Systematic Bibliographical Revision on Effective Psychotherapies and/ or Combined Treatments with Patients with Severity and Comorbidity Characteristics

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ABSTRACT

In the last decade, many authors have admitted that we are witnessing a change of paradigm in the way we understand evidence-based psychotherapy practice at its core. This new approach is far more idiographic, based on change processes, and a more dimensional understanding of psychopathology and human suffering. The need for changing paradigms becomes more apparent when facing patients with psychopathological symptoms that imply severity and comorbidity. The generic indication to treat these patients is combined treatment, medication, and psychotherapy. This systematic bibliographical review aims to collect scientific articles on effective psychotherapies and/or combined treatments with patients with severity and comorbidity to assess the state of the art. A secondary aim is to highlight the differences in the number of scientific publications in Latin American databases versus American and European ones. For this purpose, the author applied Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) declaration principles and the Population, Intervention, Comparison, Outcomes and Study (PICOS) criterion. In the first search, the author selected 95 (N=95) articles, of which 90% of the analysis units came from databases in Europe and the USA. Then, the author conducted three other searches, which selected 53 articles (N=53), excluding the findings of European and USA databases because they yielded results that were too extensive.

Keywords: Effective psychotherapy; Psychometrics; Psychophysiology; Psychopathology; Psycholinguistics

INTRODUCTION

Evidence-based psychotherapy started gaining traction around 2012 when the American Psychological Association (APA) introduced the evidence-based psychotherapy program. From the beginning, evidence-based practices implied researching different therapy techniques and integrating intervening factors like the therapistpatient relationship, clinician's experience, patient's perspective, and context. Moreover, external factors also play an important role in the treatment process and outcome. Nowadays, instead of focusing on which treatment or therapist works best for a specific problem, the approach is more about understanding the underlying change processes from a broad perspective. It is all about figuring out which bio-psycho-social processes are necessary to target to help a particular patient and the most effective way to do it [1].

In the past, researchers conducted most efficacy and effectiveness investigations with randomized controlled study methodologies with patients with well-defined diagnoses, without comorbidities [2]. However, patients rarely present themselves in the naturalistic context in such a pure fashion. Moreover, this is not the case for the patients this study deals with, who, on the opposite, would be those where there is comorbidity and severity in their psychopathological problems [3]. From an evidence-based psychotherapy perspective, we seek to know the status of scientific publications on effective psychotherapies and combined treatments with this type of patient. As has been said, although prevalence is not so high as in more common disorders, the costs are higher in comparison. These patients suffer the most, not only in terms of personal suffering but also for significant others, added to the general increase in expenses for the healthcare system that comes with treatments without good results [4]. This systematic review reflects what clinicians and researchers are doing to improve this situation. Therefore, disseminating their work may significantly contribute to good practices in mental health.

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MATERIALS AND METHODS

In order to collect scientific articles from the last ten years in databases from Latin America, Europe, and the USA on effective psychotherapies and/or combined treatments with patients with severity and comorbidity from the perspective of evidence-based practices, the author applied the PRISMA statement [5], and used the Population, Interventions, Comparators, Outcomes, and Study (PICOS) criterion for the selection of the units of analysis. In order to address the target, the author carried out four searches. 1st with the keywords "evidence-based psychotherapies AND combined treatments AND comorbidity severity," 2nd with the keywords "evidence-based psychotherapy AND combined treatments," 3rd with "psychotherapy and medication," and the fourth with "evidence-based psychotherapy." The databases used were DOAJ, PubMed, PsycNet in its free versions, and RedalyC, Scielo, Dialnet, and Bioresorbable Vascular Scaffold (BVS), as shown in Figure 1.



Inclusion criteria

Articles on effective psychotherapies and/or combined treatments based on evidence for patients who met with disorders with severity and comorbidity in the last ten years were included in the study. The units of analysis could include one or some of the elements present in the title of the review.

Exclusion criteria

Patients who do not meet the inclusion criteria, patients who had problematic drug use, crime, children and adolescents in the last ten years were excluded in the study.

The search with the keywords "evidence-based psychotherapy AND combined treatments AND comorbidity severity", in the PubMed, PsycNet and Redalyc databases, yielded a total of 784 (N=784) articles, of which 95 (N=95) were selected, taking into account that 141 PsycNet articles could not be accessed because they were not freely accessible. 687 (N=687) were discarded due to duplication or non-compliance with inclusion requirements. Of the 95 selected, 10 (N=10) came from Latin American databases, that is, 10%. There are no results in the DOAJ, Scielo, Dialnet, and BVS databases. A second search was carried out with the keywords "evidence-based psychotherapy AND combined treatments", in the DOAJ, Dialnet and BVS databases, which yielded a total of 28 (N=28) articles, of which 4 were selected (N=4), and 24 (N=24) were

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discarded due to duplication or non-compliance with the inclusion requirements. In the PubMed, PsycNet and Redalyc databases, they yielded more than 3000 items. With the keywords "psychotherapy and medication", a search was carried out that yielded a total of 64 (N=64) articles in the Scielo and Dialnet databases, of which 15 (N=15) were selected and 49 were discarded (N=49) due to duplication or non-compliance with the inclusion requirements, more than 3000 items were found in the rest of the databases. Finally, a final search was carried out with the keywords "evidence-based psychotherapy," which yielded a total of 141 (N=141) articles in the Scielo and Dialnet databases, of which 34 (N=34) were selected, and 107 (N=107) were discarded due to duplication or non-compliance with the inclusion requirements. More than 3000 items were found in the rest of the analyses.

RESULTS AND DISCUSSION

Following the PRISMA declaration [5], on the transparent reporting of systematic reviews, and the proposed flow diagram showed in Figure 1, and following the PICOS criteria based on the different groups of keywords, a total of 1017 (N=1017) articles were found, of which 148 (N=148) were selected. For relevance, the years between 2020 and 2022 were selected.

Among all the selected articles, the author rescues the importance of those highlighting the individual patient data network analysis in patients with depression with residual symptoms, which is in accordance to the more idiographic approach stated above. These types of analysis are frequent in all treatments, from cognitive therapy to antidepressant medication, and take us to the issue of personalized treatments as an intended solution for treatmentresistant patients [6-8]. About Post-Traumatic Stress Disorder (PTSD) patients, the author highlights a randomized controlled study that evaluates the effectiveness of a brief psychological intervention, which, if proven effective, could allow a significant increase in access for a larger number of patients to a brief, cost-effective and effective treatment for PTSD [9]. In the same vein, another article tries to test the effectiveness of psychological and pharmacological interventions combined in patients with PTSD with abused children [10]. Other investigations propose the construction of a computational model to better understand psychosis and its treatment, beyond pharmacological medication [11], in line with the one proposed using digital technologies to understand and evaluate the emotional regulation capacity in individuals [12]. Some other research studies focus on the supplier decision-making process in clinics with PTSD patients [13], and others examine the impact of treatment interruptions in the context of telemedicine and its consequences [14]. A seminal work, somewhat earlier, raises the resurgence of psychological interventions in the face of the limitations of widespread pharmacological interventions [15]. Along these same lines, several authors address evidence based on practice [16-18], and how practice can be considered evidence. Several articles review the effectiveness of internet interventions for different pathologies, particularly depression [19-24]. There are case studies with this type of patient [3], and articles linked to the conceptualization of evidence-based psychotherapy [25]. Most psychological interventions come from the roots of cognitivebehavioral therapy, although some articles were also found based on psychodynamic models [26,27]. There was no shortage of articles that focused on the patient's perspective [28-30], and on the training of therapists in the evidence-based perspective [31,32]. Rehabilitation techniques in psychosis and schizophrenia were also addressed [33-36].

In a later stage of this review, to delve more specifically into types of disorders with severity and comorbidity, the units of analysis were distributed according to their content in relation to evidence-based psychotherapies and/or combined treatments in the "borderline" categories (7%), "severe depression" (17%), "trans diagnosis" (12%), "post-traumatic stress" (20%), "eating disorders" (7%), "obsessive-compulsive, Tourette" (1%), "schizophrenia and psychosis", (13%) "bipolar" (4%), "generalized anxiety" (2%), "personality disorders" (3%) and "others" (12%), including comorbidities, as shown in Table 1.

Type of pathology with severity and comobility	Amount	Percentage
Borderline	10	7
Severe depression and comorbidity	23	17
Transdiagnostic	16	12
PTSD (Post-Traumatic Stress Disorder)	27	20
Bulimia nervosa, eating disorders	10	7
OCD (Obsessive-Compulsive Disorder), Tourette, comorbidity	2	1
Schizophrenia, psicosis, depression comorbidity	18	13
Bipolar	6	4
GAD	3	2
Personality disorders	4	3
Otros	17	12
Total	137	98

The largest number of articles are found in the categories "severe depression", "trans diagnosis", "post-traumatic stress disorder", "schizophrenia and psychosis (Table 2).

In the latter categories, the author searched only articles published between 2021 and 2022, containing all the search terms "psychotherapy based in evidence and combined treatments and comorbidity severity". It is observed that both in large populations [37], as in single case studies [38], the need to overcome the classification scheme of specific diagnosis, for one that addresses the complexity and comorbidity of psychiatric symptoms and

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personalization of treatment is apparent [39]. In the case of treatment resistant depressions, given their prevalence and high costs for the health system, some authors propose a new form of nosological classification that includes the complexities that come with resistant psychiatric disorders, in order to address better understanding and treatment [40]. Regarding the combination of psychotherapy and medication, most articles report on the benefits of incorporating psychological interventions for the good outcome, maintenance of the achievements and relapse prevention [41].

Table 3 presents the main results in the "other" category, which includes combined treatments, the patient perspective, the therapist's perspective and methodological approaches for the treatment of patients with these characteristics, between 2017 and 2022, based on Latin American databases. Since the perspective of patient is part of the expanded definition of "evidence-based psychotherapy", as indicated above, it is important to highlight that there are already randomized controlled studies published where the perspective of the patient is explored as an intervening variable in the treatment [42]. Now one can affirm, with scientific evidence, that its inclusion improves treatment results. Another important aspect of the broad definition of evidence-based practice is addressed, which is the context of the treatment delivery [43]. These authors demonstrated that training staff in the implementation and concept of psychological interventions in wards, improved results (Table 3).

This systematic review has allowed us to identify the shifting paradigm in mental health and in what is considered evidencebased practice with patients with severity and comorbidity.

Different authors advocate for the broadening of the concept of evidence, including practice as evidence [44-46], assessing patient's, partners and other's perspective, health care team and context [42,43,47-50]. Also, in terms of psychopathology, there is a growing trend towards more trans diagnostic perspectives and even new nosologies [40,51,52]. A more idiographic approach and personalized treatments are proposed to achieve better results with these patients, including focusing on evidence based psychological interventions [53,39,38]. In order to increase accessibility to those in need, many authors propose combining digital technologies and internet based interventions with controlled medications for severe patients [54,21]. Treatment accessibility and cost-effectiveness are targeted as well as the relevance of psychosocial effective interventions with these patients [44,55-56]. Figure 2 summarizes these achievements.

Table 2: Units of analysis: Evidence-based combined psychological interventions with patients with severity and comorbidity.

Title	Type of study	Results	Authors and year
Trans diagnostic efficacy of a group exercise intervention for outpatients with heterogeneous psychiatric disorders: A randomized controlled trial	RCT	The exercise intervention showed transdiagnostic efficacy among a heterogeneous clinical sample in a realistic outpatient setting and led to sustained exercise behavior change. Exercise may serve as an efficacious and feasible transdiagnostic treatment option improving the existing treatment gap within outpatient mental health care settings.	[37]
Combining ketamine and internet-based cognitive behavioral therapy for the treatment of posttraumatic stress disorder: Protocol for a randomized controlled trial	RCT	This will be the first experiment assessing the relationship between e-CBT and ketamine and their combined ability to treat refractory PTSD. If successful, this study will open online/asynchronous therapeutic options to patients with PTSD and will provide new insights into the functional role of glutamate in trauma-related disorders as well as in learning, memory, and fear- extinction.	[38]

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Clinical research challenges posed by difficult-to-treat depression	Nosological, descriptive	The authors propose a new clinical heuristic of 'Difficult-to-Treat Depression' (DTD) that aims to broaden our understanding and focus attention on the identification, clinical management, treatment selection, and outcomes of such individuals. Clinical trial methodologies developed to detect short-term therapeutic effects in	[39]
A randomized-controlled trial of community-based transdiagnostic psychotherapy for veterans and internally displaced persons in Ukraine	RCT	treatment-responsive populations may not be appropriate in DTD. Lack of community-based services and poor uptake of existing psychiatric services led to the current trial to determine the effectiveness of the common elements treatment approach (CETA) on anxiety, depression, and posttraumatic stress symptoms (PTS) among conflict affected adults in Ukraine. Standard CETA is more effective than brief CETA, but brief CETA also had significant effects compared with wait-controls. Given demonstrated effectiveness, CETA could be scaled up as an effective community-based approach.	[40]
Depression from a precision mental health perspective: Utilizing personalized conceptualizations to guide personalized treatments	Systematic review	The aim of this review is to provide an overview of recent findings in the conceptualization and treatment of depression from a precision mental health perspective and to discuss potential challenges and future directions in the application of precision psychiatry for the treatment of depression	[41]
The clinical and cost-effectiveness of a self-management intervention for patients with persistent depressive disorder and their partners/caregivers: Study protocol of a multicenter pragmatic randomized controlled trial	RCT	Although the revised depression treatment guidelines suggest focusing on psychiatric rehabilitation and self-management as the next treatment step for PDD, an evidence-based cost-effective self- management protocol for PDD is lacking. This study investigates the "Patient and Partner Education Program for All Chronic Illnesses" (PPEP4All) as a brief self-management protocol that could lead to lower costs, higher quality of life, and less disease burden in PDD patients and their partners/caregivers. This project will result in the implementation of a self-management intervention for patients with PDD, meeting an urgent need in mental healthcare. Using PPEP4All can optimize the quality and efficiency of care for both patients with PDD and their partners/caregivers	[42]
Study quality and efficacy of psychological interventions for posttraumatic stress disorder: A meta-analysis of randomized controlled trials	RCT-meta- analysis	Overall, study quality was not significantly associated with effect size. The findings indicate that psychological interventions can effectively reduce PTSD symptoms irrespective of study quality.	[43]
Application of the unified protocol for a Japanese patient with post-traumatic stress disorder and multiple comorbidities: A single-case study	Case study	This study examined the effects of UP treatment with trauma-focused exposure on symptoms of PTSD and comorbidities in a client who was hesitant about exposure. The UP was an effective alternative treatment for PTSD and symptoms of comorbidities in this client who was hesitant about exposure to traumatic memories, and that the inclusion of trauma-focused exposure provided sufficient therapeutic effects. Further research is needed to examine the generalizability of our findings.	[44]
Initial outcomes of transdiagnostic internet-delivered cognitive behavioral therapy tailored to public safety personnel: Longitudinal observational study	Longitudinal observational study	This study was designed to fill a gap in the literature regarding the use of ICBT tailored specifically for PSP. It examined the effectiveness of a customized ICBT program for treating depression, anxiety, and PTSD symptoms among public security personnel in the province of Saskatchewan. Customized, transdiagnostic ICBT demonstrated promising outcomes as a treatment for depression, anxiety, and PTSD among Saskatchewan PSP and warrants further investigation.	[45]
Psychosocial rehabilitation interventions in the treatment of schizophrenia and bipolar disorder	Systematic review	This review describes the psychosocial rehabilitation interventions that have been used successfully and extensively in patients with schizophrenia and bipolar disorder. Schizophrenia and bipolar disorder are chronic conditions with the early onset, higher relapse rate, and functional impairment that often persist despite optimum pharmacotherapy, underscoring the need for adjunctive psychosocial treatments and rehabilitation interventions. Evidence based psychosocial treatment and rehabilitation interventions for both illnesses are adherence therapy, psychoeducation, cognitive- behavioral therapy, interpersonal and social rhythm therapy, cognitive remediation, social skills training, family education, vocational rehabilitation, case management, assertive community treatment, occupational/art therapy, and peer support. The efficacy of these interventions has been shown in many studies	[46]

 Table 3: Unit of analysis; patients' perspective, context and evidence-based psychotherapy with severe patients.

Title	Type of study		Authors and year
Implementation of the patient version of the evidence-based (S3) guideline for psychosocial interventions for patients with severe mental illness (IMPPETUS): Study protocol for a cluster randomised controlled trial	RCT	The primary outcome is the change of empowerment, assessed by using (EPAS) scale. Inaddition, knowledge, attitudes and experiences regarding psychosocial interventions will be assessed as secondary outcomes, as well as service use, satisfaction with care, patient need and quality of life and participation and social inclusion. This study is the first to assess the effects of a structured implementation of a patient version of a psychiatric treatment guideline.	[47]
The intersection of the implementation of the Psychotherapy based on evidence and practice- oriented research	Case studies in practice oriented research (POR)	There is a pressing need to learn more about effective (and ineffective) evidence-based intervention implementation processes and outcomes in service delivery organizations. This paper traces the history of this implementation and POR effort across multiple phases, while integrating theory and research from implementation science, as well as routinely collected data from this effort. Finally, lessons from this ongoing case study may inform future efforts (both internal and external to this specific context) to implement evidence-based strategies in residential/intensive outpatient settings	[48]
Non-strategic ignorance: Considering the potential for a paradigm shift in evidence-based mental health.	Qualitative	Thematic analysis of the findings revealed an overall critique of randomised controlled trial methods. The discussion considers whether the evidence-based mental health paradigm is faced with epistemological problems of such complexity that the conditions exist for a new paradigm in which service user views are central and randomised controlled trials peripheral.	[49]
Integrating evidence-supported psychotherapy principles in mental health case management: A capacity-building pilot.	Qualitative	This pilot demonstrated that case-based consultations and training of mental health case managers within a community-of- practice in trauma-informed, culturally sensitive application of evidence-supported psychotherapy principles were feasible and acceptable with scalable potential to improve case managers' counseling self-efficacy, reflective capacity, empathy, and morale. Further research in this area is needed with a larger sample, and patient and health systems outcomes	[50]
Receipt and targeting of evidence-based psychosocial interventions for people living with psychoses: Findings from the second Australian national survey of psychosis.	Qualitative	Prior reports of limited receipt of EBPIs are reinforced. There is patchy evidence for targeting of EBPIs to those who might benefit most. Service characteristics contribute more to the prediction of receipt than clinical characteristics. Greater implementation effort and better targeting are required to bridge evidence-practice gaps, including improved evidence-based practice literacy among professionals and needs-based service re- design to improve provision and optimise consumer outcomes.	[51]
Improving implementation of evidence based practice for people with psychosis through training the wider workforce: results of the GOALS feasibility randomised controlled trial	RCT	The present study aims to examine the feasibility of training the frontline workforce, rather than accredited psychological therapists, to deliver targeted, brief evidence- based therapy in routine community services for people with psychosis. Monotherapy with medication is no longer the optimal treatment choice for people with psychosis. However, internationally there is a severe implementation challenge in extending access to additional evidence-based practices for this group	[52]
Realising the mass public benefit of evidence- based psychological therapies: The IAPT program	Longitudinal study	The English IAPT program has greatly increased the availability of empirically supported psychological therapies for depression and anxiety disorders. A session-by- session monitoring system ensures that outcomes are recorded for almost everyone. The overall outcomes are broadly in line with expectations from clinical trials. Study of the determinants of regional variation in outcomes is starting to reveal information about the optimal way to organize services. Every country is different. However, it is hoped that some of the lessons that have been learned from IAPT will help other countries in their own quests to realize the mass public benefits that can be achieved by increasing the availability of psychological therapies.	[53]

Addressing the treatment gap: A key challenge for extending evidence-based psychosocial interventions	Descriptive	Currently, in the United States (and worldwide), the vast majority of individuals in need of mental health services receive no treatment. Although there are many reasons, the dominant model of delivering psychosocial interventions in both research and clinical practice makes it difficult to scale treatment to reach the large swaths of individuals in need. That model includes one-to-one, in person treatment, with a trained mental health professional, and provided in clinical setting (e.g., clinic, private practice office, health-care facility). The article discusses the development of delivery models that would permit reaching more individuals in need, highlights criteria for developing such models, and illustrates novel models already available.	[54]
Interventions of computerized psychotherapies for depression in primary care in Spain	RCT	The objective of this work was to present the current situation in Spain regarding the use of these interventions for the treatment of depression in Primary Care. The main conclusion is that although there is scientific evidence on the effectiveness of these programs, there are still important barriers that hinder their application in the public system, and also the need to develop implementation studies that facilitate the transition from research to clinical practice.	[55]
Practice-based evidence in psychotherapy: The challenge in Latin America.	Assay	This article explains the Practice-Based Evidence in psychotherapy in depth considering its association with the research of the effectiveness in psychotherapy. Subsequently, the functioning of this last paradigm in health systems, particularly in mental health care is contextualized, emphasizing its applicability in routine evaluation and its potential to contribute to the field of research in psychotherapy and its function of bridging the gap between research and practice. Finally, some conclusions are presented on how to promote research based on the paradigm of Practice-Based Evidence in psychotherapeutic contexts, based on Practice Research Networks in Latin Ameri- can countries.	[56]



CONCLUSION

Although remarkable progress has been made in developing psychosocial interventions for a broad range of psychiatric disorders, still the vast majority of individuals in need of mental health services receive no treatment or a non-qualified one. This state of affairs is due to many diverse reasons that exceed the scope of the present article. Nonetheless, many efforts are underway to improve this situation. Among them are the efforts to bridge the gap between research and practice or increase cost-effectiveness, particularly with patients who bear the higher costs. From another perspective, the reformulation of psychopathological categories itself towards a more idiographic approach, which takes us to more personalized treatments. Trans theoretical and trans diagnostic views seem to lead to more fruitful developments in that regard. This systematic bibliographical review shows that many potential new strategies address the problem of scarce accessibility and good results with these kinds of patients. The evolution and broadening of what evidence-based practice means pose an active hope for improving the treatment delivery in mental health for the coming years, providing ongoing research and bridging the gap between research and clinical practice.

From the clinical perspective, we hope that all these changes, as they evolve and constitute an ongoing research work, will finally achieve the goal of improving the results of our treatments and, also, very

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importantly, reducing the gap between clinical practice, research and between different theoretical models, in search of a unified body for mental health assistance. Without this evolution, it surely would be impossible, and hence the great value of publications and scientific communications in our work, with its consensus and dissent.

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