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The effects of once- versus twice-weekly sessions on psychotherapy outcomes in depressed patients

Sanne J. E. Bruijniks, Lotte H. J. M. Lemmens, Steven D. Hollon, Frenk P. M. L. Peeters, Pim Cuijpers, Arnoud Arntz, Pieter Dingemans, Linda Willems, Patricia van Oppen, Jos W. R. Twisk, Michael van den Boogaard, Jan Spijker, Judith Bosmans and Marcus J. H. Huibers

Background

It is unclear what session frequency is most effective in cognitive-behavioural therapy (CBT) and interpersonal psychotherapy (IPT) for depression.

Aims

Compare the effects of once weekly and twice weekly sessions of CBT and IPT for depression.

Method

We conducted a multicentre randomised trial from November 2014 through December 2017. We recruited 200 adults with depression across nine specialised mental health centres in the Netherlands. This study used a 2 × 2 factorial design, randomising patients to once or twice weekly sessions of CBT or IPT over 16–24 weeks, up to a maximum of 20 sessions. Main outcome measures were depression severity, measured with the Beck Depression Inventory-II at baseline, before session 1, and 2 weeks, 1, 2, 3, 4, 5 and 6 months after start of the intervention. Intention-to-treat analyses were conducted.

Results

Compared with patients who received weekly sessions, patients who received twice weekly sessions showed a statistically

significant decrease in depressive symptoms (estimated mean difference between weekly and twice weekly sessions at month 6: 3.85 points, difference in effect size $d = 0.55$), lower attrition rates ($n = 16$ compared with $n = 32$) and an increased rate of response (hazard ratio 1.48, 95% CI 1.00–2.18).

Conclusions

In clinical practice settings, delivery of twice weekly sessions of CBT and IPT for depression is a way to improve depression treatment outcomes.

Declaration of interest

None.

Keywords

Depressive disorders; cognitive-behavioural therapies; individual psychotherapy; randomised controlled trial; out-patient treatment.

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Randomised trials on the effects of different psychotherapy formats showed that a more intense dose of treatment can lead to a faster response, less drop-out and better or non-inferior outcomes compared with less-intense treatments.^{1–4} In the field of depression, a meta-regression analysis showed that the number of sessions per week, and not the total number of sessions or duration of therapy, was correlated with outcome.⁵ In an observational study, a higher session frequency was associated with improvement and recovery within the first three months of treatment.⁶ However, a randomised trial on the direct effect of psychotherapy session frequency on depression is lacking. The original Beck manual for cognitive-behavioural therapy (CBT) for depression⁷ prescribes that CBT should start twice weekly in the beginning of treatment, whereas interpersonal psychotherapy (IPT) should be delivered once a week, according to Klerman's manual.⁸ In both treatments, however, a higher session frequency might lead to better depressive outcomes. Our hypothesis is that a higher session frequency leads to better recall of the content of the sessions, which will lead to a better development of therapy-specific skills and consequently better treatment outcomes.⁹ An alternative hypothesis is that a higher session frequency leads to a better working alliance, which then leads to better patient adherence and motivation, and consequently better treatment outcomes.

This is the first randomised trial to investigate the effects of once weekly versus twice weekly sessions of CBT and IPT for depression. The primary hypothesis was that twice weekly sessions in the first 16 sessions of treatment leads to greater reduction of depressive symptoms and other outcomes in the acute phase of treatment. We also assessed the effects on attrition and time to response, and potential differences between CBT and IPT session frequency.

Method

Trial design

This study was registered with the Netherlands Trial Register (registration number NTR4856). Details about the study design have been described elsewhere.⁹ Data are from a multicentre, randomised controlled trial (2 × 2 factorial design) on the effects of session frequency in CBT and IPT for depression, with a 24-month follow-up. Patients were randomly assigned to four conditions: 16 sessions of CBT twice a week, 16 weekly sessions of CBT, 16 sessions of IPT twice a week and 16 weekly sessions of IPT. In each condition, the 16th session was followed by four biweekly sessions. Data presented here concern post-treatment outcomes 6 months after the start of treatment; follow-up data will be reported in a subsequent report. Clinical outcomes on the long-term effects (Longitudinal Interview Follow-up Evaluation) and cost-effectiveness (quality of life, EuroQol-5D and the Trimbos and Institute for Medical Technology Assessment Questionnaire on Costs associated with Psychiatric Illness) outcomes will be reported in follow-up papers.

Participants and recruitment

Patients were adult out-patients referred to one of nine Dutch specialised mental healthcare centres located across the Netherlands. Inclusion criteria were as follows: (a) a primary diagnosis of a DSM-IV or DSM-5 major depressive disorder (including chronic depression) or DSM-5 persistent depressive disorder as confirmed by the Structured Clinical Interview for DSM-IV Axis I Disorders¹⁰

or the Mini International Neuropsychiatric Interview Plus¹¹, (b) aged 18 to <65 years, (c) sufficient knowledge of the Dutch language, (d) pre-treatment score ≥ 20 on the Beck Depression Inventory-II (BDI-II)¹² and (e) access to internet facilities (because some of the assessments were online). Exclusion criteria were as follows: (a) starting antidepressants or dosage change in the past 3 months, (b) acute suicide risk, (c) DSM-IV or DSM-5 diagnosis of drug or alcohol dependence, (d) presence of a DSM-IV or DSM-5 diagnosis of a cluster A or B personality disorder as evaluated by a clinician during the intake with or without help of a structured interview and (e) received more than five sessions of adequate CBT or IPT in the previous year (clinician-evaluated at intake).

Procedure

Patients were recruited during regular intakes at the clinical sites. Eligible patients were approached for participation in the study and received a general information folder. A week after the intake, an independent research assistant contacted eligible patients to give them additional study information and to check whether the patient was motivated to participate in the study. Subsequently, patients were invited for a diagnostic interview (if not completed during intake), an online baseline assessment and signing of informed consent. Informed consent for videotaping the sessions was signed separately; patients who were included in the trial were allowed to refuse videotaping of their therapy sessions. After the baseline assessment, block randomisation took place. Randomisation codes were generated by an independent computer scientist to ensure allocation concealment. Patients were randomised into one of the four conditions, using a computer script (allocation ratio: 1:1:1:1). Randomisation was stratified according to severity (high, BDI-II score ≥ 29 ; low, BDI-II score ≤ 28) and treatment site, using different blocks for high versus low severity and each treatment site. After baseline, online assessments were conducted 2 weeks after the start of treatment and every month until month 6. In addition, participants filled out the BDI-II and single questions on mood and happiness online in the therapist's office before the start of each therapy session. Post-treatment effect size for the difference in depressive symptoms between the session frequencies was estimated to be around 0.45.⁵ Therefore, 200 patients were needed for adequate power ($\alpha = 0.05$, power $(1-\beta) = 0.80$, two-tailed) to detect a difference between session frequencies, taking 25% drop-out into account.

Interventions

Treatment manuals were used for both interventions regardless of frequency and both treatments consisted of a minimum of 12 and maximum of 20 45-minute face-to-face sessions, depending on patient progress. CBT was based on the manual by Beck *et al.*⁷ and IPT was based on the manual by Klerman *et al.*⁸ Except for the structuring of session frequency, no changes were made to the original treatment manuals after the seeking advice from various CBT and IPT experts. Participants who were randomised to the condition with twice weekly sessions received 16 sessions during the first 8 weeks of treatment, and 4 sessions during the last 8 weeks (up to 20 sessions over a period of 16 weeks). Patients who were randomised to the condition with once weekly sessions received 16 sessions during the first 16 weeks and 4 sessions during the last 8 weeks (up to 20 sessions over a period of 24 weeks).

Treatment integrity

Before the study, therapists received 2 days of training by S.D.H. (CBT) or Dr Holly Swartz (IPT). During the study, therapists received supervision and consulted each other on current cases in

on-site consultation sessions. The format and the amount and frequency of supervision and consultation sessions differed per centre and therapist, varying from 30 min to 2 h biweekly (i.e. in most centres, these meetings also included discussion of patients that did not participate in the study). Therapists that were still in postgraduate clinical training received additional weekly to monthly supervision from an experienced supervisor in the context of the study. Therapists that entered the study after the training received additional training and elaborate instructions about the study and protocol. To prevent contamination, therapists were uniquely assigned to one of the treatment conditions. However, because of problems with capacity, 7 therapists treated 37 patients in both conditions.

The modified version of the Collaborative Study Psychotherapy Rating Scale version 6 (CSPRS-6^{13,14}) was used as a measure of adherence (i.e. whether the therapy protocol was followed). Treatment adherence was measured by independent expert raters (3 psychotherapists and 1 psychologist) that assessed 51 randomly selected videos of different patients drawn between sessions 6 and 12. To examine therapy competence (i.e. how well the therapy was performed), master-level clinical graduate students rated a total of 116 unique CBT videos and 131 unique IPT videos. Total scores on the Cognitive Therapy Scale¹⁵ (CTS; range 11–77), the IPT Adherence and Quality Scale (short version)¹⁶ (IPT-AQS; range 9–125) and the score on the single item 'How would you rate the clinician overall in this session, as a CBT/IPT therapist?' measured on a Likert scale ranging from 1 (poor) to 7 (excellent) were used. Details about treatment integrity can be found in Data Supplement 1 available at <https://doi.org/10.1192/bjp.2019.265>.

Primary outcomes

Primary outcome was depression severity as measured with the BDI-II.¹² The BDI-II is a 21-item self-report instrument assessing depressive symptoms over the past 2 weeks. A score of 0–13 indicated minimal depression, 14–19 indicated mild depression, 20–28 indicated moderate depression and 29–63 indicated severe depression. Reliability and validity of the BDI-II has been previously reported.¹⁷

Secondary outcomes

Secondary outcomes included a single item rating of 'current mood' (0, 'worst mood ever' to 100, 'best mood ever'); two single items rating happiness, 'general life happiness' and 'happiness today' (1, 'completely unhappy' to 7, 'completely happy'); the general health perception domain of the RAND 36-Item Health Survey (RAND-36);^{18,19} and the Remission of Depression Questionnaire²⁰ (RDQ). The RDQ measures remission as a broad construct including reduction in depressive symptoms and other depression-related domains, with lower scores representing better functioning on each subscale. The RDQ and RAND-36 were measured at baseline and at 3 and 6 months after the start of treatment. The mood and happiness questions were both included before each session and in the online assessments. For a detailed description of these instruments and their psychometric properties, we refer to our protocol paper.⁹

Data analyses

The flow chart, pre-treatment variables, treatment and study adherence, therapists characteristics and treatment integrity were described in the result section. Differences in days between sessions between frequency conditions were tested with univariate analysis of variance. Differences in attrition between session frequencies were tested with a χ^2 test.

Multilevel regression analyses with maximum likelihood estimation were conducted to investigate the effect of frequency condition on depression (BDI-II scores). Intervention was represented by two dichotomous variables: CBT (−1) versus IPT (1) and once weekly (−1) versus twice weekly (1) sessions. Because of the long waiting time (mean 35.20 days, s.d. 27.05) between baseline and session 1 (see also Data Supplement 3), we decided to add the BDI-II score measured at the start of session 1 to the outcome (i.e. dependent variable was BDI-II score measured before session 1, and 2 weeks and monthly after start of treatment up to month 6, leading to a total of eight time points). The model corrected for baseline values by adding BDI-II baseline as a covariate in the model.²¹ The initial basic model was a two-level model with repeated measurements (level 1) nested within patients (level 2) with two two-way interactions testing the difference in change of BDI-II scores over time in days for the different session frequencies (time×frequency) and treatments (time×treatment). Time in days was centred 90 days after the start of treatment and it was tested whether a quadratic or cubic function of time led to better model fit. Subsequently, the addition of random levels on therapist and treatment centre were tested, followed by a test of random slopes for time on all fitted random levels. Fit of different (co)variance structures for both the random effects and residuals errors within the lowest level (repeated measurements) were compared. To explore whether the effect of session frequency was different for CBT versus IPT, a model with a three-way interaction (frequency × treatment × time) was fitted. Analyses were intention to treat, and significance levels were set at $P < 0.05$. The same method was used to investigate effects on the secondary outcomes.

Effect sizes from session 1 to month 6 (Cohen's d)²² for the primary outcomes were computed: (estimated session 1 mean – estimated mean at time i) / estimated s.d. at session 1). Response (reliable change) was defined as a decrease of at least 9 BDI-II points from session 1 to month 6 and remission (clinically significant change) as an absolute value ≤ 9 on the BDI-II at month 6. Cox regression was conducted to examine differences in the time in days to response and remission for weekly versus twice weekly sessions, including treatment modality and the BDI-II baseline score as covariates.

Three sensitivity analyses were conducted. First, it was investigated whether the total number of sessions, the presence of a comorbid anxiety disorder or the use of antidepressants were covariates that influenced the main results. Second, because a number of the time points (week 2, month 1, month 2, month 3 and month 4) are not comparing the same number of treatment sessions between frequency conditions and this could potentially skew the estimates in the analysis, we additionally tested the change in BDI-II scores from baseline to month 6, ignoring symptom levels across the other time points. Third, a completers analysis was conducted, reporting estimated difference in BDI-II scores at month 6 and the difference in effect size between frequency conditions. Non-completers were defined as patients who discontinued therapy, deviated to other protocols or changed antidepressant use before session 12. All other patients were considered completers.

Results are reported according to the Consolidated Standards Of Reporting Trials guidelines.²³ For more details about the data analyses we refer to Data Supplement 2.

Ethics statement

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. All procedures involving human patients were approved by the Medical Ethical

Committee of VU Medical Centre Amsterdam (registration number 2014.337).

Results

Description of the sample

The flow of patients is shown in Fig. 1. A total of 3179 patients were initially screened for eligibility, of whom 2380 did not meet the inclusion criteria and 235 patients met the inclusion criteria but declined to participate. This resulted in a total sample of 200 patients (CBT weekly, $n = 49$; CBT twice weekly, $n = 49$; IPT weekly, $n = 55$; IPT twice weekly, $n = 47$).

Mean age at baseline was 37.85 years (s.d. 12.26) and 61.5% of participants were female. Mean baseline BDI-II score was 34.70 (s.d. 9.96), 43.3% of the sample experienced recurrent depression and self-reported duration of symptoms was 40.87 months (s.d. 68.31; median 20). The majority (68%) of the total sample was still actively employed. Pre-treatment characteristics per condition are presented in Table 1. Observed means (s.d.) on all outcome measures at each time point for each condition are given in Table 2.

Treatment and study adherence

Recruitment took place from November 2014 to January 2018. The patients that started treatment ($n = 191$) received a mean number of 16.54 (s.d. 4.73) sessions. There was a significant difference in days between the sessions and treatment duration between patients who received the weekly (mean 8.98 days, s.d. 3.06; mean 170 days, s.d. 67.23) versus the twice weekly (mean 4.68 days, s.d. 2.28; mean 113 days, s.d. 43.62) frequency condition ($t(177) = 10.92$, $P < .001$ and $t(165.68) = 6.98$, $P < 0.001$ for session frequency and treatment duration, respectively). There was no difference between frequency conditions in the total number of sessions. Of the 48 patients that were registered as non-completers, 14 withdrew or were lost to follow-up, 9 never started with treatment, 20 switched to another intervention or started or switched antidepressants before the 12th session, 2 received a session frequency different from the one to which they were randomised and 3 could not complete treatment because of a lack of therapists at the treatment centre. Four patients who completed treatment before session 12 were considered to be completers because their therapist indicated that therapy was successful. More patients dropped out of weekly ($n = 32$) than twice weekly ($n = 16$) treatment ($\chi^2 = 5.44$, $P = 0.02$). With regard to study adherence, the percentages of participants completing assessments on each time point were 58% for week 2, 78.5% for month 1, 76.5% for month 2, 71.5% for month 3, 68% for month 4, 65.5% for month 5 and 72.5% for month 6. Study adherence was not different between frequency conditions, except for month 3, in which there were more missing data in the weekly condition ($n = 37$ compared with $n = 20$; $\chi^2 = 5.32$, $P = 0.02$). Treatment characteristics per condition are given in Data Supplement 3.

Therapists

The 76 therapists (25–61 years of age, 81.6% female) who participated in the study were licensed mental health psychologists ($n = 38$), master-level (MSc) psychologists in post-master training ($n = 32$), psychiatrists ($n = 2$) and mental health nurses ($n = 4$). Therapists had an average of 9.55 years (s.d. 8.29; $n = 64$) of clinical experience (range 0.5–29 years). The number of patients per therapist ranged from 1 to 12 (mean 2.67, mode 1). IPT therapists had fewer years of experience with IPT than CBT therapists had with CBT (IPT: mean 4.01, s.d. 6.50; CBT: mean 6.46, s.d. 6.13). There were no significant differences in treatment outcome ($t(143) =$

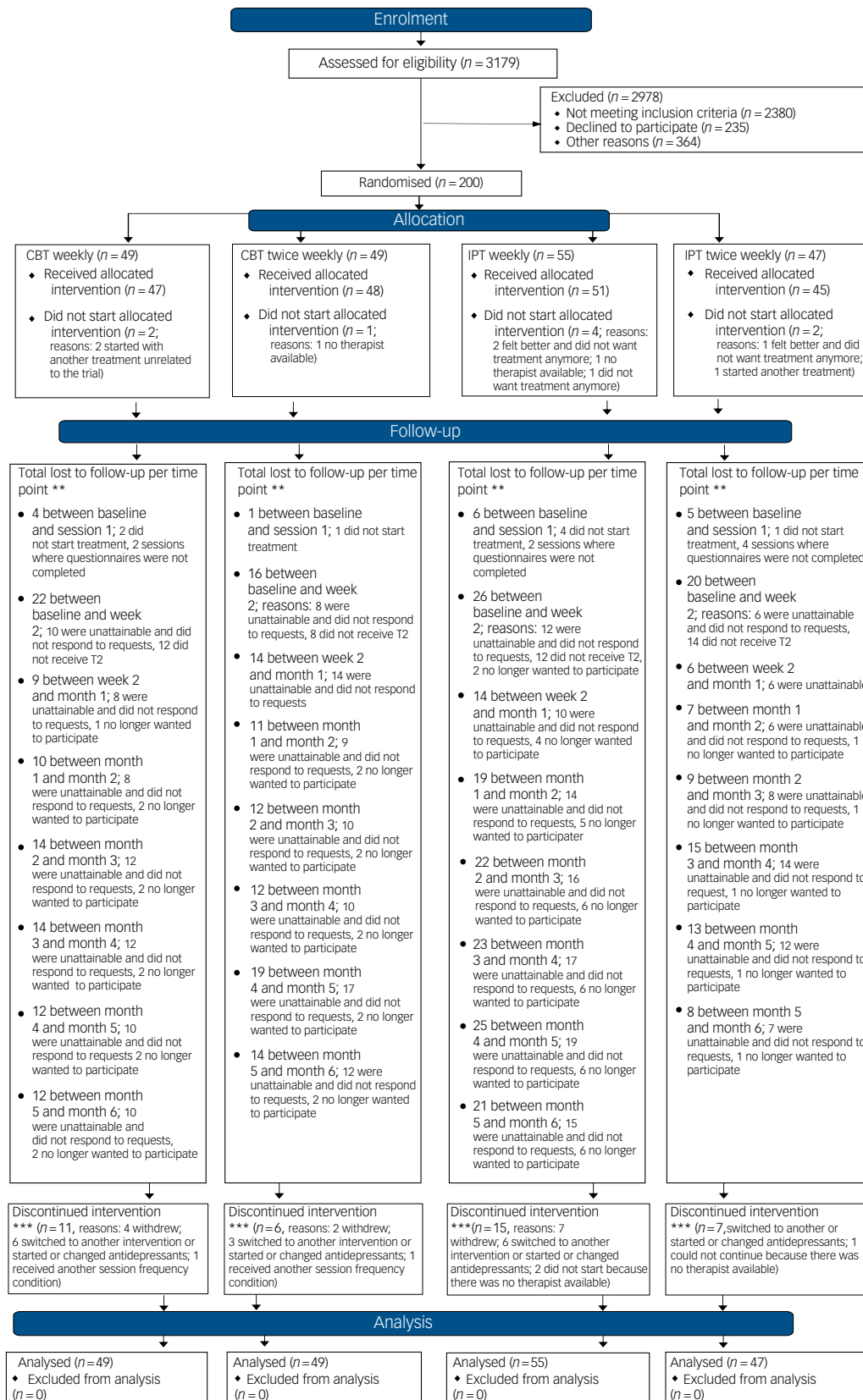


Fig. 1 Patient flow chart.

Note that 'lost to follow-up' ** presents study adherence and 'discontinued intervention' *** treatment adherence. Numbers on study adherence are based on the presence of the Beck Depression Inventory-II scores per time point. Of the 235 patients who met the inclusion criteria but declined to participate, 30 patients explicitly declined to participate because they did not want to receive therapy in a higher session frequency and 43 patients explicitly declined to participate because they preferred CBT, IPT or another treatment (e.g. antidepressants). The remaining 162 patients declined because they did not want the extra investment of completing research questionnaires (n = 21), or for unknown reasons (n = 141); 364 patients were excluded for 'other reasons', such as participation in another study, assignment to another treatment or because the reason for exclusion was unclear. Note that 3179 (screened) – 2978 (declined) = 201, but that one participant asked for complete deletion of his/her data and was therefore not included in the flow chart. CBT, cognitive-behavioural therapy; IPT, interpersonal psychotherapy.

Table 1 Pre-treatment characteristics stratified per condition

	CBT weekly (<i>n</i> = 49)	CBT twice weekly (<i>n</i> = 49)	IPT weekly (<i>n</i> = 55)	IPT twice weekly (<i>n</i> = 47)
Sociodemographic variables				
Female gender, <i>n</i> (%)	33 (67.3)	29 (59.2)	33 (60)	28 (59.6)
Age in years, mean (s.d.)	35.69 (12.67)	40.67 (11.76)	36.81 (11.67)	38.38 (12.79)
Highest completed education, <i>n</i> (%)				
Low	4 (8.2)	5 (10.2)	6 (10.9)	6 (12.8)
Medium	23 (46.9)	27 (55.1)	27 (49.1)	25 (53.2)
High	22 (44.9)	17 (34.7)	22 (40)	16 (34)
Partner, <i>n</i> (%)	17 (34.7)	17 (34.7)	16 (29.1)	22 (46.8)
Active employment, <i>n</i> (%)	33 (67.3)	35 (72.9)	37 (69.8)	29 (61.7)
Born in the Netherlands, <i>n</i> (%)	40 (81.6)	37 (75.5)	45 (81.8)	37 (78.7)
Both parents born in the Netherlands, <i>n</i> (%)	33 (67.3)	27 (55.1)	37 (67.3)	25 (53.2)
Experience of general health				
RAND-36, mean (s.d.)	42.85 (21.33)	43.97 (17.55)	43.09 (17.28)	43.61 (18.04)
Depression specifiers				
BDI-II baseline score, mean (s.d.)	36.02 (9.36)	35.65 (8.69)	33.36 (9.50)	33.91 (12.15)
First depressive episode, <i>n</i> (%)	30 (68.2)	18 (46.2)	25 (53.2)	24 (58.5)
Number of episodes (including current episode), mean (s.d.)	1.79 (1.71)	2.05 (1.29)	1.95 (1.26)	1.70 (1.03)
Severe depression, <i>n</i> (%)	36 (73.5)	39 (79.6)	36 (65.5)	31 (66)
Chronic depression, <i>n</i> (%)	23 (46.9)	24 (49)	25 (45.5)	21 (44.7)
Self-reported duration of symptoms in months, mean (s.d.)	39.85 (52.66)	50.40 (80.33)	39.47 (80.67)	33.63 (52.59)
Symptoms untenable in months, mean (s.d.)	12.61 (13.04)	13.44 (19.87)	17.67 (37.92)	13.54 (17.99)
Number of comorbid Axis I disorders, mean (s.d.)				
Comorbid anxiety disorder, <i>n</i> (%)	23 (46.9)	22 (44.9)	29 (52.7)	19 (40.4)
Comorbid PTSD, <i>n</i> (%)	3 (6.5)	2 (4.1)	6 (11.3)	2 (4.7)
Comorbid other than anxiety, <i>n</i> (%)	3 (6.1)	6 (12.2)	8 (14.5)	7 (14.9)
Self-reported use of antidepressants at baseline, <i>n</i> (%)	14 (28.6)	11 (22.4)	13 (23.6)	15 (31.9)
Received individual psychotherapy before (self-report), <i>n</i> (%)	41 (83.7)	42 (85.7)	48 (87.3)	41 (87.2)

Note that severe depression is defined as a BDI-II score >28. Low educational level has been defined as no former education or special lower education or primary school or practical training school; middle educational level has been defined as completing lower general secondary education or higher general secondary education or intermediate vocational education; and higher education level has been defined as completing higher vocational education or pre-university education or university. Note that students were also considered as active employment. The RAND-36 reports the total score of the subscale 'general experience of health', range of 5 (low perception of general health) to 25 (high perception of general health). Comorbid Axis I disorders were established with use of the MINI-Plus or SCID-I. In case of missing data, the number of available data per condition is given. Data were missing for first depressive episode and number of episodes: CBT weekly (missing *n* = 5), CBT twice weekly (missing *n* = 10), IPT weekly (missing *n* = 8) and IPT twice weekly (missing *n* = 6); and for MINI-Plus or SCID-I: CBT weekly (missing *n* = 5), CBT twice weekly (missing *n* = 1), IPT weekly (missing *n* = 3) and IPT twice weekly (missing *n* = 4). CBT, cognitive-behavioural therapy; IPT, interpersonal psychotherapy; RAND-36, RAND 36-Item Health Survey; BDI-II, Beck Depression Inventory-II; PTSD, post-traumatic stress disorder; MINI-Plus, Mini International Neuropsychiatric Interview Plus; SCID-I, Structured Clinical Interview for DSM-IV Axis I Disorders.

1.19, $P = 0.23$) or attrition ($t(198) = 0.79$, $P = 0.42$) between patients that were treated by single versus multiple modality therapists.

Treatment integrity

A total of 1771 videos of 129 patients were available. CBT-specific behaviour (adherence) as rated with the CSPRS-6 was significantly more evident in CBT than in IPT (CBT: mean 89.92, s.d. 33.84, $n = 27$ versus IPT: mean 57.56, s.d. 10.19, $n = 23$, $t(31.41) = 4.72$, $P < 0.001$). IPT-specific behaviour as rated with the CSPRS-6 was more present in IPT than in CBT (IPT: mean 95.50, s.d. 20.26, $n = 24$ versus CBT: mean 32.59, s.d. 5.38, $n = 27$; $t(25.88) = -14.75$, $P < 0.001$). CBT competence as rated with the CTS varied from poor to very good (Likert scale: mean 3.69, s.d. 1.08, $n = 61$; CTS total: mean 45.55, s.d. 9.82, $n = 60$), and 16.3% of the CBT sessions were rated good to excellent. IPT competence as rated with the IPT-AQS varied from poor to very good (Likert scale: mean 3.64, s.d. 1.27, $n = 66$; IPT-AQS: mean 66.48, s.d. 14.02, $n = 66$) and 12.1% of the IPT sessions were rated good to excellent. There were no differences in treatment adherence or treatment competence between the once weekly versus the twice weekly conditions.

Treatment outcomes

Effect of session frequency over time

Results show a significant effect of session frequency on BDI-II scores over time in favour of twice weekly sessions (estimated mean difference between weekly versus twice weekly sessions at month 6: 3.85 points on the BDI-II, difference in effect size $d = 0.55$; estimated mean scores: 31.05 (95% CI 29.29–32.81) to

23.01 (95% CI 19.45–26.57) for once weekly CBT; 32.58 (95% CI 30.84–34.32) to 20.69 (95% CI 17.18–24.21) for twice weekly CBT; 32.49 (95% CI 30.77–34.21) to 24.30 (95% CI 20.77–27.83) for once weekly IPT; and 34.02 (95% CI 32.25–35.79) to 21.98 (95% CI 18.44–25.52) for twice weekly IPT; also see Data Supplement 4). There were no differences in change over time on the BDI-II between CBT and IPT. There was no different effect of session frequency in CBT versus IPT. Change of BDI-II scores over time between conditions is given in Fig. 2. Corrected mixed-model estimated means (95% confidence intervals) on all outcome measures at each time point for each condition are given in Data Supplement 4. The mixed regression model on the BDI-II scores can be found in Data Supplement 5. Within- and between-group effect sizes can be found in Data Supplement 9.

Sensitivity and completers analyses

The total number of sessions, the presence of a comorbid anxiety disorder or the use of antidepressants were not significant covariates and did not influence the results. In addition, the effect of session frequency remained significant when testing change in BDI-II scores from baseline to month 6, without including the other time points. In congruence with the intention-to-treat analyses, results show a significant effect of session frequency on BDI-II scores over time in favour of twice weekly sessions when running the analysis in completers only ($n = 152$; estimated BDI-II mean difference between weekly versus twice weekly sessions at month 6, 3.80; difference in effect size $d = 0.53$) and there were no differences in change over time on the BDI-II between CBT and IPT.

Table 2 Observed mean scores (s.d.) for all outcome measures in the intention-to-treat sample stratified by condition

	Observed means (s.d.)			
	CBT weekly (n = 49)	CBT twice weekly (n = 49)	IPT weekly (n = 55)	IPT twice weekly (n = 47)
Primary outcome				
Beck Depression Inventory-II				
Baseline	36.02 (9.36)	35.65 (8.69)	33.36 (9.50)	33.91 (12.15)
Session 1	30.64 (10.33)	33.22 (9.42)	31.85 (10.92)	31.26 (11.47)
Week 2	28.11 (10.65)	33.51 (8.73)	33.13 (10.29)	31.77 (12.16)
Month 1	29.67 (11.76)	31.17 (11.77)	32.73 (10.57)	29.73 (13.51)
Month 2	29.05 (12.68)	27.15 (12.51)	28.27 (12.90)	26.05 (14.55)
Month 3	26.74 (13.67)	26.56 (11.92)	26.75 (11.20)	22.81 (14.18)
Month 4	23.17 (14.02)	25.51 (13.63)	24.81 (11.94)	22.53 (16.12)
Month 5	23.29 (14.72)	23.93 (14.79)	24.4 (14.19)	19.38 (15.22)
Month 6	24.16 (15.09)	21.25 (12.90)	22.91 (14.75)	20.02 (16.05)
Secondary outcomes				
Current mood				
Baseline	27.40 (18.65)	23.02 (19.29)	30.89 (21.34)	33.70 (20.82)
Session 1	41.48 (16.30)	31.68 (16.49)	34.26 (16.17)	37.73 (15.10)
Week 2	43.66 (18.34)	32.22 (14.14)	29.58 (16.69)	38.85 (20.52)
Month 1	41.65 (21.25)	37.51 (19.40)	37.85 (17.04)	41.48 (20.23)
Month 2	47.53 (20.98)	48.73 (16.77)	41.97 (20.16)	44.7 (21.95)
Month 3	45.91 (19.58)	48.29 (17.34)	46.91 (22.27)	51.58 (19.92)
Month 4	50.74 (21.83)	48.16 (21.11)	45.21 (18.33)	51.18 (21.16)
Month 5	50.02 (22.87)	51.44 (20.52)	48.06 (20.10)	54.45 (22.90)
Month 6	51.28 (23.24)	53.05 (18.68)	50.52 (22.92)	56.25 (23.11)
General life happiness				
Baseline	2.85 (0.97)	2.71 (1.09)	2.89 (0.99)	3.06 (1.18)
Session 1	2.97 (0.81)	2.64 (0.93)	2.91 (1.13)	3.04 (1.05)
Week 2	3.25 (1.02)	3.05 (0.80)	3.06 (0.75)	3.55 (1.21)
Month 1	3.30 (1.06)	3.22 (1.03)	3.04 (0.90)	3.36 (1.17)
Month 2	3.28 (1.23)	3.71 (0.86)	3.58 (1.27)	3.72 (1.21)
Month 3	3.34 (1.23)	3.86 (1.03)	3.55 (1.10)	3.92 (1.13)
Month 4	3.74 (1.14)	3.91 (1.08)	3.62 (1.07)	3.93 (1.34)
Month 5	3.70 (1.26)	3.76 (1.10)	3.80 (1.24)	4.42 (1.06)
Month 6	3.63 (1.30)	4.17 (1.16)	3.88 (1.45)	4.23 (1.15)
Happiness today				
Baseline	3.04 (1.01)	2.93 (0.89)	3.05 (1.20)	3.29 (1.08)
Session 1	3.51 (0.84)	3.16 (0.95)	3.22 (0.94)	3.40 (0.96)
Week 2	3.55 (0.89)	3.17 (0.85)	3.03 (0.77)	3.44 (1.15)
Month 1	3.42 (1.12)	3.34 (1.10)	3.09 (1.05)	3.39 (1.22)
Month 2	3.56 (1.25)	3.71 (1.01)	3.58 (1.36)	3.57 (1.21)
Month 3	3.68 (1.20)	3.86 (0.94)	3.61 (1.15)	4.05 (1.19)
Month 4	3.97 (1.20)	3.78 (1.18)	3.59 (1.13)	4.03 (1.28)
Month 5	4 (1.35)	4.03 (1.03)	3.64 (1.27)	4.34 (1.21)
Month 6	3.68 (1.29)	4.33 (0.95)	3.77 (1.41)	4.33 (1.08)
Remission of Depression Questionnaire				
Depressive symptoms				
Baseline	15.83 (3.86)	15.44 (3.58)	15.4 (4.26)	15.38 (4.52)
Month 3	12.91 (5.62)	12.81 (5.41)	13.38 (4.49)	12.51 (6.14)
Month 6	11.75 (6.87)	10.48 (6.09)	12.02 (6.06)	9.92 (6.78)
Other symptoms often present in depressed patients, such as anxiety and irritability				
Baseline	6.68 (2.44)	6.81 (1.83)	6.41 (2.43)	6.44 (1.87)
Month 3	5.17 (3.14)	5.51 (2.98)	6.05 (2.39)	5.35 (3.16)
Month 6	4.97 (3.59)	4.2 (2.78)	5.26 (2.97)	4.46 (3.43)
Coping ability				
Baseline	4.29 (1.42)	4.28 (1.45)	4.10 (1.61)	4.25 (1.59)
Month 3	3.14 (1.95)	3.45 (1.82)	3.5 (1.52)	2.91 (2.07)
Month 6	3.64 (1.95)	2.68 (1.89)	3.05 (1.92)	2.43 (2.00)
Positive health				
Baseline	17.33 (3.59)	17.48 (3.34)	17 (4.10)	16.48 (4.00)
Month 3	14.77 (5.32)	14.18 (6.51)	14.05 (4.84)	12.18 (5.96)
Month 6	13.51 (6.51)	11.37 (6.57)	12.47 (6.53)	9.74 (6.74)
Functioning				
Baseline	3.70 (1.72)	3.93 (1.32)	3.98 (1.56)	3.53 (1.53)
Month 3	2.85 (1.89)	3.13 (1.89)	3.17 (1.69)	2.44 (1.86)
Month 6	2.94 (2.01)	2.57 (1.89)	2.94 (1.81)	2.23 (2.12)
Life satisfaction				
Baseline	4.68 (1.27)	4.83 (1.23)	4.58 (1.47)	4.31 (1.46)
Month 3	3.82 (1.77)	3.83 (1.89)	3.45 (1.55)	3.21 (2.07)
Month 6	3.32 (2.13)	3.02 (1.60)	3.35 (1.87)	2.48 (2.12)

(Continued)

Table 2 (Continued)

	Observed means (s.d.)			
	CBT weekly (n = 49)	CBT twice weekly (n = 49)	IPT weekly (n = 55)	IPT twice weekly (n = 47)
General sense of well-being				
Baseline	4.91 (1.16)	4.71 (1.42)	4.6 (1.40)	4.25 (1.46)
Month 3	4.17 (2.01)	3.78 (2.13)	3.73 (1.55)	3.16 (2.07)
Month 6	3.75 (2.19)	3.11 (2.07)	3.58 (1.92)	2.53 (2.25)
RAND-36, general health perception				
Baseline	42.85 (21.33)	43.97 (17.55)	43.09 (17.28)	43.61 (18.04)
Week 2	51.34 (19.48)	44.11 (16.56)	40 (18.15)	43.88 (18.97)
Month 3	49.85 (21.53)	46.08 (21.11)	46.17 (14.46)	46.79 (20.23)
Month 6	50.13 (22.20)	51.53 (22.36)	46.80 (20.46)	53.46 (20.67)

Note that not all patients completed all measurements, total lost to follow-up per time point on the BDI-II scores can be found in Fig. 1. The RAND-36 reports the total score of the subscale 'general experience of health', range of 5 (low perception of general health) to 25 (high perception of general health). Note that for the RDQ, lower scores represent better functioning on each subscale. Missing data on the secondary outcomes differed from missing data on the BDI-II (also see flow chart) on the following time points (number of missing data is given): RAND-36 week 2, CBT weekly n = 23 and CBT twice weekly n = 15; RAND-36 month 3, IPT weekly n = 21 and IPT twice weekly n = 8; RAND-36 month 6, CBT twice weekly n = 10 and IPT weekly n = 19; current mood week 2, CBT twice weekly n = 14; current mood month 1, IPT weekly n = 13; current mood month 3, IPT weekly n = 21; current mood month 5, CBT twice weekly n = 20, IPT weekly n = 24 and IPT twice weekly n = 12; current mood month 6, CBT weekly n = 11, CBT twice weekly n = 11 and IPT weekly n = 19; happiness items week 2, CBT twice weekly = 14; happiness items month 1, IPT weekly n = 13; happiness items month 3, IPT weekly n = 21 and IPT twice weekly n = 8; happiness items month 5, IPT weekly n = 24 and IPT twice weekly n = 12; happiness items month 6, CBT twice weekly = 10 and IPT weekly = 20; RDQ depressive symptoms month 3, IPT weekly n = 21 and IPT twice weekly n = 10; RDQ depressive symptoms month 6, IPT twice weekly n = 9; RDQ coping month 3, IPT weekly n = 21; IPT twice weekly n = 10; RDQ other symptoms month 3, IPT weekly n = 21 and IPT twice weekly n = 10; RDQ positive health month 3, IPT weekly n = 21 and IPT twice weekly n = 10; RDQ functioning month 3, IPT weekly n = 21 and IPT twice weekly n = 11; RDQ life satisfaction month 3, IPT weekly n = 22 and IPT twice weekly n = 10; RDQ well-being month 3, IPT weekly n = 21 and IPT twice weekly n = 10.

CBT, cognitive-behavioural therapy; IPT, interpersonal psychotherapy; RAND-36, RAND 36-Item Health Survey; BDI-II, Beck Depression Inventory-II; RDQ, Remission of Depression Questionnaire.

Analysis of secondary outcome measures

There was a significant difference between session frequencies in current mood, happiness in general and happiness today over time in favour of twice weekly sessions (current mood estimated

mean difference at month 6, 3.98; happiness in general estimated mean difference at month 6, 0.25; happiness today estimated mean difference at month 6, 0.42). Results show trends toward significance on the RAND-36 (in favour of the twice weekly sessions;

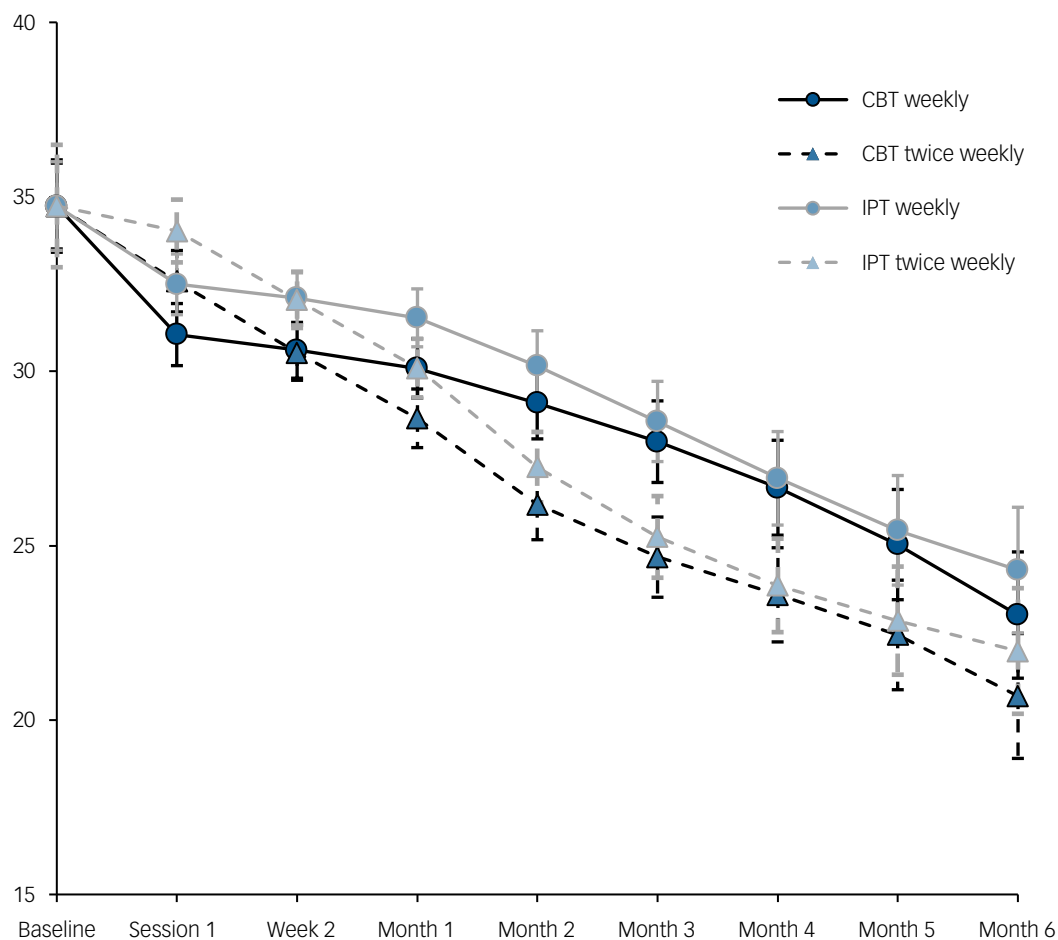


Fig. 2 Estimated means on the Beck Depression Inventory-II (BDI-II) per condition over time.

Note that for illustrative purposes the y-axis starts at BDI-II = 15. Note that BDI-II scores at baseline present the observed mean BDI-II score for all conditions at baseline. The x-axis presents the moment of measurement: baseline, before session 1, and 2 weeks and 1–6 months after the first session. Error bars present the estimated standard error (except for the baseline values that show the observed standard errors). CBT, cognitive-behavioural therapy; IPT, interpersonal psychotherapy.

estimated mean difference at month 6, 2.45) and RDQ positive health (twice weekly session estimated mean difference at month 6, 1.49; IPT estimated mean difference at month 6, 1.25). There were no differences between frequencies or treatments on change over time on the other secondary outcomes. Model descriptions can be found in Data Supplement 6. Corrected mixed-model estimated means (95% confidence intervals) on all outcome measures at each time point for each condition are displayed in Data Supplement 4.

Reliable change and clinically significant change

At month 6, 44.4% (CBT) and 32.3% (IPT) of the patients showed reliable change in the weekly conditions, whereas 60% (CBT) and 52.9% (IPT) of the patients showed reliable change in the twice weekly conditions ($\chi^2 = 4.27$, $P = 0.039$). At month 6, 21.6% (CBT) and 17.6% (IPT) of the patients showed clinically significant change in the weekly conditions, whereas 25.7% (CBT) and 33.3% (IPT) of the patients showed clinically significant change in the twice weekly conditions ($\chi^2 = 1.94$, $P = 0.16$). Reliable and clinically significant change rates are presented in Data Supplements 7 and 8.

Time to response and remission

There was a significant difference between frequency conditions in time to response, in favour of twice weekly sessions (hazard ratio 1.48, 95% CI 1.00–2.18, $P = 0.049$), when controlling for treatment modality and BDI-II baseline scores. There was no significant difference between session frequencies in time to remission (hazard ratio 1.22, 95% CI 0.68–2.18, $P = 0.49$).

Discussion

To our knowledge, this was the first randomised trial to investigate the effects of once weekly versus twice weekly sessions of CBT and IPT in patients with depression. We found that twice weekly sessions lead to a greater reduction in depressed symptoms, less time to response and lower attrition compared with weekly sessions. The effect of session frequency did not differ between CBT and IPT and there was no significant difference between frequency conditions in time to remission.

The finding that only a small proportion of the patients in the present study showed clinically significant change (17.6–33.3%) and most patients still showed moderate levels of depression post-treatment contrasts the findings of three other recent, randomised CBT-IPT studies for depression that report end scores of minimal to mild levels of depression^{13,24,25} and higher rates of clinically significant change.¹³ However, our findings are in line with a fourth CBT-IPT trial²⁶ that also reported moderate post-treatment levels of depression. This latter study was similar to ours in that they also included a large number of therapists, whereas the trials that report lower levels of depression post-treatment had less variation in settings and therapists, and provided extensive on-site supervision.^{13,24,25} One explanation for our findings might be that the large variation in therapists and treatment settings resulted in sub-optimal levels of treatment quality and subsequent high average levels of depression and low clinically significant change at the end of treatment.

A major strength of the present study is its external validity. Although the present study has certain characteristics of an efficacy study, the participation of multiple treatment centres and a large number of therapists with varying educational backgrounds (i.e. from less than a year of experience to 29 years of experience) was necessary to reach the inclusion rate of 200 patients. Therefore, the present study can best be qualified as an 'effectiveness' trial

that generalises to clinical practices outside academic research settings. Moreover, because the quality of the delivered treatments in the present study was only moderate on average, the effects of session frequency might be even larger in therapy settings with a higher level of treatment quality. Another strength of the study is the fine-grained assessment of session frequency: because patients completed online questionnaires before each session, we were able to record the exact difference in session frequency. In addition, although the implementation of a higher session frequency is a challenge that will require an organisational change, the finding that the delivery of twice weekly sessions was entirely possible in this effectiveness trial is a promising finding in regard to future implementation.

Several limitations should be considered. First, the 'pure' effect of frequency may have been confounded by the difference in treatment duration (i.e. total time being in therapy) between the frequency conditions. However, this difference was deliberate in the design of this trial, and relates to cost-effectiveness (to be reported in a follow-up paper), i.e. the assumption that more frequent sessions leads to less indirect costs (i.e. a reduction of work-days lost). Second, there were only a few patients with a low educational background and the number of patients with recurrent depression was low compared with earlier randomised controlled trials.^{2,5} These groups should therefore be considered as underrepresented in the present study. Third, the more frequent assessment of BDI-II at the beginning of each session might have contributed to the lower scores in the twice weekly condition, as two preliminary studies suggest that more frequent BDI assessments can lead to lower BDI-II scores.^{27,28} However, such an effect could have only have occurred in the first 3 months and would have disappeared in the last 3 months, when BDI-II assessments in the twice weekly condition were no longer more frequent and equalled out with the total number of BDI-II assessments in the weekly condition. Fourth, the present study was not powered to detect small effects or a difference between the four treatment conditions. The lack of an interaction between session frequency and treatment modality should therefore be considered as a preliminary result. Fifth, all outcome measures were self-reported and the clinical status of the participants at post-treatment could not be confirmed in the absence of an observer-rated outcome measure. Sixth, no psychometric properties are available for the IPT-AQS yet, and therefore conclusions about the quality of IPT should be considered preliminary.

In summary, the present study demonstrates that in clinical practice settings both CBT and IPT are best provided twice weekly. This finding implies that reorganisation of the specialised mental healthcare services for depression (going from once a week to twice a week) can lead to less attrition, quicker response and better outcomes across the course of treatment.

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Supplementary material

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Data availability

Data will be available upon request.

Author contributions

S.D.H., J.B., F.P.M.L.P., P.v.O., P.C., A.A. and M.J.H.H. obtained funding for this study. All authors contributed to the design of the study. F.P.M.L.P., P.D., L.W., P.v.O., M.v.d.B. and J.S. were involved in the recruitment of patients, therapists and coordination of the treatments. S.J.E. B. coordinated the recruitment of patients, data collection and integrity checks. S.J.E.B. conducted the analyses. S.J.E.B., M.J.H.H., J.T. and A.A. were involved in the interpretation of the analyses. S.J.E.B. wrote the manuscript with contributions from L.H.J.M.L. and M.J.H.H. All authors read, contributed to and approved the final manuscript.

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