

Why don't patients take their medicine? Reasons and solutions in psychiatry[†]

Alex J. Mitchell & Thomas Selmes

Abstract Over the course of a year, about three-quarters of patients prescribed psychotropic medication will discontinue, often coming to the decision themselves and without informing a health professional. Costs associated with unplanned discontinuation may be substantial if left uncorrected. Partial non-adherence (much more common than full discontinuation) can also be detrimental, although some patients rationally adjust their medication regimen without ill-effect. This article reviews the literature on non-adherence, whether intentional or not, and discusses patients' reasons for failure to concord with medical advice, and predictors of and solutions to the problem of non-adherence.

This is the first of two articles by Mitchell & Selmes in APT on patient engagement and retention in treatment. The second, which addresses missed appointments, will appear in the next issue of the journal (Mitchell & Selmes, 2007).

The degree to which an individual follows medical advice is a major concern in every medical specialty (Osterberg & Blaschke, 2005). Much attention has focused on methods to persuade patients to adhere to recommendations, without sufficient acknowledgement that avoidance of sometimes complex, costly and unpleasant regimens may be entirely rational (Mitchell, 2007a). Equally overlooked is the influence of communication between patients and healthcare professionals. Put simply, if no clear agreement is formed with the patient at the onset of treatment then it should be of no surprise if concordance turns out to be less than ideal. In one study the chance of premature discontinuation was found to be less than half in patients who recalled being told to take the medication for at least 6 months compared with those not given this information (Bull *et al*, 2002b). This task is made more difficult when patients lack insight into their condition (see below).

Given the necessity of therapeutic agreement, the term compliance has given way to adherence and concordance (Box 1) (Haynes *et al*, 2002). In considering the nosology of concordance and adherence a useful distinction is between individuals

who do not start a medication (similarly those who do not attend their first appointment) and those who start the course but either take medication incompletely (partial compliance or adherence) or discontinue prematurely against medical advice (Fig. 1). There has been little research on reluctance to start medication which equates to treatment refusal or overt non-adherence. Kasper *et al* (1997) found in a group of 348 newly admitted psychiatric in-patients that 12.9% refused treatment but that 90% of these ended their refusal within 4 days. Synthesising data on adherence behaviour is difficult because of the wide range of assessment methods (for review see Velligan *et al*, 2006). Few studies have examined what

Box 1 Working definitions about health behaviour

Adherence (compliance) is the extent to which an individual changes their health behaviour to coincide with medical advice

Concordance is the degree to which clinical advice and health behaviour agrees

Therapeutic alliance is an agreement between patients and health professionals to work together

Therapeutic disagreement is a divergence in the views of patients and doctors on the subject of treatment

[†]For a commentary on this article see pp. 347–349, this issue.

Alex Mitchell is Consultant and Honorary Senior Lecturer in Liaison Psychiatry at University Hospitals Leicester (Department of Liaison Psychiatry, Brandon Unit, Leicester General Hospital, Gwendolen Road, Leicester LE5 4PW, UK. Email: alex.mitchell@leicspart.nhs.uk) and author of the prize-winning book *Neuropsychiatry and Behavioural Neurology Explained: Diseases, Diagnosis, and Management* (2003). Thomas Selmes is a senior house officer on the York psychiatry scheme and was previously a medical student at Leicester University.

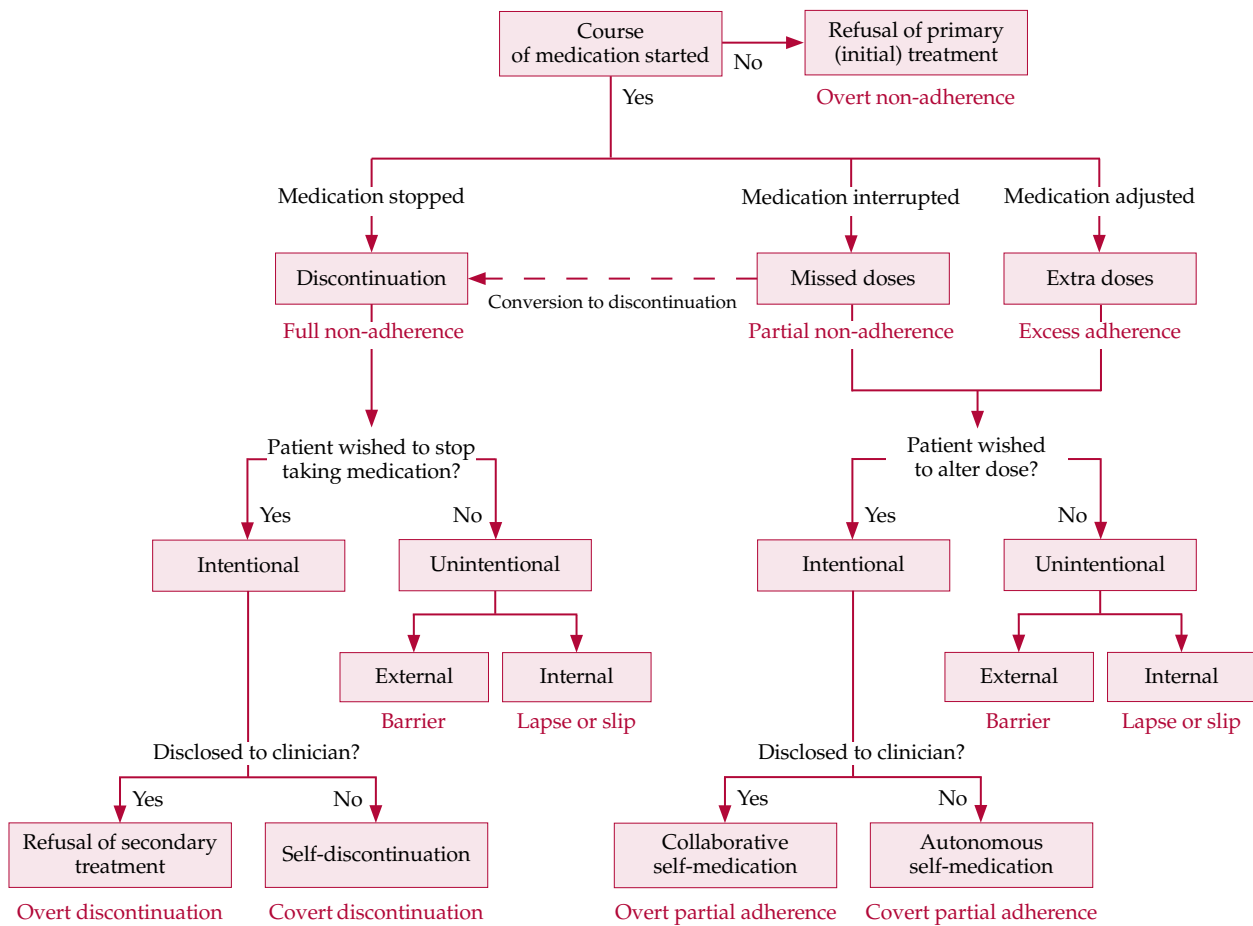


Fig. 1 Nosology of adherence behaviour.

advice patients actually receive and thus it is often impossible to test whether patient behaviour is truly at odds with what was agreed.

It is useful to remember that many predictors are generic and applicable to all patients (Box 2). Three important predictors are complexity of the regimen, duration of the course and frequency of follow-up contact. Regular contact reduces rates of both missed medication and missed appointments (Rittmannsberger *et al*, 2004; this will be discussed further in Mitchell & Selmes, 2007). The complexity of a treatment regimen (number of tablets, number of medications and drug interval) adversely affects adherence. Equally, regimens that require disruption to lifestyle, or special techniques or arrangements are less welcome by patients. A systematic review found that the number of doses prescribed per day was inversely related to adherence (Claxton *et al*, 2001). In elderly patients acceptable adherence is common in those taking only one medicine but rapidly falls in those taking four or more. Regarding the length of the prescribed course of treatment, most imagine it is relatively simple to follow a 5-day antibiotic course but in reality only two-thirds

manage to do so successfully. Ask patients to follow a 7-day course, with antibiotics four times a day, and ideal concordance is achieved by less than 40%. In psychiatry, we expect patients to agree to much longer courses of medication (occasionally for an indefinite period if risks are judged sufficiently high) (Mitchell, 2006a).

In this review, we will examine the predictors of both partial adherence and discontinuation in those taking psychotropic medication, in an attempt to understand why some patients have difficulty following the advice of mental health professionals and why adherence rates appear to be lower than in other specialties (see also Cramer & Rosenheck, 1998).

Costs of less-than-ideal adherence

There is considerable evidence that premature medication discontinuation is costly (Sullivan *et al*, 1995). Undisclosed (covert) non-adherence appears to be particularly hazardous (Task Force for Compliance, 1994). Kang *et al* (2005) examined antipsychotic adherence of individuals prior to admission to

hospital with schizophrenia: 37.1% had been totally non-adherent during the 6 months prior to admission. Although the majority had missed medication on fewer than 20% of days, many relapsed anyway. Reduced adherence weakens treatment benefits, especially when no alternatives are explored (Irvine *et al*, 1999).

Fewer studies in psychiatry have looked at the complications of partial concordance. Three of the most influential of these have been conducted in the USA. In a sample of 7864 Medicaid patients taking atypical antipsychotics, those who achieved less than 80% of ideal concordance were about 50% more likely than fully concordant patients to have been hospitalised (Eaddy *et al*, 2005). Jeste's group (Gilmer *et al*, 2004) found a hierarchy of risk of admission, from those who were non-adherent, those who took medication to excess and finally those who were partially adherent. In the largest study, Valenstein *et al* (2002) showed that those with less than 80% concordance were 2.4 times more likely to be admitted than patients with good concordance.

General predictors of missed medication

A number of authors have reviewed factors predicting non-adherence, but only a handful have considered predictors in psychiatric populations (Fenton *et al*, 1997). Predictors may be usefully divided into patient factors, clinician factors and illness factors (Box 2).

Patient factors

Intentional non-adherence

Distinguishing intentional non-adherence (missing or altering doses to suit one's needs) from unintentional non-adherence (e.g. forgetting to take medication) is a relatively recent development. In fact, in long-term studies understandable reasons for discontinuation are more common than irrational reasons. Intentional non-adherence is predicted by the balance of an individual's reasons for and against taking medication, as suggested by utility theory. Intentional non-adherence is a common reason not to start a course of medication, but it may be less common than accidental non-adherence in relation to missing individual doses (Lowry *et al*, 2005). Predictors of intentional non-adherence include less severe disease (and feeling well), the desire to manage independently of the medical profession (self-efficacy), disagreement with or low trust in clinicians, and receipt of low levels of medical information (Piette *et al*, 2005).

Box 2 Predictors of treatment concordance problems

General

- Duration and complexity of regimen
- Lack of informal support

Patient (intentional)

- Concerns about the side-effects
- Few perceived benefits
- Stigma of taking medication
- Adjustment to suit daily routine
- Concerns about cost
- Concerns about availability
- Concerns about dependency

Patient (non-intentional)

- Slips and lapses
- External distractors
- Misunderstanding instructions

Clinician

- Poor doctor-patient relationship
- Poor empathy
- Poor explanation/communication
- Inadequate follow-up

Illness

- Severe illness
- Depression or distress
- Psychosis
- Cognitive impairment

Specific adverse effects

Weight gain due to medication has been linked with non-adherence and subjective distress (Fakhoury *et al*, 2001). Obese individuals are more than twice as likely as those with a normal body mass index to miss their medication (Weiden *et al*, 2004a). Fakhoury (1999) found that more than 70% of patients described weight gain due to antipsychotics as extremely distressing, which was higher than that for any other side-effect.

Sexual dysfunction is a significant source of distress and may be linked to poor adherence. Olfson *et al* (2005) studied sexual dysfunction in 139 out-patients with DSM-IV schizophrenia who were receiving an antipsychotic but no other medications associated with sexual side-effects. Sexual dysfunction occurred in 45.3% of the group and was associated with significantly lower ratings on global quality of life. Rosenberg *et al* (2003) examined the effects of sexual side-effects on adherence. They found that 62.5% of men and 38.5% of women felt that their psychiatric medications were causing sexual side-effects; 41.7% of men and 15.4% of women admitted

that they had stopped their medications at some point during treatment because of sexual side-effects. Importantly, 50% of the sample 'never or infrequently' spoke about sexual functioning with their primary mental healthcare providers, and 80% of the women with sexual side-effects had not discussed sexual dysfunction with their mental healthcare providers.

Illness beliefs and knowledge of medication

Concepts of health and disease are important factors in adherence in mental health (Kelly *et al*, 1987). Patients' understanding of their condition and its need for treatment is positively related to adherence, and in turn adherence, satisfaction and understanding are all related to the amount and type of information given. Studies have shown that patients who understand the purpose of the prescription are twice as likely to collect it than those who do not understand (Daltroy *et al*, 1991). Awareness of treatment accounted for 20% and 34% of variation in subjective responses (satisfaction with medication and tolerability) to atypical and typical antipsychotic drugs in one recent report (Ritsner *et al*, 2004).

It is often assumed that patients understand a reasonable amount about their illness, but how often is this assumption tested? In a classic report, Joyce *et al* (1969) demonstrated that patients were unable to recall half of the information given to them by their physician. Two-thirds of individuals recently discharged from hospital did not know what time to take medication and less than 15% recalled the common side-effects (Makaryus & Friedman, 2005).

Preliminary work suggests that figures in psychiatry are comparable. Only 1 in 10 of those taking clozapine are aware of potential haematological risks (Angermeyer *et al*, 2001). Of those prescribed antipsychotics most do not feel involved in treatment decisions and state that they take medication only because they are told to (Gray *et al*, 2005). Patients typically leave the clinic with a poor understanding of the rationale for therapy (Weiden *et al*, 2004a). In one study, two-thirds of psychiatric in-patients did not understand why they were taking medication, and the vast majority could not be said to have given informed consent to their treatment (Brown *et al*, 2001). This finding was consistent in both detained and informal in-patients. Similarly, many patients misunderstand prescription instructions. Col *et al* (1990) found that 50% of patients with depression believed they did not need their antidepressants when they began to feel better or that the medication could be taken as required. The UK public campaign Defeat Depression revealed that many people were wary of taking antidepressants because they believed that individuals with depression should 'pull themselves

together' and more than three-quarters believed that the medications are addictive (Paykel *et al*, 1998). In a small sample with mood disorder or schizophrenia, Adams & Scott (2000) found that two components of the health beliefs model (perceived severity and perceived benefits) and two modifying factors (dysfunctional attitudes and locus of control beliefs regarding health) differentiated significantly between highly adherent and poorly adherent individuals. Although little work has examined how illness beliefs (good and bad) are formed, previous bad experiences are an important predictor of future non-attendance and non-adherence (Gonzalez *et al*, 2005).

Clinician factors

The doctor-patient relationship

The importance of good communication between patient and health professional is increasingly acknowledged in relation to adherence (Stevenson *et al*, 2004). At its essence this means forging a joint therapeutic agreement with full patient involvement. This is a two-way process in which willingness to discuss mental health issues with a doctor is predicted largely by the perceived helpfulness of and trust in that doctor (Wrigley *et al*, 2005). This can be quantified using a tool that measures therapeutic alliance perceived by patient or clinician.

In practice, the process of making a joint therapeutic plan is often abbreviated. Doctors tend to overestimate the amount of information they have given to patients (Makoul *et al*, 1995). At the same time, patients often misunderstand medical words. According to one study (Thompson & Pledger, 1993), 22% of patients have difficulty with the word 'symptom', 38% with the word 'orally' and 76% with the word 'stroke'.

Patients who are very unwell or without insight are unlikely to tolerate an extensive dialogue about possibilities. Yet collaborative decision-making has been shown to be a consistent predictor of health outcomes. Kaplan *et al* (1996) examined participatory decision-making style on a three-item scale. Higher scores for clinicians' participatory styles were associated with greater patient satisfaction and less likelihood of changing doctor. Bultman & Svarstad (2000) conducted an impressive study on reasons for missed antidepressants. They found that 25% of clients were not satisfied with their medication and 82% reported missing doses or stopping treatment earlier than recommended. Path analysis showed that patients with more positive beliefs about the treatment are more likely to attend for follow-up and are more satisfied with treatment after attempting medication use. Physicians' communication style during follow-up and client satisfaction were

both predictive of better medication adherence. A collaborative communication style by the clinician enhanced client knowledge of the medication, improved satisfaction with medication and improved reliability of medication use.

Predictors of missed medication in specific psychiatric disorders

Depression and antidepressants

The adherence habits of those prescribed antidepressants have recently been summarised elsewhere (Mitchell, 2006b). Roughly 10% of patients prescribed antidepressants fail to pick up their first prescription and about a third collect only the initial (typically 4-week) prescription. Of those who start medication, non-adherence rates increase with time (Bultman & Svarstad, 2002). In a study of 200 patients attending 14 family doctors in five different practices, non-adherence rates were 16% at week one, 41% at week two, 59% at week three and 68% at week four (Johnson, 1981). In those on long-term maintenance treatment, discontinuation rates for selective serotonin reuptake inhibitors (SSRIs) are above 70% (Mullins *et al*, 2005). Of all those who discontinue medication, 60% have not informed their doctor by 3 months and a quarter have not done so by 6 months (Maddox *et al*, 1994; Demyttenaere *et al*, 2001). This is sometimes referred to as covert non-adherence.

Predictors of missed antidepressant medication

Sirey *et al* (2001) found that perceptions of stigma about depression at the start of treatment predicted subsequent medication adherence. Aikens *et al* (2005) asked 81 primary care patients given maintenance antidepressant medications about their adherence. Variation in adherence could be primarily explained by the balance between patients' perceptions of need *v.* perceptions of harm, with adherence being lowest when the perceived harm of the antidepressant exceeded the perceived need. Two consistent predictors of stopping medication are feeling better and adverse effects. About 35% of patients stop after feeling better at 3 months (Maddox *et al*, 1994) and 55% stop after feeling better at 6 months (Demyttenaere *et al*, 2001). Ayalon *et al* (2005) examined both intentional and non-intentional discontinuation of antidepressants. After controlling for ethnicity and medication type, intentional non-adherence was associated with concerns about the side-effects of the medication and the stigma associated with taking antidepressants. Unintentional non-adherence was associated with greater cognitive impairment. In a study of adherence to SSRIs, Bull *et al* (2002a) found

predictors of discontinuation to be length of treatment, low-dose prescription and the occurrence of one or more moderately or extremely bothersome adverse effect. If the adverse effect had been discussed in advance then the likelihood of discontinuation was halved. This is consistent with the finding that individuals with depression generally want more information about their condition than they are offered and want to be involved in decision-making (Garfield *et al*, 2004). In depression, as in other areas, the more information that is given the better is adherence (Maidment *et al*, 2002).

Mania and mood stabilisers

Studies appear to support the observation that one-quarter to one-third of patients maintained on lithium are poorly adherent (Cochran, 1986). About a third of those prescribed lithium report that their adherence behaviour is poor and in a similar number sub-optimal serum levels indicate poor adherence (Scott & Pope, 2002). Johnson & McFarland (1996) performed a 6-year longitudinal cohort study to determine patterns of lithium use in a large US 'health maintenance organisation'. Lithium users took the drug on an average of 34% of the days. As in other areas, more patients are partially adherent than entirely non-adherent (Colom *et al*, 2000).

In contrast to the above results, MacLeod & Sharp (2001) found much higher rates of adherence, but all of their sample were attending a lithium maintenance clinic, which may have influenced this finding.

Predictors of missed mood stabiliser medication

In the handful of studies that have examined adherence predictors in bipolar disorders, adverse effects and insight are common themes. In one study 61% of patients prescribed lithium reported slight or moderate side-effects compared with 21% on carbamazepine (Greil & Kleindienst, 1999). Recently Bowden *et al* (2005) reported premature discontinuation rates of about 70% during a 1-year trial of lithium, placebo and divalproate: 23.2% of those initially dysphoric at entry who received lithium maintenance therapy and 17.1% of those treated with divalproate maintenance therapy discontinued prematurely because of side-effects compared with 4.8% of those treated with placebo. Regarding illness severity and insight, Yen *et al* (2005) found that insight at baseline predicted concordance up to 1 year later.

Schizophrenia and antipsychotics

Perhaps the most striking data come from studies of full discontinuation by people with schizophrenia.

Even in highly monitored randomised controlled trials, discontinuation rates can be greater than 50%. At least five large-scale studies have shown that adherence with both old and new antipsychotics is poor in the long term. For example, Rosenheck *et al* (1997) found that 68% of patients treated with haloperidol and 43% of those treated with clozapine had discontinued medication before the end of a 1-year trial. In the 18-month Clinical Antipsychotic Trials for Intervention Effectiveness (CATIE) study (Lieberman *et al*, 2005) a remarkable 74% of patients discontinued medication prematurely. The most common reasons for discontinuation were patient choice, lack of effect or intolerability of side-effects.

Outside of randomised controlled trials many groups have looked at more subtle forms of poor concordance, including under- and excessive dosing by people with schizophrenia. Seven studies have recruited more than 1000 patients (these are reviewed by Velligan *et al*, 2006). Rijcken *et al* (2004) found that 33% of the patients in their sample had sub-optimal prescription renewals (less than 90%), 56% had good concordance and 11% had excess prescription renewals. Weiden *et al* (2004b) found that 90% of a sample of 675 individuals with schizophrenia had some degree of partial adherence and on 36% of the study days someone had run out of medication. Patient surveys suggest that almost half (44%) have at some point stopped taking their medication without agreement of their doctor (Hogman & Sandamas, 2000).

Predictors of missed antipsychotic medication

There is a concern that people diagnosed with schizophrenia are infrequently involved in treatment decisions and sometimes not even told their diagnosis (Bayle *et al*, 1999). One patient survey (Gray *et al*, 2005) reports that most of the participants prescribed antipsychotics did not feel involved in treatment decisions and had not been given written information about their treatment, warned about side-effects or offered non-pharmacological alternatives.

Several cross-sectional studies link severity of psychopathology to medication non-adherence (Van Putten *et al*, 1976; Pan & Tantam, 1989). Grandiose thoughts and persecutory thoughts may carry particular risk (Van Putten *et al*, 1976). Low insight predicts non-adherence and, importantly, improvements in insight are often accompanied by improvements in concordance (Rittmannsberger *et al*, 2004). However, low insight may be linked to poorer cognitive function and one study suggests that during the first year of treatment, patients with poorer premorbid cognitive functioning are more likely to discontinue (Robinson *et al*, 2002).

Lack of insight has been extensively examined but other factors have been relatively overlooked. Perkins (2002) reviewed articles published up to December 2002. Correlates of poor adherence included patients' beliefs about their illness and the benefits of treatment (insight into illness, belief that medication can ameliorate symptoms), perceived costs of treatment (medication side-effects), and barriers to treatment (ease of access to treatment, degree of family or social support). More recent studies suggest that medication concerns are of prime importance. In a sample of 213 patients with schizophrenia, Lambert *et al* (2004) found that those presenting with side-effects and those with past experience of side-effects had a significantly more negative general attitude toward antipsychotics. Loffler *et al* (2003) conducted a study in which 307 people with schizophrenia were asked about their reasons for antipsychotic adherence or non-adherence, using the Rating of Medication Influences scale. A positive relationship with the therapist and a positive attitude of significant others towards antipsychotic treatment contributed to adherence. Reasons for non-adherence were lack of acceptance of the necessity for pharmacological treatment and lack of insight.

Drugs and alcohol

Batel *et al* (2004) examined risk factors of early drop-out during induction of high-dose buprenorphine substitution therapy in 1085 individuals addicted to opiates. Younger age, lack of social support and partial access to care (lack of health insurance, previous contact with the prescriber) were significantly associated with early drop-out. Herbeck *et al* (2005) looked at predictors in those with dual diagnosis. Patients with treatment adherence problems were significantly more likely to have personality disorders, lower Global Assessment of Functioning scores, and medication side-effects than those who adhered to treatment. In a study of after-care attendance by severely substance-dependent residential treatment clients, Sannibale *et al* (2003) found that younger, male, heroin-dependent clients with poly-drug use who had refused opioid pharmacotherapy were more likely to drop out of treatment and to relapse early following treatment.

Discussion

Rates of non-adherence with psychotropic medication are difficult to summarise because they vary by setting, diagnosis and type of adherence difficulty. The overall weighted mean rate of non-adherence, calculated in a sample of 23796 patients with psychosis

from a systematic literature review was 25.78% (Nose *et al*, 2003). Complete discontinuation of medication is thought to lead to about one in ten hospital admissions and one in five nursing home admissions (Sullivan *et al*, 1990). Fenton *et al* (1997) found that non-adherent individuals with schizophrenia have a 3.7-fold greater risk of relapse than those who are adherent over 6–24 months. Where medication (or appointments) are missed for predominantly illness-related reasons such as lack of insight, there is a particularly high risk of readmission. Yet illness severity probably accounts for a minority of cases of poor adherence in the community (Maddox *et al*, 1994). Further, the impact may be ameliorated if patients who have further symptoms seek help. Unfortunately, adverse experiences with medication may prejudice willingness to attend in the future (Gonzalez *et al*, 2005).

Potential solutions

A comprehensive summary of interventions that may reduce poor adherence is beyond the scope of this article. Advanced strategies such as adherence therapy and depot medication are reviewed by O’Ceallaigh & Fahy (2001) and Nadeem *et al* (2006). Many of the simpler interventions available to enhance adherence are listed in Box 3.

Barriers to healthcare are a reversible cause of poor medication and appointment adherence. Common factors that reliably influence adherence include patient expectation and knowledge (perception of benefits and hazards of therapy), involvement in medical decisions, availability of social support, and complexity and duration of the prescribed regime.

In the past it has been common to blame the individual for discontinuing medication or dropping out of treatment against medical advice (Demyttenaere, 1998). In addition, patients who do not follow medical advice are likely to be discharged early, compounding the problem. In the future this may be seen as inadequate care. Not too long ago it was considered unusual to give the patient information about their condition or, in some cases, even to reveal the truth about a diagnosis, despite the patient’s requests (Mitchell, 2007b).

Doctors do not diagnose perfectly or prescribe carefully all of the time (Nirodi & Mitchell, 2002; Grasso *et al*, 2003; Laurila *et al*, 2004). Thus the patient is not always acting irrationally if they attempt to allow for adverse effects or minimise stigma by adjusting doses or times of administration. Adverse effects are problematic in at least half of those taking psychotropic medication and may be a rational reason for their choosing to discontinue medication (Greil & Kleindienst, 1999; Bull *et al*, 2002a; Lambert *et al*, 2004). It may be surprising therefore that only about

a quarter of those discontinuing antidepressants or antipsychotics cite adverse effects as the reason (Maddox *et al*, 1994). In other words, only a minority of those experiencing significant adverse effects will discontinue medication without advice.

A substantial minority (about a quarter to a half) do not tell their doctor after stopping or interrupting medication (Hogman & Sandamas, 2000; Demyttenaere *et al*, 2001). In part this may be fear of rejection or being disbelieved, or embarrassment about discussing adverse effects such as weight gain or sexual problems (Zimmermann *et al*, 2003; Weiden *et al*, 2004a). A contributing factor may be that the frequency of side-effects such as these is greatly underestimated by doctors (Smith *et al*, 2002; Roose, 2003). About half of people who stop their medication after taking it for more than a month do so intentionally (Barber *et al*, 2004). Even when patients have discontinued medication unexpectedly, studies in general medicine suggest that more than half will offer some kind of rational explanation.

Box 3 Simple strategies to improve concordance

Basic communication

- Establish a therapeutic relationship and trust
- Identify the patient’s concerns
- Take into account the patient’s preferences
- Explain the benefits and hazards of treatment options

Strategy-specific interventions

- Adjusting medication timing and dosage for least intrusion
- Minimise adverse effects
- Maximise effectiveness
- Provide support, encouragement and follow-up

Reminders

- Consider adherence aids such as medication boxes and alarms
- Consider reminders via mail, email or telephone
- Home visits, family support, counselling

Evaluating adherence

- Ask about problems with medication
- Ask specifically about missed doses
- Ask about thoughts of discontinuation
- With the patient’s consent, consider direct methods: pill counting, measuring serum or urine drug levels
- Liaise with general practitioners and pharmacists regarding prescriptions

Clearly the emerging concept of partial adherence requires further study. The available evidence suggests that the outcome for patients who vary medication doses without consulting a professional is poorer (Svarstad *et al*, 2001). However, many patients vary regular medication in a flexible as-required manner apparently without harmful effect (Mitchell, 2007a).

The therapeutic alliance

The early period of contact between clinician and patient is important in terms of forming a therapeutic alliance and making a joint therapeutic plan. Most patients with mental health problems themselves recognise the difficulty in adhering to complex medication regimens (Irani *et al*, 2004). Before starting a new psychotropic drug we suggest that clinicians should explicitly acknowledge to the patient the difficulties of taking medication, outline realistic benefits and discuss possible adverse effects and consideration of treatment alternatives. Patients who receive this kind of communication are more knowledgeable and have more positive initial beliefs about their medication (Bultman & Svarstad, 2000). Yet analysis of doctor–patient discourses illustrates that clinicians prescribing antidepressants ask roughly one in five patients how well the drugs are working and only one in ten whether they are experiencing any side-effects (Sleath *et al*, 2003; Young *et al*, 2006). These questions may be even more rarely asked of patients in minority ethnic groups and in vulnerable groups such as those with intellectual disability (Lewis-Fernandez *et al*, 2005).

Once a person has started a course of psychotropic medication we recommend that regular follow-up contact with a clinician be arranged. In clozapine treatment, weekly rather than fortnightly monitoring reduced discontinuation rates by 10% over the course of a year and up to 50% overall (Patel *et al*, 2005).

Given the relatively high rates of missed medication and missed appointments in psychiatry we suggest that methods are developed that help patients who have adherence/attendance difficulties. These should be applicable to routine clinical care. Research will then be required to discover which methods are most effective in each setting. Further, we suggest caution before automatically discharging patients who have had initial difficulty following medical advice: at the very least clinicians should ascertain whether there are any removable barriers to continuing care.

Declaration of interest

None.

References

- Adams, J. & Scott, J. (2000) Predicting medication adherence in severe mental disorders. *Acta Psychiatrica Scandinavica*, **101**, 119–124.
- Aikens, J. E., Nease, D. E., Jr, Nau, D. P., *et al* (2005) Adherence to maintenance-phase antidepressant medication as a function of patient beliefs about medication. *Annals of Family Medicine*, **3**, 23–30.
- Angermeyer, M. C., Loffler, W., Muller, P., *et al* (2001) Patients' and relatives' assessment of clozapine treatment. *Psychological Medicine*, **31**, 509–517.
- Ayalon, L., Arean, P. A. & Alvidrez, J. (2005) Adherence to antidepressant medications in black and Latino elderly patients. *American Journal of Geriatric Psychiatry*, **13**, 572–580.
- Barber, N., Parsons, J., Clifford, S., *et al* (2004) Patients' problems with new medication for chronic conditions. *Quality and Safety in Health Care*, **13**, 172–175.
- Batel, P., Reynaud-Maurupt, C., Lavignasse, P., *et al* (2004) [Risk factors of early drop-out during induction of high-dose buprenorphine substitution therapy. A study of 1085 opiate addicts]. *Presse Medicale*, **33**, 5–9.
- Bayle, F. J., Chauchot, F., Maurel, M., *et al* (1999) Survey on the announcement of schizophrenia diagnosis in France. *L'Encephale*, **25**, 603–611.
- Bowden, C. L., Collins, M. A., McElroy, S. L., *et al* (2005) Relationship of mania symptomatology to maintenance treatment response with divalproex, lithium, or placebo. *Neuropsychopharmacology*, **30**, 1932–1939.
- Brown, K. W., Billcliff, N. & McCabe, E. (2001) Informed consent to medication in long-term psychiatric in-patients. *Psychiatric Bulletin*, **25**, 132–134.
- Bull, S. A., Hu, X. H., Hunkeler, E. M., *et al* (2002a) Discontinuation of use and switching of antidepressants: influence of patient–physician communication. *JAMA*, **288**, 1403–1409.
- Bull, S. A., Hunkeler, E. M., Lee, J. Y., *et al* (2002b) Discontinuing or switching selective serotonin-reuptake inhibitors. *Annals of Pharmacotherapy*, **36**, 578–584.
- Bultman, D. C. & Svarstad, B. L. (2000) Effects of physician communication style on client medication beliefs and adherence with antidepressant treatment. *Patient Education and Counseling*, **40**, 173–185.
- Bultman, D. C. & Svarstad, B. L. (2002) Effects of pharmacist monitoring on patient satisfaction with antidepressant medication therapy. *Journal of the American Pharmaceutical Association*, **42**, 36–43.
- Claxton, A. J., Cramer, J. & Pierce, C. (2001) A systematic review of the associations between dose regimens and medication compliance. *Clinical Therapeutics*, **23**, 1296–1310.
- Cochran, S. (1986) Compliance with lithium regimens in the outpatient treatment of bipolar affective disorder. *Journal of Compliance in Health Care*, **1**, 153–170.
- Col, N., Fanale, J. E. & Kronholm, P. (1990) The role of medication noncompliance and adverse drug reactions in hospitalizations of the elderly. *Archives of Internal Medicine*, **150**, 841–845.
- Colom, F., Vieta, E., Martinez-Aran, A., *et al* (2000) Clinical factors associated with treatment noncompliance in euthymic bipolar patients. *Journal of Clinical Psychiatry*, **61**, 549–555.
- Cramer, J. A. & Rosenheck, R. (1998) Compliance with medication regimens for mental and physical disorders. *Psychiatric Services*, **49**, 196–201.
- Daltroy, L., Katz, J., Morlino, C., *et al* (1991) Improving doctor patient communication. *Psychiatric Medicine*, **2**, 31–35.
- Demyttenaere, K. (1998) Noncompliance with antidepressants: who's to blame? *International Clinical Psychopharmacology*, **13** (suppl. 2), S19–25.
- Demyttenaere, K., Enzlin, P., Dewe, W., *et al* (2001) Compliance with antidepressants in a primary care setting. 1: Beyond lack of efficacy and adverse events. *Journal of Clinical Psychiatry*, **62** (suppl. 22), 30–33.
- Eaddy, M., Grogg, A. & Locklear, J. (2005) Assessment of compliance with antipsychotic treatment and resource utilization in a Medicaid population. *Clinical Therapeutics*, **27**, 263–272.
- Fakhoury, W. K. (1999) Extent of distress caused by adverse experiences associated with anti-psychotic treatment (abstract). *European Neuropsychopharmacology*, **9** (suppl. 5), S131–S390.

- Fakhoury, W. K., Wright, D. & Wallace, M. (2001) Prevalence and extent of distress of adverse effects of antipsychotics among callers to a United Kingdom National Mental Health Helpline. *International Clinical Psychopharmacology*, **16**, 153–162.
- Fenton, W. S., Blyler, C. R. & Heinssen, R. K. (1997) Determinants of medication compliance in schizophrenia: empirical and clinical findings. *Schizophrenia Bulletin*, **23**, 637–651.
- Garfield, S., Francis, S. A. & Smith, F. J. (2004) Building concordant relationships with patients starting antidepressant medication. *Patient Education and Counseling*, **55**, 241–246.
- Gilmer, T. P., Dolder, C. R., Lacro, J. P., et al (2004) Adherence to treatment with antipsychotic medication and health care costs among Medicaid beneficiaries with schizophrenia. *American Journal of Psychiatry*, **161**, 692–699.
- Gonzalez, J., Williams, J., Noel, P., et al (2005) Adherence to mental health treatment in a primary care clinic. *Journal of the American Board of Family Practice*, **18**, 87–96.
- Grasso, B. C., Genest, R., Jordan, C. W., et al (2003) Use of chart and record reviews to detect medication errors in a state psychiatric hospital. *Psychiatric Services*, **54**, 677–681.
- Gray, R., Rofail, D., Allen, J., et al (2005) A survey of patient satisfaction with and subjective experiences of treatment with antipsychotic medication. *Journal of Advanced Nursing*, **52**, 31–37.
- Greil, W. & Kleindienst, N. (1999) Lithium versus carbamazepine in the maintenance treatment of bipolar II disorder and bipolar disorder not otherwise specified. *International Clinical Psychopharmacology*, **14**, 283–285.
- Haynes, R., McDonald, H. & Garg, A. (2002) Interventions for helping patients to follow prescriptions for medications. *Cochrane Database of Systematic Reviews*, issue 2. Update Software.
- Herbeck, D. M., Fitek, D. J., Svikis, D. S., et al (2005) Treatment compliance in patients with comorbid psychiatric and substance use disorders. *American Journal on Addictions*, **14**, 195–207.
- Hogman, G. & Sandamas, G. (2000) *A Question of Choice*. National Schizophrenia Fellowship.
- Irani, F., Dankert, M., Brensinger, C., et al (2004) Patient attitudes towards surgically implantable, long-term delivery of psychiatric medicine. *Neuropsychopharmacology*, **29**, 960–968.
- Irvine, J., Baker, B., Smith, J., et al (1999) Poor adherence to placebo or amiodarone therapy predicts mortality: results from the CAMIAT study. *Psychosomatic Medicine*, **61**, 566–575.
- Johnson, D. A. (1981) Depression: treatment compliance in general practice. *Acta Psychiatrica Scandinavica Supplementum*, **290**, 447–453.
- Johnson, R. E. & McFarland, B. H. (1996) Lithium use and discontinuation in a health maintenance organization. *American Journal of Psychiatry*, **153**, 993–1000.
- Joyce, C. R., Caple, G., Mason, M., et al (1969) Quantitative study of doctor–patient communication. *Quarterly Journal of Medicine*, **38**, 183–194.
- Kang, S., Kim, H., Kim, C., et al (2005) Antipsychotic compliance and maintenance dosage in admitted patients with schizophrenia who had been followed up over 6 months. *European Neuropsychopharmacology*, **15**, S490.
- Kaplan, S. H., Greenfield, S., Gandek, B., et al (1996) Characteristics of physicians with participatory decision-making styles. *Annals of Internal Medicine*, **124**, 497–504.
- Kasper, J. A., Hoge, S. K., Feucht-Haviar, T., et al (1997) Prospective study of patients' refusal of antipsychotic medication under a physician discretion review procedure. *American Journal of Psychiatry*, **154**, 483–489.
- Kelly, G., Maimon, J. & Scott, J. (1987) Utility of the health belief model in examining medication compliance among psychiatric outpatients. *Social Science and Medicine*, **25**, 1205–1211.
- Lambert, M., Conus, P., Eide, P., et al (2004) Impact of present and past antipsychotic side effects on attitude toward typical antipsychotic treatment and adherence. *European Psychiatry*, **19**, 415–422.
- Laurila, J. V., Pitkala, K. H., Strandberg, T. E., et al (2004) Detection and documentation of dementia and delirium in acute geriatric wards. *General Hospital Psychiatry*, **26**, 31–35.
- Lewis-Fernandez, R., Das, A. K., Alfonso, C., et al (2005) Depression in US Hispanics: diagnostic and management considerations in family practice. *Journal of the American Board of Family Practice*, **18**, 282–296.
- Lieberman, J. A., Stroup, T. S., McEvoy, J. P., et al (2005) Effectiveness of antipsychotic drugs in patients with chronic schizophrenia. *New England Journal of Medicine*, **353**, 1209–1223.
- Loffler, W., Kilian, R., Toumi, M., et al (2003) Schizophrenic patients' subjective reasons for compliance and noncompliance with neuroleptic treatment. *Pharmacopsychiatry*, **36**, 105–112.
- Lowry, K. P., Dudley, T. K., Oddone, E. Z., (2005) Intentional and unintentional nonadherence to anti hypertensive medication. *Annals of Pharmacotherapy*, **39**, 1198–1203.
- MacLeod, M. S. & Sharp, D. M. (2001) Precursors of compliance with lithium treatment in affective disorders. *Psychiatric Bulletin*, **25**, 183–186.
- Maddox, J., Levi, M. & Thompson, C. (1994) The compliance with antidepressants in general practice. *Journal of Psychopharmacology*, **8**, 48–53.
- Maidment, R., Livingston, G. & Katona, C. (2002) Just keep taking the tablets: adherence to antidepressant treatment in older people in primary care. *International Journal of Geriatric Psychiatry*, **17**, 752–757.
- Makaryus, A. N. & Friedman, E. A. (2005) Patients' understanding of their treatment plans and diagnosis at discharge. *Mayo Clinic Proceedings*, **80**, 991–994.
- Makoul, G., Arntson, P. & Schofield, T. (1995) Health promotion in primary care: physician–patient communication and decision making about prescription medication. *Social Science and Medicine*, **41**, 1241–1254.
- Mitchell, A. J. (2006a) High medication discontinuation rates in psychiatry: how often is it understandable? *Journal of Clinical Psychopharmacology*, **26**, 109–112.
- Mitchell, A. J. (2006b) Depressed patients and treatment adherence. *Lancet*, **367**, 2041–2043.
- Mitchell, A. J. (2007a) Adherence behaviour and psychotropic medication: is it a form of self-medication? *Medical Hypotheses*, **68**, 12–21.
- Mitchell, A. J. (2007b) Reluctance to disclose difficult diagnoses: a narrative review comparing communication by psychiatrists and oncologists. *Supportive Care in Cancer*, **15**, 819. <http://www.springerlink.com/content/j18887h585211414/>
- Mitchell, A. J. & Selmes, T. (2007) Why don't patients attend their appointments? Maintaining engagement with psychiatric services. *Advances in Psychiatric Treatment*, **13**, in press.
- Mullins, C. D., Shaya, F. T., Meng, F., et al (2005) Persistence, switching, and discontinuation rates among patients receiving sertraline, paroxetine, and citalopram. *Pharmacotherapy*, **25**, 660–667.
- Nadeem, Z., McIntosh, A. & Lawrie, S. (2006) Schizophrenia: adherence to antipsychotics (follow link to Compliance therapy). *BMJ Clinical Evidence*. <http://www.clinicalevidence.com/ceweb/conditions/meh/1007/1007.jsp>
- Nirodi, P. & Mitchell, A. J. (2002) The quality of psychotropic drug prescribing in patients in psychiatric units for the elderly. *Aging and Mental Health*, **6**, 191–196.
- Nose, M., Barbui, C. & Tansella, M. (2003) How often do patients with psychosis fail to adhere to treatment programmes? A systematic review. *Psychological Medicine*, **33**, 1149–1160.
- O'Ceallaigh, S. & Fahy, T. (2001) Is there a role for the depot clinic in the modern management of schizophrenia? *Psychiatric Bulletin*, **25**, 481–484.
- Olfson, M., Uttaro, T., Carson, W. H., et al (2005) Male sexual dysfunction and quality of life in schizophrenia. *Journal of Clinical Psychiatry*, **66**, 331–338.
- Osterberg, L. & Blaschke, T. (2005) Adherence to medication. *New England Journal of Medicine*, **353**, 487–497.
- Pan, P. C. & Tantam, D. (1989) Clinical characteristics, health beliefs and compliance with maintenance treatment: a comparison between regular and irregular attenders at a depot clinic. *Acta Psychiatrica Scandinavica*, **79**, 564–570.
- Patel, N., Crismon, M., Miller, A., et al (2005) Drug adherence. Effects of decreased visit frequency on adherence to clozapine therapy. *Pharmacotherapy*, **25**, 1242–1247.
- Paykel, E. S., Hart, D. & Priest, R. G. (1998) Changes in public attitudes to depression during the Defeat Depression Campaign. *British Journal of Psychiatry*, **173**, 519–522.

- Perkins, D. O. (2002) Predictors of noncompliance in patients with schizophrenia. *Journal of Clinical Psychiatry*, **63**, 1121–1128.
- Piette, J. D., Heisler, M., Krein, S., et al (2005) The role of patient-physician trust in moderating medication nonadherence due to cost pressures. *Archives of Internal Medicine*, **165**, 1749–1755.
- Rijcken, C. A., Tobi, H., Vergouwen, A. C., et al (2004) Refill rate of antipsychotic drugs: an easy and inexpensive method to monitor patients' compliance by using computerised pharmacy data. *Pharmacoepidemiology and Drug Safety*, **13**, 365–370.
- Ritsner, M., Perelroyzen, G., Ilan, H., et al (2004) Subjective response to antipsychotics of schizophrenia patients treated in routine clinical practice: a naturalistic comparative study. *Journal of Clinical Psychopharmacology*, **24**, 245–254.
- Rittmannsberger, H., Pachinger, T., Keppelmuller, P., et al (2004) Medication adherence among psychotic patients before admission to inpatient treatment. *Psychiatric Services*, **55**, 174–179.
- Robinson, D. G., Woerner, M. G., Alvir, J. M., et al (2002) Predictors of medication discontinuation by patients with first-episode schizophrenia and schizoaffective disorder. *Schizophrenia Research*, **57**, 209–219.
- Roose, S. P. (2003) Compliance: the impact of adverse events and tolerability on the physician's treatment decisions. *European Neuropsychopharmacology*, **13** (suppl. 3), S85–92.
- Rosenberg, K. P., Bleiberg, K. L., Kosci, J., et al (2003) A survey of sexual side effects among severely mentally ill patients taking psychotropic medications: impact on compliance. *Journal of Sex and Marital Therapy*, **29**, 289–296.
- Rosenheck, R., Cramer, J., Xu, W., et al (1997) A comparison of clozapine and haloperidol in hospitalized patients with refractory schizophrenia. *New England Journal of Medicine*, **337**, 809–815.
- Sannibale, C., Hurkett, P., van den Bossche, E., et al (2003) Aftercare attendance and post-treatment functioning of severely substance dependent residential treatment clients. *Drug and Alcohol Review*, **22**, 181–190.
- Scott, J. & Pope, M. (2002) Self-reported adherence to treatment with mood stabilizers, plasma levels, and psychiatric hospitalization. *American Journal of Psychiatry*, **159**, 1927–1929.
- Sirey, J. A., Bruce, M. L., Alexopoulos, G. S., et al (2001) Perceived stigma as a predictor of treatment discontinuation in young and older outpatients with depression. *American Journal of Psychiatry*, **158**, 479–481.
- Sleath, B., Rubin, R. H. & Huston, S. A. (2003) Hispanic ethnicity, physician-patient communication, and antidepressant adherence. *Comprehensive Psychiatry*, **44**, 198–204.
- Smith, S. M., O'Keane, V. & Murray, R. (2002) Sexual dysfunction in patients taking conventional antipsychotic medication. *British Journal of Psychiatry*, **181**, 49–55.
- Stevenson, F. A., Cox, K., Britten, N., et al (2004) A systematic review of the research on communication between patients and health care professionals about medicines: the consequences for concordance. *Health Expectations*, **7**, 235–245.
- Sullivan, G., Wells, K. B., Morgenstern, H., et al (1995) Identifying modifiable risk factors for rehospitalization: a case-control study of seriously mentally ill persons in Mississippi. *American Journal of Psychiatry*, **152**, 1749–1756.
- Sullivan, S., Kreling, D. & Hazlet, T. (1990) Noncompliance with medication regimens and subsequent hospitalizations: a literature analysis and cost of hospitalization estimate. *Journal of Research in Pharmaceutical Economics*, **2**, 19–33.
- Svarstad, B. L., Shireman, T. & Sweeney, J. (2001) Using drug claims data to assess the relationship of medication adherence with hospitalization and costs. *Psychiatric Services*, **52**, 805–811.
- Task Force for Compliance (1994) *Noncompliance with Medications: An Economic Tragedy with Important Implications for Health Care Reform*. National Pharmaceutical Council.
- Thompson, C. & Pledger, L. (1993) Doctor-patient communication: is patient knowledge of medical terminology improving? *Health Communication*, **5**, 83–97.
- Valenstein, M., Copeland, L. A., Blow, F. C., et al (2002) Pharmacy data identify poorly adherent patients with schizophrenia at increased risk for admission. *Medical Care*, **40**, 630–639.
- Van Putten, T., Crumpton, E. & Yale, C. (1976) Drug refusal in schizophrenia and the wish to be crazy. *Archives of General Psychiatry*, **33**, 1443–1446.
- Velligan, D. I., Lam, Y. W. F., Glahn, D. C., et al (2006) Defining and assessing adherence to oral antipsychotics: a review of the literature. *Schizophrenia Bulletin*, **32**, 724–742.
- Weiden, P. J., Mackell, J. A. & McDonnell, D. D. (2004a) Obesity as a risk factor for antipsychotic noncompliance. *Schizophrenia Research*, **66**, 51–57.
- Weiden, P. J., Kozma, C., Grogg, A. et al (2004b) Partial compliance and risk of rehospitalization among California Medicaid patients with schizophrenia. *Psychiatric Services*, **55**, 886–891.
- Wrigley, S., Jackson, H., Judd, F., et al (2005) Role of stigma and attitudes toward help-seeking from a general practitioner for mental health problems in a rural town. *Australian and New Zealand Journal of Psychiatry*, **39**, 514–521.
- Yen, C. F., Chen, C. S., Ko, C. H., et al (2005) Relationships between insight and medication adherence in outpatients with schizophrenia and bipolar disorder: prospective study. *Psychiatry and Clinical Neurosciences*, **59**, 403–409.
- Young, H. N., Bell, R. A., Epstein, R. M., et al (2006) Types of information physicians provide when prescribing antidepressants. *Journal of General Internal Medicine*, **21**, 1172–1177.
- Zimmermann, U., Kraus, T., Himmerich, H., et al (2003) Epidemiology, implications and mechanisms underlying drug-induced weight gain in psychiatric patients. *Journal of Psychiatric Research*, **37**, 193–220.

MCQs

1 Low concordance with prescribing advice is predicted by:

- a a short course of medication
- b low number of doses per day
- c regular contact with a healthcare professional
- d concomitant psychological treatment
- e young age.

2 The following are linked with intentional non-adherence:

- a severity of illness
- b high trust in physicians
- c a desire for self-efficacy
- d receipt of adequate levels of drug information
- e missed doses after long period on treatment.

3 Regarding patients' understanding of drug therapy:

- a the majority of patients leaving hospital on medication understand why they are taking it
- b most of those taking clozapine are aware of its potentially serious haematological side-effects
- c it is usual for people with depression to understand their need for regular antidepressant therapy
- d antidepressants are commonly perceived as addictive
- e in general patients can recall significant information given by clinicians.

4 Regarding the treatment of schizophrenia:

- a patient-initiated discontinuation of medication is a rare event
- b taking too much medication is a recognised form of less-than-ideal adherence
- c a clinician may reasonably assume that patients use all medication at the prescribed dose and time
- d repeat prescription data show that almost all patients underuse medication
- e periods of missed medication typically last a few days.

5 Patients with schizophrenia commonly report that:

- a they understand the purpose of the medication they are taking
- b their diagnosis is not explained to them
- c they are given written information about their treatment
- d they are involved in treatment decisions
- e they are routinely offered non-pharmacological treatment.

MCQ answers

1	2	3	4	5
a F	a F	a F	a F	a F
b F	b F	b F	b T	b T
c F	c T	c F	c F	c F
d F	d F	d T	d F	d F
e T	e F	e F	e F	e F

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Alex J. Mitchell and Thomas Selmes

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