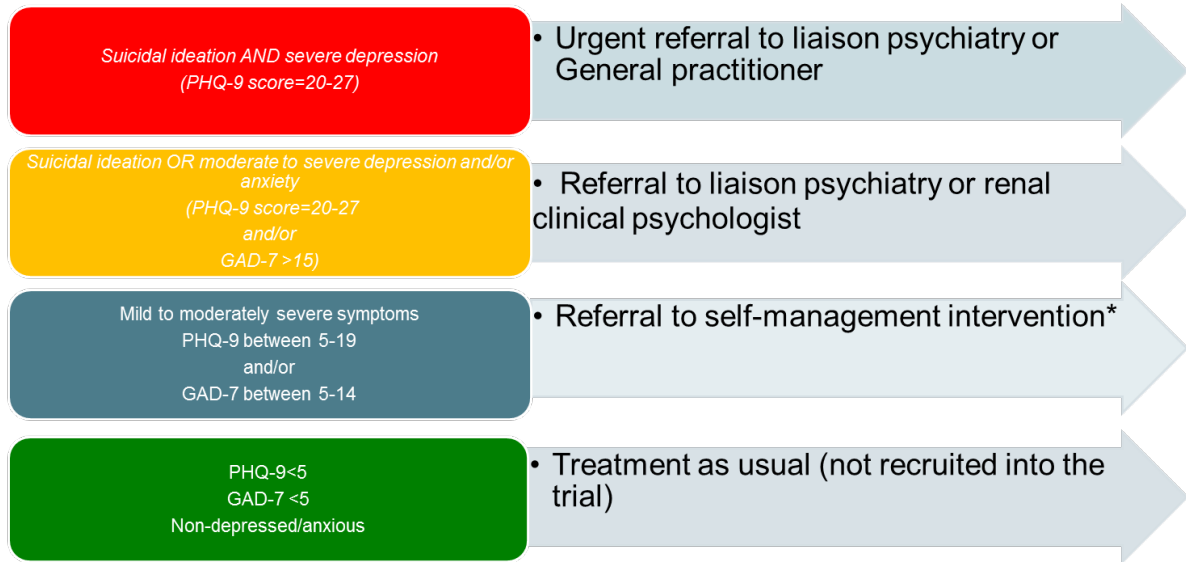
Self-report outcomes	Estimated group difference (Supported – Unsupported) ¹	Standard Error	Cohen's d ²	95% lower limit	95% upper limit
Psychological Distress (N=23)					
Depression (PHQ-9)	0.70	1.81	0.14	-0.75	1.03
Anxiety (GAD-7)	0.58	1.78	0.15	-0.74	1.04
Quality of Life (N=18)					
EQ5D – visual analogue 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;

²Positive Cohen's d value indicates that the mean difference was higher in the supported arm compared with the unsupported arm

Proposed referral pathway Stepped Care model for distress in ESRD



*Following assessment if it is felt that the patient requires further intervention they will be referred up to the appropriate level in line with the stepped care model

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

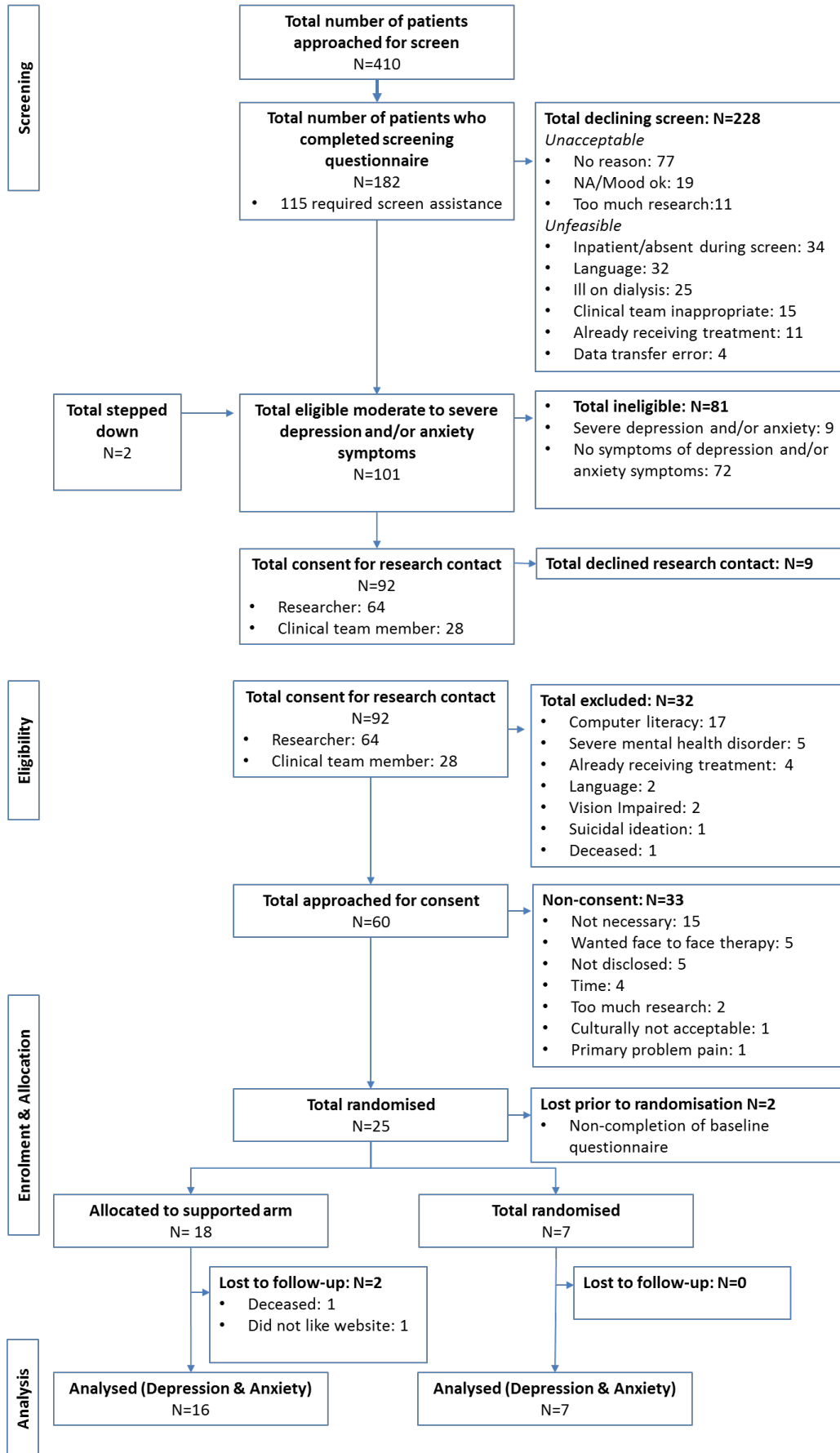


Figure 2: CONSORT flow diagram

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