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Editorial

Treatment adherence in psychoses†

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Summary
A well-conducted randomised controlled trial of an intervention to improve treatment adherence in psychosis published in this issue shows beneficial effects on self- and observer-rated adherence and trends towards fewer hospital readmissions. Partial adherence is the single most important barrier to optimal treatment. National Institute for Health and Clinical Excellence guidelines on adherence need to be revised.

Declaration of interest
A.S.D. has received lecture fees and honoraria from Janssen-Cilag, Eli Lilly and AstraZeneca for work related to antipsychotic medication.

Tony David (pictured) is Professor of Cognitive Neuropsychiatry and a consultant psychiatrist. He has a longstanding interest in treatment adherence and related topics such as insight. He is co-editor with X. Amador of *Insight and Psychosis: Awareness of Illness in Schizophrenia and Related Disorders* (2nd edn, 2004).

If someone said that they could improve on our current treatments for schizophrenia and affective psychosis, and significantly and substantially reduce relapses and prolong remission, improve social functioning, substantially reduce healthcare costs and carer burden, and probably reduce suicide and violence to others, we would think it a miraculous breakthrough, a Nobel Prize-worthy innovation or, perhaps, utterly unbelievable. Yet this is entirely within our grasp without any new discoveries. All that need happen is for our patients to adhere to their treatment better than they usually do.

This does not just apply to serious mental disorders: the same could be said for most medical conditions, especially chronic ones. In the medical field, non-adherence is estimated to affect 20–50% of patients.[1] Comprehensive systematic reviews have been published on interventions to counteract this (69 trials included),[1] with a large subset devoted to chronic conditions (37 trials).[2] In fact, between 1990 and 2005 there were as many as 38 systematic reviews on the topic, which have themselves been subject to a systematic review.[3] This may be one of those rare cases where we do not 'need more research'.

So what is the result of all this activity? It seems that simple 'technical' fixes (dosing regimen simplification, reminders, incentives, etc.) are effective in improving adherence especially for short-term treatments. Enhancing adherence to longer-term treatment is more difficult, with a number of interventions being tried from simple to complex (e.g. cognitive–behavioural therapy, CBT). Most 'work' to some extent. Some bring about improvement on adherence measures but not other relevant outcomes, while others seem to improve outcome irrespective of measured adherence. Many have initial benefits, but few are sustained. None, to my knowledge, make things worse.

Why is adherence important?

In psychiatry, non- or partial adherence is generally estimated to be higher than in medical conditions and highest of all in psychosis.[4] Defining adherence is a complex field in itself. Using the simple but quantifiable notion of 'prescribing gap', that is the proportion of time a patient goes without receiving their intended prescribed medication, used in US surveys from state or federally funded services of over 34 000 patients, we can say that 39% of patients have a score of >80% (i.e. good adherence), while 43% are inconsistent (<80%) in their adherence for at least 1 out of 4 years of their illness and 18% are persistently inconsistent (<80% for >1 in 4 years).[5] This is important because a gap of a month or less was associated with a 2.8 times risk of admission to hospital that year, whereas a gap of more than a month increased the risk by nearly four times.[6] It may be easier to visualise adherence as an exponential decay function with a half-life of 1 year. That is, about 50% of your patients will stop taking their treatment every year, so after 2 years only 25% of patients remain on their initially prescribed medication. Or put in another even simpler way: most patients with schizophrenia discontinue their medication after an average of 4 months (a bit longer if it's clozapine).[7] By the way, we all believe that our patients have above average adherence (it's the other person's patients who have the problem).

Turning to adherence enhancement in psychosis specifically, there is again no shortage of well-conducted and thorough reviews on the topic. These find that psychoeducation, although effective for many conditions, including bipolar disorder,[8] does not seem to be so for schizophrenia where a more active behaviour- and attitude-changing approach is required. Such interventions improve adherence by about 2.6 times (95% CI 2.21–3.03) according to one such review.[9]

Randomised controlled trials to improve treatment adherence in the psychoses

The first randomised controlled trial (RCT) of 'compliance therapy' was published in 1997.[10] The intervention contained elements of motivational interviewing, CBT, education and good clinical practice. When given to patients from south-east London admitted to the Maudsley Hospital with acute relapses of psychosis, their adherence and insight improved by the time they were discharged. Perhaps surprisingly, improvements in global functioning were maintained over the subsequent 12–18 months and readmission rates significantly reduced. An attempted replication in Dublin[11] was unsuccessful, perhaps because of low statistical power and less expertise in delivery of the intervention. Frustratingly, we do not know whether or not the intervention brought about any change immediately, which would help place in context the absence of an effect at 1 year. More recently, Gray *et al*[12] showed that community psychiatric nurses randomly selected to receive training in the delivery of a medication

†See pp. 448–455, this issue.

management package were able to improve their patients' symptoms and adherence compared with patients under the care of control nurses. However, in the largest RCT to date ($n = 327$), Gray and colleagues[13] carried out a multicentre European study of adherence therapy (closely modelled on compliance therapy) in comparison to a control intervention based on general health promotion. An important difference from the original trial was that it was based on selected out-patients with adherence problems. After 1 year, both groups improved functionally and on adherence measures but there was no difference between the groups.

On the basis of this contradictory evidence, the National Institute for Health and Clinical Excellence (NICE) stated in its latest clinical guidance for schizophrenia:[14] 'Do not offer adherence therapy (as a specific treatment) to people with schizophrenia'. This is despite the fact that medication adherence has an entire set of NICE guidelines all to itself with the aim of promoting 'interventions to increase adherence'. The most regrettable aspect of the peculiarly worded guidelines is the way mental healthcare providers have chosen to (mis)interpret them – that clinicians should not attempt to provide any version of adherence therapy (including those elements that are based on good clinical practice), that they should desist from it, as if it might actually be harmful.

New evidence

Against this confused backdrop comes a new, well-conducted study from The Netherlands by Staring *et al*, published in the current issue of the *Journal*.[15] The study took place in an out-patient setting, similar to the Gray *et al*[13] study, which included a Dutch centre. Consenting patients were randomised to the intervention ($n = 54$) or treatment as usual (TAU, $n = 55$) and raters were masked to treatment allocation. One innovation of this study was the attempt to tailor the intervention called treatment adherence therapy (TAT) to the more likely causes of poor adherence for each participant – although it turned out that in the majority, illness beliefs were the sticking point. The therapists were nurses with 1 week of special training. The main outcomes were engagement and self-reported adherence. Immediate and 6-month outcomes showed significant improvements in adherence but not other general or symptomatic outcomes. Tantalising trends were noted regarding reduced readmission rates: 9 (TAT) *v*. 14 (TAU), of which 1 *v*. 6 respectively were involuntary. The study lacked the power to confirm these effects. The lack of impact on symptoms seems paradoxical (see also Kemp *et al*[10]) and one might ask: what's the point of taking the medication if it doesn't make you any better? However, this ignores the powerful relapse-preventing action of antipsychotic medication. One potential weakness of the study is the rather modest training and supervision provided to the therapists. Yet this can also be seen as a strength in that it anticipates the need for generalisability of any intervention across non-academic and less well-resourced centres. Finally, an insurmountable problem for this and all RCTs in the area of adherence is the fact that most non-adherent individuals will not consent to participate, so that those with the greatest potential to benefit are absent from the scientific literature, yet are all too present in the clinic.

Let wisdom guide

So where does this leave us (and NICE guidance)? Clearly, therapies to bolster adherence in schizophrenia and related disorders should be put back in the frame. Wise advice to clinicians and mangers is that they should seek to offer additional therapies from the range available to help remedy this hugely important and costly clinical challenge. The problem remains and is not answered by the latest study – what are the key elements of these adherence interventions that really make the difference and what is the best format and setting for their application? Staring *et al*[15] had TAU as their comparator, hence the non-specific effects of the additional input (e.g. the time spent with the therapist discussing salient issues) inherent in TAT were not controlled for. If Gray *et al*[13] had included a TAU group, it is very likely that both interventions offered in that trial would have shown a beneficial effect on adherence. So it seems that we do need more research after all.

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