The outcomes of psychotherapy in mixed features personality disorders: a systematic review

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Abstract

Mixed features personality disorders (PDs) are highly prevalent and associated with significant burden of disease. Despite that, it has been an overlooked diagnostic category with respect to clinical research. This study aims to review empirical evidence about psychotherapy delivery available for these patients. We present a systematic review of clinical trials investigating the outcomes of psychotherapeutic interventions in adults with a primary diagnosis of mixed features PDs. Data were obtained from Medline/PubMed, Embase and PsycINFO. Seven studies met inclusion criteria; in one of them the whole sample was of this diagnostic group; two studies analysed psychotherapeutic intervention outcomes in this population, among other types of PDs, yet drawing specific conclusions on mixed features PDs patients; remaining studies addressed patient samples with different PDs types, mixed features included, where specific findings in this group of patients were not described – nonetheless, they included representative numbers of subjects with the diagnosis of interest. Available studies suggest that mixed features personality pathology per se does not seem to be an impediment to benefit from psychotherapeutic treatment, and Improvement in different areas of life is possible for patients undergoing psychotherapy. The extant literature is marked by multiple challenges and inconsistencies across studies.

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Introduction

Psychotherapy is the treatment of choice for personality disorders (PDs). This can be concluded from clinical guidelines, meta-analyses, and systematic or critical literature reviews. Other treatments, such as pharmacological interventions, have received less empirical support. According to the DSM-IV-TR, the category of Personality Disorder Not Otherwise Specified (PDNOS) can be used for “disorders of personality functioning that do not meet criteria for any specific personality disorder (…), the presence of features of more than one specific personality disorder that do not meet the full criteria for any one personality disorder (mixed personality), but that together cause clinically significant distress or impairment in one or more important areas of functioning”. Recently, with the DSM-5, this category does not appear under this heading. The category of Other Specified Personality Disorder applies to similar presentations but is used in situations in which the clinician chooses to communicate the specific reason that the presentation does not meet the criteria for any specific personality disorder (…) by recording Other Specified Personality Disorder followed by the specific reason (e.g., “mixed personality features”).

Some of the structured diagnostic interviews have included directions for assigning a PDNOS diagnosis mixed type. In different approaches, it should be applied when the subject is one criterion below the diagnostic threshold for 2 or more PDs; it requires the presence of at least 10 criteria from the specific PDs or it only requires that the subject meets traits from more than one specific PD, in addition to the general PD criteria. On the other hand, Verheul et al. reported that a cut-off of 5 criteria yielded an additional group of PDNOS patients with a similar level of functional impairment as groups defined according to cut-offs of 10 or 15 PD criteria. The assessment methods tend to produce different PDNOS prevalence rates.

Numerous studies suggest that PDNOS is one of the most prevalent mental disorders in clinical practice. 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. The relative prevalence, defined as the prevalence of PDNOS divided by the overall axis II percentage without PDNOS, was estimated at 21%-49%. As is the case for patients with specific PD, the burden of disease of patients with PDNOS is high, and, in terms of quality of life, patients report a quality-of-life score on the EuroQol (EQ-5D) comparable to patients with haemodialysis, rheumatic disease, lung cancer, Parkinson’s disease or diabetes type II. The diagnosis is associated with high costs for society.

In a general population study, Johnson et al. found that adolescents and young adults in the general population diagnosed with PDNOS may be as likely as those with Cluster A, B, or C PDs to have axis I psychopathology and to have behavioural, educational, or interpersonal problems that are not attributable to co-occurring psychiatric disorders. In contrast, the multicenter study of Verheul et al. found that PDNOS took an intermediate position between cluster A, B, or C PDs and no PD, regarding severity of personality pathology, symptoms, and functional impairment. Another clinical study by Karterud et al. also found that PDNOS was associated with less severe psychopathology and better treatment response compared to patients with specific PDs. Moreover, a few case reports of patients with a PDNOS diagnosis have been published.

Mixed features PDs have been an overlooked diagnostic category with respect to clinical research. Treatment studies typically focus on formal PDs and do not report results for these groups separately even when they are included in trials. According to our knowledge, there are very few treatment studies on mixed features PD patient groups, despite their high prevalence and high burden of disease, reasons why we took an interest in the subject.

Psychotherapeutic treatments can be delivered in various formats, settings, modalities, and dosages. This study aims to review the level of empirical evidence for different formats and settings that are available for psychotherapy delivery in mixed features personality disorders.
Methods
This review was performed according to the PRISMA guidelines\(^{15\_16}\), thus providing a comprehensive framework which objectively assesses indicators of quality and risk of biases of included studies.

All original studies investigating the outcomes of psychotherapeutic interventions in adults (age between 18 and 65 years) with a primary diagnosis of mixed features personality disorders were eligible for this systematic review. Further criteria adopted were: (1) publication date in the last decade, between January 2007 and June 2017, (2) empirical study, and (3) written in English, Portuguese or Spanish language. Additionally, studies were excluded from review if they were: (1) single-case report, (2) review articles, (3) repeated study population, or (4) too small sample size (less than one-third of the total sample studied in cases where specific findings in mixed features PD are not described).

As this review focused on efficacy and effectiveness of interventions, naturalistic/non-controlled studies were included.

Studies were identified by searching relevant papers via PubMed/Medline (http://www.ncbi.nlm.nih.gov/pubmed), PsycINFO and Embase using the following keywords in combination: "personality disorders"; "psychological treatment"; "psychotherapy". Finally, reference lists of retrieved studies were hand searched to identify any additional relevant studies.

After performing the initial literature searches, each study title and abstract was screened for eligibility by the first author. Full texts of all potentially relevant studies were subsequently retrieved and further examined for eligibility. The PRISMA flow diagram (Figure 1) provides more detailed information regarding the selection process of studies. Information from the included studies was then analysed and recorded in an electronic spreadsheet designed by the first author. Different types of data were extracted from each study including: (a) country in which the data were collected, (b) participants’ characteristics (including diagnosis, age and gender), (c) number of subjects, (d) type of intervention (including modality, setting and duration of treatment) (e) type of outcome measure, (f) main results, and (g) study limitations.

ROBINS-I and Cochrane Collaboration’s tool for assessing risk of bias were adopted to evaluate the risk of bias in individual studies\(^{15\_16}\). The following risk of biases were analysed: (1) bias due to confounding, (2) bias in selection of participants, (3) bias in classification of interventions, (4) bias due to deviations from intended interventions, (5) bias due to missing data, (6) bias in measurement of outcomes, and (7) bias in selection of reported results. The assessments were completed by the first and third authors independently.

Results
Seven articles investigating the outcomes of psychotherapeutic interventions in adults with primary diagnosis of mixed features PDs were included in this review. One of them specifically focused on this diagnostic group, which corresponds to the study’s whole sample\(^1\). Two other studies analysed the effectiveness of psychotherapeutic interventions in mixed features PDs, among other PDs types, yet drawing concrete conclusions for this specific patient subgroup\(^{17\_18}\). The remaining four studies\(^{19\_22}\) were concerned with intervention outcomes in samples of patients with different PD types, mixed features personality disorders included, where specific findings about this patient group were not described. Despite that, they included a representative number of subjects with the diagnosis of interest (at least one-third of the total sample studied) and, henceforth, its results were of interest to this review.

Four studies were from The Netherlands, two were from Norway, and one from Poland. Reviewed studies included 399 participants with a primary diagnosis of mixed features PD. Considering that six of the studies include varied samples and not only the mentioned diagnosis, known data related to gender distribution and average age are relative to whole samples and not only to this subgroup.

A summary of results is presented in Table 1 and risk of bias in individual studies based on ROBINS-I and Cochrane Collaboration’s tool for assessing risk of bias is presented in Table 2. As shown in this table, deviations from intended interventions was the most frequent bias, with six of seven studies assessed having moderate risk for this type of bias. No bias due to confounding and in selection of reported result were found, although the risk of bias was not always clear.

![Figure 1. PRISMA flow diagram of the study selection process.](image-url)

### Table 1. Effectiveness of psychotherapeutic interventions in adults with primary diagnosis of mixed features personality disorders

<table>
<thead>
<tr>
<th>Study</th>
<th>Country; Study design</th>
<th>Subjects</th>
<th>Type of intervention</th>
<th>Type of outcome measure; Main findings</th>
<th>Study limitations</th>
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<tr>
<td>Horn et al., 2015(^1)</td>
<td>The Netherlands; Multicenter quasi-experimental</td>
<td>PDNOS N = 205 (100% of the sample): PD mixed only (85%); Appendix PD only (17%); PD mixed and appendix PD (18%); Mean age 35.1 years (SD = 10.3) years; 72% female.</td>
<td>Short-term (&lt; 6 months) and long-term (&gt; 6 months) outpatient, day hospital and inpatient psychotherapy Psychodynamic (27%), cognitive-behavioural (21%) or integrative orientation (52%) 60 months follow-up.</td>
<td>Symptom severity; Psychosocial functioning; Quality of life 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. Short-term outpatient psychotherapy and short-term inpatient psychotherapy seem to be superior at 12-month follow-up. At 60-month after baseline, effectiveness remained but observed differences between modalities mostly diminished.</td>
<td>Not a randomized controlled trial. Difference of loss to follow-up. Did not take into account other treatment attributes – potential impact of theoretical orientation and medication use, or patient attributes – axis I comorbidity. Effectiveness is determined by self-report, without information if whether patients still meet criteria for a PD diagnosis after 5 years. Sires overlapped only partially in terms of (equal) availability of the six modalities.</td>
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<td>Horn et al., 2015&lt;sup&gt;15&lt;/sup&gt;</td>
<td>The Netherlands; Matched-control study</td>
<td>PDNOS N = 61 (42% of the STIP-TA patients and 49% of the OP patients) Mean age 39.4 (SD 9.8) years in STIP-TA, and 39.3 (SD 10.2) in OP patients 70% female.</td>
<td>Short-term (3-month) ingpatient Psychotherapy based on transactional analysis (STIP-TA) and other psychotherapies (OP) varying widely in terms of setting, duration, and theoretical orientation 36 months follow-up.</td>
<td>General psychiatric symptomatology; Psychosocial functioning; Quality of life At 36 months, 68% of STIP-TA patients were symptomatically recovered compared to 48% of OP patients. STIP-TA outperformed OP in terms of improvements in general psychiatric symptomatology and quality of life Superiority of STIP-TA was most pronounced at 12-month follow-up, but remained intact over the course of the 3-year follow-up. A very promising and effective treatment option in mainly PDNOS patients.</td>
<td>Not a randomized controlled trial. Only self-report instruments used as outcome measures. Information about the treatment fidelity and adherence was not collected. The interpretation of the results is limited by the variation of treatment modalities in the OP condition.</td>
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<td>Kvarstein et al., 2017&lt;sup&gt;20&lt;/sup&gt;</td>
<td>Norway; Naturalistic study</td>
<td>PDNOS N = 18 (17.4% of the sample) Mean age 38.5 (SD 10) years 60% female.</td>
<td>Outpatient Psychodynamic groups, mean treatment duration 1.5 (SD 0.9) years 3-year follow-up.</td>
<td>Symptom distress; Interpersonal problems; Occupational functioning; Psychiatric health service use. PDNOS benefits across all outcomes. The most favourable outcomes were found for patients with PDNOS. PDNOS patients may be well managed within outpatient group therapy.</td>
<td>Naturalistic designs limits inferences on outcome as an effect of the treatment. Dual roles of clinicians and researchers may also limit validity of patient reported ratings. Diagnostic procedures held a high standard, but reliability was not investigated.</td>
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<td>Chakhssi et al., 2015&lt;sup&gt;19&lt;/sup&gt;</td>
<td>The Netherlands; Nonrandomized exploratory study</td>
<td>PDNOS N = 38 (48.3% of the ACT patients and 42.9% of the CBT-TAU patients) Mean age 32.88 (SD 10.13) years in ACT patients, and 33.26 (SD 9.63) in CBT-TAU patients 82.7% female.</td>
<td>Specialized day hospital setting for patients with personality disorders that did not respond to previous treatments 26-week group-based acceptance and commitment therapy (ACT). Same duration group-based treatment-as-usual based on cognitive behaviour therapy (CBT-TAU) Both supplemented by arts therapy, including creative and drama therapy, and rehabilitation counselling.</td>
<td>Change in personality pathology; General psychological functioning; Experimental avoidance; Coping skills; Positive outcomes; Quality of life Group-based interventions for treatment-resistant patients with personality disorders led to significant improvements in personality pathology, general psychological functioning, coping skills and quality of life, regardless of whether participants received ACT or CBT-TAU. In group analysis, no main effect of therapy condition was observed on the outcome measures. Assessment of change on an individual level showed that a significantly higher percentage of participants receiving ACT improved on personality pathology.</td>
<td>Patients were not randomized. Treatment fidelity was not assessed. The unequal sample size across groups may have affect the results. The patients were not only provided with ACT or CBT-TAU but also with other treatments, and the effect of these treatments on the outcomes remains unknown. Medication use during the study was not measured. No independent data was available on the type and quality of previous outpatient treatment interventions. Do not report results for the PDNOS group separately.</td>
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<td>Schaap et al., 2016&lt;sup&gt;6&lt;/sup&gt;</td>
<td>The Netherlands; Naturalistic prospective study</td>
<td>PDNOS N = 24 (42.9% of treatment completers and 26.1% of dropouts) Mean age 26.94 (SD 6.45) years 72.3% female.</td>
<td>12 months group schema therapy (ST) ingpatient for patients with PDNOS who did not respond to previous psychotherapy Specific ST techniques, psychodrama, art, movement and music therapies, social services, pharmacotherapy, education about medication 6 months follow-up.</td>
<td>Maladaptive schemas; Schema modes; Maladaptive coping styles; Mental well-being; Psychological distress after treatment Over participants improved significantly on all outcome measures from pretreatment to posttreatment, and these improvements were maintained at follow-up. Experienced parenting styles was the one area that showed no improvement. These findings are comparable with treatment results for patients without such a nonresponsive treatment history.</td>
<td>Lack of a control-group. Treatment fidelity was not assessed. The patients were not only provided with ST, but also with additional therapies. Diagnosis were based on the clinical judgement and not by structured interviews. The relationship between the YSQ (Young schema questionnaire) and SMI (Short schema mode inventory) was large. Do not report results for the PDNOS group separately.</td>
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The results could be somehow applicable to this subgroup. Eighteen full-text articles assessed for eligibility were excluded due to small (up to 21% participants) sample size, making its results extrapolation inadequate.

Horn et al. specifically focuses on PDNOS patients, a group that corresponded to the total studied sample. It was the first large-scale treatment study in patients with PDNOS, having investigated the effectiveness of different psychotherapy modalities in patients with PDNOS, i.e., short-term and long-term outpatient, day hospital and inpatient psychotherapy. The treatments offered included varied theoretical orientations, such as 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). 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. Short-term outpatient
psychotherapy and short-term inpatient psychotherapy seem to be superior at 12-month follow-up, and at 60-month after baseline, effectiveness remained but observed differences between modalities mostly diminished.

In fact, cognitive-behavioural and psychodynamic approaches have been the object of the most extensive research in patients with PDs. Cognitive behaviour therapy (CBT) is well suited to address the varied and often long-standing problems of patients with PDs for several reasons. From a cognitive-behavioural perspective, PDs are maintained by a combination of maladaptive beliefs about self and others, contextual/environmental factors that reinforce problematic behaviour and/or undermine effective behaviour, and skill deficits that preclude adaptive responding. CBT incorporates a wide range of techniques to modify these factors, including cognitive restructuring, behaviour modification, exposure, psychoeducation, and skills training. In addition, CBT for PDs emphasizes the importance of a supportive, collaborative, and well-defined therapeutic relationship, which enhances the patient’s willingness to make changes and serves as a potent source of contingency. In sum, several aspects of CBT’s conceptual framework and its technical flexibility make it appropriate to address the pervasive and diffuse impairment commonly observed among patients with PDs.

Psychoanalytic psychotherapy, also referred to as psychodynamic psychotherapy, is a type of therapy that incorporates concepts such as the unconscious, the use of defense mechanisms, and the role of an individual’s past via their social processes such as attachment and early childhood experience. The approach provides useful tools for expanding, consolidating, and enriching one’s own life and one’s relationships with others. Contemporary psychodynamic therapy involves many Freudian concepts, such as the existence of the unconscious, yet it has also moved away from a purely Freudian focus on drive, ego, and conflict. Contemporary psychodynamic theory includes a rich body of theory, and now incorporates various aspects of many 20th-century psychoanalytic theories including object relations, self-psychology, interpersonal/relational theory, attachment theory, trauma theory, and intersubjective theory.

In another study, Horn et al. compared 3-month short-term inpatient psychotherapy based on transactional analysis (STIP-TA) with other psychotherapies (OP) up to 36-month follow-up. At 36 months, 68% of STIP-TA patients were symptomatically recovered compared to 48% of OP patients. This therapy outperformed OP in terms of improvements in general psychiatric symptomatology and quality of life. That superiority was most pronounced at 12-month follow-up but remained intact over the course of the 3-year follow-up. The authors concluded that it could be a very promising and effective treatment option in mainly PDNOS patients, which corresponded to 42% of the STIP-TA patients and 49% of the OP patients. Kvarstein et al. also conclude that PDNOS patients may be well managed within outpatient group therapy, in a trial involving outpatient psychodynamic groups with mean treatment duration 1.5 years and 3-year follow-up evaluating symptom distress, interpersonal problems, occupational functioning, and psychiatric health service use. The most favourable outcomes were found exactly for patients with PDNOS.

The remaining four studies included for reviews do not report results for the mixed features PDs patients group separately. Both Chakhssi et al. and Schaap et al. studied PDNOS patients, among others, that did not respond to previous treatments. The first compared day hospital group-based acceptance and commitment therapy (ACT) and group-based treatment-as-usual based on cognitive behaviour therapy (CBT-TAU), led to significant improvements in personality pathology, general psychological functioning, coping skills and quality of life in both groups. The second author and colleagues evaluated the outcomes of an inpatient group schema therapy (ST) in maladaptive schemas, schema modes, maladaptive coping styles, mental well-being, and psychological distress after treatment. Overall, participants improved significantly on all outcome measures from pretreatment to posttreatment, and these improvements were maintained at 6-month follow-up. Experienced parenting styles was the one area that had no improvement.

Cyranka et al. evaluated intensive short-term group psychotherapy in a day ward with elements of individual therapy, integrating the elements of psychodynamic, cognitive and behavioural theories, in mixed features PDs patients, which demonstrated positive changes in personality functioning which were classified as severe or moderate pathology. Hoglend et al. carried out the only randomized controlled trial included in this review, comparing 1 year of dynamic psychotherapy with low to moderate use of transference interpretations and dynamic psychotherapy without this component in a sample including PDNOS patients. After therapy with transference interpretation, patients improved significantly more in core psychopathology and interpersonal functioning, the drop-out rate was reduced to zero, and use of health services was reduced to 50%, compared to therapy without this ingredient. Three years after treatment termination, 73% no longer met diagnostic criteria for any PD in the transformation group, compared to 44% in the comparison group.

Researchers have highlighted the diversity of treatments as an obstacle to identifying efficacious treatments. In addition, some authors emphasize that instead of conducting further comparisons of different treatments, research should be concentrated on the active ingredients of treatments.

Various independent psychotherapies demonstrated efficacy for these patients. However, several factors limit our ability to draw strong conclusions from available research. Overall, the limited number of studies included, with only one randomized controlled trial, is inadequate substantial. Although certainly lacking the rigor of RCTs, uncontrolled studies can provide clinically important information about mechanisms of change and moderators of treatment outcome. In addition to their use for driving therapy and hypotheses for testing in future RCTs, uncontrolled studies can be useful for uncovering essential qualities of effective interventions and the effectiveness of psychotherapy as it is delivered in the field. Furthermore, occurring of other disorders, particularly within Axis I conditions, the possibility that maturational processes or life events may be responsible for part of the changes measured, and the use of medications along with the psychotherapy, further hampers existing research. An additional concern is substantial heterogeneity among studies included in the review. Besides, differences with respect to therapy format, the length, patient samples, gender distribution, and length of follow-up periods are very variable.

Subgroup analysis 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 diagnosis. 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.

Despite previously mentioned limitations, findings from recent studies make an important contribution to our understanding of the role of psychotherapy in mixed features PDs.

**Conclusions**

Despite the toll of mixed features PDs on healthcare systems, there are vast gaps in the treatment literature on these disorders, a frequently overlooked mental health problem, for which there are no established psychosocial treatments.

Overall, there are some psychotherapeutic approaches with different modalities and durations offered to these individuals, and the research findings we reviewed suggest that there is hope for significant and meaningful changes after psychotherapy in individuals with PDNOS.

The most important conclusion is that mixed features personality pathology per se does not seem to be an impediment to benefit from psychotherapy, and improvement in different areas of life is possible for the patients who undergo psychotherapeutic treatment. It would be important to make psychotherapy more accessible for this patient group in order to reach health gains for this vulnerable group of psychiatric patients.
Although promising in many ways, the extant literature is marked by multiple challenges and inconsistencies across studies. Further research on the effectiveness of psychotherapy for mixed features PD patients is undoubtedly needed.

References