

What's in a name? Compliance, adherence and concordance in chronic psychiatric disorders

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Abstract

About half or more of the patients with chronic psychiatric illnesses, either do not take their medications correctly, or completely stop taking them. The problem of poor initial compliance or adherence is often compounded by a continued decline in compliance/adherence over time. The failure to take medicines, adversely affects the outcome of treatment, and places a huge burden of wasted resources on the society. Three terms have been used to describe medication-taking among patients with chronic psychiatric disorders. Compliance is defined as "the extent to which the patient's behaviour matches the prescriber's recommendations". Though compliance has been frequently employed to describe medication-taking behaviour, it has proved problematic because it refers to a process where the clinician decides on a suitable treatment, which the patient is expected to comply with unquestioningly. Studies over the past few decades have emphasized the importance of patients' perspectives in medication-taking, based on their own beliefs, their personal circumstances, the information and resources available for them. Adherence has been used as a replacement for compliance in an effort to place the clinician-patient relationship in its proper perspective. Adherence refers to a process, in which the appropriate treatment

is decided after a proper discussion with the patient. It also implies that the patient is under no compulsion to accept a particular treatment, and is not to be held solely responsible for the occurrence of non-adherence. 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". To overcome certain problems in the concept of adherence, a third term concordance has been used. The concept of concordance has evolved from a narrower view, emphasizing an agreement between the clinician and the patient, which takes into account each other's perspective on medication-taking, to a broader process consisting of open discussions with the patient regarding medication-taking, imparting information and supporting patients on long-term medication. It is a process, which entertains patients' views on medication-taking, and acknowledges that patients' views have to be respected even if they make choices, which appear to be in conflict with the clinician's views. Although none of these terms are ideal solutions to understanding the complex process of medication-taking behaviour of patients, the move from compliance to adherence and concordance represents genuine progress in this field, which puts the patient's perceptions at the centre of the whole process.

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Key words: Compliance; Adherence; Concordance; Chronic psychiatric disorders

Core tip: Medication-taking in chronic psychiatric illnesses has been described using three seemingly related terms. Compliance, the degree to which patients follow the clinicians' treatment-recommendations, has adverse implications for patient autonomy and the clinician-patient relationship. Adherence, used as a replacement for compliance, puts the therapeutic relationship in its proper perspective, by focusing on

patient participation in deciding treatment choices, and being non-judgmental about patients' medication-taking behaviour. Concordance emphasizes a therapeutic relationship, which facilitates clinicians' and patients' views on treatment, and supports an informed choice of treatment by patients. The evolution of these terms represents genuine progress in understanding patients' perceptions of medication-taking.

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Keep a watch also on the faults of the patients, which often make them lie about the taking of things prescribed.

-Hippocrates

MEDICATION TAKING IN CHRONIC PSYCHIATRIC DISORDERS

A project on treatment adherence sponsored by the World Health Organization (WHO)^[1] described chronic medical conditions as: "Diseases which have one or more of the following characteristics: they are permanent, leave residual disability, are caused by non-reversible pathological alteration, require special training of the patient for rehabilitation, or may be expected to require a long period of supervision, observation or care".

The adverse impact of these chronic conditions on the life of the sufferers and their families depends on the nature of the medical illness. Some of these conditions are highly disabling, others less so. The adverse effects on the quality of life of patients and their families is also variable, with some conditions, e.g., non-communicable diseases, mental health disorders, HIV/AIDS and tuberculosis having a much greater negative impact than others^[1,2]. However, it has been acknowledged that one of the principal difficulties in the treatment of these longstanding medical illnesses is non-compliance or non-adherence with treatment by patients. Though rates vary widely across different disorders and studies, approximately 50% or more of the patients on prolonged treatment for medical illnesses, either do not take medications properly, or completely stop taking them^[1]. Estimates of compliance or adherence in chronic mental illnesses also vary widely. According to most reviews of the subject the mean rate of non-compliance/non-adherence in different psychiatric conditions lies somewhere in the range of 25% to 90%^[1,3-25]. The evidence indicates that non-compliance/non-adherence rates among mental illnesses are no different from those among physical disorders, and as many as half of those with mental illnesses are non-compliant/non-adherent at any point of time^[3-5,9,13,19,21,22,26]. Several studies also show that the problem of poor initial

compliance or adherence is compounded by a continued decline in compliance/adherence over time^[4-6,15,17,22,26-30]. This indicates that a large proportion of patients, perhaps the great majority, will stop taking their medication if the clinician waits long enough, which means that non-compliance/non-adherence at any level is more or less a universal phenomenon^[31]. The consequences of non-compliance/non-adherence are not hard to understand. Non-compliance/non-adherence is the principal underlying cause of ineffective treatment. It worsens the course and outcome of chronic disorders, impairs the quality of life of the sufferers, and increases the costs of care several fold^[1,3-26,32-36]. Consequently, health-care providers worldwide struggle to meet their targets, even after making treatment services accessible for patients^[1]. To add to the problem, the ability of clinicians to recognise non-compliance/non-adherence is limited, and interventions to improve compliance/adherence have had mixed results; successful interventions have generally proved to be complex and costly^[12,18,32-36]. The extent and the adverse consequences of poor compliance/adherence are likely to be greater for low- and middle-income countries, given the shortage of health-care resources, and the limited access to treatment for the majority in such countries^[1].

THE IMPORTANCE OF THE PATIENT'S PERSPECTIVE ON MEDICATION TAKING

Medication taking is not just dependent on the chemical properties of medications; rather, it is the outcome of a complex bio-psycho-social process, which determines the patient's choice whether or not to take medications^[37,38]. However, the traditional medical model often assumes that any treatment based on scientific evidence is always in the best interests of the patient, and it would be unwise, or even irrational for the patient not to comply with the clinician's suggestions regarding such treatment^[39,40]. Then again, according to social, cognitive and behavioural perspectives, non-compliance/non-adherence often represents a rational decision on part of patients, determined by factors such as their views on medication-taking, their life circumstances and available resources, competing priorities, the need for patients to assert their independence, and their need to carry out with their lives even while they are on long-term treatment^[1,4,22,37-43]. Recent reviews converge in concluding that non-compliance/non-adherence is far better recognized than comprehended; and, that a focus on the patient's decision making process is of equal, if not of far greater importance in understanding treatment compliance/adherence^[1,4,37-40,42,43]. Problems with compliance/adherence are complex and multidimensional. They are often determined by several variables relating to the patient, his/her condition, the medications prescribed, and factors in the patient's surroundings^[1,4,6-11,13-23,25,26,31,34,35,38,39,42,43]. Over the years, socio-demographic, treatment-related and disease-related factors have been considered to be the primary

determinants of non-compliance/non-adherence, but the role played by these factors in determining non-compliance/non-adherence has been uncertain. Moreover, these factors do not seem to predict the presence of non-compliance/non-adherence with a reasonable degree of certainty^[1,4,15,17,19,21,22,33-35,39,37-45]. On the other hand, the patient's perspective on medication-taking, which is a key component of compliance/adherence behaviour, was neglected by research in this area for a long time. However, since around the 1990s this area has been the focus of many reports on compliance/adherence. These have consistently suggested that patients' views on medication-taking play a key role in determining compliance/adherence^[1,3,4,15,17,21,22,39,42-44]. From the patient's perspective, compliance/adherence, or non-compliance/non-adherence is often a considered decision by people making their own choices about the benefits and disadvantages of treatment, based on their own beliefs, their personal circumstances, and the information available to them. The complete list of such patient-related factors has been presented in several reviews of the subject^[1,3,4,6,8,9,13-23,25,26,33-35,37-40,42-45]. They include factors such as patients' beliefs and attitudes towards medication taking, attitudes and support of their caregivers, perceived efficacy and side effects of treatment, patients' knowledge about the illness, its causes and treatment, barriers to compliance/adherence such as costs of treatment or inadequate access, the clinician-patient relationship, patients' quality of life, their satisfaction with and acceptability of treatment, and many others. Different theoretical approaches incorporating these factors and the mechanisms underlying them have been utilized to understand medication-taking behaviour^[1,4,6,7,9,21,22,34,38,39,41-48]. Examples of these include the health-belief model, the social-cognitive theory, the theory of planned behaviour (and its precursor, the theory of reasoned action), the self-regulation theory, and the protection-motivation theory. These models reflect divergent theoretical perspectives on compliance/adherence, such as the bio-medical perspective, the behavioural perspective, the communications perspective, the cognitive perspective, and the self-regulatory perspective. Their common elements include clinician-patient communication and the therapeutic relationship, psychosocial attributes of patients (*e.g.*, their attitude and beliefs), factors in the patient's immediate environment (*e.g.*, their economic status or availability of family support), and social policies and the nature of the health-care delivery system. The empirical literature on compliance/adherence is voluminous. However, even with these elaborate conceptual frameworks, the phenomenon remains far from understood^[34,41]. Studies differ greatly not only in terms of the diseases, treatment-regimens or the patients examined, but also in the way they conceptualize, define and measure compliance/adherence. Since, concepts, assessments and contexts impact the findings a great deal, considerable discrepancy in rates of compliance/adherence, their correlates, and their outcomes are the norm in such research^[1,4,5,8,11,13,17,18,33,34,39,41-43].

FROM COMPLIANCE TO ADHERENCE TO CONCORDANCE

Research in the area of compliance/adherence behaviour has often changed its preferred terminology to label such behaviour. This change is best illustrated by the use of three common and somewhat overlapping terms to describe the phenomenon.

Compliance, the oldest term to describe such behaviour, was intended to be a neutral alternative to earlier descriptions of patients who did not follow the clinician's advice, such as "untrustworthy", "uncooperative", or as proposed by Hippocrates, patients who lie about taking treatment. The most commonly used definition of compliance is "the extent to which the patient's behaviour matches the prescriber's recommendations"^[4,21,38,42,43,49]. Though compliance has been employed to describe medication-taking behaviour, it has proved problematic because it appears to portray a process, in which patient autonomy is disregarded and a genuine therapeutic relationship is automatically hampered^[1,3,4,9,16,19,21,23,33-35,38,39,42,43,49]. It seems to suggest a one-sided interaction, where the clinician decides on the suitable treatment, which the patient has to comply with regardless of its suitability. Non-compliance in this context is readily equated with either the patient's inability to understand the treatment regimen or its purported benefits, or even as a sign of irrational or maladaptive patient behaviour when he/she refuses to comply. Thus, compliance becomes synonymous with a paternalistic conceptualization of medication-taking behaviour, which disregards patients' perceptions on medication-taking. Apart from its pejorative connotations there are other problems with the term, and the traditional bio-medical model of compliance. Accumulated evidence over the last two decades or so shows that compliance, or non-compliance, is often not fully accounted for by socio-demographic characteristics of patients, the nature of the disease, efficacy and tolerability of medications, the complexity of treatment regimens, or psychosocial attributes such as insight in mental disorders, abnormal mood states like depression, or maladaptive personality traits^[1,4,6,22,38,39,42-46]. On the other hand, there has been a growing awareness of the significance of patients' perceptions regarding illnesses or medications in determining compliance. Although viewed from the clinician's perspective, refusal to comply with a treatment regimen may seem strange and irrational, on the patient's part non-compliance is often a result of having to balance the need for appropriate treatment with concerns about adverse consequences, such as side effects, costs, stigma and emotional concerns, resources available for patients and other competing priorities in their lives^[1,4,22,37-43]. It has been proposed that there are basically two notions, which need to be considered while conceptualizing medication-taking behaviour^[42]. The "scientific/clinical agenda" focuses on what has been prescribed, and the extent to which patients comply

with this advice. In contrast, the “normative” agenda involves an understanding of what is good and right about prescribing and medication-taking^[42]. Compliance is in accord with the “scientific/clinical agenda”, but not the “normative” one^[42]. In this conceptualization, compliance is always deemed to be appropriate and non-compliance is always considered to be maladaptive. However, non-compliance may not always be harmful for the patient. For example, if the treatment prescribed is inappropriate, non-compliance may actually protect the patient from the unnecessary side effects, or spare him/her from spending money on ineffective medication. Thus, while the construct of compliance may prove useful in defining and measuring the extent of non-compliant behaviour, this approach often fails to adequately account for the reasons behind such behaviour^[42].

Adherence has been used as a replacement for compliance in an effort to put the therapeutic relationship in its proper perspective. The concept of adherence places emphasis on a process, in which the appropriate treatment is decided after discussion between the prescriber and the patient. It implies that the patient is under no compulsion to accept a particular treatment, and shall not be held solely responsible for the failure of a treatment-plan because of non-adherence^[1,17,19,21,34,38,42]. Therefore, adherence has been defined as the: “extent to which the patient’s behaviour matches agreed recommendations from the prescriber”^[21,34,35,38,42,50]. Similarly, in other definitions, adherence refers to the capacity and readiness of the patient to abide by mutually agreed recommendations regarding treatment^[51]. The central focus of adherence is, thus, on an understanding between the clinician and the patient about the treatment recommended. The WHO project on treatment adherence took cognizance of the requirement to look beyond paternalistic conceptualizations of medication-taking behaviour incorporated in the term compliance, which placed the responsibility of proper medication-taking more on the patient than the clinician^[1]. The adherence project chose a definition of adherence, which was an amalgam of several previous definitions. It also extended the concept of adherence to include other elements of the patient’s behaviour, such as following recommendations about diet or lifestyle. Accordingly, this project defined adherence 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”^[1]. These definitions of adherence focus on active patient involvement while choosing the most suitable treatment, and emphasize the notion that both parties need to participate in a discussion, which yields the most appropriate medication regimen to be followed. The term is intended to be non-judgmental; it is an observation of a fact and not intended to blame either the clinician, or the patient. It is, however, more patient-centred than the clinician-centred term compliance. Thus, it has been suggested as a improvement over the term compliance, which has negative implications since it disapproves of any patient-behaviour, which does not comply with the clinician’s recommenda-

tions. In its current conceptualization, adherence is also a broader term than compliance, since its definition includes elements such as initiating a particular treatment-regimen, persisting with the agreed upon regimen, and carrying out the prescriber’s advice regarding a wide range of treatment-related behaviours^[1,3,10,11,21,23,34,35,38,39,42,43]. Moreover, adherence is not a dichotomous concept like compliance. Rather, it has been more appropriately conceptualized as a continuum of behaviours ranging from complete refusal to take medications (fully non-adherent behaviour), to following medication regimens partly (partially adherent behaviour), to precise and regular intake of medications (fully adherent behaviour)^[19,21,26]. A distinction has also been made between “unintentional” and “intentional” non-adherence^[42,52,53]. “Unintentional” non-adherence results from barriers, which prevent patients from following the prescriber’s recommendations. These include personal restrictions such as age, physical or cognitive impairments, as well as environmental hurdles such as problems in affording or accessing treatment. “Intentional” non-adherence is thought to arise from views and preferences of patients regarding medications, which may affect their willingness to adhere to the medications prescribed.

Though adherence is currently the preferred term, it still does not address the “normative” agenda, *i.e.*, whether it is “right or good to take medications,” or adhere to other treatment recommendations^[42,54]. As a compromise, the notion of “informed adherence” has been proposed^[42,54]. This term serves as bridge between the constructs of adherence and informed consent. It is intended to encapsulate a process, which consists of an informed discussion between the clinician and the patient, which leads to an agreement about the treatment regimen to be prescribed. Both parties are, thus, equally responsible for success or failure of the treatment plan, which has been agreed upon. However, despite the improvements sought in its conceptualization, the term adherence, or its derivatives are often felt to be too unwieldy for clinical use by some authors, who still prefer the term compliance^[4,9,43,55]. They suggest that using different names for the same concept only causes further confusion, and does not improve our understanding of the phenomenon.

To overcome these problems in the definition of adherence, a third term concordance has been used^[1,15,16,21,23,34,35,38,39,42,56]. The concept of concordance has evolved over time. The initial conceptualizations described a process of medication-taking reached on the basis of discussion between the clinician and the patient, where the views of both parties, especially the patient’s, were taken into account^[16,34,35,42,56]. This view acknowledged that both clinicians and patients could have equally pertinent, but somewhat contrasting perspectives on medication-taking. The clinician’s task was not only to convey to the patient his/her views, but also enable patients to express their views about medication-taking. Accordingly, in this model, the therapeutic relationship was employed to reach a consensus about medication-taking, which not only included perspective of the patient, but actually gave greater weight to the patient’s views on medication-tak-

ing. The concept of concordance has been subsequently broadened to include additional aspects such as effective communication with the patient, imparting information with the aim to help the patient make an informed choice regarding treatment, and offering support to the patient during the entire course of treatment^[42]. There are several ways that the notion of concordance improves upon the earlier terms. Firstly, it accepts that patients might have equally cogent views about treatment, which may not necessarily be similar to the clinician's views. For clinicians, the decision to adhere to treatment may depend only on clinical factors such as efficacy or tolerability, whereas for patients the decision may be based on additional factors such as adequacy of their resources, or perceived barriers to treatment. However, if the therapeutic relationship is a sound one, an agreement can usually be reached, which incorporates both these views. When the therapeutic relationship does not allow for open expression of these differing views, it more often than not leads to non-adherence on part of the patient^[16,34,35,42,56]. Consequently, a positive clinician-patient alliance is the principal element of the concept of concordance. When this alliance promotes open expression of views, and information regarding benefits and risks is properly imparted, decisions about medication-taking can be made on the basis of a truly informed choice by the patient. The chances of a patient adhering to treatment are, therefore, enhanced if this process is followed properly. In this way concordance aims to meet the "normative agenda" of medication-taking^[1,21,23,34,35,38,39,42,43,56]. Although concordance is seemingly the ideal solution to addressing the lacunae in understanding medication-taking behaviour, it is still limited in its scope, because it does not address the scientific/clinical aspect of medication-taking. It does not wholly acknowledge the possible conflict between prescribing based on scientific evidence, and decisions of patients based on personal priorities. Indeed, concordance does not seem to have a proper answer to a highly likely situation, in which the patient's preferences are in opposition to medical facts about treatment. If and when the patient chooses a treatment, which the clinician knows to be potentially harmful, this creates an ethical dilemma for the prescriber. The situation becomes more complicated when patients' decisions might threaten their health and those of others, *e.g.*, in those who lack insight or control over their behaviour because of mental illness. In such complicated situations it might be difficult to decide between the patient's freedom of choice and his/her responsibility to get better. Finally, it is evident that concordance is not only a complex construct, but also one that is still evolving. Therefore, it does not lend itself too readily to attempts to operationalize the concept, which explains why it has not been widely used in research on adherence till now^[42,56].

WHAT'S IN A NAME?

The question that often arises is whether these three terms are simply different names for an aspect of the

patient's behaviour, which is poorly understood anyway. However, careful consideration of the three terms does not support these notions. Firstly, the move away from compliance to adherence reflects the growing literature on the importance of patients' views and attitudes towards medication-taking. Secondly, it lays emphasis on the fact that patients need to be understood and helped when non-adherence is encountered. At the very least, they should never be held solely responsible for the failure to adhere to the clinician's recommendations. Finally, it addresses the fact that adherence lies on a continuum from full adherence, to partial adherence, and full non-adherence^[1,17,19,21,34,38,42]. Concordance goes one step further and focuses on adequate communication and the clinician-patient relationship as the cornerstones of the medication-taking process^[16,34,35,42,56]. Moreover, it is the only term that addresses the "normative" agenda, *i.e.*, whether it is "right or wrong" to follow the clinician's recommendations^[42]. Both compliance and adherence focus more on patient-behaviour during medication taking, while concordance highlights the processes, which underlie medication-taking, such as an equal and effective therapeutic relationship, which supports the patient during the entire course of receiving long-term treatment^[16,34,35,42,56]. Thus, these three terms are not simply different names for the same phenomena; rather, they are different concepts informed by research, which puts the patient's perceptions at the centre of the medication-taking process.

CONCLUSION

The concepts of compliance, adherence and concordance have several potential implications for the treatment of chronic mental illnesses; implications, which are diverse and wide ranging. Very briefly, they improve our understanding of the whole process of adherence behaviour, with patients' perceptions being the central tenet. They promote a research agenda, which focuses on, examines, and attempts to understand these patient related factors. For clinicians involved in the care of such patients, these concepts lay due emphasis on the critical elements of the process, such as sensitivity to patients' preferences, the need for adequate communication, and, perhaps, the most crucial aspect of all, the need for developing a healthy clinician-patient relationship. Therefore, these three terms are not simply an exercise in finding the right name, but represent real progress in the long-term treatment of chronic psychiatric disorders. However, one of the lacunae in research in this area is the relative lack of studies from developing countries^[43]. One can always argue that these concepts are far removed from clinical reality in resource-constrained, low-income countries of the developing world, with their huge patient loads and their overworked health-care services. However, even in these situations a start has to be made in understanding these vital aspects of medication taking, and then implementing some solutions to address the problem of non-adherence, as far as possible. Only by doing so, will we be

able to improve the long-term care of those who suffer from chronic psychiatric disorders in these countries.

REFERENCES

- 1 **Sabate E.** Adherence to long term therapies: evidence for action. Geneva: World Health Organization, 2003
- 2 **Murray CJ, Lopez AD.** Measuring the global burden of disease. *N Engl J Med* 2013; **369**: 448-457 [PMID: 23902484 DOI: 10.1056/NEJMr1201534]
- 3 **Blackwell B.** Treatment adherence. *Br J Psychiatry* 1976; **129**: 513-531 [PMID: 793670 DOI: 10.1192/bjp.129.6.513]
- 4 **Fenton WS, Blyler CR, Heinssen RK.** Determinants of medication compliance in schizophrenia: empirical and clinical findings. *Schizophr Bull* 1997; **23**: 637-651 [PMID: 9366000 DOI: 10.1093/schbul/23.4.637]
- 5 **Cramer JA, Rosenheck R.** Compliance with medication regimens for mental and physical disorders. *Psychiatr Serv* 1998; **49**: 196-201 [PMID: 9575004]
- 6 **Perkins DO.** Adherence to antipsychotic medications. *J Clin Psychiatry* 1999; **60** Suppl 21: 25-30 [PMID: 10548139]
- 7 **Kampman O, Lehtinen K.** Compliance in psychoses. *Acta Psychiatr Scand* 1999; **100**: 167-175 [PMID: 10493082 DOI: 10.1111/j.1600-0447.1999.tb10842.x]
- 8 **Lacro JP, Dunn LB, Dolder CR, Leckband SG, Jeste DV.** Prevalence of and risk factors for medication nonadherence in patients with schizophrenia: a comprehensive review of recent literature. *J Clin Psychiatry* 2002; **63**: 892-909 [PMID: 12416599 DOI: 10.4088/JCP.v63n1007]
- 9 **Pinikahana J, Happell B, Taylor M, Keks NA.** Exploring the complexity of compliance in schizophrenia. *Issues Ment Health Nurs* 2002; **23**: 513-528 [PMID: 12079602 DOI: 10.1080/01612840290052677]
- 10 **Keller MB, Hirschfeld RM, Demyttenaere K, Baldwin DS.** Optimizing outcomes in depression: focus on antidepressant compliance. *Int Clin Psychopharmacol* 2002; **17**: 265-271 [PMID: 12409679 DOI: 10.1097/00004850-200211000-00001]
- 11 **Nosé M, Barbui C, Tansella M.** How often do patients with psychosis fail to adhere to treatment programmes? A systematic review. *Psychol Med* 2003; **33**: 1149-1160 [PMID: 14580069 DOI: 10.1017/S0033291703008328]
- 12 **Dolder CR, Lacro JP, Leckband S, Jeste DV.** Interventions to improve antipsychotic medication adherence: review of recent literature. *J Clin Psychopharmacol* 2003; **23**: 389-399 [PMID: 12920416 DOI: 10.1097/01.jcp.0000085413.08426.41]
- 13 **Leo RJ, Jassal K, Bakhai YD.** Non-adherence with psychopharmacologic treatment among psychiatric patients. *Primary Psychiatry* 2005; **12**: 33-34
- 14 **Leucht S, Heres S.** Epidemiology, clinical consequences, and psychosocial treatment of nonadherence in schizophrenia. *J Clin Psychiatry* 2006; **67** Suppl 5: 3-8 [PMID: 16822090]
- 15 **Mitchell AJ.** High medication discontinuation rates in psychiatry: how often is it understandable? *J Clin Psychopharmacol* 2006; **26**: 109-112 [PMID: 16633137 DOI: 10.1097/01.jcp.0000205845.36042.ba]
- 16 **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]
- 17 **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]
- 18 **Byerly MJ, Nakonezny PA, Lescoufflair E.** Antipsychotic medication adherence in schizophrenia. *Psychiatr Clin North Am* 2007; **30**: 437-452 [PMID: 17720031 DOI: 10.1016/j.psc.2007.04.002]
- 19 **Julius RJ, Novitsky MA, Dubin WR.** Medication adherence: a review of the literature and implications for clinical practice. *J Psychiatr Pract* 2009; **15**: 34-44 [PMID: 19182563 DOI: 10.1097/01.pra.0000344917.43780.77]
- 20 **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]
- 21 **Kikkert MJ.** Medication adherence in patients with schizophrenia: a means to an end. Thesis, University of Amsterdam, Netherlands, 2010. Available from: URL: <http://dare.uva.nl/document/164057>
- 22 **Hardeman SM, Harding RK, Narasimhan M.** Simplifying adherence in schizophrenia. *Psychiatr Serv* 2010; **61**: 405-408 [PMID: 20360281 DOI: 10.1176/appi.ps.61.4.405]
- 23 **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]
- 24 **Sansone RA, Sansone LA.** Antidepressant adherence: are patients taking their medications? *Innov Clin Neurosci* 2012; **9**: 41-46 [PMID: 22808448]
- 25 **Acosta FJ, Hernández JL, Pereira J, Herrera J, Rodríguez CJ.** Medication adherence in schizophrenia. *World J Psychiatry* 2012; **2**: 74-82 [PMID: 24175171 DOI: 10.5498/wjp.v2.i5.74]
- 26 **Marder SR.** Overview of partial compliance. *J Clin Psychiatry* 2003; **64** Suppl 16: 3-9 [PMID: 14680412]
- 27 **Weiden P, Rapkin B, Mott T, Zygmunt A, Goldman D, Horvitz-Lennon M, Frances A.** Rating of medication influences (ROMI) scale in schizophrenia. *Schizophr Bull* 1994; **20**: 297-310 [PMID: 7916162 DOI: 10.1093/schbul/20.2.297]
- 28 **Weiden P, Rapkin B, Zygmunt A, Mott T, Goldman D, Frances A.** Postdischarge medication compliance of inpatients converted from an oral to a depot neuroleptic regimen. *Psychiatr Serv* 1995; **46**: 1049-1054 [PMID: 8829787]
- 29 **Lieberman JA, Stroup TS, McEvoy JP, Swartz MS, Rosenheck RA, Perkins DO, Keefe RS, Davis SM, Davis CE, Lebowitz BD, Severe J, Hsiao JK.** Effectiveness of antipsychotic drugs in patients with chronic schizophrenia. *N Engl J Med* 2005; **353**: 1209-1223 [PMID: 16172203 DOI: 10.1056/NEJMoa051688]
- 30 **Valenstein M, Ganoczy D, McCarthy JF, Myra Kim H, Lee TA, Blow FC.** Antipsychotic adherence over time among patients receiving treatment for schizophrenia: a retrospective review. *J Clin Psychiatry* 2006; **67**: 1542-1550 [PMID: 17107245 DOI: 10.4088/JCP.v67n1008]
- 31 **Tranulis C, Goff D, Henderson DC, Freudenreich O.** Becoming adherent to antipsychotics: a qualitative study of treatment-experienced schizophrenia patients. *Psychiatr Serv* 2011; **62**: 888-892 [PMID: 21807827 DOI: 10.1176/appi.ps.62.8.888]
- 32 **McDonald HP, Garg AX, Haynes RB.** Interventions to enhance patient adherence to medication prescriptions: scientific review. *JAMA* 2002; **288**: 2868-2879 [PMID: 12472329 DOI: 10.1001/jama.288.22.2868]
- 33 **Osterberg L, Blaschke T.** Adherence to medication. *N Engl J Med* 2005; **353**: 487-497 [PMID: 16079372 DOI: 10.1056/NEJMr050100]
- 34 **Sluijs E, Dulmen Sv, Dijk Lv, Ridder Dd, Heerdink R, Bensing J.** Patient adherence to medical treatment: a meta review. Utrecht: NIVEL, 2006: 1-142
- 35 **Gray R, Leese K, Bindman J, Becker T, Burti L, David A, Gournay K, Kikkert M, Koeter M, Puschner B, Schene A, Thornicroft G, Tansella M.** Adherence therapy for people with schizophrenia. European multicentre randomised controlled trial. *Br J Psychiatry* 2006; **189**: 508-514 [PMID: 17139034 DOI: 10.1192/bjp.bp.105.019489]
- 36 **Haynes RB, Ackloo E, Sahota N, McDonald HP, Yao X.** Interventions for enhancing medication adherence. *Cochrane Database Syst Rev* 2008; **(2)**: CD000011 [PMID: 18425859 DOI: 10.1002/14651858.CD000011.pub3]
- 37 **Morris LS, Schulz RM.** Medication compliance: the patient's perspective. *Clin Ther* 1993; **15**: 593-606 [PMID: 8364951]
- 38 **Hughes CM.** Medication non-adherence in the elderly: how

- big is the problem? *Drugs Aging* 2004; **21**: 793-811 [PMID: 15382959 DOI: 10.2165/00002512-200421120-00004]
- 39 **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]
- 40 **Donovan JL**. Patient decision making. The missing ingredient in compliance research. *Int J Technol Assess Health Care* 1995; **11**: 443-455 [PMID: 7591546 DOI: 10.1017/S026646230008667]
- 41 **DiMatteo MR**, Giordani PJ, Lepper HS, Croghan TW. Patient adherence and medical treatment outcomes: a meta-analysis. *Med Care* 2002; **40**: 794-811 [PMID: 12218770 DOI: 10.1097/01.mlr.0000114908.90348.f9]
- 42 **Horne R**, Weinman J, Barber N, Elliott R, Morgan M. Concordance, adherence and compliance in medicine taking. UK: National Co-ordinating Centre for NHS Service Delivery and Organisation R and D, 2005: 1-309
- 43 **Jin J**, Sklar GE, Min Sen Oh V, Chuen Li S. Factors affecting therapeutic compliance: A review from the patient's perspective. *Ther Clin Risk Manag* 2008; **4**: 269-286 [PMID: 18728716]
- 44 **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]
- 45 **Adams SG**, Howe JT. Predicting medication compliance in a psychotic population. *J Nerv Ment Dis* 1993; **181**: 558-560 [PMID: 7902413 DOI: 10.1097/00005053-199309000-00005]
- 46 **Adams J**, Scott J. Predicting medication adherence in severe mental disorders. *Acta Psychiatr Scand* 2000; **101**: 119-124 [PMID: 10706011 DOI: 10.1034/j.1600-0447.2000.90061.x]
- 47 **Leventhal H**, Cameron L. Behavioural theories and the problem of compliance. *Patient Educ Couns* 1987; **10**: 117-138 [DOI: 10.1016/0738-3991(87)90093-0]
- 48 **Horne R**, Weinman J. Predicting treatment adherence: an overview of theoretical models. In: Myers LB, Midence K, editors. *Adherence to treatment in medical conditions*. Amsterdam: Harwood Academic, 1998: 25-50
- 49 **Haynes RB**, Taylor DW, Sackett DL. *Compliance in health care*. Baltimore: Johns Hopkins University Press, 1979
- 50 **Barofsky I**. Compliance, adherence and the therapeutic alliance: steps in the development of self-care. *Soc Sci Med* 1978; **12**: 369-376 [PMID: 705382]
- 51 **Inkster ME**, Donnan PT, MacDonald TM, Sullivan FM, Fahy T. Adherence to antihypertensive medication and association with patient and practice factors. *J Hum Hypertens* 2006; **20**: 295-297 [PMID: 16424861 DOI: 10.1038/sj.jhh.1001981]
- 52 **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]
- 53 **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]
- 54 **Fink DL**. Tailoring the consensual regimen. In: DL Sackett DL, Haynes RB. *Compliance with therapeutic regimens*. Baltimore: John Hopkins University Press, 1976: 110-118
- 55 **Cramer JA**, Roy A, Burrell A, Fairchild CJ, Fuldeore MJ, Ollendorf DA, Wong PK. Medication compliance and persistence: terminology and definitions. *Value Health* 2008; **11**: 44-47 [PMID: 18237359 DOI: 10.1111/j.1524-4733.2007.00213.x]
- 56 **Jones G**. Prescribing and taking medicines. *BMJ* 2003; **327**: 819 [DOI: 10.1136/bmj.327.7419.819]

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