



Medication nonadherence and psychiatry

Sarah C.E. Chapman and Rob Horne

Purpose of review

Nonadherence to appropriately prescribed medication for psychiatric disorders prevents patients from realizing the full benefits of their treatment and negatively impacts on individuals, their families and the healthcare system. Understanding and reducing nonadherence is therefore a key challenge to quality care for patients with psychiatric disorders. This review highlights findings regarding the prevalence and consequence of nonadherence, barriers to adherence and new intervention methods from 2012 onwards.

Recent findings

Recent research has highlighted that nonadherence is a global challenge for psychiatry and has linked nonadherence to poorer outcomes, including hospital admissions, suicide and mortality. Optimizing medication regimens can reduce nonadherence; however, often a complex interplay of factors affects individuals' motivation and ability to follow their prescription. Psychiatrists can enable patients to develop an accurate model of their illness and treatment and facilitate adherence. However, nonadherence is often a hidden issue within consultations. Novel interventions using new technologies and tailoring techniques may have the potential to reduce nonadherence.

Summary

Nonadherence remains a significant challenge for patients with psychiatric disorders, physicians and healthcare systems. New developments demonstrate the importance of developing tailored interventions to enable patients to overcome perceptual and practical barriers to adherence.

Keywords

bipolar disorder, intervention, medication adherence, psychiatry, schizophrenia

INTRODUCTION

Taking the prescribed dose of medication, at the correct time, and for the full course of treatment is fundamental to patients realizing the full potential benefits of medications. However, between 30 and 50% of medicines for long-term conditions are not taken as prescribed, resulting in costs for individual patients and healthcare systems [1]. Research suggests that rates of nonadherence in patients with psychiatric disorders are comparable to those of patients with other long-term conditions [2,3].

The Perceptions and Practicalities Approach (PaPA) has been used to describe factors contributing to nonadherence in psychiatric disorders [4,5] (see Fig. 1). This states that nonadherence is the product of a range of perceptual factors (e.g. patients' beliefs about their illness and treatment) and practical factors (e.g. capability and resources) influencing their motivation and ability to start and continue with treatment. Specifically, the model emphasizes that, even when patients have the ability and opportunity to take their medication as prescribed, they may lack the motivation to adhere. Thus, to understand and address

nonadherence, we need to view the illness and the treatment from the patients' perspective. Within this approach, two key beliefs have been implicated in the way in which medications are prescribed: belief in personal need for medication and concerns about the potential adverse consequences of medication. This Necessity-Concerns Framework has been found to have utility in explaining nonadherence across long-term conditions, including within psychiatric disorders [6].

Effective interventions to improve adherence remain elusive; a recent Cochrane review has called for more innovative interventions [7,8]. To

Centre for Behavioural Medicine, UCL School of Pharmacy, London, UK
Correspondence to Rob Horne, Centre for Behavioural Medicine, Department of Practice and Policy, UCL School of Pharmacy, Entrance A, BMA House, Tavistock Square, London WC1H 9JP, UK. Tel: +44 0 20 7874 1281; fax: +44 0 20 7387 5693; e-mail: r.horne@ucl.ac.uk

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KEY POINTS

- Nonadherence remains a global challenge for psychiatry that has been linked to suicide rates, all-cause mortality and hospitalization for patients.
- Adherence to psychiatric medications is a complex, dynamic behaviour requiring patients to initiate treatment and continue to take their medications at the correct time, in the correct dose, for prolonged periods of time.
- Modifying practical barriers to adherence (e.g. dose frequency) can reduce nonadherence; however, patients also need to be motivated to adhere by an informed understanding of their illness and treatment.
- A strong alliance between patients and psychiatrists can protect against nonadherence in part by enabling patients to develop an accurate model of their illness and treatment.
- Effective adherence interventions remain elusive; however, new methods of tailoring content to the needs of individual patients combined with the use of technologies such as electronic monitoring and SMS may prove effective.

achieve this, we need to apply sound theories of the causes of nonadherence and theories for changing medication-taking behaviour, the why and how of nonadherence [5]. This review will therefore focus on recent developments from 2011 in the field of nonadherence within psychiatric disorders, with particular focus on the determinants of adherence and interventions to promote adherence.

NONADHERENCE IS A GLOBAL CHALLENGE FOR PSYCHIATRY

Nonadherence to psychiatric medication is a global problem. Recent research has highlighted nonadherence as a key challenge to psychiatric care in

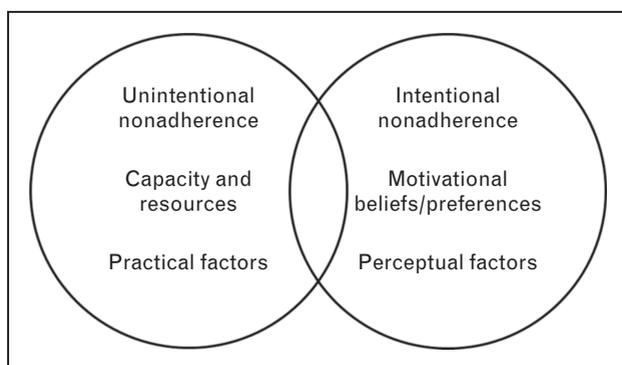


FIGURE 1. Perceptions and Practicalities Approach to nonadherence [5].

Asia [9–11], Europe [12–14,15[■]], South America [16], North America [17[■],18–20,21[■]], Australia [22], the Middle East [23[■]] and Africa [24[■]]. In Africa, Alene *et al.* [24[■]] evaluated adherence rates to antipsychotic medication in patients receiving care at an Ethiopian hospital. They found that, although 52.1% reported that they had never missed a dose or taken it outside the time instructed, only 19.6% were fully adherent if assessed using pharmacy refill records, illustrating that nonadherence can be underestimated in this setting, similarly to discrepancies shown in other settings, for example in a South Korean sample of outpatients with schizophrenia [25].

PATTERNS OF NONADHERENCE IN PSYCHIATRIC DISORDERS

Realizing the full benefits of an appropriately prescribed medication is conditional on optimal adherence. However, in practice, adherence is a complex, dynamic behaviour; patients can be non-adherent to their prescribed regimen because they do not initiate, accurately maintain or persist with their regimen. A new taxonomy of adherence terminology has been developed to promote consistency in the terminology used to describe adherence [26[■]]. This describes adherence as being composed of initiation (taking the first dose of the medication), discontinuation (no longer taking the medication) and implementation (whether the patient's actual behaviour corresponds to the prescribed dosing regimen in the period from initiation to discontinuation). Within this taxonomy, persistence refers to the time between initiation and the final dose of the medication. Implementation nonadherence can include a range of differences between the actual regimen execution and that prescribed, including missing doses, taking a different dose of medication than that prescribed and taking medication at different times.

Different assessment methods can be used to identify these differing types of nonadherence; for example, Yang *et al.* [25] used pill counts to assess whether the patient had taken the correct number of doses, and electronic monitoring to assess whether patients had taken these doses on schedule. Other researchers have used nonpersistence with a regimen to assess nonadherence, often using pharmacy refill (e.g. [21[■],27]). Through understanding the different aspects of adherence measured by these assessments, we can understand a lack of correspondence between measurements and begin to investigate whether different patterns of adherence have different causes and consequences.

Recent research has highlighted different patterns of nonadherence. Jaeger *et al.* [28] used latent class analysis to group 371 inpatients with schizophrenia on the basis of their scores on the Medication Adherence Rating Scale at baseline, a self-report/clinician-report tool. They identified five groups of patients on the basis of their adherence responses and found that different patterns of adherence were associated with different rates of later discontinuation and hospitalization. Chang *et al.* [9] categorized schizophrenic patients on the basis of type of nonadherence as measured by pharmacy refill and found that different patterns of nonadherence were associated with different antipsychotic drugs. Offord *et al.* [21[■]] found that patients with schizophrenia who had early nonadherence within 90 days of starting a new prescription had lower adherence for the following 12 months.

IMPACT OF NONADHERENCE

Evidence for an impact of nonadherence on outcomes for psychiatric patients has been consolidated within new research. Nonadherence has been found to predict poorer outcomes for patients, including hospital admission [29,30], violence [31[■]], suicide and premature mortality. San *et al.* [30] analysed the medical records of patients with schizophrenia/schizoaffective disorder admitted to acute care. Of the 1646 patients on whom data were available, for 58.6% of patients the main reason for hospital admission was listed as nonadherence.

Nonadherence can also be a risk factor for violence in psychosis, as confirmed by a recent meta-analysis [31[■]]. Witt *et al.* [31[■]] found a moderate association between violence (including a range of measures such as reported aggression and arrests) and adherence to medication [odds ratio (OR) 2.0] on the basis of nine studies.

In suicide research, adherence has been identified as the 'strongest modifiable protective factor' against suicide in patients with bipolar disorder who were followed for 10 years [32]. Lindstrom *et al.* [12] analysed the autopsy blood samples of 33 patients from a psychosis clinic who had committed suicide over a 7-year period. They found that plasma drug levels for prescribed antipsychotic and antidepressant medications suggested that three out of 24 were nonadherent to antipsychotics and 10 out of 10 were nonadherent to antidepressants at the time of their suicide. Similarly, Ruengorn *et al.* [33[■]] used a case-control methodology and estimated the odds of suicide attempts in patients with major depressive disorder as approximately twice as high for patients with low adherence.

Nonadherence has also been associated with premature mortality in schizophrenia [34[■]]. Cullen *et al.* [34[■]] retrospectively examined the records of a cohort of US patients with schizophrenia and found that low adherence to antipsychotics predicted mortality. As with previous research showing an association between mortality and adherence [35], it is unclear whether adherence *per se* is contributing to reduced mortality, or whether it is a marker for other factors. For example, as stated above, adherence could have a direct effect on psychiatric outcomes and associated risk. However, adherence may be a marker for a more direct causal effect, for example good social support or a tendency to engage in health behaviours, including exercise.

NONADHERENCE IS OFTEN A HIDDEN PROBLEM

It is very difficult for practitioners to guess which of their patients are nonadherent [11,23[■],36]. Olivares *et al.* [23[■]] surveyed 4722 psychiatrists across 36 countries. Psychiatrists estimated that 53% of their patients with schizophrenia were nonadherent, suggesting that they recognized the importance of nonadherence. However, identifying the particular patients who are not adherent may be a particular challenge. Stephenson *et al.* [37[■]] asked US physicians to rate the adherence of individual patients with bipolar disorder and/or schizophrenia, and found that 72% of patients whose prescription refill records indicated nonadherence were rated as adherent by their physician. Thus, there is evidence that nonadherence may be recognized as a general problem but remains hidden within individual consultations. Patients may fear that physicians will interpret a lack of faith in their medicine as representing a lack of faith in them, and therefore be reluctant to raise their concerns and doubts with their physicians.

A strong, trusting relationship between patients and physicians may therefore protect against nonadherence, as confirmed by a new meta-analysis that found that, where the alliance between clinicians and patients was strong, patients were more likely to adhere [38[■]]. Thompson and McCabe [38[■]] identified 23 studies relevant to this topic and suggested that future studies should focus on objective assessments of the content of clinical interactions. In one study that did directly assess consultation content, Quirk *et al.* [39[■]] analysed recordings of 92 consultations that contained discussion of antipsychotic medications between patients and nine UK psychiatrists. Nonadherence was disclosed in 22 consultations and most frequently resulted in a prescription change in

line with the behaviour of the patient [39²²]. The researchers suggest that physicians may avoid risking conflict around medication adherence in order to maintain patients' engagement with treatment. However, research on the causes of nonadherence suggests that addressing patients' doubts and concerns about medication directly may be essential to supporting adherence [6,40,41].

DETERMINANTS OF NONADHERENCE

Some medication regimens appear to be associated with greater adherence due to specific features of the medication, such as side effect profiles [27] or reduced dosing frequency (as shown by recent systematic reviews) [42,43]. However, even where regimens are optimized for adherence by reducing the number or frequency of doses, motivation is still required to maintain full adherence.

Within the PaPA, adherence to medication is determined by both practical factors (e.g. resources, patient capacity) and perceptual factors (e.g. beliefs about treatment and illness) (see Fig. 1). Hence, attempts to improve adherence by tackling practical barriers alone may not be successful if perceptual barriers (e.g. doubts about medication necessity or concerns about adverse consequences) are salient for individuals. Staring *et al.* [44] found that a lack of insight, and in particular low recognition of the need for treatment, was strongly associated with nonadherence within a sample of patients with schizophrenia. This effect was particularly strong when patients had good verbal memory. Even where practical barriers are important, they may reinforce or overlap with perceptual barriers. For example, a cross-sectional survey of 24017 US patients with chronic illnesses, including depression, found that perceptual factors predicted reported unintentional nonadherence (e.g. forgetting, running out of medication, affordability), suggesting that motivational factors can impact on both perceptual and practical barriers to adherence [45].

The key role of medication beliefs in adherence is illustrated by a recent qualitative synthesis of research on this topic in patients with schizophrenia, which highlighted beliefs about control, dependence and stigma [46]. Richardson *et al.* [47] conducted a meta-analysis of the association between medication attitudes and adherence in patients with psychoses, finding 14 studies indicating a small to moderate association. A need for more prospective and intervention studies was identified. Patients with a lack of insight into their psychiatric disorder have also been found to be at risk of nonadherence [13]. These studies demonstrate that motivational factors extend

beyond knowledge of medication efficacy and adverse effects.

Comorbid psychiatric conditions can themselves be risk factors for nonadherence. Depression and substance abuse have both been linked to nonadherence within patients with psychiatric diagnoses [32,48²²,49²²]. Psychiatric comorbidity is also a risk factor for nonadherence in physical disorders. Kronish *et al.* [50²²] found that veterans with post-traumatic stress disorder (PTSD) had increased odds of nonadherence to all medications, relative to veterans without PTSD (OR 1.47), partly due to increased concerns about the potential adverse effects of treatment [51]. Similarly, Rao *et al.* [52] found that nonadherence in HIV patients was predicted by symptoms of depression, which were also associated with increased perceived HIV stigma. Comorbid psychiatric conditions may therefore impact on both practical barriers to adherence (e.g. through increased regimen complexity) and perceptual barriers (e.g. through increased concerns).

NEW DEVELOPMENTS IN ADHERENCE INTERVENTIONS

Adherence interventions require three key components: content (e.g. information, feedback), delivery vehicle (e.g. face-to-face nurse support, telephone calls, e-mail) and a broader context (e.g. primary care setting, inpatient care); see Fig. 2 [5].

Intervention content

New developments have focused on intervention content, in particular tailoring, cognitive behavioural therapy (CBT) techniques and financial incentives. Sajatovic *et al.* [53,54] found improvements in adherence in a group of patients with bipolar disorder who were screened on factors including attitudes towards their medicines and

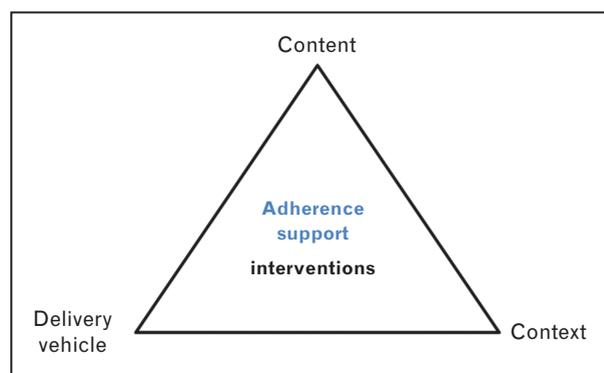


FIGURE 2. Intervention components, based on content from [5].

assigned intervention content on this basis. However, a fully controlled trial is needed before strong conclusions can be drawn regarding the utility of this tailoring process. Gleeson *et al.* [55] addressed medication adherence as part of relapse prevention therapy for first-episode psychosis, a CBT-based intervention composed of 7 months of fortnightly individual therapy sessions along with family intervention. They found that medication adherence improvements were sustained at 30 months of follow-up. The use of financial incentives in order to motivate adherence is one strategy that a new systematic review has indicated may be effective across long-term conditions, including psychiatric disorders [56]. However, questions remain regarding the ethics of this approach, in particular the implications for informed choice relating to treatments wherein there is potential for harm as well as benefit.

Delivery vehicle

Novel methods of delivering interventions have been applied within psychiatric settings, including computerized decision tools [57[■]], electronic monitoring and feedback [58[■]], SMS [15[■]] and telemonitoring [59]. Results from these approaches are promising, but the evidence for efficacy is mixed. Montes *et al.* [15[■]] reported improvements in adherence for patients with schizophrenia who were sent 3 months of daily SMS reminders; however, patients were only followed for 3 months postintervention and a substantial proportion of intervention patients who did not receive all SMS messages were excluded from the sample. Velligan *et al.* [58[■]] found that patients with schizophrenia who were given electronic pill cap reminder devices had equivalent improvements in adherence to those given 30 min of individualized support per week for 9 months. However, they found higher drop-outs in the electronic pill cap condition and did not follow up patients postintervention. Questions therefore remain about whether these new intervention delivery vehicles are suitable for all patients, and whether they result in long-term improvements in adherence.

Intervention context

Intervention content and delivery may need to be contextualized to environmental factors, including cultural variation. For example, Read [60[■]] conducted qualitative interviews with patients taking antipsychotic medication in Ghana, and highlighted reasons for nonadherence, including side effects impacting on the ability to perform physical

work, and a desire for a permanent 'cure' rather than a maintenance therapy. Thus, particular beliefs may be more relevant to some individuals within particular settings. However, it is important to recognize that variations in treatment perceptions and behaviours such as adherence are likely to be greater within cultural groups than across groups [61]. Hence, intervention content should be tailored to the individual rather than across a cultural group. Kopelowicz *et al.* [62[■]] reported a culturally adapted family intervention for Mexican American patients with schizophrenia, which improved adherence at 12 months postintervention, illustrating ways in which the intervention content and delivery can be addressed to barriers specific to the patient group without relying on generalizations about which barriers patients would face on the basis of their background. For example, they tailored intervention content on the basis of the outcomes from individual interviews with patients. By personalizing intervention content based on individual attitudes, the researchers ensured culturally relevant content without making generalizations about the typical beliefs held by a specific group.

In summary, new interventions have been developed, and questions around their long-term effectiveness and relevance across diverse patient groups remain. In addition, one key challenge for adherence intervention development is to systematically describe intervention components to enable researchers to isolate the effective components of interventions and facilitate understanding and replication interventions [7]. For example, currently, both or neither of two interventions described as psychoeducational may address concerns about side effects. Within the field of behaviour change, a taxonomy to describe intervention components has been developed over recent years [63[■]], which may be applicable to adherence interventions. By understanding the processes and active components within effective interventions, we may be able to open the 'black box' of intervention techniques and produce brief interventions tailored to the needs of individual patients [7].

CONCLUSION

Nonadherence remains a challenge for patients with psychiatric disorders, their physicians and healthcare providers, resulting in poorer outcomes for patients. New developments in the field of psychiatry shed light on key modifiable determinants of nonadherence within psychiatric disorders. Using this understanding to build theories of both adherence and behaviour change is a key challenge

[5]. New technologies may also be able to support adherence within low-resource settings.

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Conflicts of interest

There are no conflicts of interest.

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