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# PROBING THE IMPACT OF PSYCHOANALYTIC THERAPY FOR BIPOLAR DISORDERS: A SCOPING REVIEW

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# **PROBING THE IMPACT OF PSYCHOANALYTIC THERAPY FOR BIPOLAR DISORDERS: A SCOPING REVIEW**

## **ABSTRACT**

No systematic review has been conducted to provide an overview of the effectiveness of psychoanalysis on outcomes for bipolar depression and mania. The present study undertakes a scoping review on the effectiveness of psychoanalysis for bipolar disorder (BD), provides a summary of the evidence base, and identifies issues for future research in this area. A thorough search of journal articles in MEDLINE, PEP-Web, PsycINFO, Scopus, and Web of Science was carried out to obtain available studies of psychoanalytic treatment for BD published 1990-2021. We searched for either quantitative or single-case studies. Twenty-six single case reports from 21 articles and no quantitative studies met a prior inclusion criteria. Qualitative analysis suggests efficacy and cost-effectiveness but thus far there is no scientific evidence in support of psychoanalysis. Although these pilot findings suggest that psychoanalysis may impact symptoms and global functioning in patients with BD, the underlying evidence is poor and should be confirmed by experimental studies.

**KEYWORDS:** psychoanalysis, psychoanalytic psychotherapy, bipolar disorder, effectiveness

## **Probing the impact of psychoanalytic therapy for bipolar disorders: a scoping review**

### **Introduction**

Bipolar disorder (BD) is a lifelong illness characterized by severe and persistent fluctuations in mood state and energy, resulting in psychological distress and behavioral impairment (Carvalho et al., 2020; Grande et al., 2016). Although it can onset in childhood (Youngstrom et al., 2008), it usually begins in adolescence (Eric A Youngstrom et al., 2020) and affects ~1-4% of the world's population (Moreira et al., 2017; Vieta et al., 2018). The illness course is variable but often results in cognitive and functional impairments, increased mortality, and, more generally, reduced quality of life (Carvalho et al., 2020; Grande et al., 2016; Eric A. Youngstrom et al., 2020). Indeed, BD is ranked among the twenty leading causes of disability among all injuries and acute/chronic diseases worldwide (Vos et al., 2015). Furthermore, persons with BD are at high risk of developing chronic medical conditions (De Hert et al., 2011; Stefana et al., 2020) as well as of committing suicide (20/30-fold higher than in the general population) (Malhi et al., 2015; Plans et al., 2019). Identifying the most effective forms of treatment is a global health priority.

At present, pharmacotherapy represents the first-line option (Yatham et al., 2018). However, despite the effectiveness of medications in helping persons with BD in recovering from acute depressive or manic episodes, drugs alone do not enable many of these patients to significantly improve postepisode symptoms, achieve a satisfactory functional recovery, or prevent illness recurrences (Cipriani et al., 2016, 2011, 2009; Correll et al., 2010; Goodwin et al., 2016; Pacchiarotti et al., 2013; Yatham et al., 2018).

Optimal long-term management combines medications with psychosocial interventions, including psychotherapy and lifestyle approaches (Geddes and Miklowitz, 2013). Indeed, there is evidence that psychological interventions are effective for adults with BD (Oud et al., 2016), especially when combined with pharmacotherapy or psychoeducation (Chatterton et al., 2017; Miklowitz et al., 2006), capable of producing behavioral and lifestyle changes crucial for prevention of relapse and positive function (vs. simple symptom reduction) (Frank, 2007; Frank et al., 2014; Miklowitz et al., 2007). Furthermore, it should be noted that although considerable progress has been made in understanding,

managing, and treating BD in recent decades, we are still far from a personalized psychiatric approach to this disorder that allows precisely optimized biological and psychosocial interventions (Grande et al., 2016; Kalin, 2020). The treatment of these patients remains, greatly, a subjective clinical exercise (Carvalho et al., 2020).

Several therapies have growing and positive evidence-bases for effectiveness in terms of improving symptoms, social functioning, and/or risk of relapse, including cognitive-behavioral therapy (Chiang et al., 2017; Ye et al., 2016), psychoeducation (Colom et al., 2003) interpersonal and social rhythm therapy (Lam and Chung, 2021), mindfulness-based and mindfulness-informed interventions (Burgos-Julián et al., 2022; Xuan et al., 2020), functional remediation (Torrent et al., 2013), group therapy (Janis et al., 2021), and also psychodynamic therapies (Abbass et al., 2019; Caldiroli et al., 2020). Psychoanalytic methods are the oldest on this list, but relatively less studied vis bipolar disorder (*masked*). Psychodynamic therapies derived from classical psychoanalysis may be equally effective as other forms of evidence-based psychotherapy for common mental disorders (Steinert et al., 2017), including both unipolar and bipolar (Caldirola et al., 2020) depression. More generally, long-term psychoanalytic psychotherapy has been shown to be useful in improving the long-term outcome of chronic (Leuzinger-Bohleber et al., 2019) and treatment-resistant depression (Fonagy et al., 2015). However, to date, no systematic review has been conducted, focusing specifically on psychoanalytic treatment for BD. Here it should be noted that psychoanalysis and long-term psychoanalytic psychotherapy can be placed on a continuum: according to a large number of theoretical and practicing psychoanalysts, separating them (usually based on extrinsic criteria such as the weekly frequency of sessions or the use of vis-a-vis vs of couch position) is a false problem (Stefana et al., 2022).

Historically, psychoanalysis traces its origins back to the beginning of the twentieth century. It quickly became firmly entrenched in European culture due to Sigmund Freud's success in keeping up with the natural sciences of his time and integrating psychoanalysis with various trends in psychology, biology, physiology, and psychophysics (Makari, 2008). In defining psychoanalysis, Freud (Freud, 1989) distinguished three interrelated levels: a method of investigation of human functioning, a complex of psychological and psychopathological theories, and a method of treatment. Today the psychoanalytic model is unique in contributing a developmental theory (of attachment relationships) strongly supported

by empirical evidence and useful in understanding the relationship between early experience, genetic inheritance, and development of subjectivity as well as psychopathology (Cassidy and Shaver, 2018; Fonagy and Lemma, 2012; Harari and Grant, 2022).

The fundamental principles that guide the psychoanalytic approach are (a) the existence of the unconscious and its central role in mental life, (b) the implications/consequences of the interaction between childhood experiences and genetic factors in shaping the development of the individual, (c) symptoms and behaviors are determined by a complex of biological and unconscious factors, (d) transference as a primary source of understanding the personality characteristics and psychopathology of the patient, (e) countertransference as a ‘technical tool’ potentially able to provide valuable information about what happens in the relationship with the patient, (f) the analysis of the patient’s resistance to therapy, and (g) the facilitation/support of the patient to achieve a sense of authenticity (Gabbard, 2017). The aspects embodied in the principles mentioned above that jointly determine the very essence of psychoanalytic technique are technical neutrality, transference analysis, interpretation, and countertransference analysis. Notably, some of the theoretical and technical features typical of the psychoanalytic approach have been adopted by other modalities, particularly cognitive behavioral therapy (Fonagy and Lemma, 2012). Indeed, some evidence suggests that non-psychodynamic therapies may be effective in part because they utilize techniques (Gabbard, 1995; Kernberg, 2016; Stefana, 2017; Wallerstein, 1990) central to psychoanalytic theory and practice (Fonagy and Lemma, 2012).

The purpose of this study is to critically review available studies on the effectiveness of psychoanalysis / long-term psychoanalytic psychotherapy for BD, provide a summary of the evidence base, and identify issues for future research in this area.

## **Method**

The Cochrane Database of Systematic Reviews and the International Prospective Register of Systematic Reviews (PROSPERO) were searched to ensure that no similar reviews had been completed previously. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses for Scoping Reviews (PRISMA-ScR) (Tricco et al., 2018) statement was followed.

## **Eligibility Criteria**

The following eligibility criteria were applied: (1) published in a peer-reviewed journal; (2) included participants aged 18 years and older; (3) primary diagnosis of bipolar disorder; (4) administration of individual psychoanalysis or psychoanalytic psychotherapy; (5a: quantitative studies) improvement of depressive and manic symptoms, illness recurrence, or global functioning as primary outcomes; (5b: single case reports) information about the improvement of mood symptoms, illness recurrence, or global functioning.

## **Information Sources**

The databases MEDLINE, PsycINFO, Psychoanalytic Electronic Publishing [PEP-Web], Scopus, and Web of Science were searched by title and abstract. The search in PEP-Web used full-text searching because this electronic archive did not allow abstract searching and was limited to those journals not indexed in one of the other databases. Studies were also found through searching reference lists of the full articles screened and reviews of psychotherapy for BDs. The literature search was limited to English-language journal articles published from January 1990 to September 2021.

## **Search Strategy**

The words “psychoanalysis” and “psychoanalytic” were matched with “bipolar” and “manic depress\*”.

## **Study Selection**

Two raters (AS & DD) independently and sequentially reviewed and screened titles and abstracts, and then full-text articles for evidence that the studies met eligibility criteria. Any disagreements were resolved by consensus reached through discussion.

## **Data Collection Process**

A data extraction sheet for single case reports was created and pilot-tested on five randomly selected included studies. One rater extracted the data while another checked it. Disagreements were resolved by consensus.

### **Data Extraction**

The following information was extracted from each single case study. Study characteristics: Authors, year of publication, country; Patient characteristics: age, sex, DSM-5 diagnosis (derived from the patient's clinical history and symptoms as described in the respective article, when the therapist used the term "manic depression"); Treatment characteristics: psychotherapy setting, status, weekly session frequency, duration, and presence/absence of pharmacotherapy.

### **Quality Assessment**

Given the characteristics of psychoanalytic single case reports (Cena et al., 2021; Iwakabe and Gazzola, 2009) and the broader controversy regarding the critical appraisal of qualitative research (Dixon-Woods, 2004), no exclusion criteria based on quality assessment of single case studies were applied.

### **Data Analysis**

The selected clinical case studies were inspected for patients, therapists, and treatment characteristics. The qualitative meta-analysis focused on identifying treatment outcomes regarding the patient's mood symptoms, suicidality, hospitalizations, illness recurrence, or global functioning. In parallel, another analysis determined the elements and dynamics of the therapeutic relationship explicitly mentioned in the text. After these analyses were completed, two independent coders (clinical psychologists and Ph.Ds.) checked the findings by comparing the analyses with the original clinical case reports. Finally, an attempt to contact all the corresponding authors of the included studies was made to check the accuracy of the data analysis results. Seven authors replied to our request.

## **Results**

The initial search retrieved 209 items, with further examination of 7 articles captured via reverse search strategies detailed above (Figure 1). Of these, 21 articles met the full inclusion criteria; all used a single case design. A summary of the characteristics and findings of each included study is presented in the Supplemental online table S1.



### **Sample Characteristics**

A total of 26 single case reports involving adult patients affected by BD and treated with psychoanalysis (from now on called therapy) were found. Most patients were female (69%), aged between 20 and 50 years old at the start of the therapy (31% each decade age range), and met the criteria for a diagnosis of bipolar I disorder (46%). Most of the patients (92%) received psychopharmacological medication during therapy, leaving one patient who did not receive any medication and another where the status of their medication is unknown. See Table 1 for characteristics of the patients.

### **Treatment Characteristics**

Twelve therapies (46%) were still ongoing at the time of the article writing (mean duration: 5.6 years; range: 2-15 years; data based on 9 out of 12 clinical cases), and fourteen (54%) were terminated (mean duration: 4.7 years; range: 0.5-11 years; data based on 12 out of 14 clinical cases). The number of sessions per week ranged from 1 to 6. The interventions offered ranged from the more traditional one (see for instance: Jackson, 1993; Kalita, 2021) to cases where the clinician did not use the free association method to analyze the patient's conflict (Vanheule, 2017), asked the patient to fill in a daily mood chart (e.g., Salzman, 1998), or adopted a more active role in mobilizing family/environmental supports (Deitz, 1995; Salzman, 1998). See Table 1 for treatment characteristics.

### **Treatment Outcomes**

The findings indicate that 11 of 26 (42%) therapies reduced the patients' depressive and/or (hypo)manic symptoms, and 7 of 11 therapies also reported improvement in psychosocial and/or work functioning. Additionally, seven therapies resulted in some improvement in functioning, but no information specifically about mood symptoms was reported. It should be noted that only 2 out of the 14 interrupted / completed therapies did not report any of the improvements mentioned above.

Of 13 patients who had a pretherapy history of psychiatric hospitalization, six had no further hospital admissions once the therapy started, six had reduced the number or length of admissions, one experienced no significant change, and the remaining one had an unclear record of hospitalizations.

Overall, these numbers indicate that about three quarters (77%) of patients with BD that underwent therapy achieve lowering the rate of hospitalizations.

Five studies (19%) have reported an improvement in medication adherence, while four declared that due to therapy, patients required reduced medication doses (12%) or discontinued them with the knowledge of the clinician (4%).

Suicidal thoughts and attempts were reported in seven case reports, four of which claimed that therapy helped patients reduce / control / remove suicidal states. Four studies indicated a reduction in their levels regarding the patients' self-destructive behaviors and attitudes (including drinking, risky sexual behaviors, and impulsivity).

Finally, a greater acceptance of bipolar illness by patients was described in three cases.

Regarding the combined treatment of psychotherapy and pharmacotherapy, about a third of the authors (35%) underline the fundamental role of the medications in treating BD. Few of those explicitly stated that psychoanalysis (and, more generally, every talking cure) was less valuable than drugs. Some noted that psychotherapy alone was not sufficient to address the structural and functional deficits of these patients, especially during the period when they are manic or profoundly depressed.

## **Discussion**

To our knowledge, this is the first study systematically reviewing the effectiveness of psychoanalysis and long-term psychoanalytic psychotherapy in the treatment of people with BD. Although these pilot findings suggest that psychoanalysis may positively impact symptoms and global functioning in patients with BD, the underlying evidence is poor and should be confirmed by experimental studies.

This might seem somewhat not surprising, since one of the leading criticisms of psychoanalysis is that its treatment lacks empirical evidence. However, it should be noted that although there is relatively limited empirical evidence on psychoanalysis for complex mental disorders (Amir and Shefler, 2020; Beutel et al., 2004; de Maat et al., 2013; Fonagy et al., 2015; Huber et al., 2013, 2012; Knekt et al., 2011; Leuzinger-Bohleber et al., 2019; Smit et al., 2012), more several robust research studies have been done on psychoanalytically derived therapies. The latter fall under the broad umbrella of “psychodynamic psychotherapies” (Caro et al., 2019; Kealy and Ogrodniczuk, 2019) and usually are

less intensive and time-limited, have a clearly defined theoretical basis, and are manualized (e.g., transference-focused therapy, and dynamic interpersonal therapy).

In recent decades, numerous systematic reviews and meta-analyses evaluating the efficacy of short- and long-term psychodynamic therapy have found effect sizes as large as those of other main types of psychotherapy, including CBT (Abbass et al., 2006; Keefe et al., 2020; Leichsenring, 2008; Leichsenring et al., 2015, 2004; Leichsenring and Klein, 2014; Leichsenring and Rabung, 2011; Steinert et al., 2017; Zhang et al., 2022). In addition, keeping the focus narrowed to mood disorders, a recent meta-analytic review indicates that psychodynamic therapies can be effective and acceptable in the treatment of adult depression, with no significant differences from other evidence-based therapies (Cuijpers et al., 2021). Similarly, preliminary results of a review on the efficacy of intensive short-term dynamic psychotherapy suggest a positive effect of this approach on depressive symptoms for patients with major depressive disorder (Cuijpers et al., 2021; Fonagy, 2015) or BD (Caldioli et al., 2020). Another meta-analysis supports the effectiveness of psychodynamic therapy in reducing suicide attempts and self-harm in patients with heterogeneous diagnoses (Briggs et al., 2019), while a naturalistic longitudinal study indicates a significant decrease in the use of health care services, as well as a lasting reduction in absenteeism at work and days of psychiatric hospitalization over 3 years after therapy.

Overall, the above-mentioned research findings show that, contrary to widespread belief, the efficacy of the psychodynamic approaches is empirically demonstrated. On the other hand, psychoanalysis is thus far supported by less strong evidence, especially for what concerns the treatment of patients with BD as revealed by this review.

Historically, there have been various obstacles to the implementation of empirical (methodologically rigorous) empirical investigations of psychoanalysis and psychoanalytic psychotherapy, as well as to the participation of patients with BD in both therapy and research studies. These obstacles include, but are not limited to, the following four.

First, the deep skepticism about the utility of empirical research – considered an “unwanted third” in treatment (de Maat et al., 2013) – that characterized many members of the psychoanalytic community (Ortu, 2007; Yakeley et al., 2014), as well as the resistance to manualization of specific therapeutic

approaches (Yakeley et al., 2014). Such skepticism seems to be fueled by the fact that psychoanalytic training is typically provided by private institutes instead of universities, where most of the trainers are clinicians affiliated with private associations and unfamiliar with scientific research methodologies and findings (Dimitrijević, 2018; Gonzalez-Torres et al., 2016). As a result, psychoanalysts usually have little or no knowledge about the epistemological and methodological aspects of empirical psychoanalytic research and its available findings (Stefana et al., 2022).

Second, the difficulties and limitations of RCTs in the investigation of intensive and long-term treatments as psychoanalysis (Leichsenring, 2005), including limited feasibility (de Jonghe et al., 2012), which led to a situation where most psychoanalytic studies are pre/post cohort studies, lacking (randomized) control groups (de Maat et al., 2013). Moreover, many existing psychoanalytic studies are characterized by poor research methodology (Yakeley, 2018; Yakeley et al., 2014), which includes but is not limited to: unclear definition of the treatment method and/or patient sample characteristics, inadequate sample sizes, poor monitoring of adherence to the treatment model, no blinding, and lack of rigorous monitoring of inter-rater reliability.

Third, the availability of psychoanalytic psychotherapy as a treatment offered within the public health systems (where patients with BD are usually treated) of most developed countries is nowadays significantly lower than those of other forms of psychotherapy with a more substantial evidence base (Abbass et al., 2020; Kadish and Smith, 2020; Migone, 2020; Parth et al., 2020; Plakun, 2020; Yakeley, 2020). In addition, when offered within the public health care sector, psychoanalytic psychotherapy is usually time limited and conducted by trainees. At the same time, psychiatrists usually do not consider psychoanalysis as an evidence-based treatment (Paris, 2017; Salkovskis and Wolpert, 2012) nor, consequently, a therapeutic approach suitable for severe mental illnesses like BD. Consequently, recruitment for clinical studies is difficult, as psychoanalytic treatments for these people are fewer and sparse in private practice settings.

Fourth, following from the previous points, it is hard to get research funding from the main funding agencies because the latter tend to give grants for psychological treatments with greater empirical validity. This fuels a vicious circle, with analytic researchers struggling to demonstrate this validity

without being funded to perform such empirical studies (Buchholz and Kächele, 2018; McWilliams, 2013).

It has already been pointed out that the future of psychoanalysis in times of evidence-based practice could depend on proving the treatment outcomes for different patient groups (Leuzinger-Bohleber et al., 2021).

Research efforts should be directed to precisely defining conceptual and technical similarities and differences among different paradigms of psychotherapy and identifying which ones are most appropriate for patients with (a specific type of) BD within a complex context of treatment effectiveness and efficacy, cost-effectiveness, patient preference, and availability of psychological treatments (Yakeley, 2018).

A first step would be to develop manualized psychoanalytic approaches to BD, which consider the clinical and psychodynamic characteristics that accompany the different (i.e., manic or hypomanic, depressed, and euthymic) phases of bipolar illness. This approach could be quickly and easily adopted because psychoanalysis is traditionally less focused on symptoms of specific mental disorders and more inclined to observe and analyze intrapsychic and interpersonal problems and promotes a diagnostic approach that is inferential, contextual, dimensional, and appreciative of the subjective experience of the patient (Lingiardi and McWilliams, 2017; McWilliams, 2011; Stefana and Gamba, 2013) to identify the underlying mental processes. Hence, apart from the traditional treatment outcomes used in RCTs, such as symptom reduction (McIntyre et al., 2020), mood instability (Kessing and Faurholt-Jepsen, 2022), or relapse prevention (Nestsiarovich et al., 2022), researchers willing to prove the efficacy of psychoanalytic interventions for serious conditions such as bipolar disorder might want to power their studies for alternative relevant endpoints such as insight (Dell'Osso et al., 2002), cognitive reserve (Amoretti and Ramos-Quiroga, 2021), emotional and social cognition (Miskowiak and Varo, 2021; Varo et al., 2021), quality of life (Bonnín et al., 2019) or functioning (Vieta and Torrent, 2016).

Single-case studies – which historically have been quintessential for psychoanalytic research, theorization, and teaching (Desmet et al., 2013; Hinshelwood, 2013; Tuckett, 2008) – can play an important role in the study of BD only if the psychoanalytic narrative case study method will give way to quantitative single-case research methods (Kächele et al., 2015) based on audio (or video) recordings

of the whole treatment and supplemented by verbatim transcription and, possibly, computer-assisted and artificial intelligence content analysis.

After single-case, pre-post is the most common study design in psychoanalytic research. However, psychoanalytic pre-post studies often do not meet all methodological quality requirements (de Jonghe et al., 2012), thus future studies need to be improved by adhering to sound methodological principles (Barber, 2009) and using reporting guidelines such as the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statements (von Elm et al., 2007) and the CONSolidated Standards of Reporting Trials (CONSORT) (Schulz et al., 2010).

Cohort studies can provide some evidential value to the extent to which their samples are large enough and the control group is comparable to the treatment group at the start also about important aspects like having or not asked for psychological treatment or having asked for a specific type of treatment instead of others. Randomized control trials (RCTs), which have the strongest scientific evidence within the evidence hierarchy of evidence-based medicine, should be the main objective of future research work in the psychoanalytic field. They can have strong evidential value within the limits of acceptable differences in setting (especially with respect to session frequency).

Lastly, it will be important for future research to explore elements of the therapeutic relationship, such as therapeutic alliance and countertransference (originated in the psychoanalytic literature (Gelso, 2014; Stefana, 2015)) for their influence on primary outcomes.

## **Limitations**

The findings of the present review should be considered in light of several limitations. First, our review was entirely based on single case reports, therefore the underlying evidence-based is overall poor. This was despite the fact that the search criteria would have captured quantitative papers or clinical trials, and it suggests a significant gap in the literature. However, systematically aggregating and synthesizing clinical case studies has clinical and research value when it enables to cover critical areas overlooked in large-scale RCTs (Iwakabe and Gazzola, 2009) – systematic review of case studies can help combat logical errors and biases in recall that otherwise characterize clinician recall and implementation (Caspar, 2007). This is notably the case given that no clinical trials have been conducted to establish

the effectiveness of psychoanalysis for BD, as shown by our systematic literature search. Second, the data reported in the studies differed for levels of abstraction and quality of information on the outcome of the symptomatology. This could be partly because many (likely most) psychoanalytic therapists consider symptoms resulting from personality and intrapsychic problems. The latter are assumed to be the real core problem (Hill et al., 2013). They believed that symptoms improve once the personality and intrapsychic change have been obtained, but they failed to use those concepts as potential alternative endpoints for their studies. Third, the focus on English-language studies could have excluded relevant studies published in other languages. However, 65% of the journals indexed in the PEP-Web archive, formed by the American Psychoanalytic Association and the Institute of Psychoanalysis and holds all the major psychoanalytic journals, are in English. Furthermore, 10 of 13 journals indexed in the category “Psychology, Psychoanalysis” (Social Sciences Citation Index; SSCI) of Clarivate’s Journal Citation Reports publish articles only in English, while two of the remaining are multilingual (with English as one of the languages). Fourth and last, patients with different subtypes of BD are included, and most diagnoses were not based on semi- or fully structured interviews. However, in this regard, bear in mind that although solid evidence indicates that a clinician who uses unstructured interviews tends to formulate and then assign a psychiatric diagnosis based on the presenting problem (usually within the first minutes of the first encounter) (Croskerry, 2003) though these do not meet the formal criteria for a diagnosis (Miller, 2002), the therapists who treated the patients included in this review and wrote the case analysis had the benefit of considering tens or hundreds of weekly clinical interviews in formulating the diagnosis.

### **Conclusion**

These pilot findings provide no robust evidence for psychoanalysis / psychoanalytic psychotherapy as an effective treatment for people with BD. Our findings are exclusively based on a small number of psychoanalytic narrative case studies, which, from the perspective of evidence-based medicine, are of poor scientific strength. Therefore, we cannot draw conclusions about the effectiveness of psychoanalysis for BD. Experimental studies, especially randomized clinical trials, are urgently needed that (a) rely on a manualized psychoanalytic approach to BD, (b) describe patient samples in both

psychoanalytic and ICD/DSM diagnostic terms, (c) monitor the adherence of therapists to the manualized approach, (d) describe elements of the therapeutic relationship in detail, (e) apply validated process and outcome measures (including constructs such as acceptance, insight, cognitive reserve, emotional cognition, functioning, and quality of life, as well as traditional measures of symptom reduction that are often used as primary outcome measures), (f) include cost-effectiveness measures, (g) monitor mood swings, (h) monitor dropout, and (i) use long-term follow-up.

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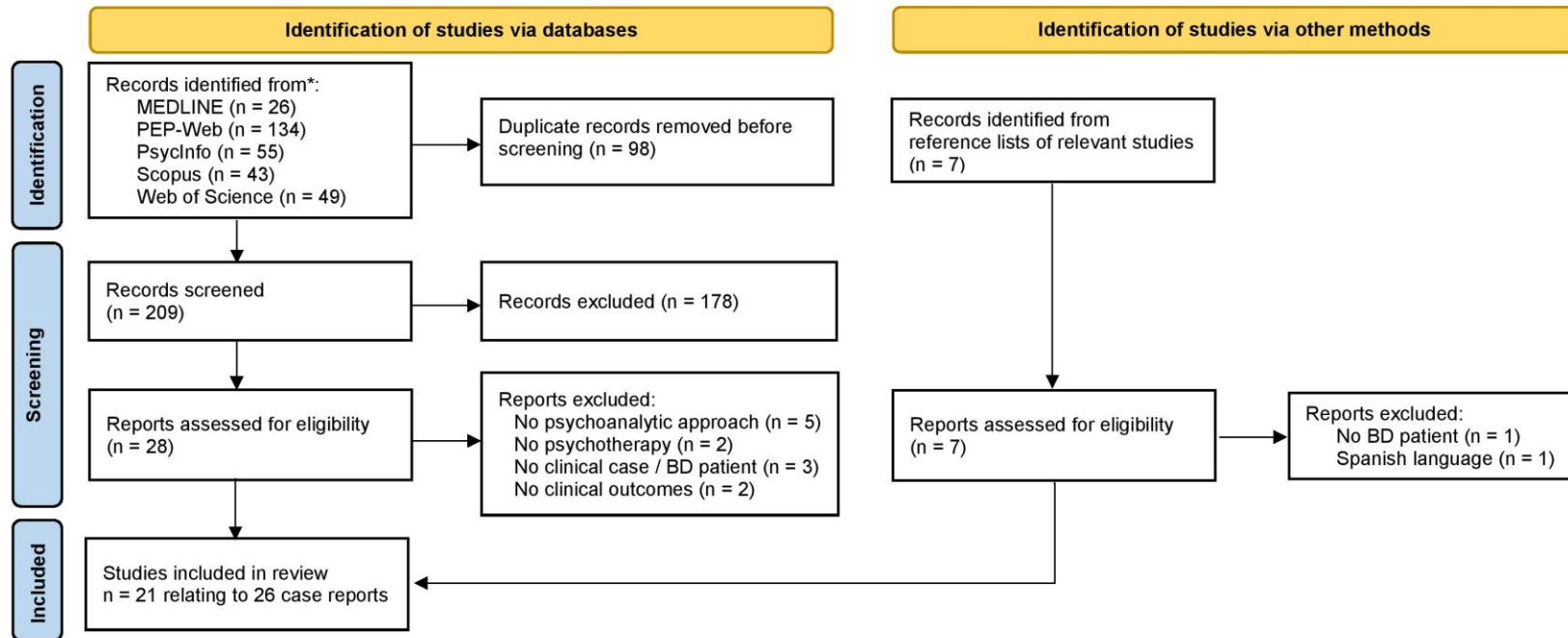
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Table I. Bipolar disorder patients and psychotherapies characteristics

	<i>n</i> = 26
<i>Age</i>	
“Young”	1 (3.8)
18–29	8 (30.8)
30–39	8 (30.8)
40–49	8 (30.8)
≥60	1 (3.8)
<i>Sex</i>	
Female	18 (69.2%)
<i>DSM diagnosis</i>	
Bipolar I Disorder	12 (46.2)
Bipolar II Disorder	6 (23.1)
Dysphoric Mania	1 (3.8)
Rapid Cycling Bipolar Disorder	6 (23.1)
Bipolar Disorder NOS	1 (3.8)
<i>Combined treatment</i>	
Yes	22 (84.8)
Yes, but only in certain periods	2 (7.6)
No	1 (3.8)
Unknown	1 (3.8)
<i>Psychotherapy setting</i>	
Private practice	14 (53.8)
Public health service	6 (23.1)
Unknown	6 (23.1)
<i>Psychotherapy status</i>	
Ongoing	12 (46.2)
Concluded	14 (53.8)
<i>Psychotherapy duration (years)*</i>	
Ongoing therapies (data on 9 out of 12), mean ± SD	5.6 (3.9) range: 2–15
Concluded therapies (data on 12 out of 14), mean ± SD	4.7 (3.8) range: 0.5–11
<i>Psychotherapy weekly session frequency</i>	
Ongoing therapies (data on 9 out of 12)	range: 1–6
Concluded therapies (data on 11 out of 14)	range: 1–6

Figure 1. PRISMA diagram of study selection process



Supplemental online table S1

Study	Patient characteristics	Treatment characteristics	Outcomes measure	Main treatment outcomes	Follow-up
Anonymous (1992) USA	- Age: 26 - Sex: F - Diagnosis: RCBD	- Setting: public health service - Weekly session(s): unknown - Duration: > 6 years - Pharmacotherapy: yes	Interview	<b>H:</b> unclear history of hospitalization both before and during therapy. <b>M:</b> improved medication adherence. <b>FO:</b> improvement in marriage and her ability to show her work. <b>S:</b> patient's suicidal episodes have significantly diminished. <b>SO:</b> it is unclear how the therapy has influenced patients' mood symptoms. <b>Other:</b> patient self-destructiveness and heavy drinking have significantly decreased.	Therapy was ongoing at the time of writing.
Wright (1992) USA	- Age: 25 - Sex: F - Diagnosis: RCBD	- Setting: private practice - Weekly session(s): 3 for the first two years, then 5 - Duration: 4 years - Pharmacotherapy: yes	Interview	<b>H:</b> not reported. <b>M:</b> antidepressant medication started after two years of therapy. <b>FO:</b> establishment of more stable work and intimate relationships. <b>S:</b> not reported. <b>SO:</b> corresponding with the start of antidepressant medication, the patient's intense affect states had diminished. Periods of depression alternating with periods of hypomania are still present. <b>Other:</b> impulsivity seemed to have given way to some degree of reflection.	Therapy was ongoing at the time of writing.
Jackson (1993) France	- Age: "young" - Sex: F - Diagnosis: BD I	- Setting: public health service - Weekly session(s): 2, sometimes more - Duration: 2 years - Pharmacotherapy: yes	Interview	<b>H:</b> the patient had stayed out of the hospital only for six months in the five years before the current psychotherapy. After two preliminary therapy sessions, the patient became acutely disturbed, with the classic symptoms of psychotic depression, which led to an eight-month hospitalization (psychotherapy suspended). At the end of the therapy, the patient had been out of the hospital for several months. <b>M:</b> not reported. <b>FO:</b> improved relationship with the parents. <b>S:</b> not reported. <b>SO:</b> dramatic switch from depression into mania and subsequent less dramatic switches or swings in both directions gradually decreased. At the end of therapy, the patient was on minimal medication and free of overt psychotic symptoms. <b>Other:</b> therapy ended when the therapist retired from the Health Service.	Undertaken psychoanalysis with another therapist. Five-year follow-up: two very brief admissions to hospital; mostly minimal medication; negotiated a miscarriage without undue disturbance, and a normal ante and postpartum period; return to and maintenance of part-time work.
Kahn (1993) USA	- Age: 37 - Sex: F - Diagnosis: RCBD	- Setting: unknown - Weekly session(s): unknown - Duration: unknown - Pharmacotherapy: yes	Interview	<b>H:</b> therapy has enabled the patient to stay out of the hospital. <b>M:</b> not reported. <b>FO:</b> not reported. <b>S:</b> suicidal gestures have been controlled <b>SO:</b> the patient's depressive symptoms have not been altered. Hypomanic episodes still occur.	Therapy was ongoing at the time of writing.
	- Age: 27 - Sex: F - Diagnosis: RCBD		Interview	<b>H:</b> not reported. <b>M:</b> not reported. <b>FO:</b> the patient moved into her apartment and began a part-time job. <b>S:</b> not reported. <b>SO:</b> mild depression and more severe manic episodes occurred during therapy. During a period, the patient became manic and required intensive nursing care at home. <b>Other:</b> better understanding of her conflicts and limits the sleep-depriving or anger-provoking behavior that seems to precede and cause manic escalations.	Therapy was ongoing at the time of writing.

Deitz (1995) USA	- Age: 43 - Sex: F - Diagnosis: BD I	- Setting: unknown - Weekly session(s): 2 - Duration: 6 months - Pharmacotherapy: yes	Interview	<b>H:</b> one hospitalization before the therapy. <b>M:</b> the patient learned to detect when she might need extra medication. <b>FO:</b> not reported. <b>S:</b> not reported. <b>SO:</b> The patient was free of any major episodes of mania or depression. <b>Other:</b> acceptance of the illness and the need to watch the stimuli.	Ten-year follow-up: the patient takes low doses of medication and did not have experienced major episodes of illness.
	- Age: late 30s - Sex: M - Diagnosis: BD II	- Setting: unknown - Weekly session(s): 2 - Duration: > 1 year - Pharmacotherapy: yes	Interview	<b>H:</b> not reported. <b>M:</b> acceptance of the need for medication. <b>FO:</b> not reported. <b>S:</b> not reported. <b>SO:</b> not reported. <b>Other:</b> greater self-confidence; greater self-acceptance; reduced medication.	Unknown.
	- Age: 42 - Sex: F - Diagnosis: DM	- Setting: unknown - Weekly session(s): unknown - Duration: unknown - Pharmacotherapy: yes	Interview	<b>H:</b> not reported. <b>M:</b> acceptance of the need for medication. <b>FO:</b> not reported. <b>S:</b> not reported. <b>SO:</b> not reported. <b>Other:</b> acceptance of illness; more attuned to the early signs of the dysphoric aspects of hypomania.	Therapy was ongoing at the time of writing.
Tizón (1997) Spain	- Age: 28 - Sex: F - Diagnosis: RCBDD	- Setting: private practice - Weekly session(s): 5, 6 at the turn of the first and second year - Duration: 8 years - Pharmacotherapy: yes, occasionally	Interview	<b>H:</b> not reported. <b>M:</b> not reported. <b>FO:</b> reduction of suicidal ideation. No more suicide attempts during therapy versus two attempts before therapy. <b>S:</b> not reported. <b>SO:</b> hypomanic periods appeared to be shorter and shorter in duration, or more mixed with melancholic feelings. <b>Other:</b> started her own family and had children; started a job she enjoyed.	Six-monthly or annual follow-ups for at least five years: the therapist has an obscure perception (which the patient says she sometimes shares) of 'hidden undercurrents' probably still lurking 'at the bottom of the well.' Occasional encounters 8, 10, 12, and more than 20 years later.
Lucas (1998) UK	- Age: 30s - Sex: F - Diagnosis: BD II	- Setting: public health service - Weekly session(s): 5 for the first thirteen years, then unknown - Duration: > 15 years - Pharmacotherapy: yes	Interview	<b>H:</b> several hospitalizations before and during the therapy. Therapy started with a three-month hospitalization for hypomania, then the patient returned to a depressive state and went outpatient. Therapy allowed the patient to be contained as an outpatient, with only a brief hospital admission lasting a week over the last three years. <b>M:</b> not reported. <b>FO:</b> no more periods in which the patient could not mix socially. <b>S:</b> not reported. <b>SO:</b> exacerbation of the length and severity of the manic phases for about the first 12 years of therapy. The propensity to manic eruptions remains.	Therapy was ongoing at the time of writing.
Salzman (1998) USA	- Age: 60 - Sex: F - Diagnosis: BD II	- Setting: private practice - Weekly session(s): unknown - Duration: > 2 years - Pharmacotherapy: yes	Interview	<b>H:</b> not reported. <b>M:</b> good adherence to medication. <b>FO:</b> not reported. <b>S:</b> not reported. <b>SO:</b> greater mood stability (nearly two years of her mood stability at the end of the therapy). <b>Other:</b> the patient felt constrained from expressing both anger and grateful for her mood stability at the therapist. After considerable debate, the therapist referred the patient to a colleague.	Undergone therapy with another therapist.
Georgaca	- Age: 23	- Setting: public health service	Interview	<b>H:</b> two hospitalizations before and one during therapy.	Therapy was ongoing at the time of writing.

(2001) UK	- Sex: F - Diagnosis: BD I	- Weekly session(s): 1 - Duration: 2 years - Pharmacotherapy: yes		<b>M:</b> good adherence to medication. <b>FO:</b> better engagement in the social world and the elaboration of ways of thinking through and coping with everyday reality and human relations demands. Improved and more stable functional relation to the world. <b>S:</b> not reported. <b>SO:</b> therapy has been helping the patient to prevent psychotic crises.	
Mills (2004) Canada	- Age: 42 - Sex: M - Diagnosis: RCBD	- Setting: first sessions in the hospital and then private practice - Weekly session(s): 1-2; 5 during hospitalizations - Duration: 4 years - Pharmacotherapy: yes	Interview	<b>H:</b> more than a dozen hospitalizations before and two during therapy. <b>M:</b> good adherence to medication. <b>FO:</b> not reported. <b>S:</b> chronic suicidality. <b>SO:</b> multiple episodes of manic psychosis have occurred. <b>Other:</b> eventual incarceration in prison for criminal theft and fraud.	Therapy was ongoing at the time of writing.
Pollack-Gomolin (2005) USA	- Age: 48 - Sex: M - Diagnosis: BD I	- Setting: unknown - Weekly session(s): unknown - Duration: > 7 years - Pharmacotherapy: yes	Interview	<b>H:</b> not reported. <b>M:</b> not reported. <b>FO:</b> not reported. <b>S:</b> not reported. <b>SO:</b> psychotic and delusional ideation characterized the first three years. Unclear changes in the clinical presentation of the patient.	Therapy was ongoing at the time of writing.
Chernus (2006) USA	- Age: 39 - Sex: F - Diagnosis: BD I	- Setting: public health service - Weekly session(s): began with 1 every other week, quickly to 1-2 times per week, depending on patient's needs - Duration: > 10 years - Pharmacotherapy: yes	Interview	<b>H:</b> several hospitalizations before therapy and none during therapy. <b>M:</b> the patient began manifesting symptoms of kidney failure, which required discontinuing her Lithium. <b>FO:</b> improvement in social and professional functioning. <b>S:</b> no suicidality before Lithium interruption. <b>SO:</b> the patient remained relatively stable over ten years. <b>Other:</b> after the interruption of lithium, the patient's depression steadily worsened, eventually culminating in her suicide approximately 18 months later.	Deceased.
Rossouw (2007) UK	- Age: mid-40s - Sex: F - Diagnosis: BD I	- Setting: private practice - Weekly session(s): 5 - Duration: 3 years - Pharmacotherapy: yes	Interview	<b>H:</b> not reported. <b>M:</b> not reported. <b>FO:</b> not reported. <b>S:</b> suicidal states were present. Therapy helped the patient to pull away from the suicidal states each time, and perhaps the intensity and duration of her episodes became less than before the onset of the therapy. <b>SO:</b> the depressed phases have been dominant during therapy, but there was one manic episode and one hypomanic episode.	Therapy was ongoing at the time of writing.
Levine (2009) USA	- Age: 23 - Sex: M - Diagnosis: BD I	- Setting: private practice - Weekly session(s): 3 - Duration: 3 years - Pharmacotherapy: no	Interview	<b>H:</b> one hospitalization before therapy. <b>M:</b> not reported. <b>FO:</b> the patient graduated, moved to another city, and was doing well at the time of termination. <b>S:</b> not reported. <b>SO:</b> not reported.	Therapy was ongoing at the time of writing
Winship (2009) UK	- Age: late 30s - Sex: M - Diagnosis: BD I	- Setting: unknown - Weekly session(s): 2-3 - Duration: unknown	Interview	<b>H:</b> not reported. <b>M:</b> not reported. <b>FO:</b> not reported.	None.

		- Pharmacotherapy: unknown		<b>S:</b> during the course of the therapy, the patient began to ruminate about ending his life. <b>SO:</b> during the course of therapy, mood swings became apparent: no information about the patient's state at the end of therapy.	
Cambray (2011) USA	- Age: late 30s - Sex: F - Diagnosis: BD I	- Setting: private practice - Weekly session(s): 2 for about a year and a half, then 1 - Duration: 4 years - Pharmacotherapy: yes	Interview	<b>H:</b> hospitalizations before therapy (it is not clear if there has been one voluntary hospitalization). <b>M:</b> not reported. <b>FO:</b> not reported. <b>S:</b> not reported. <b>SO:</b> three psychotic episodes, interspersed with periods of depression, during therapy. The third was much less debilitating and destructive than the previous two. <b>Other:</b> Therapy ended when the patient moved across the country.	No further psychotic break in more than 20 years.
Downey (2011) USA	- Age: 33 - Sex: F - Diagnosis: BD NOS	- Setting: private practice - Weekly session(s): unknown - Duration: 3 years - Pharmacotherapy: yes	Interview	<b>H:</b> no history of hospitalization either before and during the therapy. <b>M:</b> not reported. <b>FO:</b> improved intimate and social relationships. <b>S:</b> not reported. <b>SO:</b> it is not clear whether and how therapy has influenced the patient's mood state <b>Other:</b> better understanding of herself and regularizing her life: reduced anxiety and alcohol consumption and moderated sexual behaviors.	None.
Duckham (2011) USA	- Age: 28 - Sex: M - Diagnosis: BD I	- Setting: private practice - Weekly session(s): 1-2 - Duration: 11 years - Pharmacotherapy: yes	Interview	<b>H:</b> none. <b>M:</b> not reported. <b>FO:</b> improved professional career and relationship with others. <b>S:</b> not reported. <b>SO:</b> depression, anxiety, and psychosis have been contained. <b>Other:</b> improved self-concept, reduced emotional reactivity.	Therapy is still ongoing in October 2021, with a frequency of one session per week. The patient continues to make improvements, albeit slowly.
Vanheule (2017) Belgium	- Age: 46 - Sex: F - Diagnosis: BD II	- Setting: private practice - Weekly session(s): 2 - Duration: unclear >6 years - Pharmacotherapy: yes, during the first year	Interview	<b>H:</b> none. <b>M:</b> not reported. <b>FO:</b> improved relationship with parents, although it still provokes distress; resumed professional life. <b>S:</b> not reported. <b>SO:</b> not reported. <b>Other:</b> the medication was terminated after the first three years of therapy.	Therapy was ongoing at the time of writing.
Ventimiglia (2020) Italy	- Age: 45 - Sex: F - Diagnosis: BD II	- Setting: private practice - Weekly session(s): 1 or 2 (in specific, more difficult periods) - Duration: >1 year - Pharmacotherapy: yes	Interview	<b>H:</b> not reported. <b>M:</b> not reported. <b>FO:</b> not reported. <b>S:</b> not reported. <b>SO:</b> two hypomanic and one depressive phases occurred during therapy. The analytical work carried out was sufficient to reduce to a satisfactory degree both the hypomanic and depressive side of the disorder. However, it was not enough to structurally resolve the patient's condition. <b>Other:</b> the patient interrupted therapy. The onset of a new depressive malaise was evident at that time, although at a lower intensity than in prior analogous phases.	By telephone two months later: the patient reported that she was well and that the depressive signs had only lasted a short time. In person some months later: the patient confirmed that she was continuing to feel well: she had not experienced any new depressive phase or mood change.
Kalita (2021) Poland	- Age: 40s - Sex: M - Diagnosis: BD I	- Setting: private practice - Weekly session(s): 2 - Duration: many months - Pharmacotherapy: yes	Interview	<b>H:</b> one hospitalization for mania right before starting the therapy. <b>M:</b> regular intake of prescribed medication. <b>FO:</b> the overall functioning improved slightly (likely related to the psychotropic medication). <b>S:</b> not reported. <b>SO:</b> not reported.	None.

				<b>Other:</b> very little progress in understanding himself or gaining insight into his experiences.	
- Age: 31 - Sex: M - Diagnosis: BD II	- Setting: private practice - Weekly session(s): 2 - Duration: > 9 years - Pharmacotherapy: yes	Interview		<b>H:</b> two hospitalizations before and a very brief one during therapy. <b>M:</b> not reported. <b>FO:</b> significant improvement in the ability to cope with life tasks. <b>S:</b> not reported. <b>SO:</b> lasting remission of depressive and maniacal symptoms.	None.
- Age: 23 - Sex: F - Diagnosis: BD I	- Setting: private practice - Weekly session(s): unknown - Duration: 5 years - Pharmacotherapy: yes	Interview		<b>H:</b> several hospitalizations for mania before starting therapy and once during. <b>M:</b> not reported. <b>FO:</b> the patient got a master's degree, started a stable job, and entered a new relationship. <b>S:</b> not reported. <b>SO:</b> not reported. <b>Other:</b> the patient decided to terminate the therapy.	Few years of follow-up: despite her moods and some restlessness in her life, the patient did not require any hospitalization since the end of therapy. She did not experience phases of mania or clinical depression and remained in regular contact with her psychiatrist.

*Note.* BD I = bipolar I disorder; BD II = bipolar II disorder; DM = dysphoric mania; FO = functioning outcome; MA = medication adherence; H: psychiatric hospitalization; RCBD = rapid cycling bipolar disorder; SO = depressive and manic symptoms outcome; S = suicidality.

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