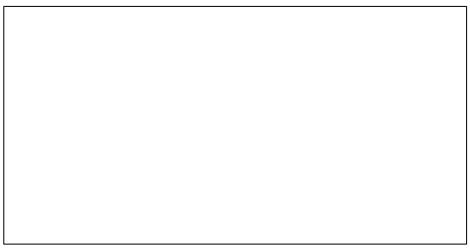

Clinical and cost-effectiveness of person-centred experiential therapy vs. cognitive behavioural therapy for moderate and severe depression delivered in the English Improving Access to Psychological Therapies national programme: A pragmatic randomised non-inferiority trial [PRaCTICED]

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Summary

Background

The UK government's implementation in 2008 of The Improving Access to Psychological Therapies (IAPT) initiative in England provided a huge increase in the availability of cognitive-behavioural therapy (CBT) for the treatment of depression and anxiety in primary care. Counselling for Depression (CfD) – a form of person-centred experiential therapy (PCET) – has since been included as an IAPT-approved therapy but there is no evidence from randomised controlled trials determining its efficacy as required by the National Institute for Clinical and Social Excellence (NICE). Given the high demand for psychological therapies, there is a need for evidence of efficacy to ensure maximum practitioner resources are available to meet this need and to offer patients choice. We aimed to determine the clinical efficacy and cost-effectiveness of PCET compared with CBT in the treatment of moderate and severe depression within the English IAPT delivery service model.

Methods

We conducted a pragmatic, non-inferiority randomised controlled trial of PCET vs. CBT for patients ≥18 years of age who met criteria for either moderate or severe depression as determined by the Clinical Interview Schedule-Revised version. We excluded participants presenting with an organic condition, psychosis, drug or alcohol dependence, or elevated clinical risk. Randomisation was carried out independent of the research team. Ethical approval was granted by the Health Research Authority (REC: 14/YH/0001). The trial registration ID is ISRCTN06461651 and the research protocol has been published. 510 patients were randomised (1:1) to PCET or CBT and were seen by appropriately trained PCET counsellors and CBT therapists respectively in accordance with IAPT service delivery

model. The primary outcome was PHQ-9 score 6-months post-randomisation. We analysed all patients randomly allocated to treatment with complete data (modified intent to treat [mITT]) as well as those who received a minimum of 4 sessions and no more than 20 sessions (per protocol [PP]). We also carried out a Complier Average Causal Effect (CACE) analysis. The non-inferiority margin was set a priori at 2 PHQ-9 points. Patient safety was monitored throughout the course of therapy and adhered to service risk procedures for monitoring SAEs.

Findings

During 11th November 2014 and 3rd August 2018, 9898 patients were referred to Step 3 treatments in the Sheffield IAPT service for common mental health problems, of whom 761 (7.9%) were referred to the trial. Of these, we recruited 510 (67% of those referred) participants (F = 293 [57.45%]; M = 217 [42.55%]) meeting criteria for a diagnosis of moderate or severe depression with 254 (49.8%; F [138, 54.3%], M [116, 45·7%]) randomly assigned to PCET and 256 (50.2%; F [155, 60·5%], M [101, 39·5%]) to CBT. The mITT analysis included those participants who completed a PHQ-9 at 6 months post-randomisation and comprised 401 (78.6%; F = 233 [58·1%]; M = 168 [41·9%]) participants (201 [79.1%] in PCET and 200 [78.1%] in CBT) while the PP analysis comprised 298 (F = 169 [56·7%]; M = 129 [43·3%]) participants (154 PCET; 144 CBT). At 6-months post-randomisation, PCET was non-inferior to CBT (mITT: PCET 12.74 PHQ-9 points [SD = 6.54], CBT 13.25 PHQ-9 points [SD = 6.35], adjusted mean difference -0.35, 95% CI [-1.53 to 0.84]; PP: PCET 12.73 [SD = 6.57], CBT 12.71 [SD = 6.33], adjusted mean difference 0.27, 95% CI [-1.08 to 1.62]; CACE: adjusted difference -0.36, 95% CI [-1.64 to 0.92]). There were two (0.4%) serious adverse events (i.e., deaths), one in each treatment arm (one suicide, one due to COPD) occurring prior to the first therapy session and both assessed by the responsible clinician as

not trial-related. Four people made more than a single use of A&E for depression-related events (3 in PCET, 1 in CBT) and 6 people made single use (3 in PCET; 3 in CBT). There was a single hospitalization for a depression-related event occurring in PCET. Outcomes at 12 months did not support non-inferiority with gains favouring CBT, especially for more severely depressed participants.

Interpretation

This is the first RCT of the two most frequently administered psychological therapies in the English Improving Access to Psychological Therapies programme. The findings of no meaningful difference in clinical outcomes between PCET and CBT at 6-months and end of therapy support the outcomes from large routine non-randomised datasets from the IAPT programme. Given the high demand for psychological therapies and the need for patient choice, these findings suggest the need for continued investment in training and delivery of PCET for short-term outcomes but suggests that CBT leads to better outcomes for more severe patients at 12 months.

Research in context

Evidence before this study

The UK's National Institute for Health and Care Excellence (NICE) requires evidence from randomised controlled trials (RCTs) in order to inform and update its 2009 clinical guidelines for depression. Since 2007, the UK has implemented a national Improving Access to Psychological Therapies (IAPT) programme delivering cognitive-behavioural therapy (CBT) and person-centred experiential therapy (PCET) on a large scale for patients experiencing depression. We carried out a literature search using Scopus and Web of Science databases from 2007 to end of 2019 of RCTs comparing PCET (or any of its theoretical precursors) with CBT in the treatment of adult depression within the IAPT programme and found none. Analyses of large observational datasets from IAPT reported no difference between counselling and CBT but these data do not meet the criteria for consideration by NICE.

We sought evidence outside of the IAPT programme for meta- or network analyses of comparisons between person-centred experiential therapy (or its theoretical precursors) and CBT for the treatment of depression using search terms person-cent* experiential therapy/person-centred therapy/counsel*/emotion focused therapy (search dates from inception to end of 2019). Evidence from network meta-analyses, traditional pairwise meta-analyses as well as RCTs showed either no significant difference between supportive counselling and CBT or small advantages to CBT. But the form of supportive counselling in these comparisons do not reflect the model of counselling delivered in the English IAPT programme as it does not convey the more active format of PCET and there is some evidence based on small trials that outcomes for person-centred therapy are improved when enhanced with emotion focused components.

In the context of the English IAPT national programme being the largest social experiment in the psychological therapies, there is no trial evidence testing the efficacy of PCET as delivered by counsellors in receipt of the specified training, monitored for their adherence to the model, and compared with CBT for the treatment of moderate or severe depression even though PCET is the second most frequently delivered high-intensity modality after CBT within IAPT.

Added value of this study

The current study is the first substantive trial to directly test PCET vs. CBT in the IAPT programme. Based on the largest trial to date of person-centred experiential therapy, and using a stringent outcome criterion, findings support the non-inferiority of PCET as compared with CBT when evaluated using the primary outcome measure, the PHQ-9 at our primary assessment (i.e., 6 months post-randomisation). This result held regardless of the population analysis. However, at 12-months, there was evidence favouring CBT for people presenting with severe depression, suggesting that any differential effect may be the result of the passage of time and presenting severity. These findings, derived from an RCT embedded within the target service model (i.e., IAPT), add to existing evidence by being the first trial confirming the yield from practice-based publications and public reports published of IAPT data by NHS Digital and addresses scientific concerns about the potential confounding effects in such non-randomised observational datasets. It therefore underpins the value of utilising observational data from IAPT in support of effectiveness data derived from large datasets. But findings suggest a need to invest in implementing longer-term follow-up of patients to determine the robustness of shorter-term gains.

Implications of all the available evidence

At a policy level, the findings provide important data for updating the NICE clinical guideline for depression. At a clinical level, in light of the high demand for psychological therapies, and particularly within the English national IAPT service, the available evidence argues for appropriate resourcing and funding for the delivery of PCET to complement CBT and thereby provide both greater treatment capacity as well as treatment choice for patients in the short-term. But a national effort within IAPT to follow-up patients as standard practice would yield important data on the durability of patient gains.

Introduction

Cognitive behavioural therapy (CBT) has consistently been shown to be both efficacious and effective in the treatment of adult depression. [1,2] CBT's robust evidence base led to it being the first-choice intervention in the UK government's Improving Access to Psychological Therapies (IAPT) initiative, which rolled out a national programme of accessible psychological therapies primarily for depression and anxiety in England. [3] However, it has been argued that CBT has no clear superiority over other psychological therapies in the treatment of depression. [4]

On current evidence, the UK's National Institute for Health and Care Excellence (NICE) guideline for depression only recommends counselling (in its various forms) as a second-line treatment and only for mild and moderate depression. [5] These guidelines are currently being reviewed. This article reports on a large randomised controlled trial (RCT) to test whether an enhanced form of counselling is non-inferior to CBT in the treatment of moderate and severe depression at 6 months post-randomisation. We designed a pragmatic RCT nested within the IAPT programme, thereby embedding the trial in a fully functioning service delivery model. IAPT is the largest national experiment in the psychological therapies to be carried out to date, reporting 1·69m referrals in England between 2019 and 2020. [6]

IAPT is based on a stepped care model comprising Psychological Wellbeing Practitioners (PWPs) acting as gatekeepers at Step 2 (low-intensity) with both counsellors and CBT therapists delivering psychological therapies at Step 3 (high-intensity). A key component of both Steps is the mandated completion of outcome measures by all patients at each attended session.

Although CBT was initially the predominant therapy delivered in IAPT [7], additional approved therapy modalities were added including what was termed Counselling for

Depression (CfD). [8] CfD is a form of therapy delivered by trained counsellors and utilises process guiding components derived from emotion-focused therapy and involves the practitioner being more active in working with clients' emotions than is the case in classical person-centred therapy. [9] The evidence-base indicates that this more active component is an essential element in treating depression. [10] Because of confusion regarding the phrase 'counselling for depression', we refer to this model by its appropriate name of person-centred experiential therapy (PCET).

An early report of IAPT data [11] as well as subsequent published outputs using large practice-based data collected from routine IAPT services [12,13] and National Health Service (NHS) Digital reports of annual recovery rates [6], have consistently reported equivalent outcomes between these two modalities. However, non-randomisation of patients in such datasets leads to the possibility of confounding by indication. Further, it is not known if all counsellors are trained in PCET and deliver high quality treatment, hence the need for an RCT in which the delivery of PCET can be quality assured.

Given the increasing prevalence of depression, exacerbated by the Covid-19 pandemic, and the NHS Long Term Plan commitment to an additional 380,000 adults being able to access IAPT services by 2023/24, there is urgency in obtaining definitive evidence of the efficacy of PCET via a non-inferiority trial with CBT as the comparator. This evidence is crucial in supporting an enlarged workforce of appropriately trained practitioners providing patients with a choice of evidenced-based high-intensity therapies. While both therapy modalities are currently offered in 85% of IAPT services, [14] there is a differential resource in the provision of CBT and PCET, specifically for depression, as indicated by the patient referral count for 2018/19 showing 58.0% for CBT, 36.2% for PCET, and 5.9% for the remaining IAPT recommended therapies. [15]

We hypothesised PCET would not be inferior to CBT by a clinically meaningful difference based on our primary outcome measure, the PHQ-9 [16] at 6 months, our primary assessment point. A cost effectiveness analysis was undertaken. We also report secondary analyses comprising treatment outcomes comparable with IAPT national reporting, 12-month follow-up data, and the effect of severity on patient improvement rates between PCET and CBT.

Method

Study design and setting

The design comprised a pragmatic non-inferiority randomised controlled trial nested within the Sheffield IAPT service in the North of England that operated a combination of services based in local GP practices as well as centrally. The service covered a population of approximately 560,000 people and the area was the 7th most deprived English region (of 39), with 17.5% of neighbourhoods in the top decile of deprivation as measured by the Index of Multiple Deprivation (IMD).

Study participants

Patients aged 18 or over and attending the IAPT service were initially seen by a PWP. If their PHQ-9 score >12 and they confirmed that depression was their major concern, they were offered the opportunity to attend an assessment that would determine whether their depression was either moderate or severe. If so, together with having no strong preference for either treatment, they would be eligible for entry into the trial. If the assessment determined that they did not meet the criteria, either in terms of level of depression or as a primary diagnosis, then they would receive treatment in the IAPT service as normal. Participants were provided with information on the trial and the treatments and, on receipt of signed consent forms, were invited to a screening interview. Assessments were carried out either by trained research staff or clinical research nurses using the Clinical Interview Schedule-Revised [17].

We excluded participants presenting with an organic condition, psychosis, drug or alcohol dependence, or elevated clinical risk. If active thoughts of suicide were indicated from the CIS-R, a risk protocol was initiated. Alcohol or substance dependency were determined by specific questions from Section I (Alcohol) and Section II (Drug) of the Mini-International Neuropsychiatric Interview [18].

Trial participants were required to meet diagnostic criteria for either moderate or severe depression on the CIS-R and, if taking medication for depression to have been on a stable regime for the previous 6 weeks. Participants meeting the diagnostic criteria then completed additional baseline measures. For trial participants, the median of low-intensity sessions prior to high-intensity therapy was 1 session (Range: 0–8) for PCET (Mean 1·35 [1·03] sessions) and 1 session (Range: 0–9) for CBT (Mean 1·45 [1·24] sessions). Of those randomised to PCET, 16.1% had two or more low-intensity sessions with a mean (SD) number of sessions of 3.22 (1.54) while for CBT the percentage was 18.0% with a mean (SD) number of sessions of 3.54 (1.79). The median for both arms was 3 sessions. All low-intensity interventions preceded the baseline assessment.

Ethical approval was granted by the Health Research Authority (REC: 14/YH/0001). Registration ID for PRaCTICED is ISRCTN06461651 and the protocol has been published. [19]. The original protocol version can be found in the Appendix pp. 27-63.

Randomisation and masking

Participants were centrally randomised (1:1) to PCET or CBT using a remote, web-based system which revealed therapy after the patient details were entered. Randomisation was stratified by site using permuted blocks of random size 2, 4 or 6. We blinded assessors to treatment allocation.

Procedures

The level of professional training for trial CBT therapists and PCET counsellors was similar in that they all met the standards of their respective professional body and were eligible to be IAPT high-intensity practitioners.

Four counsellors were already trained in PCET and we sought to train all remaining counsellors in the service (n = 25; Appendix p.1) regardless of the specific format of humanistic counselling practiced and subsequently assessed them for adherence to the new model by expert trainers using the 10-item Person-Centred Experiential Psychotherapy Scale (PCEPS). [20] Only counsellors who successfully completed the training and passed their 4 rated tapes were eligible to take part in the trial. All were also required to be accredited to a recognised professional body. A total of 18 counsellors met these criteria during the trial. We developed a treatment manual for PCET (Available from the lead author). [21]

CBT comprised the comparator intervention and all therapists in the service had received the IAPT approved training and were accredited by the British Association for Behavioural and Cognitive Psychotherapy. The modality was defined as Beckian CBT and participating therapists received refresher training (Appendix p.1). A total of 32 CBT therapists participated, comprising approximately 60% of the local IAPT CBT workforce. We developed a treatment manual for CBT (Available from the lead author). [22] The maximum number of sessions for both modalities was 20, in line with NICE depression guidelines. [5]

As the trial therapies were embedded in the routine IAPT service, participants started their randomly allocated treatment when the next appropriate PCET-trained counsellor or CBT therapist had availability in line with standard procedures. The mean (SD) waiting time between screening and first treatment session was 12.2 (7.4) weeks for PCET and 13.4 (8.8) weeks for CBT. The overall change in PHQ-9 points from randomisation to 1st session was -1.74 and the change for each therapy (PCET = -1.36; CBT = -2.11) was not significantly different ($t = 1.577$, $p = 0.115$). Ethical requirements deemed that inclusion in the trial

bestowed no advantage or disadvantage in terms of access to the service. Once participants were in receipt of therapy, treatment progressed similarly to the routine IAPT service with the exception that sessions were digitally-recorded.

Trial counsellors and CBT therapists received a combination of regular individual and group supervision that was standard within the particular IAPT service but was less frequent than stated in the IAPT manual (for details, see Appendix p.2). We assessed treatments as delivered using adherence scales designed specifically for each modality: for PCET we used the 10-item PCEPS [20] and for CBT the 12-item Cognitive Therapy Scale-Revised (CTS-R). [23] Ratings were carried out by experienced national trainers in each of the two modalities (Appendix p.2). A score of 40/60 is considered a pass mark on the PCEPS and 36/72 on the CTS-R.

Outcomes

The primary outcome measure was the PHQ-9 [16] at 6-months post randomisation. IAPT services are mandated to meet waiting time targets of 75% of patients being entered into treatment within 6 weeks and 95% within 18 weeks. [24] Given the national average treatment duration of 6-7 sessions, we reasoned that 6-months post randomisation was an appropriate time frame to assess efficacy. Secondary outcomes were scores at 6-months post-randomisation on the Beck Depression Inventory-II (BDI-II) [25], Clinical Outcomes in Routine Evaluation-Outcome Measure (CORE-OM) [26], Generalised Anxiety Disorder-7 (GAD-7) [27], Work and Social Adjustment Scale (WSAS) [28], and EQ-5D-5L including the Visual Analogue Scale (EQ-VAS) [29]. Satisfaction with treatment was collected via the Client Satisfaction Questionnaire (CSQ) [30]. An adapted form of the Patient Service Receipt Inventory was used to collect service use. [31] All outcome measures were repeated at 12-month follow-up post-randomisation. Where participants did not return trial measures, their PHQ-9, GAD-7, and WSAS scores collected by the service at the session closest to the 6-and 12-month dates were

used. All serious adverse events were recorded and reviewed by the Data Management and Ethics Committee (DMEC).

Power and sample size

We determined the margins of non-inferiority based on the recommendation that the threshold for non-inferiority be set at 50% or less than the expected difference between CBT and usual care. Based on service data, this yielded an effect size of less than 0·3. Discussions with personnel, including IAPT staff, indicated that less than 2 points on the PHQ-9 is not perceived as clinically important, which is equivalent to an effect size of just under 0·3 given the pre-post SD of 6·9 found in the local service data. Therefore, we accepted non-inferiority of PCET to CBT if the two-sided 95% confidence interval (CI) for the adjusted mean difference between treatments did not include a 2-point difference in favour of CBT.

The trial was designed to recruit 550 participants to secure 500 patients needed to test the non-inferiority hypothesis at the one-sided 2·5% significance level with a power of 90%. This assumes a standard deviation of 6·9 (derived from the aforementioned service use data, which incorporate both inter-patient and inter-therapist variability), no underlying difference between the effect of CBT and PCET, and a 10% loss to 6-month follow-up.

We carried out statistical analyses as specified in a previously written Statistical Analysis Plan (SAP) approved by both the Trial Steering Committee and the DMEC. We compared primary and secondary outcomes at 6-months post-randomisation using mixed effects models with baseline score, depression severity diagnosis and treatment arm as covariates and with therapist as a random intercept. The interclass correlation coefficient (ICC) was derived directly from the ratio of variances in the mixed model. Analyses were repeated at 12-months follow-up post-randomisation as secondary outcomes.

As per our SAP and published protocol, our primary analysis was an intention-to-treat, termed here as modified intention-to-treat (mITT), carried out on all cases who had been randomised and who completed the primary outcome measure at 6 months. We carried out a mITT analysis both on all complete cases and also used multiple imputations by chained equations (MICE) to account for missing data in the primary outcome. Missing outcome data were imputed in 100 replicates separately by randomised treatment group based on treatment region, therapist ID, baseline measures (CIS-R, GAD-7, BDI-II and WSAS) together with PHQ-9 at 6 and 12 months where available. Sensitivity analyses (not presented) were undertaken in which imputations were performed separately by treatment group to further assess the robustness. 100 burn in iterations were used and convergence assessed visually with trace plots.

In keeping with guidance on the analysis and reporting of non-inferiority trials, [32-34] we also carried out a secondary per protocol (PP) analysis. This was defined as those participants who received at least 4 sessions, shown to be the minimally acceptable dose of treatment. [35] The maximum was 20 sessions of their respective treatments as randomised at 6 and 12 months. In addition, we carried out a two-stage least squares complier average causal effects (CACE) analysis [36-38], a modification of PP analysis as a sensitivity analysis to the PP method. The CACE analysis attempted to model the difference between groups in the scenario where participants who adhered to CBT had received and adhered to PCET instead.

We also report rates of treatment response and remission and outcomes from a subgroup analysis of depression severity level, as classified by CIS-R at screening, as secondary outcomes. For direct comparisons with IAPT reports we also compared outcomes using standard IAPT procedures utilising the PHQ-9 and GAD-7 measures at the end of therapy (discharge from the service). Adverse effects and deterioration rates [39] are reported for the two treatment modalities at 6-month and 12-month follow-up.

The economic evaluation adopted a cost perspective of the NHS and social care and was limited to the 12-month trial period (for full account see Appendix pp. 3-4) and depression or mental health related service and other resource use costs from secondary care, general practitioner visits, other community care and medication were included (Appendix pp.5-6). Quality-Adjusted Life Years (QALYs) were derived from the EQ-5D-5L collected at baseline, 6 and 12 months [40]. An incremental analysis was undertaken to produce an incremental cost-effectiveness ratio (ICER) with the main analysis based on the mITT sample. The estimated ICERs were compared with the NICE cost-effectiveness threshold of £20,000 to £30,000 per QALY. [41] Narrower costs were considered in the secondary analyses. Uncertainty around the estimates from the seemingly unrelated regressions were used to generate cost-effectiveness acceptability curve (CEAC) and confidence ellipses. [42]

Analyses of the primary clinical and cost-effectiveness data were carried out by researchers outside the main research group. Treatment modalities were randomly labelled A and B to mask their identity. For the clinical analyses, treatments were only revealed once the primary analyses had been completed.

Changes to protocol

A list of amendments to the protocol after the trial start date can be found in the Appendix pp. 64-65. All amendments were approved by NHS ethics and were related to either enhancing patient recruitment or the addition of other measures to underpin related research.

Role of the funding source

The trial was designed in response to a national call from the funder to determine the efficacy of PCET compared with CBT. Beyond this, the funder had no role in the design, implementation, or analysis of the trial.

Results

During the recruitment period of the trial, 11th November 2014 to 3rd August 2018, 9898 patients were referred to Step 3 treatments in the IAPT service for common mental health problems, of whom 761 (7·9%) were referred to the trial. Towards the end of recruitment, the establishment of an IAPT long-term physical health conditions service drew a significant portion of CBT staff away from the sector that was the highest referrer to the trial, and patient recruitment slowed significantly such that recruitment ceased with the approval of the Trial Steering Committee at 510 participants, which accounted for 67% of those referred to the trial with 254 (49·8%; F [138, 54.3%], M [116, 45·7%]) randomly assigned to PCET and 256 (50·2%; F [155, 60·5%], M [101, 39·5%]) to CBT (Figure 1).

Data at baseline showed the two arms to be broadly equivalent although PCET comprised slightly more men (116 [45·7%] vs. 101 [39·5%]). More than half of participants in each arm met criteria for severe depression (PCET: 138 [54·3%]; CBT: 132 [51·6%]) and 86·7% (F: 255 [57·7%]; M: 187 [42·3%]) of participants scored either moderately severe (≥ 15) or severe (≥ 20) on the PHQ-9. Demographics and diagnoses are presented in Table 1.

Eighteen counsellors delivered PCET, of whom 16 (89%) were female and 2 (11%) were male aged, based on 10-year age categories, on average between 50–59. Their theoretical orientation prior to PCET training was varied but fell within a broad category of humanistic orientation. They had on average 4·5 years post training in PCET. Counsellors had a mean of 16·6 years (SD: 5·79, range 7–29) professional practice, while in their current role the mean (SD) was 9·6 (SD: 5·46, range 2-19) years. The median trial participants per counsellor was 8 (IQR = 2 to 12). Thirty-two CBT therapists delivered Beckian CBT, of whom 25 (78%) were female and 7 (22%) were male and aged on average between 30–39. CBT therapists had an average of 8·1(SD: 3·42, range 2–19) years professional practice, with 7·6 (SD: 2·85, range 2-11) years in their current role. The median participants per CBT therapist was 5 (IQR = 2 to

9). The mean item totals for sampled adherence ratings for PCET and CBT sessions were 39·4/60 and 40·9/72 respectively.

The primary analysis (mITT) included those participants who completed a PHQ-9 at 6 months post-randomisation. The sample comprised 401 (78·6%) participants: 201 (79·1%) in PCET and 200 (78·1%) in CBT. The mean (SD) change for PCET was 6·08 (6·12) points, while for CBT it was 5·89 (6·60). Non-inferiority of PCET was supported in the complete case analysis with an estimated mean difference of -0.35 points (95% CI -1·53, 0·84), with similar results found for the CACE -0.36 (-1.64 to 0.92) and mITT MICE -0·60 (-2·19 to 1·02). The PP analysis found non-significant mean differences in favour of CBT but non-inferiority of PCET was supported: PP 0·27, 95% CI (-1·08, 1·62); PP MICE analysis 0·40 (-0·99 to 1·79) (Table 2; Appendix p.7). The ICC for therapists was 0·002 (95% CI 0·0, 0·28) and model assumptions were assessed by visual inspection of residual plots. Cohen's *d* effect sizes at 6-months were not significant in the mITT analysis, -0·03 (95% CI -0·23, 0·17), nor in the PP analysis, 0·09 (95% CI -0·32, 0·14) (negative effects favour PCET).

The mITT analysis of secondary measures at 6 months found differences in favour of PCET on all measures but none was statistically significant. These differences (95% CI) were: BDI-II -0·48 (-3·72 to 2·76); CORE-OM -0·16 (-1·89 to 1·56); WSAS -0·82 (-2·88 to 1·23); GAD-7 -0·47 (-1·47 to 0·52), and EQ5-VAS (where higher scores indicate a better outcome), 2·54 (-2·39 to 7·47) points (Table 3). The PP analysis of secondary measures at 6 months did not show any significant difference between treatments although all between-group differences favoured CBT (Appendix p.8).

At 12 months, the mITT analysis showed a significant between group difference (1·73) for PHQ-9 in favour of CBT, with a 95% CI (0·26 to 3·19) which exceeded the 2·0-point superiority of CBT at its upper limit, a finding supported by the PP analysis: 2·05, (0·49 to 3·62) (Appendix p.8). All of the other mITT secondary measures except EQ-VAS showed

greater improvement for CBT, but no mean difference was statistically significant: BDI-II 2·01 (-1·24 to 5·27); CORE-OM 1·25 (-0·56 to 3·06); WSAS 1·75 (-0·55 to 4·06); GAD-7 0·44 (-0·96 to 1·84) and EQ-VAS 1·67 (-3·37 to 6·71) (Table3). In the PP analysis, differences were significant in favour of CBT for all secondary measures except EQ-VAS. Cohen's *d* effect sizes for PHQ-9 at 12-months were: 0·27 (95% CI 0·05, 0·49) and 0·34 (95% CI 0·09, 0·60) for mITT and PP analyses respectively with both significant and favouring CBT.

Subgroup analysis of depression severity level at baseline (moderate or severe) indicated no significant differences between treatments apart from the PP sample analysis at 12 months which showed a significant difference in favour of CBT (Appendix p.9). Similarly, depression recovery and response rates significantly favoured CBT in the 12-month PP analysis (Appendix pp.10-11). Further subgroup analysis indicated that this significant difference was for severe patients only (Appendix pp.12-13).

Comparisons with the national reporting of IAPT services were calculated using the combination of both PHQ-9 and GAD-7 and the last treatment session scores provided by the service, to determine rates of reliable recovery, recovery, reliable improvement, and reliable deterioration at the end of treatment. No significant differences were found on any of the rates (Appendix p.14).

There were two (0·4%) serious adverse events (i.e., deaths), one in each treatment arm (one suicide, one due to COPD). They occurred between screening and first therapy session and both were assessed by the responsible clinician for the trial as not being due to the trial. In terms of use of A&E for depression-related events, 4 people made more than a single use (3 in PCET, 1 in CBT) and 6 people made single use (3 in PCET; 3 in CBT). There was a single hospitalization for a depression-related event occurring in PCET. In response to the question, 'In the past week I made plans to end my life', extracted from the CORE-OM, 6 people at 6-

months scored ‘often’ or ‘most or all the time’ (4 in PCET; 2 in CBT), and at 12-months a total of 4 people (2 in PCET; 2 in CBT). Adopting a criterion of reliable deterioration [39], a total of 12 participants at 6-months (4 in PCET; 8 in CBT) and 7 at 12-months (6 PCET, 1 CBT) met this criterion compared with their baseline PHQ-9 score.

Treatment satisfaction was similar for participants at 6 months (PCET: Mean CSQ-8 score 21·48 [5·38]; CBT: Mean CSQ-8 score 20·38 [5·92]) and 12 months (PCET: Mean CSQ-8 score 24·16 [6·50]; Mean CSQ-8 score 23·92 [6·94]). The percentages of participants recorded as taking medication for depression or anxiety at each assessment were also similar – baseline: 56% (PCET), 60% (CBT); 6-months: 31% (PCET), 32% (CBT); and 12-months: 17% (PCET), 15% (CBT).

The main cost-effectiveness analysis showed a significant difference in the mean intervention costs with PCET significantly cheaper (-£66·99, $p = 0·001$) (Appendix p.15). However, no significant differences were observed in total costs (hospital, GP service, social care, and medication). The mean difference in QALYs favoured PCET (0.008, $p = 0.623$) and the higher incremental costs for PCET (15·07, $p = 0.760$) generated an ICER of £1828 (Table 4; Figure 2). The probability of PCET being cost-effective compared with CBT was 68% (Appendix p. 16) rising to 78% when secondary care costs were excluded (Table 4; Appendix pp.17-18). (Further sensitivity analyses are presented in Appendix pp. 19-23).

Discussion

In this large, pragmatic trial we found PCET to be cost-effective and yield similar outcomes to CBT at 6-months post-randomisation as determined by our pre-specified non-inferiority threshold for PHQ-9. This finding was in the context of both PCET and CBT being supported by similar training resources, delivered at similar average levels of fidelity, to a standard that yielded no therapist effects, and no differences in treatment satisfaction or medication use

between participants in the two modalities. Other outcomes at 6-months were similar between the two treatment arms. In terms of general effectiveness, while the actual PHQ-9 scores at 6 months appear modest, given the relative severity of the trial sample compared with other Step 3 IAPT studies, [43] the rate of improvement (approximately 6 PHQ-9 points) is comparable with the average rates reported from the IAPT national data base [15]. In this context, we found no evidence of any significant differences between the two therapy modalities in any analyses at either 6 months or end of treatment.

To our knowledge, the study is the only trial comparing the two major Step 3 high-intensity therapies as delivered within the IAPT programme and is therefore important in terms of validating the yield from national routine IAPT data and provision of results for NICE. Overall, results are consistent with recent analyses of large IAPT datasets where no meaningful differences were found between CBT and counselling at the end of therapy [12,13].

However, at 12-months, non-inferiority was not supported and CBT showed a small additional benefit over PCET, in particular for more severe levels of depression when participants received at least 4 therapy sessions. This specific advantage to CBT at follow-up may appear small but, when delivered at scale in a national delivery programme such as IAPT, has the potential for benefiting a significant group of patients. This finding appears to be a function of time and severity and warrants further investigation in large IAPT datasets and has potential implications for better matching of patients to these specific treatments.

Results from the economic analyses showed no significant differences in mean total costs and mean QALYs between the treatment groups at 12 months. The narrower the perspective adopted, the more PCET was likely to be cost-effective compared with CBT, mainly accounted for by the intervention costs attributable to PCET itself being significantly less than for CBT.

In terms of strengths and limitations, the results were similar for modified intention-to-treat, per-protocol and CACE analyses. Since mITT can underestimate the causal effects in the presence of non-uptake, and the per-protocol subgroup is a non-randomised comparison which can lead to bias in either direction [32,33], the consistency in these findings is an important strength. The findings were also robust to different approaches to handling missing outcome data, and were further supported by secondary outcomes including depression-specific (BDI-II), generic psychological distress (i.e., CORE-OM), and everyday functioning (i.e., WSAS) measures. Although large, we acknowledge the trial fell short of the desired target size. However, it retained sufficient power to produce 95% confidence intervals that demonstrated non-inferiority in the primary outcome.

The delay from randomisation to session 1 was, on average, longer than expected in IAPT services and there were small improvements in both treatment arms during this waiting time, However, the scores at session 1 still exceeded the respective PHQ-9 scores for each therapy as reported in IAPT national data [15]. And this delay may have contributed to the decision of some participants not to attend any therapy sessions. But whether specific to IAPT or not, that one-fifth of patients assessed at intake with moderate or severe depression did not attend any therapy sessions warrants further investigation to address potential barriers to engagement in therapy. And for participants attending therapy, we note that the regime for therapy supervision for both treatments was less frequent than stipulated in the IAPT manual and this may have impacted on the absolute level or speed of patient improvement or both. Contextually, the results are set within the English IAPT national programme and may not generalise to other delivery models although, given the international interest in the programme, the findings have wider applications.

In the context of no overall difference in cost-effectiveness and the relative severity of the trial sample compared with the extant IAPT literature, the results from our primary analysis

provide support for the effectiveness and broad equivalence of PCET compared with CBT in the short-term. The results therefore endorse findings derived from large non-randomised and routinely-collected data drawn from the English IAPT national programme where patients are not randomised and the quality of the treatment provided is not evidenced by empirical data. However, the results are qualified by the additional gains made at one year by participants in receipt of more than a minimal dose of CBT when presenting with severe depression. Taking a balanced view, in light of the increasing high demand for psychological services and importance of patient choice, a focus on appropriate levels of investment in the delivery of PCET within the national IAPT programme is needed in order to be able to provide sufficient capacity at Step 3. Clinically, however, attention should focus in PCET on strategies to enable patients in the longer term to sustain or enhance gains made in the course of therapy.

Overall, these results show that broadly similar outcomes in the short-term are not a result of potentially confounding factors. Future attention should turn to developing and implementing systematic follow-up of patients to provide robust evidence of the longer-term benefits of both PCET and CBT within the English IAPT national programme with the aim of developing evidence-based allocation of patients to these therapy modalities.

Supplementary material

See accompanying file

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Contributors

MBa was chief investigator and oversaw all aspects of the trial and, with DS, designed the trial, wrote the protocol and the manuscript together with coordinating revisions; GEH, PB,

MK, RE, MBr, SS, LG, SK, GW, and JB contributed to the design of the trial; TW was the principal investigator for the clinical service; MBr and DG conducted the statistical analyses of clinical data; NW and ADK conducted the cost-effectiveness analyses; MBa, DS, GEH, KA, LB-E, KAr, JC, PH, and SO were responsible for the conduct of the trial; DS was responsible for data management and MBr for the Statistical Analysis Plan; SK and RE contributed to the development of the treatment training manuals. MBr and DS accessed and verified the data. All contributors read, commented on, and approved the final manuscript.

Declaration of interests

MBa is on the Editorial Board of the journal published by BACP for which he is entitled to an honorarium and has previously been an unpaid member of the BACP Research Committee and Scientific Committee and received travel expenses. He was the PI on grants (1995-97) from the Mental Health Foundation to fund the development of the CORE-OM. DS has received funding from BACP to analyse routine IAPT datasets. Gillian Hardy is Director of a Clinical Psychology Unit that hosts training programmes for IAPT low- and high-intensity practitioners. PB has conducted consultancy for BACP (but not in the last 5 years) and currently sits on committees for NICE and IAPT. MK has previously been an unpaid member of the BACP Scientific Board. RE writes about, practices and delivers supervision and training on PCET and Emotion-Focused Therapy, of which he is one of the founders and receives royalties on published texts. LG is a past Chair of BACP and hosts a national training programme in PCET. SK is an IAPT Programme Director delivering training in CBT to IAPT trainees. TW is clinical director in Sheffield Health and Social Care NHS Foundation Trust and head of the Sheffield IAPT service and has previously been a NICE panel member for on-line IAPT programmes. She also contributed to the national manual for IAPT. GW receives royalties on CBT books and served on a NICE committee relating to

eating disorders. SP is in receipt of funding from NICE for the development of clinical guidelines. All other authors declare no conflict of interests.

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Data sharing

Individual participant data that underlie the results reported in this article will be made available after de-identification beginning 9 months and ending 3 years following article publication to researchers who provide a methodologically sound proposal that includes a protocol and statistical analysis plan and is not in conflict with our documented publication plan and consistent with our data sharing policy. Proposals should be directed to m.barkham@sheffield.ac.uk. To gain access, data requestors will need to sign a data access agreement.

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Table 1 Participant descriptives for person-centred experiential therapy, cognitive behavioural therapy, and combined samples

	Person-centred experiential therapy (n = 254)	Cognitive behavioural therapy (n = 256)	Combined (n = 510)
Age			
n	254	256	510
Mean (SD)	39·42 (13·32)	36·91 (12·74)	38·16 (13·08)
Median (IQR)	37·50 (28·00–50·00)	35·00 (27·00–47·00)	36·50 (27·00–48·75)
Min, Max	18, 79	17, 72	17, 79
Sex			
n	254	256	510
Female (%)	138 (54·33)	155 (60·55)	293 (57·45)
Male (%)	116 (45·67)	101 (39·45)	217 (42·55)
Ethnicity			
n	254	256	510
White (%)	225 (88·58)	226 (88·28)	451 (88·43)
Other (%)	16 (6·30)	17 (6·64)	33 (6·47)
Missing (%)	13 (5·12)	13 (5·08)	26 (5·10)
IMD Decile			
n	253	256	509
Mean (SD)	5·20 (3·33)	5·20 (3·25)	5·20 (3·29)
Median (IQR)	5·00 (2·00–8·00)	5·00 (2·00–8·00)	5·00 (2·00–8·00)
Min, Max	1, 10	1, 10	1, 10
Employment Status			
n	217	221	438
Employed (%)	135 (62·21)	131 (59·28)	266 (60·73)
Unemployed (%)	63 (29·03)	61 (27·60)	124 (28·31)
Unpaid voluntary work (%)	1 (0·46)	0 (0·00)	1 (0·23)
In education (%)	14 (6·45)	20 (9·05)	34 (7·76)
Retired (%0	4 (1·84)	9 (4·07)	13 (2·97)
CIS-R Score			
n	254	256	510
Mean (SD)	32·50 (8·21)	31·44 (8·09)	31·96 (8·16)
Median (IQR)	32·00 (27·00–38·00)	31·00 (26·00–36·00)	32·00 (26·00–38·00)
Min, Max	14, 54	12, 55	12, 55
CIS-R Depression Level Code			
n	254	256	510
Moderate (%)	116 (45·67)	124 (48·44)	240 (47·06)
Severe (%)	138 (54·33)	132 (51·56)	270 (52·94)
CIS-R Secondary Diagnosis			
n	254	256	510
Agoraphobia (%)	7 (2·76)	5 (1·95)	12 (2·35)
Generalised Anxiety Disorder (%)	154 (60·63)	167 (65·23)	321 (62·94)
Mixed Anxiety and Depression (%)	57 (22·44)	61 (23·83)	118 (23·14)
Panic Disorder (%)	18 (7·09)	10 (3·91)	28 (5·49)
Specific Phobia (%)	10 (3·94)	6 (2·34)	16 (3·14)
Social Phobia (%)	8 (3·15)	7 (2·73)	15 (2·94)

Note: SD = standard deviation; IQR = interquartile range; IMD = Index of multiple deprivation; CIS-R = Clinical Interview Schedule-Revised

Table 2: Primary assessment point at 6-months for mITT, PP, and CACE analyses

	6-months		Observed data only	Observed and imputed data (MICE): Including therapist
	PCET **M (SD)** **n**	**CBT** **M (SD)** **n**	**Adjusted between-group difference (95% CI)**	**Adjusted between-group difference (95% CI)**
Baseline	19·03 (4·12) 254	18·80 (4·09) 256		
mITT	12·74 (6·54) 201	13·25 (6·35) 200	-0·35 (-1·53 to 0·84)	-0·60 (-2·19 to 1·02)
PP	12·73 (6·57) 154	12·71 (6·33) 144	0·27 (-1·08 to 1·62)	0·40 (-0·99 to 1·79)
CACE: (Receipt of PCET)	12·68 176	13·04 180	-0·36 (-1·64 to 0·92)	

Adjusted between group differences with 95% confidence intervals were derived from a comparison of mean outcome scores at 6-months post-randomisation using mixed effects models with baseline score, depression severity diagnosis and treatment arm as covariates and with therapist as a random intercept.
PCET = Person-centred experiential therapy; CBT = Cognitive behavioural therapy; MICE= multiple imputations by chained equations: missing outcome data were imputed in 100 replicates separately by randomised treatment group based on treatment centre, therapist ID, baseline measures and PHQ-9 at 6 and 12 months where available; mITT = Modified intent-to-Treat analysis: includes all participants that completed a PHQ-9 at 6 months, comparison groups are as randomised; PP = Per Protocol analysis: participants who had not received between 4-20 sessions of their randomised treatment were excluded; CACE = Complier Average Causal Effects analysis: a sensitivity analysis to the PP method, modelling the difference between groups in the scenario where participants who adhered to CBT had received and adhered to PCET instead, estimated marginal mean scores are reported.

Table 3: mITT results for secondary outcomes at 6 months and 12 months

	PCET	CBT	Observed data only
	M (SD): n	M (SD): n	Adjusted between-group difference (95% CI)
6 months			
BDI-II Baseline mITT:	37·04 (9·18): 254 27·26 (13·95): 117	36·39 (8·06): 256 27·71 (13·52): 109	-0·48 (-3·72 to 2·76)
CORE-OM Baseline mITT:	22·56 (4·91): 253 16·96 (7·46): 117	22·27 (4·25): 255 17·11 (7·15): 114	-0·16 (-1·89 to 1·56)
WSAS Baseline mITT:	25·67 (7·60): 252 19·58 (9·79): 180	25·08 (7·31): 256 19·38 (10·06): 180	-0·82 (-2·88 to 1·23)
GAD-7 Baseline mITT:	13·80 (4·44): 254 9·99 (5·79): 183	12·84 (4·30): 256 10·46 (5·41): 186	-0·47 (-1·47 to 0·52)
EQ-VAS[1] Baseline mITT:	37·74 (16·71): 252 50·21 (19·36): 121	37·70 (15·30): 256 47·51 (20·65): 114	2·54 (-2·39 to 7·47)
12 months			
PHQ-9 Baseline mITT:	19·03 (4·12): 254 12·57 (7·48): 167	18·80 (4·09): 256 10·95 (6·58): 152	1·73 (0·26 to 3·19)
BDI-II Baseline mITT:	37·04 (9·18); 254 23·37 (14·79); 131	36·39 (8·06); 256 21·87 (13·50); 122	2·01 (-1·24 to 5·27)
CORE-OM Baseline m ITT:	22·56 (4·91); 253 15·65 (8·29); 133	22·27 (5·47);255 14·80 (7·76); 124	1·25 (-0·56 to 3·06)
WSAS Baseline mITT:	25·67 (7·60); 252 18·16 (10·71); 147	25·08 (7·31); 256 16·30 (11·22); 141	1·75 (-0·55 to 4·06)
GAD-7 Baseline mITT:	13·80 (4·44); 254 9·17 (6·10); 151	12·84 (4·30); 256 8·41 (5·78); 142	0·44 (-0·96 to 1·84)
EQ-VAS[1] Baseline mITT	37·74 (16·71);252 55·55 (21·75); 136	37·70 (15·30); 256 53·57 (22·94); 127	1·67 (-3·37 to 6·71)

BDI-II: Beck Depression Inventory; CORE-OM: Clinical Outcomes in Routine Evaluation-Outcome Measure; WSAS: Work and Social Adjustment Scale; GAD-7: Generalised Anxiety Disorder scale; EQ-VAS: Euroqol-5D-5L Visual Analogue Scale; PHQ-9: Patient Health Questionnaire. mITT = Modified intent-to-treat analysis: includes all participants that completed measures at 6 months and 12 months, comparison groups are as randomised. Adjusted between group differences with 95% confidence intervals were derived from a

comparison of mean outcome scores at 6-months and 12-months post-randomisation using mixed effects models with baseline score for each measure, depression severity diagnosis and treatment arm as covariates and with therapist as a random intercept.

[1] Higher EQ-VAS scores indicate a better outcome, therefore positive adjusted between-group differences favour PCET

Table 4: Cost-utility results for PCET vs. CBT at 12-months for mITT sample with imputed data and complete data sample

Analysis	Total costs £		QALYs		Incremental cost [£]: PCET–CBT (95% CI); p value	Incremental QALYs [1]: PCET–CBT (95% CI); p value	ICER £ per QALY gained	Probability that PCET is cost effective at the threshold £20,000/QALY)
	PCET Mean (SE); n	CBT Mean (SE); n	PCET Mean (SE); n	CBT Mean (SE); n				
Main analysis: mITT sample with imputation of missing data	512·46 (41·61); 254	497·39 (27·23); 256	.608 (.015); 254	.592 (.016); 256	15·07 (-81·74 to 111·87) 0·760	.008 (-.025 to .041) 0.623	£1828.24	68%
mITT Complete data sample	642.55 (517.04) 100	676.53 (465.59) 91	.604 (.214) 100	.609 (.240) 91	-33.98 (-173.29 to 105.33); 0.633	-.002 (-.045 to .040); 0.921	£15846.72	50%
mITT sample with imputation of missing data excluding hospital attendance & admission data	453.22 (22.07); 254	493.53 (28.13); 256	.608 (.016); 254	.589 (.016); 256	-40.31 (-110.69 to 30.08); 0.261	.011 (-.025 to .048); 0.533	£-3517.69	78%
mITT sample with imputation of missing data with same intervention costs in both groups (£53 per session)	502.62 (23.69); 254	493.53 (28.13); 256	.608 (.016); 254	.589 (.016); 256	9.08 (-63.26 to 81.43); 0.805	.011 (-.025 to .048); 0.533	£792.83	71%

Note: CBT = cognitive behavioural therapy. PCET= person-centred experiential therapy, mITT – Modified intent-to-Treat; QALYs = quality-adjusted life-years, ICER = Incremental cost effectiveness ratio.

1. Incremental QALY difference is adjusted for baseline utilities

Figure 1: CONSORT diagram for PRaCTICED Trial

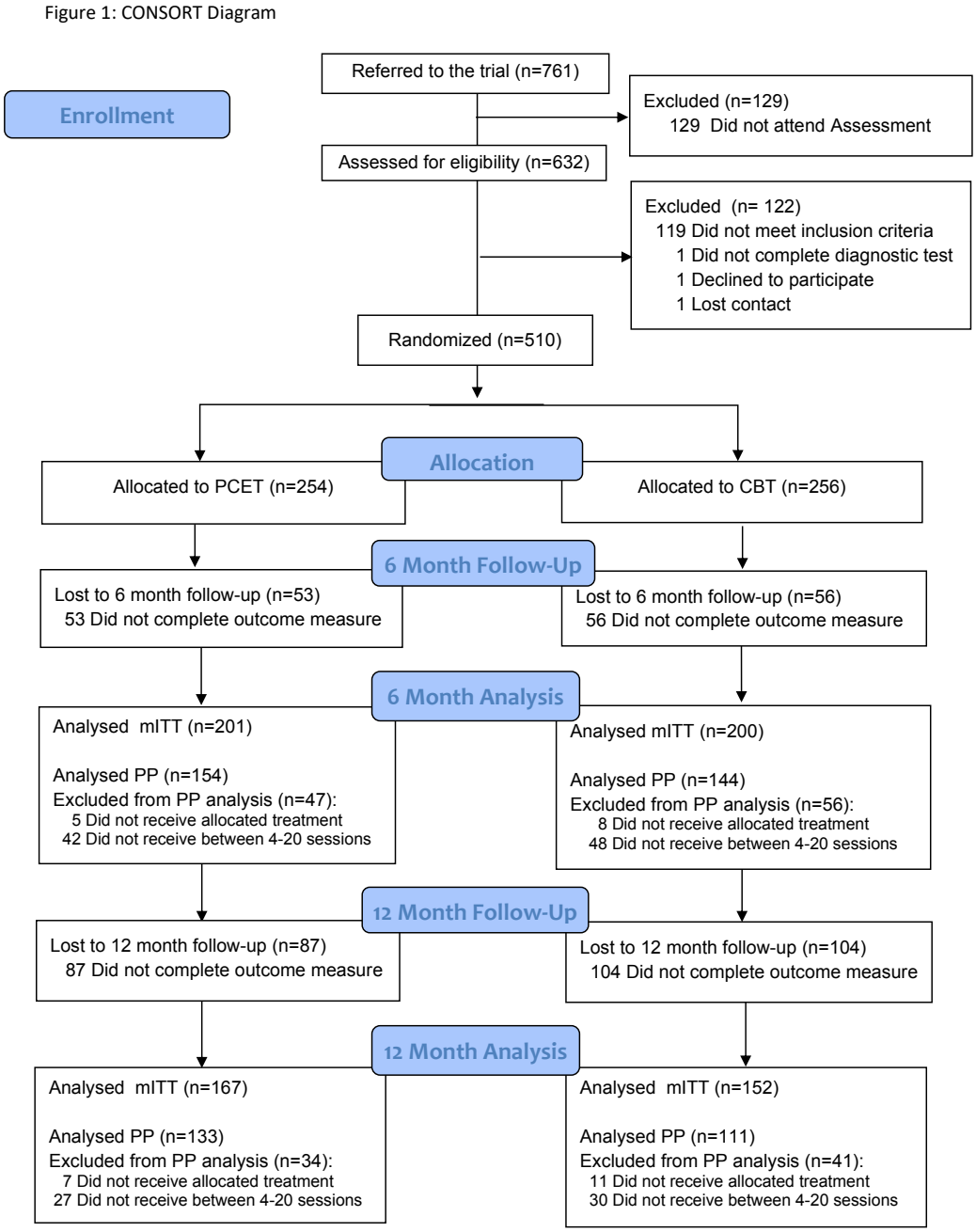

Figure 2: Confidence ellipses for person-centred experiential therapy (mITT sample with imputations)