Cognitive behavioural therapy and short-term psychoanalytical psychotherapy versus a brief psychosocial intervention in adolescents with unipolar major depressive disorder (IMPACT): a multicentre, pragmatic, observer-blind, randomised controlled superiority trial

Cognitive behavioural therapy and short-term psychoanalytical psychotherapy versus a brief psychosocial intervention in adolescents with unipolar major depressive disorder (IMPACT): a multicentre, pragmatic, observer-blind, randomised controlled superiority trial

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Summary

Background Psychological treatments for adolescents with unipolar major depressive disorder are associated with diagnostic remission within 28 weeks in 65–70% of patients. We aimed to assess the medium-term effects and costs of psychological therapies on maintenance of reduced depression symptoms 12 months after treatment.

Methods We did this multicentre, pragmatic, observer-blind, randomised controlled superiority trial (IMPACT) at 15 National Health Service child and adolescent mental health service (CAMHS) clinics in three regions in England. Adolescent patients (aged 11–17 years) with a diagnosis of DSM IV major depressive disorder were randomly assigned (1:1:1), via a web-based randomisation service, to receive cognitive behavioural therapy (CBT) or short-term psychoanalytical therapy versus a reference brief psychological intervention. Randomisation was stochastically minimised by age, sex, self-reported depression sum score, and region. Patients and clinicians were aware of group allocation, but allocation was concealed from outcome assessors. Patients were followed up and reassessed at weeks 6, 12, 36, 52, and 86 post-randomisation. The primary outcome was self-reported depression symptoms at weeks 36, 52, and 86, as measured with the self-reported Mood and Feelings Questionnaire (MFQ). Because our aim was to compare the two psychological therapies with the brief psychosocial intervention, we first established whether CBT was inferior to short-term psychoanalytical psychotherapy for the same outcome. Primary analysis was by intention to treat. This trial is registered with Current Controlled Trials, number ISRCTN83033550.

Findings Between June 29, 2010, and Jan 17, 2013, we randomly assigned 470 patients to receive the brief psychosocial intervention (n=158), CBT (n=155), or short-term psychoanalytical therapy (n=157); 465 patients comprised the intention-to-treat population. 392 (84%) patients had available data for primary analysis by the end of follow-up. Treatment fidelity and differentiation were established between the three interventions. The median number of treatment sessions differed significantly between patients in the brief psychosocial intervention group (n=6 [IQR 4–11]), CBT group (n=9 [5–14]), and short-term psychoanalytical therapy group (n=11 [5–23]; p<0·0001), but there was no difference between groups in the average duration of treatment (27·5 [SD 21·5], 24·9 [17·7], 27·9 [16·8] weeks, respectively; Kruskal–Wallis p=0·238). Self-reported depression symptoms did not differ significantly between patients given CBT and those given short-term psychoanalytical therapy at weeks 36 (treatment effect 0·179, 95% CI –3·731 to 4·088; p=0·929), 52 (0·307, –3·161 to 3·774; p=0·862), or 86 (0·578, –2·948 to 4·104; p=0·748). These two psychological treatments had no superiority effect compared with brief psychosocial intervention at weeks 36 (treatment effect –3·234, 95% CI –6·611 to 0·143; p=0·061), 52 (–2·806, –5·790 to 0·177; p=0·065), or 86 (–1·898, –4·922 to 1·126; p=0·219). Physical adverse events (self-reported breathing problems, sleep disturbances, drowsiness or tiredness, nausea, sweating, and being restless or overactive) did not differ between the groups. Total costs of the trial interventions did not differ significantly between treatment groups.

Interpretation We found no evidence for the superiority of CBT or short-term psychoanalytical therapy compared with a brief psychosocial intervention in maintenance of reduced depression symptoms 12 months after treatment. Short-term psychoanalytical therapy was as effective as CBT and, together with brief psychosocial intervention, offers additional patient choice for psychological therapy, alongside CBT, for adolescents with moderate to severe depression who are attending routine specialist CAMHS clinics.

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Research in context

Evidence before this study

Unipolar major depression emerges with the highest incidence risk rate in the second decade of life, affecting a substantial proportion of the adolescent population worldwide. Good evidence exists for psychological treatments being associated with clinical remission in about 70% of cases. By contrast, data are scarce for whether one or more of the available therapies is associated with maintenance of reduced depressive symptoms 1 year after the end of treatment. This issue is not trivial, because maintenance of depressive symptoms below a clinical threshold 12 months after the end of treatment is associated with reduced risk for diagnostic relapse into the adult years. We searched PubMed between Aug 1, 1990, and Aug 31, 2016, with the search terms "adolescence", "depression", "psychological treatments", "randomised controlled trials", "remission", "relapse", "relapse prevention", and "adverse effects". This search identified three trials of school population-based interventions, a small (n=43) feasibility study of a social media intervention for relapse prevention in patients recovered from depression, and a Cochrane database review of relapse prevention in children and adolescents with depression. No identified psychological treatments are currently recommended as effective in maintaining reduced depressive symptoms in the year after successful treatment.

Added value of this study

Our findings show that short-term psychoanalytical psychotherapy and CBT, delivered by highly trained therapists over 28 weeks and 20 weeks, respectively, were not superior to a reference brief psychosocial intervention delivered over 12 weeks by child and adolescent psychiatrists and mental health nurses. All three psychological treatments were associated with an average 49–52% reduction in depression symptoms 1 year after treatment. Prescribing of an SSRI during therapy or follow-up, as per National Institute for Health and Care Excellence guidelines, did not differ between the treatment groups and so did not mediate the outcome. Suicide and self-harm attempts over the follow-up period were lower than at baseline, as were physical side-effects. Furthermore, total costs and quality-of-life scores did not differ between treatment groups by the end of the study.

Implications of all the available evidence

To our knowledge, this is the only high-quality, fully powered, superiority and cost-effectiveness study assessing the medium-term effects and costs of psychological treatments on maintenance of reduced depression symptoms 12 months after treatment. Short-term psychoanalytical psychotherapy is as effective as CBT and, together with brief psychosocial intervention, offers an additional patient choice for psychological therapy, alongside CBT, for adolescents with moderate to severe depression who are attending routine specialist child and adolescent mental health service clinics.

Introduction

Unipolar major depression is a clinically significant mental illness affecting a substantial proportion of adolescents worldwide.[1] Although evidence exists for the effectiveness of treatments in the short term, data are scarce for whether one or more of the available psychological treatments is also able to maintain reduced depressive symptoms a year after the end of therapy.[2,3] This issue is not trivial, because maintenance of depressive symptoms below a clinical threshold level reduces the risk for diagnostic relapse into the adult years.[4] Cognitive behavioural therapy (CBT) offers plausible long-term benefits for adolescents with depression, and is recommended as such by the National Institute for Health and Care Excellence (NICE).[5] Short-term psychoanalytical psychotherapy also shows preliminary promise as a treatment for adolescents with depression. CBT has established clinical effectiveness and relapse prevention, and short-term psychoanalytical psychotherapy has shown similar clinical effectiveness in adults with depression and some clinical effectiveness in adolescents.[6–9]

We did the IMPACT trial to assess the medium-term effects and costs of psychological therapies on maintenance of reduced depression symptoms 12 months after treatment. We tested a primary superiority hypothesis that CBT and short-term psychoanalytical psychotherapy would be more likely to maintain significantly lower depressive symptoms 1 year after treatment than would a reference brief psychosocial intervention. Because our aim was to compare two psychological therapies with a brief psychosocial intervention, we first established whether CBT was inferior to short-term psychoanalytical psychotherapy for the same outcomes.

Findings from previous studies[10] of psychological treatment in adolescents with depression have shown reductions in anxiety symptoms even despite no reductions in depressive symptoms. Therefore, we tested a secondary hypothesis that, compared with participants assigned to receive brief psychosocial intervention, those assigned to receive CBT or short-term psychoanalytical psychotherapy would be more likely to maintain significantly lower self-reported anxiety symptoms, but significantly higher research interviewer-evaluated psychosocial function, 1 year after treatment. Finally, a cost-effectiveness hypothesis tested whether the additional costs of CBT and short-term psychoanalytical psychotherapy could be justified by improvements in clinical effectiveness or decreased use of health and social care services compared with brief psychosocial intervention.

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Method

Study design and participants

We did this multicentre, pragmatic, single-blind, randomised controlled superiority trial in three regions of England: East Anglia, a largely rural area of 3 million people with four urban areas each containing about 100 000 people; North London, a densely populated urban area with around 4 million people; and the North West of England, covering roughly 4 million people of whom about 1 million live in rural surroundings and 3 million live in the city of Manchester. Adolescents (aged 11–17 years) with a diagnosis of DSM IV unipolar major depressive disorder were recruited from 15 routine National Health Service (NHS) child and adolescent mental health service (CAMHS) clinics (n=5 in each region).[11,12] In the UK NHS, adolescents who do not respond to community-based treatments might be sent to specialist outpatient CAMHS. Therefore, the adolescents entered into this trial had high numbers of symptoms and concurrent personal impairments.

Exclusion criteria were generalised learning difficulties, pervasive developmental disorder, pregnancy, current use of another medication that could interact with an SSRI, current substance or alcohol abuse disorders, previous completion of one of the study treatments, and a primary diagnosis of bipolar disorder, schizophrenia, or eating disorders. The study was approved by the Cambridgeshire 2 Research Ethics Committee (reference 09/H0308/137) and local NHS provider trusts. The protocol has been previously published.[13] All patients and their parents gave written informed consent.

Randomisation and masking

Patients were randomly assigned (1:1:1), via a web-based randomisation service, to receive either CBT or short-term psychoanalytical therapy versus the brief psychological intervention. Randomisation was done by the trial coordinator, with stochastic minimisation by age (11–13 years *vs* 14–15 years *vs* 16–17 years), sex, self-reported depression sum score (≤29 *vs* 30–39 *vs* 40–49 *vs* ≥50),[8] and region (East Anglia *vs* North London *vs* North West England). In view of the nature of the interventions, patients and clinicians were aware of group allocation, but allocation was concealed from outcome assessors.

Procedures

All treatments were manualised; the appendix provides a full description of the treatment manuals, including theoretical and operational differences, and the manuals are available online. Short-term psychoanalytical psychotherapy comprised a planned programme of 28 sessions over 30 weeks, with parents or carers offered up to seven additional sessions by a separate parent worker. The techniques of this intervention are based on close and detailed observation of the relationship the child or young person makes with their therapist. The therapist introduces the therapeutic task to the young person as one of understanding feelings and difficulties in their life. The therapist is non-judgmental and enquiring, and conveys the value of self-understanding. Therapists were CAMHS clinicians with child and adolescent psychoanalytical psychotherapy training. Short-term psychoanalytical psychotherapy has been shown to be reliably and effectively delivered.[9]

CBT was based on the classic form originally developed for adults with depression.[14] We adapted the intervention to include parental involvement, focused on engagement in therapy, and emphasised the use of behavioural techniques. The focus of CBT is to identify the behaviours and information processing biases that maintain depression and low mood, and to amend these through a process of collaborative empiricism between the therapist and patient. CBT comprised a planned programme of up to 20 sessions over 30 weeks. CBT therapists were routine CAMHS clinicians and were either clinical psychologists or other clinicians who had received post-qualification training in CBT.

The brief psychosocial intervention was derived from the routine specialist clinical care delivered in the ADAPT trial, and reformulated on the basis of findings suggesting this intervention might be clinically effective.[9] Emphasis in the brief psychosocial intervention programme is on the importance of psychoeducation about depression, in addition to action-oriented, goal-focused, and interpersonal activities as therapeutic strategies. Neither self-understanding nor cognition change are components of the programme. The programme consists of 12 individual sessions, including up to four family or marital sessions delivered over 20 weeks. Therapists were drawn from routine CAMHS clinics.

For all three groups, liaison with external agencies and personnel (eg, teachers, social care) and peer group was commonly done. All therapy sessions were audiotaped. A computerised randomisation procedure was used to select tapes stratified by age, treatment, and whether obtained early (two to four sessions) or later (after four sessions) in the therapy. Randomisation was done with the Comparative Psychotherapy Process Scale and the Brief Psychosocial Intervention scale.[15] Independent raters rated each treatment session from the three treatment modalities to assess treatment fidelity and differentiation (appendix). In accordance with NICE guidelines, fluoxetine could be added if clinicians deemed that combination therapy might accelerate the time to remission.[5] A test dose of 10 mg was given for 48 h, followed by 20 mg as a single dose. If no improvement was shown within 2–4 weeks, the dose could be adjusted upwards to a maximum of 60 mg.

See Online for appendix

For the **treatment manuals** see http://dev.psychiatry.cam.ac.uk/projects

Outcomes

The primary outcome was self-reported depression symptoms at weeks 36, 52, and 86 post-randomisation (ie, end of treatment), as measured with the Mood and Feelings

Questionnaire (MFQ).[16] Secondary outcomes were self-reported sum scores on the Revised Children's Manifest Anxiety Scale (RMAS), the revised Leyton Obsessional Inventory (LOI) for adolescents, and the Health of the Nation Outcome Scales for Children and Adolescents—a measure of overall current psychosocial impairment.[17–19] A brief self-reported antisocial behaviour checklist based on DSM IV criteria for conduct disorder was used as a binary (none, one or more) measure of antisocial behavioural symptoms. Presence of major depressive disorder was also measured over time by use of the Kiddie-Schedule for Affective Disorder and Schizophrenia.[20] The study was not however powered to test a specific diagnosis hypothesis. Two additional clinical measures were assessed: the Columbia Suicide Inventory[21] and the self-report Risk and Self Harm Inventory.[22] Economic measures included the Child and Adolescent Service Use Schedule, for collection of service and other resource use data, and the EuroQol 5D questionnaire 3-level measure of health-related quality of life, for calculation of quality-adjusted life-years (QALYs).[23,24]

For **methods of the economic evaluation** see http://dev.psychiatry.cam.ac.uk/projects

Statistical analysis

The appendix details the statistical analysis plan. A 2·5% two-sided significance level was used for calculation of sample size and interpretation of analyses. Clustering of patients by therapist was assumed. Five points on the MFQ was taken to represent a clinically important difference for assessment of superiority, which corresponded to an improvement of one point on five of the 33 items of the MFQ—ie, a standardised effect size of 0·34 (small to medium), corresponding to non-overlap between treatments of about 25%. Data from the ADAPT trial gave an estimate of the SD of the primary outcome measure (14·6) and correlation between baseline and follow-up (0·41).[11] We planned for a recruited sample size of 540 individuals. With an assumption of 90% follow-up (n=486) and a 2·5% significance level to account for multiplicity, the power for the comparison of CBT with short-term psychoanalytical therapy was 84% if the intraclass correlation coefficient was zero, 76% if the coefficient was 0·025, and 69% if the coefficient was 0·05.[25] For the comparison of CBT and short-term psychoanalytical therapy with brief psychological intervention, the power was 93%, 88%, and 82% for an intraclass correlation coefficient of 0·0, 0·025, or 0·05, respectively.[25]

The marginal treatment effect was estimated with a linear mixed model, with a random effect for therapist, patient, and slope. To prevent bias due to assessments being delayed, time since randomisation was used as a continuous variable in a longitudinal mixed model (appendix). Diagnosis of major depressive disorder (present *vs* absent) was analysed with a logistic generalised estimating equation model over the same time period. To investigate non-response, a logistic generalised estimating equation model was fitted to an indicator variable for missing primary outcome data. All analyses included fixed covariates prespecified at baseline: MFQ, RMAS, LOI, Antisocial Behaviour Questionnaire (ABQ) scores, treatment allocation, region, sex, age at randomisation, comorbid behaviour disorder, and prescription of SSRI before trial entry (appendix).

There are no standardised methods for measuring the adverse effects of psychological treatments given to adolescents with depression. We derived a physical adversities score from self-reported items of breathing problems, sleep disturbances, drowsiness or tiredness, nausea, sweating, and being restless or overactive rated present or absent.

Methods of the economic evaluation have been applied previously[26] and are shown in the appendix and available online. In brief, cost-effectiveness was explored at the 86 week follow-up point, with outcomes expressed as QALYs and costs assessed from a service perspective (health, social care, and education). Unit costs were for the financial year 2011–12, and costs and QALYs were discounted at a rate of 3·5% as recommended by NICE.[27] Differences in mean costs were tested with linear regression models, with validity of the results confirmed with bias-corrected, non-parametric bootstrapping (5000 resamples).[25] For the cost-effectiveness analysis, we calculated incremental cost-effectiveness ratios (the difference in mean cost divided by the difference in mean effect) and explored uncertainty with cost-effectiveness acceptability curves, which show the probability that each of the treatments is the optimum choice, for a range of possible values of willingness to pay for additional QALYs.[28] All economic analyses were adjusted for the prespecified covariates and for baseline utility and cost, as appropriate. Complete case analysis was used, with the effect of missing data and sessions offered but not attended explored in sensitivity analyses.

We did analysis by intention to treat, subject to the availability of data. Analyses were done with Stata (version 12.0). This trial is registered with Current Controlled Trials, number ISRCTN83033550.

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

Between June 29, 2010, and Jan 17, 2013, we randomly assigned 470 patients to receive the brief psychosocial intervention (n=158), CBT (n=155), or short-term psychoanalytical therapy (n=157; figure). Five patients withdrew before starting treatment and requested data be deleted; the remaining 465 participants comprised the intention-to-treat population (figure). The patient recruitment rate was 40% in East Anglia, 33% in the

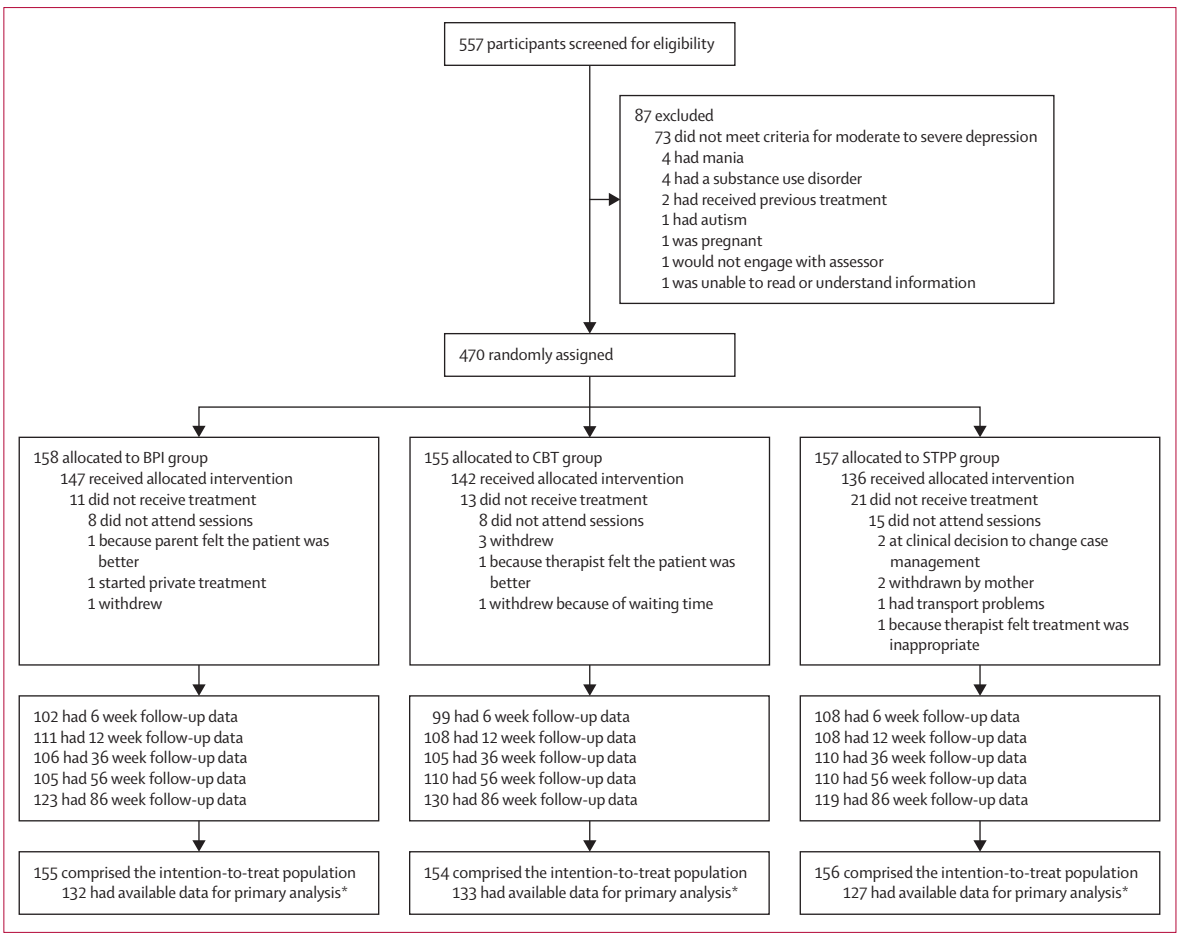

Figure: **Trial profile**
BPI=brief psychological intervention. CBT=cognitive behavioural therapy. STPP=short-term psychoanalytical psychotherapy. *The primary hypothesis was analysed in 392 (84%) of 465 patients who were randomised, accepted treatment, and provided one or more self-reported depression symptom score over the 36, 52, or 86 week assessment points. Five patients withdrew consent before starting treatment (n=3 in the BPI group, n=1 each in the CBT and STPP groups) and requested their data be deleted.

North West, and 27% in North London (table 1). 63 therapists delivered the brief psychosocial intervention, 44 therapists delivered CBT, and 38 therapists delivered short-term psychoanalytical therapy. Most (n=53) brief psychosocial intervention therapists were either psychiatrists who had passed postgraduate general training (ie, obtained membership of the Royal College of Psychiatrists) and subsequently entered specialist CAMHS psychiatry training or consultants. The primary analysis population comprised 392 (84%) patients who provided one or more self-reported depression symptom scores at weeks 36, 52, and 86 (figure). 39 (10%) patients had one MFQ score, 90 (23%) had two MFQ scores, and 263 (67%) had three MFQ scores. The number of patients with follow-up data for secondary outcomes was similar between treatment groups. The data available were within the margins suggested by the power calculation. Baseline characteristics were similar between groups (table 1).

The appendix shows the full profile of depression symptoms at baseline (appendix). The mean number of symptoms was 8·4 (SD 2·5) in patients undergoing brief psychosocial intervention, 8·7 (2·3) in patients undergoing CBT, and 8·3 (2·5) in patients undergoing short-term psychoanalytical therapy (appendix). The most prevalent symptom was sleep disturbance (n=427 [92%]) followed by depressed mood (n=390 [84%]; appendix). Psychotic symptoms were uncommon (n=48 [10%]), but a notable number of patients had current suicidal ideas (n=284 [61%]) and lifetime suicide attempts (n=177 [38%]; appendix). Symptom prevalence rates were similar between treatment groups (appendix). 225 (48%) patients had concurrent comorbid psychiatric disorders: 71 (46%) in the brief psychosocial intervention group, 80 (52%) in the CBT group, and 74 (47%) in the short-term psychoanalytical therapy group (appendix). Overall, 134 (29%) patients had one comorbidity, 60 (13%) patients had two comorbidities, and 31 (7%) patients had three or more comorbidities, with no marked differences between groups. Non-suicidal self-injury in the previous 2 weeks was reported in 85 (18%) patients: 26 (17%) assigned to the brief psychosocial intervention, 25 (16%) assigned to CBT, and 34 (22%) assigned to short-term psychoanalytical

	BPI (n=155)	CBT (n=154)	STPP (n=156)
Age (years)	15 (11–17)	15 (12–17)	15 (11–17)
Sex			
Male	40 (26%)	40 (26%)	37 (24%)
Female	115 (74%)	114 (74%)	119 (76%)
Ethnic origin			
White*	121/147 (82%)	131/152 (86%)	130/151 (86%)
Region			
East Anglia	61 (39%)	62 (40%)	62 (40%)
North London	43 (28%)	41 (27%)	43 (27%)
North West	51 (33%)	51 (33%)	51 (33%)
Conduct or oppositional disorder	20 (13%)	20 (13%)	16 (10%)
Self-reported depression score	46·2 (10·6)	46·2 (10·3)	45·4(10·8)
Number of Interviewer-assessed depressive symptoms	8·4 (2·5)	8·7 (2·3)	8·3 (2·5)
SSRI prescribed before trial entry†	29/153 (19%)	32/125 (21%)	28/155 (18%)
Prevalence of one or more comorbid DSM-5 axis 1 psychiatric diagnoses	71 (46%)	80 (52%)	74 (47%)
One or more recent suicide attempts‡	3 (2%)	2 (1%)	7 (5%)
Lifetime suicide attempts	57 (37%)	48 (31%)	55 (35%)
Recent self-harm attempts‡	26 (17%)	25 (16%)	34 (22%)
One or more lifetime non-suicidal self-injury episodes	87 (56%)	75 (49%)	84 (54%)
HoNOSCA score	18·9 (6·0)	18·4(6·0)	18·3 (6·3)
EQ-5D score	0·596 (0·27)	0·578 (0·58)	0·569 (0·59)

Data are median (range), n (%), or mean (SD). BPI=brief psychological intervention. CBT=cognitive behavioural therapy. STPP=short-term psychoanalytical psychotherapy. HoNOSCA=Health of the Nation Outcome Scales for Children and Adolescents. EQ-5D=EuroQol five dimensions questionnaire. *Excludes 15 patients for whom ethnic group or origin was not stated or missing. †Excludes five patients with missing information. ‡In the previous 2 weeks.

***Table 1*: Baseline characteristics**

therapy; lifetime non-suicidal self-injury was reported in 246 (53%) participants: 87 (56%), 75 (49%), and 84 (54%), respectively.

The number of patients starting therapy was 147 (93%) in the brief psychosocial intervention group, 142 (92%) in the CBT group, and 136 (87%) in the short-term psychoanalytical therapy group, with no differences in proportions between groups (χ^2 p=0·203). The number of individual treatment sessions given per group was less than planned (median six [IQR four to 11] in the brief psychosocial intervention group, nine [five to 14] in the CBT group, and 11 [five to 23] in the short-term psychoanalytical therapy group), but differed significantly between groups (Kruskal–Wallis p<0·0001; appendix). Of patients assigned to receive the brief psychosocial intervention, 24 (17%) had more sessions than the manual specified, compared with five (3%) assigned to receive CBT and three (2%) assigned to receive short-term psychoanalytical therapy. Mean duration of therapy did not differ significantly between treatment groups (27·5 weeks [SD 21·5] in the brief psychosocial intervention group, 24·9 weeks (SD 17·7) in the CBT group, 27·9 weeks [16·8] in the short-term psychoanalytical therapy group; Kruskal–Wallis p=0·238).

Raters assessed treatment fidelity by use of 232 audio tapes: 75 tapes for brief psychosocial intervention sessions, 76 tapes for CBT sessions, and 81 tapes for short-term psychoanalytical therapy sessions. Overall, 60 (81%) brief psychosocial intervention sessions, 61 (80%) short-term psychoanalytical therapy sessions, and 60 (74%) CBT sessions met treatment fidelity criteria (appendix). Treatment differentiation was good: the mean cognitive behavioural subscale score on the Comparative Psychotherapy Process Scale was 1·91 (95% CI 1·73–2·09) higher for CBT sessions than for short-term psychoanalytical therapy sessions (p<0·0001), whereas the mean psychodynamic interpersonal subscale score was 1·18 (1·01–1·30) higher for short-term psychoanalytical therapy sessions than for CBT sessions (p<0·0001). Patients attending brief psychosocial intervention sessions had a significantly lower mean score on the cognitive behavioural subscale than did those attending CBT sessions (mean difference –0·93, 95% CI –1·12 to –0·75; p<0·0001) and a significantly lower mean score on the psychodynamic interpersonal subscale than did those attending short-term psychoanalytical therapy sessions (–1·30, –1·48 to –1·11; p<0·0001).

The number of patients receiving an SSRI before randomisation was 29 (19%) in the brief psychosocial intervention group, 32 (21%) in the CBT group, and 28 (18%) in the short-term psychoanalytical therapy group; by the end of study, the number of patients who reported having received an SSRI at any time over the course of the trial (randomisation up to 86 weeks) was 56 (41%), 55 (40%), and 50 (36%), respectively (p=0·729; appendix).

Behavioural disorder at baseline was found to predict non-response. Because this was not a prespecified baseline covariate, it was added to all models of outcome to support the missing-at-random assumption. The appendix provides data for time from randomisation to assessment and estimates of the main effect and time with treatment interaction.

The primary outcome of self-reported depression symptoms (MFQ) at weeks 36, 52, and 86 did not differ significantly between patients in the CBT group and those in the short-term psychoanalytical therapy group, nor between those in the CBT or short-term psychoanalytical therapy groups combined versus the brief psychological intervention group (table 2). With a lower score representing improved outcome, we recorded a larger difference in favour of combined established treatments at weeks 36 and 52 (table 2), but these reductions were not statistically significant, less than the five unit difference prespecified as clinically meaningful, and not accompanied by differences in psychosocial impairment. The secondary outcomes of anxiety and obsessional symptoms were significantly reduced after the psychological treatments combined versus brief psychosocial therapy at week 36 only (table 2). The therapist intracluster correlation coefficient for therapy outcomes was calculated as the

	BPI		CBT		STPP		STPP *vs* CBT		CBT plus STPP *vs* BPI	
	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)	Treatment effect (95% CI)*	p value†	Treatment effect (95% CI)*	p value†
Primary										
MFQ										
Baseline	155	46·2 (10·6)	154	46·2 (10·3)	156	45·4 (10·8)	..	..	..	..
6 weeks	99	36·5 (14·3)	104	35·2 (11·3)	107	34·9 (13·2)	..	..	..	..
12 weeks	112	34·1 (14·4)	106	31·6 (13·3)	108	33·1 (14·2)	..	..	..	..
36 weeks	105	30·5 (16·1)	104	24·2 (15·1)	109	26·6 (15·7)	0·179 (−3·731 to 4·088)	0·929	−3·234 (−6·611 to 0·143)	0·061
52 weeks	105	25·1 (16·2)	111	25·0 (18·0)	110	23·0 (15·9)	0·307 (−3·161 to 3·774)	0·862	−2·806 (−5·790 to 0·177)	0·065
86 weeks	116	23·6 (16·2)	123	22·3 (15·7)	114	21·8 (15·5)	0·578 (−2·948 to 4·104)	0·748	−1·898 (−4·922 to 1·126)	0·219
Secondary										
RCMAS										
Baseline	155	41·1 (7·6)	154	41·2 (6·4)	155	40·5 (7·7)	..	..	..	..
6 weeks	98	35·9 (10·6)	103	37·1 (7·9)	107	36·7 (10·0)	..	..	..	..
12 weeks	110	34·2 (11·9)	105	34·4 (11·4)	108	34·3 (11·9)	..	..	..	..
36 weeks	104	32 (13·3)	102	27·0 (13·7)	107	28·6 (13·3)	0·855 (−2·530 to 4·239)	0·621	−3·832 (−6·781 to −0·884)	0·011
52 weeks	100	27·2 (14·8)	108	26·4 (14·9)	104	25·5 (14·5)	0·663 (−2·354 to 3·680)	0·667	−2·818 (−5·432 to −0·205)	0·035
86 weeks	109	24·7 (14·7)	115	24·8 (15·4)	108	23·8 (14·6)	0·254 (−2·980 to 3·489)	0·878	−0·663 (−3·460 to 2·134)	0·642
LOI										
Baseline	155	10·0 (5·3)	152	10·8 (5·4)	154	9·2 (5·0)	..	..	..	..
6 weeks	98	7·8 (5·4)	102	7·6 (5·0)	107	7·6 (5·0)	..	..	..	..
12 weeks	111	6·6 (5·6)	104	6·7 (5·2)	107	7·3 (5·1)	..	..	..	..
36 weeks	103	6·3 (5·4)	101	4·8 (4·8)	107	5·2 (4·9)	−0·816 (−1·972 to 0·341)	0·167	−1·249 (−2·258 to −0·240)	0·015
52 weeks	99	5·6 (5·8)	107	5·1 (5·5)	102	4·9 (4·7)	−0·574 (−1·601 to 0·452)	0·273	−1·120 (−2·010 to −0·231)	0·014
86 weeks	107	5·0 (5·4)	115	4·9 (5·0)	106	4·0 (4·6)	−0·062 (−1·091 to 0·967)	0·906	−0·847 (−1·736 to 0 ·042)	0·062
HoNOSCA										
Baseline	148	18·9 (6·0)	143	18·4 (6·0)	144	18·2 (6·3)	..	..	..	..
6 weeks	88	14·5 (6·5)	91	14·1 (6·4)	96	14·6 (6·9)	..	..	..	..
12 weeks	101	14·3 (7·5)	96	11·9 (6·8)	94	12·9 (6·2)	..	..	..	..
36 weeks	88	12 (8·7)	81	9·7 (7·2)	88	10·3 (7·6)	0·617 (−1·499 to 2·733)	0·567	−1·410 (−3·221 to 0·401)	0·127
52 weeks	88	9·5 (6·9)	86	8·5 (7·3)	83	8·6 (5·8)	0·620 (−1·078 to 2·318)	0·474	−1·154 (−2·601 to 0·293)	0·118
86 weeks	98	8·2 (6·2)	92	7·3 (5·2)	85	8·2 (7·2)	0·626 (−0·814 to 2·066)	0·394	−0·611 (−1·819 to 0·598)	0·322

Linear mixed model estimates of the treatment effect at weeks 36, 52, and 86 post-randomisation. Data were missing for some participants. The model was based on data for 392 (84%) of 465 patients who provided one or more self-reported depression symptom scores over the 36, 52, or 86 week assessment points. The analysis used time since randomisation as a continuous variable, with therapist, participant and slope random effects, treatment, treatment by time interaction, and other prespecified baseline covariates (appendix). BPI=brief psychological intervention. CBT=cognitive behavioural therapy. STPP=short-term psychoanalytical psychotherapy. MFQ=Mood and Feelings Questionnaire. RCMAS=Revised Children's Manifest Anxiety Scale. LOI=Leyton Obsessional Inventory–adolescent version. HoNOSCA=Health of the Nation Outcome Scale for Children and Adolescents. *The marginal mean difference at a given timepoint, with negative effects indicating treatment benefit. †To control for two comparisons, we used a 2·5% significance level to maintain a 5% significance level for any measure and timepoint combination.

***Table 2*: Primary and secondary outcomes**

proportion of the random intercept variance, and was negligible (<10^{-7}) for all the models (data not shown). Study power was therefore at the upper end of the range, because the sample size calculation included a range of values of the intracluster correlation coefficient, from 0 to 0·05.

Table 3 shows findings for the secondary binary outcomes of patients who self-reported no or one or more antisocial behaviour symptoms and patients who met clinical diagnostic criteria for major depressive disorder. Compared with brief psychosocial intervention, CBT and short-term psychoanalytical therapy led to significantly lower self-reported ABQ scores at week 36, but this difference was not maintained at week 52.

Over the follow-up period, recent suicide attempts were reported in three (3%) of 279 patients at 36 weeks (n=1 per group), two (6%) of 201 patients at 52 weeks (n=1 in the brief psychosocial intervention group, n=1 in the short-term psychoanalytical therapy group), and no patients at 86 weeks, compared with 12 (3%) of 465 patients at baseline (table 1). Similarly, non-suicidal self-injury attempts were reported in 19 (7%) of 268 patients at 36 weeks (n=10 in the brief psychosocial intervention group, n=6 in the CBT group, n=3 in the short-term psychoanalytical therapy group), 14 (4%) of 234 patients at 52 weeks (n=6, n= 2, n=6, respectively), and 16 (5%) of 257 at 86 weeks (n=7, n=5, n=4,

respectively), which compares favourably with self-harm attempts reported at baseline (n=85 [18%]; table 1). On the basis of our physical adversities score, we recorded a decline in the self-reporting of adverse physical events over the course of the study, with no observable differences between treatment groups (table 4).

The proportion of patients in diagnostic remission by 36, 52, or 86 weeks did not differ significantly between groups (data not shown). Because the present study is pragmatic, with no control group, we did a comparison of the 12 week remission rate with the rate in the TADS study,[3] which included a pill placebo control group (n=111): 145 (48%) of 305 patients were in remission at 12 weeks in our study compared with 37 (34%) placebo patients in the TADS study. Additionally, in the treatment trial of resistant depression in adolescents,[29] 203 (61%) of 334 patients were in diagnostic remission by week 72 compared with 221 (77%) of 286 by week 86 in this study. Finally, 15 (11%) of the 140 patients in remission at week 36 had relapsed by week 86 (n=5/48 [10%] in the brief psychosocial intervention group, n=4/49 [8%] in the CBT group, n=2/48 [4%] in the short-term psychoanalytical therapy group; p=0·149).

The cost of the trial interventions was lowest for CBT (mean £904·57 [SD 607·25]) and highest for short-term psychoanalytical therapy (£1396·72 [1133·41]), with the brief psychosocial intervention costing a mean of £1292·91 (851·29; appendix). The costs of use of all other services (health, social care, and education) differed little between patients in the brief psychosocial intervention group (mean £1385·4 [SD 2807·7]), the CBT group (£1459·26 [3481·02]), and the short-term psychoanalytical therapy group (£1668·51 [3425·68]) over 86 weeks (appendix). The total combined cost of trial interventions and use of other services was £2678·39 (SD 2678·39) for the brief psychosocial intervention, £2379·01 (3643·85) for CBT, and £3081·70 (3573·17) for short-term psychoanalytical therapy; neither these costs, nor QALYs (mean 1·241 [SD 0·270], 1·228 [0·304], and 1·246 [0·293] QALYs, respectively), differed significantly between groups over 86 weeks (appendix). No evidence supported the superior cost-effectiveness of short-term psychoanalytical therapy compared with brief psychosocial intervention or CBT, or CBT compared with brief psychosocial intervention (appendix).

Discussion

We found no evidence for the superiority of CBT or short-term psychoanalytical therapy compared with a brief psychosocial intervention for maintenance of reduced depression symptoms 12 months after treatment. To our knowledge, this is the first trial to show that short-term psychoanalytical therapy and brief psychosocial intervention are as clinically effective as CBT for the treatment of adolescents with depression. We note the continuing decline of symptoms and further increase in remission, which are not explained by any marked differences in post-treatment service use, costs between therapies, or reported SSRI use. However, caution is required with the findings for remission because the study was not powered for treatment group comparisons, interview data were missing at each

	BPI (n=155)	CBT (n=154)	STPP (n=156)	STPP *vs* CBT		CBT plus STPP *vs* BPI	
				Treatment effect (95% CI)*	p value†	Treatment effect (95% CI)*	p value†
MDD							
Baseline	155 (100%)	154 (100%)	156 (100%)	..	..	..	..
6 weeks	63/143 (44%)	57/95 (60%)	62/99 (63%)	..	..	..	..
12 weeks	57/ 105 (54%)	46/98 (47%)	54/99 (55%)	..	..	..	..
36 weeks	42/95 (44%)	28/89 (31%)	35/98 (36%)	–0·064 (–0·206 to 0·078)	0·375	–0·043 (–0·160 to 0·073)	0·465
52 weeks	27/92 (29%)	23/90 (26%)	23/87 (27%)	–0·018 (–0·120 to 0·084)	0·727	–0·053 (–0·142 to 0·035)	0·239
86 weeks	27/99 (27%)	24/95 (25%)	14/92 (15%)	0·057 (–0·043 to 0·157)	0·261	–0·065 (–0·152 to 0·022)	0·145
ABQ							
Baseline	121 (78%)	124/152 (82%)	128/154 (83%)	..	..	..	..
6 weeks	75/98 (77%)	71/102 (70%)	73/107 (68%)	..	..	..	..
12 weeks	78/111 (70%)	57/104 (55%)	52/107 (49%)	..	..	..	..
36 weeks	62/103 (60%)	45/101 (45%)	55/107 (51%)	–0·068 (–0·186 to 0·051)	0·263	–0·128 (–0·238 to –0·019)	0·022
52 weeks	47/99 (47%)	43/107 (40%)	41/102 (40%)	–0·040 (–0·135 to 0·055)	0·408	–0·074 (–0·163 to 0·015)	0·102
86 weeks	39/107 (36%)	49/115 (43%)	43/106 (41%)	0·018 (–0·083 to 0·120)	0·725	0·040 (–0·051 to 0·131)	0·389

Data are n (%) or n/N (%), unless otherwise specified. Logistic generalised estimated equation model estimates of the treatment effect at weeks 36, 52, and 86 post-randomisation. The model was based on data from 36 weeks post-randomisation, with therapist, participant and slope random effects, treatment, treatment by time interaction, and other prespecified baseline covariates. BPI=brief psychological intervention. CBT=cognitive behavioural therapy. STPP=short-term psychoanalytical psychotherapy. MDD=major depressive disorder. ABQ=Antisocial Behaviour Questionnaire. *The marginal mean difference at a given timepoint, with negative effects indicating treatment benefit. The study was not powered to test for treatment differences in clinical diagnostic relapse. †To control for two comparisons, we used a 2·5% significance level to maintain a 5% significance level for any measure and timepoint combination.

***Table 3*: Patients with an MDD diagnosis and one or more antisocial behaviour symptoms**

timepoint, and the control comparison could only be achieved at 12 weeks. We also note the small reduction in symptoms in favour of established treatments at the end (36 weeks) of treatment, but not by end of study, which is consistent with previous reports of psychological treatment effects on reducing anxiety in patients with depression.[10] No participants reported increases in suicidal ideation, non-suicidal self-injury, or adverse physical side-effects during the study.

Three previous randomised controlled trials similar in design to the present study have reported follow-up data beyond end of treatment. Birmaher and colleagues[30] reassessed 107 adolescents with major depressive disorder 2 years after treatment with CBT, systematic behavioural family therapy, or non-directive supportive therapy. There were no differences in outcome by original treatment group. A naturalistic follow-up study[31] of 196 adolescents with depression (45% of the original sample) recruited to a treatment trial reported that 5 year post-trial recurrence was more likely in participants with higher depressive symptom scores at the end of treatment, but was not associated with treatment type. Most recently, a 6 year follow-up study[32] of a cognitive behaviour programme aimed at prevention of depressive episodes showed that the strongest effect was early and better maintained with additional booster sessions and treatment of parental depression. Overall these findings are consistent in their suggestion that early response to treatment can be followed by continued improvement across different treatment modalities. The absence of difference between the three treatments assessed in the present study might be due to a putative shared common effect, but could also be a result of alternative explanations, including three unique effects leading to the same outcome or even to no effect, with the decline in symptoms being due to change over time.

Reports of non-response to treatment in 21–25% of trial patients are also consistent with these results.[3,11,28–30] Such non-response might be due to issues of selection of the right treatment for the right patient, noting the likelihood of resistance to a given treatment early in therapy, or to prediction of the likelihood of non-compliance. One challenge for further research is to improve the precision of the ability to select the best treatment for a given patient with depression. Despite the planned differences in treatment intensity, in practice, young people attended a median of six to 11 sessions over 25–28 weeks across all three treatment groups. A first course of therapy for adolescents with depression could be brief (six to 11 sessions) and at no difference in cost between the available treatment options assessed in this trial. The reasons for non-attendance deserve further investigation.

Our study had various strengths, including that participants were representative of the population with moderate to severe depression, with self-harm, suicidality, and non-depressive comorbid disorders at the point of referral; CAMHS referral across diverse regions of the UK; meeting of research diagnostic criteria for DSM IV major depressive disorder; and randomisation done remotely from the research team. There was a loss to follow-up, but data for the primary outcome measure (MFQ) were available in 84% of participants. The overall sample size was greater than in previous studies, and this is the first time a trial of adolescents with depression has been designed to follow up participants for 52 weeks after the end of treatment. Each of the three treatments was manualised, interventions were delivered as expected, and clear differences in approach were maintained between therapies. Some patients in all three groups received antidepressant medication. This characteristic strengthens generalisability, but restricts the interpretation of the findings. Methods of prescribing did not differ between groups over the course of the study, and fluoxetine was prescribed both during and after the end of treatment. Neither the reasons for prescribing nor medication compliance were controlled for over the study course; therefore, we cannot exclude the possibility that SSRIs might have contributed to the improvements over time. Furthermore, the declines in symptoms and improvements in wellbeing could be a function of time. The absence of a no-treatment control group restricts the assertion that any therapy was causally effective. The economic results were limited by missing data, which was higher than for the primary clinical outcome measure (40%). Multiple imputation of missing data did not, however, change the economic results of the analysis. Future research should focus on psychological mechanisms associated with treatment response, the maintenance of positive effects, non-response, and whether or not brief psychotherapies are of use in community and primary care settings.

In summary, brief psychosocial intervention, CBT, and short-term psychoanalytical therapy are all associated with maintenance of reduced depression symptoms 1 year after the end of treatment. Short-term

	BPI			CBT			STPP		
	n	Mean (SD)	Median (min–max range)	n	Mean (SD)	Median (min–max range)	n	Mean (SD)	Median (min–max range)
Baseline	155	5·0 (1·1)	5 (1–6)	154	5·1 (1·0)	5 (2–6)	156	5·0 (1·1)	5 (2–6)
6 weeks	99	4·4 (1·5)	5 (0–6)	104	4·6 (1·3)	5 (2–6)	107	4·4 (1·5)	5 (0–6)
12 weeks	112	4·2 (1·6)	4 (0–6)	106	4·0 (1·5)	4 (0–6)	108	4·2 (1·6)	4 (0–6)
36 weeks	105	4·1 (1·6)	4 (0–6)	104	3·6 (1·6)	4 (0–6)	109	3·6 (1·7)	4 (0–6)
52 weeks	105	3·5 (1·8)	3·5 (0–6)	111	3·5 (1·9)	4 (0–6)	110	3·2 (1·9)	3 (0–6)
86 weeks	116	3·3 (1·8)	3·5 (0–6)	123	3·4 (1·9)	4 (0–6)	114	3·2 (1·8)	3 (0–6)

We derived a physical adversities scores based on six self-reported adverse items: breathing problems, sleep disturbances, drowsiness or tiredness, nausea, sweating, and being restless or overactive rated present or absent. BPI=brief psychological intervention. CBT=cognitive behavioural therapy. STPP=short-term psychoanalytical psychotherapy.

Table 4: **Adverse event scores**

psychoanalytical therapy and brief psychosocial interventions offer additional patient choice, alongside CBT, for depressed adolescents attending routine specialist CAMHS clinics.

Contributors

IMG, SR, SB, BD, JH, RK, CR, MT, and PF were responsible for the original proposal, securing funding, for the trial, and for drafting the original protocol. IMG as chief investigator had overall responsibility for the management of the study. SR, RK, and IMG had responsibility for the East Anglia site; JH and BD for the North West site; and RS, NM, MT, and PF for the North London site. RK, BD, PW, and IMG were responsible for the development of the brief psychosocial intervention manual and provided training and supervision for the therapists in East Anglia. Medical leadership and supervision for the brief psychosocial intervention was provided by RK in East Anglia, RS in North London, and BD and JH in the North West. NM, MT, and PF developed the short-term psychoanalytical therapy manual and ensured and coordinated short-term psychoanalytical therapists for the study, together with JH in the North West. SR developed the CBT manual and coordinated the therapists' election, training, and supervision for the study; BD and JH coordinated CBT therapy in the North West. BW was project manager throughout the trial, developed and coordinated the randomisation and minimisation protocol with IMG and CR. BW set up and coordinated the database, with all data held in a single repository on the Cambridge site. NM, SR, RK, and BD coordinated and supervised the treatment fidelity project and analysed the data with CR. FH, CR, BB, and SB wrote the statistical analysis plan and did the analyses. BW and FH were responsible for data cleaning. IMG wrote the initial draft of the manuscript. All authors contributed to and approved the final manuscript.

Declaration of interests

All authors declare no competing interests.

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