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Erstveröffentlichung in / First published in:

Psychotherapy and Psychosomatics. 2017, 86 (6), S. 341 – 350 [Zugriff am: 19.05.2020]. Karger. ISSN 1423-0348.

DOI: https://doi.org/10.1159/000481177

Regular Article

Psychotherapy and Psychosomatics

Psychother Psychosom 2017;86:341–350
DOI: 10.1159/000481177

Received: January 11, 2017
Accepted after revision: August 30, 2017
Published online: November 3, 2017

Online Self-Help as an Add-On to Inpatient Psychotherapy: Efficacy of a New Blended Treatment Approach

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Keywords

Depression · Efficacy · Inpatient treatment · Internet-based treatment · Psychosomatic medicine · Psychotherapy · Randomized controlled trial

Abstract

Background: Depression is one of the most frequent and costly mental disorders. While there is increasing evidence for the efficacy of online self-help to improve depression or prevent relapse, there is little evidence in blended care settings, especially combined with inpatient face-to-face psychotherapy. Therefore, we evaluated whether an evidence-based online self-help program improves the efficacy of inpatient psychotherapy. ***Methods:*** A total of 229 depressed patients were randomly allocated either to an online self-help program (intervention group [IG]; Deprexis) or an active control group (CG; weekly online information on depression) in addition to inpatient psychodynamic psychotherapy. Both groups had access to their respective experimental intervention for 12 weeks, regardless of inpatient treatment duration. Reduction of depressive symptoms, as measured with the Beck Depression Inventory-II, was the primary outcome at the end of the intervention (T2). ***Results:*** Depressive symptoms were statistically significantly lower in the IG compared to the active CG at T2 with a moderate between-group effect size of $d = 0.44$. The same applied to anxiety ($d = 0.33$), quality of life ($d = 0.34$), and self-esteem ($d = 0.38$) at discharge from inpatient treatment (T1). No statistically significant differences were found regarding dysfunctional attitudes ($d = 0.14$) and work ability ($d = 0.08$) at T1. ***Conclusions:*** This is the first evidence for blended treatment combining online self-help with inpatient psychotherapy. The study opens new and promising avenues for increasing the efficacy of inpatient psychotherapy. Future studies should determine how integration of online self-help into the therapeutic process can be developed further.

Introduction

Affecting an estimated 38.2% of the population of the European Union [1], mental disorders constitute one of the most challenging global health care problems [2], often taking a chronic course and resulting in high med-

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ical, indirect, and nonmedical costs [3]. Even though effective evidence-based treatments have been established, only a minority of 10–50% of depressed individuals receives them in an adequate and timely manner [4, 5]. In order to provide instant, flexible help with low barriers, online self-help interventions have been developed. They have been found to be effective in numerous randomized controlled trials with samples recruited over the internet, particularly when combined with some degree of basic therapeutic support [6–8]. In recent meta-analyses self-guided internet-based cognitive behavioral therapy proved to be significantly more effective compared to control groups regarding depressive symptom severity [9], subthreshold depression [10], and prevention of depressive disorders [11]. Deprexis is an interactive internet-based self-help program which does not necessarily require therapist support. A recent meta-analysis [12] based on 8 studies demonstrated posttreatment effectiveness for depressive symptoms with a medium effect size of $d = 0.54$ (95% CI: 0.39–0.69). Findings on the applicability of online self-help for primary care patients have been mixed, especially when offered in usual care settings [13]. A large, independent evaluation of 2 unsupported computerized cognitive behavioral interventions, which had proved to be effective in developer-led trials, found no significant effect in a primary care setting as an add-on compared to usual care [14], mainly due to low adherence to the online treatment and probably to some extent due to the lack of therapeutic support. On the other hand, preliminary studies have indicated that web-based interventions can be combined with face-to-face psychotherapy in a meaningful way, e.g., by increasing the adherence and effectiveness of conventional therapy [15, 16] or saving therapist time [17–19].

Online programs have been used successfully to prevent relapse in patients with remitted depression [20–22] following outpatient or inpatient psychotherapy or rehabilitation in order to maintain treatment gains in recent trials [23, 24]. However, we are not aware of a trial examining the efficacy of an online self-help program in addition to inpatient psychotherapy. Inpatient psychotherapy for acute or chronic depression is indicated when symptomatology is severe and complex, and when outpatient psychotherapy or psychopharmacotherapy is not sufficient [25, 26]. Even though inpatient psychotherapy has been shown to improve depressive symptoms considerably [27–29], patients do not fully remit within 4–8 weeks, and they are at an increased risk for relapse or readmission [30, 31].

The purpose of this paper is to determine (1) if depressed inpatients accept the offer of additional online self-help, (2) if the adjunct treatment improves the outcome of inpatient psychotherapy, and (3) if it supports stabilization of positive treatment effects beyond inpatient treatment. We assume that an online self-help program is well accepted by patients and increases the efficacy of inpatient treatment.

Methods

Participants

We recruited a total of 229 patients in the Psychosomatic Clinic in Bad Neustadt/Saale, Germany, from July 2014 to February 2016. To be eligible, patients were required to be aged 18–65 years and to have private internet access, sufficient German language proficiency, a score in the Beck Depression Inventory (BDI-II) above 13, and a clinical diagnosis of depression (ICD-10: F32.x, F33.x, F34.1, F43.2). Exclusion criteria specified (1) diagnosis of psychosis (F20–F29), (2) current alcohol or drug addiction (F10–F19), (3) borderline (F60.3), antisocial (F60.2), schizoid (F60.1), and schizotypal (F21) personality disorders, (4) anorexia nervosa (F50.0), and (5) lifetime diagnoses of schizophrenia (F20–F29), schizoaffective (F25), bipolar (F31), or organic (F00–F09) mental disorder. Diagnoses were made by the individual therapist of the patient under regular supervision, based on ICD-10 criteria.

Eligible patients were invited to the weekly study information session by the study assistant where they got oral and written information about the study and the requirements for participation. The interventions were briefly presented to therapists, who were informed about their patients' study participation but had no active role in any add-on treatment.

Procedure

Patients who gave their written informed consent to participate were coded and randomized to either the intervention group (IG) or the control group (CG). After randomization, the study assistant gave each participant a login code and introduced the self-help intervention (Deprexis) and the online information platform (IG and CG, respectively). The trial protocol, including the concept for protection of data privacy, the study information, and forms for the written informed consent, were approved by the Ethics Committee of the Statutory Physician Board of the State of Rhineland Palatinate (Ref. No. 837.093.14 [9332-F]). All procedures involved in this study follow the ICH-GCP guidelines. The trial was registered at Clinicaltrials.gov (identifier: NCT02196896), and the trial protocol was published elsewhere [32].

Intervention

Inpatient psychodynamic psychotherapy consists of individual and group psychotherapy, creative psychotherapy interventions, and adjunct treatments like patient education and physical training. Additionally, a 12-week access to the online self-help intervention was offered. Deprexis is divided into 10 main modules plus 1 introductory and 1 summary module. Although labeled as cognitive behavioral, the eclectic program uses techniques from different psychotherapeutic orientations like cognitive behavioral psy-

chotherapy, positive psychology, emotion-focused therapy, and dream work. A dialogue-like concept guides the user through the intervention, presenting a text block with optional graphics, exercises, audio files, and answering options. Subsequent text blocks are based on the user's choices. A new module is presented to the user only after completing the prior module; thus the user progresses at his or her own pace. Optional reminders via e-mail and SMS can be activated [33].

Participants were assigned two 1-h time slots in their weekly treatment plan, but they were free to use the intervention beyond these slots. After discharge from inpatient treatment, participants had access to Deprexis for the remaining time of a total duration of 12 weeks. Follow-up results will be described in another publication.

Control Condition

In addition to inpatient psychotherapy (treatment as usual [TAU]) the CG had access to an online platform providing 12 weekly modules with specific topics regarding depression. This information was gathered, structured, and presented by the study center with permission from reliable and freely available internet sources. Most of the content was taken from the patient version of the German medical guidelines [34], the German network on depression [35], and health insurance companies. Information focused on clinical signs and diagnosis, etiology, course of depression, psychotherapeutic and pharmacological treatments, and self-help options. One consecutive module was automatically activated on a weekly basis over a period of 12 weeks. To ensure comparability with the IG, the CG was also given 2 different weekly time slots of equal length in their treatment plan to use the online platform.

Outcome Measures

All measures were based on self-report and collected using the online survey platform SoSci Survey [36], accessible online at https://www.soscisurvey.de.

Primary Outcome

The primary outcome was depressive symptoms at the end of inpatient treatment, as measured by the BDI-II [37]), a reliable and valid instrument [38, 39]. Cronbach's α in this study was 0.92.

Secondary Outcomes

Depressive symptoms were additionally assessed with the Patient Health Questionnaire-9 (PHQ-9), a module of the PHQ with well-established psychometric properties [40]. Anxiety was measured with the General Anxiety Disorder-7 (GAD-7), with verified reliability and validity [41]. Quality of life was assessed with the EUROHIS-QOL 8-item index [42], a shortened version of the World Health Organization Quality of Life Instrument-Abbreviated Version (WHOQOL-BREF), with proven reliability and validity [42]. Self-esteem was measured with the reliable and valid Rosenberg Self-Esteem Scale (RSE) [43]. Dysfunctional attitudes related to depressive thinking were measured with the reliable and valid Dysfunctional Attitudes Scale (DAS) [44]. Work ability was measured with the short version of the Work Ability Index (WAI) [45], a predictive, reliable, and internationally validated instrument [46].

Further Analyses

Satisfaction with the online interventions was measured on 5-point Likert scales (ranging from "not at all" to "somewhat" to "very") with the item "How satisfied are you with Deprexis?" (respectively the online information in the active control condition). The influence of the intervention on the inpatient therapy was measured with the item "How did Deprexis/online information influence the treatment outcome of your inpatient therapy?" (ranging from "very negative" to "no influence" to "very positive"). To identify the intensity of use of the intervention, patients were asked "How often did you use Deprexis/the information on the internet platform?" ("never," "less than once a week," "once a week," "several times a week").

Patients and therapists filled out the German version of the Helping Alliance Questionnaire (HAQ) [47], a standardized instrument to assess therapeutic alliance with good reliability and validity at discharge.

Sample Size Calculation

Power calculation was based on an effect size of $d = 0.50$, a power of 0.80, and an alpha error of 0.05 (2-sided). To detect this effect size, a sample size of $n = 128$ is necessary. Based on the sample size of $n = 230$, the study had a power of 0.97 to detect an effect size of $d = 0.50$ or higher. A more detailed description of power calculation is described elsewhere [32].

Randomization

Participants were randomly assigned to the IG or CG using block randomization at a ratio of 1:1. Randomization was conducted with the software Research Randomizer [48] by the Study Center of Mental Disorders, an independent institution of the University Medical Center Mainz.

Data Analyses

All analyses were based on intention to treat. Missing data were imputed with IBM SPSS Statistics 23 using a Markov Chain Monte Carlo multivariate imputation algorithm with 5 imputations, 10 estimations per missing value, and a constraint of a maximum of 60% missing data. We used unpaired *t* tests to compare responders and nonresponders for baseline differences, analyses of covariance (ANCOVA) to compare outcomes between groups at the end of treatment (controlling for baseline scores), and paired-samples *t* tests for the analysis of pre-post change in outcome measures within subjects. Reported are means and standard deviations for between-group analyses (ANCOVA), *t* test statistics, and effect sizes (Cohen's *d*). Cohen's *d* for between-group comparisons was calculated using the estimated means from the ANCOVA to control for baseline scores and the pooled standard deviations corrected for different group sizes. Cohen's *d* for within-group comparisons was calculated following the method of Dunlap et al. [49, p. 171], correcting for the correlation between the 2 measures in order to avoid overestimation of effects. All analyses were conducted on a 2-sided level of significance of 0.05. Data analyses were conducted with IBM SPSS Statistics 23 [50].

Results

Study Flow and Participant Characteristics

Figure 1 shows the flow of participants in the study until the end of the intervention (T2). Out of 611 patients assessed for eligibility, 382 (63%) were excluded from the

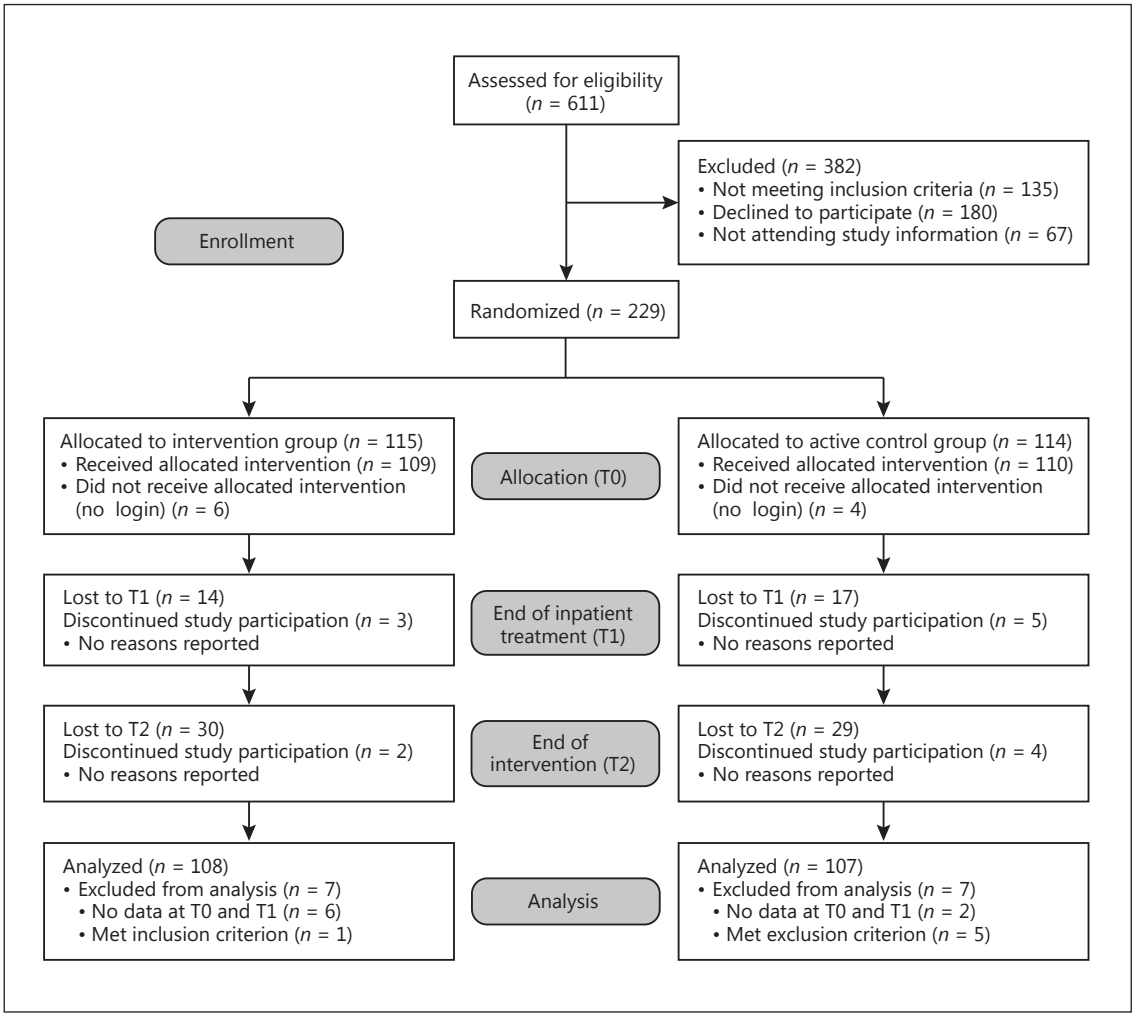

Fig. 1. CONSORT flow diagram showing the flow of participants in the study until the end of the intervention (T2).

study for not meeting inclusion criteria (22%), declining to participate (30%), or not attending the study information sessions because of organizational constraints such as scheduling problems, relocation to another clinic, or early discharge (11%). Thus, a total of 229 (37%) patients were randomized, with 115 allocated to the IG and 114 to the CG; 109 patients in the IG and 110 in the CG received the respective intervention. At the end of inpatient treatment (T1), 198 (86%) participants completed the assessment: 88% in the IG and 85% in the CG. At the end of the intervention (T2) 170 (74%) participants completed the assessment: 74% in the IG and 75% in the CG. Dropout rates were low, with 3% at T0 (did not start intervention), 4% at T1, and 3% at T2, with no differences in dropout rates between IG and CG.

Analyses revealed that the participants who completed the T2 assessments did not differ from those participants who dropped out from assessments concerning baseline mental symptoms like our primary outcome (BDI-II; $t_{213} = -0.017$; $p = 0.986$), depressive symptoms (PHQ-9; $t_{200} = 0.962$; $p = 0.337$), generalized anxiety (GAD-7; $t_{200} = 0.138$; $p = 0.890$), quality of life (EUROHIS-QOL 8; $t_{199} = 0.756$; $p = 0.450$), self-esteem (RSE; $t_{200} = 0.652$; $p = 0.515$), dysfunctional attitudes (DAS; $t_{199} = 0.483$; $p = 0.630$), or self-assessed work ability (WAI; $t_{198} = 0.030$; $p = 0.976$). For all analyses concerning the outcome measures, 14 patients were excluded due to missing assessments at T0 and T1 ($n = 8$) or meeting exclusion criteria ($n = 6$). Overall, 215 participants were analyzed after imputing missing data.

Table 1. Demographic and medical characteristics: intervention group (IG) versus control group (CG)

Variable	IG (n = 115)	CG (n = 114)	Total (n = 229)
Age (mean ± SD), years	47.36±10.38	48.61±9.16	47.98±9.79
Sex			
Male	41 (35.7)	49 (43)	90 (39.3)
Female	74 (64.3)	65 (57)	139 (60.7)
Marital status			
Single	27 (23.5)	25 (21.9)	52 (22.7)
Married	53 (46.1)	62 (54.4)	115 (50.2)
Separated	9 (7.8)	4 (3.5)	13 (5.7)
Divorced	25 (21.7)	19 (16.7)	44 (19.2)
Widowed	1 (0.9)	4 (3.5)	5 (2.2)
Graduation			
No graduation	16 (13.9)	21 (18.4)	37 (16.2)
Lower secondary	22 (19.1)	15 (13.2)	37 (16.2)
Middle secondary	34 (29.6)	31 (27.2)	65 (28.4)
Higher secondary	31 (27.0)	37 (32.5)	68 (29.7)
Other	12 (10.5)	10 (8.8)	22 (9.6)
Employment status			
Full-time	55 (47.8)	54 (47.4)	109 (47.6)
Regular part-time	29 (25.2)	17 (14.9)	46 (20.1)
Apprenticeship	3 (2.6)	1 (0.9)	4 (1.7)
Retired	3 (2.6)	8 (7.1)	11 (4.8)
Not working	14 (12.1)	24 (21)	38 (16.6)
Other	11 (9.6)	10 (8.8)	21 (9.1)
Sick leave at intake			
Yes	68 (59.2)	61 (53.5)	119 (56.3)
No	35 (30.4)	38 (33.3)	73 (31.9)
Missing	12 (10.4)	15 (13.2)	27 (11.8)
Previous medication			
No	42 (36.5)	35 (30.7)	77 (33.6)
Yes, up to 3 months	11 (9.6)	9 (7.9)	20 (8.7)
Yes, 3–6 months	10 (8.7)	13 (11.4)	23 (10.0)
Yes, 6–12 months	13 (11.3)	9 (7.9)	22 (9.6)
Yes, longer than 12 months	39 (33.9)	48 (42.1)	87 (38.0)
Previous treatment			
No	43 (37.4)	27 (23.7)	70 (30.6)
Yes, 1 treatment	31 (27.0)	39 (34.2)	70 (30.6)
Yes, 2 or more treatments	41 (35.7)	48 (42.1)	89 (38.9)
Antidepressant medication during treatment			
No	45 (39.1)	34 (30.4)	79 (34.8)
New	10 (8.7)	11 (9.8)	21 (9.3)
Stable	48 (41.7)	55 (49.1)	103 (45.4)
Reduced	8 (7.0)	7 (6.3)	15 (6.6)
Other (e.g., dose increased or change of substance)	4 (3.5)	5 (4.5)	9 (4.0)

Values are n (%) unless otherwise indicated.

Sociodemographic and medical characteristics of the study sample are shown in Table 1. Participants were predominantly female (60.7%) and had a mean age of 48 ± 9.79 years (range: 18–65). About half of the participants were married (50.2%), graduated from middle or higher secondary level (58.1%), and worked full-time (47.6%), with 56.3% being on sick leave at study intake. The mean inpatient treatment duration was 40 ± 7.51 days (range: 11–78) with no difference between IG (41 ± 7.43) and CG (40 ± 7.58). Previous psychopharmacotherapy and psy-

Table 2. Between- and within-subject analyses for the primary outcome (BDI-II)

	Baseline (T0) observed	Discharge (T1) estimated	End of intervention (T2) estimated	T1			T0–T1			T2			T0–T2		
				between-group comparisons			within-group comparisons			between-group comparisons			within-group comparisons		
				$F_{1, 212}$	p	d	t (df); r	p	d	$F_{1, 212}$	p	d	t (df); r	p	d
Study groups				12.50	0.001	0.47				11.06	0.001	0.44			
IG (n = 108)	30.63±9.39	17.51±9.47	18.69±10.38				12.73 (107); 0.54	<0.001	1.18				9.83 (107); 0.30	<0.001	1.12
CG (n = 107)	29.46±9.50	22.06±9.68	23.34±10.66				8.71 (106); 0.67	<0.001	0.69				6.50 (106); 0.60	<0.001	0.56

Values are means ± SD unless otherwise indicated. IG, intervention group; CG, control group BDI-II, Beck Depression Inventory II.

chotherapeutic treatments were comparable in the IG and CG as well as the status of antidepressant medication during inpatient treatment (Table 1).

Outcome Measures

Table 2 reports means and standard deviations for the primary outcome (BDI-II) at intake (T0), discharge (T1), and at the end of the intervention (T2), as well as test statistics and effect sizes. At baseline, there were no significant differences between the 2 groups regarding any outcome measures. At the end of the intervention (T2) both groups significantly improved concerning depressive symptoms assessed with the BDI-II, but within-group effect size was higher in the IG (d = 1.12) than in the CG (d = 0.56), reflecting a medium between-group effect size difference (d = 0.44).

At discharge (T1) within-group effect sizes for the BDI-II were similarly high (IG: d = 1.18; CG: d = 0.69), as were the between-group effect size (d = 0.48). The same applied to several secondary outcomes at T1 (see online suppl. Table 1; see www.karger.com/doi/10.1159/000481177 for all online suppl. material) such as depression scores measured with the PHQ-9 (d = 0.40). Significant between-group differences were also found regarding anxiety (GAD-7; d = 0.33), quality of life (EUROHIS-QOL 8; d = 0.34) and self-esteem (RSE; d = 0.38). No significant between-group differences were found concerning dysfunctional attitudes (DAS; d = 0.14) and work ability (WAI; d = 0.08).

Further analyses at discharge (T1) revealed that 78% of the participants in the IG were quite or very satisfied with the intervention compared to 50% in the CG (χ^2_1 = 17.59; p < 0.001; d = 0.88); 62% in the IG stated that the online intervention had a positive or very positive influence compared to 34% in the CG (χ^2_1 = 19.78; p < 0.001; d = 0.64); 83% in the IG and 78% in the CG used their respective intervention at least once per week (χ^2_1 = 1.03; p = 0.46; d = 0.13). However, 46% of the IG reported that they used their intervention several times a week compared to 24% in the CG.

At the end of the intervention (T2) 79% of the participants in the IG were quite or very satisfied with the intervention compared to 46% in the CG (χ^2_1 = 25.98; p < 0.001; d = 0.74); 42% in the IG and 25% in the CG used their respective intervention at least once per week (χ^2_1 = 7.67; p = 0.02; d = 0.39). Self-reported utilization of Deprexis compared to the active control condition is illustrated for the 2 groups and 2 time points in online supplementary Figure 1.

At study intake patient HAQ was significantly higher in the IG than in the CG (4.35 ± 0.64 vs. 4.15 ± 0.78;

t_{213} = 2.15; p = 0.03; d = 0.30), and therapist HAQ was comparable in both groups (IG: 4.50 ± 0.59 vs. CG: 4.46 ± 0.57; t_{213} = 0.61; p = 0.54; d = 0.08). HAQ scores were slightly higher at discharge in both groups (IG: 4.55 ± 0.71 vs. CG: 4.42 ± 0.71; $F_{1, 212}$ = 1.71; p = 0.202; d = 0.18), with a tendency to a higher therapist HAQ in the IG (IG: 4.74 ± 0.55 vs. CG: 4.59 ± 0.55; $F_{1, 212}$ = 3.74; p = 0.057; d = 0.26).

Discussion

While the efficacy of Deprexis has been evaluated favorably in the treatment of various depressed samples, we have little knowledge about its acceptance and efficacy in blended care approaches [12]. A recent trial with 1,013 participants [51] in different clinical and nonclinical settings demonstrated the effectiveness of Deprexis as an add-on to usual care, with a between-group effect size concerning depressive symptoms (PHQ-9) of d = 0.39 posttreatment (3 months) and d = 0.32 at the 6-month follow-up compared to care as usual alone (psychological and/or pharmacological treatments).

Multimodal inpatient psychotherapy is the treatment of choice for patients with severe, complex, and chronic depression in Germany [27]. We aimed at reducing depression further than usual by engaging self-help potentials of the patients, which may not be fully accessed by inpatient psychotherapy and bridge the gap from inpatient treatment to aftercare. The focus of this paper was on the acceptance and efficacy of blended care (inpatient psychotherapy as usual plus online self-help) versus an active CG (inpatient psychotherapy plus online information about depression) from intake to termination of online self-help after 12 weeks.

Acceptance in general – regarding participation rates of the patients recruited – was good, with only 30% of eligible patients refusing to take part in the study. Our refusal rate was lower than in similar studies, where 57% of eligible patients declined to participate in a transdiagnostic internet-based maintenance treatment after inpatient psychotherapy [23]. Patients refusing participation in our study were comparable regarding the BDI-II scores at baseline (29.60 vs. 30.04) and had a comparable age (47.4 vs. 48.0 years) and sex composition (65% vs. 61% females).

Usual care treatment augmented by Deprexis had a large effect size of d = 1.12 regarding the BDI in the within-group comparison at the end of the intervention and an additional moderate effect regarding the primary outcome compared to the active control condition. At discharge from the hospital, considerable benefits could be shown for depression (BDI-II and PHQ-9), anxiety, quality of life, and self-esteem, but not for other outcomes like depressive thinking styles or work ability. A previous study [52] concluded that dysfunctional cognitions of depressive inpatients are relatively stable compared to depressive symptoms. Similarly, self-perceived work ability is also expected to change slowly [53]. As Deprexis is geared at reducing depressive symptoms, not specifically at increasing work ability or vocational reintegration, improved work ability could only be expected as an indirect effect of depressive symptom reduction.

Overall, the great majority reported having accessed the intervention (80%) or the online material. These high proportions may result from integrating online sessions in the treatment plans. Nearly twice as many participants used Deprexis at least once a week after discharge compared to the utilization of the online information in the CG (42 vs. 25%). This corresponds to findings that online self-help (e.g., MoodGYM) was more frequently used than informational online pages alone [54].

To our knowledge this is the first study with Deprexis as an add-on to inpatient psychotherapy. Compared to previous studies an increase in efficacy was substantial – especially when considering that inpatient psychotherapy yielded medium effect sizes in the CG when assessed at the end of intervention, several weeks after discharge from the hospital. Retention in our study was excellent, with 86% completing the questionnaires at discharge and 74% at termination of the intervention, exceeding previous studies. Taken together with the high acceptance, the findings underscore the feasibility of the additional self-help on behalf of the patients.

Implementing a blended care approach in an established treatment setting also raises the issue of feasibility and acceptance on behalf of the therapists. When the program was initially presented, therapists raised concerns of overburdening depressed patients in a "full-time" treatment setting and of adversely affecting the therapeutic relationship by adding online CBT to a psychodynamic setting. Taken together, our findings on acceptance, retention, and outcome support the view that a diverse and structured setting may lend itself to adding another therapeutic online modality. Rather than overburdening them, patients achieved stronger and more lasting treatment effects, and we found no adverse effects on the therapeutic alliance from the therapist and the patient perspective.

Limitations

In order to control for the effect of additional and regular internet inquiry, we used a TAU plus online information as the CG. Thus, we had no TAU only condition. However, it seems unlikely that information had a strong impact. Effect sizes in the CG at the end of intervention were in the medium range, comparable to a previous meta-analysis on inpatient psychotherapy with comparable duration [55]. As the study was implemented under naturalistic conditions, the patients were screened by their individual therapists and scheduled for the study information session by the study assistant. Thus, we cannot preclude that depressive patients were not screened or scheduled under the time constraints of a comparatively short clinical treatment. While only 30% of eligible patients declined participation, some patients may not have attended information sessions as they were unwilling to participate in the trial. According to our assessment plan, we assessed the primary outcome – the BDI-II – at all times. However, secondary outcomes were only assessed at discharge from the hospital and at follow-up (to be analyzed and published separately). Unfortunately, as we lacked objective data on the degree of Deprexis completed to define a priori completer status, we resorted to analyzing the subjective reports of participants concerning their utilization of Deprexis as well as the control condition.

As sessions for online participation needed to be scheduled and we could not prohibit patients from talking about their study intervention to their therapist, we could not blind the therapists to the status of enrolment of their patients. As therapists had voiced concerns of whether participation might compromise collaboration of patients in the psychodynamic program, we did not expect them to explicitly encourage self-help participation. While we had therapists and patients fill out therapeutic alliance measures for their usual treatment, we had no direct measure of whether contents of online self-help were raised in face-to-face treatments. Our findings raise the issue of whether the effectiveness of a blended care approach could be further enhanced by integrating it more into the inpatient program. Furthermore, since the effect of guidance on the efficacy of internet-based interventions is still controversially discussed [56], our study would have benefitted from a subgroup of participants with therapeutic guidance to explore the effect of therapeutic interventions. Finally, we are aware that we compared treatment packages with multiple effective ingredients [57] and that we could not control how Deprexis was supported by the different members of the staff. Future investigations should determine how integration of online self-help into the therapeutic process can be developed further, e.g., by garnering and enhancing staff support.

Despite these limitations, our study delivers the first evidence for blended treatment combining online self-help with inpatient psychotherapy and opens new and promising avenues for increasing the efficacy of inpatient psychotherapy.

Acknowledgments

We would like to thank all our participating patients and the staff in the cooperating clinic for their support in patient recruitment, without whom this study would not have been possible, especially (in alphabetical order) Johanna Kraus (Dipl.-Soz.päd.), Annerose Vorndran (Dipl.-Soz.päd.), and Hiltrud Zajac, as well as our student research assistants Svenja Bidmon (BSc Psych.), Tanja Darwiesh (BSc Psych.), and Hanna Merz. The study was funded by Rhön-Klinikum AG, Bad Neustadt/Saale, Germany.

Disclosure Statement

The authors declare that they have no competing interests.

Author Contributions

R.Z. wrote the first draft of the manuscript. J.B., M.S., R.K., K.H., and M.E.B. wrote the final draft of the manuscript and critically revised it for its intellectual content. R.Z., J.B., R.K., K.H., and M.E.B. substantially contributed to the conception and design of the study. All authors read and approved the final manuscript.

References

1 Wittchen HU, Jacobi F, Rehm J, Gustavsson A, Svensson M, Jonsson B, Olesen J, Allgulander C, Alonso J, Faravelli C, Fratiglioni L, Jennum P, Lieb R, Maercker A, van Os J, Preisig M, Salvador-Carulla L, Simon R, Steinhausen HC: The size and burden of mental disorders and other disorders of the brain in Europe 2010. Eur Neuropsychopharmacol 2011;21:655–679.

2 Whiteford HA, Ferrari AJ, Degenhardt L, Feigin V, Vos T: The global burden of mental, neurological and substance use disorders: an analysis from the Global Burden of Disease Study 2010. PLoS One 2015;10:e0116820.

3 Smit F, Cuijpers P, Oostenbrink J, Batelaan N, de Graaf R, Beekman A: Costs of nine common mental disorders: implications for curative and preventive psychiatry. J Ment Health Policy Econ 2006;9:193–200.

4 Patel V, Maj M, Flisher AJ, de Silva MJ, Koschorke M, Prince M; WPA Zonal and Member Society Representatives: Reducing the treatment gap for mental disorders: a WPA survey. World Psychiatry 2010;9:169–176.
5 van Beljouw I, Verhaak P, Prins M, Cuijpers P, Penninx B, Bensing J: Reasons and determinants for not receiving treatment for common mental disorders. Psychiatr Serv 2010; 61:250–257.
6 Cuijpers P, Donker T, Johansson R, Mohr DC, van Straten A, Andersson G: Self-guided psychological treatment for depressive symptoms: a meta-analysis. PLoS One 2011;6: e21274.
7 Richards D, Richardson T: Computer-based psychological treatments for depression: a systematic review and meta-analysis. Clin Psychol Rev 2012;32:329–342.
8 Cuijpers P, Marks IM, van Straten A, Cavanagh K, Gega L, Andersson G: Computer-aided psychotherapy for anxiety disorders: a meta-analytic review. Cogn Behav Ther 2009; 38:66–82.
9 Karyotaki E, Riper H, Twisk J, Hoogendoorn A, Kleiboer A, Mira A, Mackinnon A, Meyer B, Botella C, Littlewood E, Andersson G, Christensen H, Klein JP, Schröder J, Bretón-López J, Scheider J, Griffiths K, Farrer L, Huibers MJH, Phillips R, Gilbody S, Moritz S, Berger T, Pop V, Spek V, Cuijpers P: Efficacy of self-guided internet-based cognitive behavioral therapy in the treatment of depressive symptoms. JAMA Psychiatry 2017;74: 351.
10 Zhou T, Li X, Pei Y, Gao J, Kong J: Internet-based cognitive behavioural therapy for subthreshold depression: a systematic review and meta-analysis. BMC Psychiatry 2016;16:356.
11 Sander L, Rausch L, Baumeister H: Effectiveness of internet-based interventions for the prevention of mental disorders: a systematic review and meta-analysis. JMIR Mental Health 2016;3:e38.
12 Twomey C, O'Reilly G, Meyer B: Effectiveness of an individually-tailored computerised CBT programme (Deprexis) for depression: a meta-analysis. Psychiatry Res 2017;256:371–377.
13 So M, Yamaguchi S, Hashimoto S, Sado M, A FT, McCrone P: Is computerised CBT really helpful for adult depression? A meta-analytic re-evaluation of CCBT for adult depression in terms of clinical implementation and methodological validity. BMC Psychiatry 2013;13.
14 Gilbody S, Littlewood E, Hewitt C, Brierley G, Tharmanathan P, Araya R, Barkham M, Bower P, Cooper C, Gask L, Kessler D, Lester H, Lovell K, Parry G, Richards DA, Andersen P, Brabyn S, Knowles S, Shepherd C, Tallon D, White D; REEACT Team: Computerised cognitive behaviour therapy (cCBT) as treatment for depression in primary care (REEACT trial): large-scale pragmatic randomised controlled trial. BMJ 2015;351:h5627.
15 Clough BA, Casey LM: Technological adjuncts to enhance current psychotherapy practices: a review. Clin Psychol Rev 2011;31: 279–292.
16 Clough BA, Casey LM: Technological adjuncts to increase adherence to therapy: a review. Clin Psychol Rev 2011;31:697–710.
17 Wright JH, Wright AS, Albano AM, Basco MR, Goldsmith LJ, Raffield T, Otto MW: Computer-assisted cognitive therapy for depression: maintaining efficacy while reducing therapist time. Am J Psychiatry 2005;1158–1164.
18 Romijn G, Riper H, Kok R, Donkert T, Goorden M, van Roijen LH, Kooistra L, van Balkom A, Koning J: Cost-effectiveness of blended vs. face-to- face cognitive behavioural therapy for severe anxiety disorders: study protocol of a randomized controlled trial. BMC Psychiatry 2015;15:311.
19 Kooistra LC, Wiersma JE, Ruwaard J, van Oppen P, Smit F, Lokkerbol J, Cuijpers P, Riper H: Blended versus face-to-face cognitive behavioural treatment for major depression in specialized mental health care: study protocol of a randomized controlled cost-effectiveness trial. BMC Psychiatry 2014;14:290.
20 Kok G, Burger H, Riper H, Cuijpers P, Dekker J, van Marwijk HW, Smit F, Beck A, Bockting C: The three-month effect of mobile internet-based cognitive therapy on the course of depressive symptoms in remitted recurrently depressed patients: results of a randomized controlled trial. Psychother Psychosom 2015; 84:90–99.
21 Kok G, Bockting C, Burger H, Smit F, Riper H: Mobile cognitive therapy: adherence and acceptability of an online intervention in remitted recurrently depressed patients. Internet Interv 2014;1:65–73.
22 Hollandare F, Johnsson S, Randestad M, Tillfors M, Carlbring P, Andersson G, Engstrom I: Randomized trial of Internet-based relapse prevention for partially remitted depression. Acta Psychiatr Scand 2011;124:285–294.
23 Ebert D, Tarnowski T, Gollwitzer M, Sieland B, Berking M: A transdiagnostic internet-based maintenance treatment enhances the stability of outcome after inpatient cognitive behavioral therapy: a randomized controlled trial. Psychother Psychosom 2013;82:246–256.
24 Zwerenz R, Becker J, Gerzymisch K, Siepmann M, Holme M, Kiwus U, Sporl-Donch S, Beutel ME: Evaluation of a transdiagnostic psychodynamic online intervention to support return to work: a randomized controlled trial. PLoS One 2017;12:e0176513.
25 Härter M, Klesse C, Bermejo I, Schneider F, Berger M: Unipolar depression: diagnostic and therapeutic recommendations from the current S3/National Clinical Practice Guideline. Dtsch Arztebl Int 2010;107:700–708.
26 DGPPN, BÄK, KBV, AWMF, AkdÄ, BPtK, BApK, DAGSHG, DEGAM, DGPM, DGPs, DGRW: S3-Leitlinie/Nationale VersorgungsLeitlinie Unipolare Depression – Langfassung, ed 2, version 3. 2015. www.leitlinien.de/mdb/downloads/nvl/depression/.../depression-2aufl-vers3-lang.pdf.
27 Zeeck A, Wietersheim J, Weisss H, Beutel ME, Hartmann A: The INDDEP study: inpatient and day hospital treatment for depression – symptom course and predictors of change. BMC Psychiatry 2013;13:100.
28 Franz M, Seidler D, Jenett Dr, Schäfer R, Wutzler U, Kämmerer W, Deters MA, Schauenburg H, Becher-Dortschy N, Frommhold K, Keller W, Gosda J, Tress W, Zeller A, Beutel ME, Langenbach M, Hoffmann T, Haberger R, Hartkamp N: Stationäre tiefenpsychologisch orientierte Psychotherapie bei depressiven Störungen (STOP-D) – Erste Befunde einer naturalistischen, multizentrischen Wirksamkeitsstudie. Z Psychosom Med Psychother 2015;61:19–35.
29 Schramm E, van Calker D, Dykierek P, Lieb K, Kech S, Zobel I, Leonhart R, Berger M: An intensive treatment program of interpersonal psychotherapy plus pharmacotherapy for depressed inpatients: acute and long-term results. Am J Psychiatry 2007;164:768–777.
30 Vittengl JR, Clark AL, Dunn TW, Jarrett RB: Reducing relapse and recurrence in unipolar depression: a comparative meta-analysis of cognitive-behavioral therapy's effects. J Consult Clin Psychol 2007;75:475–488.
31 Rodriguez MR, Nuevo R, Chatterji S, Ayuso-Mateos JL: Definitions and factors associated with subthreshold depressive conditions: a systematic review. BMC Psychiatry 2012;12: 181.
32 Zwerenz R, Becker J, Knickenberg RJ, Hagen K, Dreier M, Wölfling K, Beutel ME: Enhancing inpatient psychotherapeutic treatment with online self-help: study protocol for a randomized controlled trial. Trials 2015;16:98.
33 Meyer B, Berger T, Caspar F, Beevers CG, Andersson G, Weiss M: Effectiveness of a novel integrative online treatment for depression (Deprexis): randomized controlled trial. J Med Internet Res 2009;11:e15.
34 Ärztliches Zentrum für Qualität in der Medizin: Patientenleitlinie Depression. 2017. http://www.patienten-information.de/patientenleitlinien/patientenleitlinien-nvl/depression.
35 Deutsches Bündnis gegen Depression e.V.: Deutsches Bündnis gegen Depression. 2017. https://www.deutsche-depressionshilfe.de.
36 Leiner D: SoSci Survey (version 2.5.00-i) (computer software). 2014. https://www.soscisurvey.de.
37 Beck AT, Steer RA, Brown GK: Manual for the Beck Depression Inventory-II. San Antonio, Psychological Corporation, 1996.
38 Wang YP, Gorenstein C: Psychometric properties of the Beck Depression Inventory-II: a comprehensive review. Rev Bras Psiquiatr 2013;35:416–431.

39 Kuhner C, Burger C, Keller F, Hautzinger M: Reliability and validity of the Revised Beck Depression Inventory (BDI-II). Results from German samples (in German). Nervenarzt 2007;78:651–656.
40 Kroenke K, Spitzer RL, Williams JB: The PHQ-9. Validity of a brief depression severity measure. J Gen Intern Med 2001;16:606–613.
41 Spitzer RL, Kroenke K, Williams JBW, Löwe B: A Brief measure for assessing generalized anxiety disorder: the GAD-7. Arch Intern Med 2006;166:1092–1097.
42 da Rocha NS, Power MJ, Bushnell DM, Fleck MP: The EUROHIS-QOL 8-item index: comparative psychometric properties to its parent WHOQOL-BREF. Value Health 2012;15: 449–457.
43 von Collani G, Herzberg PY: Eine revidierte Fassung der deutschsprachigen Skala zum Selbstwertgefühl von Rosenberg. Z Diff Diagn Psychol 2003;24:3–7.
44 Nelson LD, Stern SL, Cicchetti DV: The Dysfunctional Attitude Scale – how well can it measure depressive thinking. J Psychopathol Behav 1992;14:217–223.
45 Tuomi K, Ilmarinen J, Jahkola A, Katajarinne L, Tulkki A: Arbeitsbewältigungsindex. Dortmund, Wirtschaftsverlag NW, 1998.
46 Radkiewicz P, Widerszal-Bazyl M: Psychometric properties of Work Ability Index in the light of comparative survey study. Int Congr Ser 2005;1280:304–309.
47 Bassler M, Potratz B, Krauthauser H: The "Helping Alliance Questionnaire" (HAQ) by Luborsky (in German). Psychotherapeut 1995;40:23–32.
48 Urbaniak GC, Plous S: Research Randomizer (version 3.0). 2011. https://www.randomizer.org.
49 Dunlap WP, Cortina JM, Vaslow JB, Burke MJ: Meta-analysis of experiments with matched groups or repeated measures designs. Psychol Methods 1996;1:170–177.
50 IBM Corp: IBM SPSS Statistics for Windows, version 23.0. Armonk, IBM Corp, 2014.
51 Klein JP, Berger T, Schroder J, Spath C, Meyer B, Caspar F, Lutz W, Arndt A, Greiner W, Grafe V, Hautzinger M, Fuhr K, Rose M, Nolte S, Lowe B, Anderssoni G, Vettorazzi E, Moritz S, Hohagen F: Effects of a psychological internet intervention in the treatment of mild to moderate depressive symptoms: results of the EVIDENT Study, a randomized controlled trial. Psychother Psychosom 2016; 85:218–228.
52 Kohler S, Unger T, Hoffmann S, Mackert A, Ross B, Fydrich T: Dysfunctional cognitions of depressive inpatients and their relationship with treatment outcome. Compr Psychiatry 2015;58:50–56.
53 Beutel ME, Zwerenz R, Bleichner F, Vorndran A, Gustson D, Knickenberg RJ: Vocational training integrated into inpatient psychosomatic rehabilitation – short and long-term results from a controlled study. Disabil Rehabil 2005;27:891–900.
54 Schneider J, Sarrami Foroushani P, Grime P, Thornicroft G: Acceptability of online self-help to people with depression: users' views of MoodGYM versus informational websites. J Med Internet Res 2014;16:e90.
55 Liebherz S, Rabung S: Do patients' symptoms and interpersonal problems improve in psychotherapeutic hospital treatment in Germany? – A systematic review and meta-analysis. PLoS One 2014;9:e105329.
56 Gieselmann A, Böckermann M, Sorbi M, Pietrowsky R: The effects of an internet-based imagery rehearsal intervention: a randomized controlled trial. Psychother Psychosom 2017; 86:231–240.
57 Fava GA, Guidi J, Rafanelli C, Sonino N: The clinical inadequacy of evidence-based medicine and the need for a conceptual framework based on clinical judgment. Psychother Psychosom 2015;84:1–3.