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Financial reinforcers for improving medication adherence: Findings from a meta-analysis

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Abstract

Background—Financial reinforcement interventions based on behavioral economic principles are being increasingly applied in health care settings, and this study examined the use of financial reinforcers for enhancing adherence to medications.

Methods—Electronic databases and bibliographies of relevant references were searched, and a meta-analysis of identified trials was conducted. The variability in effect size and the impact of potential moderators (study design, duration of intervention, magnitude of reinforcement, and frequency of reinforcement) on effect size were examined.

Results—Fifteen randomized studies and 6 non-randomized studies examined the efficacy of financial reinforcement interventions for medication adherence. Financial reinforcers were applied for adherence to medications for tuberculosis, substance abuse, HIV, hepatitis, schizophrenia, and stroke prevention. Reinforcement interventions significantly improved adherence relative to control conditions with an overall effect size of 0.77 (95% CI = 0.70–0.84), $p < .001$. Non-randomized studies had a larger average effect size than randomized studies, but the effect size of randomized studies remained significant at 0.44 (95% CI = 0.35–0.53), $p < .001$. Interventions that were longer in duration, provided average reinforcement of \$50/week, and reinforced patients at least weekly resulted in larger effect sizes than those that were shorter, provided lower reinforcers, and reinforced patients less frequently.

Conclusions—These results demonstrate the efficacy of medication adherence interventions and underscore principles that should be considered in designing future adherence interventions. Importantly, financial reinforcement interventions hold potential for improving medication adherence and may lead to benefits for both patients and society.

Keywords

reinforcement; financial; medication adherence; meta-analysis; behavioral economics

Behavioral economics is the study of psychological and cognitive factors related to decision-making processes. This field is applied increasingly in healthcare settings, often in the context of providing clinicians with incentives for meeting performance guidelines.¹ Patients can also receive reinforcers for meeting criteria associated with health outcomes,

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and randomized trials demonstrate the efficacy of financial reinforcers for reducing alcohol², illicit drug use,³⁻⁴ decreasing smoking,⁵ and losing weight.⁶⁻⁷

A problem relevant to many patient populations is poor medication adherence. Estimates indicate that 28% of new prescriptions are unfilled,⁸ and among patients who do obtain medications, adherence rates are often less than 50%.⁹ Lack of adherence interferes with therapeutic benefits of medications and can lead to additional diagnostic and treatment procedures, resulting in greater health care costs.¹⁰ Poor adherence to anti-microbials can increase disease spread and lead to development of drug resistant strains, which are transmitted to the public. Consequently, some providers are reluctant to prescribe medications to patients presumed to be non-adherent.¹¹

Interventions based on behavioral economic principles may be useful for improving medication adherence. The only prior review of this literature¹² found few studies that applied financial reinforcers for medication adherence. Among the 11 studies included, most applied reinforcers for appointment keeping alone, and only one study¹³ reinforced medication adherence in tuberculosis patients. Recently reinforcing patients for behavior change has gained popularity.¹⁴

We examined the published research on financial reinforcers to improve medication adherence, and a meta-analysis ascertained the effect size of these interventions. Furthermore, analyses evaluated the impact of reinforcement parameters on effect sizes to elucidate conditions under which beneficial effects of financial reinforcement adherence interventions may be best realized.

Methods

Identification of studies

Pubmed and PsychInfo databases were searched through April 2011, for matches in titles, abstracts and descriptors, for the terms: medication and (compliance or adhere*) and (incentive* or cash* or money or token* or payment*). Reference lists of retrieved articles were also examined.

Study inclusion and exclusion criteria

Article titles and abstracts were independently screened. If either suggested that the article might be appropriate, the article was retrieved. Financially-based reinforcers for medication adherence were defined as money, goods (bus tokens, food, etc.), or vouchers redeemable for goods (food, clothes, etc.). Both randomized and non-randomized (e.g., comparison to historical controls or reversal designs) trials were included.

Studies that provided access to treatment (including methadone doses) or reductions or eliminations of copayments as reinforcers were excluded. Studies that reinforced appointment keeping alone, when not linked to medication ingestion, and those employing a single incentive for medication ingestion (e.g., single vaccination, initial visit to a clinic) were excluded. Studies solely utilizing reimbursement payments (e.g., for travel expenses or patient time) were also not included. Studies that did not provide adequate information to derive an effect size were excluded as well. Disagreement between raters was resolved by consensus.

Data analysis

Information about the population, study design, sample size, reinforcement intervention, duration of intervention, maximal reinforcement, frequency of reinforcement, and adherence

data were tabulated. Two independent samples and reinforcement interventions were described within one publication,¹³ which are treated as two separate studies for these analyses. Objective adherence data (e.g., observed doses, Medication Event Monitoring System (MEMS) cap readings, medication completion) are reported as defined within studies.

Effect sizes (ES) were computed via $d = (M1 - M2)/SD$, where $M1$ and $M2$ refer to means of the experimental and control groups, respectively, and SD is the pooled standard deviation. In order of preference, raw data, means and SD s, or test statistics (t or F) were used to calculate ES.¹⁵ If a study had more than one reinforcement (or comparison) condition, values were averaged before determining ES.

The ESs for main adherence outcomes were calculated in each study. Consistent with recommendations,¹⁵ multiple ESs were averaged when a study had more than one adherence outcome to create one ES per sample ($N = 21$) for use in subsequent analyses. Hedge's correction¹⁵ provided unbiased ES estimates and was applied before analyses. These estimates can be interpreted using Cohen's¹⁶ conventions for small (0.20), medium (0.50), and large (0.80) ESs.

Initially, analyses evaluated whether financial reinforcement interventions impacted adherence outcomes using inverse variance weighted mean ESs.¹⁵ Publication bias was assessed using the failsafe N ,¹⁷ which estimates the number of studies with null effects needed to lower the obtained ES to a small effect ($d = 0.20$). Cochran's Q statistic¹⁸ tested for heterogeneity in ESs, and when significant, indicates variability in ESs that may be explained by moderators. In addition, the inconsistency index (I^2) is reported, which estimates the proportion of variance due to heterogeneity rather than chance.¹⁹

Analyses also evaluated whether moderators explained heterogeneity in ESs. Randomization status of the study design and three variables related to specific behavioral principles (i.e., duration, magnitude, and frequency of reinforcement) were included as moderators. Randomization was coded as a dichotomous variable (yes/no). Duration was included as a continuous variable in weeks; for studies in which duration varied across participants, the average duration was used. For two studies,^{20,21} the planned duration of 24 weeks was used, although reinforcement may have extended beyond 24 weeks for some participants. The other two behavioral moderators were dichotomized due to an inability to specifically quantify these variables in several studies. Consistent with other reinforcement literature,^{22,23} magnitudes were dichotomized into low-to-moderate ($< \$50/\text{week}$; $n = 16$) versus high ($\geq \$50/\text{week}$; $n = 5$). Reinforcement magnitudes were derived by dividing the total (or estimated total) reinforcement by the reinforcement duration. When ranges were reported (e.g., two reinforcement conditions), the average magnitude was calculated. In two cases,^{20,24} food or other individually-selected reinforcers (e.g., clothing) were provided, both presumed low-to-moderate in magnitude given the study designs. Reinforcement frequency was dichotomized into at least weekly ($n = 15$) or less frequently than weekly ($n = 6$). Modified weighted least squares regression¹⁵ assessed the effects of these design parameters, with the four variables entered into the regression simultaneously. Analyses were conducted in SPSS 19.0 using Wilson's²⁵ and Hofmann's²⁶ macros.

Results

Electronic searches identified 621 articles containing the key words. After reviewing the titles and abstracts, 46 articles were retrieved as potentially meeting the study inclusion criteria, and 32 additional articles were found through references contained in source articles. Of the 78 retrieved articles, 18 were excluded because they were reviews, 10

discussed ethical issues about payments, 8 did not provide financial reinforcers to patients, 8 did not reinforce medication ingestion, 5 provided only a single reinforcer, and 2 described designs of ongoing projects. An additional 4 studies were excluded because they compared different reinforcement interventions without a non-reinforcement control, 2 did not provide any comparison condition, and 1 non-randomized study did not provide sufficient data from which an ES could be derived.

Table 1 outlines the 21 studies evaluating financial reinforcement interventions for improving medication adherence. Tuberculosis (TB) was the medical condition for which the greatest number of studies were identified,^{13,20,21,24,27–29} and adherence was most often determined by directly observed therapy. Reinforcers were generally cash (\$5–\$10 per dose, week or month). However, one study with adolescents²⁰ employed individual reinforcement contracts with parents, and one study from Timor-Leste²⁴ used meals as the reinforcers. This study's results were impacted by civil conflicts in the region, with treatment completion rates reduced substantially during the conflict period regardless of treatment assignment. All studies providing cash reinforcement (but not those using meals or parental contracts) found significant benefits on at least one adherence measure.

One non-randomized³⁰ and four randomized^{31–34} studies reinforced adherence to naltrexone, a medication used to prevent relapse to opioid dependence. Reinforcement was contingent upon directly observed therapy, and all studies used cash or vouchers, exchangeable for retail goods and services, as reinforcers. All found significant effects or trends ($p < .10$) of the reinforcement intervention on one or more adherence measure.

Three randomized studies^{35–37} reinforced medication adherence in HIV patients, each using MEMS caps to assess adherence. Significant effects were noted with respect to the primary adherence outcomes in all studies.

Two randomized studies reinforced adherence to hepatitis vaccines.^{38,39} Both found significant benefits for overall adherence or timely receipt of injections, but the Stitzer et al.³⁹ study only found trends with respect to other outcomes.

Two non-randomized studies^{40–41} applied financial reinforcers for adherence to antipsychotic depot injections. Both demonstrated high rates of adherence or improvements in functioning related to medication administration (e.g., fewer hospitalizations) relative to pre-reinforcement periods.

One study⁴² reinforced warfarin adherence in patients at risk of stroke. Compared to historical controls, benefits of reinforcement were noted, with no differences between the two conditions that slightly varied probabilities and magnitudes of reinforcement.

Figure 1 shows ESs and confidence intervals derived from each of the 21 studies. Studies are organized by disease entity and then by publication date. Using the overall ES calculated for each study, the average corrected ES across the 21 studies was 0.77 ($SE = .03$). This ES was statistically significant, $p < .001$ (95% CI = 0.70–0.84), showing benefits of financial reinforcement for improving adherence measures. The Failsafe N indicated that 60 studies finding no effect of financial reinforcement interventions would be necessary to lower the obtained mean ES of 0.77 to a small ES of 0.20.

Significant heterogeneity was present ($Q(20) = 291.55$, $p < .001$) and the inconsistency index (I^2) suggested that 93% of the variability was due to true heterogeneity rather than sampling error. In the moderator analysis exploring this heterogeneity, randomization status and the three behavioral parameters explained significant variability in ESs [Model $Q(4) = 172.05$, $p < .001$, $R^2 = 0.59$].

All four moderators were significant predictors. Randomized studies ($n = 15$) had a significantly smaller average ES ($M = 0.44$, $SE = 0.05$) than non-randomized studies ($M = 1.22$, $SE = 0.05$; $B = -0.62$, $p < .001$). Nevertheless, the ES of randomized studies remained significant ($p < .001$; 95% CI = 0.35–0.53).

In terms of parameters of the reinforcement interventions, duration of reinforcement was significantly and positively associated with ES, $B = 0.16$, $p = .02$. Mean ES for studies providing \$50 or more in weekly reinforcement was 1.18 ($SE = 0.14$) compared to a mean ES of 0.74 ($SE = 0.04$) for studies with weekly reinforcement of less than \$50 ($B = 0.38$, $p < .001$). Studies providing at least weekly reinforcement had a significantly higher ES ($M = 1.00$; $SE = 0.04$) than studies with less frequent reinforcement ($M = 0.25$, $SE = 0.06$; $B = 0.20$, $p = .009$).

Discussion

Financial reinforcement interventions are beneficial for improving medication adherence with an overall mean ES of 0.77. An additional 60 studies would need to have been conducted, and found non-significant effects, to reverse the conclusion drawn. All four moderators evaluated significantly impact ESs. Compared to non-randomized studies, randomized studies had a smaller, but statistically significant, ES in the moderate range. Consistent with behavioral economic principles,^{43–44} greater magnitudes of reinforcement engendered larger ESs. Further, studies that reinforced patients at least weekly had large mean ES, while those with less frequent reinforcement resulted in a small mean ES. Similar issues impact ESs in studies of reinforcement interventions for treating substance use disorders,^{22–23} and suggest that reinforcement magnitude and frequency should be considered in designing reinforcement interventions to enhance medication adherence.

A positive association was found between reinforcement duration and ES. One meta-analysis of reinforcement interventions did not find that intervention duration impacts ES,²² but another found intervention duration was inversely associated with ES in substance abusing populations.²³ Differences across populations may occur because of the truncated durations of most substance abuse treatment trials (usually 12 weeks) relative to medication trials. The longer durations in which reinforcers were applied in some medication adherence studies likely related to the intended duration of medication administration. For time-limited medications for TB and vaccine series, financial reinforcers were often in place throughout the duration of the medication period, 24 to 52 weeks. In other cases, reinforcers were applied during treatment initiation (e.g., naltrexone for opioid dependence) or for relatively short durations once poor adherence was identified (e.g., HIV, stroke prevention). The larger ES in longer duration studies suggests that additional research should evaluate reinforcement duration and its impact on outcomes systematically.

For chronic medication administration, three studies in HIV-positive patients^{35–37} and one in patients at risk for stroke⁴² evaluated post-treatment effects on adherence. In the HIV trials, patients who earlier received reinforcement had numerical increases in adherence compared to those who did not receive reinforcement, but none revealed statistically significant benefits throughout follow-up. The lack of sustained effects on adherence may relate to sample size, as studies were not powered to detect significance in post-intervention periods. Some studies of financial reinforcers to reduce substance use likewise failed to achieve significant long-term benefits,^{45–48} but others find enduring benefits.^{49–51} A robust predictor of long-term effects in substance abuse treatment trials is longest duration of continuous behavior change during treatment.^{46,47,51–53} To date, only one medication adherence study³⁷ reported upon continuous days of adherence, but it did not evaluate associations between this variable and long-term adherence. More research is needed to

examine conditions under which financial reinforcers engender sustained effects for diseases that require chronic medication administration.

Across populations, different techniques were utilized to ascertain adherence. Directly observed therapy (oral or injection) was used for medications with less than daily administration, and MEMS caps for more frequent dosing schedules. Advantages of directly observed therapy are that providers can be assured the medication was ingested, a concern for medications with significant side effect profiles and those for which non-adherence may have a substantial impact on public health (i.e., infectious diseases). Primary disadvantages of reinforcing directly observed therapy relate to patient inconvenience for travel to the clinic and administrative costs for staff monitoring. These difficulties are minimized when patients are attending clinics regularly for other reasons (e.g., methadone) or when limited doses are required (e.g., a three-part vaccine or time-limited therapy). The key advantage of electronic pill caps is that patients can take medications in their natural environments. Concerns relate to the need to download data at the clinic, which places a delay between the behavior and the reinforcer. Additionally, patients can open containers without ingesting medication. Nevertheless, studies that reinforced MEMS cap openings^{35–37,42} included alternate measures of adherence and found associations between MEMS openings, self reports, and biological indicators.

A limitation of this study is that outcomes were not consistently defined across studies, and ESs were derived based upon the outcome data provided. Relatively few studies included biological indicators of medication adherence, disease progression or remission status.

Despite these limitations, this is the most comprehensive review of the literature on the use of financial reinforcement to improve medication adherence. It included a large array of patient populations and utilized multiple ESs per study to provide the most complete and unbiased overall ES per study. Overall, the ES of financial reinforcement interventions for improving medication adherence was moderate to large.

Behavioral economic studies find that individuals place a disproportionate emphasis on immediate outcomes, and they discount delayed and probabilistic events.^{54–56} In the context of medication adherence, immediate inconveniences associated with medication ingestion or its side effects may be heavily weighted while the long-term and probabilistic outcomes of disability and death are devalued. By placing more direct and immediate beneficial consequences on medication ingestion via financial reinforcers, adherence increases, resulting in potential benefits for patients and society.

One of the studies identified in this review reported upon the cost-effectiveness of financial reinforcement procedures.⁵⁷ Further evaluation of cost-effectiveness and cost-benefits of these approaches may reveal conditions under which and populations for whom financial reinforcement interventions for adherence ultimately may become a part of standard care and a reimbursable or publicly covered cost.⁵⁸ For example, Buchanan⁵⁹ reported that 16 states provide cash reinforcers for TB patients to comply with medications, and over 40 states provide meals or clothing for TB medication adherence. Other medical conditions for which financial reinforcement interventions may be useful to enhance adherence include hypertension, high cholesterol, asthma, and type 2 diabetes.

Despite demonstrated successes, providing patients with financial reinforcers is highly controversial.¹⁴ An ongoing study using these approaches with psychiatric patients in the United Kingdom⁶⁰ has been met with considerable skepticism. Decisions about which patients receive financial reinforcers require careful consideration to balance concerns about equitability, possibilities of unintended behaviors, as well as the costs and benefits of treatment. Results from this meta-analysis indicate that ethical and logistical issues should

be addressed, because providing financial reinforcers has pronounced benefits for improving medication adherence.

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Figure 1.

Effect sizes (d) and 95% confidence intervals (CI) by disease state and study. Studies are listed by the disease state for which adherence to treatment was reinforced. Morisky 1990 (a) refers to an active sample of tuberculosis patients, and Morisky 1990 (p) refers to a preventive sample of tuberculosis cases. The total effect size represents all 21 studies.

Table 1

Studies reinforcing adherence to medications.

First author, year	Design	n	Condition(s)	Duration (weeks)	Reinforcement maximum	Reinforcement frequency	Outcome(s)	d	Average d
Tuberculosis									
Morisky 1990	R	43	(a) \$10 in tokens, gift cards or cash/clinic medication visit.	24–36	Varied	Monthly (or weekly)	Took >95% of doses: (a) 71% vs (b) 57% (p<.01)	0.33	0.50
		45	(b) Usual care (active cases).				Finished treatment: (a) 98% vs (b) 91% (p=.36)		
							Appointments kept: (a) 88% vs (b) 81% (p=.08)		
Morisky 1990	R	58	(a) \$5 in tokens, gift cards or cash/clinic medication visit.	36–52	Varied	Monthly (or weekly)	Took >95% of doses: 42% vs 14% (p<.001)	0.81	0.74
		59	(b) Usual care (preventive cases).				Finished treatment: 64% vs 27% (p<.001)		
							Appointments kept: (a) 64% vs (b) 47% (p=.003)		
Tulsky 2000	R	43	(a) \$5/DOT.	24	\$240	Twice weekly	Median months on medication: (a) 5 vs (bc) 2 (p<.05)	NEI	0.55
		37	(b) Peer health advisor.				Completed treatment: (a) 44% vs (bc) 23% (p<.05)		
		38	(c) Usual care.						
Bock 2001	NR	55	(a) \$5 voucher/DOT and physician appointment.	32–52 (est.)	\$160–\$260 (est.)	Not stated, but appeared >weekly	Completed treatment (52 wks): (a) 89% vs (b) 52% (p<.05)	1.12	1.12
		52	(b) Historical controls.						

First author, year	Design	n	Condition(s)	Duration (weeks)	Reinforcement maximum	Reinforcement frequency	Outcome(s)	d	Average d
Malotte 2001	R	53	(a) \$5/biweekly DOT + outreach.	24-52	\$240-\$520	Twice weekly	Doses ingested on time: (ab) 70% vs (c) 12% (p<.001)	1.84	1.89
		55	(b) \$5/biweekly DOT.				Completed treatment: (ab) 56% vs (b) 4% (p<.001)	1.95	
		55	(c) Biweekly DOT + outreach.						
Morisky 2001	R	196	(a) Peer counseling + parental contracting/taking medication and attending clinic visits	24	Varied	Varied (recommended 3x in total)	Completed treatment: (ab) 81% vs (bc) 79% (n.s.)	0.05	0.05
		204	(b) Parental contracting.						
		199	(c) Peer counseling.						
		195	(d) Usual care.						
Jakubowiak 2007	NR	829	(a) Food, clothing, travel funds, toiletries, etc./DOT.	24	\$60-\$180 food packages	Varied, appeared to be frequent	Treatment success: (a) 99% vs (b) 90% (p<.001)	1.24	1.24
		698	(b) Usual care.						
Martins 2009	R	136	(a) Meals and food packages/visit.	32	Not stated	Daily weeks 1-8, not stated weeks 9-32	Completed treatment: (a) 76% vs (b) 78% (n.s.)	-0.05	-0.03
		129	(b) Nutritional information.				Compliance: (a) 98.2% vs (b) 98.3% (n.s.)	-0.02	
Drug abuse									
Grabowski 1979	NR	9	(a) \$3.35/DOT 3x/week.	20	(a) \$200	1-3x/week	Retained 1 month: (abcd) 89% vs (e) 59% (p<.01)	0.94	0.94
			(b) \$10.05/week on set day (regardless of DOT other days).		(b) \$200				
			(c) \$10.50/every 3rd DOT.		(c) \$200				
			(d) \$10.50/every 3rd DOT on average.		(d) \$200				
		126	(e) Historical controls.						
Preston 1999	R	19	(a) \$2.50 vouchers/DOT, increases with adherence.	12	(a) \$1155	3x/week	Doses ingested: (a) 21.4 vs (bc) 7.8 (p<.05)	1.13	1.06

First author, year	Design	n	Condition(s)	Duration (weeks)	Reinforcement maximum	Reinforcement frequency	Outcome(s)	d	Average d
Carroll 2001	R	19	(b) Yoked control vouchers.				Weeks in treatment: (a) 7.4 vs (bc) 3.6 (p<.05)	0.88	1.36
		20	(c) No vouchers.				Completed treatment: (a) 42% v. (bc) 13% (p<.05)	0.88	
							Maximum consecutive doses: (a) 19.6 vs (bc) 5.5 (p<.01)		
Carroll 2001	R	35	(a) \$0.80 vouchers/DOT and/drug-negative sample.	12	(a) \$561	3x/week	Doses ingested: (ab) 18.7 vs (c) 14.2 (p=.06)	0.35	0.40
		48	(b) Above + significant other counseling.				Weeks in treatment: (ab) 7.4 vs (c) 5.6 (p=.05)	0.37	
		44	(c) Standard care + cognitive behavioral therapy.				Completed treatment: (ab) 45% vs (c) 26% (p<.05)	0.48	
Carroll 2002	R	17	(a) \$0.80 vouchers/DOT and/drug-negative sample.	12	(a) \$561	3x/week	Doses ingested: (ab) 20.9 vs (c) 14.4 (p=.08)	0.52	0.46
		20	(b) \$2.00 vouchers/DOT and/drug-negative sample.				Weeks in treatment: (ab) 8.0 vs (c) 6.2 (p=.17)	0.40	
		18	(c) Standard care.						
Nunes 2006	R	36	(a) Motivational enhancement, cognitive-behavioral, significant other, community reinforcement therapy + \$2 voucher/DOT and/negative sample.	24	(a) \$672	2x/week	Ingested >70% doses: (a) 55.6% vs (b) 45.5% (p=.40)	0.22	0.43
							Weeks in treatment: (a) 11.9 vs (b) 7.2 (p=.04)	0.50	
		33	(b) Adherence therapy (psychoeducation, problem solving, 12 step).				Completed treatment: (a) 22.2% vs (b) 9.1% (p=.04)	0.58	

First author, year	Design	n	Condition(s)	Duration (weeks)	Reinforcement maximum	Reinforcement frequency	Outcome(s)	d	Average d
HIV									
Rigsby 2000	R	15	(a) Cue dose training + \$2–\$10/primary medication (± 2hrs) via MEMS.	4	\$280	Weekly	Doses of primary medication: (a) 90% v (bc) 69% (p<.05)	1.87	2.06
		18	(b) Cue dose training.				Doses of secondary medication: (a) 86% v (bc) 71% (p<.05)		
		22	(c) Adherence counseling.						
Rosen 2007	R	28	(a) Adherence counseling + \$1–\$100 prizes for ingestion (±3 hrs) via MEMS.	16	\$800	Weekly	Doses of primary medication: (a) 76% v (b) 44% (p=0.01)	1.30	2.18
		28	(b) Adherence counseling.				Doses of secondary medication: (a) 77% v (b) 45% (p=.09)		
							> 95% adherent: (a) 18% vs (b) 0% (p<.05)		
Sorensen 2007	R	34	(a) Adherence counseling + \$1 voucher/day for adherence (±2hrs) via MEMS.	12	\$1172	Up to twice weekly	Doses of primary medication: (a) 78% vs (b) 56% (p<.001)	1.09	0.86
		32	(b) Adherence counseling + chance to win \$1–\$80 prizes for attending.				Pill count adherence: (a) 86% vs (b) 75% (p=.02)		
							Days of continuous adherence: (a) 21 vs (b) 9 (p<.001)		
Hepatitis									
Seal 2003	R	48	(a) \$20/monthly visit (3 visits were DOT).	24	\$120	Each visit, DOT	Received all doses: (a) 69% vs (b) 23% (p<0.001)	1.10	1.10
		48	(b) Weekly outreach + reminders.						

First author, year	Design	n	Condition(s)	Duration (weeks)	Reinforcement maximum	Reinforcement frequency	Outcome(s)	d	Average d
Stitzer 2010	R	13	(a) \$10/visit for transportation, \$1–\$80 prizes for attending, and >\$20 for DOT. (b) \$10/visit for transportation.	24	\$486 prizes + \$265 DOT	Each weekly visit and DOT visits	Doses received: (a) 91% vs (b) 78% (p=.22) Doses received on time: (a) 74% vs (b) 51% (p=0.02) Received all doses: (a) 77% vs (b) 46% (p=0.11) Weeks attended: (a) 82% vs (b) 64% (p=0.14) Consecutive weeks attended: (a) 17 vs (b) 12 (p=.10)	0.54 1.11 0.75 0.65	0.75
Psychosis									
Claassen 2007	NR	4	(a) £5–15/DOT (depending on frequency of DOT). (b) Past two year's records of same patients.	3–24	Varied	Each DOT	Days hospitalized: (a) 9.3 vs (b) 214.5	1.51	1.51
Staring 2010	NR	5	(a) €10–20/DOT (depending on frequency of DOT). (b) Past year's records of same patients.	52	\$260	Each DOT	Injectons received: (a) 100% vs (b) 44% Days hospitalized: (a) 3.4 vs (b) 100.2	1.24 0.34	0.79
Stroke Prevention									
Volpp 2008	NR	10	(a) Chance to win \$10–\$100/day (\$5/day average) for MEMS adherence.	12	(a) \$420	Informed of earnings daily	Days correct pill taking: (a) 97.7% vs (c) 78.0% (b) 98.4% vs (c) 82.9%	NEI NEI	0.65

First author, year	Design	n	Condition(s)	Duration (weeks)	Reinforcement maximum	Reinforcement frequency	Outcome(s)	d	Average d
		10	(b) Chance to win \$10–\$100/day (\$3/day average) for MEMS adherence.		b) \$252		Plasma levels out of range: (a) 12.2% vs (c) 35.0%	0.75	
		25	(c) Historical patients.				(b) 40.4% vs (c) 65.0%	0.56	

d = Effect size; average d is unadjusted and unweighted. R = Randomized; NR = Not randomized; DOT = Directly observed therapy; MEMS = Medication Event Monitoring System; NEI = Not enough information to calculate effect sizes. n.s. = not stated. est = estimated.

Notes: For Morisky et al. (2001), the N analyzed differs from N randomized (794 vs 767). In Martins et al. (2009), results from the study were greatly impacted by civil conflict in the study region. In Grawbowski et al., (1979), the 9 reinforcement patients each received 2 conditions. For Rigby et al. (2000), estimates were derived from a figure. For Claassen et al. (2007), the treatment and comparison periods were not equivalent across patients. For Jakubowiak et al. (2007), reinforcement magnitude was calculated based on available data (monthly estimates for food packages only). Estimates for treatment completion in Preston et al. (1999) were reported in Nunes et al. (2006).