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EDITORIAL

Treatment alliance and adherence in bipolar disorder

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Abstract

The clinician patient relationship lies at the core of psychiatric practice and delivery of mental health care services. The concept of treatment alliance in psychiatry has its origins in psychotherapy, but has also been influenced by several other constructs such as patient-centred care (PCC) and shared decision-making (SDM). Similarly, there has been a shift in conceptualization of treatment-adherence in psychiatric disorders including bipolar disorder (BD) from illness-centred and clinician-centred approaches to patient-centred ones. Moreover, the traditional compliance based models are being replaced by those based on concordance between clinicians and patients. Newer theories of adherence in BD place considerable emphasis on patient related factors and the clinician patient alliance is considered to be one of the principal determinants of treatment-adherence in BD. Likewise, current notions of treatment alliance in BD also stress the importance of equal and collaborative relationships, sensitivity to patients' viewpoints, sharing of knowledge, and mutual responsibility and agreement regarding decisions related to treatment. Accumulated evidence from quantitative research, descriptive accounts, qualitative studies and trials of psychosocial interventions indicates that efficacious treatment alliances have a positive influence on adherence in BD. Then again, research on the alliance-adherence link in BD lags behind the existing literature on the subject in other medical and psychiatric conditions in terms of the size and quality of the evidence, the consistency of its findings and clarity about underlying processes mediating this link. Nevertheless, the elements of an effective alliance which could have a positive impact on adherence in BD are reasonably clear and include PCC, collaborative relationships, SDM, open communication, trust, support, and stability and continuity of the relationship. Therefore, clinicians involved in the care of BD would do well to follow these principles and improve their interpersonal and communication skills in order to build productive alliances with their patients. This could go a long way in confronting the ubiquitous problem of non-adherence in BD. The role of future research in firmly establishing the alliance-adherence connection and uncovering the processes underlying this association will also be vital in devising effective ways to manage non-adherence in BD.

Key words: Treatment; Alliance; Adherence; Bipolar disorder; Components; Mediators

Core tip: A collaborative treatment alliance is central to tackling the ubiquitous problem of non-adherence in bipolar disorder (BD). Studies examining the link between alliance and adherence in BD have shown that an effective alliance positively impacts adherence. However, the existing literature is relatively limited, often of variable quality, and has not been able to clearly delineate the mediators of the alliance-adherence connection. Nevertheless, the key elements of productive alliances in BD which could positively influence treatment-adherence are reasonably clear. They can be readily implemented in clinical practice to enhance adherence in BD, till future research further clarifies the alliance-adherence association.

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INTRODUCTION

The changing face of mental health care

With the introduction of the concepts of patient-centred care (PCC) and shared decision-making (SDM) since the 1990s the face of health-care delivery has undergone a remarkable transformation. The preceding years had seen many clinical, economic and social changes such as the growing numbers of elderly patients and those with chronic conditions, the increasing complexity and cost of treatments, together with repeated calls for greater patient autonomy and choice by consumer advocacy groups. The PCC and SDM approaches were driven by the need to reorient and redesign an increasingly fragmented system of health-care in order to face these challenges[1-4].

PCC and SDM

The concept of PCC began attracting increasing attention from the 1990s as a result of two landmark publications by the Picker Institute and the United States Institute of Medicine[5,6]. PCC began to be acknowledged as a central component of health-care when the Institute of Medicine included it as one on the six components of high quality care[6]. The principle attributes of PCC include responsiveness (sensitivity to patients' values and preferences), respect (according dignity to patients), autonomy (acknowledging patients' rights of informed choice), empowerment (enabling patient and family participation in care), collaboration (equal and supportive partnerships), holism (bio-psychosocial approach), individualization (personalized care), communication (information sharing), access, coordination and continuity of care[1-3,7,8]. SDM is derived from the PCC paradigm and is based on the same guiding principles of patient autonomy, informed choice and collaborative alliances between with clinicians[9-14]. Additionally, it is an evidence based and patient-centred process of decision-making consisting of information sharing, elicitation of patients' preferences, mutual deliberation and agreement on the treatment decisions between patients and clinicians[9,15,16]. The traditional, paternalistic model of clinician-centred care, which was in vogue prior to these approaches, had been criticized for vesting power in the clinician to make all treatment decisions, often overlooking patients' preferences. In contrast, both the PCC[3,7,8,17] and SDM approaches[9,12,15,18] propagated power sharing and mutual responsibility for the treatment undertaken. Thus, they shifted the locus of care from the clinician to the patient and reduced the disparity between them. These attributes made these new approaches more ethical, more acceptable to patients, and enhanced their potential to improve health-care outcomes[3,4,18-20]. Not surprisingly, the notion of collaborative treatment alliances has constituted one of the chief components of PCC[1,3,7,21,22] as well as SDM[12,23-26]. Moreover, these constructs have led to a broader understanding of the concepts of treatment-adherence and engagement with services[2,8,26-28]. The principles of autonomy, holism and humanistic care espoused by the PCC[29-31] and SDM[18,19,26,32,33] models had always been a part of mental health care. In fact, a second report of the Institute of Medicine was devoted exclusively to the application of principles of PCC to mental and substance use disorders[29,34]. Nevertheless, implementation of both PCC and SDM in mainstream psychiatric practice has been poor and there is limited research regarding their impact on mental health outcomes[18,26,32,33,35].

TREATMENT ALLIANCE IN PSYCHIATRIC PRACTICE

The concept of treatment alliance in psychiatry has its origins in psychoanalysis and psychotherapy[36-39]. However, rather than the transference based psychoanalytic concepts of therapeutic relationships, psychiatry has found it easier to adopt the pan-theoretical construct of working alliance proposed by Bordin[40], which focuses on a "here and now" approach to alliance. The central characteristic of working alliance which determines its beneficial effects is therapist and client collaboration. Within this collaborative framework working alliance is composed of three elements: An affective bond between the client and the therapist, mutually shared goals, and agreement on treatment tasks. However, even this concept is not easily extrapolated to routine psychiatric

practice because of several differences between psychotherapeutic and psychiatric settings[37,39,41-43]. These include a wider range of patients, professionals and settings; greater variability in treatment goals and interventions; and, differences in frequency and duration of contact in clinical practice. Patients with severe illnesses compromised awareness and increased risks of harm to self or others pose the greatest problems for establishing a working alliance. The necessity for use of coercive treatment measures in this group directly conflicts with the clinician's role as a therapist. Consequently, a number of other theoretical constructs have been utilized to establish the concept of alliance in psychiatry. Apart from the PCC and SDM models, these have included theories of health-behaviour, newer concepts of medication-taking such as concordance, and the use of recovery-orientated approaches to define the success of psychiatric treatment[41,44-46]. However, regardless of the conceptual framework it amply clear that collaborative partnerships, personal bonds and mutual agreement on tasks and goals between patients and clinicians lie at the heart of the treatment alliance in psychiatry. Moreover, these are the very same characteristics that determine the positive impact of effective alliances on several treatment outcomes including adherence to treatment. A systematic review by Thompson and McCabe[45] identified 10 studies, which had examined the association between treatment alliance and adherence. The majority of the studies had been conducted among patients with either depression or psychosis, while only three had included patients with bipolar disorder (BD). Eight of these 10 studies found a significant association between adherence and some component of the treatment alliance. A collaborative relationship, agreement on treatment tasks and stability of the alliance were the more salient determinants of adherence with treatment.

TREATMENT ALLIANCE AND ADHERENCE IN BD

The changing concepts of treatment-adherence

Newer approaches to medication-taking in chronic illnesses had also started to emerge around the 1990s. Much like PCC, a patient-centred view of treatment-adherence began to replace the earlier illness-centred orientations as it gradually became apparent that patients' views on medication-taking played a central role in determining adherence[47]. This change was driven by years of research on predictors of non-adherence, which revealed that demographic, clinical and treatment related determinants were not able to fully account for the extent of non-adherence. Simultaneously, the emergence of a number of health-behaviour models prompted a move away from biomedical to bio-psychosocial approaches to adherence[48]. This put the emphasis back on patients' perceptions, the clinician patient relationship, and on other influences in the patient's sociocultural environment. Eventually, traditional compliance-based approaches to medication-taking which were rooted in unequal and paternalistic clinician patient relationships, gave away to adherence and concordance based approaches[49]. The concepts of concordance, PCC and SDM are all based on the common principles of collaboration, responsiveness, open communication and mutual agreement on treatment between patients and clinicians[8,24,25,28]. It was therefore not surprising that psychiatry readily embraced these concepts in an effort to deal with the common and unrelenting problem of treatment non-adherence[50-53]. More pertinently, concordant and collaborative approaches to treatment have currently gained widespread recognition in the existing research on adherence in BD[44,54-57].

The association between treatment alliance and adherence in BD

Despite this recognition the evidence linking treatment alliance with adherence is still quite limited in BD, especially compared to other psychiatric and medical disorders. The table below summarizes this research.

The majority of studies included in the Table 1 have found a positive association between alliance and medication-adherence, while only five have failed to find such an association[58,59,67-69]. However, there was considerable variation in study designs. Measures of medication-adherence linked with alliance have varied from patient reports or clinician ratings, to persistence with treatment, dropout rates, missed medication days, and adherence with appointments or service engagement. Only about half of the studies have used validated scales of alliance; the rest have relied on self-designed questionnaires, treatment-attitude scales, or ratings of therapist interventions. Similar to studies of treatment alliance in other psychiatric disorders, the Working Alliance Inventory, based on Bordin's construct, was the most common scale used[45]. However, such overreliance on one instrument may have limited the scope of findings[37]. Though prospective studies are better indicators of the alliance-adherence link, three studies with longitudinal designs were unable to demonstrate an association between alliance and adherence on follow-up despite finding a positive association at baseline[69,72,76]. Finally, quite a few of the studies had small sample sizes and almost all included hospital attendees rather than community based patients, which meant that the results were not readily applicable to all patients with BD. Thus, the somewhat inevitable conclusion from these studies is that though there is definite evidence linking treatment alliance with adherence in BD, an unequivocal association between the two is still lacking.

Fortunately though, several other types of studies have endorsed the notion that effective treatment alliances have an important bearing on treatment-adherence in BD. Frank *et al*[78] provided their subjective impressions about "alliance building" among patients with mood disorders undergoing trials of acute and

Table 1 Treatment alliance and adherence in bipolar disorder

Ref.	Details of the studies	Findings
Connelly *et al*[58], 1982	48 outpatients on lithium; cross-sectional study; adherence by serum levels; alliance by self-designed questionnaire based on the HBM	Satisfaction with the clinician and perception of continuity of alliance was not associated with medication adherence. Perception of continuity linked to appointment adherence
Connelly *et al*[59], 1984	75 outpatients on lithium; cross-sectional study; adherence by serum levels and SCQ; alliance by self-designed questionnaire	Satisfaction with the clinician and perception of continuity of alliance was not associated with medication adherence. Perception of continuity linked to appointment adherence
Cochran and Gitlin[60], 1988	48 outpatients on lithium; cross-sectional study; adherence by self-report questionnaire; alliance as a part of an "Attitude Questionnaire"	Treatment alliance and positive attitudes to treatment explained about half of the variance in adherence. Alliance mediated the relationship between attitudes and adherence
Ludwig *et al*[61], 1990	118 outpatients and inpatients; 37 with BD; cross sectional study; adherence by physician judgment; alliance by two attitude scales: COSS and KK Skala	Adherence was associated with "reliance on the physician" using the COSS scale, but not with the KK Skala scale
Lee *et al*[62], 1992	50 Chinese outpatients on lithium; cross-sectional study; adherence by serum levels, case-notes review and patient reports; knowledge by self-designed questionnaire	A high rate of adherence was found despite inadequate knowledge about lithium. Authors concluded that an effective treatment alliance was of greater importance in ensuring adherence than imparting information
Taylor *et al*[63], 2001	30 trial patients on maintenance lithium treatment and psychotherapy; cross-sectional study; adherence by RBC lithium levels; alliance by TATIS scale to assess therapists' techniques	TATIS scores were significantly associated with RBC lithium levels. Medication adherence improved with increased focus on collaborative relationship building, positive treatment-attitudes, acceptance of BD and necessity for long-term treatment
Kleindienst and Greil[64], 2004	171 trial patients on lithium or cabamazepine; 2.5 yr follow-up; adherence indexed by time to dropout; alliance by the ICS scale	Trust in medications, trust in clinicians and absence of negative treatment expectations were associated with longer time to dropoutin those on lithium, but not carbamazepine.
Patel *et al*[65], 2005	32 African-American and Caucasian adolescent outpatients; cross-sectional study; adherence by patient reports and from records; alliance by subjective perceptions of medications and mental health contact helpfulness	Medication adherence in African-American adolescents was significantly correlated with ratings of drug usefulness and helpfulness of mental health contacts. Helpfulness of mental health contacts was not associated with adherence among Caucasian adolescents
Guandiano and Miller[66], 2006	61 trial patients on medications and family intervention; 28 mo follow-up; adherence indexed by number of months in treatment; alliance by WAI - P and C versions	Alliance was associated with number of months in treatment, dropout rate, percentage of time depressed and expectations from treatment
Sajatovic *et al*[67], 2006	184 trial inpatients; cross-sectional study; adherence by patient interviews; alliance by WAI - P and C	Alliance scores did not differ between adherent and non-adherent groups
Lecomte *et al*[68], 2008	118 patients from early intervention services; 13 with BD; cross-sectional study; adherence by the MAS scale; alliance by WAI-P	Alliance scores were not associated with medication adherence but predicted poor service engagement
Sajatovic *et al*[69], 2008	302 trial patients; 3 yr follow-up; adherence by patient interviews; alliance by WAI - P and C	Alliance scores did not differ between adherent and non-adherent groups
Zeber *et al*[70,71], 2008 and 2011	435 inpatients and outpatients; cross-sectional study; adherence by patient-report of missed medication days and MMAS; alliance by HCCQ	Overall alliance scores were associated with self-report of missed medication days and individual items of the HCCQ were linked to MMAS and missed medication days
Perron *et al*[72], 2009	429 inpatients and outpatients; 1 year follow-up; adherence by MMAS; alliance by HCCQ	Treatment alliance demonstrated a small but significant association with medication at baseline, but not at follow-up
Cely *et al*[73], 2011	124 outpatients; cross-sectional study; adherence by MMAS; alliance by self-designed questionnaire	A negative perception of the treatment alliance among patients was significantly more common in the non-adherent group compared to the adherent group
Sylvia *et al*[74], 2013	3037 outpatients from the STEP-BD study; 1 yr follow-up; adherence by a clinical monitoring form; alliance by HAQ	Patients' perceptions of the strength of the treatment alliance were associated with adherence Perceptions of collaboration, empathy and accessibility were the elements of the alliance linked to adherence
Kassis *et al*[75], 2014	628 inpatients and outpatients; 76 with BD; cross-sectional study; adherence by patient-report and from records; alliance by PDRQ	Patients in the adherent group were more satisfied with their psychiatrists, including availability and accessibility of psychiatrists and agreement with them on symptoms
Kutzelnigg *et al*[76], 2014	891 outpatients on olanzapine and mood-stabilizers; 2 yr follow-up for 657 patients; adherence by clinician judgments; alliance by self-designed scale	Patients in the highly adherent group had a better treatment alliance than those in the non-adherent group at baseline but not during the follow-up period
Novick *et al*[77], 2015	903 outpatients on olanzapine; 291 with BD; 1 yr follow-up; adherence by MARS; alliance by WAI-C	Alliance scores were associated with medication-adherence both at baseline and after 1 yr of follow-up

COSS: Compliance self-rating scale; HAQ: Helping alliance questionnaire; HBM: Health belief model; HCCQ: Health care climate questionnaire; ICS: Illness concept scale; KK Skala: Krankheits konzept skala; MARS: Medication adherence rating scale; MAS: Medication adherence scale; MMAS: Morisky medication adherence scale; PDRQ: Patient doctor relationship questionnaire; SCQ: Standardized compliance questionnaire; STEP-BD: Systematic treatment enhancement program for bipolar disorder; TATIS: Treatment adherence training interventions scale; WAI - P and C: Working alliance inventory - patient and clinician versions.

maintenance treatment. They noted that information-exchange, active patient participation and collaborative decision-making all promoted alliance and led to very high rates of medication-adherence and low dropout rates. Havens and Ghaemi[79] stated that a sound treatment alliance could have inherent mood stabilizing effects and could supplement the benefits obtained by medication treatment of BD. Scott and Tacchi[80] have shown that psychosocial interventions promoting concordant relationships have the ability to enhance medication-adherence in BD. Finally, findings from qualitative studies have found that a successful clinician patient relationship is one of the most important determinants of adherence in BD[81-84]. However, many participants of these studies seem to have found such healthy relationships hard to come by, and mostly reported unhelpful and frustrating interactions with mental health professionals[85-87].

COMPONENTS OF AN EFFECTIVE TREATMENT ALLIANCE IN BD

Since treatment alliance is a multi-dimensional concept, an understanding of specific aspects of the alliance that influence medication-taking may inform efforts to prevent non-adherence[45]. Studies of BD have revealed the following as the principal components of an effective alliance, which have a bearing on adherence.

PCC

First and foremost a successful alliance in BD is built on the principles of PCC[44,88,89]. Studies of BD have shown that patients favour a patient-centred approach and may be less likely to engage in treatment when faced with paternalistic and authoritarian approaches based on the traditional medical model[90-92]. Awareness and sensitivity to views of patients is also crucial to a patient-centred approach[74]. A large number of studies of BD have shown considerable differences between views of patients and clinicians regarding medication-taking[81,93-96]. It is obvious that this clinician patient divide can only be overcome if clinicians are aware of patients' views and preferences and respond to them appropriately[44].

Collaboration

A collaborative clinician patient relationship appears to be one of the principal facets of treatment alliance that fosters adherence in BD[44,57,97]. Sylvia *et al*[74] found that more than any other aspect of alliance, patients' perceptions of collaboration in their relationships with clinicians was associated with adherence in BD. In another qualitative study, patients with BD felt that interactive relationships with their clinicians, based on equal participation and sharing of responsibilities were more likely to result in adherence[82]. Similar results have been obtained by several other studies of BD[75,78,84,96,98]. The most compelling evidence however, comes from the growing evidence of the efficacy of psychosocial interventions in augmenting treatment-adherence in BD[99,100]. It has been proposed that the efficacy of psychosocial treatments largely stems from their collaborative and patient-focused elements[44,57,101].

SDM

Similar to PCC, SDM is not only one of key components of an efficacious treatment alliance in BD, but also the one most likely to influence adherence[56,88,102,103]. However, literature on SDM in BD is sparse. A recent systematic review found only 13 studies on the subject[89]. Nevertheless, these studies have shed light on several important aspects of SDM in BD. This review found that most treatment related decisions in BD involved those pertaining to adherence. The greater part of patients with BD preferred a SDM approach and wanted information about treatment choices, but many relied on their clinicians to take the final treatment related decisions. Certain demographic factors such as age, gender, educational level and ethnicity had some bearing on preferred involvement in SDM, though the findings were not always consistent. Similarly, it was not clear whether patients with BD sought greater involvement in decision-making than patients with other psychiatric disorders. Symptom severity, rather than diagnosis appeared to have a greater impact on patient involvement in SDM. However, regardless of the preferred level of involvement, almost all patients reported that SDM was not as commonly practiced in actual clinical settings as they had wanted. Though the implementation of SDM was low in routine care, collaborative decision-making was more likely if decisions were of complex nature and when patients initiated the process. Patients also wanted clinicians to pay attention to both interpersonal and affective elements of SDM. A sound alliance based on SDM was associated with a number of positive outcomes, mostly greater patient satisfaction, while the association with treatment-adherence was found in only two studies[74,104]. These findings were remarkably similar to what has been found among patients with medical illnesses[8,18,105,106], as well as those with other psychiatric disorders[23,25,33,107,108]. Moreover, a similar profile of patient preferences, patient and clinician involvement in SDM, and low implementation of SDM in clinical practice has been found in a number of other quantitative[109-112] and qualitative studies of BD[82-84,92,98], as well as surveys of patients with BD[96,113]. Another aspect that deserves mention is the use of decision-aids to further the process of SDM in BD. Decision-aids are tools based on updated evidence, which help patients compare different treatment options and provide them structured assistance through all steps of SDM[34,114]. Though decision-aids have been used for other psychiatric disorders[23,25,34,107], they have not yet been developed for BD[115]. A particular concern about the use

of SDM among patients with psychiatric disorders has been the problem of decisional incapacity. When acutely ill, patients might not have the capacity of making proper decisions; this may represent a significant barrier to application of SDM to psychiatric disorders. Advance directives have been proposed as a solution to this dilemma. They are documents completed by patients while still in possession of decisional capacity, regarding treatment decisions that could be made on their behalf in the event they lose the ability to make proper decisions when they are acutely ill. Some efforts have been made to implement advance directives among patients with schizophrenia[25,108], but research on such directives in BD is still at a very preliminary stage[116].

Communication

Constructive communication practices, referred to as collaborative or participatory styles of communication are based on the PCC and SDM approaches[8,45,117,118]. A participatory style of communication not only helps in building a strong alliance, but also has a positive effect on treatment-adherence by promoting positive attitudes to treatment among patients[44,45]. A meta-analysis among patients with various medical conditions found that communication practices of physicians were significantly associated with adherence and poor communication led to a 19% increase in non-adherence[119]. The review by Thompson and McCabe[45] found treatment-adherence to be associated with some or the other aspect of communication practices in eight of the 12 studies of patients with psychiatric disorders. Collaborative communication has a significant impact on adherence among patients with BD as well[44,97,120]. A two-way communication between the patients and clinicians allowing open discussions and free expression of patients' concerns appear to be the main constituents of a beneficial communication pattern in BD[78,89,98,121]. Exchange of information, particularly about medications is also accorded high priority by patients[83,96,98,113,122]. Other clinician attributes considered important by patients with BD include clinicians' ability to listen to, understand and value their views on medication-taking, along with flexibility regarding treatment options and devoting sufficient time to treatment related discussions[75,82,89,96,121].

Trust and support

Trust in the clinician is considered an important aspect of a successful alliance in BD[101,103]. Kleindienst and Greil[64] found that trust in the clinician was associated with lower dropout rates among patients on maintenance lithium treatment. Trusting and collaborative clinician-patient relationships can enhance adherence by fostering improved treatment-attitudes and aiding effective decision-making[75,82,84,86,123]. Both emotional and practical support are also essential components of a healthy alliance in BD. Strauss and Johnson[124] found that productive treatment alliances were associated with greater levels of social support among patients with BD. Similarly, the importance of a supportive relationship with the clinician in alliance building has formed a major theme in several qualitative studies of BD[83,98,125].

Stability and continuity

Continuity of care, ideally by a single treatment-team, frequent follow-ups and longer sessions with patients have all been emphasized as crucial elements of a alliance in BD[56,57,120]. Zeber *et al*[70] found that treatment-adherence was better when clinicians remained in constant contact with their patients and regularly monitored their patients' progress. Patient perceptions regarding continuity of care were found to be associated with attendance rates in other studies of BD[58,59]. Patients with BD also consider stability, consistency and continuity of treatment alliances as critical influences on their medication-taking behaviour[83,85,92,98].

Self-management

The recovery-orientated approach to care is currently being promoted as an key element of care in psychiatric disorders including BD. One aspect of recovery-orientated care is its emphasis on self-management or self-directed care[126]. Self-management strategies are adopted by many patients with BD and are also essential components of psychosocial treatments for BD[44,127]. Promoting self-management has thus been advocated as a necessary component of effective alliances in BD[88,89].

MEDIATORS OF THE ALLIANCE-ADHERENCE LINK IN BD

The positive association between treatment alliance and adherence in BD could be attributed to a number of intervening variables or mechanisms. An effective alliance results in less negative attitudes, a greater acceptance of illness, and the ability to tolerate medication side effects eventually leading to improved adherence[44,60,61,123,124]. Other potential mediators, which have demonstrated a positive association with treatment alliance in BD include reduction of symptom severity[66,72,77,124,128], enhancement of insight[77], and improvement in patient functioning or quality of life[72,77,129]. Certain psychosocial processes could also mediate the association between alliance and adherence. An efficacious treatment alliance has been linked with increased patient satisfaction[74,83,123,128,129], positive treatment expectancies[64,66], reduced stigma[124], improved self-efficacy[128], higher levels of perceived support[124,125], and some aspects of locus of control among patients with BD[130]. However, the association between all these variables and alliance in BD has often been inconsistent and largely correlational than causal. Therefore, there is still considerable uncertainty about the mechanisms underlying the beneficial effects of a successful alliance on adherence in BD.

IMPLICATIONS FOR RESEARCH AND PRACTICE

Despite the sizeable body of literature on treatment alliance and related concepts such as PCC and SDM, there is still considerable scepticism in the field of mental health regarding these approaches because of the lack of conceptual uniformity and clarity, uncertainty regarding their impact on salient patient outcomes such as treatment-adherence and barriers to their optimum implementation in routine psychiatric settings[15,44,89,108]. Doubts have also been raised about the cross-cultural validity of these concepts[89,131-133]. This is especially true for BD, where research lags behind other medical and psychiatric disorders in all these aspects. Nevertheless, several implications of the existing evidence are reasonably clear for clinicians as well as researchers. It has to be acknowledged that the locus of health-care has irrevocably shifted from the clinician to the patient. Therefore, professionals would do well to be aware of the essentials of alliance building and follow these principles in order to build productive alliances with their patients. Not only is this the right approach, but it is probably the most effective one while confronting the ubiquitous problem of non-adherence in BD. Priorities for further research are reaching a consensus on what constitutes an effective alliance in BD, establishing the connection between alliance and adherence more firmly, and working out the processes underlying this link. The success of such research endeavours will hold the key to developing successful alliances and effective treatments, both of which may reduce the burden of non-adherence in BD.

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