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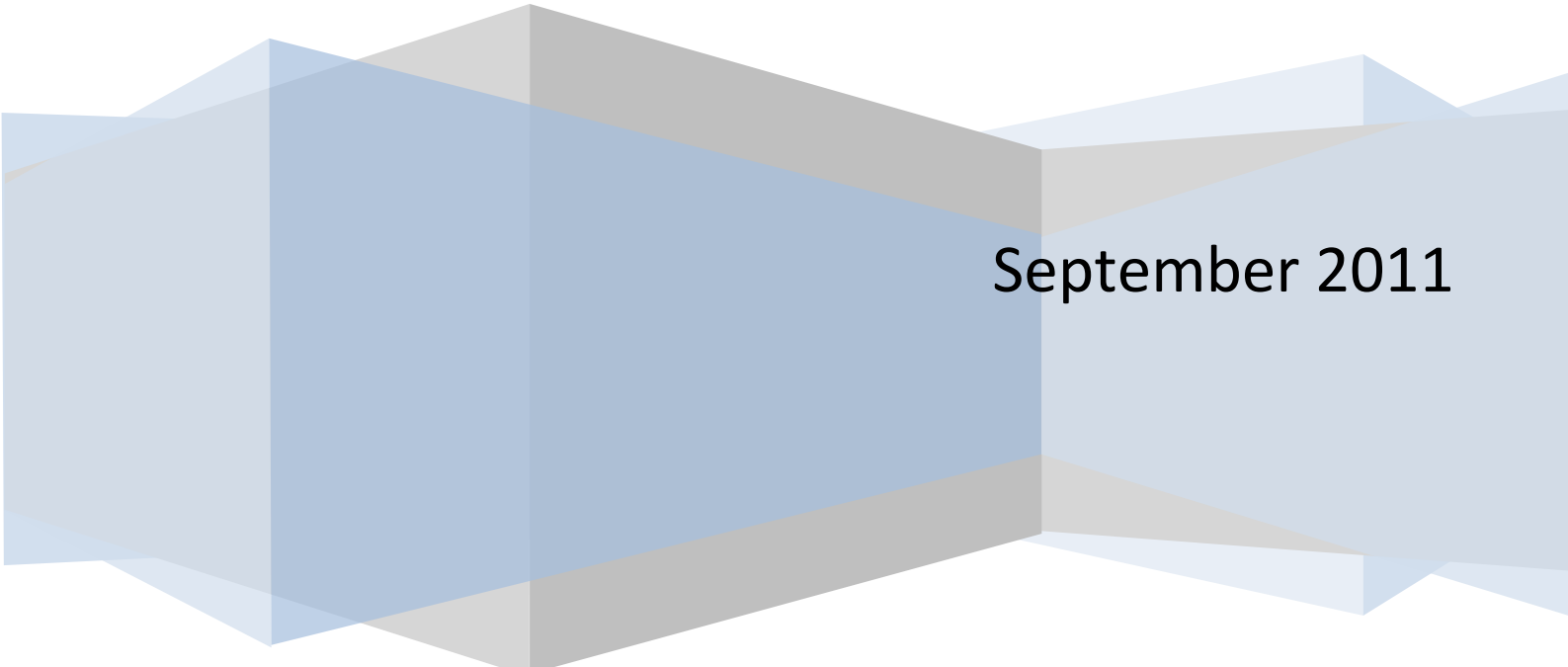
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Adherence Report No.1

The Impact of Poor Adherence in Schizophrenia

A call to action for the National Health Service



September 2011

BACKGROUND

Poor adherence to long-term treatments is a problem across the developed world. The World Health Organisation has described poor adherence as “A problem of striking magnitude.”¹ Poor adherence is associated with poor outcomes and increased healthcare costs. It is a complex phenomenon that requires interventions among both health practitioners and patients. According to the World Health Organisation, “Increasing the effectiveness of adherence may have a far greater impact on health than any improvement in specific medical treatments.”¹

In severe mental illness, poor adherence is the greatest and most important cause of **preventable** psychiatric morbidity. However, particular problems exist, including the impairment of patients’ insight and capacity and the possibility that compulsory treatments may be required.

This report gives an outline of the size of the problem, the cost to the NHS, and the factors that are known to influence adherence.

DEFINING THE PROBLEM

Adherence is difficult to define. It is a dynamic and multifactorial phenomenon which is not stable over time. Sometimes it is a dichotomous event: patients either continue to take medication or they stop. But even a complete stop may be temporary: weeks or even months later the patient resumes their consumption of medication. More commonly, adherence is irregular and varies within a continuum ranging from 100% where all doses are taken to 0% where no doses are taken over a given time period.

Adherence is also difficult to measure and evaluate clinically. There is no simple accurate way to assess adherence. Direct observation of the patient, pill counts and even measurement of blood levels are all prone to error: patients may hide pills in their mouth to dispose of later, pill counts can be distorted by the patient, and blood levels are both expensive and susceptible to variations in metabolism.²

Perhaps the best method is the Medication Event Monitoring System (MEMS). This consists of a microchip in a bottle cap that records the date and time every time the cap is removed. As a measure of adherence it is imperfect, because a patient may remove the cap without taking a pill. But as a measure of *non*-adherence it is accurate because if the cap is not removed, a pill cannot be taken. The MEMS has provided evidence that clinicians struggle to identify poor adherence accurately, with large gaps between clinicians’ perceptions of their patients’ behaviour and objective measures of adherence.^{3,4} Clinicians may use the mental state of their patients to guide them in making a judgement about adherence. However, over a period of about a year, this is likely to have only a 50:50 chance of being accurate.

HOW BIG IS THE PROBLEM?

In schizophrenia, there has been clear evidence of poor adherence with antipsychotic treatment for fifty years. In 1962, an early study of treatment adherence concluded that about half of the patients

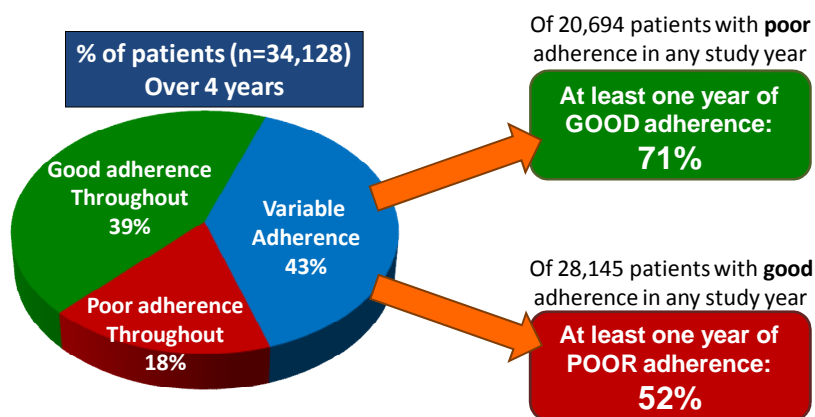
in the study were not taking their medicines as intended, and that this was associated with high rates of relapse and readmission to hospital.⁵

A systematic review of the prevalence of poor adherence in patients with schizophrenia identified 39 studies from 1980 onwards with a mean duration of illness from 9-24 years. Using a definition of acceptable adherence as “taking medication as prescribed at least 75% of the time”, the study found that 49.5% of patients could be considered to have poor adherence.⁶ In the 18-month CATIE study a remarkable 74% of patients discontinued medication prematurely.⁷

However, poor adherence is not a static phenomenon, it varies over time. A very large 4-year study in the US Veterans’ Administration, in over 34,000 patients with schizophrenia found that the cross-sectional prevalence of poor adherence was stable, at 36%-37%.⁸ Only 18% of patients showed consistently poor adherence: Of patients who showed poor adherence at any time, 71% had at least 1 year of good adherence and of those who showed good adherence at any time, 52% had one or more years of poor adherence (Figure 1). This suggests that there is a large proportion of patients in whom interventions to improve adherence could be affective. However, there is evidence that health professionals find it difficult to identify patients with poor adherence.³

Figure 1.

Variation in adherence over time



Valenstein M, Ganoczy D, McCarthy JF et al. Antipsychotic adherence over time among patients receiving treatment for schizophrenia: a retrospective review. *J Clin Psychiatry* 2006;67:1542-50

AT WHAT POINT DOES POOR ADHERENCE START TO IMPACT ON OUTCOME?

This question has been addressed in a number of studies. Two examples suffice to make the point.

In one study, in over 4,000 Medicaid patients in the USA, the relationship between poor adherence and outcome was assessed in a number of ways.⁹ Using gaps in medication as a measure, a gap of up to 10 days doubled rates of admission to hospital. Gaps of up to 30 days and over 30 days respectively trebled and quadrupled admission rates. Using a measure of medication consistency,

the study found that patients with adherence of 70% or more were significantly less likely to be admitted to hospital than those who showed less than 70% adherence.

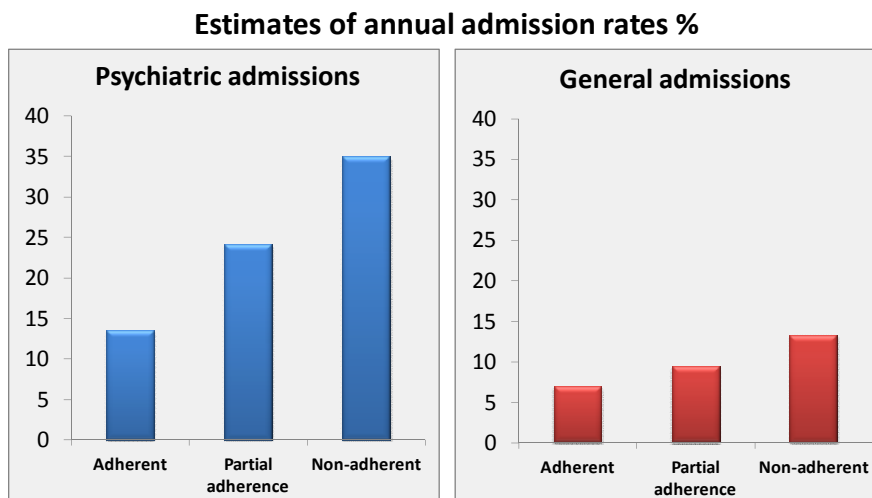
In another American study, Medicaid claims data were used to obtain 2801 person-years of data to assess adherence antipsychotic medication.¹⁰ The 'Cumulative Possession Ratio' (CPR) was calculated on an annual basis for each patient: (the number of days medications were available for consumption divided by the number of days patients were eligible). Rates of hospital admission were then obtained for three levels of adherence:

- Adherent CPR = 0.8 – 1.1 (ie. 80% to 110%)
- Partial adherence CPR = 0.5 – 0.79 (ie. 50% to 79%)
- Non-adherence CPR <0.5 (ie. less than 50%)

Poor adherence was associated with high rates of both psychiatric *and* medical admissions (Figure 3).

Figure 3.

Poor adherence in schizophrenia leads to high rates of hospital admission



Gilmer TP, Dolder CR, Lacro JP et al
Adherence to treatment with antipsychotic medication and health care costs among Medicaid beneficiaries with schizophrenia
Am J Psychiatry 2004;161:692-9

OUTCOMES IN SCHIZOPHRENIA

Adverse outcomes in schizophrenia are particularly important because of their impact at the societal level. A literature review found that schizophrenia is associated strongly with six outcomes of public concern: violence, victimisation, suicide and self-harm, substance misuse, homelessness and unemployment.¹¹ Each outcome acts as a risk factor for at least one other adverse outcome.

Violence

As a consequence of sensationalist media reporting, the public are particularly concerned about violence in schizophrenia. Varying estimates of the prevalence and relative risk of violence in schizophrenia are dependent on the type of violence measured and the location of the study. For serious violence, studies have reported relative risks of between 2 and 7.

Victimisation

People with schizophrenia are more likely to be victims than perpetrators of violence. Little is known about the impact of victimisation, though there is evidence it may lead to homelessness, and it is poorly recognised in clinical practice.

Suicide/self-harm

Suicide is a significant cause of premature death in people with schizophrenia, with lifetime estimates ranging from 5% to 13%. Nonfatal fatal acts of self-harm are also common, with a study among people with chronic schizophrenia finding that 38% had at least one episode of self-harm in a 2- to 12-year follow-up period.

Substance misuse

A substantial number of people use drugs for the first time after the onset of schizophrenia. Such patients report using street drugs to counter depression and anxiety, negative symptoms such as apathy and anhedonia, to help with sleep and to reduce extrapyramidal side-effects. Substance misuse is an important adverse outcome: it is associated with poor adherence to treatment, positive symptoms, more psychiatric admissions, higher rates of violence, unemployment, homelessness, greater likelihood of death by suicide and excessive health service costs.

Homelessness

Homelessness is a common outcome of schizophrenia. One third of the British sample of the European Schizophrenia Cohort study had experienced homelessness. Homelessness in schizophrenia predisposes to institutionalisation in prisons and hospitals, non-adherence with treatment, psychosocial problems, poor quality of life, and physical and sexual abuse. Mortality is more than 3 times higher in the homeless.

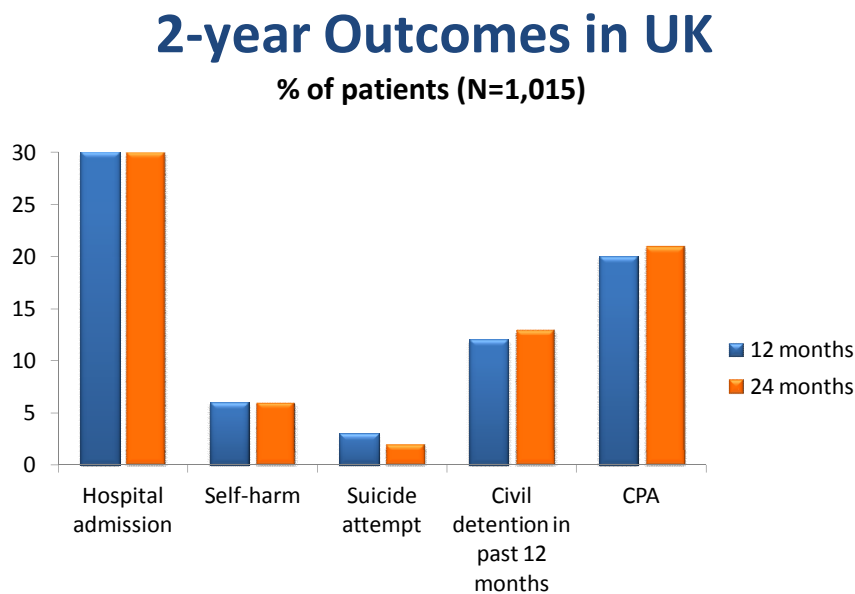
Unemployment

Nearly 90% of the British sample of the European Schizophrenia Cohort study were unemployed.

The Scottish Schizophrenia Outcomes Study collected data from a representative sample of 1,015 persons with schizophrenia, schizotypal, or delusional disorders.¹² Data were obtained on trends in outcomes and service use across Scotland over a three year period (2002–2005).

On a range of outcome measures – hospital admission, self-harm, suicide attempt, civil detention and the need for the Care Programme Approach – there was no improvement in any outcome during the study period. Indeed, HoNOS scores indicated **increased** levels of impairment (Figure 2).

Figure 2. The Scottish Schizophrenia Outcomes Study



Hunter R, Cameron R, Norrie J.
Using patient-reported outcomes in schizophrenia: The Scottish Schizophrenia Outcomes Study
Psychiatric Services 2009;60:240-245

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The authors concluded that despite the introduction of guidelines, new treatments, and new services, people with schizophrenia continue to have high levels of chronic disability.

In the management of schizophrenia, effective treatments are available, and services have been reshaped to provide care where it is most needed – in community settings. Yet outcomes remain stubbornly poor. Is this the hidden influence of poor adherence to antipsychotic treatment?

HOW CLEAR IS THE RELATIONSHIP BETWEEN POOR ADHERENCE AND POOR OUTCOME?

The literature consistently links poor adherence with poor outcome. Indeed, if this were not the case, what value would there be in prescribing antipsychotics in the long long term? Studies with second-generation antipsychotics provide strong evidence that these medicines are effective in preventing relapse.^{13, 14, 15} A meta-analysis of the effects of antipsychotic discontinuation in 4365 patients with schizophrenia found that over a 10 month period, 53% of patients who discontinued treatment relapsed compared with only 16% who continued on medication.¹⁶ This high relapse rate is reflected in hospital re-admission rates. In a sample of 7864 Medicaid patients taking atypical antipsychotics, those with adherence rates of less than 80% were 50% more likely to be admitted to hospital than those with higher rates of adherence.¹⁷ In the largest study, in over 34,000 patients, those with less than 80% adherence were 2.4 times more likely to be admitted than patients with good adherence.⁸

WHAT COSTS ARE ASSOCIATED WITH POOR ADHERENCE?

Because of the unique structure of the NHS, it is difficult, if not impossible to apply health economic data from other health economies, in the USA or Europe, to the UK. However, despite the empirical and common sense evidence that the poor outcomes resulting from poor adherence are likely to be costly, specific health economic data relating to the NHS is sparse.

There is one notable exception. Using data from the Office of Population Censuses and Surveys, A UK health economic analysis by Knapp & co-workers identified 658 schizophrenic patients for whom data were available for 1 year on in-patient care, out-patient care and community-based services. They found that poor adherence resulted in a 1.5-fold increase in in-patient care, and a 3-fold increase in demand for community-based services. At prices operating in 2004, the **added total annual cost associated with poor adherence was £5000 per patient.**¹⁸

If these costs were representative of mental healthcare in the UK, for a service with a catchment population of 750,000, given a prevalence of schizophrenia of about 1%, the added cost to the service of poor adherence could be in the region of £15 million per annum.

WHAT FACTORS ARE KNOWN TO INFLUENCE ADHERENCE?

Adherence is complex, and multiple factors are known to be important influences. Influences on adherence may be categorised into 4 broad groups.

<p>Influences that relate to the patient and their understanding and experience of treatment</p>	<ul style="list-style-type: none">• Doctors do not diagnose perfectly or prescribe carefully all of the time. Thus the patient is not always acting irrationally if they attempt to compensate for adverse effects or avoid 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 choosing to discontinue medication.¹⁹• In the CATIE study lack of effect or intolerable side-effects were among the most common reasons for discontinuation.⁷• A contributing factor may be that the impact of side-effects is often greatly underestimated by doctors.²⁰• Current and past experience of side-effects has a significant impact creating a negative general attitude toward antipsychotics.¹⁷• 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.²¹• Patients who understand the purpose of the medication are twice as likely to collect it than those who do not.²²• Most patients prescribed antipsychotics do not feel involved in treatment decisions and state that they take medication only because they are told to.²³
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<p>Influences that relate to the therapeutic relationship</p>	<ul style="list-style-type: none"> • Good communication between patients and health professionals and clear mutual agreement at the onset of treatment to support adherence is essential.²⁴ • In practice, the process of making a joint therapeutic plan is often abbreviated. Doctors may overestimate the amount of information they have given to patients and patients often misunderstand medical terminology. It is often assumed that patients understand a reasonable amount about their illness, but in a classic study, Joyce et al showed that patients were unable to recall half of the information given to them by their physician.²⁵ • Disagreement with or low trust in clinicians, and receipt of low levels of medical information predict poor adherence.²⁶
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<p>Influences that relate to the treatment regimen</p>	<ul style="list-style-type: none"> • Complexity of the regimen. A systematic review of the impact of multiple dosing on adherence found that patients receiving once-daily dosing had 22% to 41% more adherent days compared with patients receiving thrice-daily dosing and 13% to 26% more adherent days compared with patients receiving twice-daily dosing.²⁷ • Duration of the course of treatment. Generally, adherence reduces over time.
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<p>Influences that relate to the service or environment</p>	<ul style="list-style-type: none"> • Inadequate frequency of follow-up contact.²³ • Living arrangements. Patients who are homeless or who live alone show lower levels of adherence than those living with family or in supported accommodation.
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CONCLUSIONS

- In severe mental illness, poor adherence is the greatest and most important cause of **preventable** psychiatric morbidity. It is a problem that is more common than is acknowledged and realised by mental health services.
- Poor adherence is a major cause of poor outcome and impacts strongly on the mental wellbeing of patients and the people they live with.
- Poor adherence is extremely costly to the NHS.
- Poor adherence is a complex phenomenon that requires multiple interventions at a service level.
- There is an urgent need to develop or re-align existing services to improve adherence to antipsychotic treatment.
- According to a report by the World Health Organization: ***“Increasing the effectiveness of adherence may have a far greater impact on health than any improvement in specific medical treatments.”***¹

The second part of The MMH Adherence Report, with a four-point plan for improving adherence, can be obtained from www.mentalmeds.co.uk

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