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Integrated therapist and online cognitive behavioural therapy in addition to usual care versus usual care for depression in primary care in England (INTERACT): a two-group, parallel, multicentre, randomised controlled trial

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Summary

Background Online interventions can improve access to cognitive behavioural therapy (CBT). We aimed to evaluate the clinical effectiveness of a novel approach integrating therapist-delivered CBT online in reducing depressive symptoms for primary care patients in England, compared with usual care.

Methods INTERACT was a two-group, parallel, pragmatic, multicentre, randomised controlled trial recruiting patients from 67 general practices in England. Eligible participants were aged 18 years or older, scored 14 or more on the Beck Depression Inventory (BDI-II), and met ICD-10 criteria for a depressive episode. Patients who were under psychiatric care or had dementia, bipolar disorder, a psychotic illness, or a recent history of alcohol or substance abuse (within the past year) were excluded. Participants were randomly assigned (1:1, stratified by centre and minimised on gender, current antidepressant use, and depression severity) using an automated remote randomisation service to receive integrated CBT in addition to usual care (intervention) or to continue with usual general practitioner care (control). Patients, therapists, and researchers were not masked to allocation. There were no restrictions on usual care treatments. Integrated CBT comprised nine therapist-led sessions, delivered online via instant messaging within the dedicated INTERACT therapy platform. All sessions were delivered one-to-one by therapists accredited as CBT practitioners and were tailored to the individual patient's needs. Participants were followed up at 3, 6, 9, and 12 months after random assignment using self-report questionnaires. The primary outcome was depressive symptoms (BDI-II score) 6 months after random assignment, analysed using linear regression on an intention-to-treat basis without imputation for missing data. Adverse events and serious adverse events were recorded if identified as part of routine follow-up questionnaires or if reported by participants. The trial was registered with the ISRCTN registry (ISRCTN13112900) and is complete.

Findings Between Jan 28, 2021, and April 27, 2023, 451 participants were screened for eligibility and randomly assigned to the intervention (n=225) or usual care (n=226). Mean age was 39·3 years (SD 14·9). 313 (69%) of participants self-reported their gender as female, 135 (30%) as male, and three (1%) as other. 381 (84%) participants self-reported their ethnicity as White, 27 (6%) as Asian or British Asian, 14 (3%) as Mixed, 14 (3%) as Black or Black British, 12 (3%) as Other, and three (1%) as Chinese. The primary analysis included 334 (74%) participants, 171 in the intervention group and 163 in the usual care (control) group, and the median time between random assignment and 6-month follow-up was 6·2 months (IQR 6·0–6·7). At 6 months, the mean BDI-II score in the intervention group was 22·5 (SD 14·4) and in the control group was 27·4 (SD 14·0; adjusted difference in means –4·4 [–7·90 to –1·9]; p=0·0006; effect size 0·43). There were 54 adverse events (33 in the intervention group and 21 in the control group) and 14 serious adverse events (twelve in the intervention group and two in the control group) during the trial. The most common adverse events were self-harm (n=6) and referrals to a mental health team (n=6). No serious adverse events were definitely or probably related to the intervention. There were no participant deaths.

Interpretation Integrated CBT was effective for primary care patients with depression at 6 months. This novel mode of delivery could increase the availability of CBT and improve access for individuals who find in-person appointments difficult or inconvenient.

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Introduction

Most depression is managed in primary care and, although rates of antidepressant prescribing continue to increase in many countries, access to psychotherapy is important for improving outcomes and patient choice. Cognitive behavioural therapy (CBT) is an effective treatment for depression, but demand greatly exceeds supply. The growth in CBT-based computerised interventions (computerised CBT) has the potential to increase access to therapy, and some computerised CBT packages have been endorsed by the UK National Institute for Health and Care Excellence (NICE).[1] However, current evidence does not support the notion that computerised CBT materials alone are an alternative to individual high-intensity CBT. Adherence to computerised CBT that is not supported by the direct involvement of a therapist can be poor[2] and its effects more modest compared with therapy provided in person.[3,4] Furthermore, the absence of flexibility of these programmes has been previously cited as "theoretically problematic and is inconsistent with the emphasis on individual formulations that is the crux of traditional CBT".[5]

CBT is particularly suited to combining or integrating computer and mobile technology with a therapist-led approach. Delivering CBT online using instant messaging is effective.[6] However, therapy via instant messaging alone does not support the practice of CBT outside the psychotherapeutic session (termed homework) using, for example, thought records and behavioural experiments. Technological advancements make it possible to incorporate online CBT materials, such as psychoeducational resources and worksheets, as an integral part of therapy, permitting the therapist to tailor treatment to the individual. This approach aligns with the CBT competences framework[7] and the idea of meta-competences, whereby the therapist adapts CBT to each patient's needs. In this integrated treatment model, the user has easy access to CBT materials, which could increase effectiveness by encouraging homework exercises that take place outside the psychotherapeutic session.[8] Working online with interactive materials might improve adherence and engagement,[9] and use of mobile devices could allow immediate recording of thoughts and experiences. Moreover, working online with interactive materials could increase access for individuals who have difficulty in attending in-person therapy (eg, those in full-time employment, with caring responsibilities, living in more remote areas, or with social anxiety).

Previous studies have blended in-person CBT and an internet-based treatment platform.[10,11] Online content was standardised but, despite flexibility over the order in which online modules were completed, the material was not tailored to the individual.[10,11] Moreover, as these studies recruited outpatients from specialised mental health centres, the findings might not be generalisable to primary care. Other studies have used internet-based CBT support

Research in context

Evidence before this study

In a previous systematic review and meta-analysis, we searched MEDLINE, Embase, PsycINFO, and the Cochrane Central Register of Controlled Trials via the specialised register of the Cochrane Common Mental Disorders Group from database inception to June 10, 2016, for randomised controlled trials in adults with a primary diagnosis of depression that included a cognitive behavioural therapy (CBT) intervention. The search terms included MeSH Headings (eg, depressive disorder, major/ or depressive disorder, treatment-resistant/ or dysthymic disorder/); and keywords or text searches (eg, mood disorder*, affective disorder*, depression or depressive or dysthymi*), (*therap* or psychotherapy*), (cognitive) (*CBT or cognitive-behavi*). No language restrictions were applied to the searches. Our systematic review and network meta-analysis published in 2019 concluded that multimedia and hybrid CBT might be as effective as face-to-face CBT. To our knowledge, there are no other studies that incorporate online CBT materials to which the patient has independent access as an integral part of therapy delivered online in real time to primary care patients with depression. We have previously shown that CBT delivered in real time online by instant messaging is effective, but this modality alone does not support the practice of CBT outside therapy sessions (termed homework), which is a key component of CBT. Other studies have blended in-person CBT with use of an internet-based therapy platform, but this content was not tailored to the individual and the two components were not integrated. Internet-based CBT support systems or mobile applications that contain some CBT materials have been developed, but these have only been evaluated in small samples of patients recruited from psychiatric clinics.

Added value of this study

The INTERACT platform integrates computer and mobile technology with a therapist-led approach. This approach aligns with the CBT competences framework and the idea of meta-competences, whereby the therapist adapts CBT to each patient's needs. The therapy is delivered online in real time within a platform (INTERACT) that offers access to a library of CBT materials both during and outside the therapy session. To our knowledge, this work is the first large-scale randomised trial of this approach, which we showed to be clinically effective in primary care patients with depression.

Implications of all the available evidence

Implementation of the INTERACT platform has the potential to increase the availability of CBT, including for individuals who find it difficult or inconvenient to meet in person. Future research needs to identify the aspects of the platform that led to improvements and examine whether the beneficial effects of the intervention are sustained beyond 12 months.

systems or a mobile app that includes some CBT materials alongside in-person therapy, but these approaches have only been evaluated in small samples (n=33–82) of patients recruited from psychiatric clinics.[12,13]

In a novel approach to the treatment of depression, we developed and built a platform to integrate the use of online CBT materials, with therapist-led sessions taking place in real time via instant messaging. We integrated a personalised therapist-led approach with online materials that could be independently accessed outside the therapist sessions (with therapist guidance and support). These materials formed an extensive library, including animations, psychoeducation, rating scales, and worksheets for homework tasks. The Integrated Therapist and Online CBT for Depression (INTERACT) randomised controlled trial aimed to evaluate the clinical effectiveness of this integrated approach to delivering CBT in reducing depressive symptoms for primary care patients compared with usual care. The findings of the parallel economic evaluation will be reported separately.

Methods

Study design

The INTERACT trial was a two-group, parallel, pragmatic, multicentre randomised controlled trial. We recruited participants from 67 general practices in England at three trial sites: Bristol, London, and York. The trial protocol has been published.[14]

A list of approved protocol amendments is provided in the appendix (pp 12–15). Following completion of earlier pilot work and before the start of recruitment (appendix pp 2–3), flexibility was introduced to permit up to 12 therapy sessions, and brief check-in sessions were removed (amendment approved Aug 2, 2019 [version 1.2]). Additional changes (amendment approved July 31, 2020 [version 1.4]) were made before the start of recruitment due to the COVID-19 pandemic: first therapy session to take place by videocall instead of in person; option for research appointments to be conducted remotely; amendments to documentation to facilitate remote completion and e-consent; and extension of the internal pilot period from 6 months to 9 months to allow for the potential effect of the pandemic on recruitment. Later changes included an exit questionnaire and qualitative exit interviews added to 12-month follow-up (amendment approved April 25, 2022 [version 1.7]) and a £10 voucher introduced at 3-month follow-up, changes to minimum data collection measures at 6-month and 12-month follow-ups, changes to therapist and supervisor interview timing and number, recruitment extended until May 31, 2023, and end of data collection extended until June 30, 2024 (amendment approved March 27, 2023 [version 1.9]).

Individuals with lived experience of depression were involved in the design and management of the research programme. The intervention design was informed by extensive development work and included iterative user-centred design and piloting involving both patients and clinicians (appendix pp 2–3). Ethical approval was granted by the South West – Frenchay Research Ethics Committee (reference 19/SW/0038, IRAS ID 257620) and the Health Research Authority. All participants provided written informed consent in English. The trial was prospectively registered with the ISRCTN registry (ISRCTN13112900) and is complete.

Participants

Eligible patients were aged 18 years or older, scored 14 or more on the Beck Depression Inventory (BDI-II),[15] and met ICD-10 criteria for depression (assessed using the Clinical Interview Schedule–Revised [CIS-R], a computerised, self-administered, structured interview).[16] Patients who were under psychiatric care for depression; had dementia, bipolar disorder, psychosis, or schizophrenia; or had a recent history of alcohol or substance dependency (within the past year) were excluded. We also excluded those who were unable to complete questionnaires unaided or would need an interpreter, were unable or unwilling to receive online CBT, were currently receiving psychotherapy, had received high-intensity CBT in the past 4 years, or were participating in another trial.

Potential participants were identified via a search of practice electronic records or by direct referral from their general practitioner (GP). Those who agreed to be contacted were telephoned by a researcher and asked some brief screening questions. Those who met the screening criteria were invited to an appointment at which a researcher (DT, LT, SB, BCFC, BJ, or MXL) would explain the trial, obtain written informed consent, and conduct the baseline assessment to establish patient eligibility.

See Online for appendix

Randomisation and masking

Eligible participants were randomly assigned (1:1) to either usual GP care (control) or integrated CBT in addition to usual GP care (intervention). To ensure allocation concealment, randomisation was done by means of a computer-generated code from a bespoke, automated, remote randomisation service managed independently by the Bristol Trials Centre. Randomisation was stratified by centre and minimised on gender (male or female), current antidepressant use (yes or no), and depressive severity based on baseline score on the BDI-II (BDI-II score ≤25, 26–35, and ≥36), using a probability weighting of 0·8 to reduce predictability. The researcher (DT, LT, SB, BCFC, BJ, or MXL) informed the participant of their allocation at the end of the baseline appointment. Given the nature of the intervention, it was not possible to mask participants, therapists, or researchers to treatment allocation. Those analysing the data were not masked to treatment allocation but followed a pre-specified statistical analysis plan.

Procedures

There were no restrictions on the treatment options for usual care—participants could access any treatment

options available from their GP or elsewhere (eg, prescribed medication or referral to National Health Service [NHS] Talking Therapies). Usual care was administered by GPs, per their own discretion, for both the intervention and control groups.

Integrated CBT comprised nine therapist-led sessions of Beckian CBT,[17] with a further three sessions where clinically appropriate. All sessions were delivered one-to-one, remotely, and were tailored to the individual's needs. The first session took place by videocall (90 min), with subsequent 50-min therapy sessions taking place (usually weekly) online via instant messaging (typing) within the INTERACT web-based therapy platform (appendix pp 2–4). Integrated CBT was provided in addition to usual care.

Participants were granted platform access after random assignment and before their first session; those who completed therapy could maintain access until their 12-month follow-up. The platform was accessible by computer, smartphone, or tablet on participants' own devices. The platform included psychoeducational materials, worksheets for completion by participants, and short video animations. Resources covered overcoming avoidance; behavioural activation; dysfunctional assumptions, rules, and beliefs; formulation; general psychoeducation; goal setting; problem solving; relapse prevention; risk; sleep; working with thoughts; and a small number of resources related to anxiety. The psychoeducational materials and animations were all visible to participants when they registered on the platform; worksheets were released by therapists as required. Additional information on intervention development and content is provided in the appendix (pp 2–4).

Before each therapy session, participants set a brief list of topics they would like to discuss and completed a Patient Health Questionnaire-9[18] (PHQ-9) questionnaire to assess depression within the therapy platform. This topic list was used as the basis for discussion of the agenda that was agreed collaboratively between the participant and therapist at the start of each session. During therapy sessions, therapists and participants could use a collaborative workspace to view, edit, and discuss CBT resources synchronously within the platform. Therapists could also agree tasks with the participant for them to complete within the platform between sessions. Participants could access transcripts of their online instant messaging therapy sessions during and between therapy sessions.

Data on therapy session attendance and platform use were recorded by the platform. Therapists and patients could use an inbuilt messaging system between sessions; this system was predominantly for appointment scheduling and homework task queries. Therapists could view data on their patients' use of the platform.

The intervention was delivered by nine part-time CBT therapists (eight female and one male) accredited as CBT practitioners by the British Association for Behavioural and Cognitive Psychotherapies (BABCP). At the start of the trial, the median age of the therapists was 39 years (IQR 38–45) and they had been practicing as CBT therapists for a median of 6 years (3–12). Three had previously supervised other therapists, and five had previously used technology to deliver or support CBT. Therapists were employed 1 month before starting to deliver therapy in the trial and received training in use of the platform. When providing treatment in the trial, therapists at each trial site received weekly group supervision (group sizes of two or three) from an experienced CBT supervisor (12–20 years practising as a CBT therapist [AB or another supervisor]). Supervision could include review of worksheets, transcripts, and depression (PHQ-9) scores from the platform.

After all therapy provision had finished, fidelity to the CBT model was assessed in a random sample of transcripts by two independent raters, using the CTS-R. These raters were BABCP-accredited therapists and experienced CBT supervisors who had worked within NHS Talking Therapies. The CTS-R comprises 12-items, each rated zero to six, total score 0–72, with a score of 36 or higher often used as indicative of competence.

As part of the baseline assessment, data were collected on participant sociodemographic characteristics including age, self-reported gender (male, female, or other), self-reported ethnicity (using categories used in previous primary care depression trials and based on the 2001 Office for National Statistics census: White, Mixed, Asian or Asian British, Black or Black British, Chinese, or Other ethnic group), employment status, educational qualifications, housing status, and marital status. Participants were also asked for relevant medical history, including comorbidities, history of depression, and treatment (including antidepressant medication). At baseline, participants completed the following questionnaires: BDI-II,[15] CIS-R,[16] PHQ-9,[18] Generalised Anxiety Disorder-7[19] (GAD-7), Work and Social Adjustment Scale[20] (WSAS; a measure of function), and EuroQol-5 Dimension 5-Level[21] (EQ-5D-5L, a quality-of-life measure). The PHQ-9 and GAD-7 are measures of depression and anxiety used in NHS Talking Therapies services. Additional measures of neuroticism, personality, trauma, life events, financial stress, social support and alcohol use were also completed at baseline.[14]

Participants were followed up at 3, 6, 9, and 12 months after random assignment using self-report questionnaires. Participants who had not completed an earlier follow-up were re-contacted to request completion of a later follow-up unless they had withdrawn from the study. At 6 months and 12 months, participants completed the following questionnaires: BDI-II, PHQ-9, GAD-7, WSAS, and EQ-5D-5L. The PHQ-9 and GAD-7 were also completed as part of the brief 3-month and 9-month follow-ups. The use of antidepressant medication and other treatments received were self-reported at all follow-ups. Follow-ups at 6 months and 12 months were conducted via a face-to-face videocall or telephone appointment with a researcher. Alternatively, participants could complete questionnaires independently (via a secure link to an online questionnaire) or via a paper

questionnaire sent by post. The option of offering an in-person appointment (at baseline, 6 months, or 12 months) was not possible because of the COVID-19 pandemic. When possible, follow-ups at 3 months and 9 months were conducted by telephone (with alternatives of videocall, online, or post also available). Assessments were self-administered to eliminate any observer bias. Trial therapists were not involved in these outcome measurements. Further details are available in the trial protocol.[14]

Adverse events were recorded if identified as part of routine follow-up questionnaires—eg, hospital admission data collected at 6 months and 12 months—or if otherwise spontaneously reported by participants to the researcher or INTERACT therapist between baseline and end of participation.[14] A priori, more adverse event reports were anticipated in the intervention group as a result of their more frequent contact with the trial team (weekly therapy sessions and risk assessments). The clinical principal investigator at each site (DK, GL, or SG) rated each event according to expectedness, seriousness, relatedness to the intervention or trial, severity, and outcome.

Outcomes

The primary outcome was score on the BDI-II depression scale at 6 months, measured as a continuous variable. The BDI-II is a widely used outcome measure in psychotherapy trials and has been validated in various settings and populations, including primary care.[15]

BDI-II at 12 months was a secondary outcome. Additional secondary outcomes at both 6 and 12 months were response (≥50% reduction in BDI-II score relative to baseline); remission (BDI-II score <10); percentage reduction in depressive symptoms on the BDI-II (calculated at the individual level as the follow-up score minus baseline score divided by the baseline score then multiplied by 100); measures of depression and anxiety used in NHS Talking Therapy services (PHQ-9 and GAD-7); and the WSAS.

Other outcomes included use of antidepressants and other prescribed medication and other health-care resources (via participant self-report at 6 months and 12 months and GP medical records) and quality of life (EQ-5D-5L) at 6 months and 12 months. These data informed the economic evaluation, which will be reported separately.

Statistical analysis

The sample size calculation was based on 173 participants in each group providing 90% power to detect a difference of 0·35 SDs (approximately 4–5 points) on the BDI-II at a two-sided 5% significance level. Allowing for 20% attrition at 6 months, the recruitment target was 434 participants. Further details on the justification for the sample size can be found in the protocol.[14] Trial data were collected and managed using the secure web application REDCap, hosted at the University of Bristol.

Analysis and reporting were in accordance with CONSORT guidelines and followed a pre-defined statistical analysis plan agreed with the independent Trial Steering Group.[22] We used descriptive statistics to assess the baseline comparability of randomly assigned groups. Primary and secondary comparative analyses between the two randomised groups were conducted according to the intention-to-treat (ITT) principle, without imputing missing values. The primary analysis incorporated all questionnaires returned regardless of whether they were returned on time or not. Linear regression was used to compare the primary (continuous) outcome (BDI-II score) at 6 months between randomly assigned groups, adjusting for centre and minimisation variables (baseline BDI-II score, gender, and current antidepressant use). Appropriate (linear or logistic) regression models were used for secondary outcomes. We report differences in means or odds ratios (ORs), 95% CIs, and p values. Effect size is presented for the primary BDI-II outcome and was calculated on the basis of Cohen's *d* statistic. The effect of the intervention on outcomes over 12 months was summarised using a repeated-measures model, with an interaction between treatment and time to formally test whether effects varied with time. To estimate the numbers needed to treat (NNT) and associated CIs, the adjusted models for the binary treatment response and remission variables at 6 months were run. From these models, the marginal effects of treatment group were extracted, which provided the risk differences and CIs. The reciprocals of these numbers were then used to calculate the NNT and CIs.

As specified in our statistical analysis plan,[22] additional sensitivity analyses were used to examine the effect of the following on the primary outcome: (1) missing data under different assumptions—specifically, best-case and worst-case scenarios, and using multiple imputation by chained equation to impute missing data (for the latter, we generated 200 datasets with the imputation model, including all variables predictive of missingness at 6 months [p<0·20], as well as variables in the primary analysis); (2) any baseline imbalances in baseline characteristics; (3) potential clustering by therapist; and (4) actual timing of follow-up questionnaire completion.

A complier average causal effect (CACE) analysis of the primary outcome was conducted to estimate the treatment effect in compliers. We defined compliers as those who had attended at least six sessions or reached an agreed end (completing their therapy goals) in fewer sessions. Separate to the CACE analysis, another sensitivity analysis explored whether there was a dose–response relationship in terms of the number of therapy sessions attended. The primary outcome model was repeated using a numeric measure of the number of therapy sessions attended as the exposure variable. Participants allocated to usual care had exposure set to zero.

A priori-specified subgroup analyses of the primary outcome explored the potential for differential treatment effects based on chronicity of depressive symptoms (duration <1 year and 1–5 years), severity of depression (baseline BDI-II score as a continuous variable), and personality difficulties (measured using the Standardised

Assessment of Personality Abbreviated Scale score as a continuous variable).

All analyses were conducted in Stata version 18.0.

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

The trial opened to recruitment on Dec 8, 2020, with the first referral on Dec 29, 2020, and the first invitation mailing on 28 Jan, 2021. The final participant was randomly assigned on April 27, 2023 (after the recruitment target had been met). Follow-up data were collected between April 4, 2021, and April 26, 2024.

From 12 182 letters of invitation and 381 direct referrals, 1455 patients agreed to being contacted by the research team (figure). Of these, 982 were eligible to attend a baseline assessment, but 221 individuals declined. Age and gender were similar between the two groups (appendix p 5). Of the 761 individuals who attended a baseline assessment, 451 (59%) were eligible for the trial, agreed to participate, and were randomly assigned to either the intervention group (n=225) or the usual care (control) group (n=226). Details of recruitment by centre are provided in the appendix (p 6).

346 (77%) of 451 patients were followed up at 3 months, 334 (74%) at 6 months, 328 (73%) at 9 months, and 327 (73%) at 12 months (figure). Comparison of the baseline characteristics between those who did and did not provide BDI-II data at 6 months are shown in the appendix (pp 7–9). Those from higher socioeconomic backgrounds, with higher educational attainment, with a longstanding illness or disability, a longer duration of the current depressive episode, more PTSD symptoms, those who were married or cohabiting, or who were not employed were less likely to have missing BDI-II outcomes at 6 months.

313 (69%) of 451 participants self-reported their gender as female, 135 (30%) as male, and three (1%) as other. Mean age was 39·3 years (SD 14·9; table 1). 381 (84%) participants self-reported their ethnicity as White, 27 (6%) as Asian or British Asian, 14 (3%) as Mixed, 14 (3%) as Black or Black British, 12 (3%) as Other, and three (1%) as Chinese. Mean BDI-II score at baseline was 32·8 (10·3), indicative of severe depression. Most participants had a history of depression (216 [48%] had had five or more previous episodes of depression), and 314 (70%) were taking antidepressants. The duration of the current episode of depression was 2 years or more for 230 (51%) participants (table 1). Although the two treatment groups had similar characteristics at baseline, there was some evidence of imbalances (table 1). A higher proportion of participants in the intervention group were single, had five or more previous episodes of depression, reported current suicidal ideation, and reported less financial strain (living comfortably or doing all right) than those in the control group.

In the intervention group, 14 (6%) of 225 individuals had no therapy sessions, and 137 (61%) completed therapy (ie, received at least nine sessions or reached an agreed end of therapy with their therapist in fewer than nine sessions). 50 (22%) patients withdrew from therapy and 38 (17%) were discharged for non-attendance. Among the 211 participants who had at least one session, the mean duration from random assignment to final therapy session was 3·2 months (SD 1·6). 199 [94%] of 211 participants finished therapy within 6 months of random assignment. Participants received a median of eight therapy sessions (IQR three to ten); 152 (68%) of 225 participants received at least six sessions of CBT or reached an agreed end (based on completing their therapy goals) in fewer than six sessions (CACE definition). Based on a random sample of 50 transcripts, the mean CTS-R scale rating (adjusted for therapist caseload) was 28·4 (95% CI 26·8–30·0) from rater one and 32·3 (30·1–34·4) from rater two.

Among those who started therapy, the median interval from random assignment to the first therapy session was 17 days (IQR 0–29). Those assigned to the intervention group logged into the INTERACT therapy platform a median of 28 times (12–42). On average (median), ten resources (IQR five to 15; worksheets or information sheets) were shared by the therapist with each of their patients and five (two to 11) practice-at-home tasks (homework) were agreed. Use of the platform was higher among those who had received at least six sessions or who reached an agreed end in fewer sessions (median of 37 logins [27–49·5], 13 resources shared [9·5–17], and nine homework tasks set [four to 13]) than among participants in the intervention group overall. Some of the shared resources had the functionality to be completed multiple times without resharing.

The primary analysis included 334 (74%) participants, 171 in the intervention group and 163 in the control group, and the median time between random assignment and 6-month follow-up was 6·2 months (IQR 6·0–6·7). At 6 months, the mean BDI-II score in the intervention group was 22·5 (SD 14·4) and in the control group was 27·4 (14·0; adjusted difference in means –4·4 [–7·90 to –1·9]; table 2); effect size was 0·43 (using baseline pooled SD). In sensitivity analyses, adjustment for baseline imbalances slightly increased the between-group difference (difference in means –4·9 [95% CI –7·6 to –2·2]), but adjustment for actual timing of follow-up questionnaire completion had no effect (–4·4 [–7·0 to –1·9]). In other sensitivity analyses, the results of imputing missing data using multiple imputation by chained equation were consistent with the findings of the primary analysis (appendix p 10). Other scenarios for missing data that represented more extremes in the pattern of missingness were also considered. Under the better case scenarios, the differences between treatment groups were greater than observed in the primary analysis. In worse case scenarios, the differences were smaller. Assuming a 1 SD shift in the mean, in the better case scenario there was a larger difference in mean BDI-II scores (–12·1 [–14·4 to –9·7])

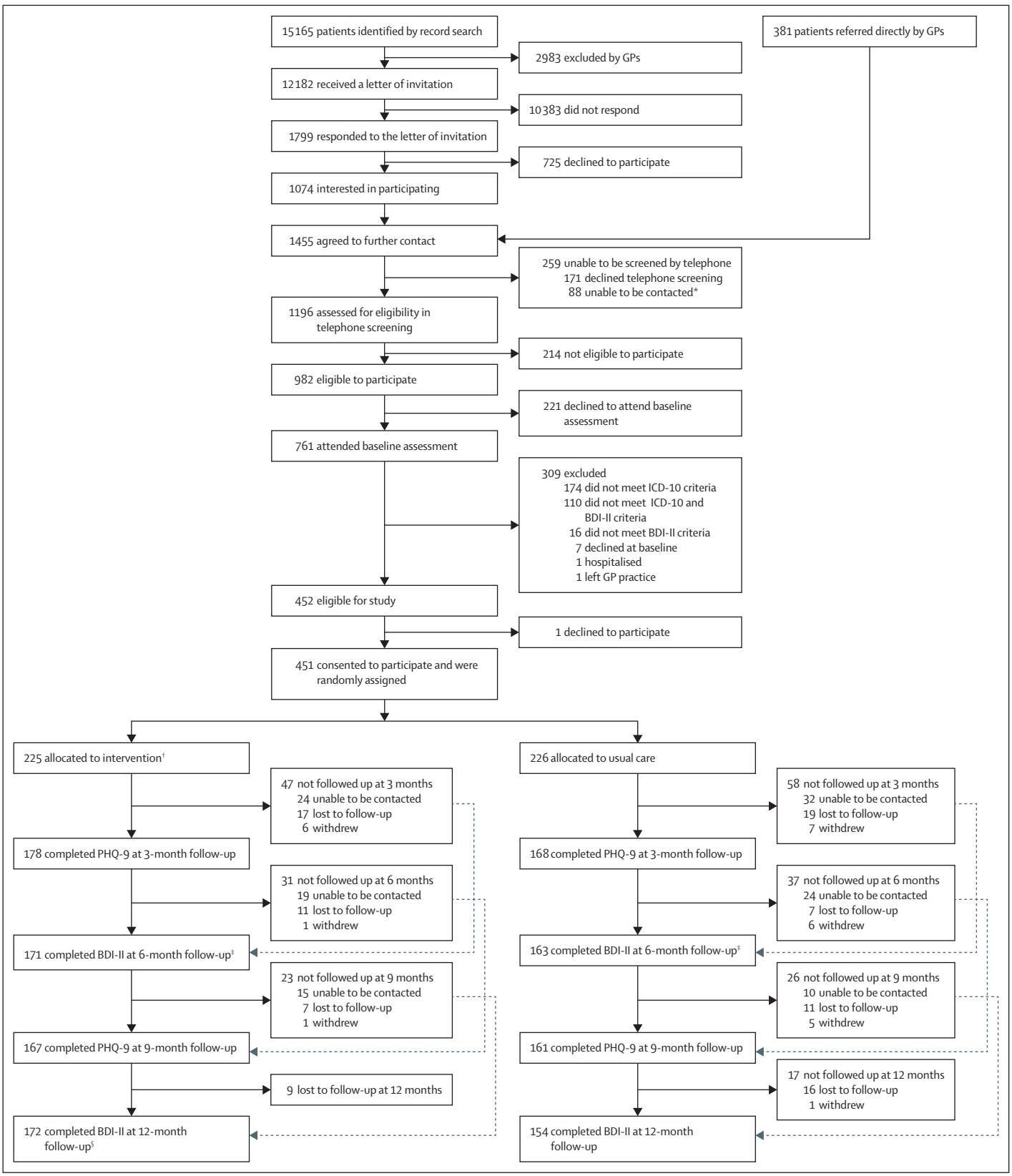

Figure: **Trial profile**

BDI=Beck Depression Inventory. GP=general practitioner. *Includes seven patients who replied too late. †211 participants started integrated CBT as planned; 137 participants completed CBT as planned. ‡Primary outcome. §One additional patient was contacted at 12 months but did not complete the BDI-II.

	Intervention group (n=225)	Control group (n=226)	Total (n=451)
Stratification variable: centre			
Bristol	139 (62%)	139 (62%)	278 (62%)
London	49 (22%)	50 (22%)	99 (22%)
York	37 (16%)	37 (16%)	74 (16%)
Minimisation variables			
Female	157 (70%)	156 (69%)	313 (69%)
Male	68 (30%)	70 (31%)	138 (31%)
Baseline BDI-II score			
≤25	60 (27%)	62 (27%)	122 (27%)
26–35	82 (36%)	83 (37%)	165 (37%)
≥36	83 (37%)	81 (36%)	164 (36%)
Currently taking antidepressants	157 (70%)	157 (69%)	314 (70%)
Sociodemographic variables			
Age, years	39·0 (15·9)	39·5 (14·0)	39·3 (14·9)
Self-reported gender			
Male	65 (29%)	70 (31%)	135 (30%)
Female	157 (70%)	156 (69%)	313 (69%)
Other	3 (1%)	0	3 (1%)
Self-reported ethnic group			
White	194 (86%)	187 (83%)	381 (84%)
Mixed	5 (2%)	9 (4%)	14 (3%)
Asian or British Asian	11 (5%)	16 (7%)	27 (6%)
Black or Black British	7 (3%)	7 (3%)	14 (3%)
Chinese	1 (<1%)	2 (1%)	3 (1%)
Other	7 (3%)	5 (2%)	12 (3%)
Marital status			
Married or living as married	78 (35%)	98 (43%)	176 (39%)
Single	123 (55%)	100 (44%)	223 (49%)
Separated, widowed, or divorced	24 (11%)	28 (12%)	52 (12%)
Employment status			
In paid employment (full-time or part- time)	134 (60%)	129 (57%)	263 (58%)
Student	31 (14%)	27 (12%)	58 (13%)
Not in employment	30 (13%)	34 (15)	64 (14%)
Unemployment due to ill health	30 (13%)	36 (16%)	66 (15%)
Educational attainment			
A-level, Higher Grade, Level 3 qualification or higher	178 (79%)	174 (77%)	352 (78%)
GCSE, Standard Grade, O-level or equivalent	38 (17%)	38 (17%)	76 (17%)
No formal qualifications	9 (4%)	14 (6%)	23 (5%)
Housing			
Homeowner	78 (35%)	91 (40%)	169 (37%)
Tenant or living with relative or friend	141 (63%)	127 (56%)	268 (59%)
Hostel or care home, homeless, or other	6 (3%)	8 (4%)	14 (3%)
Financial wellbeing			
Living comfortably or doing all right	107 (48%)	95 (42%)	202 (45%)
Just about getting by	64 (28%)	78 (35%)	142 (31%)
Finding it difficult or very difficult to make ends meet	54 (24%)	53 (23%)	107 (24%)
Information technology literacy: I am confident using computers			
Strongly agree	145 (64%)	134 (59%)	279 (62%)
Agree	63 (28%)	69 (31%)	132 (29%)
Neither agree nor disagree	11 (5%)	13 (6%)	24 (5%)

(Table 1 continues on next page)

between the intervention and control groups, but in the worse case scenario, there was a small increase in symptoms (2·5 [0·2 to 4·7]) in the intervention group compared with the control group. These scenarios, however, represent extremes in the patterns of missingness and therefore must be interpreted with caution (appendix p 10).

The number of patients per therapist ranged from ten (4%) to 36 (16%) of 225 intervention participants. There was little evidence of clustering of outcomes by therapist (intraclass correlation coefficient <0·0001). Consistent with this finding, a fully heteroscedastic model that accounted for clustering by therapist gave very similar results to the primary analysis (difference in means –4·4 [95% CI –6·9 to –1·9]). CACE analyses showed that the effect of the intervention was larger in individuals who completed treatment as intended compared with the results of the ITT analysis of the primary outcome at 6 months (table 2). In the sensitivity analysis exploring a dose–response relationship, BDI-II scores at 6 months were found to decrease by –0·50 units (–0·77 to –0·22) for each additional therapy session after adjustment for baseline BDI-II, centre, medication use at baseline, and gender.

A priori subgroup analyses of the primary outcome showed that personality difficulties (SAPAS), depression severity (BDI-II score), or chronicity of symptoms had no effect on the difference between the intervention group and control group at 6 months (numeric SAPAS score at baseline: interaction term –0·52 [95% CI –1·95 to 0·91]; p=0·47 for interaction; numeric baseline BDI-II score at baseline: interaction term –0·15 [–0·39 to 0·09]; p=0·22 for interaction; chronicity [categorical variable for the duration of symptoms]: interaction terms 1·12 [–5·00 to 7·24] for 1–5 years and –1·17 [–7·66 to 5·31] for >5 years; p=0·77 for interaction).

At 6 months, response occurred in 59 (35%) of 171 participants the intervention group and 26 (16%) of 163 in the control group (adjusted OR 2·78 [95% CI 1·63 to 4·74]). At 6 months, remission occurred in 41 (24%) of 171 participants in the intervention group and 17 (10%) of 163 in the control group (2·74 [1·46 to 5·15]; table 2). These findings can be alternatively described using NNT, which were six (95% CI four to 11) in the intervention group and eight (five to 19) in the control group. The difference in mean percentage reduction in depressive symptoms on the BDI-II was –14·6% (–22·7 to –6·6). The intervention group also had fewer depressive symptoms in terms of PHQ-9 score, fewer anxiety symptoms in terms of GAD-7, and less impairment in terms of functioning (WSAS) at 6 months compared with the control group (table 2).

The median time between random assignment and 12-month follow-up was 12·1 months (IQR 11·9–12·4) for the intervention group and 12·1 months (12·0–12·4) for the control group. In repeated-measures analyses (using data from 6 months and 12 months), participants in the intervention group had a BDI-II score that was, on average, 3·8 points lower (95% CI –6·1 to –1·5) than those in the control group (table 3). The intervention group also had

increased odds of a response (OR 2·22 [95% CI 1·45–3·41]) and of remission (2·40 [1·43–4·02]), as well as benefits in terms of function (WSAS) compared with the control group. Repeated-measures analyses for the secondary outcomes of PHQ-9 and GAD-7 scores (table 3) also incorporated scores at 3 months and 9 months. The mean PHQ-9 score at 3 months was 11·5 (SD 6·3) in the intervention group (n=178) and 13·6 (6·0) in the control group (n=168). At 9-months, the mean PHQ-9 score was 10·3 (6·6) in the intervention group (n=167) and 12·6 (6·9) in the control group (n=161). The mean GAD-7 score at 3 months was 9·4 (SD 5·5) in the intervention group (n=177) and 11·4 (5·5) in the control group (n=167); and at 9 months, the mean GAD-7 score was 8·2 (5·7) in the intervention group (n=167) and 10·4 (5·9) in the control group (n=161). In repeated-measures analyses, participants in the intervention group had a PHQ-9 score that was, on average, 2·1 points lower (95% CI –3·0 to –1·2) than those in the control group, and a GAD-7 score that was, on average, 1·9 points lower (–2·7 to –1·1) than those in the control group. There was little evidence that the effects varied over time (p values for the intervention-by-time interactions ranged from 0·12 to 0·96).

Regarding receipt of usual care treatments outside the trial, by 6 months, 13 (4%) of 324 participants had received computerised CBT (two [1%] of 166 participants in the intervention group, with a median of seven sessions [IQR six to eight], and 11 [7%] of 158 in the control group, with a median of four sessions [three to nine]). By 6 months, 74 individuals (24 [14%] of 168 in the intervention group and 50 [31%] of 161 in the control group) had received another talking therapy outside the trial. Of these, 15 individuals had received high-intensity individual CBT (five [3%] of 168 in the intervention group, median number of sessions ten [IQR eight to 12], and ten [6%] of 160 in the control group, median number of sessions ten [seven to 11]). At 6 months, 216 (65%) participants (107 [63%] of 170 in the intervention group and 109 [67%] of 163 in the control group) were taking antidepressant medication prescribed by their GP (difference –3·9% [95% CI –14·2 to 6·3]).

There were 54 adverse events and 14 serious adverse events (three expected and 11 unexpected) during the trial (table 4). More adverse events occurred in the intervention group than in the control group (45 *vs* 23). In total, 34 (15%) of 225 participants in the intervention group and 17 (8%) of 226 in the control group reported one or more adverse events or serious adverse events. Three adverse events were rated as definitely or probably related to the intervention (worsening depression, anxiety, and self-harm risk); these three participants discontinued therapy. One adverse event in the control group was probably related to trial participation (anxiety-related nosebleed). No serious adverse events were definitely or probably related to the intervention. There were no suspected unexpected serious adverse reactions or participant deaths during the trial period.

	Intervention group (n=225)	Control group (n=226)	Total (n=451)
(Continued from previous page)			
Disagree	5 (2%)	8 (4%)	13 (3%)
Strongly disagree	1 (<1%)	2 (1%)	3 (1%)
Psychosocial and clinical variables			
Alcohol consumption, AUDIT-PC score	3 (1–5)	3 (1–5)	3 (1–5)
Number of life events* in the past 6 months	1·4 (1·3)	1·5 (1·4)	1·5 (1·3)
Social support score	11·8 (3·9)	12·4 (3·6)	12·1 (3·7)
Any long-standing illness or disability	143 (64%)	146 (65%)	289 (64%)
Work and Social Adjustment Score	26·3 (7·7)	26·3 (7·3)	26·3 (7·5)
Standardised Assessment of Personality Scale	4·2 (1·8)	4·3 (1·8)	4·3 (1·8)
PC-PTSD-5: ever experienced a traumatic event	106 (47%)	108 (48%)	214 (47%)
PC-PTSD-5 score			
0	7/106 (7%)	7/108 (6%)	14/214 (7%)
1	7/106 (7%)	5/108 (5%)	12/214 (6%)
2	10/106 (9%)	7/108 (6%)	17/214 (8%)
3	21/106 (20%)	17/108 (16%)	38/214 (18%)
4	22/106 (21%)	28/108 (26%)	50/214 (23%)
5	39/106 (37%)	44/108 (41%)	83/214 (39%)
Big Five Inventory neuroticism score	4·0 (0·6)	3·9 (0·7)	3·9 (0·6)
Measures of depression			
Duration of current episode			
2 weeks to 6 months	40 (18%)	46 (20%)	86 (19%)
6 months to 1 year	37 (16%)	31 (14%)	68 (15%)
1–2 years	35 (16%)	32 (14%)	67 (15%)
2–5 years	49 (22%)	54 (24%)	103 (23%)
>5 years	64 (28%)	63 (28%)	127 (28%)
Had depression in the past (self-report)	198 (88%)	188 (83%)	386 (86%)
Number of previous episodes of depression			
0–1	40 (18%)	47 (21%)	87 (19%)
2–4	70 (31%)	78 (35%)	148 (33%)
≥5	115 (51%)	101 (45%)	216 (48%)
Family history of depression	167 (74%)	175 (77%)	342 (76%)
Previous referral to a psychiatrist for depression	64 (28%)	59 (26%)	123 (27%)
Length of current course of antidepressants in those currently taking antidepressants†			
<6 weeks	24/157 (15%)	18/157 (11%)	42/314 (13%)
6 weeks to 3 months	12/157 (8%)	22/157 (14%)	34/314 (11%)
3–6 months	20/157 (13%)	24/157 (15%)	44/314 (14%)
6–12 months	36/157 (23%)	25/157 (16%)	61/314 (19%)
>12 months	63/157 (40%)	66/157 (42%)	129/314 (41%)
Missing data	2/157 (1%)	2/157 (1%)	4/314 (1%)
Adherence to antidepressants in past 6 weeks at baseline in those currently taking antidepressants			
I have taken my tablets every day	98/157 (62%)	103/157 (66%)	201/314 (64%)
I have taken my tablets nearly every day	49/157 (31%)	48/157 (31%)	97/314 (31%)
I have taken more than half my tablets	5/157 (3%)	3/157 (2%)	8/314 (3%)
I have taken less than half my tablets	4/157 (3%)	3/157 (2%)	7/314 (2%)
I have hardly taken any of my tablets	0/157	0/157	0/314 (0%)
I have not taken any of my tablets	1/157 (1%)	0/157	1/314 (<1%)
ICD-10 primary diagnosis according to the CIS-R			
Mild	35 (16%)	24 (11%)	59 (13%)
Moderate	101 (45%)	113 (50%)	214 (47%)
Severe	89 (40%)	89 (39%)	178 (39%)

(Table 1 continues on next page)

	Intervention group (n=225)	Control group (n=226)	Total (n=451)
(Continued from previous page)			
Secondary psychiatric diagnosis according to the CIS-R			
0 No diagnosis identified	1 (<1%)	1 (<1%)	2 (<1%)
1 Mixed anxiety and depressive disorder (mild)	22 (10%)	18 (8%)	40 (9%)
2 Generalised anxiety disorder (mild)	4 (2%)	8 (4%)	12 (3%)
4 Mixed anxiety and depressive disorder	31 (14%)	31 (14%)	62 (14%)
5 Specific (isolated) phobia	8 (4%)	8 (4%)	16 (4%)
6 Social phobia	8 (4%)	4 (2%)	12 (3%)
7 Agoraphobia	7 (3%)	6 (3%)	13 (3%)
8 Generalised anxiety disorder	102 (45%)	107 (47%)	209 (46%)
9 Panic disorder	42 (19%)	43 (19%)	85 (19%)
BDI-II score	32·6 (10·4)	32·9 (10·3)	32·8 (10·3)
GAD-7 score	12·7 (5·0)	13·0 (5·1)	12·8 (5·0)
PHQ-9 score	17·2 (5·4)	17·3 (5·1)	17·2 (5·2)
EQ-5D-5L score	0·522 (0·262)‡	0·504 (0·262)	0·513 (0·262)
CIS-R score	30·6 (9·2)	31·5 (9·3)	31·0 (9·3)
Suicidal ideation (CIS-R thoughts or plans)	92 (41%)	80 (35%)	172 (38%)

Data are n (%), n/N (%), mean (SD), or median (IQR). Percentages for some categories might sum to more than 100% because of rounding. AUDIT-PC=Alcohol Use Disorders Identification Test–Primary Care. BDI=Beck Depression Inventory. CIS-R=Clinical Interview Schedule-Revised. EQ-5D-5L=EuroQol-5 Dimension-5 Level. GAD=Generalised Anxiety Disorder. GCSE=General Certificate of Secondary Education. PHQ=Patient Health Questionnaire. PC-PTSD=Primary Care Post-Traumatic Stress Screen. *Eight-item checklist including bereavement, separation or divorce, serious illness or injury, victim of crime, court appearance, unmet debts, serious dispute, and job loss. †If participant reported taking more than one antidepressant, this duration is for the first listed antidepressant. ‡Data missing for three participants.

Table 1: **Baseline sociodemographic and clinical characteristics**

Discussion

To our knowledge, this work is the first large-scale randomised controlled trial to evaluate an integrated approach to delivering CBT for depression. Integrated CBT and usual care compared with usual care was effective in reducing depressive symptoms in primary care patients with depression at 6 months. Benefit was also seen in terms of response and remission of depressive symptoms, improved function, and symptoms of anxiety; improvements were maintained over 12 months. The benefit in terms of the difference in mean depression (BDI-II) scores at 6 months, the primary outcome, is likely to be clinically important (based on previous evidence that a minimum clinically important difference is a 20% [relative] improvement in depressive symptoms, or 3·5 to 4·4 points on the BDI-II).[23] 61% of participants in the intervention group completed a course of therapy, and 22% withdrew from treatment, with a further 17% discharged for non-attendance. Participants received a median of eight therapy sessions, which aligns with the number of sessions received by those in NHS Talking Therapies.[24] The three adverse events that were definitely or probably related to the intervention were all mental health-related. The number of serious adverse events was small, and none were directly attributable to the intervention.

This large trial recruited from primary care, the setting in which most patients with depression are managed. Although we were restricted to recruiting from GP practices in the areas surrounding our three trial sites (Bristol, London, and York), participants represented a suitably heterogeneous group. Many had severe and chronic depression and had been taking antidepressant medication for more than 12 months, but 19% were experiencing their first or second episode of depression. The sample recruited was more ethnically diverse than in our previous primary care depression trials of psychotherapy (16% of participants self-reported their ethnicity as non-White, compared with 2% in a previous trial).[25] Only a small proportion of those who were invited to take part were ultimately recruited, and most of those who participated were confident using computers. However, the pragmatic nature of our trial strengthens the generalisability of our findings. Our comparison was with usual GP care, and we imposed no restrictions on this treatment. We did not explicitly specify what usual care should comprise, but we would expect GPs to refer to the NICE guidelines for the management of depression.[1] We recorded treatments received outside the trial and noted that only a small number of individuals had received high-intensity individual CBT by 6 months. The inclusion of a 12-month follow-up strengthened the trial by enhancing the validity and reliability of its findings and showing the sustained effects of the intervention. However, further work is needed to understand which aspects of the intervention and platform usage led to improvements.

The recruitment target was achieved, and, although the final follow-up rate at 6 months was slightly below the original target, retention was good (74% *vs* target 80%). Attrition was similar at 12 months, albeit with some evidence of lower retention in those randomly assigned to continue with usual care. Such differential attrition might lead to bias. However, sensitivity analyses showed that the results imputing missing data at 6 months were consistent with the findings of the primary analysis.

Some imbalances in baseline characteristics between randomised groups were identified. Importantly, the strongest predictor of the outcome of depressive symptoms is likely to be depressive symptoms at baseline, and this predictor was balanced between groups. We found no evidence that adjustment for baseline imbalances affected the conclusions. Some analyses, such as those examining the effect of the number of therapy sessions attended and subgroup analyses, were exploratory; hence, effect estimates, 95% CIs, and p values should be interpreted with caution.

Therapists were BABCP-accredited and, hence, representative of those working in NHS Talking Therapy services, so the results should be generalisable to the UK. An independent evaluation of therapist competence found mean CTS-R ratings below the traditional cutoff point for competence (score ≥36). However, scores were in line with mean scores in an earlier trial of therapy delivered using instant messaging.[6] It is important to acknowledge that, although the CTS-R is a widely used measure of fidelity, it

	Intervention group		Control group		Comparison		
	N	Mean (SD) or n (%)	N	Mean (SD) or n (%)	Adjusted odds ratio* (95% CI)	Adjusted difference in means* (95% CI)	p value
Primary outcome							
BDI-II score	171	22·5 (14·4)	163	27·4 (14·0)	..	–4·4 (–7·0 to –1·9)	0·0006
Secondary outcomes							
Response†	171	59 (35%)	163	26 (16%)	2·78 (1·63 to 4·74)	..	0·0001
Remission‡	171	41 (24%)	163	17 (10%)	2·74 (1·46 to 5·15)		0·0012
Percentage reduction in BDI-II§	171	–31·4% (38·2)	163	–16·8% (36·5)	..	–14·6% (–22·7 to –6·6)	0·0004
PHQ-9	169	10·4 (6·3)	161	12·6 (6·7)	..	–2·0 (–3·2 to –0·8)	0·0012
GAD-7	168	8·1 (5·4)	161	10·0 (6·0)	..	–1·7 (–2·7 to –0·7)	0·0013
WSAS	166	19·2 (11·3)	160	21·1 (11·3)	..	–2·1 (–4·2 to –0·03)	0·044
CACE analysis¶							
BDI-II score	171	22·5 (14·4)	163	27·4 (14·0)	..	–5·8 (–9·1 to –2·6)	0·0005

N indicates the number of individuals with data for a particular outcome measure at the 6-month follow-up. BDI=Beck Depression Inventory. CACE=complier average causal effect. GAD=Generalised Anxiety Disorder. PHQ=Patient Health Questionnaire. WSAS=Work and Social Adjustment Score. *Adjusted for the baseline measure of the outcome and stratification (centre) and other minimisation variables (gender, current antidepressant use at baseline, and depression [BDI-II] severity at baseline). †Improvement of at least 50% in BDI-II score compared with baseline. ‡BDI-II of less than 10 at 6 months. §Calculated as ([follow-up BDI-II – baseline BDI-II]/baseline BDI-II) × 100%. ¶Attended at least six sessions or reached a jointly agreed end of therapy in fewer sessions.

Table 2: **Analysis of primary and secondary outcomes at 6-month follow-up**

	Intervention group		Control group		Repeated measures analysis				
	N	Mean (SD) or n (%) at 12 months	N	Mean (SD) or n (%) at 12 months	N (number of unique individuals)	Adjusted odds ratio* (95%CI)	Adjusted difference in means‡ (95% CI)	p value	p value for treatment–time interaction
BDI-II score	172	21·6 (15·4)	154	25·2 (13·4)	660 (359)	..	–3·8 (–6·1 to –1·5)	0·0014	0·12
Response†	172	66 (38%)	154	37 (24%)	660 (359)	2·22 (1·45 to 3·41)	..	0·0003	0·24
Remission‡	172	48 (28%)	154	22 (14%)	660 (359)	2·40 (1·43 to 4·02)	..	0·0009	0·66
Percentage reduction in BDI-II§	172	–33·3% (43·7)	154	–21·6% (39·0)	660 (359)	..	–13·0% (–20·4 to –5·6)	0·0006	0·28
PHQ-9	171	10·1 (6·8)	153	12·3 (6·9)	1328 (394)	..	–2·1 (–3·0 to –1·2)	<0·0001	0·96
GAD-7	171	8·0 (5·9)	153	9·7 (6·0)	1325 (394)	..	–1·9 (–2·7 to –1·1)	<0·0001	0·82
WSAS	170	18·8 (11·9)	153	20·7 (11·3)	649 (357)	..	–1·9 (–3·8 to –0·1)	0·040	0·93

For the intervention and usual care groups, N indicates the number of individuals with data for a particular outcome measure at the 12 month follow-up; for the repeated measures analysis, N is the total number of participants across all timepoints, with the number of unique individuals included in parentheses. BDI=Beck Depression Inventory. GAD=Generalised Anxiety Disorder. PHQ=Patient Health Questionnaire. WSAS=Work and Social Adjustment Score. *Adjusted for the baseline measure of the outcome and stratification (centre) and other minimisation variables (gender, current antidepressant use at baseline, and depression [BDI-II] severity at baseline). †Improvement of at least 50% in BDI-II score compared with baseline. ‡BDI-II score of less than 10. §Percentage reduction between 12 months and baseline calculated as ([follow-up BDI-II – baseline BDI-II]/baseline BDI-II]) × 100%.

Table 3: **Repeated measures analysis of outcomes at 6-month and 12-month follow-ups**

was not designed to assess fidelity from transcripts of therapy sessions delivered via instant messaging—thus, a new measure is needed for evaluating other modes of delivery of CBT.

To our knowledge, no previous studies have integrated the use of online CBT materials with therapist-led CBT for depression delivered online. In their 2024 study, Haun and colleagues[26] evaluated the effectiveness of five sessions of therapy delivered by videocall and found a small reduction (effect size 0·21 [95% CI 0·03–0·39]) in symptoms of depression and anxiety at 6 months compared with usual care. By contrast, in this trial, the effect size for integrated CBT was substantially larger (0·43). There are several possible explanations for this finding, including the fact that INTERACT participants attended a median of eight sessions. It is also possible that the process of participants framing their thoughts in writing added to the effectiveness of the therapy in INTERACT, in that it allowed time for reflection and review. In the field of trauma therapy, there is evidence that the process of writing might have additional benefits, with emerging evidence of therapeutic gain using synchronous text-based interventions.[27,28]

Models of blended care have been proposed in previous studies,[10,11] combining individual in-person CBT sessions with a course of online treatment modules, but the online modules in these models were not tailored to the individual. Månsson and colleagues[12] developed internet-based CBT support systems that included online handouts and some CBT worksheets (eg, thought diaries), but these did not have an integrated collaborative workspace for sharing and discussing resources. Moreover, the therapy did not adhere to a specific CBT treatment manual.[12]

	Intervention group (n=45)	Control group (n=23)*	Total (n=68)
Adverse events			
Referred to mental health team	3	3	6
Self-harm	5	1	6
Musculoskeletal pain	2	2	4
Minor injury	2	2	4
Anxiety	1	2	3
Depression worse	3	0	3
Suicidal risk	2	1	3
Self-harm risk	2	0	2
Headache	0	2	2
Stress-related chest pain	0	2	2
Substance or alcohol abuse	1	1	2
Vaso-vagal episode	2	0	2
Eye surgery	2	0	2
Colonoscopy	2	0	2
Panic	1	0	1
Sleep studies†	1	0	1
Unwell after drink spiked‡	1	0	1
Femoral hernia	0	1	1
Flashback	0	1	1
Hepatobiliary pain	1	0	1
Hypertension	1	0	1
Lump in groin	0	1	1
Mechanical fall	1	0	1
Renal colic	0	1	1
Total	33	20	53*
Relatedness			
Not likely or unlikely	25	17	42
Possibly§	5	2	7
Probably or definitely¶	3	1	4
Serious adverse events—expected			
Self-harm (overdose)	1	1	2
Suicidal risk	1	0	1
Total	2	1	3
Relatedness			
Not likely, or unlikely	1	1	2
Possibly‖	1	0	1
Probably or definitely	0	0	0
Serious adverse events—unexpected			
Alcohol and injury	1	0	1
Appendicectomy	1	0	1
Ischaemic heart disease	1	0	1
Myocardial infarction	1	0	1
Cerebrovascular accident	0	1	1
Surgery for strangulated hernia	1	0	1
Hepatobiliary—gallstones	1	0	1
Infection admitted	1	0	1
Injury	1	0	1
Severe focal migraine	1	0	1
Surgery for cancer	1	0	1
Total	10	1	11

(Table 4 continues in next column)

(Continued from previous column)

	Intervention group (n=45)	Control group (n=23)*	Total (n=68)
Relatedness			
Not likely, or unlikely	10	1	11
Possibly	0	0	0
Probably or definitely	0	0	0

*One adverse event (accident and emergency department attendance for a physical health reason) was unable to be rated as the participant did not provide any details. †Pre-planned investigation. ‡Felt physically unwell and attended accident and emergency after their drink was spiked by someone else. §Intervention group: self-harm (two), self-harm risk (one), sleep studies (one), and depression worse (one); usual care group: referred to mental health team (one) and suicidal risk (one). ¶Intervention group: self-harm risk (one), depression worse (one), and anxiety (one); usual care group: anxiety (one). ‖Intervention group: suicidal risk (one).

Table 4: **Adverse events and serious adverse events**

Kalde and colleagues[13] reported a small pilot trial (n=82) of in-person CBT (12 sessions) augmented by a digital smartphone app that gave access to a depression module and additional therapeutic content released by therapists. The authors found that improvements in depressive symptoms were larger for the CBT plus app group compared with standard in-person CBT (effect size 0·21), but the study was not powered to provide definitive evidence of effectiveness, and the therapy was not standardised.

Several other studies have compared different modalities of delivering CBT. Mohr and colleagues[29] found that although CBT delivered by telephone was not inferior to in-person therapy immediately after treatment, 6 months later, those who had received in-person therapy were less depressed than those who received therapy by telephone. A network meta-analysis[30] comparing the effectiveness of different modalities of CBT showed that multimedia CBT (including books, telephone apps, and texts) and hybrid CBT (multimedia plus one or more face-to-face sessions) might be as effective as face-to-face (in-person) CBT when compared with treatment as usual. Despite uncertainty around effect estimates in this analysis,[30] it could be argued that health-care professionals should consider the practical advantages and disadvantages of the different modes of delivery when choosing treatment for individual patients.

The integrated approach evaluated in this trial is a novel approach to delivering CBT, enabling therapists to tailor treatment to the individual and share resources within sessions. Importantly, this integrated CBT approach has been found to be acceptable to patients and therapists.[31] The level of engagement with the integrated CBT approach in our trial was similar to the level observed with in-person CBT in the CoBalT randomised controlled trial (61% *vs* 68%),[25] and substantially higher than the level of engagement reported with low-intensity CBT interventions (eg, in a trial of telephone-facilitated CBT,[32] 30% of participants completed at least three sessions).

Integrated CBT is an effective treatment for primary care patients with depression. This intervention has the

potential to increase the availability of CBT and increase access for those who find it difficult to attend appointments in person (such as those in full-time employment, with caring responsibilities, living in more remote areas, or with social anxiety). This form of service delivery could be readily adapted for use by primary care mental health services such as NHS Talking Therapies and is particularly well suited to individuals who are comfortable expressing themselves via typing and prefer to avoid face-to-face interactions,[31] perhaps related to concerns about stigma.

Future research could examine which components of the integrated CBT approach and therapy platform were associated with benefit, including real-time therapist contact and access to and completion of online materials tailored to the individual. We also need to understand whether the effects are sustained beyond 12 months. Permitting continued access to the therapy platform (beyond 12 months) with periodic therapist support could offer the potential for a low-cost intervention to prevent relapse. Furthermore, the online therapy platform could be extended by the inclusion of additional online materials to enhance utility within NHS services by addressing the needs of service users with a range of mental health problems or long-term conditions. Thus, platforms such as INTERACT offer the potential to further increase utility and efficiency in terms of service provision.

Contributors

Conceptualisation: DT, JL, AB, SG, PL, GL, IN, SP, TJP, RS, KT, CW, DK, and NW. Data curation and validation: DT, JL, and SJM. Formal analysis: DT, JL, SJM, TJP, DK, and NW. Funding acquisition: SG, PL, GL, IN, SP, TJP, RS, KT, CW, DK, and NW. Investigation: DT, LT, SB, BCFC, JSH, BJ, JL, and MXL. Methodology: DT, LT, JL, SG, GL, SJM, IN, SP, TJP, RS, KT, CW, DK, and NW. Project administration: DT, LT, SB, BCFC, JSH, BJ, JL, MXL, AB, SG, GL, SJM, SP, TJP, RS, KT, CW, DK, and NW. Supervision: DT, AB, SG, GL, SP, TJP, DK, and NW. Visualisation: DT and SJM. Writing—original draft: DT, DK, and NW. Writing—reviewing and editing: all authors. Patient and public involvement expertise: PL. All authors contributed to interpretation of the data. DT and SJM directly accessed and verified the underlying data. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication. All authors read and approved the final manuscript. DT, DK, and NW are guarantors. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

Declaration of interests

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Data sharing

The INTERACT protocol[14] and statistical analysis plan[22] have been published. We encourage and will facilitate data sharing with bona fide researchers. In the first instance, all data requests should be submitted to the co-lead, NW, for consideration (nicola.wiles@bristol.ac.uk). Access to anonymised data might be granted following review. Data from the INTERACT trial (underpinning the clinical and cost-effectiveness analyses) will be made available (12 months after publication of the papers reporting the clinical and cost-effectiveness of the intervention) as a controlled dataset managed by the University of Bristol's Research Data Repository (https://data.bris.ac.uk/data). To gain access, data requestors will need to apply at http://www.bristol.ac.uk/staff/researchers/data/accessing-research-data/. Data release will be contingent on a signed data access agreement. This agreement limits use of data to non-commercial research only. Requests for any other purposes must be negotiated separately.

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evaluation, with the intention that it be made available to National Health Service partners on a not-for-profit basis should it prove effective. The authors thank the patients, therapists, supervisors, and general practices who have participated in this research. We are also grateful to the NIHR Clinical Research Network, who supported participant recruitment. We thank the people with lived experience who contributed to the development of the INTERACT intervention and advised on other aspects of the programme. We thank the INTERACT Programme Steering Group and Data Monitoring Committee for their support and guidance. We are grateful to our research programme administrators, the University of Bristol Research IT team, who developed and maintained the INTERACT CBT platform and those who kindly granted permission for their CBT resources to be used within the INTERACT platform. This trial was designed and delivered in collaboration with the Bristol Trials Centre, a UKCRC-registered clinical trials unit. This trial was also supported by the NIHR Bristol Biomedical Research Centre. Supplementary funding was provided by the NIHR School for Primary Care Research (SPCR–2014-10043 Award: L).

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