Comprehensive Psychiatry 94 (2019) 152124

Contents lists available at ScienceDirect

Comprehensive Psychiatry

journal homepage: www.elsevier.com/locate/comppsych

Inpatient treatment decreases depression but antidepressants may not contribute. A prospective quasi-experimental study☆,☆☆

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ARTICLE INFO

Available online xxxx

Keywords:
Inpatient treatment
Psychotherapy
Antidepressants
6-month follow-up
Control group

ABSTRACT

Objective: The aim of the study is the evaluation of psychiatric-psychotherapeutic inpatient treatment utilizing a naturalistic design.
Methods: In a sample of 574 consecutively admitted patients, depression (64.5%), personality disorders (19.5%), schizophrenia (4.2%), bipolar disorder (3.3%), obsessive-compulsive disorder (2.3%) or other mental disorders (6.4%) were diagnosed. All patients were treated with psychotherapy, most with antidepressants. Depression was measured using the Beck Depression Inventory–II (BDI-II). 180 patients formed a waiting list control group. The regularly discharged patients ($N = 489$) were asked to participate in a six-month follow-up, with 62.6% taking part.
Results: From the time of admission to discharge, there was a strong decline in depression (31.5 vs. 13.2 points on the BDI-II), as well as from admission to follow-up (31.2 vs. 18.3 points). In the control group, there was a weak symptom decline (34.6 vs. 32.1 points) until admission, which was independent of the waiting period duration. For the success of treatment, it did not matter whether the patients received antidepressants. In the follow-up, 81.0% of patients retrospectively considered psychotherapy to be important for treatment outcome, only 2.3% considered medications to be important.
Conclusions: Psychiatric inpatient treatment reduces depression significantly at discharge and follow-up; the decrease in depression is rather due to psychotherapy than to antidepressants.

1. Introduction

In 2016, there were 409 psychiatric departments in Germany with a total of approximately 56,000 inpatient treatment places [1]. Treatment is mostly multimodal and interdisciplinary. In addition to psycho- and pharmacotherapy – depending on the equipment available at the facility – ergotherapy and occupational therapy, milieu therapy, psychoeducation, sport activities, physiotherapy and many others are offered as adjuvant treatment processes.

Härter et al. [2] presented the results of a pilot project to evaluate the effects of inpatient psychiatric-psychotherapeutic treatment in Germany on >3000 depressed patients. However, neither control groups nor follow-ups were included. The treatment approaches among the participating hospitals differed considerably, making it difficult to compare the groups. They found high rates of short-term effect sizes for all approaches.

Beside psychopharmacotherapy, individual and group psychotherapy are key strategies in the inpatient treatment of acute mental disorders. Liebherz and Rabung [3] summarized 103 individual studies on the effectiveness of psychotherapeutic hospital treatment in German-speaking countries. At the time of discharge, they found effect sizes of 0.71 and follow-up effect sizes of 0.80. Follow-ups were performed in less than one-third of all the studies; the control groups were excluded.

Zeeck et al. [4] compared the outcomes of psychosomatic day patient and inpatient treatments. In this naturalistic study, 604 patients with unipolar depression, consecutively recorded from eight different clinics were included, over a period of 2.5 years. Furthermore, 1560 depressive patients were treated during this period and had been excluded for various reasons (for example, because of psychotic symptoms), which makes it a selective subsample. Three months after discharge, a follow-up took place. Among others, the treatment included pharmacotherapy as well as individual and group psychotherapy. The inpatients with significantly more depressive symptoms on admission were treated longer and received more frequently antidepressants. The patients benefited from both settings, with a decrease in depressive symptoms at discharge and a slight increase at the follow-up.

☆ The study is provided with the number 2014346, with a positive vote by the Ethics Committee of the Ärztekammer Nordrhein-Westfalen/Germany.
☆☆ This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.
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https://doi.org/10.1016/j.comppsych.2019.152124

Jacobi et al. [5] described a naturalistic study on behavioral therapy involving 1776 outpatients. They were primarily treated for phobia, depression, eating disorders and posttraumatic stress disorder. Depression was measured with the German version of the Beck Depression Inventory–II (BDI-II; [6]); the mean BDI-II score at the onset of therapy was 16.9 points. At the end of therapy, there were 62.7% remissions, 7.1% responses, 27.1% patients were non-response and 3.0% worsened. Nelson & Hiller [7] replicated this study involving 1866 outpatients with depression, phobia, somatoform disorders, eating disorders and personality disorders. The mean BDI-II score was averaging 18.9 points at the onset of therapy. 45.9% of all patients were completely remitted, 9.9% responded, 41.4% were non-responders, and 2.7% worsened. This corresponds to a moderate effect size (d = 0.54). There were no control groups or follow-ups in either study.

While there are some attempts to assess the effects of outpatient psychotherapy and psychosomatic inpatient treatment, studies on psychiatric inpatient treatment are rare. The studies considered by Liebherz and Rabung [3] predominantly evaluated specific therapeutic concepts for the treatment of particular diagnostic groups of patients (e.g., major depression, borderline personality disorder, eating disorders). On the other hand, there is little research on the effectiveness of "treatment as usual", although, much more in line with clinical reality. Therefore, in our study the effects of inpatient treatment on a general psychiatric ward will be examined.

2. Methods

2.1. Treatment concept

The recruitment took place on a ward with 20 inpatient treatment places,[1] belonging to the General Psychiatric Department at the Center for Mental Health Marienheide—part of the Klinikum Oberberg GmbH. It has a rather rural catchment area. The ward's therapeutic offer is suited to adult patients with all forms of psychic disorders (except organic brain disorders and substance abuse). Most of the patients treated suffer from major depression disorder or from personality disorders, anxiety disorders, obsessive-compulsive disorders and psychosis, respectively, with comorbid depression. The ward is cognitive-behavioral oriented, with a strong systemic-biographical understanding of the disorder's etiology and maintenance [8].

Upon admission, an individual aetiological model of predisposing, triggering, and maintaining factors (e.g., functionality of symptoms) is developed for each patient, which is the basis for treatment goals and strategy. The onset of a mental disorder is considered a response to acute or (more usually) chronic psychosocial loads (e.g., work pressure, partnership issues, interpersonal conflicts), combined with dysfunctional personality traits (e.g., lack of social or emotional skills, harmful cognitive beliefs) and special vulnerabilities (e.g., genetic predispositions, somatic problems), leading to overburdening and decompensation. In general, treatment is aimed to impart patients strategies to develop healthy coping mechanisms. If possible, relatives are also involved in the treatment.

Main components of the treatment concept are (1) two individual psychotherapeutic sessions per week and (2) group therapies like cognitive behavioral group therapy for depression (CBGT) [9], social skills group training [10], mindfulness-based therapy [11], metacognitive training (MCT [12]), embodiment [13], sports groups [14], and adjuvant therapies (e.g., progressive muscle relaxation, ergo therapy, occupational therapy, physiotherapy). Most patients take psychotropic drugs during treatment. The treatment plans are individualized and include all available therapeutic interventions that are required for the respective disorder; e.g. CBGT and antidepressants for depression, exposure therapy for obsessive-compulsive disorder and phobia, MCT and neuroleptics for schizophrenia.

2.2. Sample

Between October 2012 and December 2017, 574 patients were admitted and have been included in the study, without exception. There are 324 women (56.4%) and 250 men (43.6%) with an average age of 37.3 years (SD = 13.1, range 17–76). The mean length of stay was 54.2 days (SD = 24.8, range 1–120). Most patients were diagnosed with unipolar depression ($N = 370$, 64.5%). The second largest group consisted of patients with personality disorders ($N = 112$, 19.5%), including 54 cases with borderline personality disorder. Twenty-three patients (4.0%) suffered from schizophrenia, 21 of them from paranoid schizophrenia. 19 patients (3.3%) suffered from bipolar disorder, 14 (2.3%) from obsessive-compulsive disorder, and 36 patients (6.4%) had other diagnoses (e.g., somatoform disorders, anxiety disorders, M. Asperger). All diagnoses were made according to the criteria of ICD-10. If necessary, the diagnoses were confirmed using psychometric tools such as the International Diagnosis Checklists [15] or the Structured Clinical Interview for DSM-IV axis II personality disorders [16]. The assignment to the diagnostic groups (i.e., depression, personality disorder, other diagnoses) was based on the main diagnoses. Patients with a personality disorder almost always suffered from co-morbid depression, but were still assigned to the group with personality disorders. Similarly, patients with other main diagnoses (schizophrenia, obsessive-compulsive disorder, etc.) were assigned to the "other diagnoses" group, even though most of them also suffered from depression (see Table 1 for sample characteristics). In 489 patients (85.2%), the treatment ended regularly. For 81 patients (14.1%), premature discontinuation of treatment occurred, while 4 (0.7%) committed suicide during treatment. Only the 489 regularly discharged patients were asked to participate in the follow-up examination. The pharmacotherapy was carried out in accordance with the German guidelines for depression [17]. Several patients refused medication for a variety of reasons (for example, side effects, general reservations, lack of therapeutic benefit). 176 patients (30.1%) did not take any psychotropic drugs on admission. 304 patients (53.0%) took antidepressants on admission, 71 patients (12.4%) took neuroleptics, 14 (2.4%) took mood stabilizers, and 158 patients (27.5%) were admitted with sedating medications.

2.2.1. Classes of antidepressants over groups at admission

Depression group—selective serotonin reuptake inhibitors (SSRI): 108 (29.2%); selective serotonin and norepinephrine reuptake inhibitors (SSNRI): 49 (13.2%); tri- and tetracyclic antidepressants (TCA): 67 (18.1%): reversible monoamine oxidase inhibitor (rMAOI): 2 (0.5%); melatonin: 25 (6.8%); norepinephrine-dopamine reuptake inhibitor (NDRI): 2 (0.5%). Personality Disorder group—SSRI: 20 (17.8%); SSNRI: 13 (11.6%); TCA: 13 (11.6%); NDRI: 2 (1.8%); melatonin 7 (6.3%). Other disorders group—SSRI: 25 (27.2%); SSNRI 11 (12.0%); TCA: 11 (12.0%); melatonin: 4 (4.3%).

2.2.2. Classes of antidepressants over groups at discharge

Depression group—SSRI: 95 (25.7%); SSNRI: 82 (22.2%); TCA: 60 (16.2%): rMAOI: 3 (0.8%); melatonin: 46 (12.4%); NDRI: 2 (0.5%). Personality Disorder group—SSRI: 19 (17.0%); SSNRI: 17 (15.2%); TCA: 15 (13.4%); NDRI: 1 (0.9%); melatonin 13 (11.6%). Other disorders group—SSRI: 22 (23.4%); SSNRI 17 (18.5%); TCA: 7 (7.60%); melatonin: 3 (3.3%).

If a patient was admitted repeatedly within the same disease episode, the treatments were combined and considered as one case; in these cases, the interval between treatments varied between several days and a few weeks. If a patient was re-admitted because he or she suffered from a further mental disorder that developed after a remission phase and independently from the former episode of illness, he or she

[1] This ward is named after Prof. Aaron T. Beck because many of the therapeutic strategies used here are due to his cognitive therapy.

Table 1
Baseline variables among diagnosis groups.

	Depression $N = 370$	Personality disorders $N = 112$	Other diagnoses $N = 92$
Mean age (SD)	39.4 (12.8) years	34.0 (12.8) years	32.5 (12.2) years
Gender	Females 57.8% Males 42.2%	Females 66.1% Males 33.9%	Females 39.1% Males 60.9%
Mean BDI score (SD) at admission	31.7 (10.3)	33.5 (12.1)	27.6 (12.3)
Patients with AD prescribed at admission	56.5%	43.8%	48.9%
Mean duration (SD) of treatment	58.5 (22.4) days	41.8 (26.2) days	51.8 (26.9) days
Regularly discharged patients	93.0%	63.4%	80.4%
Proportion of patients who were part of the control group	32.4%	29.5%	29.3%

was considered as a new case; $N = 38$ of the 574 cases (6.6%) are re-admitted patients, the mean interval between treatments was 464 days.

2.3. Beck Depression Inventory (BDI-II)

Depressive symptoms of the patients were assessed by the BDI-II [6]. It consists of 21 items, based on the definition of major depression, in accordance to the DSM-IV. The BDI-II was selected for the following reasons: (1) depression is the psychopathological key symptom in our sample; (2) the BDI-II is an economical method with excellent psychometric properties and is a standard measure for depression; (3) as a self-assessment procedure, the BDI-II is not distorted by expectations or response tendencies of the investigators. The gold standard for depression measurement is the Hamilton Depression Rating Scale (HDRS [18]). However, the HDRS was criticized for its poor psychometric properties and outdated conception [19]. Moreover, the use of the HDRS, or other assessment methods in our study, would have led practitioners to assess the success of their own work, which would be methodologically questionable. For interpretation, the following levels of severity are proposed in the German guidelines [17]: ≤12 points = no depression; 13–19 points = mild depression; 20–28 points = moderate depression; ≥29 points = severe depression.

2.4. Procedure

The patients completed the BDI-II on admission (=T1) and at (regular) discharge (=T2). The patients who were admitted to the waiting list had already filled in the BDI at the time of the preliminary interviews (=T0). The waiting list control group was formed by these patients. They received psychiatric outpatient treatment as usual during the waiting period. 51.1% of them took antidepressants during the waiting period. The hospital admission was usually due to a recommendation from the therapist in charge. At discharge, patients were asked to participate in the 6-month follow-up (=T3). All the patients provided their informed consent. They were contacted about six months after discharge and received the BDI-II, together with an addressed, stamped return envelope. They also were asked to retrospectively assess which aspects of the treatment have been most important to them.

2.5. Statistics

Statistical analyses were carried out using SPSS (version 22). The hypothesis testing was two-tailed. Effect sizes for repeated measures according to Morris and DeShon [20] were calculated. Normal distribution was tested with the Shapiro-Wilk test [21]. Significance of differences between expected and observed frequencies were tested with the χ^2 test. Bivariate correlations were measured with Pearson's r. Group mean differences were analysed by the independent samples *t*-tests (two groups). Analysis of covariance (ANCOVA) was used to evaluate group means, while statistically controlling for the regression towards the mean effect. Scale reliability was measured by the Cronbach α.

3. Results

3.1. Treatment effects at T2 and T3

The total sample of 574 patients demonstrated a mean BDI score of 31.4 points on admission (SD = 11.1, range = 1–61), which corresponds to severe depression. Regularly discharged patients ($N = 489$) had a mean BDI score of 31.5 points (SD = 11.0) at baseline, and 13.2 points (SD = 10.2) at discharge, corresponding to an improvement from severe to mild depression. The decrease in symptoms by 18.3 points is statistically significant, the effect size is large ($t = 37.238$, df = 488, $p < .001$, d = −1.64).

306 patients (62.6% of the patients discharged, according to the rules, and 53.3% of the total number of patients) participated in the follow-up. At this time, these patients had an average BDI score of 18.3 points (SD = 12.7, range 0–55). The outcome of the BDI in the follow-up can be assessed with respect to admission (T1) or to discharge (T2). From T2 to T3, the mean BDI score increased by 5.4 points ($t = -8.32$, df = 305, $p < .001$, d = 0.56); nevertheless, even half a year after discharge, the mean BDI score still corresponds to a slight depression. From T1 to T3, there is a decrease of 12.9 points ($t = 17.36$, df = 305, $p < .001$, d = −1.06).

In the patient's retrospective assessments at T3, regarding the most important parts of the treatment, multiple answers were allowed. 81.0% emphasized psychotherapy (individual treatment, therapy groups, etc.), 49.3% emphasized inpatient setting (daily structure, silence, etc.), 14.1% emphasized adjuvant therapies (e.g. occupational therapy), 9.8% emphasized on the importance of contacts with the nursing staff and 2.3% emphasized pharmacotherapy; 11.1% named other aspects.

3.2. Control group

180 patients from the total sample formed a waiting list control group. The time between induction into the waiting list and admission averaged 39.4 days (SD = 34.5, range = 3–274). At the time of the preliminary talk, the patients had a mean BDI score of 34.6 points (SD = 9.5, range = 11–57). There was a statistically significant decrease of the mean BDI score by 2.5 points from the time of the preliminary interview to admission ($t = 4.704$, df = 179, $p < .001$). However, the effect size is small (d = −0.37). There is no linear or non-linear relationship between the BDI differences (BDI score at admission minus BDI score at induction into the waiting list) and the duration of the waiting time (r = 0.03, $p = .679$). The control group consisted to 66.7% of patients with unipolar depression, 18.3% patients with personality disorders, and 15% patients with other diagnoses. In the total sample, the corresponding percentages were 63.5%, 20.1%, and 16.5%, respectively; the differences are not statistically significant ($\chi^2 = 0.558$, df = 2, $p = .757$). The patients who formed the control group did not differ with regard to the mean age (38.4 vs. 36.7 years, $t = 1434$, df = 572, $p = .152$) or to the sex distribution (57.8% vs. 55.8% females, $\chi^2 = 0.189$, df = 1, $p = .717$) from the patients who were not part of the control group.

3.3. Effects of antidepressants (AD)

To examine the effect of AD on the course of depression, patients were divided into five groups:

- 191 patients (33.3% of the total sample) who did not receive AD at admission or discharge (abbreviated as "no AD");
- 79 patients (13.8%) who came to the ward free of AD, but who had been prescribed AD until discharge ("AD prescribed");
- 37 patients (6.4%) who received an AD on admission but were discontinued until discharge ("AD discontinued");
- 123 patients (21.4%) who received an AD on admission, which was maintained unchanged ("AD maintained");
- 144 patients (25.1%) who received a prescribed AD medication that was modified until discharge (e.g., change to another AD, change of dose, augmentation; "AD modified").

A section of patients of each of these groups dropped out of further analysis. However, both at discharge ($\chi^2 = 7.56$, df = 4, $p = .109$) and follow-up ($\chi^2 = 4.94$, df = 4, $p = .293$), this drop-out is equally distributed among all five groups of medication.

A total of 228 patients (groups "no AD" and "AD discontinued") were discharged without AD (126 with depression, 55 with personality disorder, 47 with other mental disorder). In 146 of these patients, a non-AD therapeutic strategy was followed from the outset. The other 82 patients refused AD (50 with depression, 23 with personality disorder, 9 with other mental disorder).

Fig. 1 demonstrates differences of the BDI scores of the five AD groups (T2 minus T1). Shapiro-Wilk tests yielded normal distributions for all groups. All groups showed a significant symptom decline. An ANCOVA group comparison was carried out with the BDI differences (score at discharge minus score at admission) as dependent variable. To control for the regression towards the mean (RTM) effect, the BDI scores at admission were used as covariate. This method to control for the RTM effect has been described by Yu and Chen [22] and has already been used (e.g., [2]). The RTM effect was significant, F (1, 483) = 202.97, $p < .001$. The five medication groups did not differ in the extent of the decrease in BDI scores, F (4, 483) = 0.67, $p = .613$.

To test for potential drop-out bias, this ANCOVA was repeated using the Last Observation Carry-forward method (LOCF [23]), replacing missing BDI scores at discharge by the BDI scores collected at admission, so that all 574 patients could be included. Again, there was a significant RTM effect, F (1, 568) = 120.84, $p < .001$, while the group effect was not significant, F (4, 483) = 1.21, $p = .304$.

The 199 patients who were prescribed AD at discharge demonstrated a tendentially higher BDI score at T3 than the 107 patients who were discharged without AD prescription (19.2 vs. 16.7 points, $t = 1.63$, df = 304, $p = .104$). This insignificant difference was already present at the time of discharge (13.6 vs. 11.5 points, $t = 1.79$, df = 303, $p = .0746$) and did not change until T3.

Fig. 2 shows the long-term BDI score changes of the five AD groups at follow-up (T3 minus T1), including those patients who participated in all three measurement times ($N = 306$). Shapiro-Wilk tests showed for all groups that the difference values were normally distributed. Again, an ANCOVA of the medication's effect on the BDI differences with the AD group as an independent variable and the BDI scores at T1 as co-variate, was performed. The co-variate was again statistically significant, F (1, 300) = 74.27, $p < .001$. Similarly, there was no difference between the AD groups, F (4,300) = 0.49, $p = .743$. The LOCF analysis (see above) showed comparable results; the RTM effect was significant, F (1, 568) = 93.32, $p < .001$, the group effect was not, F (4, 586) = 0.95, $p = .434$. There was also no AD group difference in the increase of BDI scores from T2 to T3.

3.4. Reliability of the BDI

The internal consistency (Cronbach α) of the BDI was 0.85 at the time of inclusion in the control group, 0.90 during admission, and 0.94 during discharge and follow-up, respectively.

3.5. Drop-out analysis

3.5.1. Discharge (T2)

The lowest drop-out rate was recorded in the group with unipolar depression. 93.0% were discharged according to the rules and asked to participate in the follow-up. The largest drop-out rate was seen in personality disorders group, with only 63.4% being discharged on a regular basis. Patients with other diagnoses were grouped together and 80.4% of them were regularly discharged. These differences are statistically significant ($\chi^2 = 61.60$, df = 2, $p < .001$). The drop-out patients do not differ from the regular, discharged patients in BDI score at T1, age or gender distribution.

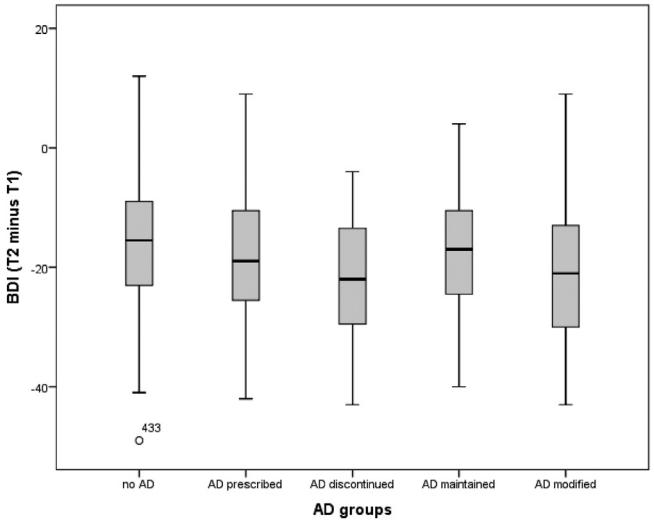

Fig. 1. Comparison of the BDI-II differences in the five AD groups, from admission (T1) to discharge (T2). Only patients who have been discharged regularly ($N = 489$).

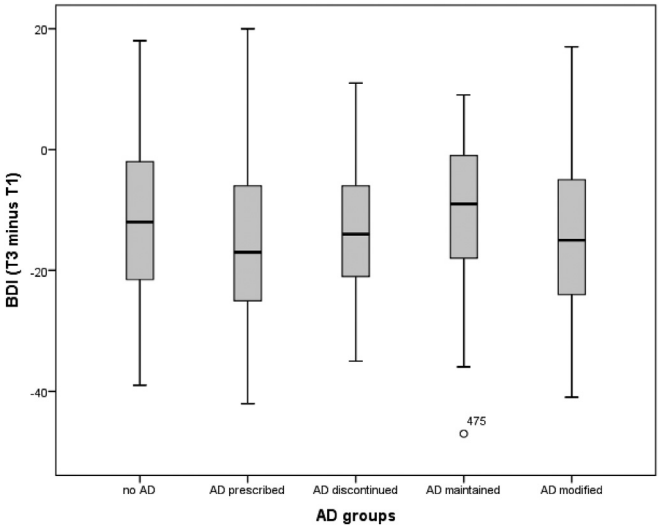

Fig. 2. Comparison of the BDI-II differences in the five AD groups, from admission (T1) to follow-up (T3). Only patients who participated in all three measurement times ($N = 306$).

3.5.2. Follow-up (T3)

66.0% of the regularly discharged patients with unipolar depression participated in the follow-up, compared to the 56.3% of the patients with personality disorders and 52.7% of patients with other diagnoses. These differences miss statistical significance ($\chi^2 = 5.97$, df = 2, $p = .051$). The patients who participated in the follow-up are somewhat older than those who did not (38.9 vs. 35.0 years, $t = 3.258$, df = 487, $p = .001$). There are no differences in gender distribution or BDI scores.

Overall, the drop-out analysis shows that the relevance of this study is greatest for patients with unipolar depression and least for patients with personality disorders due to differences in participation. 61.4% of patients admitted for unipolar depression participated in the follow-up, compared to only 35.7% of patients admitted for with a personality disorder.

4. Discussion

4.1. Treatment effects

The inpatient treatment leads to a significant decrease in depression. The large effect size is higher than that of comparable studies [2,3]. When admitted, the mean BDI score of the patients corresponded to severe depression; at discharge, the mean BDI score corresponds to mild depression, similar to outpatients at the begin of an outpatient psychotherapy [5,7].

The slight increase in BDI scores from discharge (T2) to follow-up (T3) can be explained by the re-emergence of psychosocial stressors in the patients' environment, which may have contributed to the development of a mental disease in the first place. The 306 patients examined during admission, discharge and follow-up showed a decrease of 18.2 points from admission to discharge and an increase of 5.4 points from discharge to follow-up. Thus, in terms of overall diagnoses, >70% of the effect of treatment sustains at least for six months.

While the mean BDI score at discharge corresponded to mild depression, 56.4% of the patients reached complete remission with regard to the BDI categories (≤12 points). On the other hand, 20.7% still suffered from moderate or severe depression (≥20 points). This is important since residual symptoms have been shown to be associated with chronic depression and impaired social functioning in the long-term [24].

4.2. Control group

With regard to age, sex and diagnosis, the control group is representative of for the total sample. The symptom decrease in the control group is small. Hence, a spontaneous remission, as an explanation of the symptom decrease from T1 to T2, is unlikely. On the other hand, the symptom decline from T0 to T1 is probably a placebo effect; the patients associate admission with the hope for recovery.

There are two limitations to the control group. First, the mean waiting period amounts to about 39 days while the mean treatment duration was about 54 days. However, there was no correlation between the length of the waiting period and the decrease in the BDI scores ($r = 0.03$), so that this difference may be of minor importance. Second, the control group is part of the treatment group, so that - unlike RTCs - both groups are not independent of each other.

4.3. Antidepressants

The more depressed the patients of our sample, the more likely the prescription of AD; this relationship has been described earlier [4,25]. In contrast, no therapeutic AD effect was seen either at discharge or at follow-up. How can this be explained?

As previously reported, studies on the effectiveness of antidepressants carried out under naturalistic conditions lead to substantially lower effects than randomized control trials (RCTs [26,27]). The therapeutic effect of AD is often overestimated, even by professionals. This is attributed to the well-known "publication bias" [28]. Another reason is the neglect of the RTM effect in evaluation studies. Because in repeated measurements the magnitude symptom reduction relies on the initial values [29], and AD are more likely to be prescribed to more severely depressed patients, the RTM effect and the AD prescribing tendency are confounded variables. Hence, in pre-post analyses the RTM effect must be controlled for. Goldberg et al. [24] did so and found no drug effect in the treatment of depression as well. Brugha et al. [30] reassessed 119 out of 130 inpatients, suffering from an episode of depressive disorder, 4 months post discharge. Very similar to our results, they found that the prescribed AD did not appear to have affected the clinical outcome. Instead, there was a weak trend for a worse outcome in patients on drug treatment.

Another significant methodological problem that is largely ignored in psychiatric research is the so-called "breaking blind" effect. The effectiveness of AD is defined in RCTs as the difference in symptom decline between the verum and placebo groups; the placebo effect accounts for approximately 75% of the verum effect [31]. Presumably, this proportion is even greater. Because of the side effects of AD, both patients and investigators in RCTs can identify which patient received the drug and which received the placebo [32,33], thus breaking the double-blind condition. This may cause the placebo effect to be greater in the verum groups than in the placebo groups, increasing the difference between the placebo and verum groups; the difference between the two varying placebo effects would then be misinterpreted as a specific verum effect. This consideration is confirmed by the fact that using a placebo that causes similar side effects as the verum, almost completely eliminates the differences between the ADs and the placebo [34].

Thus, there are valid reasons to believe that the pharmacological therapeutic effect of AD is very low and without substantial clinical relevance. In contrast, the strong placebo effect of AD has been demonstrated time and time again. Therefore, the question arises as to why no placebo effect has occurred in the present study. There might be given two explanations. (1) Most of our patients have experienced that the AD did not protect them from depression and resulting admission to hospital; (2) the psychological explanation for the onset of depression, developed during the inpatient treatment (see above), might reduce the expectation into additional pharmacological aid, compared to psychotherapy. However, expectation is crucial to the size of a placebo effect [35]. Therefore, in our sample there were poor conditions for the development of a placebo effect of AD. This assumption is supported by the fact that >80% of patients at T3 retrospectively considered psychotherapy to be important, whereas medication was of negligible importance to them.

In summary, our findings suggest that inpatient psychiatric-psychotherapeutic treatment favours a strong decrease in depression, both at the time of discharge and at the 6-month follow-up. Antidepressants do not seem to contribute to this effect. This result might be obtained only within a naturalistic study design since RCTs may lead to a systematic overestimation of AD effects, due to fundamentally methodical problems (i.e., "breaking blind").

4.4. Limitations

As mentioned above, there were a number of key benefits that spoke in favor of using BDI-II as the main outcome measure (e.g., independence from the therapists). Nevertheless, self-rating scales such as the BDI-II also have some disadvantages that should not be ignored. In self-ratings, patient's tendencies to falsify responses (e.g., social desirability) may have greater impact than in observer ratings [36]. The accordance between self-ratings and observer ratings of depression in general is high; e.g., Svanborg and Åsberg [37] reported a correlation of r = 0.87 between BDI and the Montgomery Åsberg Depression Rating Scale (MADRS). On the other hand, the agreement between self-rating and observer rating is more limited when depressive

symptomatology is severe, as at the time of inpatient admission. This is probably connected to the greater limitation of the capacity for self-observation among the severely depressed [36]. Moreover, Lambert et al. [38] reported that the BDI showed significantly less change in depression following treatment than did the Hamilton Rating Scale for Depression (HRSD). Svanborg and Åsberg [37] showed that the BDI tapped more maladaptive personality traits compared to the MADRS (see also [39]). This may be the reason why patients with personality disorders in our study have higher BDI scores than other groups. Hence, it cannot be ruled out than the use of other instruments than the BDI for the measurement of depression would have led to slight different results. However, because the limitations of using a self-rating affect all groups equally, there is no evidence of serious falsification of our results.

We have shown that the control group is similar in important characteristics to the study group (age, gender, diagnoses). Nevertheless, it cannot be ruled out that there still are other differences that we did not record in our study.

5. Conclusions

An intensive psychiatric-psychotherapeutic inpatient treatment reduces depression significantly, and about 70% of the symptom improvements achieved during discharge are still present six months after discharge. The prescription of antidepressants seems to have no substantial effect on the treatment outcome at discharge or follow-up.

Declaration of competing interest

None.

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