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Original Article

Dosage effects of psychodynamic and schema therapy in people with comorbid depression and personality disorder: four-arm pragmatic randomised controlled trial

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Background

Higher intensity of psychotherapy might improve treatment outcome in depression, especially in those with comorbid personality disorder.

Aims

To compare the effects of 25 individual sessions (weekly) of two forms of psychotherapy – short-term psychoanalytic supportive psychotherapy (SPSP) and schema therapy – with the same treatments given for 50 sessions (twice weekly) in people with depression and personality disorder. Trial registration: NTR5941.

Method

We conducted a pragmatic, double-randomised clinical trial and, over 37 months, recruited 246 adult out-patients with comorbid depression/dysthymia and personality disorder. A 2 × 2 factorial design randomised participants to 25 or 50 sessions of SPSP or schema therapy. The primary outcome was change in depression severity over 1 year on the Beck Depression Inventory II (BDI-II). Secondary outcomes were remission both of depression and personality disorder.

Results

Compared with 25 sessions, participants who received 50 sessions showed a significantly greater decrease in depressive symptoms over time (time × session dosage, $P < 0.001$), with a mean difference of 5.6 BDI points after 1 year ($d = -0.53$, 95% CI −0.18 to 0.882, $P = 0.003$). Remission from depression was also greater in the 50-session group (74% *v.* 58%, $P = 0.025$), as was remission of personality disorder (74% *v.* 56%, $P = 0.010$).

Conclusions

Greater intensity of psychotherapy leads to better outcomes of both depression and personality status in people with comorbid depression and personality disorder.

Keywords

Depressive disorders; personality disorders; schema therapy; psychodynamic psychotherapy; randomised controlled trial.

Depression and personality often appear to be interwoven, with personality pathology as one of the drivers of mood symptoms.[1] This is reflected in the high prevalence of comorbidity: 45% of people with major depressive disorder and up to 60% of people with a persistent depressive disorder also have a personality disorder.[2] In people whose susceptibility to depression is rooted in personality, an integrated treatment approach that aims to change enduring personality patterns related to depression may improve outcome and reduce the probability of relapse.[3] Schema therapy and short-term psychodynamic supportive psychotherapy (SPSP) are examples of integrated psychotherapies. Secondary analyses in randomised trials showed improvement in both depression and personality disorder after these interventions.[4,5]

To adequately treat both depression and underlying vulnerability, greater intensity of psychotherapy in terms of session frequency and number may be required: in patients with various diagnoses higher session frequencies are believed to accelerate improvement and recovery, with larger effect sizes found with twice-weekly sessions than with less frequent sessions.[6–9] For personality disorder, evidence-based treatments generally consist of at least 40–50 sessions, and more sessions are often recommended to achieve characterological change (i.e. change in personality traits).[10]

Individuals with depression and personality disorder often receive treatment for depression in short-term or low-intensity formats, but these therapies tend to take longer when personality disorder underlies the depression.[11] It is plausible that these patients are better served by more or more frequent treatment sessions but research on this subject is limited. The subject is important as resources need to be used wisely, but if higher intensity of psychotherapy improves outcome in this group extra resources could be justified. This is the first study to compare two levels of intensity of psychotherapy in people with both depression and personality disorder.

Method

Trial design

The delivery of schema therapy and SPSP was planned in either 25 weekly sessions or 50 twice-weekly sessions over a period of 9–12 months. We hypothesised that 50 sessions would lead to both a greater reduction in the severity of depression over time and higher remission rates for depression and personality disorder after 1 year. A secondary aim was to examine whether SPSP and schema therapy are feasible and effective treatment modalities for people with co-occurring depression and personality disorder. The study was registered with The Netherlands Trial Register (now International Clinical Trials Registry Platform; registration number NTR5941). Details of the study design have been published elsewhere.[12] In summary, the protocol described the study as a single-centre, pragmatic randomised controlled trial with a 2 × 2 factorial design involving 200 patients with a depressive disorder

and personality disorder(s), recruited from a Dutch mental health-care centre for personality disorders. Participants would be randomised by therapy dosage (25 *v.* 50 sessions in a year) and type of therapy (schema therapy *v.* SPSP). The primary clinical outcome measures were depression severity and remission.

The protocol was followed but with some violations. Owing to limited therapist availability the allocation ratio (1:1:1:1) was temporarily changed to 1:3 for SPSP:schema therapy and later reversed to 3:1. In this paper we report on data collected from baseline up to the end of treatment. Two other minor corrections made to the protocol article, concerning type of randomisation and sample size, are described elsewhere.[13]

Participants

Participants were recruited from regular referrals to a specialised centre for personality disorders in Amsterdam, The Netherlands. They were adult out-patients who met the diagnostic criteria for DSM-IV depression or dysthymia and had one or more personality disorders, including non-specified or other groups (PD-NOS; OSPD) according to DSM-IV and DSM-5, based on a minimum of five personality disorder traits (DSM-5 was introduced in The Netherlands during the trial). Patients were excluded if they had psychotic symptoms, a bipolar disorder, inadequate mastery of the Dutch language or an indication for immediate hospital admission or intensive treatment, such as acute suicidality. Individuals with a history of addiction were excluded in case of current alcohol or substance dependence (including benzodiazepines). Individuals without a history of addiction were excluded if the intake clinician decided that the current addiction needed treatment before (or in parallel with) depression/personality disorder treatment. In addition, the treatment centre excluded individuals with a main personality disorder diagnosis in cluster A or antisocial personality disorder. In line with the pragmatic nature of the trial the use of antidepressants was allowed, as were changes in prescription during the course of treatment.

Procedure

Participants were recruited through regular assessment procedures. Once informed about the trial, they had at least 48 h to consider participation, after which they were further assessed for eligibility using a semi-structured interview for depression (section A for Depression and section B for Dysthymia in the Mini-International Neuropsychiatric Interview-Plus; MINI-Plus).[14] As part of the regular assessment procedure individuals were screened for personality disorder (SCID-PQ/SCID-5-SPQ) and those with scores at or above the cut-off minus 1 on the personality disorder sections were further assessed with the Structured Clinical Interview for DSM-IV Axis II Personality Disorders (SCID-II) or DSM-5 Personality Disorders (SCID-5-PD).[15–18] The interviews were conducted by research assistants with a bachelor's degree in psychology and additional training for the semi-structured interviews. Interrater agreement for the SCID interviews was excellent (intraclass correlation coefficient ICC = 0.76 for trait scores by personality disorder and ICC = 0.86 for sum scores by personality disorder based on 27 double-rated interviews).

Randomisation took place after the diagnostic assessment. To ensure allocation concealment, randomisation codes were generated by an independent researcher, not working at one of the clinical departments. Research assistants assessing outcomes were masked for trial condition. Masking was successful: correctly guessed treatment allocations did not differ significantly from random guessing (30 and 25% respectively, $P = 0.294$). Participants were stratified according to depression severity assessed using the Beck Depression Inventory-II (low: BDI-II $\leq$ 29; high: BDI-II $\geq$ 30) and randomly assigned to one of four groups (25 or 50 sessions; schema therapy or SPSP) with random allocation sequences that were generated using the SPSS random number generator (SPSS, Chicago). All participants signed informed consent forms. A difference of 0.45 in the post-treatment effect size for depressive symptoms was estimated as clinically meaningful.[8] Using this difference, a minimum of 211 participants were needed for adequate power, taking 25% drop-out into account ($\alpha = 0.05$, power $(1 - ß) = 0.80$, two-tailed). (Owing to a miscalculation, the required minimum that was reported in the protocol paper was 200 participants. This was rectified in consultation with, and with the approval of, the medical ethics committee. The appropriate amendment was made in the trial register and a correction to the protocol article was published[13]).

Interventions

Both treatment modalities consider depression and enduring personality patterns to be interwoven and both aim to alleviate depression and the underlying susceptibility to depression. However, they differ in some key elements: SPSP is a psychodynamic psychotherapy, originally proven effective for treating depression, with a concurrent positive effect on personality measures.[19,20] Schema therapy is an integrative approach that combines elements from cognitive–behavioural therapy, attachment and object relation theories, Gestalt therapy and experiential therapies.[21] It has proven effective in treating personality disorder and has yielded promising results for the treatment of (persistent) depression.[22,23] The manuals for SPSP and schema therapy for chronic depression were used and the interventions were provided in either 25 or 50 sessions.[19,24] Participants in the 25-session condition received 16 weekly sessions, followed by 9 sessions every 2 weeks. Participants in the 50-session condition received 32 twice-weekly sessions, followed by 18 weekly sessions. Duration of therapy was at least 8 months but owing to holidays and sick days on both sides a duration of 9–12 months was expected in all conditions.

Treatment integrity

Therapists were psychiatrists or psychologists with at least a post-Masters degree in psychology, registered as SPSP or schema therapy therapists or who had at least completed a basic course in SPSP (3 days) or schema therapy (25 h), had 6 months of experience in the given form of treatment and had attended additional biweekly supervision sessions led by a registered supervisor for SPSP or schema therapy. All schema therapists received an additional 1-day course in schema therapy for depression. To improve adherence to the model, therapists were allowed to treat patients in only one treatment modality. To reduce potential therapist bias they were assigned to both dosage conditions.

Adherence (i.e. whether the protocol was followed) and competence (i.e. how well the therapy was performed) were rated by four masked experts (psychologists with a post-master's degree in psychology and 12–16 years of clinical experience), who scored a total of 160 audiotapes of sessions with 80 randomly selected participants. Further details on the adherence and competence scales and procedures are given in Data supplement 1, available at https://doi.org/10.1192/bjp.2024.56. In addition, adherence and competence were checked and enhanced in biweekly peer supervision at which current cases and audiotaped material were discussed. Issues that were not solved in supervision were discussed during biweekly meetings with research staff and supervisors on the trial's advisory committee.

Primary outcomes

The primary outcome was the change in depressive symptoms over time on the Dutch version of the revised Beck Depression

Inventory-II (BDI-II-NL-R).[25] The BDI-II assessments were made at the start of treatment, at 1, 2, 3 and 6 months, and at the end of treatment (9–12 months).

Secondary outcomes

Secondary outcomes included remission of depression (MINI-Plus) and remission of personality disorder (during the past 6 months, assessed using the SCID-II/SCID-5-PD) measured at the end of treatment.[14,16,17] Secondary personality outcomes were improvement over time in terms of psychodynamic and schema therapy constructs assessed using the Severity Indices of Personality Problems (SIPP), the Developmental Profile Inventory (DPI), the Young Schema Questionnaire-Short Form (YSQ-SF) and the Schema Mode Inventory (SMI) planned at inclusion (SIPP), baseline (YSQ-SF, SMI), 6 months (SIPP, DPI, YSQ-SF, SMI) and at the end of treatment (SIPP, DPI, YSQ-SF, SMI).[26–29] Assessments of the reduction of general psychological symptoms (using the Brief Symptom Inventory (BSI) and the Outcome Questionnaire's Symptom Distress subscale (OQ-SD)) and improvement in quality of life (EuroQol 5-Dimension, EQ-5D) were planned at inclusion (BSI, OQ-SD), baseline (BSI, EQ-5D), 3 months (BSI, OQ-SD, EQ-5D), 6 months (BSI, OQ-SD, EQ-5D) and at the end of treatment (BSI, OQ-SD, EQ-5D).[30–32] The happiness item was included in every measurement.[33] For a detailed description of these instruments and psychometric properties, we refer to our protocol paper.[12]

Data analysis

An outline of the analysis strategy is provided in the published protocol.[12] Data Supplement 1 describes the analysis of treatment integrity. Differences in number of sessions, session frequency and therapy duration were tested with Mann–Whitney tests. Primary analyses used intention to treat. To investigate the effect of psychotherapy dosage on depression (BDI-II) multilevel regression analyses with restricted maximum likelihood estimation were conducted. Interventions were represented by two dichotomous variables: 25 (0) versus 50 (1) sessions and SPSP (0) versus schema therapy (1). The initial basic model was a two-level model with repeated measurements (level 1) nested within participants (level 2) with two two-way interactions testing the difference in the change in BDI-II scores over time (in days) for the different psychotherapy dosages (time × dosage) and treatments (time × treatment). When available (BDI, SIPP, OQ-SD), we used the inclusion measurement as a covariate.

The addition of random levels for therapist was tested, as well as the addition of random slopes for time. Time in days was used as the time variable. Various covariance structures for the repeated part were tested (SPSS options AR1, ARMA11, CS, ARH1, CSH). Potential additional quadratic functions of time were compared with the linear model for the best model fit. The additional quadratic parameters were tested in the following sequence: first time-squared, then time-squared and time-squared × dosage, and then time-squared and time-squared × treatment (eventually combined with time-squared × dosage if that led to significantly better fit in the previous step). To explore whether the effect of psychotherapy dosage differed between SPSP and schema therapy, the addition of a three-way interaction (dosage × treatment × time) was tested separately. To investigate differences in remission from depression/dysthymia (MINI-Plus), the groups were analysed with χ^2 tests.

Estimated marginal means were derived from the linear mixed models for all continuous measures. Within-group effect sizes from start to 1 year (Cohen's *d*) were computed: (estimated mean at start of treatment − estimated mean at 1 year)/(observed s.d. at start of treatment). Between-group effect sizes at 1 year were derived from linear mixed model analysis. For the SIPP and OQ-SD, measurement at start of treatment was not available to calculate the effect sizes, and we therefore used the observed measures at inclusion as the reference point and the standard deviation of the inclusion measurement as the denominator. For the BDI we also reported the effect sizes after 308 days, which was the mean treatment duration. Reliable change (response) was defined as a minimum decrease of 9 BDI-II points, based on Jacobson & Truax.[34] Response differences between treatment groups were tested using generalised estimating equations (GEE). Differences in remission from personality disorder between the groups were analysed using χ^2. A sensitivity analysis was performed with completers only (>72% session attendance). Differences in drop-out rates were analysed using χ^2. Differences in time until drop-out were tested using Kaplan–Meier survival analysis with log rank tests. This analysis was done for (a) completers + participants who did not start the intervention + those who dropped out during treatment and for (b) completers + those who dropped out during treatment. Significance levels were set at $P < 0.05$. All statistical analyses were performed in SPSS Statistics 27.0 for Windows. The results are reported in line with CONSORT guidelines.[35]

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 patients were approved by the Medical Ethical Committee of Vrije Universiteit Amsterdam (registration number NL55916.029.15).

Results

Participants

Recruitment took place from April 2016 through to May 2019. After initial screening, 369 patients were interviewed for eligibility, of whom 246 were eligible and willing to participate. After randomisation, 132 participants were assigned to the 25-session arm (54%; 64 in schema therapy and 68 in SPSP) and 114 to the 50-session arm (46%; 60 in schema therapy, 54 in SPSP). The intervention was completed (attendance of at least 72% of the sessions) by 50 participants in 25-session schema therapy (78%), 53 participants in 25-session SPSP (78%), 43 participants in 50-session schema therapy (72%) and 39 participants in 50-session SPSP (72%). All 229 participants with at least one post-randomisation measurement were included in intention-to-treat analysis. The flow of participants is shown in Fig. 1. End-of-treatment assessments were conducted between March 2017 and October 2020.

The sample was predominantly female (70%) and the average age was 40 years (s.d. = 12; range 19–65). Most participants had severe depression (65%; mean BDI score 33.3) and had experienced a depressive episode before (69%). Cluster C personality disorders were the most frequently diagnosed personality disorders (avoidant 44%; obsessive–compulsive 29%), followed by borderline personality disorder (26%). Note that 29% were diagnosed with more than one personality disorder. Baseline demographics for each condition and for the 25- versus 50-session conditions are presented in Data supplements 2 and 3. The use of antidepressants increased slightly during treatment, from 32% at inclusion to 37% during and 33% at the end of treatment, with no differences between conditions (Data supplement 4).

Treatment and study adherence

Although the intention was to deliver both dosage conditions with the same duration of therapy, the 25-session condition was

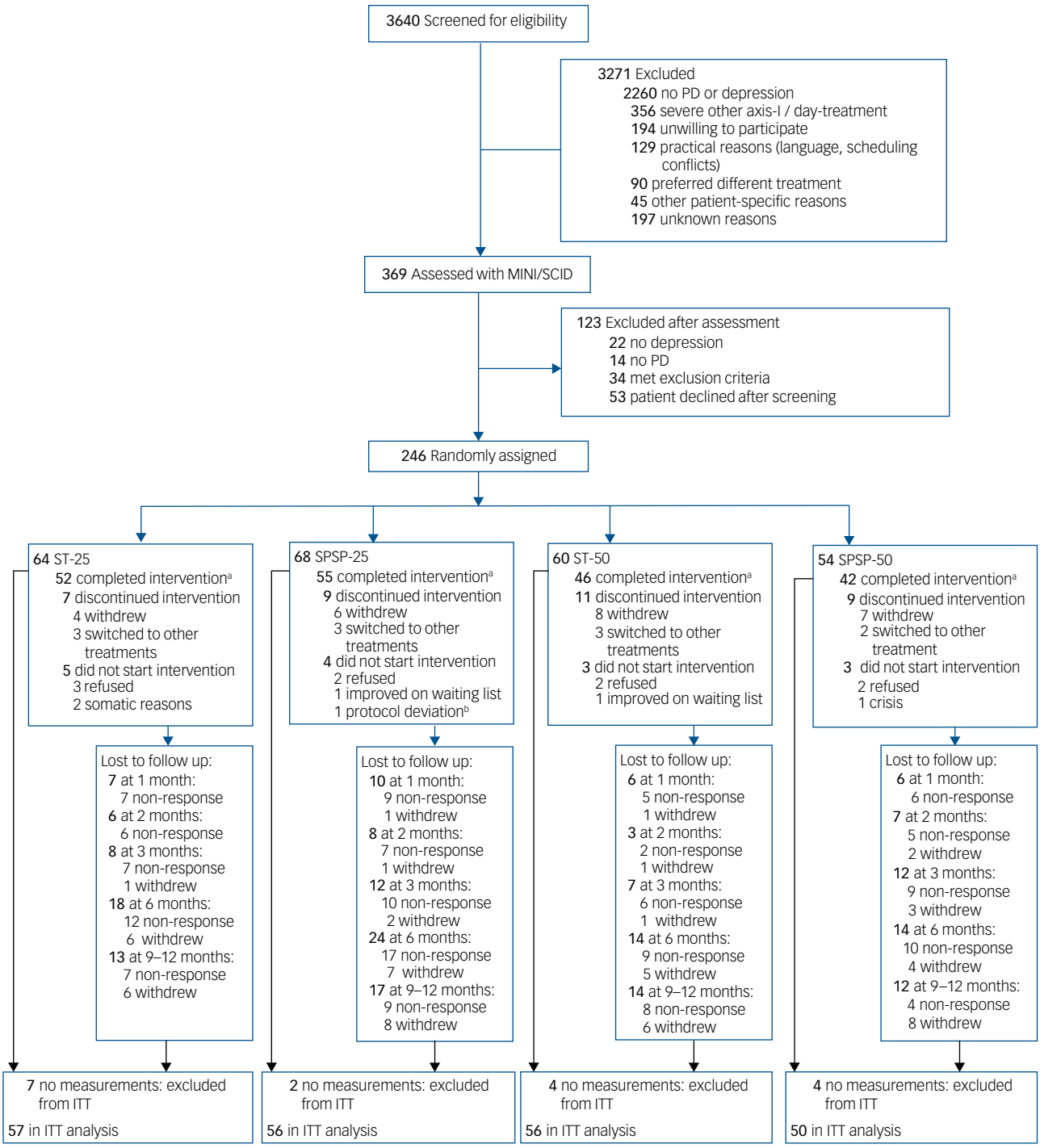

Fig. 1 Participant flowchart.

PD, personality disorder; MINI, Mini-International Neuropsychiatric Interview-Plus, sections A (depression) and B (dysthymia); SCID, Structured Clinical Interview for Personality Disorder for Axis II Personality Disorders (SCID-II) or DSM-5 Personality Disorders (SCID-5-PD); ITT, intention to treat; a, received at least 72% of allocated treatment (minimum of 18 and 36 sessions in 25- and 50-session conditions respectively); b, therapist provided 50 instead of 25 sessions by accident. Non-response per time point was measured for each patient participating in the trial at that moment. Withdrawals from the study were measured monthly, adding up to a total of 6 withdrawals from 25-session schema therapy (ST-25), 8 from 25-session short-term psychoanalytic supportive psychotherapy (SPSP-25), 6 from 50-session schema therapy (ST-50) and 8 from 50-session SPSP (SPSP-50) by the end of the study.

significantly shorter (9.6 months, 293 days, s.d. = 48.4) than the 50-condition (10.9 months, 331 days, s.d. = 58.8, $P < 0.001$). Supplementary Table 4 lists the treatment characteristics for each condition. No differences in drop-out rates nor in time until drop-out were found between the 25- and 50-session conditions nor between the schema therapy and SPSP conditions (Data supplement 5).

Therapists

Thirty-nine professionals delivered the therapies. They were between 34 and 63 years of age and 85% were female. They had an average of 15.2 years of clinical experience (s.d. = 6.0, range 8–36 years), with no differences between SPSP and schema therapy therapists. They each treated 5.7 patients in the trial on average (range 1–12).

Treatment integrity

Schema therapy and SPSP were discriminated: schema therapy-specific elements (adherence) were more evident in schema therapy (mean 18.0, s.d. = 4.4, $n = 40$) than in SPSP (mean 13.3, s.d. = 2.5, $n = 12$, $P = 0.001$) and SPSP-specific elements were more evident in SPSP (mean 12.7, s.d. = 2.5, $n = 40$) than in schema therapy (mean 8.1, s.d. = 2.3, $n = 12$; $P < 0.001$). In 90% of the schema therapy sessions therapists' competence was rated as adequate to excellent (on a 6-item Likert-scale ranging from very poor to excellent: mean 4.4, s.d. = 0.8, $n = 40$). For SPSP, adequate to good competence was found for 78% of the sessions (on a 4-item Likert scale ranging from very poor to good: mean 3.0, s.d. = 0.5, $n = 40$). There were no significant differences in treatment competence between the 25- and 50-session conditions in either schema therapy or SPSP (Data supplement 1).

Primary outcomes

The 50-session arm of the trial was significantly more effective in reducing depression scores than the 25-session one (time × session difference, $P = 0.004$) (Table 1). Note that the best fit was achieved with a quadratic model for the overall effects of time, linear time × dosage and linear time × treatment effects. This effect did not differ between SPSP and schema therapy. Based on the primary analysis, mean differences per time point were estimated at 5.6 BDI points after 1 year, with an effect size difference of $d = 0.53$ (95% CI 0.18–0.88) between the 25- and 50-session conditions. Figure 2 and Supplementary Table 6 show the estimated means for each condition by time point of planned BDI-II assessments.

Secondary outcomes

More participants no longer satisfied the diagnosis of depression or dysthymia on the MINI-Plus ($n = 63$, 74%) after 50 sessions than after 25 sessions ($n = 58$, 58%; $P = 0.025$). The 50-session condition also was superior to the 25-session condition over time on functional and dysfunctional schema modes (SMI), neurotic and primitive levels of development (DPI), self-control, identity integration, responsibility and relational capacities (SIPP), general happiness, symptomatic distress (OQ-SD) and general mental health (BSI). Table 2 shows the results of the multilevel analyses on all secondary outcome measures. Note that the best fit was reached with a quadratic model for the effect of time on most outcome measures except for SIPP relational capacities, IPD adaptive and primitive, SMI negative, Happiness, OQ-SD and BSI, for which linear time models had the best fit. For the models with a quadratic time effect, the interactions between time and dosage treatment, respectively, involved only a linear slope of time, because the addition of the interactions with time-squared did not improve the fit significantly. The only exception was observed for the Functional Modes SMI outcome, where the addition of the dosage × time-squared interaction improved the fit significantly. Session dosage × time-squared (quadratic) interaction was included in the model. The time-squared × dosage interaction implied that there was a curvilinearly increasing difference between 25- and 50-sessions dosages, with more improvement in the 50-sessions dosage (resulting in start to 12 month estimated means of 3.03 (95% CI 2.92–3.13) to 3.36 (95% CI 3.15–3.57) in the 25-session condition and 3.13 (95% CI 3.01–3.24) to 3.72 (95% CI 3.54–3.89) in the 50-session condition; $d = 0.62$).

In addition to the estimated means on the BDI at 1 year, we estimated the differences at the mean therapy duration (308 days) and found BDI-II scores to be 4.7 points lower in the 50- than in the 25-session condition, with an effect size difference of $d = 0.44$ (95% CI 0.14–0.74). Data supplement 7 shows estimated means and effect sizes for all primary and secondary outcomes.

Changes in personality status were also greater in the 50-session arm of the trial. At the end of treatment, personality disorder was no longer diagnosed in 74% ($n = 63$) of the group who received 50 sessions, compared with 56% ($n = 56$) of the group who received 25 sessions ($P = 0.010$). Looking at personality disorder and depression together, more patients in the 50-session condition than in the 25-session condition had lost both their depression and personality disorder diagnoses ($n = 52$, 63% and $n = 40$, 40% respectively; $P = 0.003$), whereas recovery from neither diagnosis was seen more often in the 25-condition ($n = 25$, 25% and $n = 9$, 11% respectively; $P = 0.013$).

We found no difference in the effectiveness of schema therapy and SPSP over time between the treatment conditions.

Sensitivity analyses

The completers analysis showed, in line with the intention-to-treat analyses, a significant effect of session dosage on BDI-II scores over time in favour of the 50-session condition ($n = 185$, time × session dosage, $P = 0.001$), with an estimated BDI-II mean difference between 25 and 50 sessions after 1 year of 7.4 and a difference in effect size of $d = 0.70$ (95% CI 0.34–1.06), with again no difference between schema therapy and SPSP.

Adverse events

Two serious adverse events were reported: one patient died by suicide after the initial research assessment but before randomisation and one patient attempted suicide in the 50-session SPSP condition.

Discussion

This study shows that people with comorbid depression and personality disorder had a better outcome when treated in 50

Table 1 Results of multilevel analyses: the effect of psychotherapy dosage and type of treatment over time (continuous model)

	B	s.e.	95% CI	*T*	*P*
Intercept	6.85	1.86	3.18 to 10.53	3.68	<0.001
BDI score at inclusion[a]	0.71	0.05	0.61 to 0.80	14.56	<0.001
Session dosage	−0.16	1.03	−2.19 to 1.86	−0.16	0.873
Treatment	1.08	1.02	−0.94 to 3.10	1.05	0.295
Time	−0.05	0.01	−0.07 to −0.04	−6.75	<0.001
Time × session dosage	0.02	0.01	0.01 to 0.03	2.92	0.004
Time × treatment	-2.18×10^{-3}	0.01	−0.01 to 0.01	−0.40	0.686
Time-squared	4.00×10^{-5}	1.96×10^{-5}	1.50×10^{-6} to 7.83×10^{-5}	2.04	0.042

BDI, Beck Depression Inventory–II.
a. BDI score at start of treatment, after 1, 2, 3 and 6 months, and at end of treatment (9–12 months) was the dependent variable.

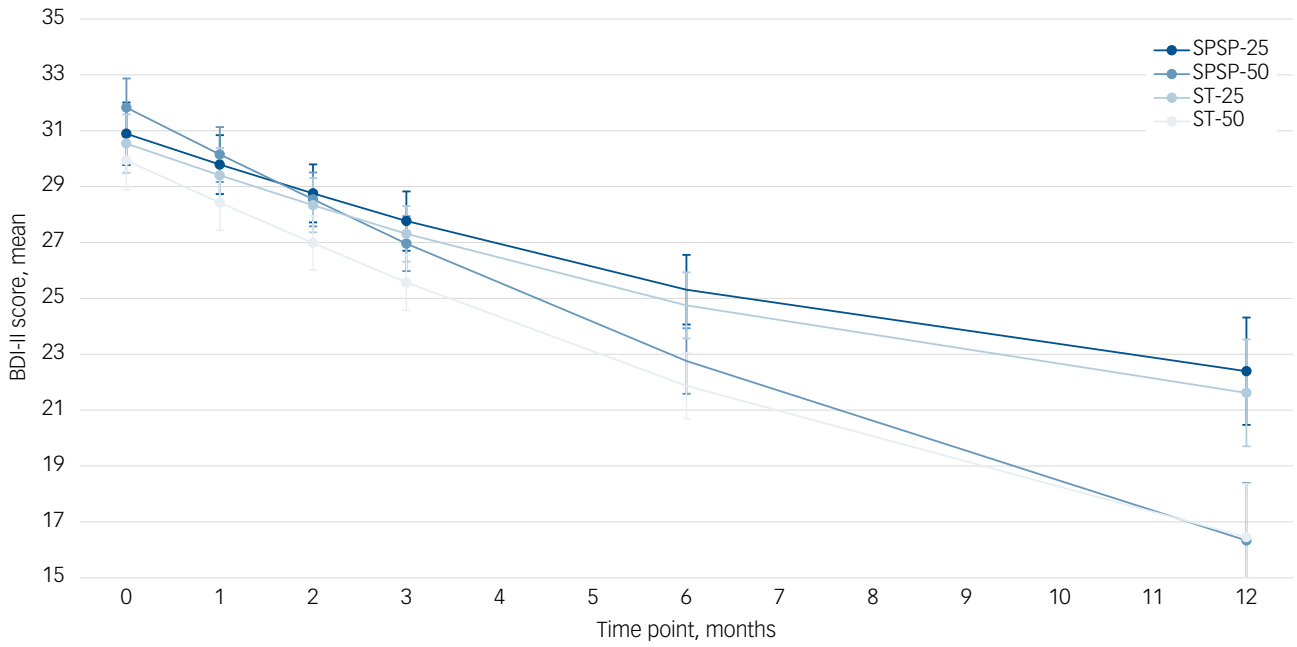

Fig. 2 Estimated means on the Beck Depression Inventory-II (BDI-II) per intervention condition and by time point.

SPSP-25 and SPSP-50 denote 25- and 50-session short-term psychoanalytic supportive psychotherapy; ST-25 and ST-50 denote 25- and 50-session schema therapy. The *y*-axis starts at a BDI-II mean score of 15 for presentation purposes. The *x*-axis presents the moments at which assessments were planned: treatment start, 1, 2, 3, 6 and 12 months (the analysis was based on the actual moment the assessment was done (in days)). Error bars present the estimated standard error.

Table 2 Results of multilevel analyses: the effect of psychotherapy dosage over time on the secondary outcome measures[a]

	B	s.e.	95% CI	*T*	*P*
Depression					
Reliable change (BDI change ≥9)	1.76×10^{-3}	1.08×10^{-3}	-0.35×10^{-3} to 3.99×10^{-3}	2.67	0.102
Personality					
Dysfunctional schemas (YSQ-SF)	6.77×10^{-4}	3.55×10^{-4}	-2.41×10^{-5} to 1.38×10^{-3}	1.91	0.058
SMI					
Functional modes					
Time × dosage	7.50×10^{-4}	7.32×10^{-4}	-6.90×10^{-4} to 2.19×10^{-3}	1.03	0.306
Time-squared × dosage	-4.03×10^{-6}	2.37×10^{-6}	-8.69×10^{-6} to 6.26×10^{-7}	−1.70	0.090
Chi-squared fit test of combined time × dosage and time-squared × dosage effects				$\chi^2 = 0.20$	**0.034**
Dysfunctional modes	4.88×10^{-4}	2.19×10^{-4}	5.62×10^{-5} to 9.19×10^{-4}	2.23	**0.027**
DPI					
Adaptive level of development	-4.51×10^{-3}	4.70×10^{-3}	-1.38×10^{-2} to 4.76×10^{-2}	−0.96	0.339
Maladaptive neurotic level	1.21×10^{-2}	5.49×10^{-2}	1.31×10^{-3} to 2.30×10^{-2}	2.21	**0.028**
Maladaptive primitive level	9.46×10^{-3}	4.50×10^{-3}	5.91×10^{-4} to 1.83×10^{-2}	2.10	**0.037**
SIPP					
Self-control	-2.19×10^{-3}	9.46×10^{-4}	-4.06×10^{-3} to -3.14×10^{-4}	−2.31	**0.023**
Identity integration	-1.98×10^{-3}	8.66×10^{-4}	-3.70×10^{-3} to -2.70×10^{-4}	−2.29	**0.024**
Responsibility	-1.91×10^{-3}	6.85×10^{-4}	-3.27×10^{-3} to -5.56×10^{-4}	−2.79	**0.006**
Relational capacities	-1.69×10^{-3}	8.54×10^{-4}	-3.38×10^{-3} to 1.70×10^{-6}	−1.98	**0.050**
Social concordance	-1.34×10^{-3}	8.47×10^{-4}	-3.02×10^{-3} to 3.33×10^{-4}	−1.59	0.115
Quality of life					
General life happiness	-1.43×10^{-3}	5.12×10^{-4}	-2.44×10^{-3} to -4.28×10^{-4}	−2.80	**0.005**
Quality of life (EQ–5D)	-9.08×10^{-5}	1.05×10^{-4}	-2.98×10^{-4} to 1.16×10^{-4}	−0.86	0.388
Other					
Symptomatic distress (OQ-SD)	2.38×10^{-2}	1.08×10^{-2}	2.44×10^{-3} to 4.51×10^{-2}	2.20	**0.029**
General psychological symptoms (BSI)	2.60×10^{-2}	1.28×10^{-2}	8.15×10^{-4} to 5.12×10^{-2}	2.03	**0.043**

BDI, Beck Depression Inventory-II, second edition; YSQ-SF, Young Schema Questionnaire-Short Form; SMI, Schema Mode Inventory; DPI, Developmental Profile Inventory; SIPP, Severity Indices of Personality Problems; EQ-5D, EuroQol 5-Dimension; OQ-SD, Outcome Questionnaire – Symptom Distress subscale; BSI, Brief Symptom Inventory.
a. Mean item scores were used for the YSQ-SF, SMI functional modes (Happy child and Healthy adult subscales) and SMI dysfunctional modes (all the other subscales). For the DPI and SIPP, subscale scores were used. No measures were available at treatment start for the SIPP and OQ-SD. Bold denotes significance at $P < 0.05$.

psychotherapy sessions (starting twice weekly) than in 25 (starting weekly), with no differences between schema therapy and SPSP being found. A randomised trial can only assess one specific hypothesis well and the effect of the other variables, type of intervention or whether differences found were due to the frequency of sessions, to the amount of sessions or to their combination cannot be judged. It is also possible that the optimal intensity of therapy could be greater than in the 50-session condition as the beneficial effects did not tail off, unlike in other longer-term treatments.[36]

Possible explanations for the superior effects of 50 sessions include the need for those with personality disorders for more input to strengthen learning processes and to implement psychotherapy content better in everyday live, or that the additional and more frequent sessions strengthened the therapeutic alliance.[37,38]

Although previous research in the field of depression emphasised the need for higher session frequency in the initial phase of therapy, our study shows that the dosage effects only start to appear in the second half of therapy.[8,9] This happened just after session frequencies were halved in all conditions (after 6 months). This could indicate that the difference between one session every 2 weeks and one session a week (in the second half of therapy) is more substantial than between one and two sessions a week (in the first half of therapy). Another possibility is that the effect of psychotherapy dosage in the initial phase of therapy takes longer to show in this patient group.

Strengths and limitations

A major strength of this pragmatic trial is that many aspects resemble clinical reality (broad eligibility criteria, no detailed treatment manuals, no pilot treatment prior to the start of the study, no regulation of medication). This enhances the generalisability of the results. Other strengths are the large sample, the intention-to-treat analysis, an extensive treatment integrity check and the availability of both self-reports and observer-rated measures for depression and personality disorder. In addition, the double-randomised design provided an opportunity to compare differences between psychotherapy dosages independently of treatment type and, conversely, to compare differences between the treatment types independently of psychotherapy dosage.

This brings us to the first limitation of the study: it was not powered to detect differences between all four treatments as separate conditions, or to demonstrate the equivalence of SPSP and schema therapy. The lack of interaction between psychotherapy dosage and treatment type and the fact that no differences were found between SPSP and schema therapy should be interpreted with caution. A second limitation is that longer-term data are not included in the analyses, making it uncertain whether the found effects are maintained after treatment termination. Third, we did not include a waiting-list or treatment-as-usual condition. For ethical reasons we did not want patients to be deprived of specialised therapy for a year. Clearly, this means we could not rule out possible effects of natural course and do not know the additional value of these integrated treatment forms compared with regular care. Fourth, since our study was conducted in a centre specialised in personality disorder, the generalisability to broader settings needs to be explored. Compared with a sample in a depression setting, our sample had more cluster B personality disorders and more personality disorders per participant, indicating higher personality disorder severity.[39] Fifth, we cannot rule out the possibility that depression has to some extent influenced personality disorder measures, although we tried to minimise this effect by explicit training of the assessors on this distinction. Sixth, some participants did not complete any questionnaires and could therefore not be included in the intention-to-treat analysis, which increased the risk of an attrition bias. Finally, an imbalance in allocation occurred by chance. Owing to the large sample size, however, the power to detect differences between the groups remained sufficient. In retrospect we may have tried to test too many hypotheses in this study and the comparison of the two forms of psychotherapy could not be adequately tested in our design. Although the differences in antidepressant use were non-significant, it would have been better if the prescription of antidepressants had been controlled by the researchers during the trial.

Implications

Clinicians should consider the intensity of psychotherapy for depression in people with personality disorder, as both SPSP and schema therapy were more effective in terms of both depression and personality measures when delivered in 50 sessions than in 25 (spread over 1 year). Long-term studies are needed to determine whether higher dosages can reduce recurrence of depression, to identify additional treatment needs, and to assess direct and indirect costs.

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Supplementary material

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Data availability

All data generated or analysed during this study are included in this article and its supplementary material files.

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Author contributions

M.K., H.V. and J.D. were involved in designing and initiating the study. M.K., as the primary investigator, oversaw data collection and wrote the drafts of the manuscript. A.B. provided guidance throughout the project organisation and data collection phase of the study. J.P. conducted the statistical analysis and wrote the statistical analysis section. H.V., A.A. and J.D. supervised the study. A.B., H.V., A.A. and J.D. commented on all manuscript drafts. L.D. and K.d.B. supervised the trial therapists, sat on the advisory committee (as did A.B.) and commented on the final draft of the manuscript. All authors have contributed to and approved the final manuscript.

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