Appendix

PCET counsellor training & CBT therapist refresher training

PCET training

PCET training comprised five intensive days conducted in April and May 2013 by national experts, structured as three initial days followed by two further days training three weeks later, a two-day workshop on the PCET model, and a pre-publication copy of a key text.

Sanders, P. & Hill, A. (2014). *Counselling for depression: A person-centred and experiential approach to practice*. SAGE publications.

In addition, counsellors also attended a full day workshop on emotion focused therapy (EFT) implemented in December 2013 at the service base and led by Robert Elliott.

See: Nye, A., Connell, J., Haake, R., & Barkham, M. (2019) Person-centred experiential therapy (PCET) training within a UK NHS IAPT service: experiences of selected counsellors in the PRaCTICED trial, *British Journal of Guidance & Counselling, 47*(5), 619-634, http://doi/.org10.1080/03069885.2018.1544608

Completion of the training required a total of 80 hours supervised client contact working in the model and meeting a pass mark on four tapes (from a maximum of 6) assessed for adherence by the expert trainers using the 10-item Person-Centred Experiential Psychotherapy Scale (PCEPS). Only counsellors who successfully completed the training and passed their 4 rated tapes were eligible. All PCET counsellors were also required to be accredited to a recognised professional body.

CBT refresher

CBT comprised the comparator intervention in the trial and the modality was defined as Beckian CBT and all trial therapists delivering CBT took part in a 3-day training delivered by national experts focusing specifically on this model. Therapists had access to a standard text: Beck, J. (2011). *Cognitive behavior therapy: Basics and beyond*. 2nd Ed. Guilford Press

We developed a treatment manual for CBT therapists. We carried out annual refresher courses for all the trial CBT therapists during the duration of the trial.

Supervision and monitoring of fidelity

Supervision

All trial counsellors and CBT therapists received a combination of standard IAPT supervision comprising fortnightly individual supervision amounting to 1·5 hours per month together with group supervision twice a month totaling 3 hours, thereby providing approximately 4.5 hours of supervision per month. Most counsellors and CBT therapists received individual supervision with a PCET qualified or senior CBT supervisor respectively and all groups were facilitated by either PCET qualified supervisors or senior CBT therapists.

Separately, supervisors monitored the adherence and competence of therapists and counsellors at the supervision occurring closest to sessions 2, 6, and 12 via completion of the Session Adherence and Competence Scale (SACS), a separate form relating to each modality and comprising the higher-order elements of the PCEPS and CTS-R rating forms. These forms were completed for each participant in the trial

Supervision of supervisors

PCET and CBT supervisors also attended monthly peer group supervision, where supervisors' work with trial therapists were discussed. PCET counsellors also received bi-monthly consultation meetings online with a national expert.

Calibration and feedback

An initial sample of digital tapes were calibrated for future target ratings in the full sample by national trainers for PCET and by the Oxford Cognitive Therapy Centre for CBT. The expert feedback from these calibrated tapes was relayed back to the pool of counsellors and therapists. A sample of approximately 50 audio-tapes from each modality were selected using a design ensuring that sessions of all practitioners were selected and the number of sessions sampled reflected the proportion of participants seen in the trial by any one counsellor/therapist.

Ratings were carried out by experienced national trainers in each of the two modalities with checks made against the initial calibration tapes – PCET: Kate Hayes, Trish Hobman, Lynne Laycock, & Emma Tickle; CBT: Clare Crole-Rees, David Hitt, Kate Rosen, & Louise Waddington

Cost-effectiveness methodology

The economic evaluation adopted a cost perspective of the NHS and social care and was limited to the 12-month trial period. Intervention costs were provided by the NHS Trust. 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 p.4). To calculate the total cost, a unit cost was applied to the number of times each participant used the services and differences in costs between PCET and CBT groups were tested using non-parametric t-tests. Utilities were derived from the EQ-5D-5L collected at baseline, 6 and 12 months [1] and Quality-Adjusted Life Years (QALYs) were estimated using the area under the curve method. The main analysis was based on the mITT sample with imputation of missing data. Costs and QALYs assumed to be missing at random were imputed by treatment group using chained equations to create 50 complete datasets. [2] A seemingly unrelated regression (SUR) model was fitted for estimating differential mean total costs and QALYs adjusting for within person differences in baseline utility, accounting for the correlation between costs and QALYs. [3] Differences in costs and QALYs, significance level and 95% CI between PCET and CBT groups were derived from the SUR regression. An incremental analysis was undertaken by dividing the mean incremental cost and QALYs from the SUR analyses to produce an incremental cost effectiveness ratio (ICER). The estimated ICERs were compared with the NICE cost-effectiveness threshold of £20,000 to £30,000 per QALY. [4] The uncertainty around the ICER was addressed using the parametric method and key parameters were derived from the SUR regression. These were used to produce the cost-effectiveness acceptability curve (CEAC) and confidence ellipses. [5] To assess the robustness of the estimates, three sensitivity analyses were performed: (1) only mITT sample with complete data for costs and QALYs; (2) a narrower cost perspective excluding hospital admission and attendance; and (3) costing PCET at the same higher costs associated with the delivery of CBT. Data were analysed using Stata V·16. [6]

References

1. Van Hout B, Janssen MF, Feng Y-S, et al. Interim scoring for the EQ-5D-5L: Mapping the EQ-5DL to EQ-5D-3L. *Value in Health* 2012; **15**: 708–15.
2. Faria R, Gomes M, Epstein S, White IR. A guide to handling missing data in cost-effectiveness analysis conducted within randomised controlled trials. *PharmacoEconomics* 2014; **32**: 1157–70.
3. Willan AR, Briggs AH, Hoch JS. Regression methods for covariate adjustment and subgroup analysis for non-censored cost-effectiveness data. *Health Econ* 2004; 13:461–75.
4. National Institute for Health and Care Excellence. Guide to the methods of technology appraisal 2013. 2013. http://www.nice.org.uk/article/pmg9/resources/non-guidance-guide-to-the-methods-of-technology-appraisal-2013-pdf. Accessed 9 Dec 2016.
5. Hoch JS, Briggs AH, Willan AR. Something old, something new, something borrowed, something blue: a framework for the marriage of health econometrics and cost-effectiveness analysis. *Health Econ* 2002; **11**: 415–30
6. StataCorp. 2019. *Stata Statistical Software: Release 16*. College Station, TX: StataCorp LLC.

Costs used in the cost-utility analyses and sources

	Unit cost £	Unit	Referenced/ assumed time	Mean used £	Source
Intervention costs [a]					
Person-centred experiential therapy	44	Per session	60 mins	44	Provided by the local Trust: Band 6
Cognitive behavioural therapy	53	Per session	60 mins	53	Provided by the local Trust: Band 7
Resource use - health care costs [b]					
Secondary care					
A&E attendance (Mental Health Liaison Services)	198	Per visit	Per visit	198	NHS Reference costs 17/18
Short inpatient stay	3116	6 days	6 days	3116	NHS Reference costs 17/18
Day hospital	606	Per day	1 day	606	NHS Reference costs 17/18
Psychiatric outpatient	103	Per visit	Per visit	103	NHS Reference costs 17/18
Primary care					
General practitioner (GP) – clinic	31	9.22 mins	9.22 mins	31	PSSRU 17/18
General practitioner (GP) – home	31	9.22 mins	9.22 mins	31	PSSRU 17/18
General practitioner – practice nurse	36	60 mins	15.5 mins	9.3	PSSRU 17/18
District nurse	59	60 mins	20 mins	19.7	PSSRU 17/18
Health visitor	44	60 mins	20 mins	15.8	PSSRU 15/16 (adjusted for 17/18)
Community and Social care					
Other Improving Access to Psychological Therapies (IAPT)[c]	34	60 mins	60 mins	34	PSSRU 17/18
Community Psychiatric nurse	59	60 mins	30 mins	29.5	PSSRU 17/18
Psychologist	75	60 mins	60 mins	75	PSSRU 17/18
Counselling	53	60 mins	60 mins	53	PSSRU 17/18
Physio	34	60 mins	55.6 mins	31.5	PSSRU 17/18
Occupational therapist	43	60 mins	30 mins	21.5	PSSRU 17/18
Social care worker	44	60 mins	30 mins	22	PSSRU 17/18
Care assistant	32	60 mins	30 mins	16	PSSRU 17/18
Home care worker	27	60 mins	30 mins	13.5	PSSRU 17/18
Family support worker	31	60 mins	30 mins	15.5	PSSRU 17/18
Medications	-	-	-	(different prices)	British national Formulary

[a] Cost of training therapists/refresher courses were not included due to lack of accurate data and geographical differences.
[b] Only depression/mental health related attendance have been included
[c] There were different descriptions for other IAPT services – individual costs could not be found; therefore, we assumed the same rate for all other IAPT services provided by psychological wellbeing

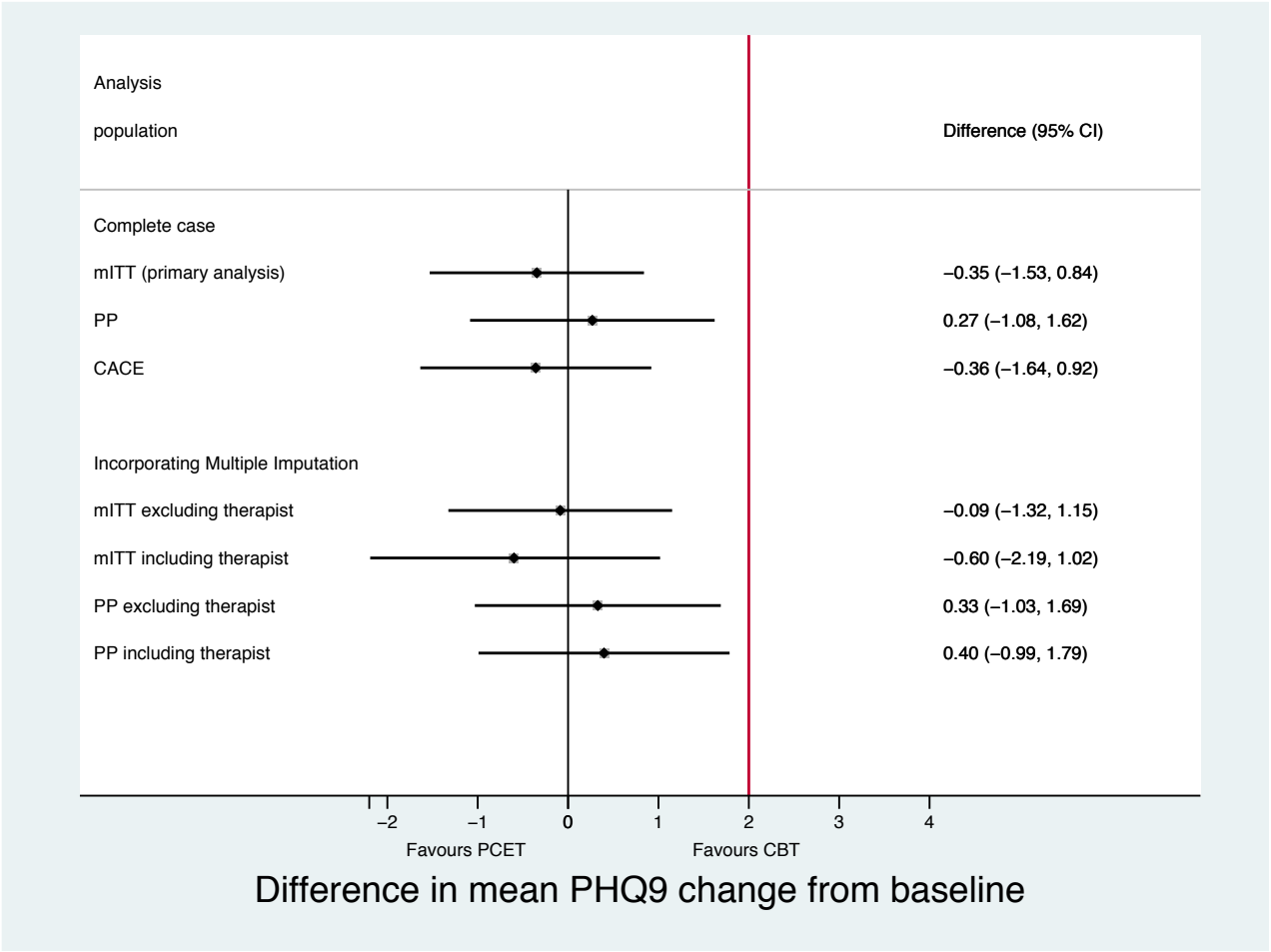
practitioners (band 5).

References

Curtis, L. & Burns, A. (2019) *Unit Costs of Health and Social Care 2019*, Personal Social Services Research Unit (PSSRU), University of Kent, Canterbury. DOI: 10.22024/UniKent/01.02.79286

Department of Health, Team FaC. *National Schedule of Reference Costs 2018-19*. Department of Health, London; 2019.

Differential PHQ-9 outcomes for PCET vs. CBT at 6 months post-randomisation



Note: mITT = Modified intent-to-Treat; PP = Per Protocol; CACE = Complier Average Causal Effects

Per Protocol analysis of secondary outcomes at 6 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	37·04 (9·18): 254	36·39 (8·06): 256	
PP:	27·51 (13·56): 99	26·60 (13·08): 81	0·96 (-2·62 to 4·54)
CORE-OM			
Baseline	22·56 (4·91): 253	22·27 (4·25): 255	
PP:	17·10 (7·38): 99	16·24 (7·24): 84	0·89 (-1·06 to 2·85)
WSAS			
Baseline	25·67 (7·60): 252	25·08 (7·31): 256	
PP:	19·90 (9·46): 153	18·43 (9·80): 135	0·80 (-1·26 to 2·86)
GAD-7			
Baseline	13·80 (4·44): 254	12·84 (4·30): 256	
PP:	9·90 (5·67):155	9·74 (5·36): 139	0·18 (-0·93 to 1·30)
EQ-VAS[1]			
Baseline	37·74 (16·71): 252	37·70 (15·30): 256	
PP:	49·99 (18·61): 103	50·01 (20·10): 84	-0·01 (-5·40 to 5·37)
12 months			
PHQ-9			
Baseline	19·03 (4·12): 254	18·80 (4·09): 256	
PP:	12·10 (7·09): 133	10·16 (6·26): 111	2·05 (0·49 to 3·62)
BDI-II			
Baseline	37·04 (9·18); 254	36·39 (8·06); 256	
PP:	23·38 (14··3); 108	20·22 (12·73); 89	4·13 (0·61 to 7·64)
CORE-OM			
Baseline	22·56 (4·91); 253	22·27 (5·47);255	
PP:	15·84 (8·16); 109	13·99 (7·62); 91	2·28 (0·27 to 4·30)
WSAS			
Baseline	25·67 (7·60); 252	25·08 (7·31); 256	
PP:	18·46 (10·62); 122	15·09 (10·88); 107	3·34 (0·80 to 5·88)
GAD-7			
Baseline	13·80 (4·44); 254	12·84 (4·30); 256	
PP:	9·02 (6·12); 125	7·65 (5·46); 106	1·48 (0·07 to 2·90)
EQ-VAS[1]			
Baseline	37·74 (16·71);252	37·70 (15·30); 256	
PP:	56·00 (21·20); 112	55·30 (22·07); 93	0·04 (-5·53 to 5·61)

Note: PCET = Person-centred experiential therapy; CBT = Cognitive behavioural therapy; BDI-II = Beck Depression Inventory-II; CORE-OM = Clinical Outcomes in Routine Evaluation-Outcome Measure; WSAS = Work and Social Adjustment Scale; GAD-7 = Generalised Anxiety Disorder-7; EQ-VAS = EuroQol-5D-5L Visual Analogue Scale; PP = Per Protocol.

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

Subgroup Analyses for CISR diagnosis groups (moderate/severe)

Comparison of PHQ-9 outcomes for depression severity subgroups at 6 and 12 months

	PCET	CBT	Observed data only
	M (SD): n	M (SD): n	Adjusted between-group difference (95% CI)
6 months			
CISR Diagnosis: Moderate			
PHQ-9 Baseline	17·61 (3·83): 116	16·80 (3·74): 124	
mITT	11·71 (6·44): 92	11·96 (6·13): 89	-0·31 (-2·06 to 1·45)
PP	11·26 (5·94); 74	11·48 (5·97): 61	-0·24 (-2·25 to 1·77)
CISR Diagnosis: Severe			
PHQ-9 Baseline	20·22 (4·00): 138	20·69 (3·48): 132	
mITT	13·61 (6·53): 109	14·29 (6·40): 111	-0·03 (-1·79 to 1·73)
PP	14·10 (6·85): 80	13·61 (6·47): 83	0·93 (-1·12 to 2·99)
12 months			
CISR Diagnosis: Moderate			
PHQ-9 Baseline	17·61 (3·83); 116	16·80 (3·74); 124	
mITT	11·66 (7·54); 80	10·39 (6·25); 74	1·08 (-1·02 to 3·19)
PP	10·31 (6·62); 61	9·10 (5·05); 51	1·02 (-1·29 to 3·33)
CISR Diagnosis: Severe			
PHQ-9 Baseline	20·22 (4·00); 138	20·48 (3·48); 132	
mITT	13·41 (7·37); 87	11·49 (6·88); 78	1·35 (-0·79 to 3·48)
PP	13·61 (7·16); 72	11·07 (7·05); 60	2·70 (0·39 to 5·01)

Recovery and response rates for PCET vs. CBT based on PHQ-9 at 6 months

	PCET n/total (%)	CBT n/total/ (%)	Odds ratio (95% CI)	p-value
6 months				
Depression recovery				
mITT	67/198 (34%)	55/197 (28%)	0·76 (0·49 to 1·16)	0·203
PP	53/151 (35%)	45/141 (32%)	0·87 (0·53 to 1·41)	0·565
Depression response				
mITT	59/198 (30%)	55/197 (28%)	0·91 (0·59 to 1·41)	0·680
PP	44/151 (29%)	45/141 (32%)	1·14 (0·69 to 1·88)	0·607

Note: PCET = Person-centred experiential therapy; CBT = Cognitive behavioural therapy; mITT = Modified intent-to-Treat; PP = Per Protocol. Response = at least 50% fall in intake score; recovery = score of <10; ORs below 1·00 favour PCET.

Recovery and response rates for PCET and CBT based on PHQ-9 at 12-month follow-up

12 months	PCET n/N (%)	CBT n/N (%)	Odds ratio (95% CI)	p-value
Depression recovery				
mITT	62/165 (38%)	73/151 (48%)	1·56 (0·99 to 2·44)	0·054
PP	51/131 (39%)	59/110 (54%)	1·82 (1·09 to 3·03)	0·023
Depression response				
mITT	60/165 (36%)	69/151 (46%)	1·47 (0·94 to 2·31)	0·092
PP	50/131 (38%)	56/110 (51%)	1·68 (1·01 to 2·81)	0·048

Note: PCET = Person-centred experiential therapy; CBT = Cognitive behavioural therapy; mITT = Modified intent-to-Treat; PP = Per Protocol. Response = at least 50% fall in intake score; recovery = score of <10; ORs below 1·00 favour PCET.

Recovery and response rates for PCET and CBT based on PHQ-9 at 6 months for moderate and severe groups

Recovery & Response	PCET n/N (%)	CBT n/N (%)	Odds ratio (95% CI)	p-value
Moderate				
Depression recovery				
mITT	41/91 (45.1%)	29/86 (33.7%)	0·62 (0·34 to 1·14)	0·124
PP	33/73 (45.2%)	22/58 (37.9%)	0·74 (0·37 to 1·50)	0·403
Depression response				
mITT	33/91 (36.3%)	25/86 (29.1%)	0·72 (0·38 to 1·36)	0·309
PP	25/73 (34.2%)	19/58 (32.8%)	0·94 (0·45 to 1·94)	0·858
Severe				
Depression recovery				
mITT	26/107 (24.3%)	26/111 (23.4%)	0·95 (0·51 to 1·78)	0·879
PP	20/78 (25.6%)	23/83 (27.7%)	1·11 (0·55 to 2·24)	0·767
Depression response				
mITT	26/107 (24.3%)	30/111 (27.0%)	1·15 (0·63 to 2·12)	0·645
PP	19/78 (24.4%)	26/83 (31.3%)	1·42 (0·71 to 2·84)	0·326

Recovery and response rates for PCET and CBT based on PHQ-9 at 12-month follow-up for moderate and severe groups

Recovery & response at 12-months	PCET n/N (%)	CBT n/N (%)	Odds ratio (95% CI)	p-value
Moderate				
Depression recovery				
mITT	35/79 (44.3%)	39/73 (53.4%)	1·44 (0·76 to 2·73)	0·262
PP	30/60 (50.0%)	30/50 (60.0%)	1·50 (0.72 to 3·20)	0·295
Depression response				
ImTT	33/79 (41.8%)	33/73 (45.2%)	1·15 (0·61 to 2·19)	0·670
PP	29/60 (48.3%)	26/50 (52.0%)	1·16 (0·55 to 2·45)	0·702
Severe				
Depression recovery				
mITT	27/86 (31.4%)	34/78 (43.6%)	1·67 (0·89 to 3·20)	0·108
PP	21/71 (29.6%)	29/60 (48.3%)	2·23 (1·09 to 4·57)	0·029
Depression response				
mITT	27/86 (31.4%)	36/78 (46.2%)	1·87 (0·99 to 3·54)	0·053
PP	21/71 (29.6%)	30/60 (50.0%)	2·38 (1·16 to 4·88)	0·018

End of treatment comparisons based on the national criteria for reporting of IAPT services: reliable recovery, recovery, reliable improvement, and reliable deterioration

	PCET n/N (%) meeting criterion	CBT n/N (%) meeting criterion	Odds ratio (95% CI)	p-value
Reliable recovery	80/188 (42·6%)	86/180 (47·8%)	1·23 (0·82 to 1·84)	0·310
Recovery	81/188 (45·3%)	87/180 (48·3%)	1·13 (0·76 to 1·69)	0·543
Reliable Improvement	127/193 (65·8%)	129/191 (67·5%)	1·08 (0·71 to 1·65)	0·718
Reliable deterioration	9/193 (4·7%)	13/191 (6·8%)	0·67 (0·28 to 1·61)	0·369

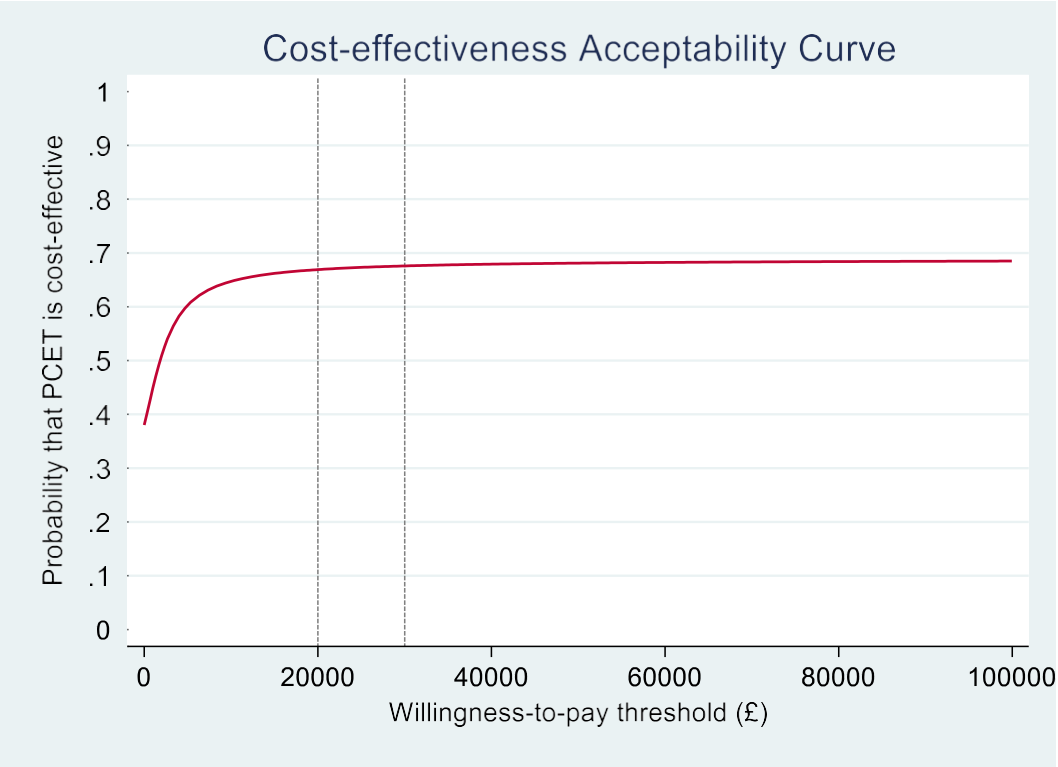
Note: PCET = Person-centred experiential therapy; CBT = Cognitive behavioural therapy; ORs below 1·00 favour PCET.

Resource use at 12 months and EQ-5D-5L utility scores for mITT sample with imputation and mITT sample with complete data

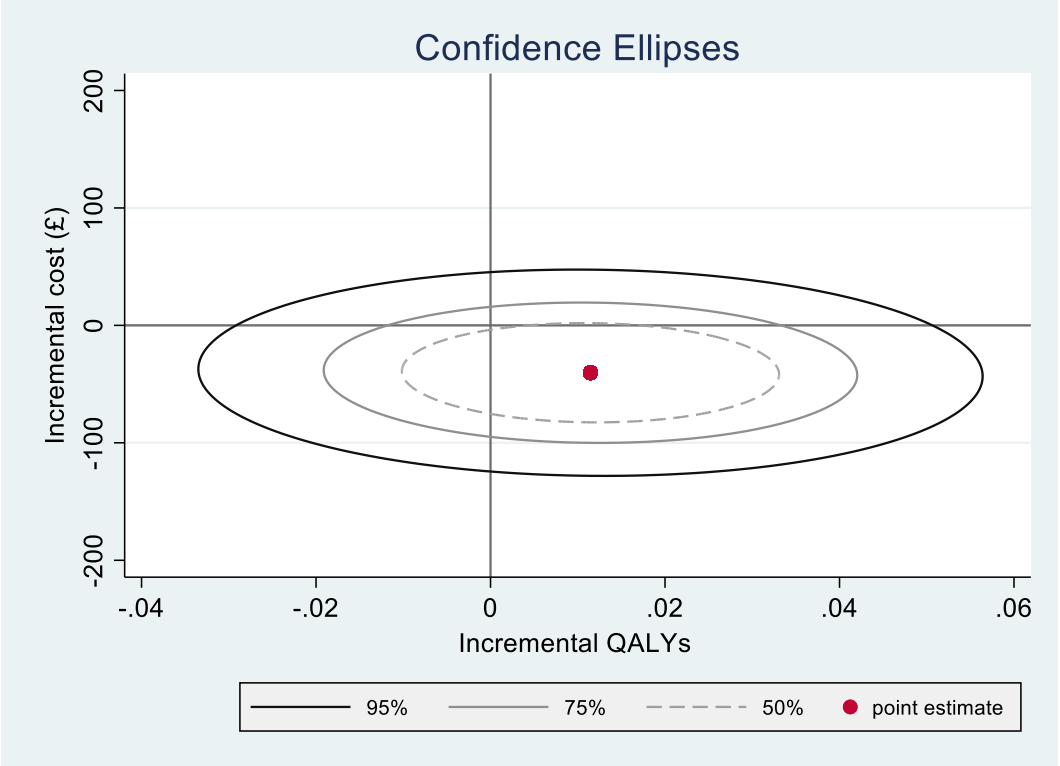
Full mITT sample				
Costs per participant (£)				
	PCET (n = 254) Mean (SE); n[a]	**CBT (n = 256) Mean (SE); n[a]**	**Mean Difference (95% CI)**	**p value**
Intervention	241·48 (12·27); 205	308·48 (16·61); 205	-66·99 (-107·61 to -26·38)	0·001
Hospital	61·21 (33·32); 5	6·54 (3·32); 4	54·67 (-11·41 to 120·74)	0·104
GP health care	99·48 (9·90); 98	71·70 (7·53); 93	27·79 (3·01 to 52·58)	0.028
Community social care	88·04 (14·70); 48	93·83 (14·22); 50	-5·79 (-45·90 to 34·32)	0·776
Medication	22·25 (3·62); 83	16·86 (1·43); 89	5·40 (-2·41 to 13·20)	0·174
Total costs	512·46 (41·61); 223	497·39 (27·23); 212	15·07 (-81·74 to 111·87)	0·760
EQ-5D-5L utility score				
Baseline	·549 (·014); 252	·537 (·015); 256	·013 (-·028 to ·053)	0·544
6 months	·619 (·019); 120	·594 (·021); 113	·025 (-·030 to ·080)	0·369
12 months	·646 (·020); 135	·643 (·020); 127	·003 (-·052 to ·058)	0·910
mITT sample with complete data for costs and QALY				
	PCET (n = 100) Mean (SD); n	**CBT (n = 91) Mean (SD); n**	**Mean Difference (95% CI)**	**p value**
Costs per participant (£)				
Intervention	349·8 (167·85); 99	433·9 (275·16); 83	-84·10 (-148·52 to -19·68)	0·011
Hospital	44·1 (357·83); 3	4·41 (29·39);3	39·69 (-34·96 to 114·34)	0·296
GP health care	118·17 (129·55); 76	93·52 (123·71); 64	24·65 (-11·70 to 61·00)	0·183
Community social care	113·36 (221·87); 39	133·78 (231·86);35	-20·42 (-85·38 to 44·56)	0·536
Medication	26·33 (53·53); 100	20·09 (26·03); 91	6·24 (-8·76 to 21·24)	0·412
Total costs	642·55 (517·04);100	676·53 (465·59);91	-33·98 (-173·29 to 105·33)	0·633
EQ-5D-5L utility score				
Baseline	·545 (·221);100	·550 (·255);91	-·005 (-·073 to ·063)	0·882
6 months	·620 (·247);100	·615 (·282);91	·005 (-·070 to ·081)	0·896
12 months	·630 (·264);100	·658 (·264);91	-·028 (-·103 to ·047)	0·465

CBT = cognitive behavioural therapy; PCET= person-centred experiential therapy; mITT = Modified intent-to-Treat; n[a] is the observed n prior to imputation.

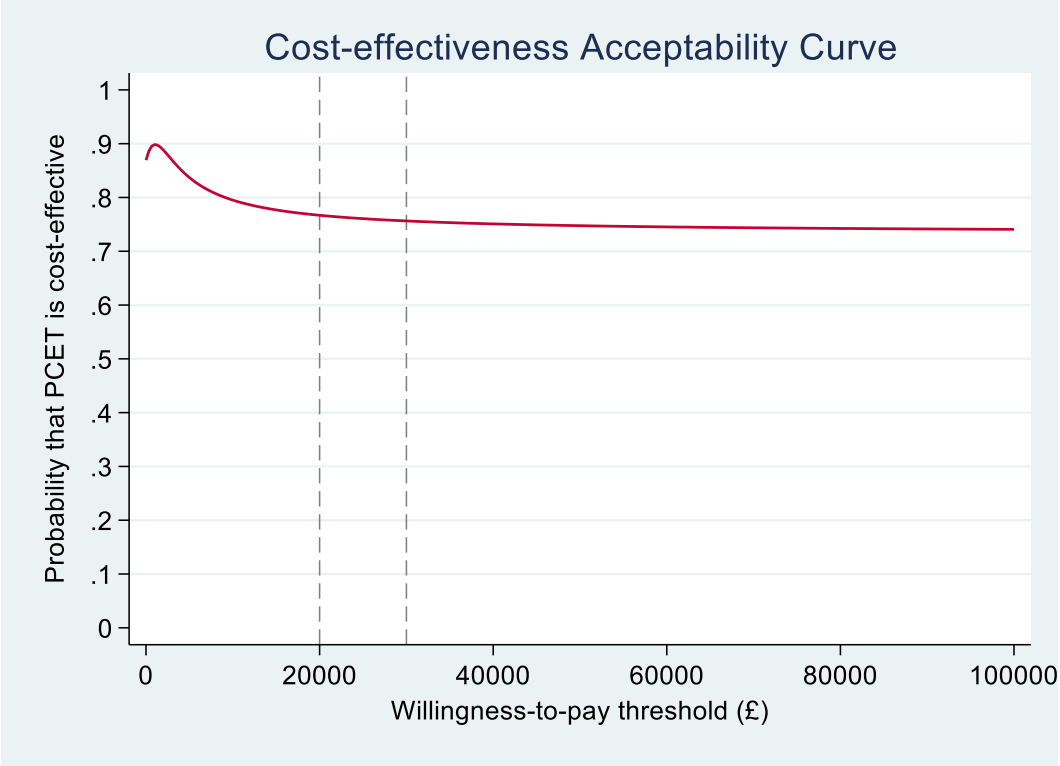
Cost-effectiveness acceptability curve for person-centred experiential therapy (mITT sample with imputation of missing data)



Confidence Ellipses for person-centred experiential therapy (Excluding hospital attendance & admission data on mITT sample with imputation)



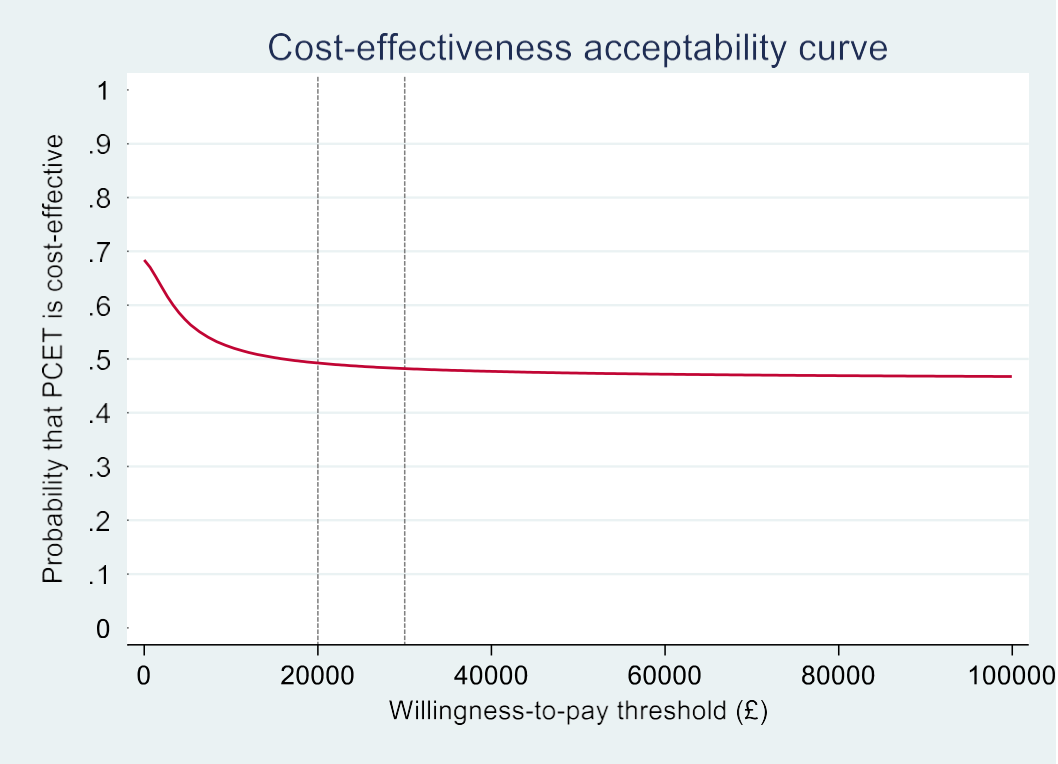
Cost-effectiveness acceptability curve for person-centred experiential therapy (Excluding hospital attendance & admission data on mITT sample with imputation)



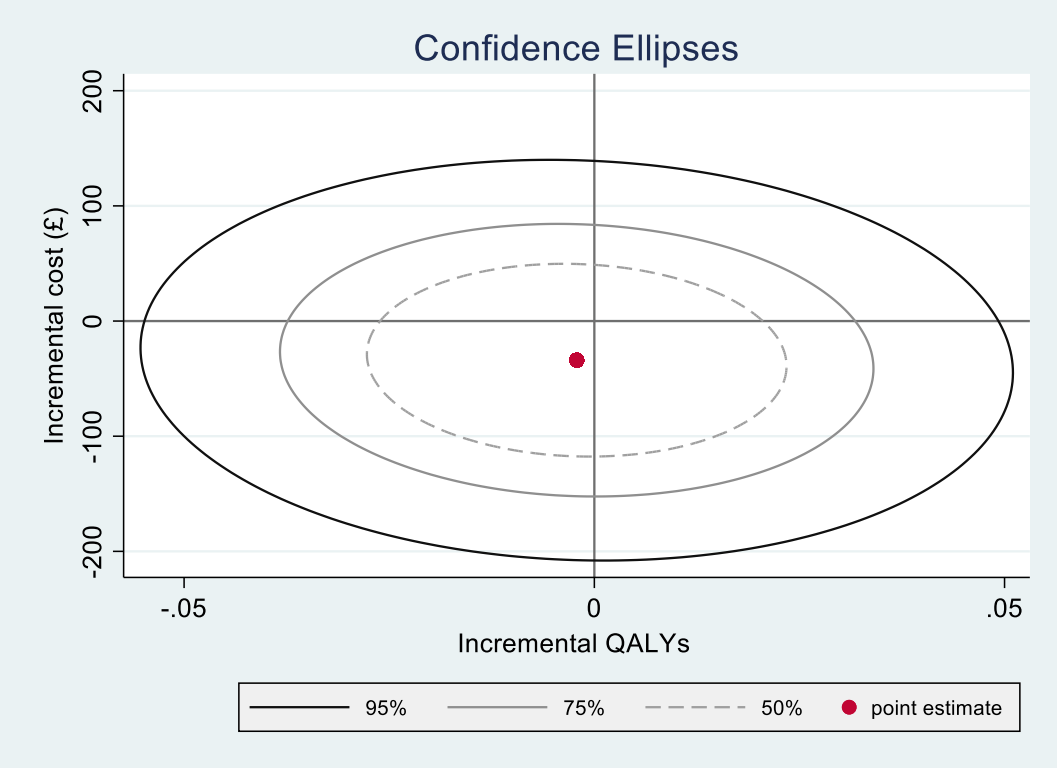
Cost-effectiveness analyses

The main analysis showed a significant difference in the mean intervention costs with PCET significantly cheaper (-£66·99, p = 0·001) (Appendix p.25). 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 6). The probability of PCET being cost-effective compared with CBT was 68% (Appendix p.26). The confidence ellipses spread across all four quadrants of the cost-effectiveness plane providing a visual representation of the large uncertainty around the point estimate (Figure 3). Sensitivity analyses showed the incremental total costs and QALYs were consistently non-significant between the modalities. In the sample with complete data, the lower total costs for PCET (-£33·98, p = 0.633) and less effective outcomes (-0.002, p = 0.921) resulted in an ICER of £15847 with a 50% probability of PCET being cost-effective compared with CBT (Appendix p.27,28). Excluding secondary care costs and assuming the same intervention costs for both PCET and CBT, the probability of PCET being cost-effective rose to 78% (Appendix p.29,30) and 71% (Appendix p.31,32) respectively.

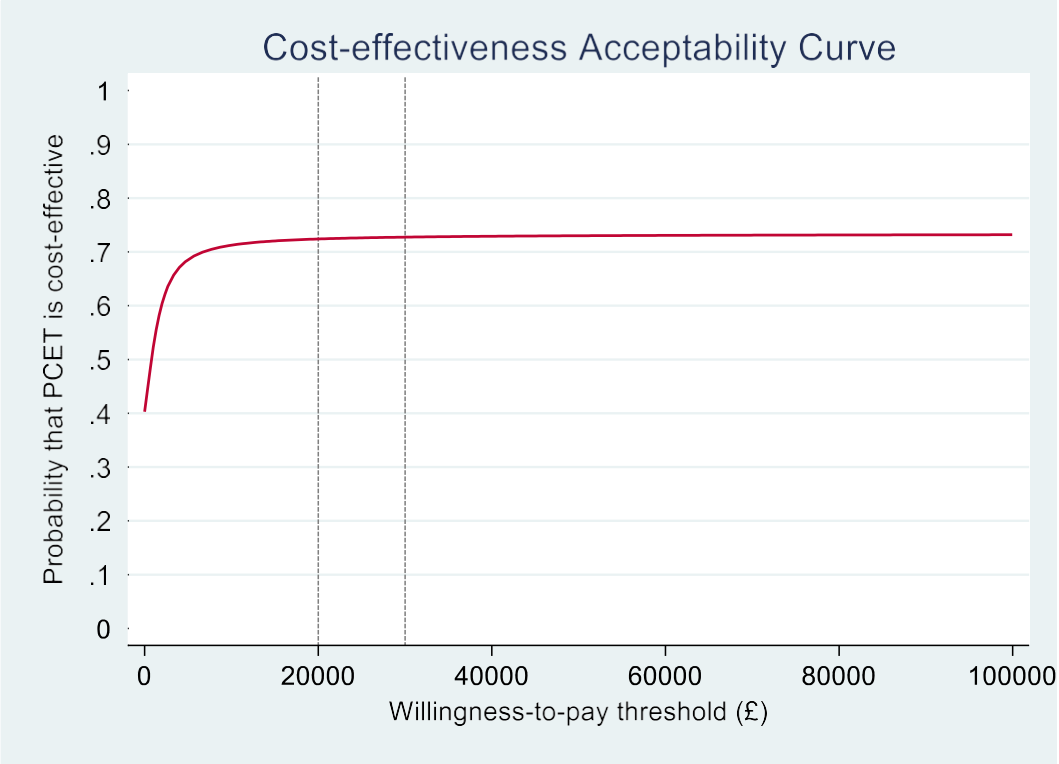
Cost-effectiveness acceptability curve for person-centred experiential therapy (Complete case)



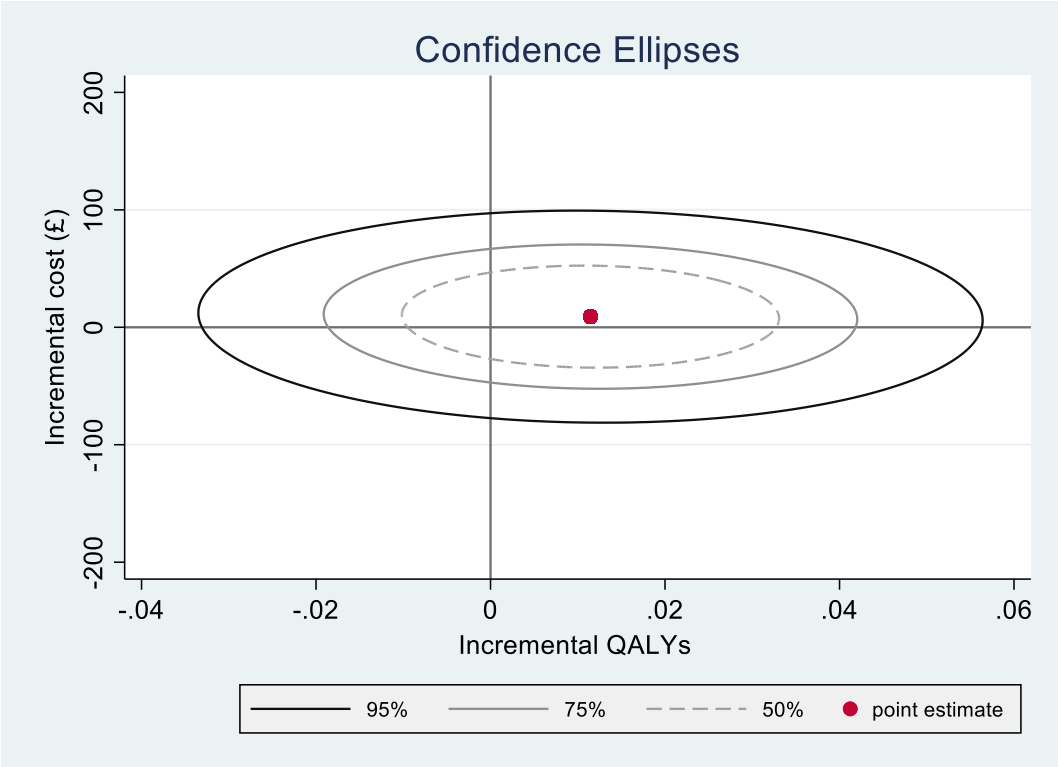
Confidence Ellipses for person-centred experiential therapy (Complete case)



Cost-effectiveness acceptability curve for person-centred experiential therapy (Intervention cost the same in both groups @ £53 per session on mITT sample with imputation)



Confidence Ellipses for person-centred experiential therapy (Intervention cost the same in both groups @ £53 per session on mITT sample with imputation)



CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	1
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	1-3
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	6-8
	2b	Specific objectives or hypotheses	8
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	8 & 10
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	
Participants	4a	Eligibility criteria for participants	9
	4b	Settings and locations where the data were collected	8
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	10-11
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	12
	6b	Any changes to trial outcomes after the trial commenced, with reasons	N/A
Sample size	7a	How sample size was determined	12-13
	7b	When applicable, explanation of any interim analyses and stopping guidelines	N/A
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	10
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	10
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	10
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	10
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those	Statisticians 10

		assessing outcomes) and how	
	11b	If relevant, description of the similarity of interventions	10-11
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	13-14
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	14-15
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	17-18
	13b	For each group, losses and exclusions after randomisation, together with reasons	17-18(Figure 1)
Recruitment	14a	Dates defining the periods of recruitment and follow-up	15-16
	14b	Why the trial ended or was stopped	16
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	16 (Table1)
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	17 (Figure 1)
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	17-18 (+ Appendix)
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	N/A
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	19 – 20 (+Appendix)
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	19
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	22-23
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	23
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	21, 23
Other information			
Registration	23	Registration number and name of trial registry	10
Protocol	24	Where the full trial protocol can be accessed, if available	Available from lead author
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	24

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials.

Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.

Counselling for Depression: The PRaCTICED Trial

Research Protocol

Full title: A pragmatic non-inferiority randomised trial of the clinical and cost-effectiveness of counselling for depression versus cognitive-behaviour therapy, for clients in primary care meeting a diagnosis of moderate or severe depression.

Brief title: **P**ragmatic, **Ra**ndomised **C**ontrolled **T**rial assessing the non-**I**nferiority of **C**ounselling and its **E**ffectiveness for **D**epression

Acronym: PRaCTICED

Funder: BACP Research Foundation

Date: 20th November 2013

Doc ref: Version 1.0

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Contents

OVERVIEW

Full title of study:
A pragmatic non-inferiority randomised trial of the clinical and cost-effectiveness of counselling for depression versus cognitive behaviour therapy, for clients in primary care meeting a diagnosis of moderate or severe depression.

Brief title of study:
Pragmatic, **Ra**ndomised **C**ontrolled **T**rial assessing the non-**I**nferiority of **C**ounselling and its **E**ffectiveness for **D**epression (PRaCTICED)

Main research question
To determine the clinical and cost-effectiveness of counselling for depression (CfD) compared with cognitive behaviour therapy (CBT) as delivered in primary care for clients with moderate or severe depression.

Lay summary
There is good evidence showing that CBT can and does help many people. However, it does not help everyone all the time. For people experiencing moderate or severe depression, there is an alternative treatment, called *counselling for depression*. Service evaluation evidence indicates that counselling for depression is as effective as CBT but we need to test whether this is really the case by conducting a scientifically rigorous trial – and that is the purpose of this research project.

Our study requires a total of 550 people to enter treatment and 500 people to complete treatment – half receiving Counselling for Depression (CfD) and half Cognitive Behaviour Therapy (CBT). We will base our research within the Sheffield IAPT service that already delivers both counselling (and is training them in CfD) and CBT and we will compare these two interventions. We will ask people presenting with depression that the Psychological Well-being Practitioner (PWP) feels needs a more intensive therapy (i.e., CfD or CBT) and who meet certain criteria, to take part in the trial. They will stand an equal chance of receiving either therapy and the PWP will provide information and will explain the trial to them and what it involves. They will be invited to attend an assessment interview and, if they meet the criteria, then they will be talk through an informed consent form. This sets out the elements of the trial that are additional to what would be asked of them if they attended the service as normal. These procedures will not delay treatment. However, it is important that people have sufficient time to consider what is being offered. Once people have entered the trial, their experience of the service will be the same as other people not in the trial apart from filling in the questionnaires. Their therapy will be for up to 20 sessions, but most people have fewer sessions. People will complete some forms that will help us to know how effective the therapy is for them.

Ending treatment is something that the therapist and client discuss and agree together. Once treatment has finished, clients will be sent a questionnaire pack 6-months and 12-months after their entry into the trial. We will also, with their agreement, contact them by telephone to carry out a short exit interview on their experience of treatment, whether they have terminated treatment with the agreement of their practitioner or by their own decision. This will help us understand why some people decide to leave treatment.

We will write up the results of the study and disseminate them widely. In particular, we will feed the results of the study back to the Sheffield service, service user organisations, and to the participants themselves.

WHY THERE IS A NEED FOR A TRIAL NOW

BACKGROUND LITERATURE

A review of six RCTs showed clients who were assigned to counselling demonstrated a significantly greater reduction in psychological symptoms such as anxiety and depression than clients receiving usual GP care when followed up at up to 6 months. [1] These psychological benefits were modest: the average counselled patient was better off than approximately 60% of clients in usual GP care. However, there were no significant differences between counselling and usual care in the 4 RCTs reporting longer-term outcomes (8 to 12 months).

An HTA-funded trial comparing counselling with CBT yielded no differences between the two therapies in their overall effectiveness at short- or long-term follow-up. [2] Both therapies were superior to usual GP care in the short-term but provided no significant advantage in the long-term. Findings from this trial were not included in the Depression Guidelines due to a confounding of diagnoses. However, a subsequent re-analysis of data focusing on those clients meeting a diagnosis of depression confirmed the earlier results. [3]

A meta-analysis of psychological therapies for depression compared non-directive supportive therapy with CBT and yielded an effect size advantage to CBT of d= 0.05. [4] However, the authors commented that this difference is small, its clinical relevance is unclear, and the collection of studies included under the broad heading of supportive psychotherapy may have been overly heterogeneous. Further, CBT had the highest relative risk of drop out (k = 26, RR=1.16).

A state-of-the art review of the literature regarding person centred and experiential therapies, reported that Person Centred Therapy (PCT) appeared to be consistently, statistically and practically equivalent in effectiveness to CBT (22 studies, including 17 RCTs, with effect sizes of -.06 and -.1 respectively. [5] Further, evidence from practice-based studies indicate that PCT, as defined by the practitioners and as delivered in the NHS, is effective and not significantly different from CBT [6,7]. In response to the IAPT initiative [8], several studies have reported outcome data from IAPT services and a recent review of data from the one-year rollout indicated counselling to be as effective as CBT. [9]

The collective evidence from the studies reported above suggests comparisons between CBT and counselling to yield small or broadly equivalent results. However, these results may be due to a number of factors, for example the heterogeneity of non-CBT comparators and the over sampling of mild depression. What is required is a rigorous pragmatic trial that is acceptable to the Guideline Development Group in terms of methodology and provides a definitive answer as to the relative effectiveness of CfD compared with CBT for moderate and severe depression

The proposed trial will: (1) provide the largest UK trial to date of a protocol driven counselling intervention delivered by counsellors trained to a specific standard for a specific presenting condition (depression) and enable an evaluation of the non-inferiority of counselling set against the current standard of CBT (effectiveness argument); (2) yield findings regarding the comparative satisfaction between counselling for depression and CBT (acceptability argument); (3) enable a test of the cost-efficiency of counselling for depression in terms of whether gains achieved by counselling for depression can be obtained more quickly (efficiency argument); and (4) yield the best evidence to date of the comparative cost per QALY gained for counselling (economic argument).

RATIONALE FOR THE STUDY

Although counselling has a long and valued tradition within primary care, evidence derived from trials has not kept pace with changes in service configurations and delivery. This situation makes counselling vulnerable when the evidence is reviewed by NICE, in terms of treatments for levels of depression other than of mild severity. This is in stark contrast to the body of evidence supporting interventions based on CBT. As a consequence, the NICE review of psychological interventions for depression identified CBT as the front-line psychological intervention while counselling was assigned to situations in which first-line interventions were either not successful or were not preferred by the patient with the evidence for counselling being 'uncertain'. [10]

The robust evidence base for CBT was a key factor in the UK government's funding of the IAPT initiative [8] and the drive to train large numbers of practitioners in CBT as part of workforce development in Primary Care. [11] Subsequent funding for the IAPT initiative has, however, invested in supporting selected additional interventions, one of which is Counselling for Depression (CfD) [12,13], which is now seen as a *bona fide* and appropriate intervention within the IAPT framework. However, a number of caveats have been applied to its implementation within NICE guidance relating to the range of client severity for which it is deemed appropriate as well as the level of evidence supporting the modality and the requirement to convey this situation to prospective clients. The overall purpose of the proposed trial is to provide a robust and rigorous evidence base to inform these issues.

Counselling for Depression (CfD) is currently one of the NICE-recommended psychological therapies for mild to moderate depression made available within IAPT services, to support patient choice and ensure there is a range of therapies to meet patients' needs. However, low-cost interventions (e.g., self-help, computerised interventions) are being supported for mild depression while CBT is advocated for severe depression. There are no trial data pertaining specifically to CfD and the moderate band of depression is probably too narrow to sustain a specific intervention (i.e., counselling) and its associated practitioners (i.e., counsellors). Accordingly, there is an urgent need for a randomised controlled trial of CfD for moderate/severe depression. Furthermore, given that CBT is the current treatment of choice for moderate/severe depression, there is a need to know the relative efficacy of CfD as compared with CBT (rather than, for example, a no-treatment condition). Hence, it is important that all stakeholders have access to better quality evidence as to the efficacy and efficiency of counselling for depression. It is the purpose of this trial to provide such evidence.

The Sheffield IAPT service routinely delivers both CfD and high-intensity CBT to clients with depression, who have not responded to a low-intensity treatment (step 2 in the stepped care model). Organisationally and philosophically the service is in a position of equipoise regarding the two interventions. From previous research and analysis of service data, there is sufficient evidence to move to a definitive trial to establish the efficacy of CfD, particularly in comparison to CBT that, in general, is the usual care among this patient population. Although there is little evidence to suggest that CfD is superior to CBT, CfD would nonetheless be a valuable intervention were it shown to achieve broadly the same effect. Therefore, we propose a *non-inferiority randomised trial* comparing CfD against CBT at step 3. [6]

The study design has been overseen by the University of Sheffield Clinical Trials Research Unit (CTRU). Co-I Bradburn (Senior Medical Statistician from the CTRU) has contributed to the sample size calculations, and will devise the analysis plan for the trial. The

randomisation schedule will be carried out by CTRU and analyses carried out by statistician blinded to treatment conditions.

The trial will be embedded within a cohort of patients seen within the Sheffield IAPT service, a large, established IAPT service, in which there is common and concurrent measurement of the primary outcome for both trial and service. Accordingly, outcome data from trial patients can be compared with those who decline the trial in order to provide a test of the external validity of the results. The combination of trial and cohort data frames the study as a *comprehensive cohort design*, thereby yielding added value to the trial. [14-17]

The added value of external validity also presents a number of challenges for the design. These have centred on maintaining the integrity of the trial whilst causing minimum disruption to routine service delivery and the client experience. A subgroup of the proposed research team comprising CI Barkham and Co-Is Hardy, Kellett, and Saxon have collaborated with the Sheffield IAPT service for over a year, analysing counselling and high-intensity CBT interventions within anonymised data from the first 18 months of the service (1/4/09-30/9/10). From this we have assessed current and projected procedures, client throughput and waiting times. This analysis has informed the study design, the recruitment and the sample size calculation. In effect, this collaboration has provided the same opportunity as would be afforded by a platform trial, enabling us to be confident of key components in the methodology. The relationship between the University and the IAPT service is defined by collaboration across training, supervision, and research.

PSYCHOLOGICAL INTERVENTION BEING EVALUATED

The intervention being evaluated is Counselling for Depression (CfD) [12,13]. CfD is a form of Person-Centred/Experiential (PCE) therapy derived from the competences required to deliver effective humanistic psychological therapies [3]. CfD is drawn from those humanistic approaches with the strongest evidence for efficacy, based on outcomes of controlled trials (for a review, see [5]). CfD is specifically designed to address depression and is delivered within IAPT and related programmes.

Whilst counselling has long been available in NHS Primary Care settings, service design and treatment approaches in practice have proved very variable. Providing CfD training has facilitated a move towards standardised practice and evidence-based service evaluation. CfD training standardises counselling work with depressed clients and aligns therapist interventions with the evidence-base underpinning NICE guidelines.

The CfD training is aimed at experienced person-centred and humanistic practitioners, as a 'top-up' provision. The training consists of a five-day taught programme that is delivered across a one-week or two-week block. Feedback from the CfD External Examiner (Co-I Gabriel) suggests a two-week model of delivery better facilitates student engagement, learning and knowledge retention), followed by a period of supervised clinical work. During clinical practice associated with CfD training, a minimum of 80 hours of supervised practice must be completed.

METHOD

DESIGN

A non-inferiority randomized controlled trial embedded within a comprehensive cohort design.

SETTING AND SERVICE

Sheffield is a city with a population of around 650,000 that has large urban and rural areas and is average in terms of a number of demographic characteristics compared with other major cities. For example, the BME population (8.8%) approximates the national average (8.7%). [18,19] The Sheffield IAPT service was established by Sheffield Health and Social Care Trust (SH&SCT) in 2009. Previously each of four PCTs had their own configuration of psychological therapy services that included well established counselling services. Sheffield IAPT unified the different services and incorporated the counselling services within it. Counsellors and CBT therapists can offer up to 20 sessions of one-to-one therapy, although service data indicate only 2% of clients had 20 sessions and 95% received up to 16 sessions.

As dictated by the IAPT stepped-care model, the PWP is the first point of contact for step 2 interventions and a gateway for clients being stepped up to step 3. Because of this, PWPs play a key role in the proposed trial as they are the gatekeeper and initial assessor for entry into the trial. The proposal funds the equivalent of 0.2 wte PWP within the IAPT service for an 36 month period (i.e., spanning the whole project) as a co-ordinator to ensure maximum liaison with the research team in terms of client flow, throughput in terms of keeping client recruitment on target, and assistance in assesmsnts. Where service support costs are appropriate according to the revised AcoRD [20] documentation, these will be sought.

Analyses and reports of Sheffield IAPT minimum data set (MDS) data indicate service outcomes, comparable to other IAPT services nationally, with a client recovery rate of 48.6%. [21,22]

The Service aims to provide a step 3 therapy within 12 weeks of the stepping-up decision and provide equal access to both CBT and CfD. Practice sites within the service that have waits longer than 12 weeks, or where the difference in wait for the two therapies is greater than three weeks will be excluded. These criteria will be applied to the site at the point where each client is stepped-up, therefore sites may be included or excluded at different times during the recruitment period.

PRACTITIONERS

The Sheffield IAPT service comprises approximately 30 counsellors and 35 high-intensity CBT therapists (the exact numbers can fluctuate as a function of changes in the workforce). While most the the CBT practitioners are fulltime, a majority of the counsellors are part-time (reflecting the historical nature of the profession). Currently around 15% of counsellors (in terms of wte) have been trained in CfD and the remaining counsellors will be trained during the initial part of the project prior to commencement of the trial. All practitioners will be trained to the predetermined level required for CfD before being assigned to the trial. The amount of time required to achieve this is likely to vary depending on the number of hours worked by counsellors, but by start of client recruitment it is estimated that at least 50% of counsellor capacity will be fully CfD trained and this will rise to 100% by the seventh month of recruitment. Sites will become eligible for the study as their counsellors become trained. CBT therapists will enter the study as their site becomes eligible. During the pre-recruitment phase, all CBT therapists will receive a refresher workshop on high-intensity CBT as consistent with the IAPT guidance. Supervision for CfD and CBT practitioners will be monitored and logged by supervisors as part of ensuring that the interventions are delivered as per protocol.

Training in CfD will be required for the trial and these skills will remain with the service after the trial has finished. A bid for NHS treatment costs will be made to cover the costs of the training according to the AcoRD arrangements [20].

PARTICIPANTS

Participants will be clients meeting the following inclusion criteria: aged 18+ with a diagnosis of major depression, having been deemed to require stepping up by a PWP within the Sheffield IAPT service. Clients whose stated treatment preference would make them unwilling to be randomised to the other treatment if randomised to it, will have been excluded from the trial at Stage 1 assessment. Other exclusion criteria are: presence of organic condition, psychosis, drug or alcohol dependence, or elevated clinical risk. Clients may be in receipt of medication for depression but it must the regime must be stable at the point of entry to the trial. If they are in receipt of medication, this will be recorded.

Target population: Adults aged 18 and above who are eligible to receive either high-intensity CBT or CfD for a primary presentation of depression.

A. Inclusion criteria:

Stage 1

1. An initial indication by the client that depression is a major focus (ascertained by the PWP during initial assessment of presenting issues).
2. The trial will be broached with clients if their weekly PHQ-9 [23] scores are ≥12 at the 3rd or 4th appointment with the PWP (See Appendix 1).
3. If they state no strong objection to either treatment sufficient for them to be unwilling to enter the trial should they be allocated to the alternate treatment, then they will be given an first-stage Informed Consent form (See Appendix 2) to indicate their willingness to be contacted by the member of the research team that would then enable them to progress to Stage 2. If the patient has a strong objection, then they will progress as normal within the IAPT service and their consideration acknowledged.

Stage 2

4. Client meets an ICD-10 diagnosis of moderate or severe depression using the Clinical Interview Schedule-Revised (CIS-R) [24] carried out by an independent assessor. (See Appendix 3).

B. **Exclusion criteria:**

Stage 1

1. Presence of prior diagnosis of personality disorder, bipolar disorder, schizophrenia as indicated in the IAPT Outcomes Toolkit within the service data or from GP referral notes to the service.
2. Organic origin of presentation (e.g., dementia) as indicated on referral to the service by the GP.
3. Long-term physical condition as denoted in service notes.

Stage 2

4. Elevated risk of suicide: If active thoughts of suicide are indicated from the CIS-R, we will implement a risk protocol to inform the PWP or identified practitioner. (See Appendix 4).
5. Alcohol or substance dependency: these will be determined by Questions 1 and 2 from Section I (Alcohol) and Section II (Drug) of the Mini-International Neuropsychiatric Interview (M.I.N.I.) [25], which yield diagnoses of current alcohol or drug dependency (See Appendix 3)

INTRODUCTION OF THE TRIAL TO PARTICIPANTS & 2-STAGE INFORMED CONSENT PROCESS

Stage 1

As outlined above, potential clients will be given a summary of the aims of the trial and a brief description of the two treatments (see Appendix 1). The trial will be labelled for clients as followed:

A randomized trial to compare the effectiveness of cognitive behaviour therapy and counselling for depression.

This title provides the key information and components of the trial for clients. The name PRaCTICED will be used for shorthand – the same as used in the formal title of the trial.

If clients are eligible in terms of their PHQ-9 scores at the 3rd to 4th session and do not have a strong preference, they will be asked to complete a first-stage informed consent (consent to contact) agreeing to a researcher/clinical support officer contacting them to arrange an appointment for an assessment (see Appendix 2). They can take the form away and consider it and check any questions with the PWP at the following session. Clients will be asked about their preferred means of being contacted (letter, email, phone, text) and they will be told that they will be sent a one-day bus pass to cover any travel cost of attending the assessment interview.

Stage 2

Patients will be contacted by a member of the research team and posted a fuller description of the study (See Appendix 1) and a second-stage consent form regarding their participation in the study (Appendix 2). This consent form provides the opportunity for the patient to attend the research assessment but await signing the informed consent until they have clarified any questions relating to the research study.

When attending for the research interview, patients will be asked if there is anything that needs clarifying and then will be consented into the research assessment and explained that the assessment procedure to determine whether the trial is appropriate for them.

The interview will comprise the following:

1. Introduction to the trial, outline of treatments, and informed consent into the main trial (see Appendix 2)
2. Treatment preference question [26] (Appendix 3)
3. Administration of the CIS-R [24] (Appendix 3)
4. Follow-up questions on risk of suicide if necessary: If active thoughts of suicide are indicated from the CIS-R, we will implement a risk protocol to inform the PWP or identified practitioner. (Appendix 4)
5. Questions 1 and 2 from Section I (Alcohol) and Section II (Drug) of the Mini-International Neuropsychiatric Interview (M.I.N.I.) [25] will be administered, which yield diagnoses of current alcohol or drug dependency. (Appendix 3)
6. Expectations Questionnaire (6 items) [27] (Appendix 3)
7. Administration of 7 outcome questionnaires (totalling 82 items): (Appendix 3)
    a. The PHQ-9 (9 items) [23]
    b. The Beck Depression Inventory-II (21 items) [28]
    c. CORE-OM (34 items) [29]

   d. GAD-7 (7 items) [30]
   e. WSAS (5 items) [31]
   f. EQ-5D-L (5 items) [32] and Quality of Life Scale (1 item) [33]
8. Moderator questionnaire - The Connor-Davidson Resilience Scale (25 items) [34]
9. By interview - Client Service Receipt Questionnaire (adapted) [35]

The Stage 2 assessment will be carried out by a member of the research team or a clinical support officer (CSO). All assessors will have received training in administration of the assessment tool – the CIS-R – and will be monitored regularly by the lead assessor. The lead assessor is Janice Connell who has previously carried out CIS-R interviews for the Sheffield arm of the OCTET trial.

If the patient meets a diagnosis of moderate or severe depression with no excluding factors, they will be invited to enter the trial and assigned to one of the treatment arms via remote access to the randomisation procedure run by the University of Sheffield Clinical Trials Research Unit (EpiGenysis). This assignment takes 1 minute.

They will be provided with their first appointment and location of the appointment. The location will be the same as if they were not in the trial (i.e., acceptance into the trial does not change the venue for receiving the intervention).

SAMPLE SIZE

Published findings [2-4] and Sheffield IAPT service data (1/4/09 – 30/9/10), indicate only small differences in outcomes between CBT and counselling. In a meta-analysis, a comparison of CBT with therapy similar to counselling (non-directive supportive therapy) yielded a null effect size advantage to CBT of d= 0.05 (95% CI -0.08, 0.18) [4]. In the analysis of clients with PHQ-9 intake scores ≥12 in the Sheffield service data, the overall mean (SD) pre-last change in PHQ-9 was 6.8 (6.9) and there was no significant difference between counselling and CBT (difference=+0.5 points on the PHQ-9 in favour of counselling; 95% CI -0.3, +1.3).

From these findings, we predict the actual difference in change means to be zero. The margin, within which CBT could not be considered statistically or clinically more effective than CfD was determined as follows; First, treatment effects of 0.2 to 0.3 are conventionally viewed as ‘small’ and of limited clinical value [e.g. 36,37]. Second, it has been recommended that the threshold for non-inferiority be set at 50% or less than the expected difference between CBT and usual care which would mean an effect size of less than 0.3 (i.e. 0.6/2). [38] Finally, discussions with psychologists on the research team and IAPT staff indicate 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-last SD of 6.9 found in the service data above). Therefore, a pre-last change difference of less than 2 on PHQ-9 in favour of CBT was adopted as the limit for non-inferiority of CfD.

It is estimated that 550 clients (275 per arm) would need to be recruited in order 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 incorporates both inter-patient and inter-therapist variability); no underlying difference between the effect of CBT and counselling; and a 10% loss to 6-month follow-up. As the trial is within a service with few additions to routine practices and procedures, it is expected that there will be relatively few participants who leave the trial and do not provide a 6-month follow-up PHQ-9.

ASSESSMENT MEASURES

A client score of 12 or more on the PHQ-9 [23] at the 4th session of Step 2 intervention will provide the initial point of possible suitability for the trial. The weekly administration of the PHQ-9 is part of routine practice within the IAPT service and is mandated nationally by the Department of Health. This will be used as the filter for the administration of the CIS-R. The threshold score of 12 on the PHQ-9 denotes the mid-point score within the moderate severity banding. The CIS-R is a computer run programme that filters out unnecessary questions thereby marking out the quickest route through the questions without asking redundant questions. Please note: a copy of the CIS-R is not included as it is a computer disk.

Diagnosis

Clients scoring 12 or more on the PHQ-9 will be invited to attend a screening interview where the computerised CIS-R will be administered. [24] The CIS–R is a standardised interview for assessing common psychiatric disorders and is designed to be administered by non-clinicians. It comprises 14 sections covering areas of neurotic symptoms: somatic symptoms, fatigue, concentration and forgetfulness, sleep problems, irritability, worry about physical health, depression, depressive ideas, worry, anxiety, phobias, panic, compulsions and obsessions. Each section has a lead-in question relating to symptoms experienced over the previous month; the response to this question is not included in the scoring. A positive response to the initial question leads to four further questions (five for depressive symptoms) relating to the frequency, duration and severity of the symptom over the past 7 days. Each positive response scores 1; thus, for each section, scores range from 0 to 4 (or 0 to 5 for depressive ideas). The total score is the sum of all 14 sections, giving a possible range of 0–57. A score of 12 or above on the CIS–R indicates caseness [24] a score of 6–11 indicates some symptoms of mental disorder and a score of 0–5 indicates little evidence of mental disorder. [39] The CIS-R also provides a primary and secondary ICD-10 diagnosis and clients meeting an ICD-10 primary diagnosis of moderate or severe major depression will be eligible to enter the trial.

The CIS-R has been used in ONS National Survey of Psychiatric Morbidity [40,41] and in primary care studies of depression. [e.g., 42-46] It has been used in Sheffield IAPT service as part of a trial of treatments of obsessive compulsive disorder (OCTET, often referred to as OCTET1: ISRCTN number is ISRCTN73535163). Patients have found the CIS-R acceptable as an assessment procedure. The CIS-R will be administered by members of the research team and/or clinical support officers at designated practices across the city.

Baseline measures

On meeting criteria for the trial, providing consent, and being randomised, clients will also complete the remaining baseline outcome measures as follows (See Appendix 3 for all measures): the PHQ-9 [23] (primary outcome measure of depression), BDI-II (depression severity measure) [28], the CORE-OM [29,47] (generic presenting problems), the EQ-5D-5L [30,48] (health status utility measure), and Quality of Life Scale [33]. In addition, clients and therapists will complete the Connor-Davidson Resilience Scale (CD-RISC) [34], which will be used as a predictor variable in secondary analyses.

Because clients entering the trial are also embedded within the IAPT service, clients will complete the IAPT minimum dataset (MDS) [49] comprising the PHQ-9 [23] (depression), GAD-7 [30](anxiety), and WSAS [31] (functioning). These data will be available as trial data. As is mandatory within the UK national IAPT initiative, the PHQ-9, GAD-7, and WSAS will

also be completed at each session, as required by the IAPT service and the IAPT minimum dataset (MDS).

A brief exit interview will be administered by telephone at 4 weeks post treatment. (See Appendix 3) This will be presented to the patient via their preferred method (i.e., postal questionnaire or web-based survey). The experiences aspect of the questionnaire will be depend on whether the patient left therapy unexpectedly (i.e., unilaterally) or had a mutually agreed ending. The baseline measures will be repeated at 6-months and 12-month follow-up post-randomisation.

From respondents, we will use purposive sampling to interview – with patients' consent – upwards of 50 patients (i.e., 10%) to gain richer material. The topic guide for this interview, focusing on how patients experienced the intervention, is outlined in Appendix 5. Patients will be free not to answer questions and to withdraw at any time. The venue for the interview will be at the University of Sheffield but patients will be given a choice that would include a visit to their home. Our experience from another trial (OCTET) is that most patients prefer a neutral setting (i.e., University, which is sited conveniently in the city centre).

We will access data from the service record recorded on the Trust's Data Management System, termed Insight, which records basic patient demographics and past and present service utilization. The database also includes postcode information that can be converted to the Index of Multiple Deprivation (IMD) [51] within the Trust prior to electronic download to the research team. We will also retrieve service resource costs from the INSIGHT system. Data will be stripped of strong identifiers prior to any analyses by the research team.

Primary outcome measure

Our primary outcome will be depression severity and symptomatology as measured by the PHQ-9 at 6-months and at 12-month follow-up. The PHQ-9 is a widely used measure of depression in primary care services in England and part of the MDS for IAPT and is now common currency in major UK trials of depression (CADET [40], REEACT [42], COBRA [43], and CoBAIT [44]

Secondary outcome measures

We will also collect the CORE-OM, BDI-II, EQ-5D-5L, WSAS and GAD-7. In addition we will collect health care utilisation by an adaptation of the Client Service Receipt Inventory (See Appendix 3).

We will administer a patient satisfaction questionnaire, the Client Satisfaction Questionnaire (CSQ), at 6-months (Appendix 3).

Summary of measurement of outcomes and duration of follow up

Primary outcome: Our primary outcome is PHQ-9 score at 6-months post-randomisation adjusting for baseline score.

Secondary outcome measures: Our secondary outcome measures are PHQ-9 scores at 12 month follow-up, adjusting for baseline and CORE-OM, BDI-II, EQ-5D-5L, GAD-7 and WSAS at 6 and 12-month follow-up, adjusting for baseline. We will also collect client service receipt data at 6- and 12-months. In addition, outcomes will be compared at the last therapy session using routinely collected PHQ-9, GAD-7 and WSAS.

At 4-weeks post their last session (whether an agreed ending or not), patients will contacted by their preferred means with a brief questionnaire asking them about their experiences with the treatments. Completion of this questionnaire will also be considered via a secure website portal.

PSYCHOLOGICAL INTERVENTIONS BEING COMPARED

Candidate intervention

As outlined earlier, the intervention being evaluated is Counselling for Depression (CfD) [12,13]. It is specifically designed to address depression and to be delivered within IAPT services. It is a form of Person-Centred/Experiential (PCE) therapy derived from the competences required to deliver effective humanistic psychological therapies [12,13] CfD is drawn from those humanistic approaches with the strongest evidence for efficacy, based on outcomes of controlled trials [for a review, see [5].

CfD is premised on the assumption that people have a natural tendency to develop to their full potential. However, when they become depressed, the assumption is that many people lose this natural tendency and that CfD may help them to get back on track. CfD has two central tenets.

First, the development of a trusting relationship between the counsellor and client. The counsellor aims to ensure that the client feels accepted and understood and that their counsellor is not judging them in any way. Second, rather than focusing on symptoms, CfD views the client as a whole person and tries to understand their world from their point of view. Accordingly, CfD places a special emphasis on building an effective therapeutic relationship. This is because it is seen as the starting point for helping clients, and that without this trusting relationship change is unlikely to occur. [12]

The CfD curriculum was developed by BACP (the British Association for Counselling and Psychotherapy; sponsored by DH) and the work of the design team informs this protocol. The programme trains counsellors to provide a depression-specific therapy for individual clients (in an IAPT setting where a client has not responded to low intensity intervention or actively opts for counselling). The CfD competences are outlined in an IAPT-endorsed framework drawn from a number of NICE-endorsed research studies and from key texts identified by the Humanistic Psychological Therapies Expert Reference Group that describe the modality and underpin its effectiveness. [52] Person-Centred Counselling [53] and Emotion-Focused Therapy [54] have much in common both theoretically and in terms of their methods. When used in combination they are often referred to as Person-Centred/Experiential Therapy.

Training of counsellors in Counselling for Depression (CfD)

Training the counsellors to a standard of CfD is taking place comprising two-key stages of training.

Stage 1: Training events & materials

A total of 27 counsellors from the Sheffield IAPT service attended a 5-day training in CfD led by Trish Hobman and Lynne Lacock (York St John) in April/May 2013. The 5-day training followed an established agenda as set out by associated training providers. All counsellors attending the training provided a videoed example of their work as carried out with a counsellor colleague at the training event (i.e., not involving clients). The tapes were assessed for basic competence in the CfD model by the trainers at York St John. All the counsellors passed this initial assessment. A second 2-day training workshop is planned for 25th/26th November 2013 for the counsellors to receive in-depth training in the emotion-focused component of CfD. This workshop will be led by Professor Robert Elliott (co-investigator) and Lorna Carrick (University of Strathclyde).

The training is supported by the publication of a key text on CfD to which the counsellors are being given pre-publication access and then a copy once published in March: Hill, A. & Sanders, P. (in press). *Counselling for Depression*. SAGE publications. In addition, a CfD Manual has been written, termed a Clinical Practice Guide (CPG), in order to guide the delivery of CfD in the trial. The CPM has been developed with input from co-applicant Gabriel, CfD trainers (Lacock & Hobman), and the lead CfD practitioner in the Sheffield IAPT service (Davies). It does not present any new component of CfD but simply acts as a reminder to all practitioners to adhere to the treatment model being delivered

Stage 2: Determining competence of counsellors working in the CfD model

The counsellors are required to complete 80 hours CfD experience in four blocks of 20 hours with these sessions being audio-taped. It is standard practice within the IAPT model of competencies and within Sheffield IAPT for counsellors (and CBT therapists) to audio-record sessions in order to receive quality supervision. This is consistent with the CfD national curriculum (points 4.7.2, 4.7.7, & 6.1 in National Curriculum). The procedure for rating audiotapes will be used as a template for obtaining competence ratings.

Practitioners will select one tape from each of the 4 blocks of 20 tapes submitted to the expert trainers to be assessed on a developmental trajectory. The final tape assessment determines their competency as a CfD practitioner. These standards are set out in the IAPT national document and are, therefore, national standards that are expected for any person working as a CfD practitioner. The tape will be rated on the PCEPS.

Comparator intervention

The comparator will be high-intensity CBT as delivered within the Sheffield IAPT service. The curriculum for high intensity CBT states that CBT is now known to be an effective treatment option for many problems. In the National Institute for Health and Clinical Excellence's (NICE) guidelines for anxiety disorders and depression CBT was strongly recommended. [10] CBT within the IAPT service comprises two protocol driven interventions: Beckian cognitive therapy [56,57] and Martell's behavioural activation. [58] These interventions are delivered by high-intensity CBT practitioners in accordance with NICE guidance in which CBT and BA are recommended for the treatment of mild to moderate depression but only CBT for the treatment of severe depression. Although the current COBRA trial is addressing the comparative efficacy of BA versus CBT for depression [43] the comparator treatment in this trial will be confined to CBT only so as to ensure clarity of the comparator and to maximize comparison with other trial evidence using CBT. To ensure equal commitment to the comparator treatment, a top-up workshop for the CBT practitioners will be organised before the trial starts, so that all practitioners have received up-to-date training in their respective treatment method prior to the trial. Clinical supervision will be carried out as standard in line with IAPT guidelines. This will be monitored and logged. This process and procedure is separate from the evaluation of treatment competence, which is addressed later.

The delivery of CBT will be standardised by adoption of the Judith Beck text '*Cognitive behaviour therapy: Basics and beyond*' (2nd edition) [57], which will be made available to all CBT practitioners supporting the trial. In addition, a CBT Manual has been written, termed a Clinical Practice Guide (CPG), in order to guide the delivery of CBT in the trial. This has been based on a similar CPM written for two recent major UK trials of CBT: CoBaLT and COBRA (Kuyken & Kidney, 2011) [59]. The CPM has been adapted and developed with input from trial co-applicants (Kellett & Waller) and the lead CBT practitioner in the Sheffield IAPT service (Bliss). It does not present any new component of CBT but simply acts as a reminder to all practitioners to adhere to the treatment model being delivered.

Re-fresher training of CBT practitioners in Beckian CBT

The CBT practitioners all meet the IAPT training standards. However, they will be provided with additional training directed to ensuring that their delivery is consistent with Beckian CBT. Four half-day workshops focusing on CBT treatment of depression will be led by Paul Bliss (Lead CBT therapist) and Dr Stephen Kellett (IAPT CBT Manager, and Co-Investigator). To ensure that CBT practitioners are adherent to the model prior to starting the trial, a single audio-tape will be rated blind by an expert using the CTS-R.

TREATMENT FIDELITY AND PROCESS ANALYSES

All therapy sessions will be routinely taped with consent from clients as a standard part of practice within the IAPT service. The service policy is for therapists to take tapes to clinical supervision. The use of selected tapes will be made for two main purposes: (a) *treatment fidelity (i.e., competence)*, and (b) *process analyses* of common factors and therapy-specific mechanisms of change.

Treatment fidelity

Regarding assessing treatment fidelity, our strategy will ensure that tapes from each practitioner are sampled in order to establish that each treatment arm is being delivered according to the specified standard. The procedures for assessing treatment fidelity will be identical for both interventions. The description here applies to each intervention arm. The raters for the two interventions will be independent in order to minimise contamination.

Stage 1 (Calibration): A sample of 5 tapes (one from 5 practitioners selected at random) will be rated by 1 national expert and 2 local raters in order to determine the level of inter-rater agreement using the national rater as the target. These will be used as a source for establishing agreement for the locally recruited raters. The national rater for CfD will be Peter Pearce (Metanoia) or person appointed by them, and for CBT will be based at the Oxford Cognitive Therapy Centre (OCTC; Helen Kennerley), or person appointed by them.

Stage 2 (Competence ratings: local). Digital recordings of sessions will be selected at random using the following procedure:

Therapist level: For each therapist, one case will be selected at random per block of 5 seen cases (or upwards of 5). This translates into the following sampling: 1-9 cases = 1 tape; 10-14 cases = 2 tapes; 15-20 cases = 3 tapes. Hence, the sampling strategy ensures that (a) all therapists are sampled, and (b) that the pool of rated tapes and overall competence ratings reflect the differential loading carried by therapists.

Session level: For each case sampled, the selected session will be randomly selected from early (excluding session 1), middle, or late (excluding final session).

Based on a therapist sample of 25 practitioners per treatment arm (i.e., 50 in all) and 500 completed client cases, if all practitioners saw equal numbers of patients, then this would result in each practitioner seeing 10 clients in the trial. This would result in 2 cases being selected on average and the 2 sessions being randomly selected from early, middle, or later sessions. Hence, each therapist would have 2 tapes rated. Hence, 2 tapes x 25 CBT practitioners yields a total of 50 tapes, and the same number for CfD. This yields a theoretical total of 100 tapes to be rated in the trial although the actual number will be a function of any differential loading of cases on practitioners. However, the actual number of tapes will be a function of the caseload of practitioners and so the number may be less.

Stage 3 (Competence ratings: national): A subsample of the rated tapes will be rated blind by national experts at a sampling density of 20%.

The samples from CfD and CBT will be rated by independent sets of raters, so as to avoid contamination, using the Person-Centred and Experiential Scale [PCEPS; 60] for CfD and the Cognitive Therapy Scale-Revised [CTS-R; 61,62] for CBT sessions. We will also require supervisors to log practitioners' presentations and record a simple index of competence.

This combined sampling strategy will ensure that the work of all practitioners is sampled in accordance with their wte but it will not be possible – nor it is required – for all clients to be sampled. However, the supervisor log will provide information on the percentage caseload that is presented at supervision for each practitioner. Co-I Elliott is experienced in the use of the PCEPS and Co-Is GW and SK similarly so in the CTS-R. Raters will be drawn from the community of CBT practitioners in Sheffield (not involved in the trial) and CfD practitioners and experts nationally.

Process analyses

In order to achieve a fuller understanding of patients' experiences of CBT and CfD and how these impact of the course of treatment, we will carry out a programme of process studies using a defined sampling frame comprising (A) Therapy non-completion and account of change (based on questionnaire returns and selective interviews), (B) Patient engagement, resilience, and therapeutic alliance (based on subsample of routinely collected tapes); and (C) the phenomenon of sudden gains and deteriorations (based on routinely collected sessional PHQ-9 scores).

A. Therapy non-completion and accounts of change (Hardy as lead co-investigator**)**

A key finding within psychotherapy research literature as well as IAPT services is the relatively high dropout rate, with clients who drop out of therapy having, generally poorer outcomes than those who complete therapy. [63] In the Sheffield IAPT routine data, the rate of clients who did not complete their scheduled therapy was 37.7%. Using the trial data we will compare the dropout rate for the two therapies and will use the routinely collected data to compare PHQ-9 scores at last session attended for those clients who do not complete therapy.

In addition, we will seek the agreement of participants, during the consenting process, for us to contact them by telephone or method of their choice, when they either complete their therapy by agreement with their practitioner *or* if they unilaterally stop attending therapy, to take part in a brief exit interview.

If they have unilaterally terminated therapy, the aim is not to persuade them to return, but to identify factors that have led to their decision to leave. We will carry out a brief semi-structured telephone interview (see Appendix 5) from which responses will be coded. Responses will enable us to distinguish between those clients who leave unilaterally due to perceived improvements versus those who exit for negative reasons. The results of these analyses have the potential for improving practice and addressing the pressing issue of non-completion of therapy.

In addition, we will contact a subsample of clients on completion of their treatment (CfD and CBT) to carry out an interview to ascertain qualitative accounts of the changes (or not) in understanding, functioning and approach in their lives. In effect, we are seeking evidence for what has changed in their lives and in their social context. (See Appendix 5 for topic guide.) We will seek to interview 25 people from each treatment arm using purposive sampling.

Our reasoning for this line of research is the need to triangulate evidence of the outcomes of self-report measures following psychological interventions with clients' accounts of the intervention. While self-report outcome measures are highly valued, they yield statistical accounts of recovery based on cut-off scores and invariant items. It is important to be able to translate accounts of statistical recovery into meaningful accounts and also to identify cases where clients' accounts do not tally with statistical accounts. We will provide training for the team members carrying out any telephone interviews and they will need to be blinded to the self-report outcomes to ensure they do not lead the respondent. We will address this requirement via an experienced colleague (Connell) who has carried out many client interviews in previous studies. We will use King's Template Analysis to analyse clients' accounts of change/no change. [64-66]

B. Patient engagement, resilience, and therapeutic alliance (Hardy as lead Co-Investigator**)**

We will investigate the contribution and role of resilience in clients' responses to treatment and differential therapist outcome. This proposed work builds on work carried out in a D.Clin.Psy dissertation supervised by CI Barkham and Co-I Kellett in which therapist resilience as measured by the CD-RISC was the only variable that differentiated between the most and least effective PWPs. The proposed study will have both clients and step 3 therapists complete the CD-RISC prior to their entry into the trial and will determine the extent to which resilience predicts patients' outcomes in both therapies and therapist resilience predicts better overall outcomes. [67-69]

Building on the above work strand, we will analyse a selected subset of the audio recordings of sessions 1-3 to identify helpful and unhelpful therapist activities, relationship patterns, and levels of patient engagement that characterise sessions of patients who completed and those who dropped out of therapy. We will also consider whether the characteristics of CfD and CBT differ and if so whether these characteristics are related to outcome.

This study will utilise the first three session recordings of a subsample of patients to identify potential markers in the initial 3 sessions that predict outcome. A sample of 100 tapes, one from each of 100 clients would make it possible to detect a correlation of .27 with a statistical power of .80 (alpha = .05); this is about the size of effect commonly found in meta-analyses of the relation between alliance and client outcome. We will use this power calculation to derive an independent N of 100 cases (each x 3 sessions) based on 2 (good/poor) outcome types x 2 (CfD/CBT) treatments. These selected sessions will be rated for engagement and specific markers identified that distinguish between the good and poorer outcome cases.

Analyses of these sessions will be carried out in the context of client-reported outcomes and their own accounts of change/no change. This strand of work will provide data that will enable an analysis of the process from engagement in therapy to differential outcomes. Analyses will include qualitative analysis of audiotapes, and will be the area assigned for the PhD studentship due to the relatively high resource needed. The work will be supervised by Co-I Hardy and CI Barkham, both of whom have a track record in carrying out process studies within the context of trials [70-73]

We will enhance this work by investigating the key common factor of the therapeutic relationship [74-75] We will utilise the same data set as above and the research will be carried out by D.Clin.Psy trainees under supervision. The aim will be to investigate differences in the components of the therapeutic alliance between CfD and CBT but also to consider the role of the therapeutic relationship together with resilience. We will use the Working Alliance Inventory to elicit independent ratings of the alliance, using multiple raters, with raters blinded to the treatment condition. [76,77]

C. Sudden gains and deterioration (Hardy as lead co-investigator lead**)**

Subsequent to the completion of the trial, we will test for the presence of *sudden gains* in both therapies using the session-by-session data that is collected as standard (i.e., PHQ-9) as part of IAPT MDS. There is currently considerable interest in this phenomenon within CT [78-80] but has not been examined to the same extent in counselling. There is also a related literature on *gradual gains* as well as *sudden deterioration.* A fundamental component of studies investigating these related phenomena are the collection of session-by-session measures that tracks change over time. We will use the PHQ-9 to carry out these analyses. We have analysed data from a practice-based study from the Sheffield IAPT data and have found the method appropriate and sensitive to detecting sudden gains. [Hardy/Thorpe] We will consider the relationship of sudden gains to outcome for both treatment arms. This is a research area in which Co-I Hardy has established an international reputation and will lead research in this area. [81-83]

PLANNED ANALYSES

Analyses will be carried out by a statistician (Mukuria) supervised by a senior statistician from CTRU (Co-I Bradburn). Neither will be involved in the administration of the trial and both will be blinded to the randomisation. Key variables (i.e., treatment assignment) will be coded as non-identifiable variables (e.g., variable A, variable B) in order to minimise potential biasing in analyses.

Primary analysis

The baseline-to-6 month follow-up change in PHQ-9 will be analysed using multilevel modelling in which therapists are a random intercept and the fixed effect covariates will include the treatment group and baseline PHQ-9 (plus other possibly significant covariates such as number of sessions and medication use). The difference between the treatment groups and its two-sided, 95% confidence interval (CI), will be calculated. Non-inferiority of counselling to CBT will be concluded if the CI lies entirely above the non-inferiority limit of -2 units (i.e., that a difference as large as 2 units in favour of CBT has been ruled out). The primary analysis will be undertaken on all clients randomised (ITT) alongside per-protocol and complier-average causal effect (CACE) analyses as recommended by the extension to the CONSORT statement for non-inferiority trials [84] The use of ITT for the primary analysis is in keeping with the real life setting in which a substantial proportion of patients do not attend all sessions. However, protocol adherence (non-attendance, early termination of therapy, switchover) will be monitored and reported in detail for each arm, along with the reason (where known) for non-adherence.

Secondary analysis

This will consider baseline to 6 month and baseline to 12-month change in PHQ-9, BDI-II, EQ-5D-5L, CORE-OM, GAD-7 and WSAS using the same methodology as for the primary outcome. Similarly, change from baseline to the routinely collected end of therapy score on PHQ-9, GAD-7 and WSAS. The proportions of clients making reliable and clinically significant change [85] on PHQ-9, BDI-II, and CORE-OM will also be compared. Additional exploratory analyses will be used to identify characteristics of clients and therapists that are predictive of better outcomes overall and within each therapy. In addition, the number and effect on outcome of clients experiencing sudden gains in each treatment arm will be compared as will the reasons why clients leave therapy prematurely.

Routine service data for client cohort (Bradburn as lead co-investigator**)**

For the period spanning client recruitment into the trial (i.e., approximately 15 months), all clients who are stepped up to step 3 will define the client cohort within which the trial is embedded. Data collected routinely as part of the service for non-trial participants will be made available in anonymised form as a comparator. These data will provide added value in terms of external validity and will allow comparisons to be made between trial participants and non-participants, to consider the representativeness of our research sample. The ability to derive this comparison as a function of the comprehensive cohort design addresses a key limitation of trials methodology in terms of external validity. Crucially, we will be able to determine the relative outcomes of those clients who were offered entry into the trial as compared with those who were excluded because of a strong preference or other reason. Because the primary outcome measure is standard throughout the IAPT services, the outcomes of trial and non-trial clients can be compared with those from published literature on counselling and CBT within routine IAPT services. [86-89]

This approach does not place any additional burden on non-trial participants, as the measures they complete are routine and mandatory as part of the IAPT service agreement. Further, it does not add cost to the proposed study and therefore is clear added value. In addition, as the data will contain sessional PHQ-9 scores, including a last session attended (end of therapy) score, it will be used in conjunction with trial data for further analyses. The adoption of a comprehensive cohort design has been specifically espoused in response to the provision of evidence for future NICE guidance on depression and the proposed trial provides a unique opportunity to deliver such a design that will add credibility to all stakeholders and the wider scientific community.

Missing data

By recruiting sufficient numbers to account for trial dropout to 6 month follow-up, it is planned that primary endpoint data will be adequate to address the main research question. Routinely collected PHQ-9 scores will be available for sessions attended prior to drop-out, and these will be used as part of the imputation process where the 6-month endpoint data are missing. It is also expected that in most cases (80%), the client will remain under follow-up and will continue to provide research data at 12 months post randomization. Isolated instances of missing data will be imputed by linear interpolation. Multiple imputation methods will be used for clients with more substantial missing data, and the sensitivity of the results will be further assessed by imputing alternative values based on the reason for drop-out.

Economic analysis

In line with NICE guidance for assessing interventions, an economic analysis will be conducted to establish the cost-effectiveness of CfD compared to CBT. [90] This aims to establish what the additional benefit and resource implications of CfD are relative to CBT. The primary analysis will be from a health and social care perspective, and will therefore include costs to the NHS and social care services.

The method used to conduct this economic analysis will depend on treatment outcomes. Where treatment outcomes are found to be equivalent based on the primary measure of efficacy, a cost minimisation analysis will be conducted. In this case, the focus will be in assessing any cost differences between CfD and CBT. Total costs of each intervention will be estimated using the number of sessions multiplied by national unit costs and data from the local trust. The consequences for the use of other health and social care resources (including hospital admissions, outpatient attendance, GP visits, other therapy and medication) will be measured using a patient completed resource use questionnaire and

service data and costed with national unit costs. Individual level mean costs (intervention and other resource use) for CfD and CBT will be compared; uncertainty around the costs estimates will be generated using probability sensitivity analysis. One-way sensitivity analysis will be conducted on key assumptions such as the number of sessions.

Where one intervention proves to be more effective, then a cost effectiveness analysis (CEA) will be undertaken using the estimated incremental cost per quality adjusted life year (QALY), that is, the difference in outcomes divided by the difference in costs for CfD and CBT. The primary outcome measure for the CEA will be the EQ-5D-5L. The EQ-5D-5L is a generic preference-based measure of health designed for calculating QALYs. It is composed of 5 dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression, each with 5 levels which describes 3125 health states in total. The EQ-5D-5L is a revision of the EQ-5D, the NICE recommended measure for economic evaluation, offering better sensitivity. [46] Valuation of the EQ-5D-5L is ongoing and these values will be used to generate utility values for the health states described by the measure. If these values are not published, then an existing method to generate utility values from the EQ-5D will be used [91] QALYs will be estimated from the EQ-5D-5L collected from patients at baseline, 6 and 12 months. Individual patient level data on costs and QALYs over 12 months will be used to estimate the mean cost effectiveness of CfD compared to CBT and the underlying uncertainty around it by a probabilistic sensitivity analysis. One-way analysis of key assumptions will be undertaken and where differences persist at 12 months then the analysis will be extrapolated beyond 12 months.

Additional analysis will include assessing outcomes for CfD compared to CBT in terms of the proportion who achieve reliable and clinically significant improvement based on the PHQ-9. [92] Patients will be classified as having had a reliable and clinically significant improvement if they change by 6 points *and* move from a clinical population at baseline (10 and above) to a non-clinical population (9 or less) at 12 months. This will be combined with incremental costs to establish the incremental costs associated with reliable and clinically significant improvements.

PROJECT TIMETABLE INCLUDING RECRUITMENT RATE

Recent service figures indicate a large client throughput and service capacity with 3310 clients receiving a step 3 treatment in a 12-month period. However, the need to maintain the integrity of the trial, to impose inclusion/exclusion criteria and avoid excessive or differential waiting times means that the number of suitable participants will be considerably less. Appendix A shows the study recruitment procedure for each site, while Appendix B and C are CONSORT diagrams showing trial throughput for different phases of recruitment (Waves 1 and 2 – see below) respectively. Estimates for inclusion at each stage of recruitment, outlined below, have been derived from service data, literature and discussions with service managers and are in general conservative. They will be monitored along with monthly and quarterly recruitment figures from the start of recruitment and any serious deviations or problems with recruitment will be addressed immediately.

Recruitment and recruitment rate is based on the following:

At the point where the client is considered suitable for stepping-up (Stage 1), they will only be considered for the trial if both therapies at the recruitment site have a waiting time of between 2 to 12 weeks and the difference in waiting times between treatments does not exceed 3 weeks. Additional therapy funded by excess treatment costs may provide a means of maintaining equilibrium of waiting times between treatments to some degree but we expect up to 40% of clients may be excluded from the trial for this reason.

Service data indicate that 30% of clients have a PHQ-9 score < 12 at the start of a step 3 treatment, therefore clients will also be excluded if their score on PHQ-9 is <12 at the stepping-up assessment.

The number of clients having no strong preference for treatment type has been estimated at 70% therefore a further 30% of clients are likely to be excluded at Stage 1. Clients still eligible will be given information about the trial and will be placed on the waiting lists for both therapies and will be invited to attend a screening interview 1-2 weeks prior to their start of therapy date. We expect around 80% of eligible clients to attend the screening interview. Although all will have scored ≥12 on PHQ-9 at the initial assessment stage, it is likely that those meeting a formal diagnosis will be fewer. In a comparison between SCID diagnosis and a PHQ-9 cut-off of 12, 15% of those scoring 12 or more on PHQ-9 did not meet diagnosis criteria on SCID. Therefore we expect a further 15% of clients will be excluded.

It is expected that no more than 10% of clients will withhold consent to the trial after attending the screening assessment. Following randomisation clients will be removed from the waiting list of the therapy not randomised to.

Using these estimates we expect 595 clients per annum (around 50 per month) to be eligible for recruitment and randomisation. However, only those sites with a CfD trained counsellor could refer clients to the trial. Following the CfD training course and subsequent experiential training, it is estimated that CfD counselling capacity will be at least 50% by the start of recruitment, with other sites joining the study as their counsellors complete the training, this could rise to 100% by the seventh month of recruitment.

To ease feasibility and client flow considerations, we have estimated a 50% capacity (25 per month) for the first 6 months of recruitment (Wave 1) followed by 90% capacity (45 per month) for a further 9 months (Wave 2). Approximately 152 clients could be recruited in Wave 1 and 404 in Wave 2 over a 15-month recruitment period. With a 10% loss to follow-up, those providing 6 month follow-up data will number 136 from Wave 1 and 364 from Wave 2, a total of 500, therefore meeting our sample size requirement (Appendix B and C).

Planned recruitment would begin at the start of month 6 and cease in month 21. However, if necessary recruitment could continue for a further 2 months which would still allow the collection of the last 12 month follow-up data, at month 35.

Summary of project timetable

0-4 mth	Project set up time, research staff recruitment, and infrastructure set up. Road testing procedures
3 mth	PWPs begin introducing the trial and screening appointments arranged
6-12 mth	Wave 1 recruitment; training competence raters
12-21 mth	Wave 2 recruitment
12-27 mth	Wave 1 & Wave 2: 6-month follow-up assessment
18-33 mth	Wave 1 & Wave 2: 12-month follow-up assessment

Project timeline, indicating key milestones and objectives with dates

Milestone	Month	Objectives
1	1-4	Project begins; Secure ethics and initiate governance approvals; Establish infrastructure and test; Appoint staff
2	3	PWPS begin introducing the trial and arranging screening appointments
3	6	First client enters trial with Wave 1 practitioners
4	8	Pool of competence raters secured
5	11	Competence raters trained
6	12	First client enters trial with Wave 2 practitioners
7	21	Last client enters trial
8	24	Competence ratings completed
9	27	All 6-month post-randomisation follow-up data collected
10	28	Analysis and report writing initiated
11	33	All 12-month post-randomisation follow-up data collected
12	34 - 38	Dedicated analysis and report writing. Write up completed

1. The 12 milestones listed above set out the major stages of the proposed trial and the timeline for its successful completion. Each is commented on below. On receipt of funding, some processes can begin (e.g., staff recruitment, preparation of materials/equipment). The project will officially commence on 1/1/14 and the dedicated new RA appointment and PhD student will start as soon afterwards. The CI (MB) and Project Manager (DS) will initiate the ethics and governance procedures prior to 1/1/14and the milestone is to have these agreed and the infrastructure in place by March 2014.
2. Following ethics approval, PWPs will begin informing suitable clients about the trial.
3. The first client to enter the trial with the Wave 1 practitioners at 6 months (June 2014). This will enable a recruitment period of 15 months (to end August 2015).
4. Raters for competence and a suitable pool of raters will be identified by 8 months (August 2014)

5. Wave 2 practitioners can begin seeing clients in the trial at month 10 (October 2015).
6. Pool of raters trained at 12 months (December 2015).
7. At 21 months (September 2015), the last client is randomised and enters the trial. A further 2 months of recruitment is available to account for any slippage.
8. Competence ratings completed.
9. All 6-month follow-up data in (March 2016).
10. Analysis of 6 month data
11. 1-year follow-up data collected (October 2016)
12. Full report writing (completed March 2017

GOVERNANCE AND MANAGING RISKS

We will ensure good governance of the trial and reduce risks to patients through management processes within the trial and in collaboration with the Trust. The overarching processes of trial management will be in accordance with the current (2013) version of the Declaration of Helsinki [93]. The trial will be conducted to protect the human rights and dignity of the participant as reflected in the Declaration.

In order to protect the trial participants the following provisions will be made/upheld; the trial has been designed to minimise pain, discomfort and fear and any foreseeable risk in relation to the treatments involved, the explicit wishes of the participant will be respected including the right to withdraw from the trial at any time, the interest of the patient will prevail over those of science and society, provision will be made for indemnity by the investigator and sponsor and a contact name for further information will be provided. In addition, the trial will be registered on an open database before the first patient enters the trial and there will be an undertaking to publish or make publically available the results of the trial to the wider scientific community, including negative and inconclusive results.

Risk procedures and reporting of adverse events

We will set out and follow standard operating procedures in relation to assessing patient risk and reporting and acting upon serious adverse events. All associated research staff will be trained in the recognition of and response to distress and risk. Written protocols will be followed, based on the standard operating procedures of the Clinical Trials Research Unit (CTRU).

Governance of the trial

A Trials Management Group (TMG) will oversee the day-to-day management of the trial and will comprise the core members of the team (i.e., Chief Investigator, Project Manager, and direct research staff). A Trial Steering Group (TSG) will be convened with an independent Chair and include the Chief Investigator and key members of the trial team (for reporting purposes). It will include the Trust R&D Manager, representatives from Depression Alliance, inter alia.

An independent Data Management and Ethics Committee (DMEC) will be established with an independent chair. This will adhere to the Standard Operating Procedure of the Clinical Trials Research Unit. It will meet twice during the trial, first at the end of Wave 1 or 6-months after start of recruitment, and second at 12-months. The DMEC will consider recruitment, data issues and any adverse events. It will report to the Trial Steering Group (TSG).

IMPACT ON POLICY, PRACTICE AND SERVICE DELIVERY

The study has been designed in order to give it the best likelihood of impacting on policy makers and to be considered as appropriate evidence to inform the next Guideline Development Group for depression. The results will provide evidence for CfD as compared with high-intensity CBT. Our focus has been on delivering the best methodology within the cost-limits of the funding. Further, the research team has been established with this agenda specifically in mind. To that end, we have not only assembled a top-rate team of researchers, but we have also actively involved key academics in the team who are well attuned to policy initiatives and who have very specific roles in ensuring that the trial has the best probability of meeting this agenda whilst also holding a position of equipoise.

The results will inform, and thereby impact on, policies in the four areas that the research study targets: (1) acceptability, satisfaction, and choice, (2) effectiveness, (3) cost-efficiency, and (4) economics of counselling for depression.

1. Acceptability, satisfaction, & choice

There is a preference for talking therapies in contrast to medication. This is allied with a national drive towards reducing the public's reliance on medication and the associated financial burden to the NHS. This requires there to be sufficient breadth of options within the talking therapies to meet demand and provide choice. That is, the provision of counselling for depression has workforce planning implications (to meet demand) and client preference implications (to address choice). At present, it may be the case that some clients base their choice on misunderstandings or misperceptions of the evidence. The current guidance from the Guideline Development Group for depression regarding the caveat on counselling is one that urgently needs to be addressed in order to give clear and unequivocal evidence on the comparative outcomes of counselling versus CBT for moderate and severe depression. In addition, initial data from our practice-based studies suggest a lower dropout rate for clients in counselling compared with CBT. This finding needs to be replicated within trials methodology.

2. Effectiveness

Notwithstanding issues of acceptability and choice, psychological therapies and counselling need to be evidence-based. Although there is substantial evidence from meta-analyses and practice-based studies (see Section C5), it is crucial that evidence is provided that is acceptable to the GDG for depression. The findings also have important implications for GPs appropriately referring clients to IAPT services and for the commissioning of counselling for depression services more generally.

3. Cost-efficiency

Data from the practice-based analyses of the Sheffield IAPT services indicate that counsellors see clients for fewer sessions, a finding, which if replicated in the trial, may have implications in terms of gains being achieved more efficiently.

4. Economics

The economic analysis via health utilities will provide robust data upon which to base counselling for depression for commissioners and workforce planning.

DISSEMINATION OF RESULTS AND PROJECTED OUTPUTS

We will set out clear outputs aimed to have an impact at different levels.

- We will seek to publish the trial protocol in *Trials*, a standard route of informing the scientific community of the trial and promoting transparency.
- We will provide feedback on the end-point analyses as well as the 12-month follow-up to the Sheffield IAPT service and SH&SCT. We would envisage this being a one-day open event, with associated reports produced.

We will identify key national platforms for providing speedy dissemination to the broad scientific and practice community. Foremost amongst these would be the following conferences:

- Annual BACP Research Conference held May/June. The audience would be the broad constituency of UK counsellors
- British Association for the Person-centred Approach (BAPCA)
- Person-centred Therapy Scotland (PCT Scotland)
- World Association for Person-Centred and Experiential Psychotherapy and Counselling (WAPCEPC)
- Annual Savoy Conference. This conference would provide a platform to reach a wider audience within the NHS, particularly IAPT services, as well as the voluntary sector.
- Annual BABCP Conference. The audience would be the broad constituency of cognitive-behavioural practitioners in the UK and Europe.

We will commit to establishing a group responsible for developing a publication plan in order to maximise the yield and impact of the study. Consideration needs to be given to whether to await the 12-month follow-up results in order to publish the main outcome or whether to decouple the 12-month follow-up. An additional consideration relates to the results arising from analyses of clients in the trial versus those who declined the trial and were seen within the standard IAPT service (yielding primary outcome measures at end-point). Possible outputs include: (1) end-point and 6-month efficacy data; (2) economic analysis of end-point and 6-month follow-up; (3) benchmarking trial outcomes with non-trial clients and broader IAPT outcomes locally and nationally; (4) satisfaction with therapies. We will take advice from the TSG.

Notwithstanding these points, we will aim to secure the highest quality publication possible for the main outcome analysis. We would likely target high quality UK journals but would take advice from the TSG and others. We will aim to secure a mainstream journal rather than one allied with either intervention. We will also seek dissemination via the network of service users and also to GPs via their research networks. We will also seek an international approach to dissemination through presentations at meetings of the Society for Psychotherapy Research and international meetings of BABCP.

TEAM EXPERTISE

The team comprises a core Sheffield group and key national figures and has been assembled to reflect a position of equipoise comprising experts in both psychological interventions and an equal emphasis on robust research design as well as maximising the potential for informing policy.

Sheffield group:

Centre for Psychological Services Research (CPSR, University of Sheffield):

Applicants

Michael Barkham (CI: Professor of Clinical Psychology & Director of CPSR); expertise in trial design & effectiveness studies, outcomes measurement, reporting on very large routine data sets. Role: Overall management and delivery of project.

Dave Saxon (Co-I: 0.8wte Project manager); expertise in managing large data sets and preparation for analysis (e.g., IAPT), experience managing projects in SH&SCT, statistics, multilevel modelling. Role: Project management and oversight of client data quality.

John Brazier (Co-I: Professor of Health Economics); expertise in valuation of health costs, cost effectiveness trials and health utility measures. Role: Supervision of economic analyses

Gillian Hardy (Co-I: Professor of Clinical Psychology & Director of Clinical Psychology Unit); expertise in organisational and qualitative methods for researching patient experience. Role: Lead on process studies of resilience, client engagement, and therapeutic alliance.

Glenn Waller (Co-I: Professor of Clinical Psychology – wef November 2012); expertise in CBT. Role: Lead on CBT quality and competence across both treatment conditions.

Stephen Kellett (Co-I; IAPT Progamme Director); BABCP accredited; expertise in IAPT CBT and PWP training. Role: Lead on CBT training and quality.

Sue Shaw (CPSR Service user); user perspective and linked with a network of users in Sheffield. Role: Provision of client perspective and ensuring appropriate procedures with clients

Employees

Janice Connell (0.6wte; Research Associate); Lead CIS-R interviewer; qualitative interviewing of clients.

Research Assistant (1 wte; TBA): Supporting all aspects of the trial and responsible to PM

DClinPsy trainees aligned with the research team and supervised by co-applicants:

1. Kim Campbell (supervised by Professor Hardy [Co-Investigator]): Therapeutic dropout: a mixed methods study of factors affecting dropout in a counselling intervention for depression.

2. Carole Dunsmuir-White (supervised by Professor Hardy [Co-Investigator): Therapist competence to the CBT model in the treatment of depression in primary care and the impact of therapist competence for dropout.

PhD students (1 wte; TBA): Supporting the RA and process research and reporting to PM/CI

Jo-Ann Pereira: Completing PhD student working with the IAPT service

Administrative support

Sue Ridgway (0.3wte: Clerical support)

Abby Constantine (0.2wte: Administrative support)

School of Health and Related Research

University of Sheffield Clinical Trials Research Unit (CTRU):

Mike Bradburn (Co-I; Senior medical statistician); trial design and consultant on statistical analysis. Role: Independent overview and steering of statistical analysis of trial data

Health Economics and Decision Science

Clara Mukuria (Months 6/12s; Economics analyst/statistician). Role: Outcomes and economic analysis; blinded to trial; data analysis for DMEC

Sheffield Health & Social Care NHS Foundation Trust:

Simon Bennett (Co-I: Head of Sheffield IAPT Service); responsible for Sheffield IAPT service; currently supporting an HTA-funded trial, OCTET). Role: Overall responsibility for PWP and high-intensity practitioners and liaising with research team.

PWP seconded (0.2wte over 36 months) liaison with Trust. Role: Co-ordination of client flow into trial

National group (in alphabetical order):

Pete Bower (Co-I: Professor of Health Services Research, University of Manchester) - design & trials expertise, primary care focusing on complex interventions. Role: Oversight of trial procedures

Robert Elliott (Co-I: Professor of Counselling, University of Strathclyde) – Expertise in Person centred and experiential therapies, methodologist. Role: Lead on CfD quality and competence

Lynne Gabriel (Co-I: Reader in Counselling and Relational Ethics, York St. John University) – training in CfD. Role: Responsible for overseeing the delivery of Counselling for Depression training and supervision.

Michael King (Co-I: Director of Mental Health Sciences & joint Director of PRIMENT Clinical Trials Unit, University College London) – Primary Care; trials design. Role: Oversight on trial procedures.

Steve Pilling (Co-I: Professor of Clinical Psychology & Clinical Effectiveness, and Director of CORE, UCL & Director of National Collaborating Centre for Mental Health) – mental health policy. Role: Oversight of trial procedures in relation to NICE Guideline Development Group.

Non-paid international advisors: Professor Louis Castonguay (Penn State University), Emeritus Professor William B Stiles (Miami University), & Professor Wolfgang Lutz (University of Trier). Inputs to be derived via ongoing collaborations at international meetings.

Non-paid consultant: Emeritus Professor Sue Wheeler (University of Leicester) for expert advice on supervision.

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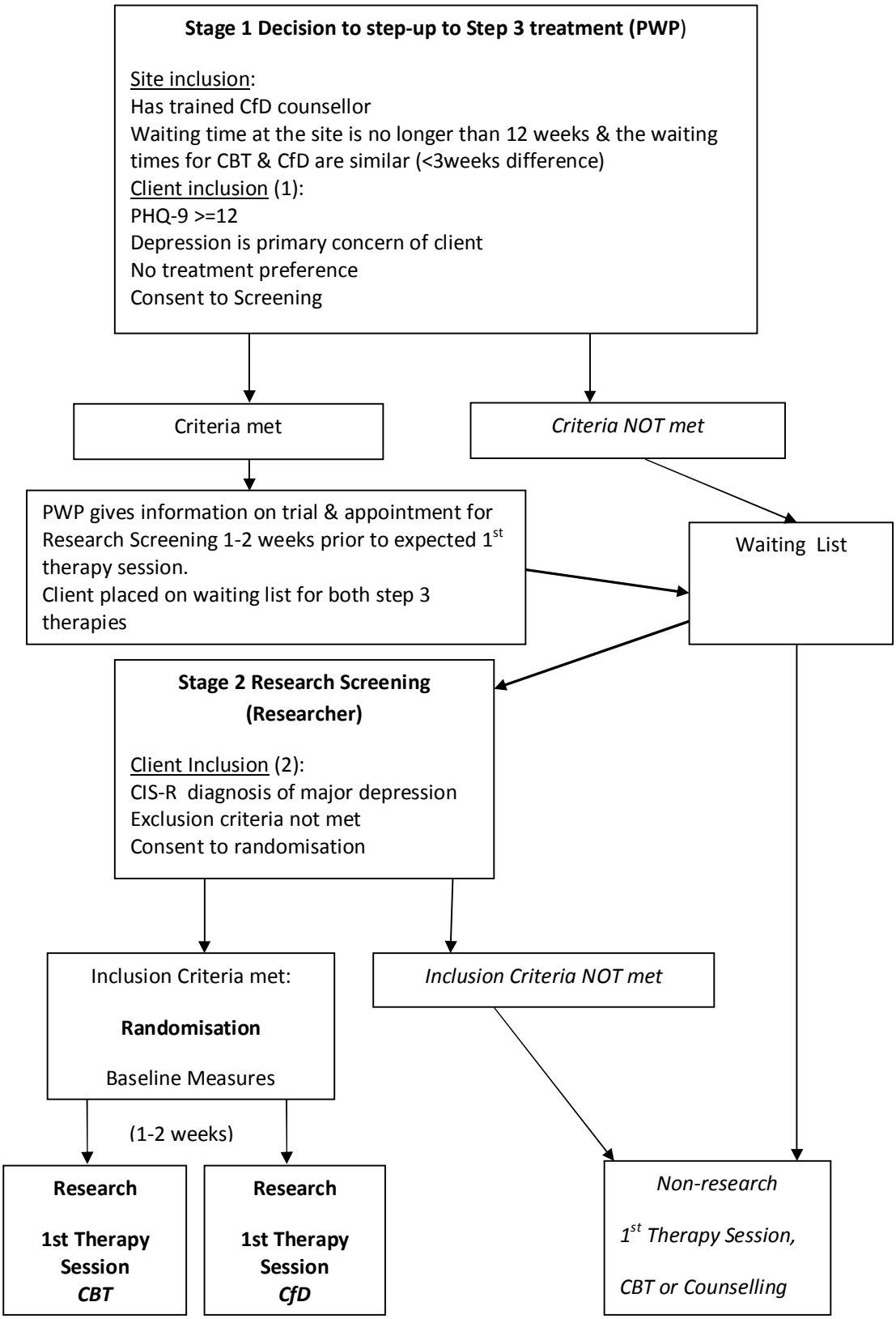
APPENDIX A: Recruitment Procedure

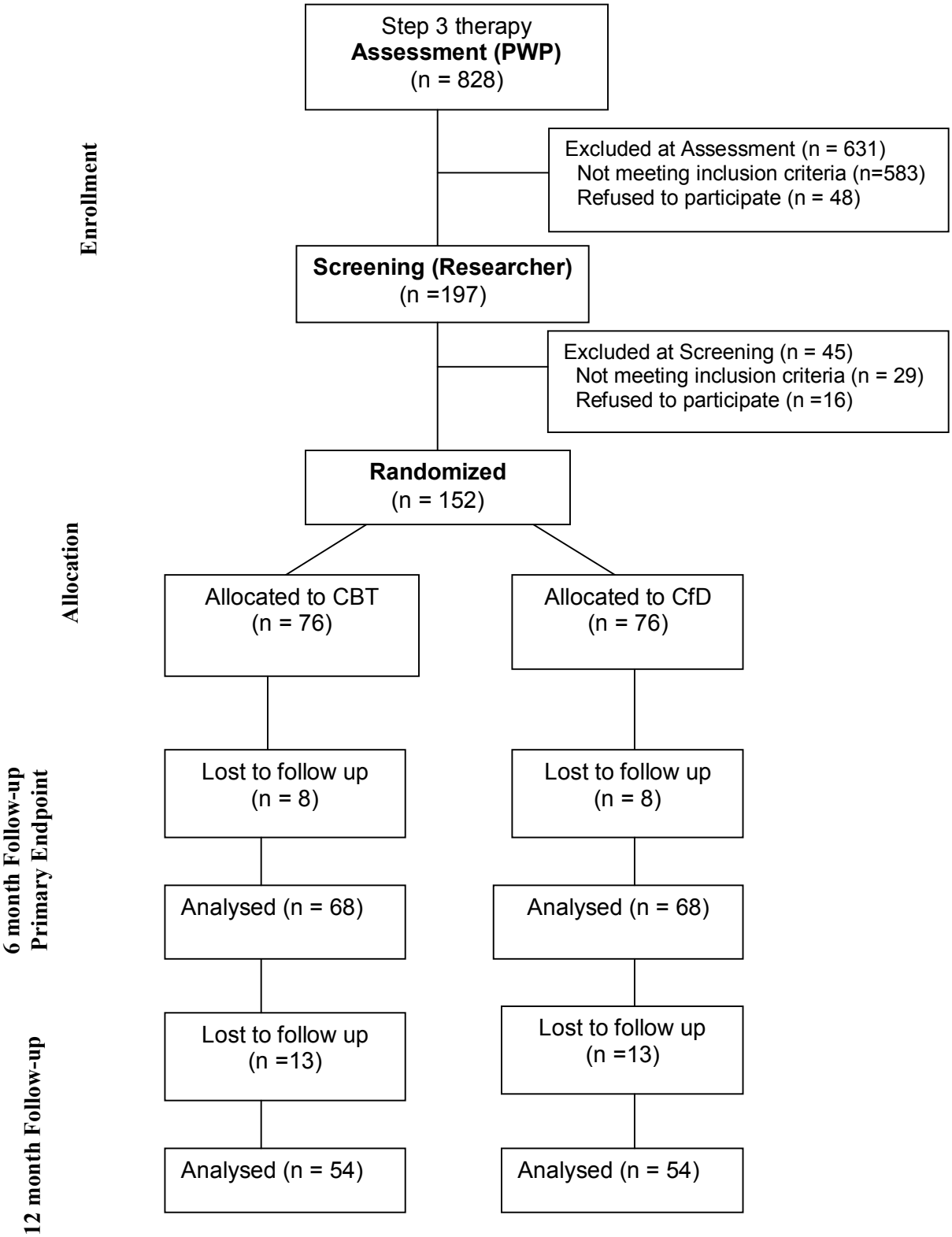
Pragmatic, **Ra**ndomised **C**ontrolled **T**rial assessing the non-**I**nferiority of **C**ounselling and its **E**ffectiveness for **D**epression (PRaCTICED)



APPENDIX B: CONSORT diagram 1

Pragmatic, **Ra**ndomised **C**ontrolled **T**rial assessing the non-**I**nferiority of **C**ounselling and its **E**ffectiveness for **D**epression (PRaCTICED)

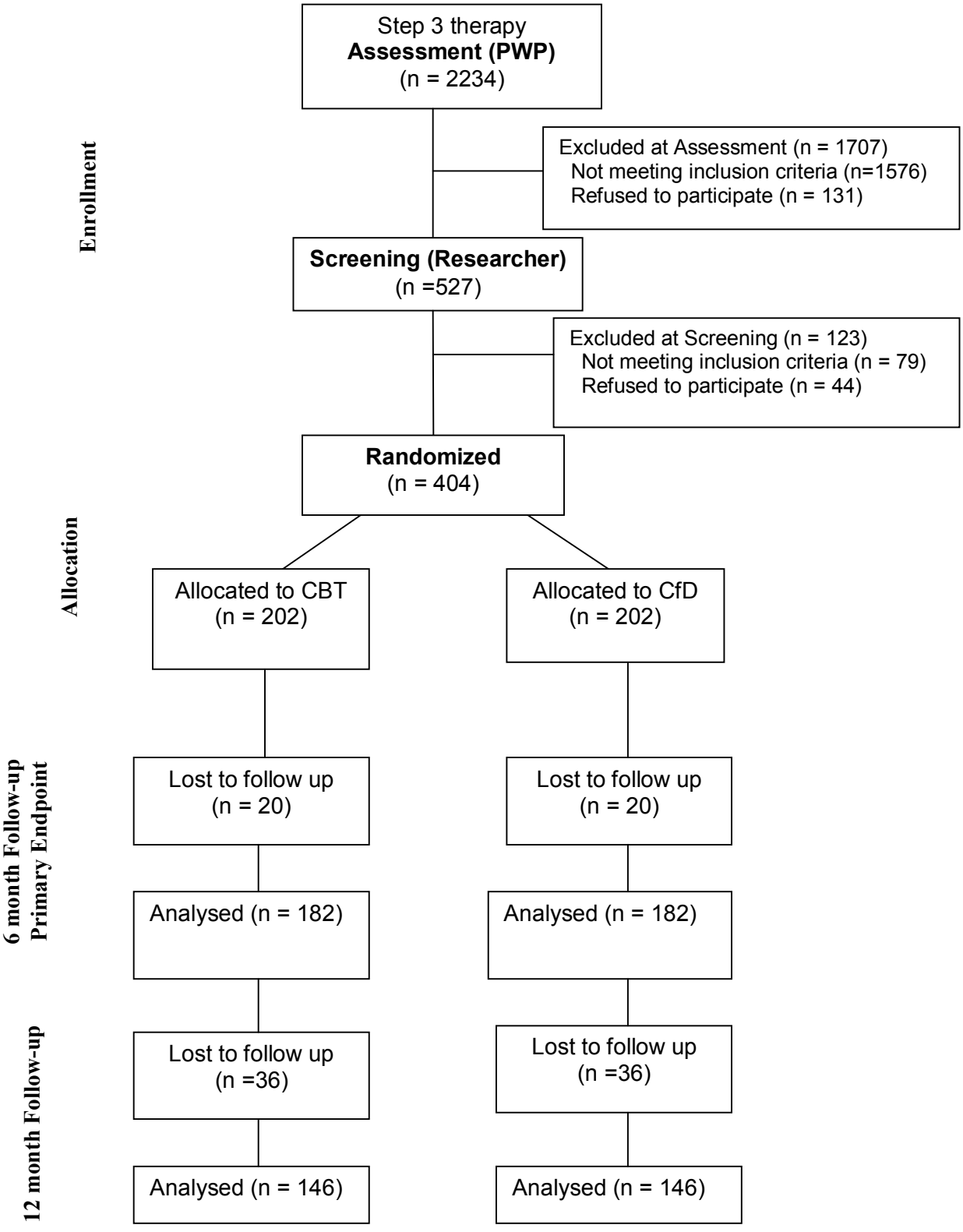
Wave 1 Trial Recruitment (6 months at 50% capacity)



APPENDIX C: CONSORT diagram 2

Pragmatic, **Ra**ndomised **C**ontrolled **T**rial assessing the non-**I**nferiority of **C**ounselling and its **E**ffectiveness for **D**epression (PRaCTICED)

Wave 2 Trial Recruitment (9 months at 90% capacity)



History of amendments to PRaCTICED protocol

Protocol version & date	Specific change	Rationale
V1 20.11.13	This is the pre-trial version	
V2 18.05.15	A holding BDI sent to patient while waiting for treatment	To monitor patient status while waiting for treatment
V3 23.11.15	Inclusion of direct referral procedure Interview procedure/attendance at interview if not attended therapy	To enhance patient referrals
V4 26.01.16	Introduction of central waiting list	To enhance patient referrals
V5 12.04.16	Addition of Sheffield Engagement in Therapy Scale	To support PhD program investigating prediction of outcomes
V6 25.09.16	Addition of ReQoL measure	To provide data on the development of a new outcome measure
V7 23.11.17	Addition of seeking basic demographics information that was not guaranteed from the IAPT log	To ensure better quality information on patient demographics

The changes to earlier revisions to the protocol focused on enhancing patient recruitment while the latter ones focused on securing more information in relation to predicting outcomes, monitoring change, and demographics.

There were no changes made to the primary outcome measure, which was the PHQ-9. Protocol V6 introduced the Recovering Quality of Life (ReQoL-10) measure but the purpose was to gather information on the ReQoL measure rather than to use it to enhance the outcome data on the trial. We never intended to use it in the write-up of the trial and have not done so.

There have been no changes to the end-points, with the primary one being 6-months. The secondary end points are 12-months and end of treatment.

There have been no changes to the analysis plan, which was approved and signed off by the Trial Steering Committee and the DMEC.

There have been no changes to inclusion or exclusion criteria.

The aimed for sample size at recruitment was 550 allowing for 10% attrition in order to secure 500 patients at intake. The power analysis was premised on these figures. Service reconfigurations within the local IAPT service led us, with the support of the Trial Steering Committee, to stop recruiting at 510.