Effectiveness of financial incentives to improve adherence to maintenance treatment with antipsychotics: cluster randomised controlled trial (REC 09/H070/35)

Background

Non adherence to antipsychotic long acting injectable (LAI) medication for patients with psychotic disorders remains a significant problem within mental healthcare, with the cost of non-adherence having implications on both an individual (relapse, rehospitalisation, increased suicide risk, poorer subjective quality of life) and societal level (increased healthcare costs).

Despite interventions developed to improve adherence, there is little evidence suggesting which intervention is most effective. Financial incentives have demonstrated some effectiveness in improving adherence to medication/treatment in both general and mental healthcare. Furthermore, a recent pilot study within the UK found financial incentives to be effective in improving LAI adherence and reducing the number of hospital admissions. So far, no wider research on the use of financial incentives to improve LAI adherence has been investigated.

The use of financial incentives to improve adherence levels to LAI medication is a contentious issue, with a range of concerns highlighted by focus groups with stakeholders prior to the trial. Stakeholders felt that research evaluating the effectiveness of financial was crucial. Furthermore, it is important to understand the experiences of the clinicians and patients offering the incentives to determine whether the concerns highlighted from these groups would be borne into reality if financial incentives were offered in practice.

Objectives

- To examine the effectiveness and cost-effectiveness of offering financial incentives to patients with psychotic disorders who demonstrate poor adherence to LAI medication (i.e. adherence ≤75%).
- To examine the views and experiences of both patients and clinicians with offering financial incentives to improve adherence to LAIs.

Method

The study was a cluster-randomised controlled trial. Mental health teams (assertive outreach and community mental health teams) across the UK were recruited and identified patients with schizophrenia and other psychotic disorders that showed poor adherence to their anti-psychotic LAI medication (≤75% adherence). Teams (and therefore patients) were randomised to receive financial
incentives (£15 per LAI) over a 12-month period, or to continue treatment as usual with no incentives. Randomisation was conducted by an independent Clinical Trials Unit using a computer-generated sequence. Teams were randomly allocated, with equal probability to the intervention or control group, and stratified by levels of socio-economic deprivation as it was assumed that teams in areas with higher deprivation would have more eligible (and more challenging) patients. The trial statistician was blinded to treatment allocation until the analysis was complete.

Participants

Patients were eligible for the trial if aged between 18-65 years of age, an established diagnosis of schizophrenia, schizo-affective psychosis or bipolar illness (according to the ICD-10), being cared for in a mental health team for at least four months, having the capacity to give informed consent, being described anti-psychotic LAI medication, poor adherence to LAI medication (≤75% adherence) and other methods to improve adherence have failed. Patients were not included in the trial if they had a learning difficulty or poor command of English which may impair their ability to consent to their involvement in the trial.

Procedure

Community mental health and assertive outreach teams across the UK were approached and teams interested in the study were visited by research assistants. Written informed consent was provided by the team manager, consultant psychiatrist, or both. Clinicians from recruited teams approached eligible patients and if agreeable, were visited by a research assistant to explain the study in more detail. If written informed consent was provided, patients completed short questionnaire rating their subjective quality of life. After all eligible patients in a team had been contacted and consent obtained, the team was randomised and a researcher later informed them of their allocation.

For teams allocated to the intervention group, research assistants visited the teams to further explain the procedure of the incentives and to provide the required money for the intervention period. Over the course of 12 months, patients within the trial received £15 each time they attended an appointment for their LAI medication, which was signed for by both the nurse administering the medication and the patient. Towards the end of the 12-month period, research assistants contacted the teams to inform them that the incentives would be ending shortly, and to explain this to patients. Teams allocated to the intervention group received treatment as usual, with no incentives.

For data collection for all time points, research assistants contacted the teams to arrange a visit to collect data off electronic medical records. At the end of the intervention, research assistants contacted patients again to complete another questionnaire rating their subjective quality of life and an optional qualitative interview.
The primary outcome was analysed using a linear mixed effects model with a random effect of mental health team. In the main analysis, patients who had at least four months’ of complete adherence data at baseline and end of intervention were included. Separate analyses were carried out excluding patients with protocol violations for diagnoses, not meeting the inclusion criterion or those who were at least 75% adherent in the four months prior to screening for eligibility. Further sensitivity analysis were conducted without adjusting for baseline, for patients only with a diagnosis of schizophrenia and excluding patients who were at least 75% adherent throughout the whole baseline period (as opposed to at least four months prior). Secondary outcomes (achieving adherence of at least 95%) were analysed using mixed effects logistic regression models. Subjective quality of life was analysed using a mixed effects model fitted by least generalised squares. Hospital admissions and adverse events were reported descriptively as these were expected to be infrequent. For all regression analyses, all models adjusted for the stratification variable, average LAI treatment cycle at baseline and where possible, for baseline measures of outcomes (excluding clinical global improvement which was assessed at end of intervention only).

Outcome measures

The main study aimed to assess outcomes at baseline (up to 12 months prior to randomisation), at the end of the 12-month intervention and at six months follow-up. These were as follows:

- **Primary outcome**: Adherence to LAIs - defined as the percentage of received LAIs out of those prescribed over a 12 month period. Calculating adherence also took into account periods where LAIs would not be received in the community (e.g. hospitalisation, imprisonment). This was assessed at baseline (up to 12 months prior to intervention), at the end of intervention and six months follow-up.

- **Secondary outcomes**: Percentage of patients with adherence of at least 95%; ‘slippage’ (the percentage of the prescribed time interval that has expired before the next LAI is administered); clinical global improvement; subjective quality of life; satisfaction with medication; hospitalisation; and adverse events. All secondary outcomes were assessed at baseline and end of intervention, with all but clinical global improvement, subjective quality of life and treatment satisfaction assessed at 6-months follow-up.

- **Cost-effectiveness**: Adjusted cost difference between experimental groups, the incremental cost per patient of improving adherence by 20% and the incremental cost per patient of achieving at least 95% adherence. The probability of cost-effectiveness was also calculated. Cost-effectiveness was calculated at baseline, end of intervention and at six months follow-up.

- **Interviews**: Interviews with clinicians of patients allocated to the intervention group were carried out during the intervention (at six months and 12 months), and at six months follow-up to assess their experiences of offering financial incentives. Interviews with patients
allocated to the intervention were conducted at the end of the intervention to explore the experiences of receiving financial incentives.

*Follow-up study*

The trial was granted permission by the HTA to extend the project for a further 19 months to assess whether financial incentives were continued with patients and to examine the longer term impact of the financial incentives on adherence and other outcomes. This extension included following up teams and patients for a further 18 months after the six month follow-up (i.e. 24 months after the end of the intervention). Outcomes measured included the primary outcome (adherence) and fewer secondary outcomes (patients with at least 95% adherence, ‘slippage’, hospitalisation and adverse events only). Follow-up interviews were conducted with patients at 24 months to address how the incentives influenced adherence, did their adherence affect other outcomes and how patients experienced the use of financial incentives. Follow-up interviews were conducted with clinicians at 24 months to assess whether financial incentives had been continued, reasons for/against continuation and the long term impact of the incentives on the patient adherence, the therapeutic relationship and other outcomes.

*Results*

73 mental health teams (24 assertive outreach, 48 community mental health, and one Recovery team) across 29 different NHS trusts were recruited and 141 patients across these teams were consented into the trial. Thirty seven teams were randomised to the intervention (n=78 patients) and 36 teams randomised to the control condition (n=63 patients). Patients in the trial had a mean age of 43.7 years (SD=9.8), 74% of them were male and 80% of patients were diagnosed with schizophrenia.

*End of intervention*

Primary outcome data was available for 35 intervention teams with 75 patients and for 31 control teams with 56 patients. *Primary outcome*: The average adherence level at baseline was 69% in the intervention group and 67% in the control group. At the end of the intervention, adherence was 85% in the intervention group, and 71% in the control group. Adherence was significantly higher in the intervention group than control group at the end of the intervention (adjusted $\beta=11.5\%$, 95% CI 3.9% to 19.0%, $p=0.003$). *Secondary outcome*: Patients reaching adherence levels of at least 95% was achieved in 28% of the intervention group and 5% of the control group (adjusted odds ratio 8.21, 95% CI 2.00 to 33.67, $p=0.003$). Patients in the intervention group reported more favourable subjective quality of life ($\beta=0.71$, 95% CI 0.26 to 1.15, $p=0.002$). No statistically significant differences in the clinical improvement scale, hospital admissions, and adverse events were found.
Six months follow-up

Primary outcome data was available for 106 patients. Adherence in the intervention group had fallen to 71%, compared to 78% in the control group, however the difference between groups were not statistically significant (adjusted $\beta=-7.4\%$, 95% CI -17.0 to 2.1, $p=0.127$). No statistically significant differences between groups in the number of patients reaching adherence levels of at least 95% or for time slippage. No differences were found in the number of hospital admissions or adverse events were found.

Twenty four months follow-up

Primary outcome data was available for 116 patients. Adherence in the intervention group was 68%, compared to 74% in the control group. Medication adherence between the two groups at 24 months follow-up was not significantly different ($\beta=-5.7$, 95% CI -13.1% to 1.7%, $p = 0.123$). There were a higher number of hospital admissions in the intervention group compared to the control.

Cost-effectiveness

At the end of intervention, the costs of patients in the intervention group were not significantly higher than costs of patients in the control group (adjusted cost difference = £598, 95% CI -£4 533 to £5 730, $p=0.818$).

Patient interviews

Interviews were conducted with 45 of the 78 patients allocated to the intervention group, with 11 patients interviewed both the end of intervention and at 24-months follow-up. All patients felt that the incentives acted as a motivator or reward for receiving their LAI medication, however many patients highlighted a range of personal dilemmas that arose for them as a result of being offered the incentives. The majority of patients felt that the incentives being discontinued did not have a negative impact on them.

Clinician interviews

Interviews during the intervention period (six and 12 months of the intervention) were conducted with 59 clinicians for 73 or the 78 patients allocated to the intervention. In 77% of cases clinicians reported the benefits of the incentives on clinical management through improved adherence, contact, patient monitoring, communication and trust. Clinicians also reported improvements in insight, mental health and social functioning. In 33% of cases clinicians reported problems in patient management as a result of the incentives such as increased drug and alcohol use, and the monetarisation of the therapeutic relationship.
Interviews after the end of the intervention (six months and 24 months follow-up) were conducted with 57 clinicians for 59 of the 78 patients. No clinicians continued to use the incentives with patients within the trial or with any new patients, with financial constraints being the most common reason as to why the incentives were not implemented. The majority of clinicians reported no negative impact once the incentives were stopped, however there were reports of patients whose adherence and mental health, and their relationship with their patients had deteriorated as a result. The majority of clinicians expressed positive opinions over the use of financial incentives, which was maintained both before and after the intervention. Around a fifth had negative opinions over the use of incentives and another fifth had mixed opinions.

Conclusions

Offering financial incentives is an effective and cost-effective method in improving adherence amongst patients with psychosis who demonstrate poor adherence to LAI medication. However, once the incentives have been discontinued, levels of adherence are not maintained in the long term. Whilst the incentives were welcomed by the majority of clinicians and patients, both report negative aspects as a result of the incentives. Once the incentives were discontinued, a number of clinicians reported that outcomes or interactions with patients remained the same and patients said that the incentives stopping had no effect on them. However, there were also reports by both clinicians and patients whereby the incentives stopping had a negative impact. This seems to suggest that the incentives may benefit some but not all patients and a cost vs. benefit approach must be taken if implemented into routine practice.