

# Effectiveness of cognitive–behavioural therapy for depression in advanced cancer: CanTalk randomised controlled trial

Marc Serfaty, Michael King, Irwin Nazareth, Stirling Moorey, Trefor Aspden, Kathryn Mannix, Sarah Davis, John Wood and Louise Jones

## Background

Depression is one of the most common mental disorders in people with advanced cancer. Although cognitive–behavioural therapy (CBT) has been shown to be effective for depression in people with cancer, it is unclear whether this is the case for people with advanced cancer and depression.

## Aims

We sought to determine whether CBT is more clinically effective than treatment as usual (TAU) for treating depression in people with advanced cancer (trial registration number ISRCTN07622709).

## Method

A multi-centre, parallel-group single-blind randomised controlled trial comparing TAU with CBT (plus TAU). Participants ( $n = 230$ ) with advanced cancer and depression were randomly allocated to (a) up to 12 sessions of individual CBT or (b) TAU. The primary outcome measure was the Beck Depression Inventory-II (BDI-II). Secondary outcome measures included the Patient Health Questionnaire-9, the Eastern Cooperative Oncology Group Performance Status, and Satisfaction with Care.

## Results

Multilevel modelling, including complier-average intention-to-treat analysis, found no benefit of CBT. CBT delivery was proficient, but there was no treatment effect ( $-0.84$ , 95% CI  $-2.76$  to

$1.08$ ) or effects for secondary measures. Exploratory subgroup analysis suggested an effect of CBT on the BDI-II in those widowed, divorced or separated ( $-7.21$ , 95% CI  $-11.15$  to  $-3.28$ ).

## Conclusions

UK National Institute for Health and Care Excellence (NICE) guidelines recommend CBT for treating depression. Delivery of CBT through the Improving Access to Psychological Therapies (IAPT) programme has been advocated for long-term conditions such as cancer. Although it is feasible to deliver CBT through IAPT proficiently to people with advanced cancer, this is not clinically effective. CBT for people widowed, divorced or separated needs further exploration. Alternate models of CBT delivery may yield different results.

## Declaration of interest

M.S. is a member of the Health Technology Assessment General Board.

## Keywords

Cognitive behavioural therapies; depressive disorders; individual psychotherapy; randomised controlled trial; psychosocial interventions.

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With increasing life expectancy, more people are living with advanced cancer. Clinical depression in this group has a pooled prevalence of 16.5%.<sup>1</sup> Depression, which is distinct from adjustment disorder, is associated with a negative impact on quality of life and, untreated, is a predictor of early death.<sup>2</sup> The UK National Institute for Health and Care Excellence (NICE) guidelines recommend that people with advanced cancer are routinely screened and treated for depression.<sup>3</sup> Antidepressants may be helpful, but they may worsen cancer symptoms or interact with chemotherapy<sup>4</sup> and, given that people with advanced cancer face particular challenges, including life-threatening illness, symptom burden, and personal, family and practical problems, psychological interventions may be preferred. Cognitive–behavioural therapy (CBT) is one of the most widely evidenced psychological interventions for depression.<sup>5</sup> However, evidence of its effectiveness for treating depression in advanced cancer is limited and previous research has focused on those affected by specific tumour groups.<sup>6</sup> The CanTalk study (trial registration number ISRCTN07622709) was a multicentre randomised controlled trial (RCT) evaluating the clinical and cost-effectiveness of CBT delivered through NHS England's Improving Access to Psychological Therapies (IAPT) programme compared with treatment as usual for reducing depressive symptoms in people with advanced cancer. The CBT was manual-based and context-specific for advanced cancer. The research, reported in detail in the full National Institute for Health Research report,<sup>7</sup> formed part of the UK's National Cancer Research Network (NCRN) clinical trials portfolio, registration

number 10255. This paper reports on whether manualised IAPT-delivered CBT was more effective than treatment as usual in treating depressive symptoms in people with advanced cancer.

## Method

### Design

The CanTalk study was a multi-centre parallel-group single-(researcher)-blind RCT undertaken between 5 March 2012 and 30 November 2016. A summary of methods from the protocol<sup>8</sup> is provided in this section.

### Ethics and consent

We assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. All procedures involving human patients were approved by the London–Camberwell St Giles Research Ethics Committee, reference 11/LO/0376. Written informed consent was obtained from all participants.

### Patient involvement

Cancer and mental health patients helped with: formulating the research, trial design, preparing materials, ethics, trial meetings,

optimising recruitment, interpreting results and deciding how to distribute results.

### Eligibility and screening

People with a diagnosis of cancer not amenable to curative treatment were screened for depression using the two-item Patient Health Questionnaire (PHQ-2).<sup>9</sup> Participants were recruited from general practices, a hospice, and oncology departments in England; if positive ( $\geq 3$  on the PHQ-2), they were assessed against the inclusion and exclusion criteria.

#### Inclusion criteria

Diagnosis of advanced cancer; DSM-IV diagnosis of major depressive disorder using the Mini-International Neuropsychiatric Interview (MINI);<sup>10</sup> sufficient understanding of English; eligible for treatment in an IAPT centre.

#### Exclusion criteria

Clinician-estimated survival <4 months; high suicide risk; receipt in past 2 months of a psychological intervention for depression recommended by NICE; alcohol dependence (Alcohol Use Disorders Identification Test, AUDIT<sup>11</sup>). We avoided recruiting in areas where oncology care included routine referral to CBT.

### Randomisation

Participants were randomised to CBT plus treatment as usual (TAU) or TAU alone, with a 1:1 ratio. The random allocation sequence was generated by PRIMENT, a UK Clinical Research Collaboration (UKCRC) registered clinical trials unit, using a web-based system. Randomisation used permuted blocks with sizes of 4 or 6, stratified for antidepressant prescription (yes/no).

### The intervention

TAU involved routine assessment and treatment, including care from general practitioners (GPs), clinical nurse specialists, oncologists and palliative care clinicians.

In CBT (plus TAU), IAPT therapists were trained to adapt their existing skills and use context-specific CBT according to the CanTalk study intervention manual. They provided up to 12 sessions of individual CBT delivered, usually weekly and within 3 months, either face to face or by telephone.

#### Context-specific CBT manual and training

A treatment manual informed by previous work (available from the corresponding author) was developed for the trial by members of the research team.<sup>11</sup> CBT therapists attended a 1-day course on how to use the manual and adapt their standard CBT work for people with advanced cancer. This included adapting techniques within the constraints of physical illness, working with realistic negative thoughts, dealing with fears about death and dying, and including carers in sessions where appropriate.

#### Delivery of CBT

Since 2008 a stepped-care approach for people with depression and anxiety disorders has been available in some areas of England through NHS England's IAPT programme, delivered through IAPT/well-being centres<sup>12</sup> located in the community or in GP practices. Our study used only high-level (level 3) 'high-intensity therapists' with at least 2 years postgraduate diploma experience in CBT. IAPT therapists offer face-to-face evidence-based therapy for people with complex problems using an

adaptation of CBT developed by Beck *et al.*<sup>13</sup> High-intensity therapists are required to have at least a proficient level of delivery of therapy, judged by the Cognitive Therapy Scale-Revised<sup>14</sup> (CTS-R).

#### Supervision

In our study, regular supervision, usually monthly, was provided by IAPT supervisors, reflecting routine IAPT practice. In addition, the therapists were offered the opportunity to contact members of the trial team (M.S., S.M. and K.M.) for specialist advice in CBT applied to cancer.

### Study measures

Potential participants were screened by University College London (UCL) researchers, National Cancer Research Network support staff and GP practice nurses and followed up by UCL researchers and/or National Cancer Research Network support staff.

#### Screening measures

Before study entry, initial screening used the PHQ-2 (the first two questions of the PHQ-9<sup>9</sup>), a validated depression screening measure.

After assessment for eligibility, second screening used the MINI,<sup>10</sup> a short structured diagnostic interview, widely used in people with cancer.

#### Demographic and related information (baseline)

We recorded gender, date of birth, marital status, ethnicity, employment status, education, history of depression and cancer diagnosis.

#### Outcome measures

- (a) Primary outcome (baseline, 6, 12, 18 and 24 weeks):
  - (i) the Beck Depression Inventory-II<sup>15</sup> (BDI-II), a 21-item self-report measure, used previously in advanced cancer.<sup>16</sup>
- (b) Secondary outcomes (baseline, 12 and 24 weeks):
  - (i) the Patient Health Questionnaire<sup>9</sup> (PHQ-9), a validated nine-item screening tool measuring severity of depression;<sup>17</sup>
  - (ii) EuroQol's EQ-5D,<sup>18</sup> a generic utility measure of quality of life across five domains;
  - (iii) Satisfaction with Care: we assessed overall care, continuity of care, supportive care, information needs and quality of communication (scored 0–10 towards higher satisfaction);<sup>19</sup>
  - (iv) Eastern Cooperative Oncology Group Performance Status<sup>20</sup> (ECOG-PS), an observer-rated scale assessing physical functioning in people with cancer: 0, asymptomatic; 1, symptomatic, fully ambulatory; 2, symptomatic, in bed less than 50% of time; 3, symptomatic, in bed more than 50% of time; 4, 100% restricted to bed; 5, dead.

#### Measures of potential bias

- (a) Antidepressant use (baseline, 12 and 24 weeks): we recorded any prescribed antidepressants.<sup>21</sup>
- (b) Other psychological therapies (baseline, 12 and 24 weeks): we noted any psychological intervention reported by participants.
- (c) Expectations of therapy (baseline): participants were asked to predict the degree to which they thought their mood would improve during the trial using a 10-point Likert scale ('not at all' to 'completely').

- (d) Treatment preference (baseline): patients indicated their group preferences (CBT, TAU, no preference).
- (e) Attrition (6, 12, 18 and 24 weeks): we recorded reasons for missing follow-up assessments.

#### Therapy-related measures

- (a) Non-attendance for CBT: we recorded reasons for not attending therapy sessions.
- (b) Competence and adherence to treatment:
  - (i) competence: an accredited member of the British Association of Behavioural and Cognitive Psychotherapies independently rated recordings of therapy using the Cognitive Therapy Scale-Revised<sup>14</sup> (CTS-R); the recordings were a randomly selected sample of 1 in 10 therapy sessions, stratified by phase (early: sessions 1–4; mid: sessions 5–8; or late: sessions 9–12).
  - (ii) adherence to the CBT manual: therapists recorded the components of therapy they delivered using a Therapy Components Checklist (TCC; available from the corresponding author); the independent rater also completed this checklist.

### Statistical considerations

We agreed an analysis plan before locking the database for analysis.

#### Power and sample size

The study was powered to detect the overall effect of treatment on depression as measured on the BDI-II over the 24-week follow-up period, assuming a difference between the TAU and CBT groups of three points when measured at 6 weeks, rising further to six points after 12 weeks and sustained at that level thereafter (i.e. at 18 and 24 weeks). We assumed a standard deviation of 12 for each individual BDI-II measurement, based on the BDI-II manual.<sup>15</sup> We assumed a 70% follow-up rate after 6 weeks, decreasing to 65% at 12 weeks and 60% at 24 weeks.

The correlation between two successive BDI-II measures taken 6 weeks apart is obtained from the BDI-II manual, which reports a correlation of 0.93 for sessions 1 week apart.<sup>15</sup> If we assume an autoregressive decay of order 1, our best estimate of the correlation between BDI-II measures at 6 weeks is  $0.93^6 = 0.65$ .

Assuming the attrition rates and correlation reported above, then the sample size required to detect an overall difference between the groups, at 90% power and 5% significance, is 109 patients per arm (using a multilevel model adjusting for baseline BDI-II). To account for clustering by therapist, the sample size needs to be inflated by a factor of 1.10.  $(1 + (\text{average cluster size} - 1) \times \text{intraclass correlation coefficient})$ . This is based on an intraclass correlation coefficient of 0.02<sup>22</sup> and an average of 6 patients per therapist post-intervention. We therefore intended to recruit 120 patients per arm.

#### Statistical analysis

The primary analysis, conducted on an intention-to-treat basis, tested for an overall treatment effect on the BDI-II over the four follow-up points, using multilevel modelling allowing for repeated measurements with equal weighting for each time point. The model comprised three levels: (a) repeated measures; (b) individuals; and (c) therapists. Baseline BDI-II score and antidepressant prescribing (yes/no) were included as fixed effects. The model was

fitted using a linear mixed-effects model assuming Gaussian error distribution. Normality assumptions were checked.

Supportive analyses repeated the primary analysis with modifications: (a) using clustering by IAPT service; (b) without clustering; (c) including baseline history of depression, EQ-5D score, duration of current depression and duration from primary diagnosis to baseline as fixed effects; and (d) conducting separate analyses for each follow-up.

The original analysis<sup>8</sup> was modified to include a complier-average intention-to-treat (CAITT) analysis,<sup>23</sup> which adjusts for adherence by generating a 'per-session' treatment effect. Clustering by therapist was ignored in the CAITT model, as there was no evidence of such a clustering effect in the main analysis and so the simpler model is more robust here.

To test for bias, we compared baseline scores between the groups on: (a) non-pharmacological treatment for depression; (b) group preference; and (c) expectations of improvement with CBT. To compare antidepressant doses, these were converted into equivalent fluoxetine doses.<sup>24</sup>

We included exploratory analysis of the interaction of treatment with (a) time, (b) marital status and (c) education.<sup>25</sup> This was done by adding the relevant interaction term into the primary analysis model.

#### Analysis of secondary outcomes

Analysis of PHQ-9 and Satisfaction with Care scores mirrored the primary analysis. For the ECOG-PS a non-parametric comparison of change from baseline at each time point was made between groups.

A detailed analysis plan is available from the corresponding author on request.

### Data sharing

The study's data-set is available from the corresponding author on request.

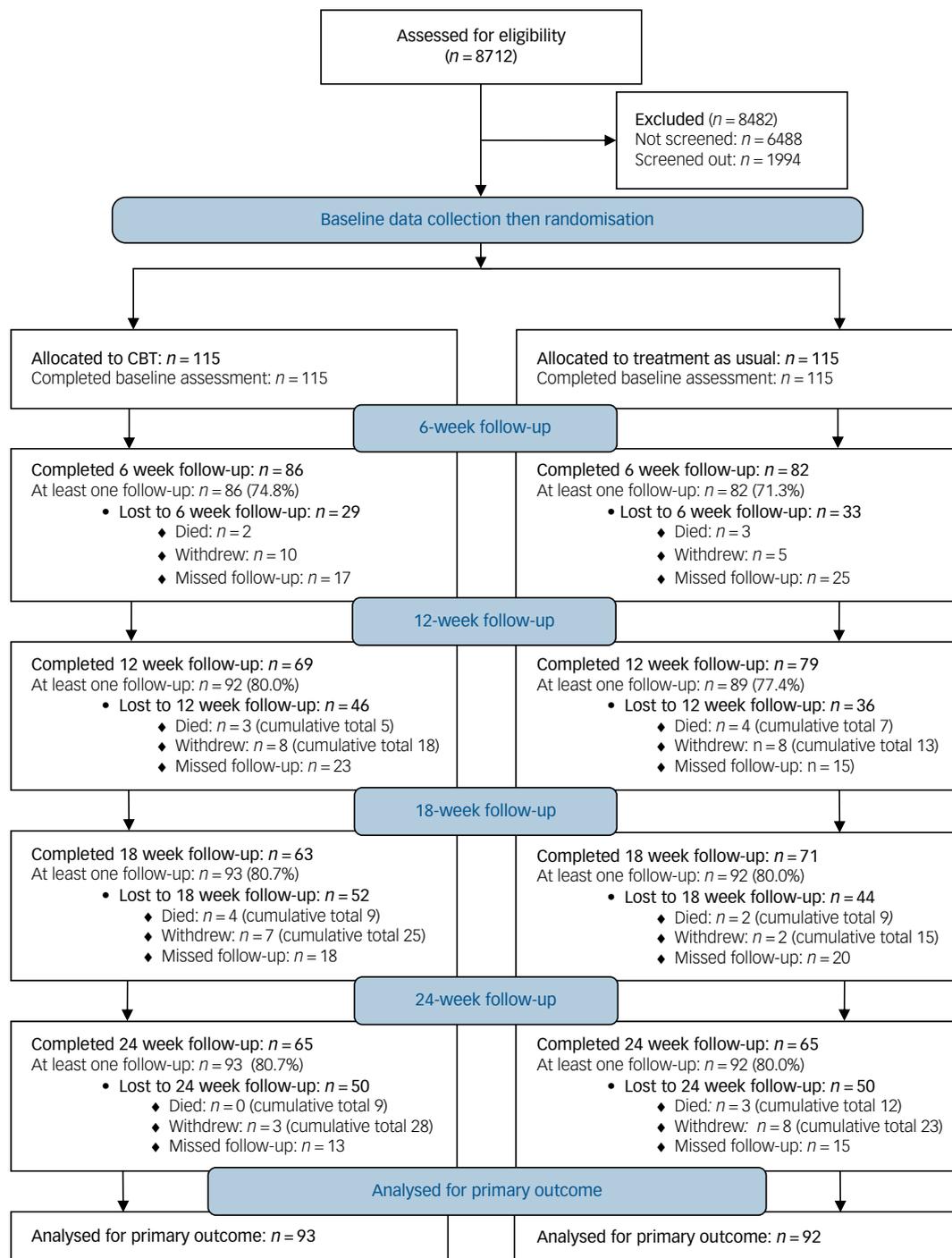
## Results

Of 8712 patients considered, 6488 were excluded (Fig. 1) for the following reasons (note that some had more than one reason for exclusion). In the pre-screening phase: IAPT unavailable,  $n = 2614$ ; no advanced cancer,  $n = 1668$ ; not screened (other reason),  $n = 1250$ ; declined to participate,  $n = 1021$ . Post-screening: declined to participate,  $n = 1241$ ; PHQ-2 score  $\leq 3$ ,  $n = 532$ ; other reason,  $n = 221$ .

Two hundred and thirty participants were randomised. At least one follow-up was available for 80% of participants; some were missed because of fluctuations in health (Fig. 1). Fifty-one reasons for withdrawing from the study were recorded; 18 (35.3%) were for ill health, and the remainder mixed, with no reason given for 11 (21.6%). Of the 71 reasons given for missed follow-ups in the CBT groups, 21 (29.2%) were due to physical health, 19 (26.4%) participants could not be contacted, and the remainder were mixed, with no reason given for 17 (23.6%).

### Demographic characteristics

Demographic characteristics were similar across trial arms (Table 1). Recruitment sources were as follows: oncology departments ( $n = 196$ ), hospices ( $n = 28$ ) and GPs ( $n = 6$ ). The cancer types were as follows: breast 31.3% ( $n = 72$ ), haematological 18.6% ( $n = 43$ , comprising myeloma ( $n = 10$ ), lymphoma ( $n = 17$ ) and



**Fig. 1** CONSORT flow diagram for the trial.

CBT, cognitive-behavioural therapy.

leukaemia ( $n = 5$ ), colon 12.6% ( $n = 29$ ), lung 11.7% ( $n = 27$ ), prostate 5.2% ( $n = 12$ ), other 20.4% ( $n = 47$ ).

### Diagnosis of depression, psychiatric history and treatment

The duration of current depression was skewed, with a median of 12 weeks; two people had been depressed for 40 years. The number of previous episodes of depression, the duration of the current depressive episode and antidepressant use were all similar between groups (Table 2).

### Delivery and receipt of CBT

Mean time from referral to first appointment was 29.4 days (s.d. = 26.7). Of a potential 1380 CBT sessions, 543 (39.3%) were taken up by 74/115 (64%) participants randomised to CBT. Mean number of sessions received was 4.7 (s.d. = 4.9); 41 people (35.6%) had no sessions. Thirty-two sessions (5.9%) were delivered by telephone. We rated for quality 55 sessions (28% of recorded sessions), 1 in 10 of sessions delivered. Mean CTS-R score was 47.6 (s.d. = 13.8), which was at the upper end of the 'proficient' range. Cognitive techniques were used in 57% of assessed sessions, behavioural techniques in 37% and topics specific to cancer in 70%.

**Table 1** Baseline demographic characteristics by randomisation group

	TAU arm ( <i>n</i> = 115)	CBT arm ( <i>n</i> = 115)	Total ( <i>n</i> = 230)
Age, years: mean (s.d.), min., max.	59.5 (12.4), 27, 93	59.5 (10.3), 37, 81	59.5 (11.4), 27, 93
Gender, <i>n</i> (%)			
Male	37 (32.2)	41 (35.7)	78 (33.9)
Female	78 (67.8)	74 (64.3)	152 (66.1)
Total	115 (100.0)	115 (100)	230 (100)
Marital status, <i>n</i> (%)			
Married	55 (48.2)	59 (51.3)	114 (49.8)
Partner, living with	9 (7.9)	9 (7.8)	18 (7.9)
Partner, not living with	1 (0.9)	2 (1.7)	3 (1.3)
Divorced/separated	18 (15.8)	13 (11.3)	31 (13.5)
Widowed	9 (7.9)	10 (8.7)	19 (8.3)
Single, never married	20 (17.5)	22 (19.1)	42 (18.3)
Other	2 (1.8)	0 (0)	2 (0.9)
Total	114 (100)	115 (100)	229 (100)
Ethnicity, <i>n</i> (%)			
White	84 (73.0)	83 (72.2)	167 (72.6)
Black British/African/Caribbean	17 (14.8)	14 (12.2)	31 (13.5)
Indian/Pakistani/Bangladeshi	6 (5.2)	7 (6.1)	13 (5.6)
Other	8 (7.0)	11 (9.6)	19 (8.3)
Total	115 (100)	115 (100)	230 (100)
Employment, <i>n</i> (%)			
Employed	16 (14.3)	27 (23.7)	43 (19.0)
Self-employed	5 (4.5)	13 (11.4)	18 (8.0)
Unemployed	12 (10.7)	14 (12.3)	26 (11.5)
Homemaker	2 (1.8)	0 (0)	2 (0.9)
Retired	49 (43.8)	38 (33.3)	87 (38.5)
Unable to work owing to health	24 (21.4)	20 (17.5)	44 (19.5)
Other	4 (3.6)	2 (1.8)	6 (2.7)
Total	112 (100)	114 (100)	226 (100)
Education, <i>n</i> (%)			
Degree/higher degree	42 (36.5)	44 (38.3)	86 (37.4)
A-level/HNC/HND/NVQ	36 (31.3)	36 (31.3)	72 (31.3)
GCSE (or equivalent)	16 (13.9)	24 (20.9)	40 (17.4)
No qualification	8 (7.0)	7 (6.1)	15 (6.5)
Other	13 (11.3)	14 (12.2)	27 (11.7)
Total	115 (100)	115 (100)	230 (100)

TAU, treatment as usual; CBT, cognitive-behavioural therapy; HNC, Higher National Certificate; HND, Higher National Diploma; NVQ, National Vocational Qualification; GCSE, General Certificate of Secondary Education.

## Main outcome

BDI-II scores at baseline and follow-up are provided in supplementary Table 1, available at <https://doi.org/10.1192/bjp.2019.207>. The primary analysis of CBT (*n* = 93) *v.* TAU (*n* = 92) indicated that there was no benefit from CBT with time, adjusted for therapist clustering, antidepressant use or educational level (Table 3).

Additional analyses found no evidence of clustering (at therapist or IAPT level) on the primary outcome and so these results are not given.

### CAITT analysis

A total of 153 individuals were included in the CAITT model (those with relevant data (for the control and intervention groups) and with number of CBT sessions available (for the intervention group)). Assuming a linear relationship between number of sessions and change in outcome, the estimated per-session effect on the BDI-II was  $-0.295$  (95% CI  $-0.760$  to  $0.170$ ;  $P = 0.213$ ). Thus, every CBT session would be expected to decrease the total BDI-II score by 0.3 points.

### Exploratory analysis

There was an improvement in BDI-II of around five points for both groups at 6 months. People who were widowed, separated or divorced and who did not receive CBT continued with depressive symptoms (treatment effect  $-7.21$ , 95% CI  $-11.15$  to  $-3.28$ ;  $P < 0.001$ ) (Table 4).

## Secondary outcomes

Baseline scores for secondary outcomes were similar in both trial arms (supplementary Table 2). There were no significant between-group differences at 12 and 24 weeks. The ECOG-PS suggested that, at baseline, 19.6% of participants (*n* = 45) were fully active, 42.2% (*n* = 97) had restricted movement, 27.4% (*n* = 63) were ambulatory, 10.9% (*n* = 25) had limited movement and 0% (*n* = 0) were disabled. Both groups were similar on the ECOG-PS at baseline. Non-parametric analysis of the change in ECOG-PS scores found no significant difference between groups at 12 or 24 weeks.

## Discussion

In this trial, we compared CBT (plus TAU) delivered by IAPT therapists for the treatment of depression in people with advanced cancer with TAU alone. No benefit of CBT was found, and the per-session effect of CBT was too small to scale up to a clinically significant change even if the full 12 sessions were delivered. CAITT analysis found a non-significant change in BDI-II depression scores with CBT of 0.3 points per therapy session, which would equate to a 3.6-point change over 12 sessions. This is well below the 6-point change generally regarded as the minimum clinically important change on this scale. An exploratory analysis suggested that CBT for people widowed, separated or divorced was helpful. There were no significant between-group differences for secondary

**Table 2** History, sources of bias and treatment of depression

	TAU arm (n = 115)	CBT arm (n = 115)	Total (n = 230)
Previous episodes of depression: mean (s.d.), min., max. (n <sub>e</sub> )	2.2 (1.9), 1, 10 (n <sub>e</sub> = 63)	2.6 (2.4), 1, 12 (n <sub>e</sub> = 59)	2.4 (2.1), 1, 12 (n <sub>e</sub> = 122)
Duration of depression, weeks: mean (s.d.), min., max. (n <sub>w</sub> )	74.3 (242.7), 0, 2080 (n <sub>w</sub> = 90)	86.6 (266.5), 0, 2080, (n <sub>w</sub> = 84)	80.3 (253.8), 0, 2080 (n <sub>w</sub> = 174)
CBT treatment expectation: mean (s.d.), min., max., (n) <sup>a</sup>	7.0 (1.9), 1, 10 (n <sub>t</sub> = 111)	7.2 (1.8), 4, 10 (n <sub>t</sub> = 113)	7.1 (1.9), 1, 10 (n <sub>t</sub> = 224)
Previous depression, n (%)			
Yes	69 (60.0)	68 (59.1)	137 (59.6)
Total	115 (100)	115 (100)	230 (100)
Previously received CBT			
Yes	12 (10.4)	12 (10.4)	24 (10.4)
Total	115 (100)	115 (100.0)	230 (100)
Currently being treated for depression, n (%) <sup>b</sup>			
Yes	33 (29.2)	33 (29.2)	66 (29.2)
Total	113 (100)	113 (100.0)	226 (100)
Treatment preference, n (%)			
The CBT group	92 (80.0)	87 (75.7)	179 (77.8)
The group with no CBT	3 (2.6)	2 (1.7)	5 (2.2)
Do not have a preference	20 (17.4)	26 (22.6)	46 (20.0)
Total	115 (100)	115 (100)	230 (100)
Current antidepressant use, n (%)			
At baseline	26 (22.6)	29 (25.2)	55 (23.9)
At 12-week follow-up	20 (17.4)	22 (19.1)	42 (18.3)
At 24-week follow-up	16 (13.9)	20 (17.4)	36 (15.7)
Other current psychological therapy (not CBT), n (%)			
At baseline	5 (4.3)	3 (2.6)	8 (3.5)
At 12-week follow-up	6 (5.2)	1 (0.9)	7 (6.1)
At 24-week follow-up	5 (4.3)	3 (2.6)	8 (7.0)

TAU, treatment as usual; CBT, cognitive-behavioural therapy; n<sub>e</sub>, number of participants reporting previous episodes; n<sub>w</sub>, number of participants reporting weeks of depression; n<sub>t</sub>, number of participants reporting treatment expectation.  
a. Treatment expectation estimated improvement from 'not at all' (scored 0) to 'very much improved' (scored 10).  
b. Includes prescribed medications, over-the-counter remedies and complementary therapies/self-help books to treat depression.

outcomes. The benefits of CBT for people with advanced cancer had been previously unclear because of underpowered trials, poor diagnosis and measurement of depression, lack of detail about interventions and concerns about generalisability.

Integrative collaborative-care approaches have previously been demonstrated to be effective in treating depression in poor-prognosis cancer.<sup>26</sup> Such integrative approaches, in which cancer nurses and psychiatrists collaborate with primary care physicians, may be more appropriate for treating depression in this population than referral to IAPT services.

### Clinical effectiveness and trial power

Our achieved power was sufficient to detect a 3-point change on the BDI-II. Even if our treatment effect of 0.84 change on the BDI-II were statistically significant, it is not clinically important. Although a recent study found a statistically significant benefit for psychotherapy,<sup>27</sup> the change of 1.29 points on the PHQ-9 is of questionable clinical significance given accepted standards.<sup>28</sup> Indeed, the beneficial effects of CBT for depression may be overestimated<sup>29</sup> and the benefit of psychosocial therapies,<sup>6</sup> including CBT,<sup>30</sup> for depression in advanced breast cancer is questionable. Our trial does not support CBT for depression in a wide range of cancers.

### Diagnosing and measuring depression in advanced cancer

The MINI has been widely used to diagnose depression in cancer. However, in people with life-limiting physical illnesses it may be difficult to distinguish depressive disorder from an adjustment disorder with a prolonged depressive reaction (ICD-10 code F43.21). As the mean duration of depression was 1.4 years and no one had symptoms lasting less than 4 weeks, it is unlikely that our findings were accounted for by adjustment disorder. The BDI-II is widely used for measuring depression in advanced cancer.<sup>16,30,31</sup>

Its cognitive components mitigate the problem of mislabelling physical symptoms that can occur with somato-affective components.

### CBT as an intervention

A recent meta-analysis<sup>29</sup> suggested that physical illness does not affect the outcomes of psychological treatments, but these data were not specific to a population with advanced cancer. With the exception of one underpowered study,<sup>30</sup> previous work in a palliative care population<sup>31</sup> and a population with metastatic breast cancer<sup>6</sup> does not support the use of CBT for depression in advanced cancer. Our clinical experience was that physically ill people had difficulty in managing the demands of CBT.<sup>32</sup>

#### Delivery of CBT

Time from referral to receiving therapy (mean 29.4 days) was shorter than in typical IAPT services, where 75% of referrals are seen within 42 days.<sup>33</sup> Our qualitative interviews confirmed that a small number were delayed because of physical problems.<sup>32</sup> Our trial aimed to test effectiveness, rather than efficacy of CBT. Sixty-four per cent (74/115) took up at least one CBT session. The mean number of sessions was 4.7. This is similar to therapy uptake for general IAPT practice (70%) and some improvement is observed after two therapy sessions.<sup>34</sup> Our CTS-R ratings suggest delivery of good-quality CBT, adherence to the manual, and a balance of cognitive and behavioural techniques and cancer-related issues.

Therapists in the present study described the experience of working with this population as positive, although they perceived the rigidity of IAPT policies as problematic when treating this population.<sup>32</sup> Therapists also emphasised the need for specialist supervision when delivering therapy to people with advanced cancer.<sup>32</sup>

**Table 3** BDI-II treatment effect adjusted for potential predictors of outcome

	Treatment effect (CBT – TAU)	95% CI	P
Model with baseline BDI-II, baseline antidepressant use, time and group – clustering by therapist <sup>a</sup> Number in model = 185 Estimates	–0.836	–2.755 to 1.083	0.393
Model with baseline BDI-II, baseline antidepressant use, time and group – clustering by therapist, plus baseline history of depression, baseline EQ-5D health score, baseline duration of current depression (weeks): duration between primary diagnosis and baseline visit (days) Number in model: 122 Estimates	0.105	–2.273 to 2.483	0.931
Model with baseline BDI-II, baseline antidepressant use and group – clustering by therapist: 6-week follow-up only Number in model: 168 Estimates	–0.136	–2.157 to 1.884	0.895
Model with baseline BDI-II, baseline antidepressant use and group – clustering by therapist: 12-week follow-up only Number in model: 148 Estimates	–1.504	–3.714 to 0.707	0.182
Model with baseline BDI-II, baseline antidepressant use and group – clustering by therapist: 18-week follow-up only Number in model: 134 Estimates	–0.964	–4.133 to 2.205	0.551
Model with baseline BDI-II, baseline antidepressant use and group – clustering by therapist: 24-week follow-up only Number in model: 130 Estimates	–1.875	–4.845 to 1.096	0.216

BDI-II, Beck Depression Inventory-II; CBT, cognitive-behavioural therapy; TAU, treatment as usual.  
a. The pre-determined primary analysis for the trial.

### Effect of bias

The BDI-II is self-report and this should minimise researcher bias. Differential attrition may bias outcome; however, retention of participants was similar between the trial arms.

### Limitations

A large number of patients (8712) had to be considered to recruit 230 into this trial. Although many were excluded because they did not have advanced cancer or depression, others were excluded owing to lack of access to participating IAPT centres, and a

substantial number also declined to participate in the study. The majority (two-thirds) of participants were female, which may raise concerns about generalisability of the findings, as men are more likely to develop and die from cancer. However, depression is more common in women, suggesting that our sample is representative of depression in the population with a range of advanced cancers. Uptake of therapy was limited, with only 64% of those randomised to the CBT group receiving treatment, and the mean number of sessions taken was 4.7 (out of a possible 12). Although this may have reduced the overall treatment effect, the CAITT analyses indicated that the per-session effect was insufficient to provide

**Table 4** BDI-II Total scores by time point, marital status and level of education

	Treatment effect (CBT – TAU)	95% CI	P
Model with baseline BDI-II, baseline antidepressant use, time and group – clustering by therapist, plus group × time interaction Number in model, 185 P = 0.471 for interaction Estimates			
6 weeks	0.127	–2.202 to 2.456	0.915
12 weeks	–0.847	–3.281 to 1.586	0.495
18 weeks	–1.365	–3.875 to 1.146	0.287
24 weeks	–1.728	–4.262 to 0.806	0.181
Model with baseline BDI-II, baseline antidepressant use, time and group – clustering by therapist, plus group × marital status interaction Number in model, 183 P = 0.002 for interaction Estimates			
Married/partner	0.645	–1.791 to 3.081	0.604
Divorced/separated/widowed	–7.211	–11.147 to –3.276	<0.001
Single, never married	0.836	–3.372 to 5.044	0.697
Model with baseline BDI, baseline antidepressant use, time and group – clustering by therapist, plus group × educational status interaction Number in model, 170 P = 0.710 for interaction Estimates			
Below A-level	–0.463	–3.558 to 2.631	0.769
A-level and above	–1.234	–3.862 to 1.395	0.358

BDI-II, Beck Depression Inventory-II; CBT, cognitive-behavioural therapy; TAU, treatment as usual.

a clinically meaningful change, even if all 12 sessions were taken up. TAU could not be standardised and we could not preclude it including a psychosocial intervention. However, very few participants in the TAU group reported receiving any psychological intervention and none reported receiving CBT. Lastly, diagnosing depression can be problematic in people with cancer, where symptoms of the disease and treatment can overlap with symptoms of depression; although this cannot be fully mitigated, we chose the BDI-II as the primary outcome measure, as it has been validated and widely used in trials involving people with cancer.

### Implications of findings

CBT in advanced cancer may be delivered in three ways: CBT specialists may be trained to apply existing skills to cancer-specific problems; cancer specialists may be trained in CBT skills; specialist CBT therapists may be imbedded in a cancer service. IAPT is expanding to treat long-term medical conditions. This research suggests that delivering CBT in this context for advanced/incurable cancer, rather than early curable disease, is not effective. Training clinical nurse specialists in a palliative care service to use CBT techniques is not effective for depressive symptoms.<sup>31</sup> Embedding CBT therapists within cancer and palliative care teams requires evaluation. Integrated collaborative care, which includes elements of CBT, has been shown to be beneficial for depression in lung cancer.<sup>26</sup> Testing this approach in other tumour groups may offer greater promise than embedding a CBT therapist in a palliative care team. Although under a quarter of people in this trial were prescribed an antidepressant, evidence for their use for depression in people with cancer remains to be evaluated.<sup>35</sup> The long duration of depression observed in this trial (mean 80 weeks) suggests that in people with advanced cancer, depression may either be missed (71% of participants in this trial were not receiving treatment for depression) or be unresponsive to treatment (in the 29% receiving treatment).

This trial was not powered to examine the observed benefit of CBT for depressive symptoms in participants who were widowed, separated or divorced. However, these are known moderators of response to CBT in adults.<sup>25</sup> We postulate that isolated, bereaved or separated participants may have benefited from the non-specific components of CBT (e.g. having someone friendly to talk to).

### Summary

A meta-analysis<sup>29</sup> suggested that the effectiveness of CBT for depression in general may be overestimated, possibly owing to publication bias, small sample size and a lack of suitable control groups. Although IAPT practitioners can be trained to deliver CBT to people with advanced cancer, our results suggest that resources for a relatively costly therapy such as IAPT-delivered CBT should not be considered as a first-line treatment for depression in advanced cancer. Indeed, these findings raise important questions about the need to further evaluate the use of IAPT for people with comorbid severe illness.

**Marc Serfaty** , MD(Res), Associate Professor in Psychiatry, Division of Psychiatry, University College London, UK; **Michael King** , PhD, Professorial Research Associate, Division of Psychiatry, University College London, UK; **Irwin Nazareth**, PhD, Professor of Primary Care and Population Science, Research Department of Primary Care and Population Health, University College London, UK; **Stirling Moorey**, MBBS, Consultant Psychiatrist in CBT, South London and Maudsley NHS Foundation Trust, King's College London, UK; **Trefor Aspden** , PhD, Senior Research Associate, Division of Psychiatry, University College London, UK; **Kathryn Mannix**, MBBS, Consultant in Palliative Medicine and Cognitive Behaviour Therapist, Palliative Care Service, Newcastle upon Tyne Hospitals NHS Foundation Trust, UK; **Sarah Davis**, MA, Senior Research Nurse, Marie Curie Palliative Care Research Department, University College London, UK; **John Wood**, MSc, Principle Research Associate, Research Department of Primary Care and Population Health, University College London, UK; **Louise Jones**, FRCP, Honorary Clinical Senior Lecturer, Marie Curie Palliative Care Research Department, University College London, UK

**Correspondence:** Dr Marc Serfaty, Division of Psychiatry, University College London, 6th Floor Maple House, 149 Tottenham Court Road, London W1T 7NF, UK. Email: [m.serfaty@ucl.ac.uk](mailto:m.serfaty@ucl.ac.uk)

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### Supplementary material

Supplementary material is available online at <https://doi.org/10.1192/bjp.2019.207>.

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