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Behavioral economic incentives to improve adherence to antiretroviral medication

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Abstract

Objective—Fixed incentives have been largely unsuccessful in improving adherence to antiretroviral medication. Therefore, we evaluate whether small incentives based on behavioral economic theory can increase adherence to antiretroviral medication among treatment-mature adults in Kampala, Uganda.

Design—A randomized control trial design tests whether providing small incentives based on either attending timely clinic visits (intervention group 1) or achieving high medication adherence (intervention group 2) can increase antiretroviral adherence. Antiretroviral adherence is measured by medical event monitoring system (MEMS) caps.

Methods—Overall, 155 HIV-infected men and women age 19–78 were randomized into one of two intervention groups and received small prizes of US \$1.50 awarded through a drawing conditional on either attending scheduled clinic appointments or achieving at least 90% antiretroviral adherence. The control group received the usual standard of care.

Results—Preliminary results based on pooling the intervention groups showed individuals receiving incentives were 23.7 percentage points more likely to achieve 90% antiretroviral adherence compared with the control group [95% confidence interval (CI), 6.7–40.7%]. Specifically, 63.3% (95% CI, 52.9–72.8%) of participants in the pooled intervention groups maintained at least 90% mean adherence during the first 9 months of the intervention, compared with 39.6% (95% CI, 25.8–54.7%) in the control group.

Conclusion—Small prize incentives resulted in a statistically significant increase in antiretroviral adherence. Although more traditional fixed incentives have not produced the desired results, these findings suggest that small incentives based on behavioral economic theory may be more effective in motivating long-term adherence among treatment-mature adults.

Keywords

behavioral economics; HIV; medication adherence; Uganda

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Conflicts of interest

There are no conflicts of interest.

Introduction

Antiretroviral therapy has improved the life expectancy of HIV-infected patients dramatically [1–4]. However, the success of these drugs is dependent on high medication adherence, which is a difficult behavior for patients to maintain not only in Uganda but worldwide [5–8]. The growing evidence of suboptimal adherence is pronounced among patients who have been on antiretroviral medication for a number of years and have been found to take ‘drug holidays’ from their antiretroviral regimen when they feel overwhelmed by daily pill taking [9]. These gaps in adherence dramatically reduce the effectiveness of antiretroviral medication, and highlight the importance of motivation and self-control in fighting treatment fatigue.

For many health behaviors, people have difficulty following through on their good intentions and end up in situations they later regret, such as overeating or smoking [10,11]. Behavioral economists interpret these situations as people overly discounting the future and giving in to short-term temptation at the expense of long-term benefits [12]. Such ‘present bias’ is particularly damaging for chronic conditions such as HIV/AIDS where the benefits of a healthier and longer life occur in the distant future, but the costs of taking antiretroviral drugs are incurred daily [13].

Incentives, such as conditional cash transfers [14] or contingency management style payments of large monetary value that have a long tradition in the psychology literature [15], show promising but sometimes mixed results [16]. In the field of HIV, recent studies using large conditional rewards to prevent HIV [17–19] and link HIV-infected individuals to HIV care have not delivered the desired results [20], and novel, more effective ways to provide incentives are needed.

Behavioral economics suggests that instead of the magnitude of the incentive, the way incentives are delivered – and at what time intervals – significantly determines their effectiveness [13]. Small incentives provided frequently and close to observations of the desired behavior may be more effective than larger, infrequent payments at increasing an individual’s internal motivation and sustaining behavioral improvements [21]. Some recent studies in the field of HIV have begun to apply smaller, more frequent incentives to increase the uptake of safe male circumcision [22] and mother-to-child HIV transmission care [23]. Incentives allocated by a drawing may be more effective than equivalent fixed payments [24,25] by leveraging the motivational power and joy of games of chance. Such incentives also leverage overestimation bias to reduce the cost of the intervention, as individuals respond more to these small incentives relative to a larger fixed payment [26,27].

The ‘Rewarding Adherence Program’ (RAP) described in this paper examines whether providing small incentives allocated by a drawing conditional on either attending timely clinic visits (intervention group 1) or achieving high medication adherence (intervention group 2) can increase antiretroviral adherence among 155 adult clients in HIV care in Uganda. We did not test the relative effectiveness of incentives as traditionally used (i.e. those of relatively large, fixed monetary value) versus those inspired by behavioral economics after discussions with the implementing clinic who decided that larger incentives

would not be sustainable or acceptable to clinic leaders. In this article, we report on the effects over the first 9 months of a 26-month study that is currently ongoing.

Methods

Study setting

RAP was implemented at Mildmay Uganda, an HIV clinic in Uganda's capital Kampala that provides antiretroviral therapy to over 11 000 clients and has been caring for HIV-infected Ugandans for over 17 years.

Study design and participants

Ethics approval was obtained from RAND's Human Subjects Protection Committee, the Research Ethics Committee at Mildmay clinic, and the Uganda National Council for Science and Technology. There were no adverse events reported in any of the study groups.

Clients of the Mildmay clinic were eligible for participation if they were at least 18 years of age, had documented adherence problems (either missed at least one clinic visit in the last 6 months or self-reported adherence problems), and were on antiretroviral medication for at least 2 years; these criteria were chosen as we hypothesized that small incentives may be particularly appropriate for treatment-mature clients who likely have overcome more structural barriers to adherence (such as transportation costs or lack of appropriate food) and for whom motivational barriers are likely of key importance. Based on a list of all clients conforming to these study eligibility criteria, potential participants were randomized to either one of two intervention groups or the control group in a 1 : 1 : 1 ratio. Written informed consent was then obtained in the patient's preferred language. Afterwards, consenting participants completed a 45 min baseline survey that measured respondents' demographics, socioeconomic status, and health history. Recruitment took place between March and August 2013.

Of the initial 201 eligible Mildmay clients, 46 approached by the study coordinator were not recruited because of refusal, scheduling problems, language barriers, and other circumstances, until the final study sample size of 155 participants was reached. These participants were evenly divided between the three study groups, and sample attrition during the first 9 months of the RAP program was equally experienced across groups. Figure 1 outlines the flow of study participation during the recruitment phase and the first 9 months of the project.

Intervention groups

After completing the baseline survey, participants were informed of their random assignment to either of the intervention groups, whereby participants were eligible for small incentives, or to the control group. Eligibility for in-kind incentives allocated by a drawing was based on timely clinic visits – that coincide with drug refills at the clinic pharmacy – for intervention group 1 and antiretroviral adherence of 90% or higher for intervention group 2. Intervention group 1 was included at the request of our local partner to test whether incentives could be successfully implemented without the cost-intensive use of medical

event monitoring system (MEMS) caps to measure adherence. The control group received the usual standard of care.

The eligibility for incentives in intervention group 1 was defined as attending the clinic appointment on the scheduled day and was verified by the study coordinator who checked the client's scheduling booklet. Clients who visited the clinic before their scheduled visit would only become eligible again based on the date for their following appointment. If the client was overdue by 3 days or more, the study coordinator would first verify that the participant had not come to the clinic without being seen by study personnel, and if not, then a new schedule for clinic appointments was established. Eligibility was then determined based on this new schedule, which maintained an approximate 2-month gap between appointments (the observed time between clinic visits during the study period was approximately 52 days for all three groups). The eligibility for incentives in intervention group 2 was defined as being more than 90% adherent and was confirmed by downloading patients' latest MEMS data.

Eligible participants would then draw a number out of a bag with cards numbered 1 through 6, and would receive the in-kind incentive if they drew a '6.' They were offered the choice of one of three items (to avoid boredom, as some patients were expected to win more than once): a coffee mug, an umbrella, or a water bottle. All three items had a monetary value of about 6000 Ugandan shillings, or approximately \$1.50 USD. The incentives and other intervention parameters were developed in collaboration with key stakeholders as part of an extensive formative phase preceding the intervention.

Primary outcome adherence measurement

Given evidence in the medical literature that adherence levels of 80–100% are necessary to achieve viral suppression [28–32], and levels above 90% significantly reduce the likelihood of virologic failure and drug resistance [33], the main outcome of interest was achieving 90% adherence or higher.

A MEMS cap was placed on the pill bottle containing antiretroviral medication for all participants of this study. The MEMS cap electronically records the time and date of each bottle opening. Clients were asked to bring the MEMS cap to each clinic visit to download their adherence data. Participants were encouraged to take their medication only from the pill bottle with the MEMS cap. Of note, as it was important to determine if a lower cost approach could be used to increase adherence, eligibility for participating in the prize drawing in intervention group 1 was based on timely clinic attendance only. However, providing the intervention group 1 and the control group with MEMS caps not only assured that we could use a fully comparable adherence measure for all three groups, but also largely eliminated any potential confounding effects brought about by the use of MEMS caps.

Statistical analyses

We conducted an impact analysis to compare the proportion of participants with 90% mean adherence or higher in each intervention group to the control group using probit regression analysis, and F-tests were used to compare the treatment impact between intervention group 1 and intervention group 2. Kernel densities were used to additionally compare the

distribution of patients' mean adherence in each study group using the Epanechnikov kernel function with equal bandwidths for each group. The analysis also estimated probit models adjusted for participant's age, educational attainment, sex, wealth, marital status, and physical and mental health. Age was defined in years and was measured as an integer, and education was defined as a binary variable indicating whether the participant had completed at least primary education. Participants' wealth was measured by an asset index defined as the sum of affirmative responses to the ownership of 10 common household items. These 10 items represent the most common household items included in the Demographic and Health Survey's (DHS) Uganda survey [34], and the asset index places equal weight on participants' self-reported ownership of each item. Marital status was defined as a binary variable indicating whether the participant was married at the time of the baseline survey. Physical and mental health were defined by participants' responses on a 5-point Likert-type scale to the statements: 'My health keeps me from working at a job, doing work around the house, or going to school,' and 'Over the past 2 weeks, I have felt down, depressed, or hopeless.' All statistical tests were two-sided and performed using Stata version 14.0 (StataCorp. LP, College Station, Texas, USA). Coefficient standard errors were estimated using heteroskedasticity robust procedures for all linear regression specifications.

The planned sample size for the intervention was 150, with 50 participants in each study group. Power calculations indicated that with a sample size of 50 per study group and 45% of participants in the control group maintaining mean adherence rates equal to or above 90%, there would be 80% power to detect a difference in the proportion of participants with high mean adherence as small as 17% between study groups. At the time that power calculations were performed, there were no data available on the actual mean adherence rates of patients at the Mildmay HIV clinic, but self-reported measures indicated that fewer than half of clients were maintaining at least 90% mean adherence.

Results

Baseline data

Baseline demographic characteristics of participants were similar across the three study groups (Table 1). Roughly half of the participants had at least completed their primary education (53%). The majority of clients in this sample (63%) were women, which is representative of the total client population at the Mildmay clinic that is also predominantly female, and participants were on average 39 years old. Median monthly disposable income was US \$58 [interquartile range (IQR), \$29.20–\$87.20] of which travel costs to the clinic represented roughly 5%; median travel costs were US \$2.90 (IQR, \$2.03–\$4.35), according to the prevailing exchange rate of 1 USD to 3450 Ugandan Shillings. The average participant's household contained 4.7 (SD 2.8) members, and 49% of participants were married at the time of the baseline survey. Roughly 12% of participants are physically limited by their health, and over 65% have had feelings of depression or hopelessness.

Table 1 also illustrates that the randomization procedure successfully led to a balanced sample across the control and intervention groups. The only significant differences occurred between the control group and intervention group 1, where two-sided *t*-tests indicated that the fraction of participants being married was lower and the percentage of participants who

had completed primary school was higher in intervention group 1 (P values of 0.10 and 0.06, respectively). This difference in educational attainment across study groups is not correlated with participants' self-reported knowledge of the HIV treatment protocol or observed mean adherence rates so it is unlikely to bias the impact analyses. In light of these small and generally statistically insignificant observable differences between intervention groups, the preferred analytic specification for analysis is the unadjusted regression model comparing mean adherence rates between intervention groups and the control group. To account for the small changes in baseline variables between the three groups, however, we also present results controlling for the main observable demographic differences between intervention groups, and find that the demographic controls are statistically insignificant in all regression models.

Impact of behavioral economic incentives on antiretroviral adherence

Table 2 shows the impact of the incentives on mean adherence rates separately for the two intervention groups, as well as when the intervention groups are combined. Although adherence in the control group was 80.9% [95% confidence interval (CI), 74.8–87.1%], those in the intervention group 1 show adherence that was 88.3% (95% CI, 84.7–91.9%), which is 7.4% higher, and those in intervention group 2 had a mean adherence level of 86.7% (95% CI, 81.9–91.6%). In the unadjusted regression, these differences in mean adherence are statistically significant only for intervention group 1, and marginally significant at conventional significance levels for the combined treatment groups.

These intervention impacts were unlikely to be experienced equally by all members of the target population for this study. For example, small incentives are likely to be least effective for clients with structural adherence barriers such as high clinic commuting costs or family/social stigma. To investigate the heterogeneity of intervention effects, Fig. 2 displays the observed distribution of 9-month mean adherence rates across each study group. The kernel density distributions are estimated using equal size bandwidths and the Epanechnikov kernel function. This figure shows that the intervention impacts are most pronounced around the 90% mean adherence threshold, which suggests that the outcome measure of the proportion of clients maintaining at least 90% mean adherence is likely capturing the key impact of the behavioral change induced by RAP.

Table 3 presents the probit regression results for a binary outcome measure that takes on the value of 1 for clients who show at least 90% adherence over the first 9 months of RAP, and shows positive improvements in both intervention groups. Although 39.6% (95% CI, 25.8–54.7%) of the participants in the control group showed a mean adherence level of at least 90%, the fraction in the combined intervention groups was 63.3% (95% CI, 52.9–72.8%). Probit regression analysis indicates that those in either one of the intervention groups were more likely to have adherence of at least 90%; (intervention group 1 marginal effect, 21.5%; 95% CI, 0.9–42.1%; intervention group 2 marginal effect, 26.2%; 95% CI, 6.2–46.3%), and this increase was statistically significant at the 5% level among both intervention groups. The effects are larger in intervention group 2 than in intervention group 1, but this difference is not statistically significant (P value = 0.45; 4.7%; 95% CI, –0.4 to 9.8%). Results from the adjusted probit regression analyses were similar, with slightly smaller increases in the

marginal effects estimated (intervention group 1 marginal effect, 20.5%; 95% CI, -1.3 to 42.3%; intervention group 2 marginal effect, 24.8%; 95% CI, 4.0–45.7%), and only the intervention group 2 marginal effect is statistically significant at the 5% level (P value = 0.02). Additional adjusted regression models were estimated using the measures of physical and mental health status, and the inclusion of these additional variables does not alter the magnitude or significance of the estimated intervention effects.

Discussion

In this study, we present evidence that it is feasible and effective to use small behavioral economics incentives to increase antiretroviral adherence. Using in-kind prizes valued at less than \$2 USD, the intervention resulted in a 23.7 percentage point increase in the fraction of clients showing mean adherence of 90% or higher. These improvements were made using items valued at roughly half of the cost of travel to the HIV clinic, which represent significantly smaller transfers than employed in most other interventions targeting antiretroviral adherence [16]. These beneficial effects occurred both in intervention group 2, in which adherence was directly incentivized, and intervention group 1 in which participants were eligible for prize drawings if they came to the clinic on their scheduled appointment days. This finding is important as it indicates that such an intervention may not have to rely on expensive MEMS cap-based adherence measurement to increase adherence, but can instead be based on timely clinic attendance, which is easier and less costly to verify. However, we do find some evidence that direct adherence incentivization may be more effective, but a fully powered study is necessary to provide more conclusive evidence on this question. Interventions leading to increased adherence can be cost-effective if they lead to lower levels of adherence support needed, and subsequently lower rates of drug resistance and the need to switch to expensive (and in sub-Saharan Africa not always available) second or third-line treatment. Given the low payouts used in our intervention we expect that it is likely cost-effective, which we intend to test in the fully powered trial based on the current study.

The RAP study is to our knowledge the first to use small incentives based on insights from behavioral economics and allocated by a drawing for improving antiretroviral adherence, and contributes to a growing body of literature that uses such incentives to improve chronic health behaviors [35,36]. Our study suggests that designing incentives based on behavioral economic insights can increase their effectiveness, and get beyond the often at best mixed results of recent interventions aimed at behavioral change in the HIV field based on traditional, fixed incentives of relatively large monetary value. A larger, fully powered study is needed to confirm these early promising results, and would allow the results to additionally detect demographic subgroup differences to shed light on the characteristics of patients most likely to benefit from the intervention. In the current study, those with already relatively high (but not optimal) adherence seem to be benefitting disproportionately from the intervention, which is in line with our hypothesis that for our sample of treatment-mature clients motivational rather than structural barriers are addressed by the small incentives offered. A larger study would also be able to quantify the potentially differential treatment impact across participants' behavioral biases, which our study was not powered to detect. In particular, clients' present bias may play an important role for medication adherence in

chronic conditions, and such clients may also be particularly likely to respond to the relatively short-term rewards underlying the current intervention [37].

There are several limitations to our study. First, it does not have a biological endpoint such as viral load for cost reasons, which should be a goal for a larger study. Although adherence was measured using MEMS caps, which is currently one of the most accurate ways to measure adherence, we cannot exclude the possibility that some participants consciously manipulated the pill bottle openings to increase their chances of receiving the incentives. However, as we observe similar adherence improvements in the group incentivized for keeping their scheduled clinic appointments, this seems to be a limited problem. Second, the incentives provided were in-kind and of very small monetary magnitude (umbrellas, coffee mugs, water bottles). We can therefore not speak to the (potentially greater) effectiveness of different types of incentives (such as cash versus in-kind), or larger prizes that may still be cost-effective. Third, as this article provides evidence of the impact of incentives for the first 9 months of an ongoing study, we cannot verify the longer term effects of these incentives, or whether any effects persist after the incentives are withdrawn. The evaluation of treatment effects over the full 20 months study duration and 6 months postintervention will be better positioned to investigate such effects. However, being able to improve adherence over 9 months using in-kind incentives that cost \$1.50–2 USD is a significant achievement.

In conclusion, small in-kind incentives based on insights from behavioral economics were found to result in improved adherence to antiretrovirals over 9 months among HIV-positive, treatment-mature adults in HIV care in a clinic in Kampala, Uganda. These adherence improvements were experienced by participants in an intervention group eligible for incentives based on MEMS caps-measured adherence directly, as well as participants in a group that received incentives for timely clinic visits. The impact of offering different incentive types and amounts will require further research.

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S.L. and C.S. had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. S.L. was responsible for study design, data analysis, and manuscript preparation; C.S. contributed to data analysis and manuscript preparation; B.M. contributed to study design and manuscript preparation.

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The study is registered at <https://clinicaltrials.gov/ct2/show/NCT02503072?term=linnemayr&rank=2>, NCT02503072.

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Fig. 1. Flow of study participants for the Rewarding Adherence Program study
MEMS, medical event monitoring system.

Fig. 2.
Observed distribution of 9-month mean adherence.

Table 1

Balanced demographics across study groups.

	Full sample <i>N</i> = 155)	Control <i>N</i> = 50)	Intervention groups	
			Group 1 <i>N</i> = 51)	Group 2 <i>N</i> = 54)
Men, no. (%)	57 (37)	19 (38)	20 (39)	18 (33)
Age, mean (SD), years	39 (10.3)	37.4 (9.8)	40.1 (10.9)	39.3 (10.0)
Education, no. (%)				
Some primary education or none	74 (48)	24 (48)	23 (45)	27 (50)
Completed primary education	63 (41)	23 (46)	19 (37)	21 (39)
Greater than primary education	18 (12)	3 (6)	9 (18)	6 (11)
Wealth based on asset index, mean (SD) ^a	5.0 (2.0)	4.8 (2.0)	5.3 (2.1)	4.9 (2.0)
Own home, no. (%)	115 (74)	35 (70)	39 (76)	41 (76)
Monthly disposable income, median (IQR), US \$ ^b	58.00 (29.00–87.00)	43.50 (23.20–79.75)	58.00 (34.80–87.00)	58.00 (34.80–87.00)
Travel cost to HIV clinic, median (IQR), US \$	2.90 (2.03–4.35)	2.90 (2.03–4.35)	2.90 (2.90–4.35)	2.90 (1.74–4.35)
Married, no. (%)	76 (49)	21 (42)	30 (59)	25 (46)
Household size, mean (SD)	4.7 (2.8)	4.3 (2.5)	5.1 (3.1)	4.7 (2.8)
Health limits physical activity, no. (%)	18 (12)	9 (18)	4 (8)	5 (9)
Feelings of depression or hopelessness, no. (%)	102 (66)	33 (66)	34 (67)	35 (65)

^aWealth was measured using an asset index defined as the sum of affirmative responses to questions about ownership of 10 household items. These 10 items represent the most common household items included in the Demographic and Health Survey's (DHS) Uganda survey and the index places equal weight on participants' self-reported ownership of each individual item.

^bBecause of varying exchange rates, US dollar conversions (from Ugandan shillings) are approximate, and are based on the prevailing rate of 1 USD to 3450 Ugandan Shillings during this study period.

Table 2

Impact of incentives on mean antiretroviral adherence over 9 months.

	Control	Intervention groups			<i>P</i> value for test of equality ^c
		Group 1	Group 2	Groups 1 + 2	
No. of participants	48	46	52	98	
Mean adherence % (95% CI)	80.9 (74.8–87.1)	88.3 (84.7–91.9)	86.7 (81.9–91.6)	87.5 (84.4–90.5)	
Unadjusted ^a impact (95% CI)	1 (Reference)	7.4 (0.3–14.4)	5.8 (–1.9 to 13.6)	6.6 (–0.2 to 13.3)	0.510
<i>P</i> value		0.040	0.140	0.057	
Adjusted ^b impact (95% CI)	1 (Reference)	6.4 (–0.7 to 13.5)	4.7 (–2.9 to 12.3)	5.2 (–1.6 to 11.9)	0.511
<i>P</i> value		0.077	0.225	0.131	

CI, confidence interval.

^aResults from ordinary least squares (OLS) regression model of mean adherence during the first 9 months of Rewarding Adherence Program with indicators of intervention groups (control group is the reference standard).^bResults from OLS regression model with indicators of intervention groups and controls for age, sex, education, wealth, and marital status.^c*P* value from F-test of equality between treatment group 1 and treatment group 2.

Table 3

Impact of incentives on reaching 90% mean antiretroviral adherence over 9 months.

	Control	Intervention groups			<i>P</i> value for test of equality ^c
		Group 1	Group 2	Groups 1 + 2	
No. of participants	48	46	52	98	
Mean adherence above 90% No.	19	28	34	62	
% (95% CI)	39.6 (25.8–54.7)	60.9 (45.4–74.9)	65.4 (50.9–78.0)	63.3 (52.9–72.8)	
Unadjusted ^a ME (95% CI)	1 (Reference)	21.5 (0.9–42.1)	26.2 (6.2–46.3)	23.8 (6.4–41.2)	0.453
<i>P</i> value		0.040	0.010	0.007	
Adjusted ^b ME (95% CI)	1 (Reference)	20.5 (–1.3 to 42.3)	24.8 (4.0–45.7)	21.2 (3.0–39.4)	0.457
<i>P</i> value		0.065	0.020	0.023	

CI, confidence interval; OR, odds ratio.

^a Marginal effects from probit regression model of attaining at least 90% mean adherence during the first 9 months of Rewarding Adherence Program with indicators of intervention groups (control group is the reference standard).^b Marginal effects from probit regression model with indicators of intervention groups and controls for age, sex, education, wealth, and marital status.^c *P* value from F-test of equality between treatment group 1 and treatment group 2.