The Effect of Financial Incentives on Adherence to Antipsychotic Depot Medication:
Does It Change Over Time?

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ABSTRACT

Objective: A recent cluster-randomized controlled trial found that offering financial incentives improves adherence to long-acting injectable antipsychotics (LAIs). The present study investigates whether the impact of incentives diminishes over time and whether the improvement in adherence is linked to the amount of incentives offered.

Method: Seventy-three teams with 141 patients with psychotic disorders (using *ICD-10*) were randomized to the intervention or control group. Over 1 year, patients in the intervention group received £15 (US $23) for each LAI, while control patients received treatment as usual. Adherence levels, ie, the percentage of prescribed LAIs that were received, were calculated for quarterly intervals. The amount of incentives offered was calculated from the treatment cycle at baseline. Multilevel models were used to examine the time course of the effect of incentives and the effect of the amount of incentives offered on adherence.

Results: Adherence increased in both the intervention and the control group over time by an average of 4.2% per quarterly interval (95% CI, 2.8%–5.6%; $P < .001$). Despite this general increase, adherence in the intervention group remained improved compared to the control group by between 11% and 14% per quarterly interval. There was no interaction effect between time and treatment group. Further, a higher total amount of incentives was associated with poorer adherence ($\beta_{bootstrapped} = -0.11$; 95% $CI_{bootstrapped}$, −0.20 to −0.01; $P = .023$).

Conclusions: A substantial effect of financial incentives on adherence to LAIs occurs within the first 3 months of the intervention and is sustained over 1 year. A higher total amount of incentives does not increase the effect.

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Poor adherence to antipsychotic medication remains a major problem in the treatment of patients with psychotic disorders, resulting in exacerbation of symptoms, avoidable hospitalizations, and overall suboptimal outcomes.[1] Furthermore, medication nonadherence has been consistently reported as a factor substantially increasing health care costs.[2]

Various psychosocial interventions have been tested to improve poor adherence to antipsychotic medication, including psychoeducation, cognitive-behavioral therapy, compliance therapy, motivational interviewing, text prompting, or a combination of approaches.[3] However, evidence for the effectiveness of psychosocial interventions in enhancing medication adherence remains mixed at best.[4–6] There is no consistent evidence that any intervention significantly improves medication adherence in community patients with psychotic disorders. In addition, so-called compliance therapy has been explicitly contraindicated for patients with psychotic disorders.[7]

Against this background, offering financial incentives to improve treatment adherence has been considered as an option. In patients with severe mental disorders, financial incentives have been successfully employed to promote a number of health-related behaviors.[8,9] Examples include abstaining from smoking,[10,11] alcohol,[12] marijuana,[13,14] and other illicit drugs.[15]

The potential effect of financial incentives to improve adherence to antipsychotic medication was first suggested by 2 very small observational studies in assertive outreach teams in London[16] and the Netherlands.[17] These studies were followed by a multicenter randomized controlled trial in the United Kingdom.[18,19] Over a 1-year period, patients in the intervention group were offered financial incentives (£15 [US $23]) for each long-acting injectable (LAI), while patients in the control condition received treatment as usual without incentives. Patients in the intervention group had significantly improved adherence and also reported significantly higher subjective quality of life. In line with the study protocol, the original analysis considered effects on patients' adherence over the 1-year period as a whole, and did not explore whether the effect changed over time.

Studies on financial incentives for abstaining from smoking[20–22] and illicit drugs[23] suggest that the effect of incentives might diminish over time. It has been demonstrated that the value of the incentives has to be increased to sustain patients' abstinence up to 18 months.[22] At the same time, Petry et al[24] suggested that financial incentives might have more effect on adherence to medication in both psychiatric and nonpsychiatric patients when administered over longer periods of time. Their suggestion, however, was based on a meta-analysis of overall effects observed in controlled and noncontrolled studies. It did not reflect analyses of changing effect sizes over time within randomized controlled trials.

Clinical Points

- Incentives have been found to be effective, more so than any other method so far tested in trials. For using incentives in clinical practice, evidence is required on whether the effect lasts or diminishes over time, as has been suggested in other health-related behaviors using financial incentives such as smoking cessation.
- The findings of this article clearly show that the effect of financial incentives remains practically unaltered over a 1-year period (even when compared to an increasing percentage of adherence in the control group), which may be explained by the nature of behavior motivated by incentives, characteristics of the patient population, or both.
- Less frequent long-acting injectable cycles are likely to result in improved adherence, even in the light of potential financial gains.

When financial incentives are utilized in practice, clinicians may plan to offer them over longer periods of time. They therefore need to know whether the effect tends to decrease after a few weeks or months or (vice versa) whether the effect can still occur after an initial period of having no impact. Evidence on the consistency of the effect over time is therefore of high clinical relevance.

Another pertinent question concerns the effect of the amount of financial incentives offered to patients. A number of previous studies have reported an association between the value of incentives and behavioral change observed.[25–27] Whether a similar mechanism operates in medication adherence–related behaviors in patients with psychotic disorder is unknown.

Using data from the Priebe et al trial,[19] we explored whether the effect of consistent financial incentives on adherence to antipsychotic maintenance medication would change over the 1-year period, ie, whether it would diminish as has been found in smoking cessation[20–22] or increase as has been suggested for medication based on a comparison of effects between studies across medicine.[24] Further, whether the overall LAI adherence is associated with the amount of incentives offered over the 1-year period has been explored.

METHOD

One hundred forty-one patients with an *ICD-10* diagnosis of schizophrenia, schizoaffective disorder, or bipolar disorder whose adherence to LAI over the preceding 4 months was, at most, 75% were recruited from 73 community mental health teams across England and Wales. Data from both baseline and intervention periods were available from 123 patients within 62 teams. Adherence levels were calculated as the percentage of prescribed LAIs that were actually administered during the observation period. Written informed consent was obtained from both patients and consultant psychiatrists/team managers. This study was approved by the National Research Ethics Service Ealing and West London Research Ethics Committee (reference no: 09/H0710/35). It was registered on ISRCTN.com (identifier: ISRCTN77769281) and adopted into the UKCRN portfolio (UKCRN.org identifier: 7033).

Mental health teams were randomized to either the intervention group, with patients receiving £15 (US $23) for each LAI, or the control group, continuing with treatment as usual with no financial incentives. The intervention period lasted for 12 months. Recruitment and randomization procedures, sample size calculations, and overall findings are reported in detail elsewhere.[18,19] During the baseline period, the mean adherence was 69% (SD = 16%) in the intervention group and 67% (SD = 16%) in the control group. During the intervention period, mean adherence in the intervention group was 85% (SD = 15%) and 71% (SD = 22%) in the control group. The difference was statistically highly significant (adjusted difference in mean values: $\beta = 11.5\%$; 95% CI, 3.9%–19.0%; $P = .003$).

Statistical Analyses

Time course. Adherence levels were calculated as the percentage of prescribed LAIs that were received within each consecutive 3-month period.

The assumptions are described in detail elsewhere[19]; briefly, the number of LAIs due during each interval for each patient was calculated based on his or her prescribed treatment cycle, accounting for any changes in cycle and any periods spent out of the community longer than the prescribed cycle. Periods out of the community longer than a treatment cycle (eg, in hospital or prison) were removed from the denominator. When there were changes in treatment cycle, the average time between prescribed LAIs in weeks was calculated.

As partitioning of the intervention period and calculating associated adherence levels may, on occasion, result in a "shrinkage effect" (for example, when the number of LAI appointments in 1 interval is increased due to when the weekend falls), the denominator of expected LAIs was rounded down to the nearest integer.

We fitted a multilevel linear model with adherence per quarter (ie, every 3 months) of the intervention period as the outcome variable and included a linear time trend per quarters as a continuous covariate. The time trend was calculated per quarterly interval to give a reasonable minimum number of data points on which to calculate adherence and examine the time course. Even shorter periods of time, for example months, would result in unstable adherence estimates for patients on less-frequent cycles. (That is, for a patient on a monthly cycle, adherence would be either 100% if they received the depot or 0% if they did not.) We included fixed effects for the group allocation variable adjusted for adherence across the baseline period, the average time between prescribed depot medications during the baseline, and the Mental Illness Needs Index category,[6] which was the team-level stratification factor used in the randomization of clusters. An interaction term between group allocation and time trend was included to test whether change in adherence over time differed between groups.

Table 1. Patient Baseline Sociodemographic and Clinical Characteristics[a]

Variable	Missing Data, n	Total (N = 141)	Intervention (n = 78)	Control (n = 63)
Demographics				
Age, mean (SD), y	0	43.7 (9.8)	44.4 (9.6)	42.7 (10.2)
Male sex	0	105 (74)	59 (76)	46 (73)
Years of education, mean (SD)	29	11.0 (1.6)	10.9 (1.7)	11.2 (1.5)
Ethnicity	3			
White		83 (60)	49 (63)	34 (54)
Black		31 (22)	17 (22)	14 (23)
Asian		9 (7)	5 (6)	4 (7)
Mixed and other		15 (11)	7 (9)	8 (13)
Living situation				
Married/cohabiting	3	18 (13)	8 (10)	10 (16)
Independent accommodation	4	102 (74)	53 (68)	49 (83)
Living alone	20	75 (62)	41 (62)	34 (62)
Paid employment (any)	3	4 (3)	3 (4)	1 (2)
Receiving benefits	7	134 (99)	76 (99)	58 (100)
Clinical status	0			
Schizophrenia		113 (80)	61 (78)	52 (82)
Schizoaffective disorders		17 (12)	9 (12)	8 (12)
Bipolar disorder		7 (5)	6 (8)	1 (2)
Other psychosis		3 (2)	2 (2)	1 (2)
Other diagnosis		1 (< 1)	0 (0)	1 (2)
Clinical history				
Duration of illness, mean (SD), y	14	17.8 (8.5)	18.2 (8.6)	17.3 (8.5)
No. of psychiatric hospitalizations in the last 2 years, mean (SD)	4	0.8 (2.2)	0.9 (2.7)	59 (0.6)
≥ 1 Hospital admissions in past year	3	32 (23)	20 (26)	12 (20)
Recreational drugs during baseline	5	104 (76)	57 (74)	47 (80)
Criminal convictions during baseline	4	2 (1)	1 (1)	1 (2)
Imprisonment during baseline	3	4 (3)	1 (1)	3 (5)
Community treatment order at time of randomization	4	7 (5)	3 (4)	4 (7)

[a]Values are presented as n (%) unless stated otherwise.

Table 2. Numbers of Patients and Mean Adherence According to Depot Treatment Cycle During the Intervention Period

Treatment Cycle During Intervention[a]	Intervention Period (n = 123)			
	Intervention, n = 71		Control, n = 52	
	n	Mean Adherence, %	n	Mean Adherence, %
1/52	2	82	1	49
2/52	49	83	27	74
3/52	4	97	3	44
4/52	12	92	16	73
Variable treatment cycle	4[b]	72[b]	5[c]	72[c]

[a]Treatment cycle 1/52, 2/52, 3/52, and 4/52 denotes once per week, once per fortnight, once every 3 weeks, and once per month, respectively.
[b]n = 1 moved from 2/52 to 4/52 to 1/52 to 2/52 to 4/52; n = 1 moved from 3/52 to 2/52; n = 1 moved from 3/52 to 4/52 to 3/52; n = 1 moved from 2/52 to 1/52 to 2/52.
[c]n = 1 moved from 2/52 to 4/52; n = 1 moved from 1/52 to 2/52; n = 1 moved from 2/52 to 1/52; n = 2 moved from 2/52 to 3/52.

The relatedness of adherence at each time quarter within each patient and similarity of adherence for patients under the care of the same mental health team were accounted for by including random effects for patient and mental health team, respectively (both with an exchangeable covariance structure).

Amount of money. Further, we examined whether the amount of money patients were offered to receive affected their adherence as calculated over the whole of the intervention period, as opposed to quarterly. The estimate of the money due, rather than money actually received, has been used, as, arguably, patients would be motivated by the prospect of what they may gain. The money-due estimate was calculated as the number of depot injections to be received (given by treatment cycle) multiplied by £15 (US $23). Due to the unusual distribution, we dichotomized the amount of money at £300 (US $466) or more versus less than £300. A multilevel model with adherence during the intervention period as the outcome variable and money due as the predictor was estimated. Subsequently, a model was estimated while data were controlled for the adherence at baseline. Given the nonnormal distribution of patient-level residuals, bootstrapping was applied to the regression analyses (3,000 replications).[28] All analyses were undertaken in Stata version 12.1.[29]

RESULTS

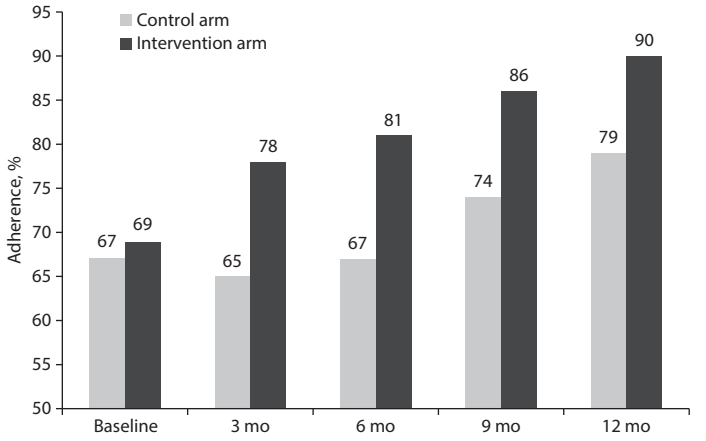
Demographics

The baseline demographic and clinical characteristics were similar in both groups and are presented in Table 1. The number of patients on different treatment cycles and associated adherence levels at the end of the intervention are presented in Table 2.

The Time Course of Adherence to Medication

Adherence levels in the intervention group and the control group are shown for each 3-month interval in Figure 1. Four patients in the intervention group and 5 in the control group

Figure 1. Medication Adherence Levels in the Intervention and Control Groups



had an adherence of at least 90% in each quarter for which it was possible to calculate adherence.

Adherence improved in both groups over time, and the general increase was statistically significant (adjusted quarterly increase = 4.2%; 95% CI, 2.8%–5.6%; $P < .001$; ie, a mean of 4.2% increase in adherence per quarter).

The effect of group allocation was found to be highly significant (adjusted difference in mean values = 11.8%; 95% CI, 6.5%–17.1%; $P < .001$). The difference in mean adherence between the intervention and control groups was similar for each quarter, ie, 13%, 14%, 12%, and 11% at 3, 6, 9, and 12 months, respectively. There was no evidence of an interaction effect between time quarters and group allocation ($\beta = -0.01$; 95% CI, −0.04% to 0.02%; $P = .491$), a finding that strongly indicates the effect of financial incentives did not change in magnitude over time.

The team-level intracluster correlation coefficient (ICC) (ie, correlation between adherence of any 2 randomly selected patients within each mental health team) was 0.04 and the within-patients ICC (ie, correlation of adherence at each quarter within each patient) was 0.22.

The Effect of Monetary Value

A highly significant negative association between the amount of money and adherence was identified ($\beta_{bootstrapped} = -0.10$; 95% $CI_{bootstrapped}$, −0.18 to −0.03; $P = .009$). After we controlled for baseline adherence, the strength and direction of the association was unchanged ($\beta_{bootstrapped} = -0.11$; 95% $CI_{bootstrapped}$, −0.20 to −0.01; $P = .023$), while baseline adherence showed no association with intervention adherence ($P = .764$).

DISCUSSION

Adherence increased in both groups over time. This general trend of improving adherence may be seen as a regression to the mean of patients recruited to the study because of poor adherence at baseline. The impact of financial incentives took immediate effect within the first 3 months after implementation and was maintained over the whole 1-year period. In each 3-month time interval, adherence was improved by between 11% and 14%. In regard to the effect of the amount of financial incentives on the overall adherence, contrary to our hypothesis, we found that there was a negative association between the amount of financial incentives offered and treatment adherence.

The findings have been generated from a rigorous randomized controlled trial. The findings are clear with very similar effect sizes for each 3-month period.

The major limitations of the study are (1) almost all patients were of low socioeconomic status and received social benefits; (2) we studied the effect of financial incentives of a single fixed value, ie, £15 (US $23) per LAI, which is tightly linked to the effect of the treatment cycle; and (3) the study duration was only 1 year. Thus, it remains unclear as to which extent the findings can be generalized to patients with a different socioeconomic status, to incentives with a different value, and to periods of more than 1 year.

So far, only a handful of studies have analyzed the time course of the effect of financial incentives within a randomized controlled trial. To our knowledge, none of them investigated adherence to medication in patients with psychotic disorders. The few studies[21–23] exploring the time course of the effect of financial incentives on health behaviors in randomized controlled trials reported decreasing effects over time. For example, in a study testing the effect of a voucher-based intervention for cocaine dependency in people with psychotic disorders, Roll et al[23] found a statistically significant improvement only during the first 2 weeks of the intervention. Further, there have been indications of a diminishing effect of interventions for smoking cessation utilizing fixed payments as opposed to progressively increasing payment schedules[30] or even schedules including a reset component whereby increasing payments are reset to their original values when participants fail to carry out incentivized behavior.[31]

There are at least 2 explanations that might explain why, inconsistent with reports of effects of financial incentives on other types of health behaviors, the effect of financial incentives in the present study did not diminish over time. The first is linked to the characteristics of the patients and the amount of the incentives in this study. It has been suggested that offering incentives greater than 1.2% of one's personal disposable income is associated with a trend toward greater effect.[32] In this study, almost all patients were in receipt of social benefits, and the amount of money offered to patients (ie, £15 [US $23]) was therefore substantially higher than the proposed threshold. The second explanation relates to the facilitated behavior. In smoking cessation and other forms of abstinence, the incentivized behavior has to be sustained all the time. Patients are encouraged to avoid a critical behavior and need to achieve this for 24 hours every day. Adhering to LAIs does not require maintaining

a changed behavior all the time. Patients are expected only to attend their appointments and receive the LAI. Thus, it is something that patients do rather than avoid doing, and the frequency of the required behavior ranges from once per week to once a month. It might be easier to respond to financial incentives and sustain the effect over time when receiving the incentives does not require a constant behavior change but rather sporadic acts confined to certain occasions.

In terms of the effect of the amount of financial incentives, the present findings contrast the previous literature. Although money has not always been utilized as a reward and some studies used vouchers,[15,23] the positive relationship between the magnitude of incentives and their effect has been unequivocally reported in a number of areas, including smoking-cessation programs,[25,27] illicit drug dependency,[26] and medication adherence.[24] In their meta-analysis, Petry et al[24] have shown that using rewards of greater value, as well as reinforcing participants at least weekly, is associated with greater effect in adherence to medication in a range of health conditions. Furthermore, in behaviors difficult to modulate, such as weight control, offering incentives greater than 1.2% of personal disposable income has been associated with a trend toward a greater effect.[32]

In spite of the fact that the amount of incentives was far higher than suggested by Paul-Ebhohimhen and Avenell,[32] we found that patients due to receive a greater amount of money had lower adherence than those with lower potential profits. We can argue that the amount of £15 (US $23) is high enough to motivate behavioral change, and a further increase in the amount of incentives does not lead to a stronger motivation. As the amount of money received is tightly linked to the treatment cycle (as discussed earlier), and it is impossible to disentangle the effect of the two, we might also argue that the frequency of required behavior remains the driving factor despite the potential financial gains. It may be easier to increase adherence if the required behavior, ie, making oneself available for the injection, is required more rarely.

There are 3 main tasks for future research. Mediating factors explaining the sustained effect should be explored so that the intervention can be further improved and specified for different target groups. Longer-term studies are needed to establish whether the effect is maintained beyond a 1-year period, when such long treatments are appropriate. Finally, evidence is required on whether the effect of financial incentives undermines adherence once incentives have been removed, a type of rebound phenomenon that has been referred to as "crowding out."[33]

There are different ways of understanding adherence and its improvement. One way of assessing percentages of adherence is the stringent method used in this study (ie, calculating adherence and its increase out of the possible maximum 100%). Following this method, the percentage improvement was between 11% and 14%, which may seem small. Yet, if we analyze the proportion by which adherence has been improved related to the adherence in the control group, the percentage is higher, ie, over 20%. In case one focuses on nonadherence as the clinical problem rather than adherence, one may want to quantify the reduction of nonadherence. Taking the difference between the adherence in the control group and full adherence as the potentially reducible nonadherence, the reduction of nonadherence was between 37% and 52% of the maximum effect in each quarter. In other words, the intervention achieved, on average, almost half of the potentially possible maximal effect. Also, the previously reported findings[19] of a statistically significant increase in subjective quality of life in the intervention group further point to the clinical relevance of adherence improvement achieved through the financial incentives.

The success of the intervention is likely to be apparent very early after the implementation. If there is no improvement within the first 3 months, one should be skeptical as to whether the intervention will be successful later. In cases where financial incentives do have an impact initially, there is reason to be optimistic that the effect can be sustained, at least for a period of 1 year. Moreover, our results indicate that, unlike in other areas of health beahviors such as smoking cessation, there is no need for increasing payments to motivate patients to sustain their improved adherence to LAIs. Finally, less frequent LAI cycles are likely to result in improved adherence, even in the light of potential financial gains.

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