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RESEARCH ARTICLE

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Recovery from chronic depression and structural change: 5-year outcomes after psychoanalytic and cognitive-behavioural long-term treatments (LAC depression study)

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Abstract

Objective: Psychotherapy of chronic depression has remained a challenge due to limited prognosis and high rates of recurrence. We present 5-year outcome data from a multicentre trial comparing psychoanalytic (PAT) and cognitive-behavioural (CBT) long-term treatments with randomized and preferred allocations analysing symptom ($N = 227$) and structural change ($N = 134$) trajectories.

Method: Self- and blinded expert ratings of depression symptoms were performed at yearly intervals using the Beck Depression Inventory-II (BDI-II) and Quick Inventory of Depressive Symptoms (QIDS-C). Blinded expert ratings of Operationalized Psychodynamic Diagnosis (OPD) and the Heidelberg Restructuring Scale (HRS) at baseline, 1, 3, and 5 years assessed structural change in a subsample.

Results: Lasting and comparable symptom changes were achieved by PAT and CBT. However, compared to CBT, PAT was more successful in restructuring, a major goal of long-term psychodynamic treatments with high frequency and duration.

Limitations: Due to practical reasons, the time criterion for chronic depression of an acute phase had to be defined for over 1 year in the present study, which does not correspond to the DSM-5 criterion of 2 years. Therapy duration and session frequency were not incorporated into the statistical models.

Conclusion: Long-term psychotherapy helps patients with a yearlong history of depression and often multiple unsuccessful treatment attempts to achieve lasting symptom changes. Future follow-up will clarify whether restructuring promotes further sustainable improvements.

KEYWORDS
chronic depression, cognitive behavioural treatment, psychoanalysis, restructuring, structural change, symptom change

1 | INTRODUCTION

Depression has remained a major challenge for mental health care. Despite a range of evidence-based psychotherapeutic and pharmacological treatments (Cuijpers et al., 2020), the majority of patients do not achieve remission during their first course of treatment, and large proportions suffer from recurrent or chronic courses (Maj et al., 2020). Treatment-resistant depression, the failure to respond or remit to pharmacological or psychological bona fide treatments has remained an ambiguous and debated concept (Brown et al., 2019). In the newly defined category of persistent depressive disorder, the DSM-5 has fused the concepts of chronic major depression and dysthymic disorder, considering common antecedents (e.g., childhood adversity, depression in relatives, and early onset), functional impairment, and diminished response to psychotherapy. Chronic depression may necessitate longer treatments in order to achieve sustaining effects (Fonagy et al., 2015; Knekt et al., 2011; Leuzinger-Bohleber, Kaufhold, et al., 2019; Steinert et al., 2014), yet the great majority of trials have been limited to short-term treatments and outcomes (Cuijpers et al., 2020, 2021).

Recently, we published results from long-term psychoanalytic (PAT) and cognitive-behavioural (CBT) treatments of a sample of 252 adults with chronic depression 3 years after treatment assignment (Leuzinger-Bohleber, Hautzinger, et al., 2019). In a two-step procedure, patients first indicated either a treatment preference or the willingness to be randomly assigned. Those consenting were randomized to PAT or CBT. Patients with a preference for either CBT or PAT were allocated to their preferred treatment type. Symptom change was assessed by two main outcome measures, the self-report Beck Depression Inventory-II (BDI-II; Hautzinger et al., 2006) and the blinded expert rating conducted using the Quick Inventory of Depressive Symptomatology (QIDS-C; Rush et al., 2003). Both treatments were effective with effect sizes of $d = 1.83$ (BDI-II), and $d = 2.08$ (QIDS-C) and full remission rates of 45% (BDI-II), and 61% (QIDS-C). Contrary to our expectations, we found no significant differences between PAT and CBT with respect to the decrease of depressive symptoms or between preferential and randomized allocation 3 years after treatment start, maybe due to the relatively small sample size of the randomized arm (Leuzinger-Bohleber, Hautzinger, et al., 2019). Yet, there was evidence of more structural change in the PAT group after 3 years. After 3 years, structural change, as assessed by the Heidelberg Restructuring Scale (HRS; Rudolf et al., 2000), was only associated with outcome in the PAT but not the CBT group (Leuzinger-Bohleber, Kaufhold, et al., 2019). In the present study, we report the 5-year outcome data, analysing long-term symptomatic and structural change.

A basic claim of psychoanalytic long-term treatments has been not only to alleviate symptoms, but also to achieve structural change, that is a profound and lasting change of psychic, interpersonal or personality functioning (Kernberg, 1984, 1988; Wallerstein, 1988). Initial findings have indicated that higher levels of structural change predict better outcomes of psychoanalytic treatments (Grande et al., 2009; Leuzinger-Bohleber et al., 2022; Leuzinger-Bohleber, Kaufhold, et al., 2019). Gaining insight into central conflicts (e.g., dependency vs. autonomy) as well as structural vulnerabilities (e.g., self-other differentiation) and eventually assuming responsibility for consequences pertaining to these (Grande et al., 2001; Rudolf et al., 2000) improves the capacity for social (e.g., intimate and professional) relationships, enlarges creativity in personal and professional contexts, and reduces symptom burden. The introduction of dimensional assessment of personality disorders in the DSM-5 (American Psychiatric Association [APA], 2013) and the ICD-11 (World Health Organization [WHO], 2022) has drawn attention to the concept of personality functioning (Bach et al., 2020, 2022). Psychoanalytic theories as well-established roots of the Alternative model of personality disorders (AMPD) conceive of personality structure as "… the dynamic interplay of repetitively activated psychological processes that normally serve adaptive functions but can become dysfunctional" (Zimmermann et al., 2012, p. 523). Consistent with major theories of personality disorders, the DSM-5 Level of Personality Functioning Scale (LFPS) assesses the self and the interpersonal domains by the four dimensions, identity, self-direction, empathy, and intimacy (Bender et al., 2011; Hopwood et al., 2018). These show striking similarities with the psychoanalytic concept of personality structure as conceptualized by the working group of the Operationalized Psychodynamic Diagnostic (OPD Task Force, 2008). Here, structural vulnerabilities are captured by capacities pertaining to self and object in the domains of self-perception, self-regulation, defence, the perception of the other, communication, and attachment. Conceptual as well as empirical overlaps between the LFPS and the OPD-Level of structural integration axis (OPD-LSIA) are well documented (Zimmermann, 2014). Through the concepts of schemas and skills, a link to personality structure can be drawn from a cognitive behavioural perspective (e.g., Huber et al., 2017), making it a potentially relevant outcome for CBT as well. As long-term psychotherapy trials remain scarce, structural change and related domains of functioning, representing their main target, are understudied.

Key Practitioner Message

- Long-term cognitive behavioural and psychoanalytical treatments achieved lasting changes regarding depressive symptoms.
- Both treatments resulted in structural change, with greater changes following psychoanalytic treatment.

To this end, our study is relevant and innovative as it investigated both, the change of depressive symptomatology, and structural change of chronically depressed patients in long-term CBT and psychoanalytic therapies. The aim of this paper was to analyse 5-year outcome data regarding changes in symptoms and restructuring for the two treatment approaches, PAT and CBT. Based on the higher intensity and longer duration, respectively, of PAT, we hypothesized that changes in CBT would start earlier but PAT would achieve more stable effects (Beutel et al., 2012; Leuzinger-Bohleber, Kaufhold, et al., 2019).

2 | METHODS

2.1 | Study design and participants

The study design has been described extensively elsewhere (Leuzinger-Bohleber, Hautzinger, et al., 2019). We included 252 patients between 21 and 60 years of age who gave written informed consent to study participation. Because many of the depressed patients reported having short periods where they felt better for a few days in the last 2 years, we decided that eligible patients had to be depressed without such short periods of subjective improvements for more than 1 year and meet diagnostic criteria of major depressive episode or dysthymia to be included. Their current depression severity had to meet a BDI-II score above 17 (Hautzinger et al., 2006), and an expert-rated Quick Inventory of Depressive Symptoms (QIDS-C) score of more than 9 points (Rush et al., 2003). Patients with antidepressant medication were included if they had been on a stable dosage for more than four weeks. The trial allocated patients either to be randomized or to their treatment preference leading to four original treatment arms. Patients consenting to randomization were coded by the respective study site and assigned by the independent statistic centre, which generated separate random allocation sequences for the study sites. Patients articulating a preference for either CBT or PAT were allocated accordingly. In the present study, we combined the random and preferential allocation groups due to the small sample size and long-term attrition rates. For sample size calculation, see Beutel et al. (2012), and Leuzinger-Bohleber, Hautzinger, et al. (2019). The study was registered (Clinical Trial Register ISRCTN91956346) and approved by the Ethics Committee of the Physician Board of Rhineland-Palatinate, Mainz, Germany (Ref: 837.124.075659). 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.

2.2 | Interventions

Psychoanalytic therapy (PAT) for depression is well described (Bleichmar, 2010; Leuzinger-Bohleber et al., 2022). All study PAT therapists ($N = 73$) had finished their psychoanalytic training for at least 3 years and were state licensed. In training workshops based on the empirically validated PAT-manual for treatment of chronic depression (Taylor, 2015), therapists were taught to uncover and modify the unconscious idiosyncratic fantasies and conflicts due to developmental deficits and traumatic experiences underlying chronic depression. Unconscious mental functioning (e.g., manifested in dreams, current object relationships) is observed and worked through in the 'here and now' of the transference relationship with the aim to change the psychic structure (Lane et al., 2015).

Cognitive Behaviour Therapy (CBT) for depression is based on the work of Beck, Lewinsohn and others, as integrated in a nationally widely used and well-accepted treatment protocol (Hautzinger, 2013). CBT therapists used five modules (problem analysis, goals, psychoeducation, and rationale for treatment; behavioural activation and increasing pleasant activities; cognitive interventions to re-structure basic assumptions and schemata; social skill training, problem-solving and stress management; maintenance and relapse prevention). State licensed CBT therapists ($N = 44$) with at least 3 years of clinical practice participated in training workshops.

Adherence to treatment protocol was assessed by the Comparative Psychotherapy Process Scale (CPPS; Hilsenroth et al., 2005). Based on randomly selected 137 audiotapes of therapy sessions, adherence ratings were high (inter-rater reliability ICC > .85).

2.3 | Outcome measures

Main outcome measures were the BDI-II (Hautzinger et al., 2006) and the short form of the QIDS-C (Rush et al., 2003). We assessed the BDI-II and QIDS-C yearly, at baseline, and over the course of 5 years following treatment start. All patients were diagnosed using the Structured Clinical Interview for DSM-IV (SCID-I and -II) and followed over the 5-year study period with the Longitudinal Follow-up Evaluation (LIFE). All ratings (QIDS-C) were conducted by independent, trained clinicians, blinded to treatment. Inter-rater reliability for the QIDS-C ratings was high (Pearson correlation $r = .95$ [CI: 0.889–0.999]).

A video-recorded, semistructured interview, conducted by interviewers trained in the Operationalized Psychodynamic Diagnosis (OPD), was evaluated independently by at least two blinded raters, then discussed together and rated on the axes internal (neurotic) conflicts (axis 3) and psychological structural features (axis 4). The latter included self-perception and object perception, self-regulation, or different aspects of the quality of object relations (Bahrke & Grabhorn, 2020). Comprehensive validation studies have demonstrated good psychometric properties ($\kappa = .71$ to .83; Grande et al., 2001; Rudolf et al., 2000).

The HRS is an individualized tool to assess insight into the dysfunctional patterns indicating structural change over time. Its formal setup is based on Stiles' Assimilation of Problematic Experiences Scale (APES; Stiles et al., 1990). Based on the blinded OPD pretreatment expert ratings, which included an unconscious conflict and a structural feature, five individual core problems or foci were defined by trained and blinded raters for each patient. The reliable

($\kappa = .70$) scale (Grande et al., 2001; Rudolf et al., 2000) assesses different levels of awareness of these foci on a seven-stage scale from 1 = focus problem warded-off to 7 = resolution of the focus. While patients often begin psychoanalytic therapy at stage 2 (involuntary engagement with focus) or stage 3 (vague problem perception), after passing stage 4 (acceptance and exploration of the focus), they may proceed to stages 5 (dissolution of old structures) or 6 (reorganization of the focus area). A visual depiction of these stages can be found in the supporting information (Figure S1). Higher levels of structural outcome have been shown as positive predictors of follow-ups of psychoanalytic treatments (Grande et al., 2009). For the main analysis the average stage achieved across the five foci per patient was used. According to Rudolf et al. (2012), relevant stages indicating structural change pertain to stages 4 and 5. Therefore, we also applied a different scoring procedure indicating no structural change (less than two defined foci at stage 4 or higher AND mean change across 5 foci < 1.5), mixed change (either two foci at stage 4 or higher OR mean change across 5 foci ≥ 1.5), positive change (two foci at stage 4 or higher AND mean change across 5 foci ≥ 1.5), restructuring (two foci at stage 5 or higher AND mean change across 5 foci ≥ 1.5). Due to the time- and cost-intensive assessment of the OPD, out of 190 initial HRS interviews, only $N = 134$ patients could be pursued in a consecutive subsample 1, 3, and 5 years after treatment start, resulting in four measurement points. Participants with at least two available ratings were considered eligible for analysis.

2.4 | Data analysis

Statistical analyses were carried out using the R software package lme4 (v1.1-27; Bates et al., 2015) and SPSS 25 for macOS. Following up on our 3-year analysis, we performed linear mixed models with patient-specific random intercepts to estimate change over time. As previous analyses by the independent statistical centre (Leuzinger-Bohleber, Hautzinger, et al., 2019) had found no differences between preference and random assignment, we only compared two conditions, PAT and CBT, regardless of random or preferential assignment to increase power. Patients with at least two valid assessments were incorporated in the analyses. Model estimation was performed separately for the three different outcome variables to evaluate change in symptoms (BDI-II, QIDS-C), and structural change (HRS). We built five nested models per outcome and sequentially added the following predictor variables to estimated course trajectories: Mean centred baseline score of the respective outcome variable (BDI-II, QIDSC-C, and HRS), psychopharmacological medication, treatment, and time. Therapy group (CBT, PAT), time points, and baseline psychopharmacological medication (medication, no medication, no information available) were included as categorical independent variables. Time points and medication were incorporated using effect coding.

Our baseline (null)-models estimated the linear independent effects of a patient-specific random intercept, the mean centred baseline score of the dependent variable (BDI-II, QIDSC-C, and HRS), and of psychopharmacological medication at baseline. To test for a general effect of time, the time variable was added in a subsequent model and tested against the nested baseline model. The same was repeated with the treatment variable in order to test for overall differences between CBT and PAT. To test for differences between time points, treatment groups, and different time courses in treatment groups, we built our full model by adding the variables time, treatment group, and interactions between time points and treatment groups to the baseline model. We tested the full model against a model including only the main effects of time and treatment in addition to the baseline model. We computed 95% confidence intervals for model estimates. Nested models were tested using approximate *F* tests for each of the two models. Degrees of freedom of the corresponding test statistic where calculated using the R software package pbkrtest (v0.5.1; Halekoh & Højsgaard, 2014). Mean-centred baseline scores were calculated with the R software package QuantPsyc (v1.5; Fletcher, 2010). We performed multiple sensitivity analyses (Supporting Information): (1) While missing data was assumed to be missing at random in the main analysis, we repeated the analysis on data in which missing BDI-II/QIDS-C, or HRS scores, respectively, were imputed based on the last available score of the respective participant using R package zoo (v1.8-9; Zeileis & Grothendieck, 2005). (2) To account for the study's multicentre character, we estimated models in which patients were further clustered in study centres. (3) As the original design considered randomized and preferential allocation, we performed sensitivity analyses incorporating the four original treatment conditions.

3 | RESULTS

3.1 | Trial flow and baseline characteristics

Of a total of 554 interviewed individuals, 252 were included as study patients. In the naturalistic setting, treatment ended upon mutual agreement of therapist and patient. Figure 1 (cf. Leuzinger-Bohleber, Hautzinger, et al., 2019) shows the participants included, reasons for exclusion, and available main outcome assessments, BDI-II and QIDS-C, at baseline (T0), after 1 (T4), 2 (T6), 3 (T8), 4 (T9), and 5 years (T10), separately for PAT and CBT. Based on the total sample of 252 study patients, at least one outcome criterion (BDI-II or QIDS-C) was available for 73.4% after 1 year, 63.9% after 2 years, 65.5% after 3 years, 55% after 4 years, and 60% after 5 years. HRS ratings were performed for a subsample and the following assessment points: At baseline, 190 HRS ratings were conducted, year one: 128; year three: 106, year five: 80. The baseline assessment plus at least one additional rating was available for 134 patients.

Table 1 summarizes baseline demographic and clinical characteristics of total study participants analysed, drop-outs, and the subsample with ratings of structural change (HRS sample). The analysed patients ($N = 227$) suffered from chronic depression with high symptom severity (BDI: $M = 31.8$, $SD = 7.91$; QIDS-C: $M = 14.2$, $SD = 3.03$). These scores correspond to percent ranks above 75 in large samples of depressed patients (Hautzinger et al., 2006). The majority had had

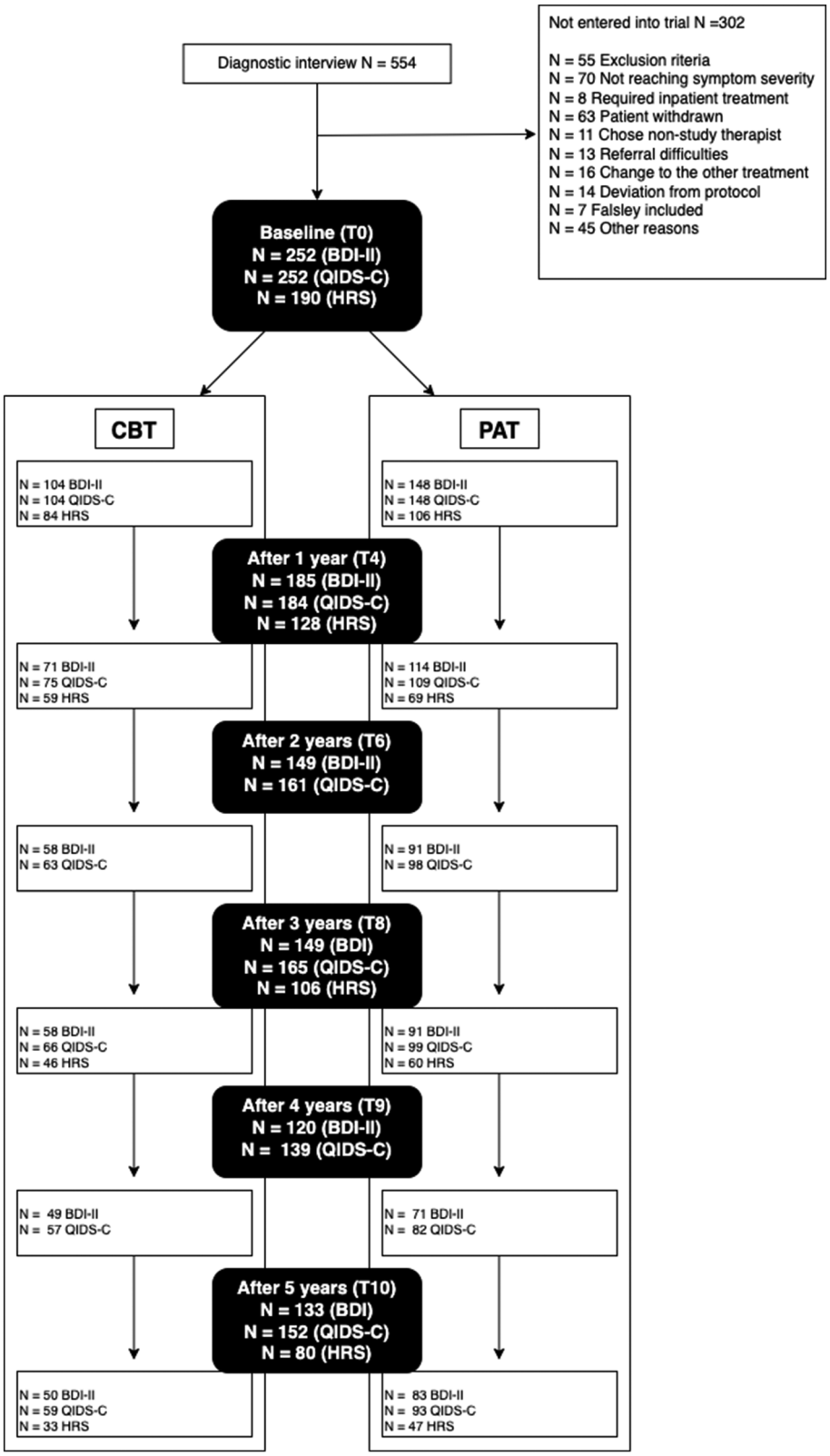

FIGURE 1 Patient flow diagram. The number of patients with available measures over the course of 5 years is depicted for the overall sample and according to treatment conditions CBT (cognitive-behavioural therapy) or PAT (psychoanalytical therapy), respectively. Symptom ratings of BDI-II (Beck Depression Inventory II) and QIDS-C (Quick Inventory of Depressive Symptoms) were assessed every year (T0-T10). Personality functioning with the HSCS (Heidelberg structure scale) was rated at baseline, one (T4), three (T8), and five (T10) years after treatment start.

prolonged periods of sick leaves from work during the past year. More than 70% had had previous psychotherapies. More than one third of our sample had been admitted to inpatient psychotherapy, and 42% were on antidepressant medication. According to DSM-IV, 58% fulfilled MDE criteria, 13% suffered from Dysthymia, and 29% from Double Depression.

We analysed 227 (90%) patients with at least one available outcome score in addition to the baseline score. As Table 1 shows, drop-

TABLE 1 Sociodemographic and medical characteristics of study participants at baseline

Variable	Analysed ($N = 227$) M (SD)	Dropouts ($N = 25$) M (SD)	t test[a] T (df)	p	HRS sample ($N = 134$) M (SD)	t test[b] T (df)	p
Age	40.40 (10.8)	42.20 (9.71)	−0.85 (30.92)	.403	41.00 (10.90)	−0.63 (247.78)	.523
BDI-II	31.8 (7.91)	34.8 (8.20)	−1.73 (29.13)	.094	30.0 (7.01)	4.61 (229.58)	≤.001
QIDS-C	14.2 (3.03)	15.0 (3.18)	−1.20 (29.02)	.239	13.7 (2.70)	3.22 (227.17)	.001
HRS	2.27 (0.45)	2.33 (0.40)	−0.49 (9.07)	.635	2.33 (0.40)	−2.51(90.77)	.014
			χ^2 test[c]			χ^2 test[d]	
	% (N)	% (N)	$\chi^2(df)$	p	% (N)	$\chi^2(df)$	p
Gender							
Men	33.04% (75)	28.00% (7)	0.082 (1)	.775	33.58% (45)	0.06 (1)	.809
Women	66.96% (152)	72.00% (8)			66.42% (89)		
Job status							
Full- or part-time work	69.27% (151)	70.83% (17)	2.50 (3)	.475	75.00% (96)	4.32 (3)	.229
Not working	15.60% (34)	12.50% (3)			11.72% (15)		
In school/training	5.50% (12)	n.a.			4.69% (6)		
Unemployed	9.63% (21)	16.67% (4)			8.59% (11)		
Education							
Lower secondary or middle school	29.41% (65)	45.83% (11)	14.75(2)	≤.001	27.13% (35)	2.534(2)	.282
High school	70.14% (155)	45.83% (11)			72.09% (93)		
Did not graduate/other	0.45% (1)	8.33% (2)			0.78% (1)		
Marital status							
Single	60.18% (133)	54.17% (13)	0.806 (3)	.848	57.36% (74)	3.35 (3)	.341
Married	25.34% (56)	33.33% (8)			25.58% (33)		
Separated	14.03% (31)	12.50% (3)			17.05% (22)		
Widowed	0.45% (1)	n.a.			n.a.		
Work disability (12 months)							
None	43.46% (93)	34.78% (8)	8.13 (3)	.043	41.46% (51)	2.18 (3)	.537
1–4 weeks	20.56% (44)	8.70% (2)			21.95% (27)		
5–12 weeks	15.89% (34)	39.13% (9)			15.45% (19)		
>13 weeks	20.09% (43)	17.39% (4)			21.14% (26)		
Diagnosis							
Double depression	28.63% (65)	36.00% (9)	1.98 (2)	.371	28.36% (38)	0.397 (2)	.820
Dysthymia	13.22% (30)	4.00% (1)			13.43% (18)		
Major depression	58.15% (132)	60.00% (15)			58.21% (78)		
Previous outpatient treatments							
None	27.85% (61)	25.00% (6)	11.62 (2)	.003	27.91% (36)	13.63 (2)	.001
1	28.77% (63)	n.a.			34.88% (45)		
2 or more	43.38% (95)	75% (18)			37.21% (48)		
Antidepressant medication at baseline							
Yes	41.85% (95)	48.00% (12)	4.88(2)	.087	41.04% (55)	20.59 (2)	≤.001
No	49.78% (113)	32% (8)			56.72% (76)		

Note: BDI-II = Beck Depression Inventory Revision; QIDS-C = Clinician-rated Quick Inventory of Depressive Symptomatology; HRS = Heidelberg Restructuring Scale; baseline sociodemographic characteristics and mean scores of the analysed sample, dropouts (patients terminating treatment prematurely or with less than two valid assessments), and the subsample evaluated on the HRS.

[a]Two-sided t tests between analysed and dropout sample.

[b]Two-sided t test between participants of the HRS subsample and those who were not evaluated on the HRS.

[c]χ^2 difference test between analysed and dropout sample.

[d]χ^2 difference tests between participants of the HRS subsample and those who were not evaluated on the HRS.

outs did not differ from this sample regarding age, depression and HRS scores, gender, job, marital status, diagnosis, and antidepressant intake. However, drop-outs were less likely to have high school diploma, less likely on sick leave, and had undergone more outpatient treatments. The HRS subsample ($N = 134$) resembled the analysed total sample. However, the HRS sample had a lower symptom load and higher HRS ratings at baseline. They also were more likely to have undergone one previous outpatient treatment and less likely to have undergone two or more. Moreover, they were more likely to receive antidepressant medication.

Tables S1 and S2 show data separately for PAT and CBT, as well as for the original four treatment arms. At baseline, BDI-II and HRS scores were comparable, but the PAT group had higher (mean) QIDS-C scores compared to the CBT group. Using ANOVAs with Tukey post-hoc corrections, we find elevated symptom levels according to QIDS-C ratings in the PAT randomized group, compared to the CBT randomized ($p = .01$) and the CBT preference ($p = .04$) group. Hence, the effect is mainly driven by the PAT randomized group but no consequence of merging preference and randomized cells. No statistically significant differences between PAT and CBT were found regarding age, gender, job status, sick leave, education, diagnosis, previous outpatient treatments, and antidepressant medication. Comparing the original four treatment conditions with X^2 difference tests showed that patients who preferred PAT were less likely to have sick leaves >3 months during the last year ($p = .03$). A primary diagnosis of dysthymia was overrepresented in the CBT randomized group ($p = .02$).

3.2 | Changes on outcome measures

Pre-post effect sizes for both treatment groups, between treatment groups effect sizes, and the number of participants with full data at each time-point are depicted in Table 2. After 4 years, full remission rates (cut-offs: BDI-II ≤ 12, QIDS-C ≤ 5) of the analysed sample were 45.83% for the BDI-II (CBT = 44.9%, PAT = 46.48%) and 57.55% (CBT = 54.39%, PAT = 59.76%) for the QIDS-C. According to BDI-II scores, 57.14% (CBT = 58%, PAT = 56.63%) showed full remission 5 years after treatment. This was true for 59.21% (CBT = 61.02%, PAT = 58.06%) of patients according to QIDS-C scores. Table 3 shows structural changes according to Rudolf et al. 2012 criteria. During the first year of treatment, the majority of patients did not achieve structural changes. At the 5-year measurement point, more than 80% of patients in PAT had achieved positive or complete restructuring, while this was the case for less than 50% of patients in CBT.

Table 4 presents the statistical model of the mixed effect analyses for the two symptom measures, BDI-II and QIDS-C, and Table 5 for structural change (HRS). Figure 2 shows mean values and standard errors over time.

BDI-II scores decreased over the 5 years. The corresponding test of time (against the baseline model) rejects the null-hypotheses of no differences in expected BDI-II scores at the five different time points ($p \leq .001$). We found no differences of BDI-II scores between the two treatment groups, adding treatment group to the baseline model did not lead to an increase in explained variance ($p = .43$). No differences in expected values for the treatment groups over all time points were found, and there was no interaction between time points and treatment groups ($p = .37$). Medication and mean-centred BDI-II score at baseline were included as covariates. The performed sensitivity analyses, replacing missing values with the last available observation carried forward, the analysis incorporating clustering by trial centre, as well as the analysis of the four treatment groups (randomized vs preference CBT/PAT), yielded the same results (Tables S3, S5, and S7).

Consistent with these findings, QIDS-C scores also decreased over the 5 years. For the QIDS-C scores, the null hypothesis of no time differences over treatment groups could be rejected as well ($p \leq .001$). Yet, the interaction effect between time points and treatment groups was statistically significant ($p \leq .02$) as 1 year after treatment start, a significantly steeper decline in symptoms could be observed in the CBT group. Again, medication and mean-centred QIDS-C score at baseline were included as covariates. The same results were observed when performing sensitivity analysis with participants' last observation carried forward (Table S3), and when clustering according to trial centres was considered (Table S5). Sensitivity analysis with the four treatment groups yielded similar results (Table S7). Here, the significant full model ($p \leq .001$) indicated that 1 year after treatment start, the CBT preference group reported the lowest level of symptoms of all groups. In the CBT randomized group, symptom levels decreased up to 3 years after treatment start but significantly increased from the fourth year onward.

Regarding restructuring (HRS), we found an improvement over time ($p \leq .001$). Treatment groups differed significantly ($p = .006$), and their interaction with time was also significant ($p \leq .001$); that is, the increase was steeper in PAT and levelled off in CBT after 3 years. Sensitivity analysis using last observation carried forward (Table S4), and analysis considering the study centre as a source of variation, showed similar results (Table S6). When performing sensitivity analysis with the four treatment groups (Table S8), we did not find a significant main effect of the group variable. The full model estimated a significant interaction effect of time and treatment, with the PAT-preference group performing best after 5 years. However, this group incorporated the largest number of participants and the full model did not explain more variance compared to the main effects model ($p = .056$). Scores of the HRS increased more strongly in PAT after 3 or 5 years, respectively.

3.3 | Treatment intensity

PAT and CBT offer different treatment intensity and duration due to their divergent conceptualizations of treatment process and outcome. One major aim of PAT is to achieve so-called "structural changes" by longer and more intensive treatment as a presupposition for sustaining change in patients (Leuzinger-Bohleber, 2015; Leuzinger-Bohleber et al., 2022). In the total sample, the median number of sessions in

TABLE 2 Means and standard deviations of all outcome variables over the course of 5 years and effect sizes (Cohen's *d*) between and within (pre-post) treatment arms in the analysed sample

	Baseline (year 0)			Year 1				Year 2				Year 3				Year 4				Year 5			
	N	*M* (*SD*)	$d_{CBT/PAT}$	*N*	*M* (*SD*)	$d_{CBT/PAT}$	$d_{Y0\text{-}Y1}$	*N*	*M* (*SD*)	$d_{CB/PAT}$	$d_{Y0\text{-}Y2}$	*N*	*M* (*SD*)	$d_{CBT/PAT}$	$d_{Y0\text{-}Y3}$	*N*	*M* (*SD*)	$d_{CBT/PAT}$	$d_{Y0\text{-}Y4}$	*N*	*M* (*SD*)	$d_{CBT/PAT}$	$d_{Y0\text{-}Y5}$
BDI-II																							
CBT	91	31.75 (7.16)	0.02	71	18.21 (12.06)	0.2	1.08	58	17.48 (12.66)	0	1.25	58	14.28 (10.01)	0.11	1.50	49	14.10 (11.47)	0.13	1.45	50	14.22 (11.77)	0.12	1.52
PAT	136	31.87 (8.40)		114	20.68 (12.51)		0.96	91	17.52 (11.92)		1.13	91	15.47 (11.61)		1.51	71	15.63 (12.16)		1.48	83	12.73 (12.19)		1.50
QIDS-C																							
CBT	91	13.56 (2.70)	0.36	75	6.44 (4.44)	0.4	1.59	63	6.13 (4.90)	0.07	1.45	66	5.02 (4.48)	0.18	1.73	57	5.65 (4.85)	0.08	1.64	59	5.12 (4.76)	0.04	1.72
PAT	136	14.62 (3.17)		109	8.43 (5.25)		1.33	98	6.43 (4.34)		1.79	99	5.89 (5.22)		1.59	82	5.27 (4.55)		1.92	93	4.92 (5.00)		1.83
HRS																							
CBT	59	2.32 (0.45)	0.02	58	3.37 (0.90)	0.05	1.19					46	3.75 (1.00)	0.47	1.49					33	3.68 (1.04)	0.83	1.39
PAT	70	2.33 (0.35)		69	3.42 (0.79)		1.44					60	4.23 (1.03)		1.72					47	4.50 (0.94)		2.46

Note: BDI-II = Beck Depression Inventory Revision; QIDS-C = Clinical-rated Quick Inventory of Depressive Symptomatology; HRS = Heidelberg Restructuring Scale; CBT = cognitive behaviour therapy; PAT = psychoanalytic therapy.

TABLE 3 Structural change

Structural change % (*N*)	Year 1 (124)		Year 3 (102)		Year 5 (78)	
	CBT (59)	PAT (65)	CBT (46)	PAT (56)	CBT	PAT
None[a]	61.0% (36)	50.8% (33)	30.4% (14)	19.6% (11)	36.4% (12)	6.7% (3)
Mixed[b]	16.9% (10)	23.1% (15)	32.6% (15)	21.4% (12)	15.2% (5)	22.2% (10)
Positive[c]	5.1% (3)	9.2% (6)	4.3% (2)	8.9% (5)	24.2% (8)	15.6% (7)
Restructuring[d]	16.9% (10)	16.9% (11)	32.6% (15)	50.0% (28)	24.2% (8)	55.6% (25)

[a]< Two foci at stage 4 or higher AND mean change across 5 foci < 1.5.
[b]≥ Two foci at stage 4 or higher OR mean change across 5 foci ≥ 1.5.
[c]≥ Two foci at stage 4 or higher AND mean change across 5 foci ≥ 1.5.
[d]≥Two foci at stage 5 or higher AND mean change across 5 foci ≥ 1.5.

TABLE 4 Estimated coefficients of the mixed-effects models of the symptom outcomes BDI-II and QIDS-C

	BDI-II				QIDS-C			
	B	*SE*	95% CI (*LL*; *UL*)	*T*	B	*SE*	95% CI (*LL*; *UL*)	*T*
Intercept	14.38	2.39	9.72; 9.56	6.01	6.30	0.93	4.50; 8.11	6.80
Baseline score	0.51	0.08	0.35; 0.68	6.07	0.45	0.09	0.28; 0.62	5.13
$Year_1$	0.89	1.80	−2.63; 4.40	0.49	0.70	0.37	−0.02; 1.14	1.90
$Year_2$	0.73	1.95	−3.06; 4.54	0.37	0.52	0.83	−1.10; 2.15	0.63
$Year_3$	−0.62	1.92	−4.35; 3.11	−0.32	−0.78	0.81	−2.36; 0.81	−0.96
$Year_4$	−2.05	2.08	−6.10; 2.00	−0.99	0.78	0.86	−0.91; 2.46	0.90
$Year_5$	1.05	2.05	−2.95; 5.05	0.51	0.32	0.53	−1.34; 1.98	0.03
No medication	−0.64	1.06	−2.70; 1.41	−0.61	−0.74	0.40	−1.52; 0.05	0.07
Medication	2.23	1.08	0.12; 4.34	2.06	0.37	0.42	0.44; 1.19	0.89
Missing information regarding medication	−1.58	1.63	−4.76; 1.59	−0.97	0.36	0.62	−0.85; 1.57	0.58
Therapy group (PAT)	0.87	1.35	−1.76; 3.51	0.65	0.02	0.53	−1.02; 1.05	0.03
$Year_1$ × therapy group	1.69	1.07	−0.40; 3.77	1.58	1.54	0.47	0.61; 2.46	3.24
$Year_2$ × therapy group	0.16	1.16	−2.10; 2.42	0.14	−0.18	0.50	−1.15; 0.78	−0.37
$Year_3$ × therapy group	−0.41	1.14	−2.63; 1.82	−0.36	0.21	0.49	−0.74; 1.16	0.43
$Year_4$ × therapy group	0.51	1.25	−1.92; 2.94	0.41	−0.85	0.45	−1.86; 0.17	−1.63
$Year_5$ × therapy group	−1.95	1.21	−4.31; 0.41	−1.61	−0.71	0.51	−1.70; 0.27	−1.41
Model tests	$F_{(4,\ 549.00)} = 14.83$, $p \leq .001$[a]				$F_{(4,\ 609.90)} = 13.54$, $p \leq .001$[a]			
	$F_{(1,\ 207.66)} = 0.614$, $p \leq .434$[b]				$F_{(1,\ 215.22)} = 0.4$, $p \leq .85$[b]			
	$F_{(4,\ 545.09)} = 1.08$, $p \leq .367$[c]				$F_{(4,\ 605.64)} = 3.09$, $p \leq .015$[c]			

Note: BDI-II = Beck Depression Inventory Revision; QIDS-C = Clinical-rated Quick Inventory of Depressive Symptomatology; PAT = psychoanalytic therapy; CI = confidence interval; *LL* = lower limit; *UL* = upper limit.
[a]Refers to the effect of time, tested against the null-model including mean centred baseline score, effect of medication.
[b]Refers to the effect of treatment, tested against the null-model including mean centred baseline score, effect of medication.
[c]Refers to the effect of different time courses in the treatment groups (interactions), tested against main effects model including mean centred baseline score, effect of medication, main effects of time and treatment.

PAT was 242 and 59 in CBT. Seventeen PAT patients and one CBT patient were in ongoing treatment at the 5-year outcome assessment.

4 | DISCUSSION

To our knowledge, this is the longest controlled trial for persistent depression comparing two major treatment approaches, cognitive behaviour, and psychoanalytic psychotherapy. It fills several gaps in the fast-expanding literature on the treatment of depression regarding long-term outcomes of depression and structural changes. In light of these current debates, the LAC study can make an innovative contribution.

Suffering from chronic depression, patients in our study had undergone a multiplicity of outpatient and inpatient psychotherapy and antidepressant treatments. More than 70% had previous outpatient treatments, without lasting success. The initial severity of symptoms appeared high with a mean BDI-II score of 32, and 58% were

TABLE 5 Estimated coefficients of the mixed-effects model of structural change (HRS)

	HRS Estimate	*SE*	95% CI (*LL*; *UL*)	*T*
Intercept	3.32	0.27	2.80; 3.85	12.23
Baseline score	0.61	0.16	0.30; 0.91	3.84
$Year_1$	0.11	0.20	−0.27; 0.49	0.56
$Year_3$	0.14	0.20	−0.26; 0.54	0.69
$Year_5$	−0.25	0.22	−0.69; 0.19	−1.12
No medication	−0.22	0.17	−0.55;0.10	3.08
Medication	−0.02	0.17	−0.35; 0.31	−0.10
Missing information regarding medication	0.24	0.31	−0.37; 0.84	0.76
Therapy group (PAT)	0.40	0.13	0.15; 0.65	3.08
$Year_1$ × therapy group	−0.35	0.12	−0.58; −0.11	−2.86
$Year_3$ × therapy group	0.01	0.12	−0.23; 0.25	0.09
$Year_5$ × therapy group	0.33	0.14	0.07;0.60	2.45
Model tests	$F_{(2,\ 198.42)} = 24.68$, $p \leq .001$[a]			
	$F_{(1,\ 117.61} = 7.71$, $p \leq .006$[b]			
	$F_{(2,\ 196.53} = 4.68$, $p \leq .010$[c]			

Note: HRS = Heidelberg Restructuring Scale; CI = confidence interval; *LL* = lower limit; *UL* = upper limit; PAT = psychoanalytic therapy.

[a]Refers to the effect of time, tested against the null-model including mean centred baseline score, effect of medication.

[b]Refers to the effect of treatment, tested against the null-model including mean centred baseline score, effect of medication.

[c]Refers to the effect of different time courses in the treatment groups (interactions), tested against main effects model including mean centred baseline score, effect of medication, main effects of time and treatment.

diagnosed with Major Depression, 13% with Dysthymia, and 29% with Double Depression. Patients with this symptom severity and treatment history have been labelled difficult-to-treat or treatment-resistant (Fonagy et al., 2015). With two-year relapse rates of about 50%, stability of improvement is a crucial issue in the treatment of depression (Steinert et al., 2014). This is consistent with growing evidence showing that chronic depression, associated with worse prognosis than non-chronic depression (Schramm et al., 2020), requires long-term treatments (Heerlein et al., 2021). Overall, in our trial long-term psychotherapy was very successful improving depression and achieving full remission in the long run. Yet about 4% of patients were still in treatment at the last follow-up, as treatment length was not predetermined. The finding that PAT and CBT were comparably successful in achieving symptom reduction is consistent with a recent meta-analysis (Cuijpers et al., 2021). While our analyses indicate stable improvements with respect to overall mean symptom scores, differentiating individual courses of remission represents an important task of future research.

Compared to CBT, PAT was superior in improving insight into dysfunctional patterns, indicating improved psychological capacities. A major goal in PAT is the improvement of the functioning of the inner object world, the unconscious fantasies and conflicts and thus modify pathological psychic and psychosocial developments which influence their social relationships, quality of life and symptoms. PAT focuses on transformations of the unconscious dimensions of patients' psychological capacities, characteristically using analysis of transference/countertransference, dreams, or Freudian slips to observe such changes (Leuzinger-Bohleber et al., 2022) Based on the OPD and HRS, the LAC study showed that such changes indeed take place more often in psychoanalytic long-term therapies than in CBT. Achieving these objectives may need more time and a greater treatment intensity (Lindfors et al., 2019). In our study, greater structural changes were accomplished in PAT versus CBT. However, PAT used more sessions over a longer time period compared to CBT. Yet, we did not examine dose–response relations, and cannot determine whether the finding is related to dose or technique. Alterations of the structure after long-term psychodynamic psychotherapy promoted sustainability of psychological changes after treatment termination (Lindfors et al., 2019) and in the face of adversity following treatment (Huber et al., 2017). Given the high rates of chronicity, recidivism, and health care utilization in chronic and treatment-resistant depression (Li et al., 2020) and the more general role of personality functioning in health costs (Hajek et al., 2020), the finding of restructuring is very encouraging. Further analyses of health care data will show whether these are indeed associated with less health care use and better long-term outcomes.

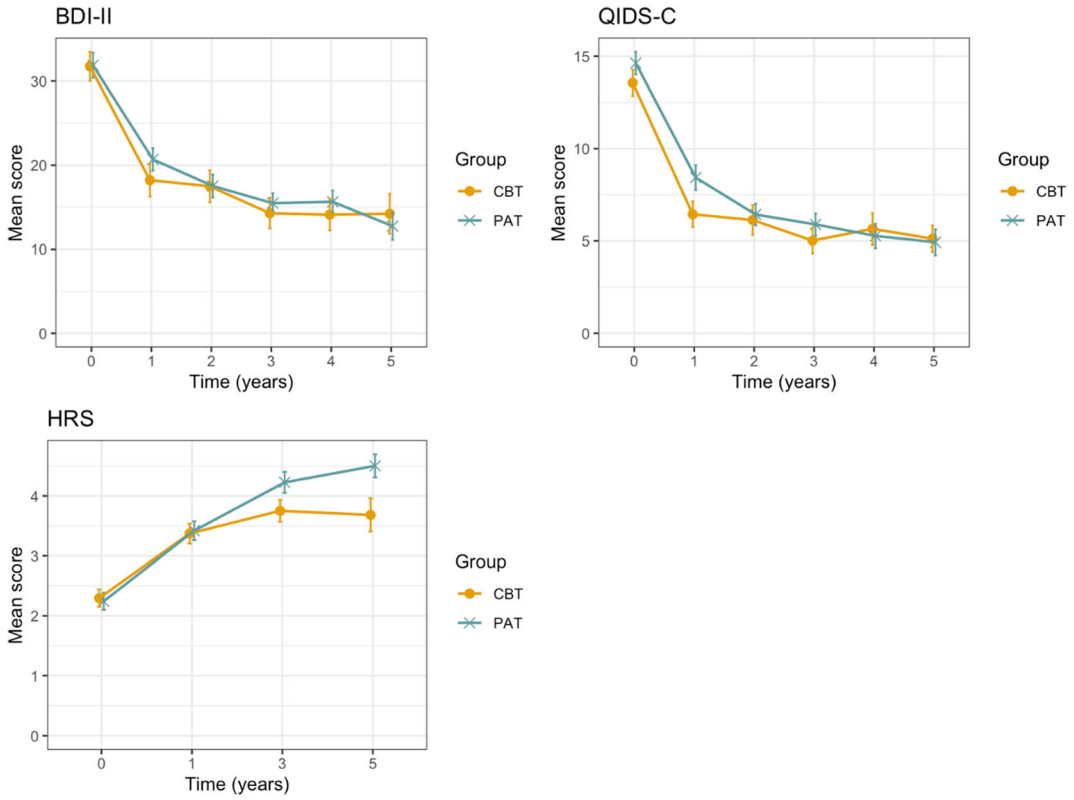

FIGURE 2 Mean scores and standard errors of depressive symptoms (BDI-II; QIDS-C) and structural change (HRS) over time in the CBT (cognitive behavioural therapy) and PAT (psychoanalytic therapy) treatment groups [Colour figure can be viewed at wileyonlinelibrary.com]

4.1 | Limitations

Our naturalistic, controlled trial with four arms, two different active treatments and two kinds of allocation suffers from several shortcomings limiting our conclusions. First, we powered our design to detect treatment differences of an effect size of 0.5. Due to unavailable previous studies, we might have over-estimated this difference and therefore underpowered our design. Given their complexity and costs, OPD and HRS assessments could only be performed in about half the sample. Due to the limited sample size of patients followed with these instruments, we had to combine randomization and preference cells. Though we controlled for baseline severity, we must concede that we thereby gave up the randomized controlled design. However, as the sensitivity analyses show, findings on symptoms were consistent with analyses of the full design (Table S7).

Second, the complexity of the design, recruitment of difficult-to treat patients and the long duration of the trial led to a considerable proportion of missing data at single time points. However, by our statistical mixed model analysis approach we handled missing data including all available assessments. The missing at random assumption could be problematic. Different imputation techniques could have led to slightly different results. Therefore, we also conducted a sensitivity analysis using the last available assessment for missing data (Tables S3 and S4). Third, we could not thoroughly control the effect of antidepressant medication over the duration of study time. Withholding medication in this group of severely ill patients would have been unethical. We considered only baseline medication in our analyses. Fourth, in principle, the study could have been enhanced by adding a "treatment-as-usual" group in the design. However, given their high rates of previous treatments, we would have expected this group of patients to take up medication or CBT or PAT, respectively, in a treatment-as-usual arm. Fifth, the HSR is an instrument assessing structural change, a proposed outcome and mechanism of change in psychodynamic therapies. Although a connection can be made between personality structure and CBT concepts like schemas and skills (Huber et al., 2017), we did not assess mechanisms of change rooted in cognitive-behavioural theories. Because of the high costs, structural change could only be evaluated in a subsample. Participants in this sample differed from those who did not with respect to symptomatic burden and structural capacities. Sixth, while we took care to include patients with a chronic course of depression for at least 1 year, the time criterion is below the DSM-5 criterion of 2 years of ongoing depression, due to practical reasons. As discussed in previous publications (Leuzinger-Bohleber et al., 2013, 2020) most of the patients had a yearlong history of severe depression but sometimes mentioned that they had a short period in the last 2 years (e.g., vacations) where they felt "a bit better". Therefore, we lost many patients in

the first phase of the LAC study during which we tried to fulfil the two-year criterion of DSM-5 and thus modified our design to 1 year. The finding that more than 70% of the patients had previous treatment attempts further speaks to the chronicity of depression in our sample. Seventh, we are aware that chronically depressed individuals are frequent users of a variety of health care services. However, within the scope of this investigation, we were only able to evaluate the psychotherapy provided in the study. Additional follow-up investigations are currently conducted to determine if and when additional treatments were sought. Eighth, due to missing data (exact termination date of treatments, individual follow-up data), we could not include the number of sessions and date of treatment termination in the statistical models.

5 | CONCLUSION

Long-term psychotherapy helps chronically depressed patients with a history of unsuccessful treatments achieve lasting symptom changes. However, PAT was more successful achieving structural change, a major goal of long-term psychodynamic treatments with high frequency and duration. Future follow-up will clarify whether structural change promotes further sustainable improvements and its interrealation with symptomatic change.

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CONFLICTS OF INTEREST

The authors declare no competing interest.

AUTHOR CONTRIBUTIONS

MB, MLB, and MH collectively designed and led the study. UB and AG were responsible for reviewing OPD interview material. GF, ME, LKK, and JK were involved in the data collection, data management, and the implementation at different study sites. BR developed the original statistical analysis plan. LK and JK did the statistical analysis. MB, MLB, and LK wrote the first draft of the manuscript. All authors reviewed and commented on the manuscript and approved the final version and submission to Clinical Psychology and Psychotherapy.

DATA AVAILABILITY STATEMENT

The data supporting the findings of this study are available on request from the corresponding author, L. Krakau. The data are not publicly available due to their containing information that could compromise the privacy of research participants.

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REFERENCES

American Psychiatric Association. (Ed.) (2013). *Diagnostic and statistical manual of mental disorders: DSM-5* (5th ed.). American Psychiatric Association. https://doi.org/10.1176/appi.books.9780890425596

Bach, B., Kerber, A., Aluja, A., Bastiaens, T., Keeley, J. W., Claes, L., Fossati, A., Gutierrez, F., Oliveira, S. E. S., Pires, R., Riegel, K. D., Rolland, J.-P., Roskam, I., Sellbom, M., Somma, A., Spanemberg, L., Strus, W., Thimm, J. C., Wright, A. G. C., & Zimmermann, J. (2020). International assessment of DSM-5 and ICD-11 personality disorder traits: Toward a common nosology in DSM-5.1. *Psychopathology*, *53*(3–4), 179–188. https://doi.org/10.1159/000507589

Bach, B., Kramer, U., Doering, S., di Giacomo, E., Hutsebaut, J., Kaera, A., De Panfilis, C., Schmahl, C., Swales, M., Taubner, S., & Renneberg, B. (2022). The ICD-11 classification of personality disorders: A European perspective on challenges and opportunities. *Borderline Personality Disorder and Emotion Dysregulation*, *9*(1), 12. https://doi.org/10.1186/s40479-022-00182-0

Bahrke, U., & Grabhorn, A. (2020). Zwischen Patenschaft und Rating. Die OPD-Mitarbeit in der LAC-Depressionsstudie [Between sponsorship and rating. The OPD Collaboration in the LAC Depression Study]. In M. Leuzinger-Bohleber, A. Grabhorn, & U. Bahrke (Eds.), *Was nur erzählt und nicht gemessen werden kann. Einblicke in psychoanalytische Langzeitbehandlungen chronischer Depressionen (pp. 83–98)*. Psychosozial-Verlag. https://doi.org/10.30820/9783837976991-83

Bates, D., Mächler, M., Bolker, B., & Walker, S. (2015). Fitting linear mixed-effects models using lme4. *Journal of Statistical Software*, *67*(1), 1–48. https://doi.org/10.18637/jss.v067.i01

Bender, D. S., Morey, L. C., & Skodol, A. E. (2011). Toward a model for assessing level of personality functioning in DSM–5, part I: A review of theory and methods. *Journal of Personality Assessment*, *93*(4), 332–346. https://doi.org/10.1080/00223891.2011.583808

Beutel, M. E., Leuzinger-Bohleber, M., Rüger, B., Bahrke, U., Negele, A., Haselbacher, A., Fiedler, G., Keller, W., & Hautzinger, M. (2012). Psychoanalytic and cognitive-behavior therapy of chronic depression: Study protocol for a randomized controlled trial. *Trials*, *13*(1), 117. https://doi.org/10.1186/1745-6215-13-117

Bleichmar, H. (2010). Rethinking pathological mourning: Multiple types and therapeutic approaches. *The Psychoanalytic Quarterly*, *79*(1), 71–94. https://doi.org/10.1002/j.2167-4086.2010.tb00440.x

Brown, S., Rittenbach, K., Cheung, S., McKean, G., MacMaster, F. P., & Clement, F. (2019). Current and common definitions of treatment-resistant depression: Findings from a systematic review and qualitative interviews. *The Canadian Journal of Psychiatry*, *64*(6), 380–387. https://doi.org/10.1177/0706743719828965

Cuijpers, P., Noma, H., Karyotaki, E., Vinkers, C. H., Cipriani, A., & Furukawa, T. A. (2020). A network meta-analysis of the effects of psychotherapies, pharmacotherapies and their combination in the treatment of adult depression. *World Psychiatry*, *19*(1), 92–107. https://doi.org/10.1002/wps.20701

Cuijpers, P., Quero, S., Noma, H., Ciharova, M., Miguel, C., Karyotaki, E., Cipriani, A., Cristea, I. A., & Furukawa, T. A. (2021). Psychotherapies for depression: A network meta-analysis covering efficacy, acceptability and long-term outcomes of all main treatment types. *World Psychiatry*, *20*(2), 283–293. https://doi.org/10.1002/wps.20860

Fletcher, T. D. (2010). 'QuantPsyc' Package: Quantitative Psychology Tools (R package version 1.5). https://www.rdocumentation.org/packages/QuantPsyc/versions/1.5/topics/QuantPsyc-package

Fonagy, P., Rost, F., Carlyle, J., McPherson, S., Thomas, R., Pasco Fearon, R. M., Goldberg, D., & Taylor, D. (2015). Pragmatic randomized controlled trial of long-term psychoanalytic psychotherapy for treatment-resistant depression: The Tavistock Adult Depression Study (TADS). *World Psychiatry*, *14*(3), 312–321. https://doi.org/10.1002/wps.20267

Grande, T., Dilg, R., Jakobsen, T., Keller, W., Krawietz, B., Langer, M., Oberbracht, C., Stehle, S., Stennes, M., & Rudolf, G. (2009). Structural change as a predictor of long-term follow-up outcome. *Psychotherapy Research*, *19*(3), 344–357. https://doi.org/10.1080/10503300902914147

Grande, T., Rudolf, G., Oberbracht, C., & Jakobsen, T. (2001). Therapeutische Veränderungen jenseits der Symptomatik: Wirkungen stationärer Psychotherapie im Licht der Heidelberger Umstrukturierungsskala Umstrukturierungsskala [Therapeutic changes beyond the symptoms—Effects of inpatient treatment according to the Heidelberg Structural Change Scale]. *Zeitschrift für Psychosomatische Medizin und Psychotherapie*, *47*(3), 213–233. https://doi.org/10.13109/zptm.2001.47.3.213

Hajek, A., Kretzler, B., & König, H.-H. (2020). Personality, healthcare use and costs—A systematic review. *Healthcare (Basel, Switzerland)*, *8*(3), 17. https://doi.org/10.3390/healthcare8030329

Halekoh, U., & Højsgaard, S. (2014). A Kenward-Roger approximation and parametric bootstrap methods for tests in linear mixed models—The R package pbkrtest. *Journal of Statistical Software*, *59*(9), 1–32. https://doi.org/10.18637/jss.v059.i09

Hautzinger, M. (2013). *Cognitive behavior therapy of depression* (7th ed.). Beltz Edition

Hautzinger, M., Keller, F., & Kühner, C. (2006). *BDI-II Beck-Depressions-Inventar [Beck-Depression-Inventory]*. Harcourt Test Services.

Heerlein, K., Perugi, G., Otte, C., Frodl, T., Degraeve, G., Hagedoorn, W., Oliveira-Maia, A. J., Perez Sola, V., Rathod, S., Rosso, G., Sierra, P., Malynn, S., Morrens, J., Verrijcken, C., Gonzalez, B., & Young, A. H. (2021). Real-world evidence from a European cohort study of patients with treatment resistant depression: Treatment patterns and clinical outcomes. *Journal of Affective Disorders*, *290*, 334–344. https://doi.org/10.1016/j.jad.2021.03.073

Hilsenroth, M. J., Blagys, M. D., Ackerman, S. J., Bonge, D. R., & Blais, M. A. (2005). Measuring psychodynamic-interpersonal and cognitive-behavioral techniques: Development of the comparative psychotherapy process scale. *Psychotherapy: Theory, Research, Practice, Training*, *42*(3), 340–356. https://doi.org/10.1037/0033-3204.42.3.340

Hopwood, C. J., Good, E. W., & Morey, L. C. (2018). Validity of the DSM–5 levels of personality functioning scale–self report. *Journal of Personality Assessment*, *100*(6), 650–659. https://doi.org/10.1080/00223891.2017.1420660

Huber, D., Zimmermann, J., & Klug, G. (2017). Change in personality functioning during psychotherapy for depression predicts long-term outcome. *Psychoanalytic Psychology*, *34*(4), 434–445. https://doi.org/10.1037/pap0000129

Kernberg, O. F. (1984). *Object relations theory and clinical psychoanalysis*. Jason Aronson.

Kernberg, O. F. (1988). Psychic structure and structural change: An ego psychology-object relations theory viewpoint. *Journal of the American Psychoanalytic Association*, *36*, 315–337.

Knekt, P., Lindfors, O., Laaksonen, M. A., Renlund, C., Haaramo, P., Härkänen, T., Virtala, E., & Helsinki Psychotherapy Study Group. (2011). Quasi-experimental study on the effectiveness of psychoanalysis, long-term and short-term psychotherapy on psychiatric symptoms, work ability and functional ccity during a 5-year follow-up. *Journal of Affective Disorders*, *132*(1–2), 37–47. https://doi.org/10.1016/j.jad.2011.01.014

Lane, R. D., Ryan, L., Nadel, L., & Greenberg, L. (2015). Memory reconsolidation, emotional arousal, and the process of change in psychotherapy: New insights from brain science. *The Behavioral and Brain Sciences*, *38*, e1. https://doi.org/10.1017/S0140525X14000041

Leuzinger-Bohleber, M. (2015). Working with severely traumatized, chronically depressed analysands. *The International Journal of Psychoanalysis*, *96*(3), 611–636. https://doi.org/10.1111/1745-8315.12238

Leuzinger-Bohleber, M., Bahrke, U., & Negele, A. (2013). *Chronische depression: Verstehen, behandeln, erforschen [Understanding, treating, and researching chronic depression]*. Vandenhoeck & Ruprecht.

Leuzinger-Bohleber, M., Beutel, M. E., Fischmann, T., & Beutel, M. E. (2022). *Chronische depression: Analytische Langzeitpsychotherapie [Chronic depression: Analytic longterm psychotherapy]*. Hogrefe Verlag. https://doi.org/10.1026/03142-000

Leuzinger-Bohleber, M., Grabhorn, A., & Bahrke, U. (Eds.) (2020). *Was nur erzählt und nicht gemessen werden kann: Einblicke in psychoanalytische Langzeitbehandlungen chronischer Depressionen [What can only be told but not measured: Insights into Psychoanalytic Long-Term Treatments of Chronic Depression] (Originalausgabe)*. Psychosozial-Verlag.

Leuzinger-Bohleber, M., Hautzinger, M., Fiedler, G., Keller, W., Bahrke, U., Kallenbach, L., Kaufhold, J., Ernst, M., Negele, A., Schoett, M., Küchenhoff, H., Günther, F., Rüger, B., & Beutel, M. (2019). Outcome of psychoanalytic and cognitive-behavioural long-term therapy with chronically depressed patients: A controlled trial with preferential and randomized allocation. *The Canadian Journal of Psychiatry*, *64*(1), 47–58. https://doi.org/10.1177/0706743718780340

Leuzinger-Bohleber, M., Kaufhold, J., Kallenbach, L., Negele, A., Ernst, M., Keller, W., Fiedler, G., Hautzinger, M., Bahrke, U., & Beutel, M. (2019). How to measure sustained psychic transformations in long-term treatments of chronically depressed patients: Symptomatic and structural changes in the LAC Depression Study of the outcome of cognitive-behavioural and psychoanalytic long-term treatments. *The International Journal of Psychoanalysis*, *100*(1), 99–127. https://doi.org/10.1080/00207578.2018.1533377

Li, G., Zhang, L., DiBernardo, A., Wang, G., Sheehan, J. J., Lee, K., Reutfors, J., & Zhang, Q. (2020). A retrospective analysis to estimate the healthcare resource utilization and cost associated with treatment-resistant depression in commercially insured US patients. *PLoS ONE*, *15*(9), e0238843. https://doi.org/10.1371/journal.pone.0238843

Lindfors, O., Knekt, P., Lehtonen, J., Virtala, E., Maljanen, T., & Härkänen, T. (2019). Effectiveness of psychoanalysis and long-term psychodynamic psychotherapy on personality and social functioning 10 years after start of treatment. *Psychiatry Research*, *272*, 774–783. https://doi.org/10.1016/j.psychres.2018.12.082

Maj, M., Stein, D. J., Parker, G., Zimmerman, M., Fava, G. A., Hert, M. D., Demyttenaere, K., McIntyre, R. S., Widiger, T., & Wittchen, H.-U. (2020). The clinical characterization of the adult patient with depression aimed at personalization of management. *World Psychiatry: Official Journal of the World Psychiatric Association (WPA)*, *19*(3), 269–293. https://doi.org/10.1002/wps.20771

OPD Task Force. (Ed.) (2008). *Operationalized psychodynamic diagnosis OPD-2* (1st ed.). Hogrefe & Huber Publishers.

Rudolf, G., Grande, T., & Oberbracht, C. (2000). Die Heidelberger Umstrukturierungsskala [The Heidelberg scale of structural change]. *Psychotherapeut*, *45*(4), 237–246. https://doi.org/10.1007/PL00006720

Rudolf, G., Jakobsen, T., Keller, W., Krawietz, B., Langer, M., Oberbracht, C., Stehle, S., Stennes, M., & Grande, T. (2012). Umstrukturierung als Ergebnisparadigma der psychodynamischen Psychotherapie - Ergebnisse aus der Praxisstudie Analytische Langzeittherapie [Restructuring as an Outcome Paradigm of Psychodynamic Psychotherapy- Results from the Long-Term Analytic Therapy Practice Study]. *Zeitschrift Für Psychsomatische Medizin Und Psychotherapie*, *58*(1), 55–56.

Rush, A. J., Trivedi, M. H., Ibrahim, H. M., Carmody, T. J., Arnow, B., Klein, D. N., Markowitz, J. C., Ninan, P. T., Kornstein, S., Manber, R., Thase, M. E., Kocsis, J. H., & Keller, M. B. (2003). The 16-item quick inventory of depressive symptomatology (QIDS), clinician rating (QIDS-C), and self-report (QIDS-SR): A psychometric evaluation in patients with chronic major depression. *Biological Psychiatry*, *54*(5), 573–583. https://doi.org/10.1016/S0006-3223(02)01866-8

Schramm, E., Klein, D. N., Elsaesser, M., Furukawa, T. A., & Domschke, K. (2020). Review of dysthymia and persistent depressive disorder:

History, correlates, and clinical implications. *The Lancet Psychiatry*, *7*(9), 801–812. https://doi.org/10.1016/S2215-0366(20)30099-7

Steinert, C., Hofmann, M., Kruse, J., & Leichsenring, F. (2014). Relapse rates after psychotherapy for depression—Stable long-term effects? A meta-analysis. *Journal of Affective Disorders*, *168*, 107–118. https://doi.org/10.1016/j.jad.2014.06.043

Stiles, W. B., Elliott, R., Llewelyn, S. P., Firth-cozens, J. A., Margison, F. R., Shapiro, D. A., & Hardy, G. (1990). Assimilation of problematic experiences by clients in psychotherapy. *Psychotherapy: Research, Practice, Training*, *27*(3), 411–420. https://doi.org/10.1037/0033-3204.27.3.411

Taylor, D. (2015). Treatment manuals and the advancement of psychoanalytic knowledge: The treatment manual of the Tavistock Adult Depression Study. *The International Journal of Psychoanalysis*, *96*(3), 845–875. https://doi.org/10.1111/1745-8315.12360

Wallerstein, R. S. (1988). Assessment of structural change in psychoanalytic therapy and research. *Journal of the American Psychoanalytic Association*, *36*, 241–261.

WHO. (2022). *ICD-11 clinical descriptions and diagnostic guidelines for mental and behavioural disorders*. World Health Organisation. gcp.network/en/private/icd-11-guidelines/disorders

Zeileis, A., & Grothendieck, G. (2005). zoo: S3 infrastructure for regular and irregular time series. *Journal of Statistical Software*, *14*(6), 1–27. https://doi.org/10.18637/jss.v014.i06

Zimmermann, J. (2014). Assessing the DSM-5 level of personality functioning and the OPD level of structural integration amounts to the same thing. *European Society for the Study of Personality Disorders Newsletter*, *3*(1), 9–10.

Zimmermann, J., Ehrenthal, J. C., Cierpka, M., Schauenburg, H., Doering, S., & Benecke, C. (2012). Assessing the level of structural integration using operationalized psychodynamic diagnosis (OPD): Implications for DSM–5. *Journal of Personality Assessment*, *94*(5), 522–532. https://doi.org/10.1080/00223891.2012.700664

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