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Use of contingency management incentives to improve completion of hepatitis B vaccination in people undergoing treatment for heroin dependence: a cluster randomised trial



Tim Weaver*, Nicola Metrebian*, Jennifer Hellier, Stephen Pilling, Vikki Charles, Nicholas Little, Dilkushi Poovendran, Luke Mitcheson, Frank Ryan, Owen Bowden-Jones, John Dunn, Anthony Gasper, Emily Finch, John Strang



Summary

Background Poor adherence to treatment diminishes its individual and public health benefit. Financial incentives, provided on the condition of treatment attendance, could address this problem. Injecting drug users are a high-risk group for hepatitis B virus (HBV) infection and transmission, but adherence to vaccination programmes is poor. We aimed to assess whether contingency management delivered in routine clinical practice increased the completion of HBV vaccination in individuals receiving opioid substitution therapy.

Methods In our cluster randomised controlled trial, we enrolled participants at 12 National Health Service drug treatment services in the UK that provided opioid substitution therapy and nurse-led HBV vaccination with a super-accelerated schedule (vaccination days 0, 7, and 21). Clusters were randomly allocated 1:1:1 to provide vaccination without incentive (treatment as usual), with fixed value contingency management (three £10 vouchers), or escalating value contingency management (£5, £10, and £15 vouchers). Both contingency management schedules rewarded on-time attendance at appointments. The primary outcome was completion of clinically appropriate HBV vaccination within 28 days. We also did sensitivity analyses that examined vaccination completion with full adherence to appointment times and within a 3 month window. The trial is registered with Current Controlled Trials, number ISRCTN72794493.

Findings Between March 16, 2011, and April 26, 2012, we enrolled 210 eligible participants. Compared with six (9%) of 67 participants treated as usual, 35 (45%) of 78 participants in the fixed value contingency management group met the primary outcome measure (odds ratio 12·1, 95% CI 3·7–39·9; $p < 0·0001$), as did 32 (49%) of 65 participants in the escalating value contingency management group (14·0, 4·2–46·2; $p < 0·0001$). These differences remained significant with sensitivity analyses.

Interpretation Modest financial incentives delivered in routine clinical practice significantly improve adherence to, and completion of, HBV vaccination programmes in patients receiving opioid substitution therapy. Achievement of this improvement in routine clinical practice should now prompt actual implementation. Drug treatment providers should employ contingency management to promote adherence to vaccination programmes. The effectiveness of routine use of contingency management to achieve long-term behaviour change remains unknown.

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Introduction

Poor adherence to treatment is a widespread problem that reduces the individual and public benefit from numerous health interventions.¹ For addiction, evidence-based treatments exist (eg, opioid substitution treatment),² but do not provide their full benefit because of poor adherence and high progressive dropout.³ Building on the behavioural principles of operant conditioning, contingency management involves the systematic application of positive reinforcement⁴ (use of financial or material incentives) to promote adherence to treatment or behaviour consistent with treatment goals and thereby amplify the benefits of existing treatment. Substantial interest exists in the application of contingency management as an adjunct to treatments

delivered in various contexts,⁴ and particularly within treatment for addictions.⁵

Strong evidence from the USA supports the effectiveness of contingency management to improve outcomes of existing addiction treatments.⁶ However, the generalisability of these findings might be restricted by the extensive use of specialist therapists employed solely to deliver contingency management, and its frequent assessment within specialist research centres. The UK National Institute for Health and Care Excellence (NICE) recommends that contingency management should be applied and assessed in routine clinical practice in the UK,^{7,8} and identifies adherence to time-limited health interventions such as hepatitis B virus (HBV) vaccination^{9,10} as a potential intervention target. However,

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See [Comment](#) page 113

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despite international evidence for contingency management, in common with most other developed and developing health-care systems, the UK has no track record in this area. Hence the feasibility, acceptability, and clinical and cost-effectiveness of this intervention need to be assessed in routine drug-treatment settings.¹¹

HBV infection (and associated health sequelae) is a global health problem.¹² Injecting drug users are a major risk group for infection and transmission¹³ and an important target population for vaccination.¹⁴ In the UK, HBV infection affects about 22% of injecting drug users.¹⁵ Clinical guidance recommends routine HBV vaccination be offered to people receiving addiction treatment,¹⁶ but although prison-based programmes have improved vaccination uptake in recent years,¹⁷ a need remains to improve the uptake and completion of vaccination programmes offered to people entering community treatment.¹⁸ We aimed to assess the effectiveness of contingency management in promoting the completion of HBV vaccination in community drug-treatment settings, comparing the offer of fixed and escalating incentives for on-time attendance at vaccinations with the offer of vaccination without incentive.

Methods

Study design and participants

In our cluster randomised trial, we enrolled participants at 12 National Health Service drug treatment clinics in the UK. All sites provided opioid substitution therapy and nurse-led blood-borne virus services. We trained clinic staff to deliver contingency management as part of routine care. In accordance with clinical guidelines, all sites offered HBV vaccination to patients starting new treatment episodes according to a super-accelerated vaccination schedule (three injections on days 0, 7 and 21).^{16,19}

Local clinical teams assessed eligibility of patients in participating services within the first 2 months of a new period of opioid substitution therapy. Adults aged 18–65 years were eligible if they had previous, current, or future risk of injecting drug use and agreed to receive vaccination, participate in the trial, and provided written informed consent. Individuals were excluded if they were pregnant or breastfeeding or not clinically eligible to receive HBV vaccination (ie, previously received vaccination or had HBV infection).

The trial was reviewed by the North London Research Ethics Committee 2 and received a favourable ethical opinion on Sept 27, 2010 (reference 10/H0724/56).

Randomisation and masking

Randomisation was undertaken independently by the Kings Clinical Trials Unit (Institute of Psychiatry, King's College London, London, UK). Clusters were assigned to treatments with a random permuted blocks approach, with a block size of 3 in a 1:1:1 allocation ratio. Sites were randomly allocated to provide HBV vaccination without contingency management (treatment-as-usual group),

HBV vaccination with fixed-value incentive (fixed group; service users received up to an aggregate total of £30, provided as a £10 voucher at each of three vaccinations), or HBV vaccination with contingency management of an incentive that increased in value (escalating group; participants received up to an aggregate total of £30 in vouchers, provided as a £5 voucher at first vaccination visit, a £10 voucher at second vaccination visit, and a £15 voucher at third vaccination visit). In both contingency management groups, eligibility to receive a voucher was conditional on attendance at the appointment on time and compliance with the vaccination schedule as clinically indicated.

In most sites, vaccination was offered to all patients whose clinical eligibility was established through a verbal assessment. However, some sites used blood tests to establish a patient's HBV antibody concentrations either before or during the vaccination schedule. Where this practice was followed, if the blood test showed the patient had sufficiently high concentrations of antibodies, the service would either not start the vaccination schedule or would not continue with the vaccination schedule if it had been started. Because of the potential effect of this difference in practice on our primary outcome, randomisation was stratified by whether sites undertook blood tests and acted upon the results within 7 days of the first vaccination appointment (ie, before vaccination 2). Three of 12 sites undertook blood testing. An open-label design was used for this trial owing to the nature of the intervention; researchers, clinicians, and statistician were unmasked to treatment allocation.

Procedures

The vaccination schedule offered in each site was identical apart from the absence or presence (and type) of financial incentive. We used a super-accelerated vaccination schedule in accordance with best clinical practice as recommended by the UK Department of Health^{16,19} for use with injecting drug users or individuals at risk of injecting. These individuals are at high risk of contraction and transmission of the disease and should be immunised as rapidly as possible.

Patients completed a research interview before enrolment into the trial. The research interview assessed sociodemographic variables, drug and alcohol use, and drug treatment history (Opiate Treatment Index²⁰ and Alcohol Use Disorders Identification Test²¹) and health status (EQ-5D²² and Short Form-36²³). On conclusion of the interview, site treatment allocation was revealed and when relevant, scripted information was provided explaining eligibility for receipt of the financial incentives. Patients were given a first vaccination appointment (day 0) at least 24 h after enrolment. Attendance at the three HBV vaccination appointments was recorded for up to 3 months.

Nurses providing HBV vaccinations received training on trial procedures and, if working in an intervention site, the principles and practice of contingency

management (panel 1).⁵ All trial appointments were recorded as audio and a random sample of 40 recordings (stratified by treatment allocation and first or subsequent vaccination) were rated for adherence to the intervention protocol according to a bespoke measurement scale. We regarded good adherence as a score of at least 66% and poor adherence as a score of less than 33%.

Outcomes

The primary outcome was the completion of HBV vaccination within 28 days of the first vaccination (day 0). Patients were defined as completers if they attended all scheduled, clinically relevant vaccination appointments, or attended but were not vaccinated because of existing immunity. We chose 28 days as the primary endpoint because this timeframe was consistent with some rescheduling of appointments by patients (permitted by our protocol if agreed in advance) and the occasional necessary rescheduling of appointments by clinics. Sensitivity analyses examined completion of the vaccination schedule with a strict definition of completer requiring on-time attendance at all relevant vaccination appointments, and a more relaxed definition requiring patients to complete all relevant vaccination appointments within 3 months.

We also recorded incidence of serious adverse events, which we assessed for seriousness and relatedness to vaccination.

Statistical analysis

We calculated the sample size to allow a separate comparison of treatment as usual versus fixed and escalating contingency management approaches. No directly comparable data exist from which to base a power calculation, but we used data from a similar study⁹ that compared contingency management with an outreach programme promoting completion of HBV vaccination that reported large differences (69% for the CM approach *vs* 23% for the outreach programme). The sample size was based on the assumption that the percentage of participants completing clinically relevant vaccination would increase from 23% in the treatment as usual conditions to 69% in the two contingency management conditions.

A randomised controlled trial would require an overall sample size of 29 participants per group to provide 90% power for a two-sided test at 5% significance to detect a difference of completers of 69% in contingency management and 23% in treatment as usual (allowing 5% attrition). To account for possible cluster effects, we increased the sample size by an inflation factor of 1.75, calculated on assumption of intraclass correlation of 0.05 on the basis of previous studies²⁴ with a planned 16 participants per cluster. This increase equated to 51 participants per intervention group, with at least three clusters per intervention needed to achieve 90% power. We therefore planned to trial each intervention in four clusters, with 16 participants per cluster (192 participants

Panel 1: Training and supervision of nurses

All staff delivering hepatitis B virus (HBV) vaccination with or without contingency management were registered nurses working within substance misuse services and employed as either keyworkers (providing HBV vaccinations as part of their role) or specialist nurses providing a range of blood-borne virus interventions (including HBV vaccinations). All nurses had previously received training in provision of HBV vaccinations.

Nurses responsible for provision of HBV vaccinations were instructed on trial procedures and those working in sites allocated to contingency management also received a bespoke 1 day training course in the principles and practice of contingency management, including simulation and role play from psychologists on the research team. A training manual was written by the research team and provided to all nurses.

All HBV vaccination appointments were recorded as audio. Supervision (either face-to-face or telephone) was provided to nurses working in sites allocated to contingency management throughout the trial by a psychologist from the research team after review of selected audio recordings. 40 audio recordings were reviewed and rated for adherence to the contingency management protocol by use of a specifically developed adherence measure.

overall, 64 participants per trial intervention, and 12 clusters) because recruitment of 192 participants provides 90% power for a two-sided test at 5% significance between each contingency management treatment versus treatment as usual. The study was also powered sufficiently if the trial resulted in unequal cluster sizes based on an average of 16 per site with minimum cluster size of six and maximum of 26.²⁵

The statistical analysis plan was approved by the trial steering and data monitoring committees. We regarded $p < 0.05$ as significant for all analyses. We analysed all data at the individual level, accounting for clustering at the site level and based on the intention-to-treat sample. We summarised continuous variables as mean (SD) and categorical variables as n (%). The unadjusted comparison of categorical variables was by Fisher's exact test. Our primary outcome analysis measured on-time attendance for vaccination and did not depend on post-intervention follow-up of the patient. Therefore, attrition contributed to our outcome measure and thus no outcome data would be regarded as missing.

For the primary analysis, we assessed the binary outcome completer status with a generalised estimating equation (GEE) to account for potential correlations of outcomes within sites, specifying an exchangeable correlation matrix. We adjusted the GEE logistic regression (specifying a binomial family and logit link) for trial group and the randomisation stratification factor (blood test) with a fixed-effects approach.²⁶ We also calculated the number needed to treat (NNT) to achieve completer status.

In the sensitivity analyses, we recategorised data into the outcome completer status, adjusted for the two time assumptions. We analysed the binary outcomes within a GEE, specifying an exchangeable correlation matrix and adjusting the GEE logistic regression (with a binomial family and logit link) for trial group and the randomisation stratification factor with a fixed-effects approach. We

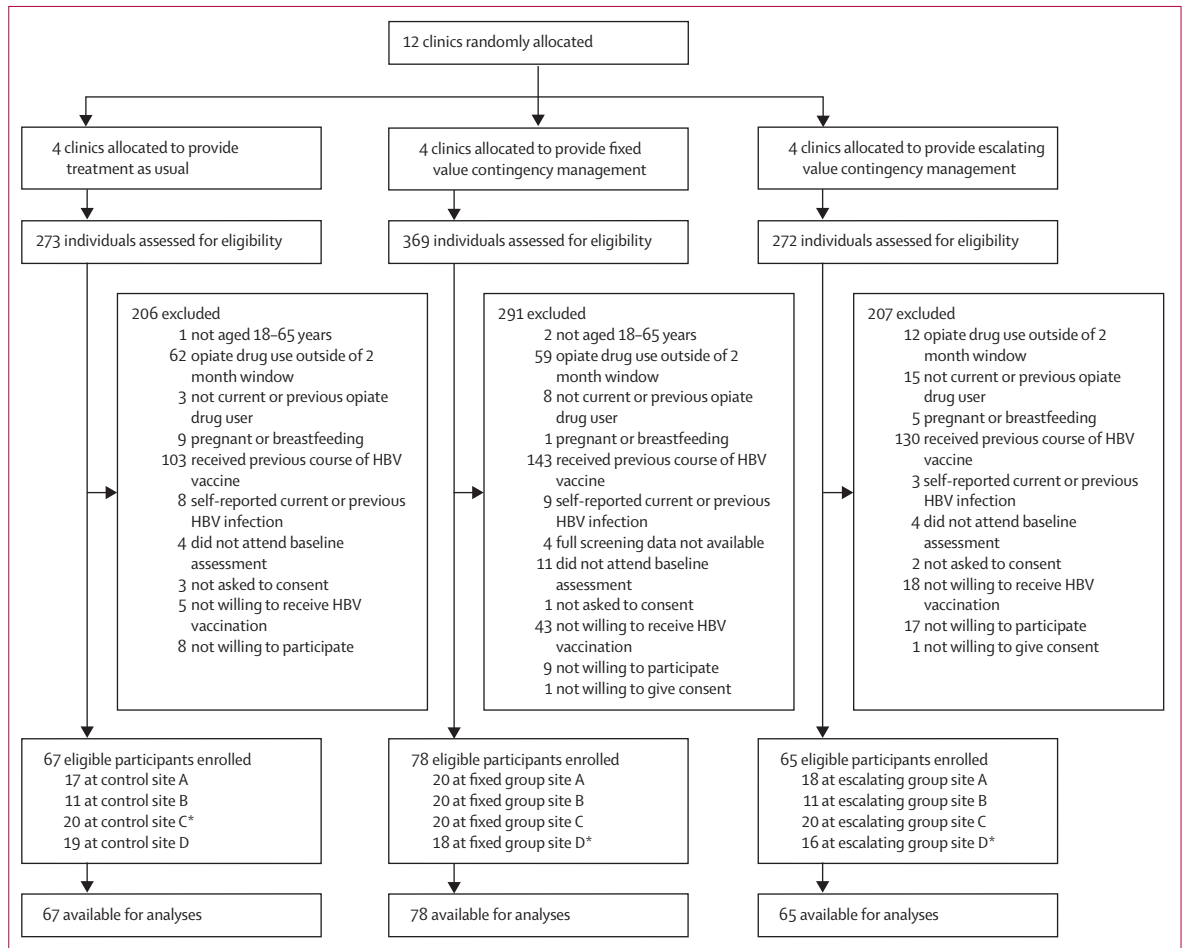


Figure 1: Trial profile
 HBV=hepatitis B virus. *Site undertook blood testing for HBV.

	Treatment as usual (n=67)	Fixed value contingency management (n=78)	Escalating value contingency management (n=65)	Overall (N=210)
Age, years	37.7 (8.6, 18–59)	35.5 (8.1, 21–51)	35.5 (7.9, 18–55)	36.2 (8.2, 18–59)
Sex				
Male	51 (76%)	66 (85%)	50 (77%)	167 (80%)
Female	16 (24%)	12 (15%)	15 (23%)	43 (20%)
Ethnicity				
White	51 (76%)	62 (79%)	45 (69%)	158 (75%)
Black	4 (6%)	1 (1%)	1 (2%)	6 (3%)
Asian	2 (3%)	11 (14%)	14 (22%)	27 (13%)
Other	10 (15%)	4 (5%)	5 (8%)	19 (9%)
Employment				
Unemployed	61 (91%)	69 (88%)	53 (82%)	183 (87%)
Employed or student	6 (9%)	9 (12%)	10 (15%)	25 (12%)
Other	0	0	2 (3%)	2 (1%)
Normal living arrangement				
With partner or spouse	9 (13%)	12 (15%)	15 (23%)	36 (17%)
With friends	8 (12%)	3 (4%)	5 (8%)	16 (8%)
Alone	28 (42%)	35 (45%)	31 (48%)	94 (45%)
Other	22 (33%)	28 (36%)	14 (22%)	64 (30%)

(Table 1 continues on next page)

	Treatment as usual (n=67)	Fixed value contingency management (n=78)	Escalating value contingency management (n=65)	Overall (N=210)
(Continued from previous page)				
Accommodation				
Owner occupied	2 (3%)	8 (10%)	1 (2%)	11 (5%)
Rented private	10 (15%)	18 (23%)	19 (29%)	47 (22%)
Rented (LA, HA)	30 (45%)	16 (21%)	26 (40%)	72 (34%)
Living with relatives	0	8 (10%)	9 (14%)	17 (8%)
Bed and breakfast or hotel	2 (3%)	1 (1%)	2 (3%)	5 (2%)
Hostel	12 (18%)	9 (12%)	1 (2%)	21 (10%)
NFA	9 (13%)	11 (14%)	6 (9%)	26 (12%)
Other	2 (3%)	8 (10%)	1 (2%)	11 (5%)
Prison history				
Ever imprisoned (sentenced or remand)	47 (70%)	41 (53%)	26 (40%)	106 (50%)
Ever been in prison (on remand)	41 (61%)	32 (41%)	18 (28%)	91 (43%)
Ever been in prison (sentenced)	39 (58%)	39 (50%)	25 (38%)	103 (49%)
Offered hepatitis B vaccination in prison	24 (36%)	18 (23%)	7 (11%)	49 (23%)
Health status				
EuroQOL (VAS score 0–100)	50.0 (20.5, 0–90)	52.2 (22.4, 0–96)	55.2 (21.4, 10–95)	52.4 (21.5, 0–96)
SF-36 mental health component (0–100)	46.0 (10.5, 20–67)	46.1 (11.8, 16–69)	46.1 (11.3, 13–66)	46.1 (11.2, 13–69)
SF-36 physical health component (0–100)	28.6 (14.4, 2–60)	30.0 (14.8, 4–62)	32.1 (14.4, 4–64)	30.2 (14.6, 2–64)
Drug use				
Age of first opiate use, years	23.5 (9.1, 12–51)	21.7 (7.8, 12–45)	23.9 (7.9, 12–51)	22.9 (8.3, 12–51)
Age of regular opiate use, years	25.1 (8.8, 13–51)	24.2 (7.9, 12–46)	26.1 (7.8, 14–51)	25.1 (8.2, 12–51)
Age first injected, years	26.4 (7.8, 12–49)	25.1 (7.3, 12–45)	24.7 (6.5, 16–41)	25.5 (7.2, 12–49)
Age first received help, years	30.7 (8.8, 17–54)	29.3 (8.4, 13–49)	30.4 (8.3, 17–54)	30.1 (8.5, 13–54)
Times in opiate treatment	2.9 (3.5, 0–20)	2.2 (3.1, 0–20)	1.8 (2.5, 0–10)	2.3 (3.1, 0–20)
Alcohol use				
AUDIT score (0–40)	12.2 (11.9, 0–36)	10.4 (11.5, 0–37)	7.5 (9.2, 0–37)	10.1 (11.1, 0–37)
AUDIT score <8 (non-harmful use)	31 (46%)	45 (58%)	44 (68%)	120 (57%)
AUDIT score 8–15 (problem use, medium)	15 (22%)	11 (14%)	10 (15%)	36 (17%)
AUDIT score 16–<20 (problem use, high)	4 (6%)	5 (6%)	4 (6%)	13 (6%)
AUDIT score ≥20 (possible dependency)	17 (25%)	17 (22%)	7 (11%)	41 (20%)
Drug use in previous 30 days				
Heroin	51 (76%)	72 (92%)	54 (83%)	177 (84%)
Crack	45 (67%)	44 (56%)	32 (49%)	121 (58%)
Cocaine	8 (12%)	9 (12%)	5 (8%)	22 (10%)
Bezodiazapines	16 (24%)	28 (36%)	14 (22%)	58 (28%)
Amphetamines	2 (3%)	4 (5%)	2 (3%)	8 (4%)
Cannabis	35 (52%)	30 (38%)	28 (43%)	93 (44%)

Data are mean (SD, range) or n (%). LA=local authority. HA=housing association. NFA=no fixed abode. VAS=visual analogue scale. SF-36=Short Form-36. AUDIT=alcohol use disorders identification test.

Table 1: Baseline characteristics

checked model assumptions by use of diagnostic plots. All analyses were done in Stata version 11.2.

The trial is registered, number ISRCTN72794493.

Role of the funding source

The sponsor of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

Between Feb 1, 2011, and Jan 31, 2012, we randomly allocated 12 services (clusters) to three treatment groups (figure 1). 210 (23%) of 914 patients screened for eligibility consented to enrolment (figure 1). Study participants were broadly representative of patients entering opioid substitution therapy in the UK,²⁷ in that they were mostly men (167 [80%] participants) and white (158 [75%] participants) with a mean age of 36.2 years (SD 8.2). The three study groups were well matched on key

sociodemographic and health variables and previous drug use and treatments received (table 1).

About half of the participants treated as usual attended their first vaccination appointment compared with about three-quarters of those receiving contingency management (table 2). At the second appointment, about a third of participants in the treatment as usual group attended compared with nearly two-thirds in the contingency management groups (table 2). At the third vaccination appointment, only a fifth of patients in the treatment as usual group attended compared with half of participants in the contingency management groups (table 2).

Figures 2 and 3 show the proportions of the expected attendees who did attend (ie, individuals offered each successive vaccination as opposed to the total enrolled population), showing the increased attrition in the treatment as usual group at all timepoints. The highest rate of attrition in all treatment groups occurred at the first vaccination and attrition in the control group was

higher than in both contingency management conditions at vaccinations 2 and 3 even in patients who attended vaccination 1 in the absence of reinforcement (figure 3).

Of participants in the contingency management groups who attended vaccinations, at least 80% did so on time and received clinically appropriate vaccinations at each of the three appointments (ie, achieved the target behaviour; table 2). By contrast, only 50–65% of the lower overall numbers of participants in the treatment as usual group who attended appointments did so on time (table 2).

Most attendances resulted in vaccination. 13 participants attended appointments but did not have a clinical need for (further) vaccination because they were identified as having immunity (three in the treatment-as-usual group, four in the fixed contingency management group, and six in the escalating contingency management group). All were regarded as completers in our outcome analyses. Four participants attended but refused vaccination (two in

	Vaccination 1 (day 0)*				Vaccination 2 (day 7)				Vaccination 3 (day 21)			
	Treatment as usual (n=67)	Fixed (n=78)	Escalating (n=65)	Total (n=210)	Treatment as usual (n=67)	Fixed (n=78)	Escalating (n=65)	Total (n=210)	Treatment as usual (n=67)	Fixed (n=78)	Escalating (n=65)	Total (n=210)
Attendance												
Enrolled and expected to attend	67 (100%)	78 (100%)	65 (100%)	210 (100%)	31 (46%)	58 (74%)	47 (72%)	136 (65%)	22 (33%)	46 (59%)	39 (60%)	107 (51%)
Attended	34 (51%)	60 (77%)	49 (75%)	143 (68%)	23 (34%)	50 (64%)	42 (65%)	115 (55%)	14 (21%)	37 (47%)	33 (51%)	84 (40%)
Did not attend	33 (49%)	18 (23%)	16 (25%)	67 (32%)	8 (12%)	8 (10%)	5 (8%)	21 (10%)	8 (12%)	9 (12%)	6 (9%)	23 (11%)
Compliance with appointment time												
Attended scheduled appointment on time†	21/34 (62%)	52/60 (87%)	45/49 (92%)	118/143 (83%)	15/23 (65%)	46/50 (92%)	38/42 (90%)	99/115 (86%)	7/14 (50%)	32/37 (86%)	32/33 (97%)	71/84 (85%)
Attended, but not scheduled appointment date or time‡	13/34 (38%)	8/60 (13%)	4/49 (8%)	25/143 (17%)	8/23 (35%)	4/50 (8%)	4/42 (10%)	16/115 (14%)	7/14 (50%)	5/37 (14%)	1/33 (3%)	13/84 (15%)
Compliance with vaccination												
Vaccinated	30/34 (88%)	56/60 (93%)	46/49 (94%)	132/143 (92%)	20/23 (87%)	45/50 (90%)	39/42 (93%)	104/115 (90%)	14/14 (100%)	37/37 (100%)	32/33 (97%)	83/84 (99%)
Not vaccinated (immunity established)	3/34 (9%)	1/60 (2%)	2/49 (4%)	6/143 (4%)	0/23 (0%)	3/50 (6%)	3/42 (7%)	6/115 (5%)	0/14 (0%)	0/37 (0%)	1/33 (3%)	1/84 (1%)
Not vaccinated (other valid clinical reason)	0/34 (0%)	1/60 (2%)	1/49 (2%)	2/143 (1%)	2/23 (9%)	2/50 (4%)	0/42 (0%)	4/115 (3%)
Not vaccinated (refused)	1/34 (3%)	2/60 (3%)	0/49 (0%)	3/143 (2%)	1/23 (4%)	0/50 (0%)	0/42 (0%)	1/115 (1%)
Achievement of target behaviours and reinforcement protocol fidelity												
Achieved target behaviour (on time and vaccination and immunity established)§	21/34 (62%)	49/60 (82%)	44/49 (90%)	113/143 (79%)	13/23 (57%)	44/50 (88%)	38/42 (90%)	95/115 (83%)	7/14 (50%)	32/37 (86%)	32/33 (97%)	71/84 (85%)
Did not achieve target behaviour (non-compliant with appointment schedule)¶	13/34 (38%)	11/60 (18%)	6/49 (12%)	30/143 (21%)	10/23 (43%)	6/50 (12%)	4/42 (10%)	20/115 (17%)	7/14 (50%)	5/37 (14%)	1/33 (3%)	13/84 (15%)

Data are n (%) or n/n (%). *For vaccination 1 the base date (day 0) was defined as the first appointment date offered to the participant unless rescheduled by the clinic or the participant (but only in advance and with the agreement of the nurse); under these circumstances, the rescheduled appointment was regarded as day 0. Thus, any vaccinations given after day 0 will have been given because the patient did not attend the first appointment offered and then received the vaccination at a later date. †Participants who attended the vaccination appointment on the scheduled date and time, including those who attended at a date and time rescheduled by the client in advance and with the agreement of the clinic. ‡Participants who attended on the appointment date but outside the appointed timeframe, or on a rescheduled date made after a previous non-attendance of one or more appointments. §Participants who achieved target behaviour (ie, attended the appointment on time and either received the vaccination or were not vaccinated because they had established immunity). ¶Participants non-compliant with appointment schedule required to receive vaccination describes participants who attended but were not on-time, refused vaccination, or were required to attend on a subsequent day (eg, for clinical reasons) and did not do so.

Table 2: Participant flow through the vaccination schedule

the treatment as usual group, two in the fixed contingency management group).

Incentives were given in error when the target behaviour was not achieved in ten (4%) of 271 appointments in the contingency management groups. These errors mostly occurred when participants received a vaccination but had not attended on time. However, adherence, expressed as a mean percentage of the total adherence score was modest at 53%. Of the 40 audio recordings assessed, 13 (33%) were rated as good adherence and 13 (33%) were rated as poor adherence. Poor adherence scores were mainly due to failure to explain the schedule, offer sufficient praise, or check that participants understood the schedule. Tapes were independently rated by two reviewers and good inter-rater reliability was achieved (intraclass correlation 0.873, 95% CI 0.773–0.930).

Table 3 shows the proportion of participants in each group who completed the vaccination schedule in 28 days, the number of participants classified as completers who were identified as immune and received up to three vaccinations (three in the treatment-as-usual group, four in the fixed contingency management group, and five in the escalating contingency management group), and the results of the GEE modelling.

In the primary outcome analysis, we noted significantly increased completion rates for HBV vaccination in both contingency management groups compared with treatment as usual (table 3). Participants in both contingency management groups were more likely to complete the vaccination schedule within 28 days than were those in the treatment as usual condition (table 3). The intraclass correlation coefficient for the site clustering was estimated at 0.097.

Figure 2 shows the predictive probability from the fully adjusted GEE modelling of completion of vaccination within each group and confirms that the differences in vaccination completion rates were significant. Unadjusted χ^2 statistics show differences in the completion rates between the fixed contingency management group and the treatment as usual group (35 of 78 in the fixed group vs six of 67 in the treatment as usual group; χ^2 22.9, $p < 0.0001$) and escalating contingency management and treatment as usual (32 of 65 participants in the escalating group vs six of 67 participants in the treatment as usual group; χ^2 26.1, $p < 0.0001$).

Compared with treatment as usual, the NNT was 2.78 (2.05–4.36) for fixed contingency management and 2.48 (95% CI 1.84–3.80) for escalating contingency management.

Our first sensitivity analyses assessed whether contingency management was associated with increased full compliance with the vaccination schedule, through comparison of the proportions of participants who completed their vaccinations with the strict definition of completer that required on-time attendance at all relevant vaccination appointments. This measure might

thus be regarded as a proxy for improved clinic efficiency. We noted substantially improved rates of completion for both contingency management groups versus treatment as usual (table 3, figure 2)

Our second sensitivity analysis assessed whether the benefit of contingency management remained if a longer follow-up period was used, through comparison of the proportions of participants who completed their vaccinations with a relaxed definition of completer that required participants to complete all relevant vaccination appointments within 3 months of recruitment. In this analysis, completion rates were higher in all treatment groups, with the proportion of completers in the treatment as usual group increasing to 25% (17 of 67 participants). However, completion rates

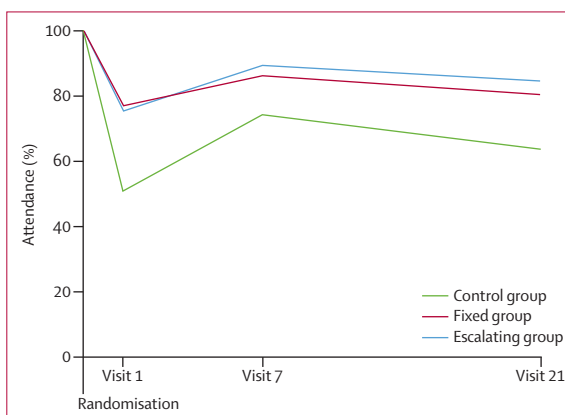


Figure 2: Attrition of study participants over the course of vaccination schedule (attendance/expected attendance)

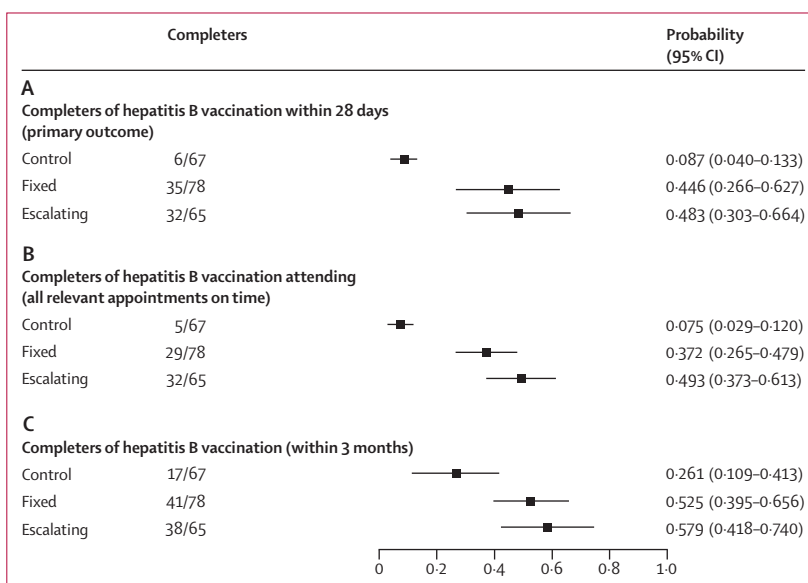


Figure 3: Predictive margins for the primary and sensitivity analyses (A) Completers of hepatitis B vaccination within 28 days (primary outcome). (B) Completers of hepatitis B vaccination attending all relevant appointments on time. (C) Completers of hepatitis B vaccination within 3 months. Predictive margins (95% CIs) are derived from fully adjusted generalised estimating equation model, controlling for the blood test status and allowing for site at the cluster level.

	Treatment as usual (n=67)	Fixed value contingency management (n=78)	Escalating value contingency management (n=65)
Completers within 28 days (primary endpoint)			
Completers (all)	6 (9%)	35 (45%)	32 (49%)
Completed 1 of 1	3 (4%)	1 (1%)	2 (3%)
Completed 2 of 2	0	3 (4%)	2 (3%)
Completed 3 of 3	3 (4%)	31 (40%)	28 (43%)*
Odds ratio†	..	12.13 (7.37, 3.68–39.92; p<0.0001)	13.95 (8.53, 4.21–46.25; p<0.0001)
Completers attending all appointments on time (sensitivity analysis)			
Completers (all)	5 (7%)	29 (37%)	32 (49%)
Completed 1 of 1	3 (4%)	1 (1%)	2 (3%)
Completed 2 of 2	0	2 (3%)	2 (3%)
Completed 3 of 3	2 (3%)	26 (33%)	28 (43%)*
Odds ratio†	..	9.89 (4.80, 3.82–25.59; p<0.0001)	16.68 (8.61, 6.06–45.88; p<0.0001)
Completers within 3 months (sensitivity analysis)			
Completers (all)	17 (25%)	41 (52%)	38 (58%)
Completed 1 of 1	3 (4%)	1 (1%)	2 (3%)
Completed 2 of 2	0	3 (4%)	3 (5%)
Completed 3 of 3	14 (21%)	37 (47%)	33 (51%)*
Odds ratio†	..	3.38 (1.64, 1.30–8.76; p=0.012)	4.18 (2.32, 1.41–12.40; p=0.010)
Time to complete vaccination, days			
First vaccination after day 0‡	6.2 (14.2)	1.9 (5.1)	0.6 (3.1)
Second vaccination after day 0§	25.3 (25.5)	11.0 (9.1)	9.5 (7.0)
Third vaccination after day 0§	50.5 (24.5)	24.3 (7.8)	23.2 (5.7)

Data are n (%), odds ratio (SE, 95% CI; p value), or mean (SD). *Includes one participant whose immunity was established after receipt of the second vaccination; the participant attended vaccination 3 but was informed of their immunity status and not given a third vaccination. †From the fully adjusted generalised estimating equation model, controlling for the blood test status and allowing for site at the cluster level. ‡For vaccination 1 the base date (day 0) was defined as the first appointment date offered to the participant unless rescheduled by the clinic or the participant (but only in advance and with the agreement of the nurse); under these circumstances, the rescheduled appointment was regarded as day 0. Thus, any vaccinations given after day 0 will have been given because the patient did not attend the first appointment offered and then receiving the vaccination at a later date. §The base time was used for the calculation of the time to vaccination 2 and 3.

Table 3: Completers of hepatitis B vaccination schedule and outcome analysis

remained highest in the contingency management groups (table 3).

Three participants died in the treatment as usual group (one cardiac arrest, one deep vein thrombosis, and one unknown cause in a patient not administered vaccine). Other serious adverse events were one case of pneumonia in the treatment as usual group and one psychiatric admission in a participant in the fixed contingency management group. No other serious adverse events were reported, and none was regarded as related to treatment. We noted no association between serious adverse events and trial condition (Fisher’s exact test p=0.50).

Discussion

NICE has identified contingency management as a behavioural intervention with the potential to increase adherence to physical health interventions amongst drug users.^{7,8} In our study of HBV vaccination in routine clinical

practice, we noted improved rates of completion of vaccination and adherence to appointment schedules when the offer of vaccination was combined with contingency management with financial incentives (panel 2).

That incentives increase adherence is unremarkable, but the size of increase we noted was striking. The findings of our health economic analysis are ongoing and will be presented elsewhere but, notably, increased vaccination was associated with relatively modest levels of financial reinforcement. Our primary outcome measure was completion of the 21 day vaccination schedule within 28 days. We noted a significant advantage with each of the contingency management reinforcement conditions (49% and 45%) compared with treatment as usual (9%). In addition to the increased rate of completion, participants receiving contingency management mostly attend appointments on time, which offers providers an additional advantage in terms of efficient use of resources.

In our primary analysis, the completion rate with treatment as usual was very low and merits comment. Ideally, we would be able to compare our findings with data from routine practice. However, no information is available at present about vaccination completion rates as a proportion of patients offered opioid substitution therapy or compliance with vaccination schedules. The completion rate in our treatment as usual group seems substantially worse than that recorded in injecting drug users in other settings (notably prison vaccination programmes),¹⁷ but comparison with data from such settings needs to be made with caution. The completion rate in our sensitivity analysis, which included vaccination up to 3 months, was substantially higher than it was in the primary analysis (25% vs 9%) and was close to the completion rates noted by Seal and colleagues (23%).⁹ This analysis probably provides a better comparison with routine completion rates. Nevertheless, even with this 3 month timeframe, the benefit of contingency management over treatment as usual remained substantial, with completion rates exceeding 50% in both contingency management groups.

Our study was not powered to examine differences between the two contingency management conditions but the gains achieved by each of the two schedules were much the same (odds ratio 12.1 and NNT of 2.78 for fixed contingency management and odds ratio 13.9 for escalating contingency management and NNT of 2.48). Although clinician adherence to some aspects of the intervention protocol was modest (mainly failure to explain the schedule, offer sufficient praise, or check understanding of the participants), the incentive was given correctly in 261 (96%) of 271 appointments. One interpretation of these findings is that these poorly delivered aspects of the protocol might be less powerful influences on outcome than the tangible financial reinforcement which was invariably delivered appropriately. We are also mindful that, despite the high

Panel 2: Research in context**Systematic review**

Evidence increasingly supports the effectiveness of contingency management for improvement of outcomes of drug users receiving substance misuse treatment. NICE^{7,8} identifies that contingency management can directly target the desired behaviour change (eg, drug abstinence) or can work synergistically by targeting intermediate behaviours (eg, attendance or medication adherence): two major meta-analyses report effectiveness of contingency management in reducing drug use.^{6,28}

Use of contingency management for time-limited interventions to produce irreversible health benefits (eg, hepatitis B virus [HBV] vaccination) was mooted by NICE^{7,8} but has received little attention in contingency management research; no meta-analysis has been published. Likewise for attention to physical comorbidities, apart from studies of contingency management to reinforce attendance for tuberculosis testing,²⁹ adherence to tuberculosis medication,²⁹⁻³¹ and to antiretroviral treatment for HIV.³²

In addition to small observational studies^{33,34} reporting increased uptake and completion of HBV vaccination associated with provision of financial incentives to injecting drug users, there have been three randomised controlled trials examining contingency management targeted specifically at HBV vaccinations. One trial,⁹ despite modest sample size (n=96), found contingency management (monthly monetary incentives) was significantly more effective than an outreach programme (weekly contact with outreach worker) in achieving completion of HBV vaccination within 6 months (69% vs 23%).⁹ A second trial¹⁰ found contingency management (prize incentives) more successful than no contingency management with non-significantly increased attendance of weekly sessions (82% vs 64%), increased compliance with all injections (77% vs 46%) and significantly more injections received on the originally scheduled day (74% vs 51%).¹⁰ A third randomised controlled trial,³⁵ from Australia, found monetary incentives (vouchers) more effective than no contingency management for completion of three-dose HBV vaccination (days 0, 7, 21) by injecting drug users. Monetary incentives not only improved compliance with HBV vaccination but also frequently achieved this within specified appointment times.³⁵

Interpretation

The findings from our properly powered trial accord with previous studies, providing compelling evidence that contingency management significantly improves completion of the three-injection vaccination schedule, so that approximately half of patients complete vaccination as scheduled. Further work is now required to refine the contingency management method to improve further the capture and completion of these vaccination schedules.

odds ratios, only about half the participants completed the vaccination schedule in the contingency management groups. Elsewhere, we will present the results of secondary analyses in which clinician adherence, treatment fidelity, and competence to behavioural principles are included as predictors of outcome.

Our findings suggests that contingency management for HBV vaccination is an effective and robust intervention—irrespective of schedule—despite variation in staff adherence to some aspects of the reinforcement protocol. Three main conclusions can be drawn from our findings.

First, we identified a powerful beneficial effect of contingency management in relation to a time-limited physical health intervention, which nevertheless has enduring benefit.³⁶ Our findings were obtained in real-world clinical circumstances, and therefore support the conclusions of NICE^{7,8} that this adjunctive technique should be routinely applied to increase the individual and public benefit of vaccination programmes in drug-treatment settings. The low NNT and high odds ratios should attract the close attention of public health practitioners and clinicians working in the field. These findings might also have relevance to other areas of clinical practice in which clinical and public health benefit could be achieved by incentivised improvement of treatment adherence in the short-term (eg, early antenatal care or tuberculosis testing).

Second, although differences in attrition at first and subsequent vaccinations might attract some further debate and analysis, attrition was highest in the control arm at each vaccination. Our interpretation of these data is that (modest) reinforcement at each vaccination is probably necessary and prudent to achieve the clinically significant health gains that are dependent on compliance with the full vaccination schedule. We would caution against too much further research focus on the precise schedule and instead we recommend concentrating energies on implementation.

Third, a strong case now exists for further rigorous assessment of contingency management in the UK for other areas of health-care provision. Investigators working in other clinical settings in which the patient and public health benefit of current treatments would be enhanced by measures that improve compliance could benefit from our findings. Within the specialty of substance misuse, attention should now shift to more challenging areas of behaviour change (eg, reduction in illicit drug use),^{7,8} in which long-term robustness of the change is necessary for any health benefit to be maintained.

Contributors

JS, TW and SP originally conceived the trial and secured research grant support. All authors made substantial contributions to the conception and design of the study, acquisition, or analysis of data, and writing and revision of the report. All authors were involved in interpretation of data and critical revision of the manuscript on behalf of the Contingency Management Programme team. JS was the principal investigator and guarantor of the study. TW was principal investigator

and (with NM [coordinator and trial manager] and SP [principal investigator]) responsible for day-to-day management of the trial, and co-led (with NM) writing of the report and coordination of contributions from coauthors. VC, NL, and DP were trial researchers, who contributed to study design, acquired data, interpreted findings, and contributed to the writing and revision of the report. JH was the trial statistician and did all statistical analysis, wrote the description of the statistical analysis and (in consultation with coauthors) produced the figures and tables. LM, SP, and FR was responsible for the training and supervision of clinicians and the analysis of adherence to the clinical protocol. OBJ, JD, AG, and EF were site principal investigators. Made substantial contributions to study design, acquisition of data, the interpretation of findings and contributions to the drafting and critical revision of the manuscript.

Contingency Management Programme team

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Declaration of interests

JS and SP have contributed to UK guidelines on the potential role of contingency management in the management of opioid addiction (NICE, 2007; convened by SP, chaired by JS). SP receives funding from NICE for the production of clinical guidelines, and JS has chaired the broader-scope pan-UK working group preparing the 2007 Orange Guidelines for the UK Departments of Health, providing guidance on management and treatment of drug dependence and misuse, including guidance on possible inclusion of contingency management. JS (and his institution) have received support and funding from the Department of Health (England) and National Treatment Agency (England), and JS (and his institution) have provided funded consultancy advice on possible new addiction treatments, products, and formulations to various pharmaceutical companies. All other authors declare that they have no competing interests.

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