Effectiveness of Psychotherapy in Personality Disorders Not Otherwise Specified: A Comparison of Different Treatment Modalities

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Objective: Although personality disorder not otherwise specified (PDNOS) is highly prevalent and associated with a high burden of disease, only a few treatment studies in this patient group exist. This study is the first to investigate the effectiveness of different modalities of psychotherapy in patients with PDNOS, i.e., short-term (up to 6 months) and long-term (more than 6 months) outpatient, day hospital, and inpatient psychotherapy.

Method: A total of 205 patients with PDNOS were assigned to one of six treatment modalities. Effectiveness was assessed over 60 months after baseline. The primary outcome measure was symptom severity, and the secondary outcome measures included psychosocial functioning and quality of life. The study design was quasi-experimental, and the multiple propensity score was used to control for initial differences between treatment groups.

Results: All treatment modalities showed positive outcomes, especially in terms of improvements of symptom severity and social role functioning. At 12-month follow-up, after adjustment for initial differences between the treatment groups, short-term outpatient psychotherapy and short-term inpatient psychotherapy showed most improvement and generally outperformed the other modalities concerning symptom severity. At 60 months after baseline, effectiveness remained but observed differences between modalities mostly diminished.

Conclusion: Patients with PDNOS benefit from psychotherapy both at short-term and long-term follow-up. Short-term outpatient psychotherapy and short-term inpatient psychotherapy seem to be superior to the other treatment modalities at 12-month follow-up. At 60-month follow-up, treatments showed mostly comparable effectiveness. Copyright © 2014 John Wiley & Sons, Ltd.
According to the DSM-IV-TR, the category of personality disorder (PD) not otherwise specified (PDNOS) can be used for ‘disorders of personality functioning (…) that do not meet criteria for any one personality disorder (…), but that together cause clinically significant distress or impairment in one or more important areas of functioning’ (American Psychiatric Association, 2000). Numerous studies showed that PDNOS is one of the most prevalent mental disorders in clinical practice (Coid, Yang, Tyer, Roberts, & Ullrich, 2006; Verheul, Bartak, & Widiger, 2007; Wilberg, Hummelen, Pedersen, & Karterud, 2008; Zimmerman & Coryell, 1989; Zimmerman, Rothchild, & Chelminski, 2005). A meta-analysis on the prevalence and use of PDNOS diagnoses showed that 3–6% of the general population and 8–13% of clinical samples met the diagnostic criteria for a PDNOS diagnosis (Verheul & Widiger, 2004). The relative prevalence, defined as the prevalence of PDNOS divided by the overall axis II percentage without PDNOS, was estimated at 21–49% (Verheul & Widiger, 2004). As is the case for patients with specific PD, the burden of disease of patients with PDNOS is high (Soeteman, Hakkaart-van Roijen, Verheul, & Busschbach, 2008; Soeteman, Verheul, & Busschbach, 2008; Verheul & Widiger, 2004). In terms of quality of life, PDNOS patients report a quality-of-life score on the EuroQol (EQ-5D) of between 0.42 (negativistic PD) and 0.62 (mixed PD). Such EQ-5D scores represent a range comparable to patients with haemodialysis, rheumatic disease, lung cancer, Parkinson’s disease or diabetes type II (Soeteman, Verheul, et al., 2008). In terms of the economic burden, a PDNOS diagnosis is associated with high costs for society (Soeteman, Hakkaart-van Roijen, et al., 2008). As is the case for PD patients in general, patients with PDNOS show a wide range of problems, such as substance use or self-mutilation (Johnson et al., 2005; Verheul et al., 2007; Wilberg et al., 2008). In terms of severity of symptoms, personality problems and relational problems, patients with PDNOS seem to fall within an intermediate position between patients without PD and patients meeting the full criteria for 1 of the 10 formal PDs in DSM-IV-TR (Verheul et al., 2007; Wilberg et al., 2008). However, patients with a diagnosis of PDNOS in addition to a formal PD diagnosis have typically higher symptom severity, more personality problems and more relational problems than those with a formal PD diagnosis alone (Verheul et al., 2007).

Since 2000, researchers and clinicians have become increasingly interested in psychotherapy for PD patients. This has resulted in numerous studies and the development of new evidence-based therapies. There is now sufficient evidence that psychotherapy is the treatment of choice in PDs (Karterud et al., 2003; Leichsenring & Leibing, 2003). This is reflected in treatment guidelines (e.g., Landelijke Stuurgroep Richtlijnontwikkeling in de GGZ, 2008; National Institute for Health and Clinical Excellence, 2009a, 2009b). Specialized psychotherapeutic treatments have proven to be effective for PD in general (Gabbard, 2000; Leichsenring & Leibing, 2003), to be more effective than being on a waiting list or general psychiatric outpatient care and to be associated with faster recovery rates compared with natural recovery (Bateman & Fonagy, 2008; Perry, Banon, & Ianni, 1999; Petersen et al., 2008). Approximately 75 years ago, Rosenzweig suggested that common factors were responsible for the effectiveness of psychotherapies making them equally effective in outcome. This effect was later called the ‘dodo-bird effect’ by Luborsky et al. (e.g., Wampold et al., 1997). Indeed, comparative trials have not yet provided conclusive evidence for the superiority of one theoretical orientation over another. Furthermore, the available studies suggest that other treatment characteristics, such as dosage (Bartak, Soeteman, Verheul, & Busschbach, 2007) or level of destabilization (van Manen, Horn, Stijnen, Busschbach, & Verheul), might be more important determinants of (cost) effectiveness than theoretical orientation per se (e.g., Leichsenring & Leibing, 2003).

According to our knowledge, there are no explicit treatment studies on PDNOS patient groups, despite their high prevalence and high burden of disease. Treatment studies on PD populations typically focus on formal PDs and do not report results for the PDNOS group separately (e.g., Gabbard et al., 2000; Winston et al., 1994; Zanarini, 2009; Zanarini, Frankenburg, Reich, & Fitzmaurice, 2010). We found one general PD treatment study reporting results separately for PDNOS patients following short-term and long-term day hospital treatment.

**Key Practitioner Messages:**

- The effectiveness of different modalities of psychotherapy in patients with PDNOS (i.e., short-term vs long-term; outpatient versus day hospital versus inpatient psychotherapy) has not yet been compared.
- Different modalities of psychotherapy are effective for patients with PDNOS, and positive effects remain after 5 years.
- In patients with PDNOS short-term (less than 6 months) outpatient psychotherapy and short-term inpatient psychotherapy seem to be superior to the four other treatment modalities at 12-month follow-up.
- At 60-month follow-up, treatments showed mostly comparable effectiveness.

**Keywords:** Personality Disorders, Personality Disorder Not Otherwise Specified, Long-term Treatment Effectiveness, Psychotherapy, Mixed Personality Disorder.
The paper reported on the results obtained from the Study on Cost-Effectiveness of Personality Disorder Treatment (SCEPTRE), which is a large multi-centre study in the Netherlands (trial register ISRCTN: 73817429).

**METHODS**

**Study Population and Design**

During a 3-year period (2003–2006), 1379 patients completed the intake procedure in six mental health centres in the Netherlands and were selected for treatment (De Viersprong Netherlands Institute for Personality Disorders, Halsteren; GGZ WNB, Bergen op Zoom and Roosendaal; Centre of Psychotherapy Pro Persona, Lun tener; Altrecht, Utrecht; Zaans Medical Centre, Zaandam; Centre of Psychotherapy Arkin, Amsterdam). The six centres offer outpatient, day hospital and/or inpatient psychotherapeutic treatments, tailored to PD patients. Patients had to go through an extensive intake procedure prior to treatment allocation. The intake procedure consisted of one or two assessment sessions with an intake clinician, a semi-structured interview for PD diagnosis and questionnaires (Assessments), after which allocation to treatment was discussed by an intake team and afterwards with the patient (van Manen et al., 2011). Of the 1379 patients who participated in the intake procedure, 959 (70%) were enrolled in the SCEPTRE study (Figure 1). To avoid overlap with earlier studies on the effectiveness of different treatment modalities in PD patients (Bartak et al., 2010; Bartak, Andrea, Spreeuwenberg, Ziegler, et al., 2011), selecting PDNOS patients and extending the follow up period to 60 months. We expected a similar pattern of results compared with cluster C PDs as the problem severity in both groups is similar (Verheul et al., 2007).

**Aim of the Study**

The present study aimed to extend the evidence of the effectiveness of psychotherapy to patients with PDNOS. Effectiveness of six treatment modalities in patients with PDNOS, i.e., short-term (up to 6 months) and long-term (more than 6 months) outpatient, day hospital and inpatient psychotherapy, was investigated over 60 months after baseline.

The two questions we addressed in this study were:

- Did PDNOS patients profit from psychotherapy in terms of severity of symptoms, relational functioning and quality of life, and did the results remain stable over time?
- Were there differences in effectiveness between different treatment modalities in PDNOS patients, and did these differences remain stable over time?
had 14.9 ± 10.1 years of postgraduate clinical experience. All treatment centres offered treatments with varying theoretical orientations, such as a psychodynamic orientation (27% of all given treatments), a cognitive–behavioural orientation (21% of all given treatments) or an integrative orientation (combining different theoretical frameworks, 52% of all given treatments).

The study focused on different treatment modalities in terms of setting and duration. The duration of treatments was defined as ‘short-term’ for treatments, which lasted up to 6 months, and ‘long-term’ for treatments, which lasted more than 6 months. The settings were defined as outpatient psychotherapy (i.e., individual or group psychotherapy sessions, up to two sessions per week), day hospital
psychotherapy (i.e., at least one morning/afternoon per week, various forms of psychotherapeutic and psychosocial treatments, where patients sleep at home) and inpatient psychotherapy (i.e., patients stay at the institutions 5 days a week, various forms of psychotherapeutic and psychosocial treatments, where patients sleep in the institutions). Day hospital and inpatient programmes typically consisted of group psychotherapy as a core element, mostly in combination with one or more non-verbal or expressive group therapies, individual psychotherapy, milieu therapy, coaching for social problems, discussions about household tasks and living together, community meetings and/or pharmacological treatment. Before the start of the treatment, psychotherapists were asked to register the intended treatment in terms of setting and duration. When the treatment was finished, therapists were asked once more to register the setting and duration of the actual treatment received. Since this study conformed to the intention-to-treat principle, the treatments described are the intended treatments and are not necessarily the actual treatments received.

The six treatment modality groups in this study had the following characteristics (intended treatments, mean (SD)):

1. short-term outpatient psychotherapy (N = 17): sessions per week: 0.84 (0.26), duration: 4.82 (1.27) months, 57% group therapy, 43% individual therapy;
2. long-term outpatient psychotherapy (N = 47): sessions per week: 0.88 (0.46), duration: 16.34 (7.22) months, 32% group therapy, 68% individual therapy;
3. short-term day hospital psychotherapy (N = 24): days per week: 3.06 (1.31), duration: 5.75 (0.74) months;
4. long-term day hospital psychotherapy (N = 33): days per week: 3.02 (1.39), duration: 12.30 (2.56) months;
5. short-term inpatient psychotherapy (N = 52): days per week: 5.00 (0.00), duration: 4.06 (1.43) months; and
6. long-term inpatient psychotherapy (N = 32): days per week: 4.94 (0.21), duration: 11.22 (3.12) months.

**Assessments**

An extensive standard assessment battery of instruments was administered to the patients before treatment assignment.

**Diagnosis of PD**

Personality disorders were assessed using the Dutch version of the Structured Interview for DSM-IV Personality (De Jong, Derks, van Oel, & Rinne, 1996; Pfohl, Blum, & Zimmerman, 1997). This interview covers the 10 formal DSM-IV axis II diagnoses, as well as the two appendix diagnoses, i.e., depressive and negativistic PD. Furthermore, the self-defeating PD was assessed (American Psychiatric Association, 1987). Interviewers were thoroughly trained masters-level psychologists who received monthly booster sessions to avoid drift from the interviewer guidelines. Inter-rater reliability was evaluated in 25 videotaped interviews that were rated by three observer-raters. Percentage of agreement between observer-raters ranged from 84% (avoidant PD) to 100% (schizoid) (median 95%). To estimate the intraclass correlation coefficients (ICC(2,1)) for the sum of DSM-IV PD traits present (i.e., scores ‘2’ or ‘3’), 25 videotaped interviews were rated by three (out of 25) random observers, which resulted in 75 observations. With analysis of variance, the between patients, the between observers and the residual variance components were calculated. The ICCs were calculated as the between patients variance divided by the total variance. The ICC ranged from 0.31 (schizotypal PD) through 0.88 (depressive PD) (median 0.66). A diagnosis of PDNOS can be obtained in two ways: (1) meeting the diagnostic criteria for an appendix PD (DSM-IV-TR depressive or negativistic PD, DSM-III-R self-defeating PD) but not for any specific cluster PD, or (2) meeting the criteria for a mixed PD: meeting 10 or more diagnostic criteria of various PDs but not for any specific PD. The definition of mixed PD in the current study is in agreement with some earlier studies (Pagan, Oltmanns, Whitmore, & Turkheimer, 2005; Wilberg et al., 2008) but not with other studies in which a cut-off of only five criteria was suggested (Coccaro, Nayar, & McCloskey, 2012; Verheul et al., 2007). Since in clinical practice mostly 10 or more criteria have to be met, we chose to use this definition.

**Outcome Measures**

The primary outcome measure was symptom severity. This was measured using the Dutch version of the Brief Symptom Inventory (De Beurs & Zitman, 2006; Derogatis & Melisaratos, 1983), a validated self-report scale derived from the revised Symptom Checklist-90 (Arrindell & Ettema, 2003; Derogatis, 1983). In this study, we used the mean score of the 53 items of the Brief Symptom Inventory, i.e., the Global Severity Index (GSI), ranging from zero to four. Cronbach’s Alpha was α = 0.96. The secondary outcome measures included psychosocial functioning and quality of life. Psychosocial functioning was measured using two subscales of the Outcome Questionnaire-45 (OQ-45), i.e., Interpersonal Relations and Social Role (Lambert et al., 2004). Cronbach’s Alpha was α = 0.74 for Interpersonal Relations and α = 0.58 for Social Role. Furthermore, health-related quality of life was measured using the EQ-5D (EuroQolGroup, 1995). A recent study in the Netherlands elicited valuations for the EQ-5D, resulting in the Dutch EQ-5D value set, which is used to calculate utilities for EQ-5D health states (Lamers, Stalmeier, McDonnell, Krabbe, & van Busschbach, 2005). Cronbach’s was α = 0.50. All outcome measures were assessed at baseline and several follow-up points. Three treatment centres conducted their assessments at baseline, at end of treatment, at 6 and 12 months after the end of
treatment and at 36 and 60 months after baseline. Three other centres conducted their assessments at baseline and at 12, 24, 36 and 60 months after baseline. Different assessment points were used due to logistic reasons.

**Additional Baseline Measures**

The assessment battery at baseline included three supplementary instruments to assess variables that were used as potential confounders for the propensity score (PS) estimation. First, the Dutch version of the Dimensional Assessment of Personality Pathology-Basic Questionnaire was used to measure type and degree of personality pathology in four domains, i.e., emotional dysregulation, dissocial behaviour, inhibition and compulsivity (Livesley, 2002; van Kampen, 2002). Second, to measure patients’ motivation for treatment, the two scales of the Motivation for Treatment Questionnaire were used: Need for Help and Readiness to Change (van Beek & Verheul, 2008). Third, the core components of personality pathology were measured using the Severity Indices of Personality Problems-118, a 118-item questionnaire aimed to measure five core domains of personality pathology, i.e., Self Control, Identity Integration, Responsibility, Relational Functioning and Social Concordance (Verheul et al., 2008).

**Data Completeness**

Follow-up response was high, thereby enhancing the robustness of the multi-level analyses. We included all patients with at least one follow-up measure as multi-level models make optimal use of incomplete repeated measures data and are robust for selective dropout when the dropout is missing at random (Little & Rubin, 1987). Figure 2 illustrates the proportion of patients who provided different numbers of follow-up assessments.

Dropouts (6%) and completers (94%) differed significantly on only one baseline measure of the four assessed outcome variables (OQ-45 Social Role: t(213) = 2.54, p = 0.012). Dropouts had a higher mean score (M = 18.00, SD = 3.36) compared with completers (M = 14.59, SD = 4.75), which implies that they experienced more difficulties adjusting to their social role.

**Statistical Analyses**

We used multilevel modelling to deal with the following: (1) the dependency of the repeated measures within the same subject in time and (2) the longitudinal data with observations unequally spaced in time (Outcome Measures).

First, we examined the uncorrected results on all outcome measures over 60 months after baseline in 12-month intervals. To estimate the uncorrected treatment effects over 60 months after baseline, we used a random intercept and random slope model with time as level I and patient number as level II. In addition to a linear time effect, we postulated knots (or splines) every 6 months, which allowed the estimated course of the dependent variable to bend at these time points. Non-significant knots (p < 0.05) were deleted from the models until a parsimonious model was reached that did not differ significantly from the original saturated model. This resulted in a final best fitting model with the change scores (from baseline) observed.

![Proportion of follow-up assessments](image)
during follow-up for each of the outcome measures as dependent variables and the following independent variables: time, a spline (knot point at 3 years), dummy variables indicating group membership, interaction between time and group membership, and interaction between spline and group membership. Subsequently, we calculated within-group effect sizes (ES, Cohen’s d) using the estimated pooled standard deviations from the models to describe change from baseline over 60 months in each group (Cohen, 1988).

Second, since this is a non-randomized study, the comparisons of the groups had to be corrected for the influence of potential confounders, i.e., initial patient differences between treatment groups that are related to outcome. We included a multiple PS in our analyses to adjust for these differences and avoid bias in effect estimation. The classic PS is defined as the conditional probability of assignment to one of two treatment groups given a set of observed pre-treatment variables (Bartak et al., 2009; Rosenbaum & Rubin, 1983). The PS is designed to reduce selection bias by equating groups on the basis of their pre-treatment variables and to reduce the number of covariates by combining these pre-treatment variables into one PS. By using the PS, the random assignment to one of two treatments is imitated as the PS adjusts for (observed) baseline differences between patients in different treatment groups. After adjustment, the distribution of these pre-treatment variables is similar in the two treatment groups (for an illustration refer to Bartak et al., 2009). The multiple PS is an extension of the classic PS to more than two treatment groups, and its feasibility in mental health research has been illustrated earlier (Spreeuwenberg et al., 2010). To identify relevant confounders, we considered a broad list of social, economic and diagnostic variables carefully selected by both clinicians and researchers, which were based on literature and clinical knowledge (Bartak et al., 2009). Only pre-treatment characteristics significantly related to the studied outcome variables were used to estimate the multiple PSs. A simulation study of Brookhart et al. (2006) showed that the addition of variables that were related to treatment but were not related to the outcome led to an increase of the variance of the estimated treatment effect and removed only a small amount of bias. The multiple PSs were achieved by a multinomial regression analysis, with group membership as the dependent variable and pre-treatment variables significantly related to the outcome as independent variables (Appendix 1). The PS method allows the possibility of visualization and judgment of the overlap in PS distributions (and thus the overlap in relevant variables) between treatment groups. The overlap on the PS distributions showed that these were sufficient for the comparison of the six treatment groups. The overlap on the PS distributions showed that these were sufficient for the comparison of the six treatment groups. Furthermore, significance testing on variables related to the outcome showed that by correcting for the multiple PS initial significant differences between treatment groups disappeared. In earlier investigations in patients with cluster A, B and C PDs, this visual judgment led to a less firm interpretation of the results (cluster A) or to the exclusion of treatment groups (cluster C), as the PS distributions were too far apart (Bartak et al., 2010; Bartak, Andrea, Spreeuwenberg, Thunnissen, et al., 2011; Bartak, Andrea, Spreeuwenberg, Ziegler, et al., 2011).

After the analyses of the uncorrected results with the first multi-level model, a second multilevel model was used to compare change in outcome variables across treatment groups. This model included the multiple PSs to correct for initial patient differences. Dependent variables were the change scores (from baseline) observed during follow-up for each of the outcome measures. Independent variables were time, a spline (knot point at 3 years), dummy variables indicating group membership, the multiple PSs, interaction between time and group membership, interaction between spline and group membership, and the mutual interactions of the multiple PSs. This model was used to estimate differences in change scores over 60 months after baseline in pairwise comparisons of the six treatment groups. Unstandardized coefficients (b) were used to describe the size of the effect.

The analyses of outcomes were based on the intention-to-treat principle. The analyses were performed using IBM SPSS Statistics 20.0 for data preparation and the estimation of the multiple PSs and SAS 9.2 for multilevel modeling. The study protocol was approved by the Medical Ethics Committee of the Erasmus University Medical Centre in Rotterdam, the Netherlands.

RESULTS

Sample

The sample consisted of 205 patients with a diagnosis of PDNOS and at least one follow-up measurement (Figure 1). The mean age of the sample was 35.1 (SD = 10.3) years, and 72% of the sample were female. Educational level was high (European Qualifications Framework [EQF] ≥ 6) for 33%, medium (EQF 3 to 5) for 43% and low (EQF ≤ 2) for 23% (van der Sanden, Smit, & Dashorst, 2012). About one quarter (24%) of the patients were married or were in steady relationships, and about one quarter (27%) of the sample lived together with children. Two-thirds (66%) of the sample was employed or was studying (Table 1). One hundred and thirty-four patients (65%) met the criteria for a mixed PD only, 34 patients (17%) met the criteria for an appendix diagnosis only, and 37 patients (18%) met the criteria for both a mixed and an appendix PD. On average, 14.6 (6–29) diagnostic criteria were fulfilled. For patients with a mixed PD, traits from one or more of the appendix diagnoses were most common (M = 5.4, SD = 2.4), followed by traits from cluster C (M = 4.8, SD = 1.9) and traits from cluster B (M = 3.2, SD = 2.5). The least number of traits came from cluster A
(M = 1.5, SD = 1.8). Of the patients with an appendix diagnosis, the majority (64 patients, 90%) had a depressive PD, five patients (7%) had a self-defeating PD and five patients (7%) had a negativistic PD.1 A significant difference was found on one of the assessed outcome scales at baseline (OQ Interpersonal Relations) between patients with a mixed PD only (M = 18.38, SD = 5.79), patients with an appendix PD only (M = 17.70, SD = 6.16) and patients with both a mixed PD and an appendix PD (M = 21.44, SD = 5.87; F(2,202) = 4.68, p = 0.01). Patients with both diagnoses reported a more dysfunctional interpersonal functioning compared with patients with a mixed PD (p = 0.006) or appendix PD only (p = 0.008).

1Because patients could have more than one appendix diagnosis, the sum of the prevalence is higher than 100%.
**Treatment Adherence**

Forty-five patients (22%) changed their intended treatment group: Of these, 38 patients stayed in the same setting but for a longer (N = 16) or shorter (N = 22) period than planned. Three patients changed their treatment setting and their treatment lengths, and four patients changed their treatment setting only. Of these, five patients followed a less intensive treatment and two patients a more intensive treatment (in terms of setting). When the intended treatment was stopped earlier than planned, this was mostly carried out in agreement with the treatment staff (N = 13 [48%]), or because of the patient dropping out (N = 13 [48%]). One patient was forced to leave earlier by the treatment staff (4%).

**Effectiveness Results**

**Uncorrected Outcomes**

Sixty months after baseline, within-group ESs of the uncorrected scores of symptom severity (GSI) ranged from 0.91 (large effect, short-term outpatient) to 1.42 (very large effect, short-term day hospital; Table 2). A positive significant change was found for all treatment modalities. Refer to Figure 3 for the course of the GSI scores.

Improvements also appeared in terms of psychosocial functioning and quality of life. ESs for these outcome measures were somewhat smaller compared with symptom severity, but a positive significant change was evident in most measures at 60 months (except for OQ-45 Interpersonal Relations in short-term day hospital, and EQ-5D in short-term outpatient and short-term day hospital). ESs ranged from 0.30 (small effect, OQ-45 Interpersonal Relations, short-term day hospital) to 1.46 (very large effect, OQ-45 Interpersonal Relations, long-term inpatient) (Table 3).

**Corrected Outcomes**

We concluded that the overlap in the PSs was sufficient for all between-group comparisons, indicating that the PS was capable to correct for initial baseline differences (Methods). After correction for all relevant pre-treatment differences with the multiple PS, no significant differences were found between treatment modalities concerning either of the outcome measures at 60-month follow-up (Table 4). However, analyses on the intervening time points on the primary outcome measure did show significant differences up to 36-month follow-up. Strongest differences were found at 12-month follow-up (less at 24 months), mainly because of the low gains of long-term inpatient psychotherapy. Significant differences were found in favour of short-term outpatient psychotherapy compared with long-term inpatient psychotherapy (b = −0.57, p = 0.01), long-term outpatient psychotherapy compared with long-term inpatient psychotherapy (b = −0.34, p = 0.05), short-
term inpatient psychotherapy compared with short-term day hospital \((b = 0.33, p = 0.02)\) and finally short-term inpatient psychotherapy compared with long-term inpatient psychotherapy \((b = -0.60, p = 0.00)\). Over time, these differences diminished, and from 48-month follow-up onwards, all significant differences had disappeared. Concerning the secondary outcome measures, no significant differences at 60 months after baseline were found.

The results of this study were based on the classification of treatments on the basis of intention to treat (Methods). When completion of the intended treatment was introduced as a covariate, no significant differences were found between patients who followed their intended treatment and the ones who did not on the primary outcome measure (GSI). There was a trend that the initial (statistical insignificant) differences between these two
groups became even smaller over time ($b = 0.17$, $p = 0.07$ at 12-month follow-up, $b = -0.01$, $p = 0.95$ at 60-month follow-up). In the secondary outcome measures, the same pattern and insignificant differences were found.

DISCUSSION

This is the first study to compare the effectiveness of various treatment modalities in patients with PDNOS. Patients in all treatment modalities showed positive outcomes at short-term and long-term follow-ups, especially in terms of improvements of symptom severity and social role functioning. This study provides evidence that PDNOS patients profit from psychotherapy and that accomplished changes are maintained over time. Strongest differences were found at 12-month follow-up. In terms of symptom severity, short-term outpatient, long-term outpatient and short-term inpatient psychotherapy were found to be superior to long-term inpatient psychotherapy. Short-term inpatient psychotherapy was found to be superior to short-term day hospital treatment. At 60-month follow-up, the observed differences between modalities were diminished. The higher ESs of the short-term outpatient and short-term inpatient psychotherapies decreased, whereas the lower ESs of the long-term outpatient and long-term inpatient psychotherapies increased. Concerning day hospital treatment, we found a deviant course over time, i.e., an increase in ES of the short-term modality, and a stable effectiveness over time for the long-term modality.

Embedding in Previous Studies

To the best of our knowledge, the study of Karterud et al. (2003) on day hospital treatment in PD patients is the only study reporting treatment results separately for PDNOS patients. The admission GSI score of PDNOS patients in their study ($M = 1.4$, $SD = 0.6$) was comparable with the baseline GSI score in our day hospital patients (short-term day hospital $M = 1.37$, $SD = 0.57$, long-term day hospital $M = 1.53$, $SD = 0.62$). However, mean GSI scores at 1-year follow-up were lower in the current sample (short-term day hospital $M = 0.75$, $SD = 0.59$/long-term day hospital $M = 0.83$, $SD = 0.60$), and ESs were therefore higher than in the sample of Karterud et al. ($M = 1.1$, $SD = 0.7$). It is
difficult to explain why these differences emerged, given the same GSI score at baseline and no other variables to compare the samples on.

Within the same SCEPTRE project, three studies were published on the effectiveness of different modalities of psychotherapy in patients of the DSM-IV-TR cluster A, B and C PDs, respectively. These studies revealed invariably positive effects at 12 or 18 months after baseline (long-term follow-up is not available yet [Bartak et al., 2010; Bartak, Andrea, Spreeuwenberg, Thunnissen, et al., 2011, and Bartak, Andrea, Spreeuwenberg, Ziegler, et al., 2011]). A comparison with these populations showed that PDNOS patients reported the healthiest scores on all outcome measures at baseline, thus reporting the least psychological distress, a better psychosocial functioning and a higher quality of life, which is in accordance with earlier studies (Verheul et al., 2007; Wilberg et al., 2008). Given the different follow-up time points (12 and 18 months) and treatment groups (three, five and six groups), it was possible to compare the effectiveness between PDNOS and cluster A, B and C patient groups in a general way only. This comparison demonstrated that concerning symptom severity, PDNOS patients in outpatient and inpatient psychotherapies showed higher ESs compared with cluster A, B and C PD patients. PDNOS patients in day hospital psychotherapies, however, seemed to benefit more compared with cluster A and C patients, but benefitted less compared with cluster B patients. Furthermore, three long-term studies on the effectiveness of psychotherapeutical treatments lasting 1 to 3 years in PDs showed results comparable with the current study. First, in the study of Chiesa and Fonagy (2003) and Chiesa, Fonagy, and Holmes (2006), a steady drop in the GSI score and therefore a steady increase in effectiveness were found in a group of PD patients of which more than half met the criteria for a PDNOS diagnosis. Treatments consisted of an inpatient and a step-down programme (consisting of inpatient treatment, which was followed by outpatient treatment) and results were presented at 3-year and 6-year follow-ups. Second, in studies on mainly BPD patients, Giesen-Bloo et al. (2006) showed stable differences for outpatient schema-focused therapy versus transference-focused therapy at 3-year follow-up, and finally, Bateman and Fonagy (2008) showed stable effectiveness for day hospital mentalization-based treatment versus treatment as usual (general psychiatric services) at 8-year follow-up. These studies support the notion that PDNOS patients have a similar development in psychotherapy compared with other PDs.

Possible Explanations of Findings

Generally, we found higher but decreasing effects in short-term outpatient and short-term inpatient psychotherapies and lower but increasing effects in long-term outpatient and long-term inpatient psychotherapies. This led to insignificant differences between treatment groups at long-term follow-up, which is in line with earlier effectiveness studies on psychotherapeutical treatments and supports the conclusion that differences in effectiveness of active treatments in PD are negligible, also called ‘equivalence effect’ or ‘dodo-bird effect’ (Wampold et al., 1997; Budge et al., 2013). Five possible explanations for the results found are set out hereafter.

First, the axis-I study of Knekt et al. (2008) on the effectiveness of short-term (i.e., 5 to 6 months) and long-term (i.e., up to 3 years) psychodynamic psychotherapy for patients with mood and anxiety disorders showed similar results. Within the first year after the start of the treatment, the short-term psychotherapy group showed better results than the long-term group in terms of psychiatric symptoms, whereas at 3-year follow-up, the long-term group even exceeded the short-term group in terms of treatment success. Knekt et al. explained this difference as being due to the difference in duration of treatment, which influences the orientation and aim of therapy. In short-term therapies, an active and problem-based orientation is applied, which patients can make use of, and profit from, in a short period. On the other hand, long-term therapies aim for ‘more global changes by affecting the patient’s long-term vulnerability to stressors’, requiring more time to achieve good results.

Second, explanations for the superiority of the short-term psychotherapies in the short-term are that these typically have a highly structured format, have a consistently applied theoretic orientation and are focused with respect to treatment targets right from the start of treatment. Such aspects are typically less pronounced in long-term treatments. Both the level of structure and the consistent application of a comprehensible coherent theoretical orientation can be considered key components of effective psychotherapies (Bateman & Fonagy, 2000).

Third, high pressure in the therapy might accelerate the therapy effect. However, high pressure is difficult to imagine bearable in long-term treatment. Short-term treatments are therefore in a better position to use high pressure, facilitating changes to come more quickly.

Fourth, since this PDNOS population is characterized by slightly milder symptoms compared with patients with formal PD diagnoses, potential iatrogenic effects could occur in long-term hospitalization, which could account for the poorer short-term effects for the long-term inpatient psychotherapy (Fonagy & Bateman, 2006).

Fifth, evidence suggested that the best outcome is usually apparent a few weeks or months after the termination of treatment, followed by some relapse and a consolidation of results (Perry et al., 1999). This would give the short-term treatments an advantage on short-term follow-up as these treatments had already finished and could explain part of the results found.
Strengths and Limitations

The most important strength is the inclusion of a large number of patients as well as the rather equal division of patients over various treatment modalities. Another strength is its representativeness and therefore high external validity due to the naturalistic design of the study, a minimal set of exclusion criteria and a long-term follow-up period of 5 years.

This study has also several limitations. First, the study is limited by the fact that patients were not randomized. However, comparisons between markedly different treatment modalities or dosages, as were made in this study, are not feasible in a randomized study. Most patients would probably refuse to be randomly assigned to a condition, which consists of either 3-months outpatient psychotherapy or 12-months inpatient psychotherapy (an example of the greatest contrast). However, this limitation is mitigated by the fact that we controlled as rigorously as possible for initial patient differences as potential confounders by means of the multiple PS. It is important to acknowledge that this score corrects for observed differences only, and it cannot correct for unobserved differences. Therefore, it is possible that the treatment groups differed on aspects that we did not measure and therefore could not control. However, we controlled for a substantial number of social and diagnostic variables, which minimizes the possibility that important variables were overlooked. Second, another limitation is the difference of loss to follow-up, which was higher in the long-term psychotherapies compared with the short-term psychotherapies. This concern is somewhat mitigated since we found no significant differences in the outcome measures at baseline between patients with and without follow-up, with one exception, and the general low loss to follow-up. Third, this study focused on treatment dosage and did not take into account other treatment attributes such as the potential impact of theoretical orientation and medication use or patient attributes, such as axis I comorbidity. However, we came across two complications to investigate the impact of theoretical orientation. First, more than 50% of the given treatments were considered integrative treatments (e.g., schema-focused therapy, dialectical behaviour therapy and mentalization-based treatment). Second, as theoretical orientation was associated with setting and duration, a different research design would have been necessary to explore the effect of theoretical orientations in addition to treatment modalities. Furthermore, studies for PD typically show that theoretical orientations only account for small differences in effectiveness (Bartak et al., 2007). Nevertheless, we consider this study to be a starting point for further research. Future studies are recommended to take these other treatment and patient attributes into account. Fourth, the absence of a control condition without psychotherapy or a placebo condition makes it less straightforward to conclude that psychotherapy works in patients with PDNOS. Part of the effectiveness could also be due to natural recovery or regression towards the mean. Nevertheless, in the review of Perry et al. (1999), it was concluded that psychotherapeutic treatments may lead to a sevenfold increase in speed of recovery in comparison with natural recovery. Fifth, a limitation is that effectiveness is determined by self-report. From the present study, we know that patients report less complaints and a better functioning, but we do not have information whether patients still meet criteria for a PD diagnosis after 5 years. Sixth and finally, sites overlapped only partially in terms of the (equal) availability of the six modalities. Disentangling the site effect would reduce statistical power. The reason why we did not do so is that we could not think of any valid reason why, given the specialist expertise of the six sites involved in this study, sites would have a clinically important and interpretable impact on treatment effectiveness.

Clinical and Scientific Implications

As this is the first large-scale treatment study in patients with PDNOS, it is difficult to translate the results into definitive conclusions and strong recommendations for clinical practice. It might be that short-term psychotherapeutic treatments are preferred for this patient population since patients in these treatment modalities improved quickly. Furthermore, since all treatment modalities seemed to be equally effective in the long run, it might be preferable to make treatment choices based on pragmatic reasons. Therefore, a treatment with the least impact on everyday life and—for economic reasons—the least costly treatment could be the way forward.

Our results have several implications for future research. First, a cost-effectiveness study is essential to inform policy makers in a budget-constrained health care system. The cheapest treatment is not necessarily the most cost-effective treatment. Patients who have followed an intensive—and therefore expensive—but effective treatment might function better and consume less additional care after treatment compared with patients who followed less intensive and less effective treatments. In other words, intensive and expensive treatments might provide more long-term benefits thereby ultimately proving superior to cheaper and less intensive therapies. Therefore, a state-of-the-art cost-effectiveness analysis should be performed, as has already been carried out for cluster B and cluster C PDs (Soeteman et al., 2010; Soeteman et al., 2011). Since the costs of short-term treatments are generally lower compared with their longer counterparts (especially compared to long-term inpatient psychotherapy) and they show a rather high effectiveness, it might be expected that short-term outpatient and inpatient psychotherapies in PDNOS are more cost-effective than longer-term alternatives.
Second, subgroup analyses directed at ‘what works for whom’ could give more valuable information for clinical practice about which treatments work best for which category of patients instead for which category of diagnoses. This is even more important in this patient group since various definitions of PDNOS are used in clinical practice and across studies, limiting the comparability and generalizability of study findings (Coccaro et al., 2012; Verheul & Widiger, 2004; Wilberg et al., 2008). Third, more research about the effect of dosage would be valuable. In the current study, dosage was defined as a product of setting in three and duration in two stratifications. The study of a further division in smaller units of time could give more useful information for clinical practice.

CONCLUSIONS

In conclusion, on the basis of long-term follow-up, all treatment modalities were shown to be approximately

APPENDIX A

POTENTIAL CONFOUNDERS TESTED FOR PROPENSITY SCORE

<table>
<thead>
<tr>
<th>Potential confounder</th>
<th>GSI</th>
<th>OQ-45 social role</th>
<th>OQ-45 interpersonal relations</th>
<th>EQ-5D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td>x</td>
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<tr>
<td>Alcohol abuse</td>
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<tr>
<td>Care for children</td>
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<tr>
<td>Civil status</td>
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<tr>
<td>DAPP-BQ compulsivity</td>
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<tr>
<td>DAPP-BQ dissocial behaviour</td>
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<td>x</td>
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<tr>
<td>DAPP-BQ emotional dysregulation</td>
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<td>x</td>
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<tr>
<td>DAPP-BQ inhibition</td>
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<tr>
<td>Drug use</td>
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<tr>
<td>Duration of problems</td>
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<tr>
<td>Level of education</td>
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<td>x</td>
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<tr>
<td>EQ-5D</td>
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<tr>
<td>GSI</td>
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<tr>
<td>Living situation</td>
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<td>x</td>
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<tr>
<td>MTQ-8 need for help</td>
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<tr>
<td>MTQ-8 readiness to change</td>
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<tr>
<td>OQ-45 interpersonal relations</td>
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<tr>
<td>OQ-45 social role</td>
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<tr>
<td>OQ-45 symptom distress</td>
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<td>Previous inpatient treatment</td>
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<td>x</td>
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<td>Previous medical treatment</td>
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<tr>
<td>Previous outpatient treatment</td>
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<tr>
<td>Sex</td>
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<tr>
<td>SIDP-IV appendix depressive PD</td>
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<td>SIDP-IV appendix negativistic PD</td>
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<td>SIDP-IV appendix self-defeating PD</td>
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<td>SIDP-IV dimensional score cluster A PD</td>
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<td>SIDP-IV dimensional score cluster B PD</td>
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<td>SIDP-IV dimensional score cluster C PD</td>
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<tr>
<td>SIDP-IV dimensional score PD Total</td>
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<tr>
<td>SIDP-IV PD mixed</td>
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<tr>
<td>SIPP identity integration</td>
<td></td>
<td>x</td>
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<tr>
<td>SIPP relational functioning</td>
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<td>x</td>
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<td>x</td>
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<tr>
<td>SIPP responsibility</td>
<td></td>
<td>x</td>
<td></td>
<td>x</td>
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<tr>
<td>SIPP self-control</td>
<td></td>
<td>x</td>
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<td>x</td>
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<tr>
<td>SIPP social concordance</td>
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<tr>
<td>Working situation</td>
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</tbody>
</table>

PD, personality disorder; DAPP-BQ, Dimensional Assessment of Personality Pathology-Basic Questionnaire; EQ-5D, EuroQol-5D; GSI, Global Severity Index; MTQ-8, Motivation for Treatment Questionnaire; OQ-45, Outcome Questionnaire-45; SIDP-IV, Structured Interview for DSM-IV Personality; SIPP, Severity Indices of Personality Problems-118.

x: p < 0.05, variable used for propensity score estimation for the concerned outcome measure.
equally effective treatments in a PDNOS population. However, short-term outpatient and short-term inpatient psychotherapy, limited to a duration of 6 months, displayed higher ESs on short-term follow-up. This study provides the first evidence for the benefit of different treatment modalities for one of the most prevalent mental disorders in clinical practice: PDNOS. Further state-of-the-art cost-effectiveness studies will inform us about the most cost-effective treatments.

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REFERENCES


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