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REVIEW

Treatment-adherence in bipolar disorder: A patient-centred approach

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Abstract

About half of the patients diagnosed with bipolar disorder (BD) become non-adherent during long-term treatment, a rate largely similar to other chronic illnesses and one that has remained unchanged over the years. Non-adherence in BD is a complex phenomenon determined by a multitude of influences. However, there is considerable uncertainty about the key determinants of non-adherence in BD. Initial research on non-adherence in BD mostly limited itself to examining demographic, clinical and medication-related factors impacting adherence. However, because of inconsistent results and failure of these studies to address the complexities of adherence behaviour, demographic and illness-related factors were alone unable to explain or predict non-adherence in BD. This prompted a shift to a more patient-centred approach of viewing non-adherence. The central element of this approach includes an emphasis on patients' decisions regarding their own treatment based on their personal beliefs, life circumstances and their perceptions of benefits and disadvantages of treatment. Patients' decision-making processes are influenced by the nature of their relationship with clinicians and the health-care system and by people in their immediate environment. The primacy of the patient's perspective on non-adherence is in keeping with the current theoretical models and concordance-based approaches to adherence behaviour in BD. Research over the past two decades has further endorsed the critical role of patients' attitudes and beliefs regarding medications, the importance of a collaborative treatment-alliance, the influence of the family, and the significance of other patient-related factors such as knowledge, stigma, patient satisfaction and access to treatment in determining non-adherence in BD. Though simply moving from an illness-centred to a patient-centred approach is unlikely to solve the problem of non-adherence in BD, such an approach is more likely to lead to a better understanding of non-adherence and more likely to yield effective solutions to tackle this common and distressing problem afflicting patients with BD.

Key words: Non-adherence; Bipolar disorder; Attitudes; Health-beliefs; Treatment-alliance; Familial influences; Knowledge; Stigma

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Core tip: Treatment non-adherence in bipolar disorder (BD) is a complex phenomenon determined by a multitude of influences, but its critical determinants are yet to be identified with certainty. Demographic and illness-related factors have not been able to explain or predict non-adherence in BD. On the other hand, patient-centred variables such as attitudes and beliefs regarding medications, treatment-alliance, family attitudes, knowledge, stigma and access to treatment may be the more seminal influences on medication-taking in BD. A move from an illness-centred to a patient-centred approach is more likely to lead to a better understanding and more effective solutions for non-adherence in BD.

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INTRODUCTION

To write prescriptions is easy, but to come to an understanding with people is hard. A country doctor: Franz Kafka, 1917.

Bipolar disorder (BD) is a commonly prevalent and enduring condition characterized by recurrent episodes and often followed by residual symptoms. The high rates of comorbidity, suicide and functional impairment in BD also ensure that it is a common cause of disability as well as economic and social burden[1,2]. Pharmacological treatments are efficacious in both acute and long-term treatment of BD in clinical trials of these medications. Nevertheless, the effectiveness of medication treatments, particularly long-term treatment with medications is less impressive in day-to-day practice. Inadequate treatment-adherence is the single most important hurdle in translating efficacy in research settings into effectiveness in clinical practice[3]. In common with other chronic medical conditions with intermittent symptoms and delayed effects of discontinuing treatment, non-adherence is widespread in BD and is associated with several adverse consequences. Apart from undermining the usefulness of treatment and leading to poor outcomes, non-adherence also increases the risk of relapse, re-hospitalization and suicide several folds[2,4]. Non-adherence in individuals with BD leads to greater utilization of health-care services and increased mental health expenditures[5-7]. Finally, the poorer quality of life, stigmatization and functional impairment which accompany non-adherence lead to added burden on the family and society as a whole[8].

HOW COMMON IS NON-ADHERENCE IN BD?

Adherence has been defined as "the extent to which a person's behaviour, taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a health care provider"[9]. Studies of BD have largely focused on medication non-adherence rather than other aspects of treatment-adherence. Not surprisingly, there is a considerable variation between the rates of such non-adherence ranging from universal adherence in some studies to more or less universal non-adherence in others[10-12]. Much of this variability in rates can be attributed to methodological differences across studies. Adherence has been defined and assessed differently in different studies. Studies also differ in the settings in which they have been conducted (*e.g.,* clinics or community), in their designs (*e.g.,* cross-sectional or longitudinal), in the patient samples included, and in the phase of illness or the duration during which non-adherence has been estimated[13-17]. Extremely high or low rates have usually been obtained from studies with small patient samples and from specialized settings, or from randomized controlled trials of medication efficacy[10-12,18-20]. If these extremes are ignored most studies report non-adherence rates from 20% to 50%, with a few reporting rates from 60% to 70% for all patients with BD[21-23]. This is very similar to the estimates of several reviews on the subject, which conclude that on the average about 40% to 50% of patients with BD (range 9%-66%) do not take their medications regularly[2,4,24-28]. These rates are essentially the same regardless of whether patients are on mood stabilizers or antipsychotics. Moreover, rates of non-adherence seem to have remained unchanged or even increased over the years despite the introduction of several new medications[1,4,13,26,29]. The fact that about half of patients with BD become non-adherent during long-term treatment puts it on par with several other chronic psychiatric and medical disorders[4,9,30-32]. Moreover, a large part of this commonly prevalent non-adherence remains undetected in real-world treatment of BD as well; clinicians appear to be particularly likely to underestimate non-adherence among their patients[17,33-36]. However, the blame for lack of detection in day-to-day practice cannot be entirely laid at the clinician's door, because it is notoriously difficult to predict who is likely become non-adherent. Non-adherence is obviously a complex phenomenon determined by a multitude of influences. However, despite best efforts it is still unclear as to which of these factors is most critical in determining non-adherence in BD[4,13,26].

DEMOGRAPHIC AND ILLNESS-RELATED DETERMINANTS OF NON-ADHERENCE IN BD

In a seminal article about 40 years ago Jamison *et al*[37] proposed four mutually interacting domains to explain non-adherence to prescribed lithium among patients with BD. These included factors related to the patient (*e.g.*, demographic characteristics), the illness (*e.g.*, severity), the effect of medications (*e.g.*, side effects) and characteristics of the clinicians (*e.g.*, relationship with patients). These determinants have been subsequently adopted by others working in the field, but some significant additions have been made in each category. For example, patient-related factors have come to include personal attitudes and beliefs about medication-taking in addition to demographic factors. Clinician-related factors has been broadened to include an environmental domain, which encompasses the influence of clinician-patient interactions and health-system related factors on adherence, as well as the influence of the family and significant others in the patient's life[13,25,28,38,39].

In the 1980s and 1990s research on treatment non-adherence amongst those diagnosed with psychiatric disorders including BD mostly limited itself to examining demographic, clinical and medication-related factors impacting adherence[2,17,38,40]. The exclusive focus on these factors appeared to be driven by biologically and medically orientated conceptualizations of the illness, although the primacy of the biological approach had been the object of criticism for long. Unfortunately, these efforts to predict non-adherence on the basis of demographic and illness-related factors were not very successful[40-44]. This failed quest could be due to several reasons, the principal one being the equivocal and inconsistent results obtained from different studies[40,45,46]. For example, although certain demographic correlates have emerged as likely determinants in some studies[4,26,27,42], several other studies have found no association between demographic variables and non-adherence in BD[17,47-51]. Among individual demographic attributes there has been some evidence for an association of non-adherence in BD with younger age[13,27,39,52,53], minority ethnicity[7,54-58], and social disadvantage[27,34,52,56,57,59], but the evidence for such links is either limited or often contradictory[2,4,34,38,48,49,60]. The role of clinical factors in determining non-adherence in BD seems to have been similarly inconsistent and ambiguous[42,61]. Overall severity of the illness in terms of symptom-burden, greater number of episodes and prior hospitalizations appeared to influence non-adherence in some[25,27,28,35,62], but not all studies[2,16,47,51,59]. A majority of studies among patients with BD found that poor insight and denial of the illness was associated with non-adherence[4,24,26,38,63-65]. However, though it might be difficult for a patient to be adherent without a basic level of insight, simply having insight may not be sufficient to ensure adherence[1,16,36,65,66]. The presence of comorbid disorders, particularly substance use disorders has also emerged as a consistent correlate of non-adherence in BD[26,28,39,42,46], but the evidence for associations with most other clinical variables has been either scarce or inconsistently replicated[35,62,67-70]. Among medication-related factors the role of the efficacy-tolerability balance in determining adherence has been the focus of most studies in BD. A large number of studies have found that treatment side effects negatively influenced adherence in BD[7,35,46,59,70], though many of these have exclusively investigated the side effects of lithium[34,67,71-74]. On the other hand, an almost equally large number of studies and patient surveys have revealed that side effects are not associated with non-adherence in BD[2,4,26,27,39,75]. It appears that fear or concerns regarding side effects rather than their actual prevalence may be more important in determining non-adherence in BD[17,26,41,45,76,77]. The influence of treatment-efficacy on adherence has been examined less often, though some studies suggest that medications alleviating depressive symptoms are more likely to promote adherence[7,51,78-80].

The uncertain influence of clinical and demographic factors on adherence in BD could also be due to the fact that many of the studies examining this association have failed to take into account complex interactions between several such variables, which could eventually determine the risk of non-adherence in BD[28]. For example, the higher prevalence of non-adherence during manic episodes could well be due to a lack of insight or the presence of cognitive impairment during such episodes[1,4,41]. Similarly, the greater risk of non-adherence in men could be related to the more frequent use of substances among them[81,82]. Additionally, the simple and dichotomous categorizations of demographic, clinical and treatment-related factors adopted by these studies ignored the subjective experience of medication-taking and the importance of factors such as attitudes and health-beliefs, which might underlie the link between demographic and clinical factors and non-adherence[28,81,83]. Accordingly, there is ample evidence to suggest that variables such as age, gender, severity of illness, effects of substance use, side effects and other treatment-related factors may impact adherence through their effects on subjective patient experiences such as their attitudes to medications, their knowledge of the illness and the availability of social support[2,19,51,84-88]. Moreover, while certain demographic and clinical variables such as young age, symptom-severity, substance use comorbidity and lack of insight may be useful in delineating groups at high risk for non-adherence, they do not accurately predict non-adherence at the level of the individual patient[11,40,41,45]. Finally, because many of these factors may not be amenable to change they do not provide opportunities for adherence enhancement through targeted psychosocial interventions[48,49]. These limitations of attempting to predict and target non-adherence based on demographic and illness-related factors indicates the need for an alternative perspective on treatment-adherence. The newer perspective lays greater emphasis on the patient's point of view of medication-taking, while acknowledging that problems with adherence are likely to be determined by complex interactions between the patient, the illness, its treatment and the wider socio-cultural environment in which such treatment takes place[11,27,41,61].

A PARADIGM SHIFT TO A PATIENT-CENTRED APPROACH TO ADHERENCE IN BD

As with other chronic medical conditions, research on predictors of non-adherence in BD over the last two decades has undergone a gradual shift in thinking from an illness-centred to a patient-centred approach[40,89]. In this patient-centred paradigm, adherence is viewed as a dynamic rather than a static process which is influenced by many factors within and outside the patient[2,13,26,42,43]. At the core of this process lie the patients' abilities to make decisions about their own treatment[11,27,90]. Patients are the "final decision-makers" who have a right to choose whether or not continue treatment based on their own beliefs, personal circumstances and their perceptions of benefits and disadvantages of treatment. This right of patients to have a say in their treatment is acknowledged and prioritized in the patient-centred approach to medication-taking[2,7,27,32,50,90]. The emphasis on the patient's decision-making prompts a shift in the patient-clinician relationship to one in which both are equal and active collaborators. This approach is in keeping with the move away from earlier compliance-based models to those that place emphasis on concordant relationships between patients and clinicians[1,4,32,50,89,90]. While compliance-based paradigms treated patients as passive recipients of treatments and ignored the centrality of their viewpoints, the currently prevalent adherence- and concordance-based approaches place greater stress on the need for an agreement on decisions regarding treatment between patients and clinicians. The cornerstone of the concordance approach rests on open discussions of mutual views about taking medications, and a shared decision-making alliance between patients and clinicians while retaining the primacy of patients' choices. This shift in paradigms has been further propelled by the formulation of a number of health-behaviour models, which have been used to explain non-adherence in BD with a certain degree of success[11,41,45,76,90,91]. Though consisting of divergent social, cognitive and behavioural perspectives on adherence, they give central importance to the very same elements such as patients' attitude and health-beliefs, the treatment-alliance and factors in patients' immediate environments influencing adherence. Finally, the move from illness-related determinants to patients' perspectives on adherence has aided the development of several adjunctive psychosocial interventions to enhance medication-adherence in BD. These treatments, which use the framework of a collaborative alliance with patients and families to address non-adherence through educative, cognitive and behavioural means have had some success in optimizing adherence in BD[2,4,26,28,38,61].

PATIENT-CENTRED DETERMINANTS OF NON-ADHERENCE IN BD

Attitudes and beliefs regarding medications

In the research on adherence a distinction is often made between unintentional and intentional non-adherence. Unintentional non-adherence arises from personal or environmental restrictions which hamper medication-taking, while intentional non-adherence arises from patients' views on medications which affect their willingness to take them[92,93]. In an influential study, Horne and Weinman[94] categorized patients' beliefs about medications into general beliefs related to the intrinsic nature of medicines and ways in which medicines are used by doctors, and specific beliefs comprised of the perceived necessity of taking medications coupled with concerns about their adverse consequences. Both general health-beliefs and specific beliefs (attitudes) regarding medications have been examined among patients with BD. Barring a few exceptions[10,27,74,80,95], the majority of such studies of patients with BD have found that both health-beliefs and attitudes to medications are associated with non-adherence in BD[2,4,13,26,28]. Some of the studies have actually concluded that adverse attitudes and health-beliefs among patients have a much greater influence on non-adherence than demographic, illness or treatment-related factors such as side effects[17,26,45,51,76]. In other studies attitudinal factors such as doubts about the need for medications, as well as concerns about their adverse effects have been found to account for a substantial proportion of variance in intentional non-adherence[11,19,37,41,87,96]. All kinds of negative attitudes have been found in these studies though the commonest ones appear to be fear of side effects and harm caused by medications[17,19,37,51,75,97], denial of severity of illness and the need for treatment[11,41,46,86,98,99], the negative impact of long-term medications on daily routines and competing priorities of life[37,85,86,98,100,101], perceived ineffectiveness of medications[19,51,69,46,98,102], fears regarding dependence, being controlled or stigmatized by taking medications[35,37,60,75,103], and missing the pleasure experienced during manic episodes because of the mood-controlling effects of medications[37,44,101,104,105]. On the other hand, some patients perceive medications to be helpful and seem to realize the necessity of taking medications to prevent relapses, hospitalizations and other negative consequences[11,69,79,98,106,107]. Attitudes towards medications among patients might be relatively independent of their demographic and clinical characteristics[50,51,108,109], or they might differ according to age and illness-related factors such as the severity of the illness and its course, comorbid substance use and side effects of medications[85,100,110-113]. Additionally, patients' attitudes are more likely to be influenced by their knowledge of the illness, attitudes among their family members and ethno-cultural groups, the clinician-patient relationship and the overall quality of life among patients[35,60,84,101,103,114]. However, regardless of the substantial evidence in favour of attitudes and health-beliefs influencing adherence behaviour in BD, the number of studies is relatively small. Moreover, because of the cross-sectional designs and the small numbers of patients in most studies it is not possible to make any inferences about causality[41,86].

Treatment alliance

Apart from attitudes and health-beliefs the other principal influence on non-adherence in BD is the treatment-alliance between the doctors or clinicians and patients. The concept of the treatment-alliance as a collaborative and affective bond between clinicians and patients has its origin in psychoanalytic and psychotherapeutic literature[115,116]. In keeping with the research-evidence on treatment-alliance in psychotherapy and other psychiatric disorders such as schizophrenia[115-117], an effective alliance appears to have a significant influence on treatment-adherence in BD as well. Though research on the influence of treatment-alliance on adherence is relatively scarce, the more or less unequivocal finding from several studies is that a strong therapeutic alliance is associated with improved adherence among patients with BD[18,58,91,114,118-120]. A strong alliance appears to enhance treatment-adherence in BD in several ways such as fostering more positive attitudes to treatment and enhancing the acceptance of treatment among patients[1,2,13,14,26,78]. The importance of a genuinely collaborative alliance in determining adherence is also in accord with the current emphasis on the active involvement of patients in decision-making and concordance-based approaches to understanding adherence in BD[1,13,52,78,121]. Moreover, a patient-centred approach and a collaborative clinician-patient alliance appear to be essential ingredients of all psychosocial interventions designed to enhance adherence in BD[1,7]. Definitions of therapeutic alliance in psychotherapy have three common elements including the collaborative nature of the relationship, the affective bond between patients and therapists, and the patient's and therapist's ability to agree on treatment goals and tasks[115]. Research among patients with BD indicates that the very same components of treatment-alliance are intimately related to adherence behaviour. Forging a successful treatment-alliance in BD begins with a two-way, reciprocal communication between the patient and the clinician[18]. There are a number of studies among patients with BD showing that not only do clinicians tend to overestimate the degree of adherence among patients, but there is also considerable discrepancy between clinicians and their patients regarding the reasons for non-adherence as well as the meaning of non-adherence[3,24,43,76,96]. Clinicians might also fail to acknowledge the patient's concern or distress about long-term treatment. Therefore, clinicians first need to create an atmosphere in which patients are able to freely discuss their problems about taking medications. Clinicians also need to play an active role in attempting to understand the patient's views on illness and medication-taking. To further this open and active stance clinicians must not only listen more effectively, but also learn to value this communication with patients in order to forge effective links with them[18,26,107,122]. Empathy, compassion and skilful counselling are much valued by patients and positively associated with adherence in BD[120,123]. This bi-directional communication also forms the vehicle for imparting information about the illness and its treatment since patients frequently express the need for such information[75,106,122]. Moreover, information can be used to effectively dispel incorrect beliefs about medications, reduce feelings of stigma and foster positive attitudes to treatment among patients[50,114]. The other necessary component of an effective treatment-alliance is a genuinely collaborative relationship between the patients and clinicians. This collaborative relationship is built on respect for patients' rights to decide about their own treatment and a shared decision-making process with patients and clinicians as active and equal partners[8,18,121]. Evidence suggests that patients place substantial emphasis on this interactional component of the treatment-alliance and that the degree of agreement between clinicians and patients on decisions regarding treatment is a high priority for patients[18,122]. Adherence is also enhanced when both patients and clinicians agree on their roles and responsibilities within the alliance. Patients also want this interactional relationship to be flexible and responsive to changes in clinical status and their treatment needs[18]. Feelings of trust also help in building a strong treatment-alliance as studies have found that trust in medication, trust in the clinician and absence of negative treatment expectations are all associated with adherence in BD[85]. Other elements of importance are regular contacts and reviews by clinicians, ongoing support and the long-term stability of the clinician-patient relationship[49,58,106,114,124]. Finally, factors such as attitudes of patients about the illness and its treatment, their perception of the clinician, ethnic and cultural backgrounds of patients, expectations of patients and the extent to which these have been met, and personality attributes such as locus of control have emerged as some of the more significant influences on the treatment-alliance[60,86,114,118,125,126].

Knowledge about the illness and its treatment

Another potential determinant of adherence in BD is the knowledge about the illness and its treatment among patients. Lack of such knowledge is widespread and a prevailing source of dissatisfaction among patients with BD[75,101,106,113,127,128]. Patients appear particularly unhappy with the lack of information provided on side effects and other aspects related to medication-treatment[75,86,127-129]. Although enhancing knowledge should improve adherence among patients, results of studies in BD have been somewhat equivocal in this regard. While several studies have found that inadequate knowledge of the illness among patients appears to affect treatment-adherence[19,75,80,95,102,128], quite a few others have concluded that patients' level of knowledge is not associated with adherence in BD[10,34,51,84,118,130]. Similarly, psychosocial interventions imparting information in an effort to reduce non-adherence have met with mixed success[38,90,109,126,131,132]. There could be several reasons for these unexpected results including factors such as old age and longer duration of treatment, which influence the levels of knowledge and may act as potential confounders[10,19,84,86,130,133]. Insufficient knowledge could be due to insufficient efforts and ineffective means of imparting information by clinicians, as well as cognitive impairments, lack of insight and motivation among patients[127,128,134]. Patient's perceptions about their need for information and the extent to which these are met also have some bearing on adherence. Provision of information is more likely to be effective only if it is tailored to the specific needs of patients[128].

The role of the family and significant others

Families influence patients' medication-adherence in several ways. A disorganized or dysfunctional family environment has been associated with higher prevalence of non-adherence in BD[101,135,136]. A disturbed family atmosphere often leads to non-adherence by reducing the social support available to the patient[108,137]. Such an outcome would be more likely among patients who are more dependent on family members. This probably explains why a number of studies have found that patients with a greater external locus of control are more likely to become non-adherent[50,83,95,126]. Perceived criticism, negative affective responses and stigmatization or rejection within the family are also associated with non-adherence among patients with BD[75,138]. Finally, attitudes and health-beliefs of family members and their knowledge of the illness and treatment have been shown to have a significant influence of the patient's own beliefs and attitudes. Accordingly, negative attitudes and improper understanding of the illness among family members may affect the patient's decision whether or not to continue treatment[2,4,75,91,101,138].

Stigma, patient satisfaction and system-related factors

For many people with BD the stigma of having a chronic mental illness and needing to take long-term treatment for it may deter adherence. Consequently, studies among patients with BD have found their perceived sense of stigma to be associated with non-adherence[75,100,135,139]. Feelings of stigma regarding BD and its treatment also appear to promote negative attitudes towards treatment and adversely affect the treatment-alliance[114]. Patient satisfaction with various aspects of treatment has been found to be a determinant of non-adherence in BD. Dissatisfaction with the efficacy of treatment, with lack of information, with clinicians and with the treatment-alliance have all been found to adversely affect adherence in BD[59,80,106]. On the other hand, patients who are contended with their own lives are more likely to adhere with treatment[28,103,140]. Access to treatment and affordability of treatment also constitute significant barriers to continued adherence in BD. Bhugra *et al*[141] have suggested that only about half of the patients receive appropriate treatment BD because of systemic barriers to gaining access to appropriate care. This has been endorsed by the results of a number of other studies[38,49,80,101,119]. Finally, further elaboration of the concepts of shared decision-making, personal recovery and integrated or collaborative care are being increasingly applied to understand treatment-adherence in chronic medical disorders[142]. However, as of now these concepts have been only sparingly used to explain treatment-adherence in psychiatric disorders such as schizophrenia and depression. They have not yet been widely applied to BD. A discussion of the importance of these factors is thus beyond the scope of this brief review.

CONCLUSION

This brief examination of the literature on treatment-adherence in BD clearly suggests that research in this area is in the process of making a decisive shift towards the patient's perspective on non-adherence. Given the failure of demographic, illness and treatment-related factors to explain and predict non-adherence in BD, greater emphasis on factors such patients' attitudes and health-beliefs, the clinician-patient relationship and the impact of the immediate environment on treatment-adherence, certainly appears to be more appropriate. Moreover, such a stance is congruent with the current theoretical perspectives of adherence and concordance-based models of adherence. However, non-adherence continues to be rife in BD and simply adopting a patient-centred approach is unlikely to be a panacea for the problem. Nevertheless, it seems to be the only way forward for both research and clinical practice. Research focusing on non-adherence from the viewpoint of patients is more likely to lead to a greater understanding of this complex phenomenon in BD. A patient-centred approach also encourages clinicians to improve their understanding of the critical elements of adherence behaviour, to enhance their sensitivity to their patients' needs and to develop a collaborative and trusting relationship with them while attempting to tackle the problem of non-adherence. Thus, while there is no looking back to an earlier era of considering non-adherence to be only a patient's problem, we can only hope that adopting a patient-centred approach will lead us to find effective solutions to this common and distressing problem of non-adherence in BD.

REFERENCES

1 **Berk M**, Berk L, Castle D. A collaborative approach to the treatment alliance in bipolar disorder. *Bipolar Disord* 2004; **6**: 504-518 [PMID: 15541066 DOI: 10.1111/j.1399-5618.2004.00154]

2 **Berk L**, Hallam KT, Colom F, Vieta E, Hasty M, Macneil C, Berk M. Enhancing medication adherence in patients with bipolar disorder. *Hum Psychopharmacol* 2010; **25**: 1-16 [PMID: 20041478 DOI: 10.1002/hup.1081]

3 **Guscott R**, Taylor L. Lithium prophylaxis in recurrent affective

illness. Efficacy, effectiveness and efficiency. *Br J Psychiatry* 1994; **164**: 741-746 [PMID: 7952980 DOI: 10.1192/bjp.164.6.741]

4 **Colom F**, Vieta E, Tacchi MJ, Sánchez-Moreno J, Scott J. Identifying and improving non-adherence in bipolar disorders. *Bipolar Disord* 2005; **7** Suppl 5: 24-31 [PMID: 16225557 DOI: 10.1111/j.1399-5618.2005.00248]

5 **Gianfrancesco FD**, Sajatovic M, Rajagopalan K, Wang RH. Antipsychotic treatment adherence and associated mental health care use among individuals with bipolar disorder. *Clin Ther* 2008; **30**: 1358-1374 [PMID: 18691997 DOI: 10.1016/S0149-2918(08)80062-8]

6 **Rascati KL**, Richards KM, Ott CA, Goddard AW, Stafkey-Mailey D, Alvir J, Sanders KN, Mychaskiw M. Adherence, persistence of use, and costs associated with second-generation antipsychotics for bipolar disorder. *Psychiatr Serv* 2011; **62**: 1032-1040 [PMID: 21885581 DOI: 10.1176/appi.ps.62.9.1032]

7 **Johnson FR**, Ozdemir S, Manjunath R, Hauber AB, Burch SP, Thompson TR. Factors that affect adherence to bipolar disorder treatments: a stated-preference approach. *Med Care* 2007; **45**: 545-552 [PMID: 17515782 DOI: 10.1097/MLR.0b013e318040ad90]

8 **Rakofsky JJ**, Levy ST, Dunlop BW. Conceptualizing Treatment Nonadherence in Patients with Bipolar Disorder and PTSD. *CNS Spectr* 2011; **16**: 11-20 [PMID: 24725297 DOI: 10.1017/S1092852912000119]

9 **Sabate E**. Adherence to long term therapies: evidence for action. Geneva: World Health Organization, 2003

10 **McCleod MS**, Sharp DM. Precursors of compliance with lithium treatment in affective disorders. *Psychiatr Bull* 2001; **25**: 183-186 [DOI: 10.1192/pb.25.5.183]

11 **Clatworthy J**, Bowskill R, Rank T, Parham R, Horne R. Adherence to medication in bipolar disorder: a qualitative study exploring the role of patients' beliefs about the condition and its treatment. *Bipolar Disord* 2007; **9**: 656-664 [PMID: 17845282 DOI: 10.1111/j.1399-5618.2007.00434]

12 **Sylvia LG**, Reilly-Harrington NA, Leon AC, Kansky CI, Calabrese JR, Bowden CL, Ketter TA, Friedman ES, Iosifescu DV, Thase ME, Ostacher MJ, Keyes M, Rabideau D, Nierenberg AA. Medication adherence in a comparative effectiveness trial for bipolar disorder. *Acta Psychiatr Scand* 2014; **129**: 359-365 [PMID: 24117232 DOI: 10.1111/acps.12202]

13 **Crowe M**, Wilson L, Inder M. Patients' reports of the factors influencing medication adherence in bipolar disorder - an integrative review of the literature. *Int J Nurs Stud* 2011; **48**: 894-903 [PMID: 21481391 DOI: 10.1016/j.ijnurstu.2011.03.008]

14 **Gaudiano BA**, Weinstock LM, Miller IW. Improving treatment adherence in bipolar disorder: a review of current psychosocial treatment efficacy and recommendations for future treatment development. *Behav Modif* 2008; **32**: 267-301 [PMID: 18391049 DOI: 10.1177/0145445507309023]

15 **Jónsdóttir H**, Opjordsmoen S, Birkenaes AB, Engh JA, Ringen PA, Vaskinn A, Aamo TO, Friis S, Andreassen OA. Medication adherence in outpatients with severe mental disorders: relation between self-reports and serum level. *J Clin Psychopharmacol* 2010; **30**: 169-175 [PMID: 20520290 DOI: 10.1097/JCP.0b013e3181d2191e]

16 **Jónsdóttir H**, Opjordsmoen S, Birkenaes AB, Simonsen C, Engh JA, Ringen PA, Vaskinn A, Friis S, Sundet K, Andreassen OA. Predictors of medication adherence in patients with schizophrenia and bipolar disorder. *Acta Psychiatr Scand* 2013; **127**: 23-33 [PMID: 22900964 DOI: 10.1111/j.1600-0447.2012.01911]

17 **Scott J**, Pope M. Nonadherence with mood stabilizers: prevalence and predictors. *J Clin Psychiatry* 2002; **63**: 384-390 [PMID: 12019661 DOI: 10.4088/JCP.v63n0502]

18 **Sajatovic M**, Davies M, Bauer MS, McBride L, Hays RW, Safavi R, Jenkins J. Attitudes regarding the collaborative practice model and treatment adherence among individuals with bipolar disorder. *Compr Psychiatry* 2005; **46**: 272-277 [PMID: 16175758 DOI: 10.1016/j.comppsych.2004.10.007]

19 **Rosa AR**, Marco M, Fachel JM, Kapczinski F, Stein AT, Barros HM. Correlation between drug treatment adherence and lithium treatment attitudes and knowledge by bipolar patients. *Prog Neuropsychopharmacol Biol Psychiatry* 2007; **31**: 217-224 [PMID: 16982121 DOI: 10.1016/j.pnpbp.2006.08.007]

20 **Manwani SG**, Szilagyi KA, Zablotsky B, Hennen J, Griffin ML, Weiss RD. Adherence to pharmacotherapy in bipolar disorder patients with and without co-occurring substance use disorders. *J Clin Psychiatry* 2007; **68**: 1172-1176 [PMID: 17854240 DOI: 10.4088/JCP.v68n0802]

21 **Keck PE**, McElroy SL, Strakowski SM, Stanton SP, Kizer DL, Balistreri TM, Bennett JA, Tugrul KC, West SA. Factors associated with pharmacologic noncompliance in patients with mania. *J Clin Psychiatry* 1996; **57**: 292-297 [PMID: 8666570]

22 **Miasso AI**, do Carmo BP, Tirapelli CR. Bipolar affective disorder: pharmacotherapeutic profile and adherence to medication. *Rev Esc Enferm USP* 2012; **46**: 689-695 [PMID: 22773491 DOI: 10.1590/S0080-62342012000300022]

23 **Montes JM**, Maurino J, de Dios C, Medina E. Suboptimal treatment adherence in bipolar disorder: impact on clinical outcomes and functioning. *Patient Prefer Adherence* 2013; **7**: 89-94 [PMID: 23378745 DOI: 10.2147/PPA.S39290]

24 **Cochran SD**. Compliance with lithium regimens in the outpatient treatment of bipolar affective disorders. *J Compliance Health Care* 1986; **1**: 153-170

25 **Goodwin F**, Jamison JK. Manic depressive illness. New York: Oxford University Press, 1990

26 **Lingam R**, Scott J. Treatment non-adherence in affective disorders. *Acta Psychiatr Scand* 2002; **105**: 164-172 [PMID: 11939969 DOI: 10.1034/j.1600-0447.2002.1r084]

27 **Perlick DA**, Rosenheck RA, Kaczynski R, Kozma L. Medication non-adherence in bipolar disorder: a patient-centered review of research findings. *Clin Approaches Bipolar Disord* 2004; **3**: 56-64

28 **Leclerc E**, Mansur RB, Brietzke E. Determinants of adherence to treatment in bipolar disorder: a comprehensive review. *J Affect Disord* 2013; **149**: 247-252 [PMID: 23489403 DOI: 10.1016/j.jad.2013.01.036]

29 **Schou M**. The combat of non-compliance during prophylactic lithium treatment. *Acta Psychiatr Scand* 1997; **95**: 361-363 [PMID: 9197898 DOI: 10.1111/j.1600-0447.1997.tb09646]

30 **Cramer JA**, Rosenheck R. Compliance with medication regimens for mental and physical disorders. *Psychiatr Serv* 1998; **49**: 196-201 [PMID: 9575004]

31 **DiMatteo MR**. Variations in patients' adherence to medical recommendations: a quantitative review of 50 years of research. *Med Care* 2004; **42**: 200-209 [PMID: 15076819 DOI: 10.1097/01.mlr.0000114908.90348.f9]

32 **Chakrabarti S**. What's in a name? Compliance, adherence and concordance in chronic psychiatric disorders. *World J Psychiatry* 2014; **4**: 30-36 [PMID: 25019054 DOI: 10.5498/wjp.v4.i2.30]

33 **Stephenson BJ**, Rowe BH, Haynes RB, Macharia WM, Leon G. The rational clinical examination. Is this patient taking the treatment as prescribed? *JAMA* 1993; **269**: 2779-2781 [PMID: 8492406 DOI: 10.1001/jama.1993.03500210079036]

34 **Aagaard J**, Vestergaard P. Predictors of outcome in prophylactic lithium treatment: a 2-year prospective study. *J Affect Disord* 1990; **18**: 259-266 [PMID: 2140378 DOI: 10.1016/0165-0327(90)90077-L]

35 **Baldessarini RJ**, Perry R, Pike J. Factors associated with treatment nonadherence among US bipolar disorder patients. *Hum Psychopharmacol* 2008; **23**: 95-105 [PMID: 18058849 DOI: 10.1002/hup.908]

36 **Vieta E**, Azorin JM, Bauer M, Frangou S, Perugi G, Martinez G, Schreiner A. Psychiatrists' perceptions of potential reasons for non- and partial adherence to medication: results of a survey in bipolar disorder from eight European countries. *J Affect Disord* 2012; **143**: 125-130 [PMID: 22840608 DOI: 10.1016/j.jad.2012.05.041]

37 **Jamison KR**, Gerner RH, Goodwin FK. Patient and physician attitudes toward lithium: relationship to compliance. *Arch Gen Psychiatry* 1979; **36**: 866-869 [PMID: 454105 DOI: 10.1001/archpsyc.1979.01780080040011]

38 **Busby KK**, Sajatovic M. REVIEW: Patient, treatment, and

systems-level factors in bipolar disorder nonadherence: A summary of the literature. *CNS Neurosci Ther* 2010; **16**: 308-315 [PMID: 21050421 DOI: 10.1111/j.1755-5949.2010.00191.x]

39 **Depp CA**, Moore DJ, Patterson TL, Lebowitz BD, Jeste DV. Psychosocial interventions and medication adherence in bipolar disorder. *Dialogues Clin Neurosci* 2008; **10**: 239-250 [PMID: 18689293]

40 **Scott J**. Cognitive and behavioural approaches to medication adherence. *Adv Psychiatr Treat* 1999; **5**: 338-345 [DOI: 10.1192/apt.5.5.338]

41 **Clatworthy J**, Bowskill R, Parham R, Rank T, Scott J, Horne R. Understanding medication non-adherence in bipolar disorders using a Necessity-Concerns Framework. *J Affect Disord* 2009; **116**: 51-55 [PMID: 19101038 DOI: 10.1016/j.jad.2008.11.004]

42 **Basco MR**, Smith J. Faulty decision-making: impact on treatment adherence in bipolar disorder. *Primary Psychiatry* 2009: **16**: 53-58

43 **Mączka G**, Siwek M, Skalski M, Grabski B, Dudek D. Patients' and doctors' attitudes towards bipolar disorder – do we share our beliefs? *Archives of Psychiatry and Psychotherapy* 2010; **2**: 43-50

44 **Johnson SL**, Fulford D. Development of the treatment attitudes questionnaire in bipolar disorder. *J Clin Psychol* 2008; **64**: 466-481 [PMID: 18357575 DOI: 10.1002/jclp.20465]

45 **Scott J**. Using Health Belief Models to understand the efficacy-effectiveness gap for mood stabilizer treatments. *Neuropsychobiology* 2002; **46** Suppl 1: 13-15 [PMID: 12571427 DOI: 10.1159/000068022]

46 **Arvilommi P**, Suominen K, Mantere O, Leppämäki S, Valtonen H, Isometsä E. Predictors of adherence to psychopharmacological and psychosocial treatment in bipolar I or II disorders - an 18-month prospective study. *J Affect Disord* 2014; **155**: 110-117 [PMID: 24262639 DOI: 10.1016/j.jad.2013.10.032]

47 **Colom F**, Vieta E, Martínez-Arán A, Reinares M, Benabarre A, Gastó C. Clinical factors associated with treatment noncompliance in euthymic bipolar patients. *J Clin Psychiatry* 2000; **61**: 549-555 [PMID: 10982196 DOI: 10.4088/JCP.v61n0802]

48 **Sajatovic M**, Bauer MS, Kilbourne AM, Vertrees JE, Williford W. Self-reported medication treatment adherence among veterans with bipolar disorder. *Psychiatr Serv* 2006; **57**: 56-62 [PMID: 16399963 DOI: 10.1176/appi.ps.57.1.56]

49 **Sajatovic M**, Biswas K, Kilbourne AK, Fenn H, Williford W, Bauer MS. Factors associated with prospective long-term treatment adherence among individuals with bipolar disorder. *Psychiatr Serv* 2008; **59**: 753-759 [PMID: 18586992 DOI: 10.1176/appi.ps.59.7.753]

50 **Sajatovic M**, Ignacio RV, West JA, Cassidy KA, Safavi R, Kilbourne AM, Blow FC. Predictors of nonadherence among individuals with bipolar disorder receiving treatment in a community mental health clinic. *Compr Psychiatry* 2009; **50**: 100-107 [PMID: 19216885 DOI: 10.1016/j.comppsych.2008.06.008]

51 **Schumann C**, Lenz G, Berghöfer A, Müller-Oerlinghausen B. Non-adherence with long-term prophylaxis: a 6-year naturalistic follow-up study of affectively ill patients. *Psychiatry Res* 1999; **89**: 247-257 [PMID: 10708271 DOI: 10.1016/S0165-1781(99)00108-0]

52 **Frank E**, Prien RF, Kupfer DJ, Alberts L. Implications of noncompliance on research in affective disorders. *Psychopharmacol Bull* 1985; **21**: 37-42 [PMID: 3983336]

53 **Jamison KR**, Akiskal HS. Medication compliance in patients with bipolar disorder. *Psychiatr Clin North Am* 1983; **6**: 175-192 [PMID: 6889171]

54 **Keck PE**, McElroy SL, Strakowski SM, Bourne ML, West SA. Compliance with maintenance treatment in bipolar disorder. *Psychopharmacol Bull* 1997; **33**: 87-91 [PMID: 9133756]

55 **Strakowski SM**, Keck PE, McElroy SL, West SA, Sax KW, Hawkins JM, Kmetz GF, Upadhyaya VH, Tugrul KC, Bourne ML. Twelve-month outcome after a first hospitalization for affective psychosis. *Arch Gen Psychiatry* 1998; **55**: 49-55 [PMID: 9435760 DOI: 10.1001/archpsyc.55.1.49]

56 **Sajatovic M**, Valenstein M, Blow F, Ganoczy D, Ignacio R. Treatment adherence with lithium and anticonvulsant medications among patients with bipolar disorder. *Psychiatr Serv* 2007; **58**: 855-863 [PMID: 17535948 DOI: 10.1176/ps.2007.58.6.855]

57 **Sajatovic M**, Valenstein M, Blow FC, Ganoczy D, Ignacio RV. Treatment adherence with antipsychotic medications in bipolar disorder. *Bipolar Disord* 2006; **8**: 232-241 [PMID: 16696824 DOI: 10.1111/j.1399-5618.2006.00314.x]

58 **Zeber JE**, Copeland LA, Good CB, Fine MJ, Bauer MS, Kilbourne AM. Therapeutic alliance perceptions and medication adherence in patients with bipolar disorder. *J Affect Disord* 2008; **107**: 53-62 [PMID: 17822779 DOI: 10.1016/j.jad.2007.07.026]

59 **Bates JA**, Whitehead R, Bolge SC, Kim E. Correlates of medication adherence among patients with bipolar disorder: results of the bipolar evaluation of satisfaction and tolerability (BEST) study: a nationwide cross-sectional survey. *Prim Care Companion J Clin Psychiatry* 2010; **12**: pii: PCC.09m00883 [PMID: 21274363 DOI: 10.4088/PCC.09m00883yel]

60 **Fleck DE**, Keck PE, Corey KB, Strakowski SM. Factors associated with medication adherence in African American and white patients with bipolar disorder. *J Clin Psychiatry* 2005; **66**: 646-652 [PMID: 15889954 DOI: 10.4088/JCP.v66n0517]

61 **Byrne N**, Regan C, Livingston G. Adherence to treatment in mood disorders. *Curr Opin Psychiatry* 2006; **19**: 44-49 [PMID: 16612178 DOI: 10.1097/01.yco.0000191501.54034.7c]

62 **Aagaard J**, Vestergaard P, Maarbjerg K. Adherence to lithium prophylaxis: II. Multivariate analysis of clinical, social, and psychosocial predictors of nonadherence. *Pharmacopsychiatry* 1988; **21**: 166-170 [PMID: 3205885 DOI: 10.1055/s-2007-1014670]

63 **Velligan DI**, Weiden PJ, Sajatovic M, Scott J, Carpenter D, Ross R, Docherty JP. The expert consensus guideline series: adherence problems in patients with serious and persistent mental illness. *J Clin Psychiatry* 2009; **70** Suppl 4: 1-46; quiz 47-48 [PMID: 19686636 DOI: 10.4088/JCP.7090su1cj]

64 **Yen CF**, Chen CS, Ko CH, Yeh ML, Yang SJ, Yen JY, Huang CF, Wu CC. Relationships between insight and medication adherence in outpatients with schizophrenia and bipolar disorder: prospective study. *Psychiatry Clin Neurosci* 2005; **59**: 403-409 [PMID: 16048445 DOI: 10.1111/j.1440-1819.2005.01392.x]

65 **Copeland LA**, Zeber JE, Salloum IM, Pincus HA, Fine MJ, Kilbourne AM. Treatment adherence and illness insight in veterans with bipolar disorder. *J Nerv Ment Dis* 2008; **196**: 16-21 [PMID: 18195637 DOI: 10.1097/NMD.0b013e318160ea00]

66 **Mathew AJ**, Samuel B, Jacob KS. Perceptions of illness in self and in others among patients with bipolar disorder. *Int J Soc Psychiatry* 2010; **56**: 462-470 [PMID: 19651694 DOI: 10.1177/0020764009106621]

67 **Maarbjerg K**, Aagaard J, Vestergaard P. Adherence to lithium prophylaxis: I. Clinical predictors and patient's reasons for nonadherence. *Pharmacopsychiatry* 1988; **21**: 121-125 [PMID: 3406049 DOI: 10.1055/s-2007-1014662]

68 **Perlis RH**, Ostacher MJ, Miklowitz DJ, Hay A, Nierenberg AA, Thase ME, Sachs GS. Clinical features associated with poor pharmacologic adherence in bipolar disorder: results from the STEP-BD study. *J Clin Psychiatry* 2010; **71**: 296-303 [PMID: 20331931 DOI: 10.4088/JCP.09m05514yel]

69 **Eker F**, Harkın S. Effectiveness of six-week psychoeducation program on adherence of patients with bipolar affective disorder. *J Affect Disord* 2012; **138**: 409-416 [PMID: 22316565 DOI: 10.1016/j.jad.2012.01.004]

70 **Belzeaux R**, Correard N, Boyer L, Etain B, Loftus J, Bellivier F, Bougerol T, Courtet P, Gard S, Kahn JP, Passerieux C, Leboyer M, Henry C, Azorin JM. Depressive residual symptoms are associated with lower adherence to medication in bipolar patients without substance use disorder: results from the FACE-BD cohort. *J Affect Disord* 2013; **151**: 1009-1015 [PMID: 24051101 DOI: 10.1016/j.jad.2013.08.028]

71 **Bech P**, Vendsborg PB, Rafaelsen OJ. Lithium maintenance treatment of manic-melancholic patients: its role in the daily routine. *Acta Psychiatr Scand* 1976; **53**: 70-81 [PMID: 1251757 DOI: 10.1111/j.1600-0447.1976.tb00060.x]

72 **Jamison KR**, Gerner RH, Hammen C, Padesky C. Clouds and silver linings: positive experiences associated with primary affective disorders. *Am J Psychiatry* 1980; **137**: 198-202 [PMID: 7352574 DOI: 10.1176/ajp.137.2.198]

73 **Gitlin MJ**, Cochran SD, Jamison KR. Maintenance lithium treatment: side effects and compliance. *J Clin Psychiatry* 1989; **50**: 127-131 [PMID: 2925600]

74 **Nilsson A**, Axelsson R. Factors associated with discontinuation of long-term lithium treatment. *Acta Psychiatr Scand* 1989; **80**: 221-230 [PMID: 2510458 DOI: 10.1111/j.1600-0447.1989.tb01331.x]

75 **Morselli PL**, Elgie R. GAMIAN-Europe/BEAM survey I--global analysis of a patient questionnaire circulated to 3450 members of 12 European advocacy groups operating in the field of mood disorders. *Bipolar Disord* 2003; **5**: 265-278 [PMID: 12895204 DOI: 10.1034/j.1399-5618.2003.00037.x]

76 **Scott J**. Predicting medication non-adherence in severe affective disorders. *Acta Neuropsychiatr* 2000; **12**: 128-130 [PMID: 26975270 DOI: 10.1017/S0924270800035584]

77 **Scott J**, Pope M. Self-reported adherence to treatment with mood stabilizers, plasma levels, and psychiatric hospitalization. *Am J Psychiatry* 2002; **159**: 1927-1929 [PMID: 12411230 DOI: 10.1176/appi.ajp.159.11.1927]

78 **Foster A**, Sheehan L, Johns L. Promoting treatment adherence in patients with bipolar disorder. *Current Psychiatry* 2011: **10**: 45-52

79 **Sajatovic M**, Jenkins JH, Cassidy KA, Muzina DJ. Medication treatment perceptions, concerns and expectations among depressed individuals with Type I Bipolar Disorder. *J Affect Disord* 2009; **115**: 360-366 [PMID: 18996600 DOI: 10.1016/j.jad.2008.10.002]

80 **Savaş HA**, UnalA,Vırıt O. Treatment adherence in bipolar disorder. *JMOOD* 2011; **1**: 95-102 [DOI: 10.5455/jmood.20110827015615]

81 **Kriegshauser K**, Sajatovic M, Jenkins JH, Cassidy KA, Muzina D, Fattal O, Smith D, Singer B. Gender differences in subjective experience and treatment of bipolar disorder. *J Nerv Ment Dis* 2010; **198**: 370-372 [PMID: 20458200 DOI: 10.1097/NMD.0b013e3181da8ef7]

82 **Vega P**, Alonso M, Alberich S, Barbeito S, de Azúa SR, Ugarte A. Why do bipolar men not comply with treatment? The Spanish CIBERSAM data. *Eur J Psychiatr* 2009; **23** (Suppl): 63-69

83 **Sajatovic M**, Micula-Gondek W, Tatsuoka C, Bialko C. The relationship of gender and gender identity to treatment adherence among individuals with bipolar disorder. *Gend Med* 2011; **8**: 261-268 [PMID: 21763217 DOI: 10.1016/j.genm.2011.06.002]

84 **Dharmendra MS**, Eagles JM. Factors associated with patients' knowledge of and attitudes towards treatment with lithium. *J Affect Disord* 2003; **75**: 29-33 [PMID: 12781347 DOI: 10.1016/S0165-0327(02)00027-7]

85 **Kleindienst N**, Greil W. Are illness concepts a powerful predictor of adherence to prophylactic treatment in bipolar disorder? *J Clin Psychiatry* 2004; **65**: 966-974 [PMID: 15291686 DOI: 10.4088/JCP.v65n0713]

86 **Kessing LV**, Hansen HV, Bech P. Attitudes and beliefs among patients treated with mood stabilizers. *Clin Pract Epidemiol Ment Health* 2006; **2**: 8 [PMID: 16712717 DOI: 10.1186/1745-0179-2-8]

87 **Teter CJ**, Falone AE, Bakaian AM, Tu C, Ongür D, Weiss RD. Medication adherence and attitudes in patients with bipolar disorder and current versus past substance use disorder. *Psychiatry Res* 2011; **190**: 253-258 [PMID: 21696830 DOI: 10.1016/j.psychres.2011.05.042]

88 **Medina E**, Salvà J, Ampudia R, Maurino J, Larumbe J. Short-term clinical stability and lack of insight are associated with a negative attitude towards antipsychotic treatment at discharge in patients with schizophrenia and bipolar disorder. *Patient Prefer Adherence* 2012; **6**: 623-629 [PMID: 22969293 DOI: 10.2147/PPA.S34345]

89 **Vermeire E**, Hearnshaw H, Van Royen P, Denekens J. Patient adherence to treatment: three decades of research. A comprehensive review. *J Clin Pharm Ther* 2001; **26**: 331-342 [PMID: 11679023 DOI: 10.1046/j.1365-2710.2001.00363.x]

90 **Scott J**, Tacchi MJ. A pilot study of concordance therapy for individuals with bipolar disorders who are non-adherent with lithium prophylaxis. *Bipolar Disord* 2002; **4**: 386-392 [PMID: 12519098 DOI: 10.1034/j.1399-5618.2002.02242.x]

91 **Cochran SD**, Gitlin MJ. Attitudinal correlates of lithium compliance in bipolar affective disorders. *J Nerv Ment Dis* 1988; **176**: 457-464 [PMID: 3404137 DOI: 10.1097/00005053-198808000-00001]

92 **Clifford S**, Barber N, Horne R. Understanding different beliefs held by adherers, unintentional nonadherers, and intentional nonadherers: application of the Necessity-Concerns Framework. *J Psychosom Res* 2008; **64**: 41-46 [PMID: 18157998 DOI: 10.1016/j.jpsychores.2007.05.004]

93 **Gadkari AS**, McHorney CA. Unintentional non-adherence to chronic prescription medications: how unintentional is it really? *BMC Health Serv Res* 2012; **12**: 98 [PMID: 22510235 DOI: 10.1186/1472-6963-12-98]

94 **Horne R**, Weinman J. Patients' beliefs about prescribed medicines and their role in adherence to treatment in chronic physical illness. *J Psychosom Res* 1999; **47**: 555-567 [PMID: 10661603 DOI: 10.1016/S0022-3999(99)00057-4]

95 **Even C**, Richard H, Thuile J, Friedman S, Rouillon F. Characteristics of voluntary participants versus nonparticipants in a psychoeducation program for euthymic patients with bipolar disorder. *J Nerv Ment Dis* 2007; **195**: 262-265 [PMID: 17468688 DOI: 10.1097/01.nmd.0000258302.82957.db]

96 **Pope M**, Scott J. Do clinicians understand why individuals stop taking lithium? *J Affect Disord* 2003; **74**: 287-291 [PMID: 12738048 DOI: 10.1016/S0165-0327(02)00341-5]

97 **Mert DG**, Turgut NH, Kelleci M, Semiz M. Perspectives on reasons of medication nonadherence in psychiatric patients. *Patient Prefer Adherence* 2015; **9**: 87-93 [PMID: 25609930 DOI: 10.2147/PPA.S75013]

98 **Devulapalli KK**, Ignacio RV, Weiden P, Cassidy KA, Williams TD, Safavi R, Blow FC, Sajatovic M. Why do persons with bipolar disorder stop their medication? *Psychopharmacol Bull* 2010; **43**: 5-14 [PMID: 21150842]

99 **Weiss RD**, Greenfield SF, Najavits LM, Soto JA, Wyner D, Tohen M, Griffin ML. Medication compliance among patients with bipolar disorder and substance use disorder. *J Clin Psychiatry* 1998; **59**: 172-174 [PMID: 9590667 DOI: 10.4088/JCP.v59n0405]

100 **Hajda M**, Kamaradova D, Latalova K, Prasko J, Ociskova M, Mainerova B. Self-stigma, treatment adherence, and medication discontinuation in patients with bipolar disorders in remission – a cross sectional study. *Act Nerv Super Rediviva* 2015; **57**: 6-11

101 **Sajatovic M**, Levin J, Fuentes-Casiano E, Cassidy KA, Tatsuoka C, Jenkins JH. Illness experience and reasons for nonadherence among individuals with bipolar disorder who are poorly adherent with medication. *Compr Psychiatry* 2011; **52**: 280-287 [PMID: 21497222 DOI: 10.1016/j.comppsych.2010.07.002]

102 **Moon E**, Chang JS, Kim MY, Seo MH, Cha B, Ha TH, Choi S, Cho HS, Park T, Ha K. Dropout rate and associated factors in patients with bipolar disorders. *J Affect Disord* 2012; **141**: 47-54 [PMID: 22410504 DOI: 10.1016/j.jad.2012.02.025]

103 **Darling CA**, Olmstead SB, Lund VE, Fairclough JF. Bipolar disorder: medication adherence and life contentment. *Arch Psychiatr Nurs* 2008; **22**: 113-126 [PMID: 18505693 DOI: 10.1016/j.apnu.2008.02.004]

104 **Van Putten T**. Why do patients with manic-depressive illness stop their lithium? *Compr Psychiatry* 1975; **16**: 179-183 [PMID: 1120419 DOI: 10.1016/0010-440X(75)90064-4]

105 **Greenhouse WJ**, Meyer B, Johnson SL. Coping and medication adherence in bipolar disorder. *J Affect Disord* 2000; **59**: 237-241 [PMID: 10854641 DOI: 10.1016/S0165-0327(99)00152-4]

106 **Gibson S**, Brand SL, Burt S, Boden ZV, Benson O. Understanding treatment non-adherence in schizophrenia and bipolar disorder: a survey of what service users do and why. *BMC Psychiatry* 2013; **13**: 153 [PMID: 23714262 DOI: 10.1186/1471-244X-13-153]

107 **Miasso AI**, Cassiani SH, Pedrão LJ. [Affective bipolar disorder and ambivalence in relation to the drug treatment: analyzing the

causal conditions]. *Rev Esc Enferm USP* 2011; **45**: 433-441 [PMID: 21655795 DOI: 10.1590/S0080-62342011000200019]

108 **Chang CW**, Sajatovic M, Tatsuoka C. Correlates of attitudes towards mood stabilizers in individuals with bipolar disorder. *Bipolar Disord* 2015; **17**: 106-112 [PMID: 24974829 DOI: 10.1111/bdi.12226]

109 **Soares JJF**, Stintzingc CP, Jackson C, Skoldin B. Psychoeducation for patients with bipolar disorder: An exploratory study. *Nord J Psychiatry* 2009; **51**: 439-446 [DOI: 10.3109/08039489709090741]

110 **Barraco A**, Rossi A, Nicolò G. Description of study population and analysis of factors influencing adherence in the observational Italian study "Evaluation of Pharmacotherapy Adherence in Bipolar Disorder" (EPHAR). *CNS Neurosci Ther* 2012; **18**: 110-118 [PMID: 21199448 DOI: 10.1111/j.1755-5949.2010.00225.x]

111 **Hou R**, Cleak V, Peveler R. Do treatment and illness beliefs influence adherence to medication in patients with bipolar affective disorder? A preliminary cross-sectional study. *Eur Psychiatry* 2010; **25**: 216-219 [PMID: 20005683 DOI: 10.1016/j.eurpsy.2009.09.003]

112 **Revicki DA**, Hanlon J, Martin S, Gyulai L, Nassir Ghaemi S, Lynch F, Mannix S, Kleinman L. Patient-based utilities for bipolar disorder-related health states. *J Affect Disord* 2005; **87**: 203-210 [PMID: 16005983 DOI: 10.1016/j.jad.2005.03.017]

113 **Rosa AR**, Andreazza AC, Sanchez-Moreno J, Gazalle FK, Santin, A, Stein A. Validation of the Portuguese version of the Lithium Attitudes Questionnaire (LAQ) in bipolar patients treated with lithium: cross-over study. *Clin Pract Epidemiol Ment Health* 2006; **2**: 32 [DOI: 10.1186/1745-0179-2-32]

114 **Strauss JL**, Johnson SL. Role of treatment alliance in the clinical management of bipolar disorder: stronger alliances prospectively predict fewer manic symptoms. *Psychiatry Res* 2006; **145**: 215-223 [PMID: 17079023 DOI: 10.1016/j.psychres.2006.01.007]

115 **Martin DJ**, Garske JP, Davis MK. Relation of the therapeutic alliance with outcome and other variables: a meta-analytic review. *J Consult Clin Psychol* 2000; **68**: 438-450 [PMID: 10883561 DOI: 10.1037/0022-006X.68.3.438]

116 **Mitchell AJ**, Selmes T. Why don't patients take their medicine? Reasons and solutions in psychiatry. *Adv Psychiatr Treat* 2007; **13**: 336-346 [DOI: 10.1192/apt.bp.106.003194]

117 **McCabe R**, Bullenkamp J, Hansson L, Lauber C, Martinez-Leal R, Rössler W, Salize HJ, Svensson B, Torres-Gonzalez F, van den Brink R, Wiersma D, Priebe S. The therapeutic relationship and adherence to antipsychotic medication in schizophrenia. *PLoS One* 2012; **7**: e36080 [PMID: 22558336 DOI: 10.1371/journal.pone.0036080]

118 **Lee S**, Wing YK, Wong KC. Knowledge and compliance towards lithium therapy among Chinese psychiatric patients in Hong Kong. *Aust N Z J Psychiatry* 1992; **26**: 444-449 [PMID: 1417630 DOI: 10.3109/00048679209072068]

119 **Perron BE**, Zeber JE, Kilbourne AM, Bauer MS. A brief measure of perceived clinician support by patients with bipolar spectrum disorders. *J Nerv Ment Dis* 2009; **197**: 574-579 [PMID: 19684493 DOI: 10.1097/NMD.0b013e3181b08bc6]

120 **Sylvia LG**, Hay A, Ostacher MJ, Miklowitz DJ, Nierenberg AA, Thase ME, Sachs GS, Deckersbach T, Perlis RH. Association between therapeutic alliance, care satisfaction, and pharmacological adherence in bipolar disorder. *J Clin Psychopharmacol* 2013; **33**: 343-350 [PMID: 23609394 DOI: 10.1097/JCP.0b013e3182900c6f]

121 **Frank E**, Kupfer DJ, Siegel LR. Alliance not compliance: a philosophy of outpatient care. *J Clin Psychiatry* 1995; **56** Suppl 1: 11-16; discussion 16-17 [PMID: 7836346]

122 **Lewis L**. Patient perspectives on the diagnosis, treatment, and management of bipolar disorder. *Bipolar Disord* 2005; **7** (Suppl 1): 33-37 [DOI: 10.1111/j.1399-5618.2005.00192.x]

123 **Cochran SD**. Preventing medical noncompliance in the outpatient treatment of bipolar affective disorders. *J Consult Clin Psychol* 1984; **52**: 873-878 [PMID: 6501672 DOI: 10.1037/0022-006X.52.5.873]

124 **Connelly CE**, Davenport YB, Nurnberger JI. Adherence to treatment regimen in a lithium carbonate clinic. *Arch Gen Psychiatry* 1982; **39**: 585-588 [PMID: 6807256 DOI: 10.1001/archpsyc.1982.04290050057011]

125 **Gaudiano BA**, Miller IW. Patients' expectancies, the alliance in pharmacotherapy, and treatment outcomes in bipolar disorder. *J Consult Clin Psychol* 2006; **74**: 671-676 [PMID: 16881774 DOI: 10.1037/0022-006X.74.4.671]

126 **Even C**, Thuile J, Kalck-Stern M, Criquillion-Doublet S, Gorwood P, Rouillon F. Psychoeducation for patients with bipolar disorder receiving lithium: short and long term impact on locus of control and knowledge about lithium. *J Affect Disord* 2010; **123**: 299-302 [PMID: 19815295 DOI: 10.1016/j.jad.2009.09.008]

127 **Delany N**. How much do patients on lithium know about their medication? *Psychiatric Bulletin* 1991: **15**: 136-137 [DOI: 10.1192/pb.15.3.136]

128 **Bowskill R**, Clatworthy J, Parham R, Rank T, Horne R. Patients' perceptions of information received about medication prescribed for bipolar disorder: implications for informed choice. *J Affect Disord* 2007; **100**: 253-257 [PMID: 17174406 DOI: 10.1016/j.jad.2006.10.018]

129 **Agyapong VI**, Nwankwo V, Bangaru R, Kirrane R. Sources of patients' knowledge of the adverse effects of psychotropic medication and the perceived influence of adverse effects on compliance among service users attending community mental health services. *J Clin Psychopharmacol* 2009; **29**: 565-570 [PMID: 19910722 DOI: 10.1097/JCP.0b013e3181befa3e]

130 **Schaub RT**, Berghoefer A, Müller-Oerlinghausen B. What do patients in a lithium outpatient clinic know about lithium therapy? *J Psychiatry Neurosci* 2001; **26**: 319-324 [PMID: 11590971]

131 **Harvey NS**, Peet M. Lithium maintenance: 2. Effects of personality and attitude on health information acquisition and compliance. *Br J Psychiatry* 1991; **158**: 200-204 [PMID: 2012911 DOI: 10.1192/bjp.158.2.200]

132 **Dogan S**, Sabanciogullari S. The effect of patient education in lithium therapy on quality of life and compliance. *Arch Psych Nursing* 2003; **17**: 270-275 [DOI: 10.1053/j.apnu.2003.10.001]

133 **Rosa AR**, Andreazza AC, Gazalle FK, Sanchez-Moreno J, Santin, A, Stein A. Adaptation and validation of the Portuguese version of the Lithium Knowledge Test (LKT) of bipolar patients treated with lithium: cross-over study. *Clin Pract Epidemiol Ment Health* 2006; **2**: 34 [DOI: 10.1186/1745-0179-2-34]

134 **Glover KJ**, Lawley D. How safe is lithium prescribing? Audit of a local prescribing framework and patient survey. *Psychiatric Bulletin* 2005; **29**: 98-100 [DOI: 10.1192/pb.29.3.98]

135 **Cely EEP**, Fierro M, Pinilla MI. Prevalence and factors associated with non-adherence in drug maintenance treatment in adults with bipolar affective disorder. *Rev Colomb Psiquiatr* 2011; **40**: 85-98 [DOI: 10.1016/S0034-7450(14)601062]

136 **Drotar D**, Greenley RN, Demeter CA, McNamara NK, Stansbrey RJ, Calabrese JR, Stange J, Vijay P, Findling RL. Adherence to pharmacological treatment for juvenile bipolar disorder. *J Am Acad Child Adolesc Psychiatry* 2007; **46**: 831-839 [PMID: 17581447 DOI: 10.1097/chi.0b013e31805c7421]

137 **da Cruz LP**, Miranda PM, Vedana KGG, Miasso AI. Medication therapy: adherence, knowledge and difficulties of elderly people from bipolar disorder. *Rev Latino-Am Enfermagem* 2011; **19**: 944-952

138 **Scott J**, Colom F, Pope M, Reinares M, Vieta E. The prognostic role of perceived criticism, medication adherence and family knowledge in bipolar disorders. *J Affect Disord* 2012; **142**: 72-76 [PMID: 22944191 DOI: 10.1016/j.jad.2012.04.005]

139 **Sajatovic M**, Jenkins JH. Is antipsychotic medication stigmatizing for people with mental illness? *Int Rev Psychiatry* 2007; **19**: 107-112 [PMID: 17464788 DOI: 10.1080/09540260701278911]

140 **Kutzelnigg A**, Kopeinig M, Chen CK, Fábián A, Pujol-Luna MG, Shin YC, Treuer T, D'yachkova Y, Deix C, Kasper S, Doby D. Compliance as a stable function in the treatment course of bipolar disorder in patients stabilized on olanzapine: results from a 24-month observational study. *Int J Bipolar Disord* 2014; **2**: 13 [PMID: 25360398 DOI: 10.1186/s40345-014-0013-x]

141 **Bhugra D**, Flick GR. Pathways to care for patients with bipolar disorder. *Bipolar Disord* 2005; **7**: 236-245 [PMID: 15898961 DOI: 10.1111/j.1399-5618.2005.00202.x]

142 **Tibaldi G**, Salvador-Carulla L, García-Gutierrez JC. From treatment adherence to advanced shared decision making: new professional strategies and attitudes in mental health care. *Curr Clin Pharmacol* 2011; **6**: 91-99 [PMID: 21592062 DOI: 10.2174/157488411796151101]

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