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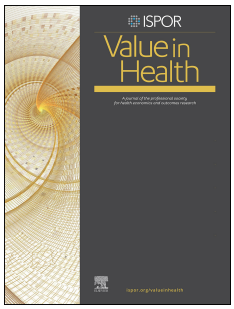

The cost-effectiveness of financial incentives to achieve heroin abstinence in individuals with heroin use disorder starting new treatment episodes: A cluster randomised controlled trial-based economic evaluation

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Title: The cost-effectiveness of financial incentives to achieve heroin abstinence in individuals with heroin use disorder starting new treatment episodes: A cluster randomised trial-based economic evaluation

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Financial incentives used as contingency management to reward heroin abstinence in individuals with heroin use disorder starting opioid agonist treatment was not cost effective.

1. A major barrier to implementing contingency management (CM) is the lack of evidence for cost-effectiveness and evidence that CM is value for money.

2. This report analyses real world evidence on the costs, outcomes and cost effectiveness from data collected alongside a large, rigorous and pragmatic trial of CM.

3. The implications for the treatment of heroin use disorder in the UK is that incentivising individuals to stop using heroin is not a cost-effective use of limited public funds. However, incentivising individuals with heroin use disorders with modest or small incentives to engage with heroin treatment services does work, but only while patients are being rewarded with financial incentives to attend.

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The cost-effectiveness of financial incentives to achieve heroin abstinence in individuals with heroin use disorder starting new treatment episodes: A cluster randomised controlled trial-based economic evaluation

Abstract

Objectives: Cost-effectiveness analysis of two 12-week contingency management (CM) schedules targeting heroin-abstinence or attendance at weekly keyworker appointments for opioid agonist treatment (OAT), compared to treatment as usual (TAU).

Methods: Cost-effectiveness analysis was conducted alongside a cluster randomised trial of 552 patients from 34 clusters (drug treatment clinics) randomly allocated 1:1:1 to OAT plus weekly keyworker appointments with either: i) CM targeted at heroin-abstinence (CM Abstinence); ii) CM targeted at on-time attendance at weekly appointments (CM Attendance); or, iii) no CM (TAU). The primary cost-effectiveness analysis at 24 weeks post-randomisation took a societal cost perspective with effects measured in heroin-negative urine samples.

Results: At 24-weeks, mean differences in weekly heroin-negative urine results compared with TAU were 0.252 (95%CI -0.397 to 0.901) for CM Abstinence and 0.089 (95%CI -0.223 to 0.402) for CM Attendance. Mean differences in costs were £2562 (95%CI £32 to £5092) for CM Abstinence and £317 (95%CI -£882 to £1518) for CM Attendance. Incremental cost-effectiveness ratios were £10,167 per additional heroin-free urine for CM Abstinence and £3,562 for CM Attendance with low probabilities of cost-effectiveness of 3.5% and 36%, respectively. Results were sensitive to timing of follow-up for CM Attendance, which dominated TAU (better outcomes, lower costs) at 12-weeks, with an 88.4% probability of being cost-effective. Probability of cost-effectiveness remained low for CM Abstinence (8.6%).

Conclusions: Financial incentives targeted toward heroin-abstinence and treatment-attendance were not cost-effective over the 24-week follow-up. However, CM Attendance was cost-effective over the treatment period (12-weeks), when participants were receiving keyworker appointments and incentives.

Highlights: a) what is already known about the topic? There is evidence that CM may be an effective strategy in heroin treatment, however, there is limited evidence of cost-effectiveness; b) what does the paper add to existing knowledge? CM is not a cost-effective strategy for promoting heroin abstinence and treatment engagement in England; and c) what insights does the research provide for informing health care related decision making? Further research into the duration and the target of incentives is needed before CM could be considered value for money in English drug treatment services.

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Introduction

Heroin use is a serious and persistent problem in the United Kingdom and throughout the World. Heroin use in England in 2020 accounted for nearly half of all drug related deaths. Deaths from heroin overdose doubled between 2012 and 2020 with an increase recorded in every year. (1) The economic burden of heroin use is considerable with multisectoral impacts on the health and well-being of heroin users, their families, their communities, health services and the criminal justice system. (2) In England and Wales, the social and economic cost of Class A drug use was estimated at £15.4 billion (2003/2004), with 99% of this attributed to heroin and crack cocaine use. (3)

The economic consequences of heroin use include drug-related crime, drug-related deaths, and health and social care service use. Drug-related crime accounted for most of the social and economic costs of heroin use in England and Wales in 2003/2004 (90% or £13.9 billion). Most drug-related crime associated with heroin use was acquisitive or property-related crimes committed to fund drug use. These included fraud (32%, £4.8 billion), burglary (26%, £4.1 billion), robbery (16%, £2.5 billion) and shoplifting (12%, £1.9 billion). (3) Drug-related deaths in individuals who use heroin or crack cocaine was the second largest cost category (6%, £923 million) consisting of health care costs, lost productivity and the human costs from the years of life lost. (4) Health and social care service use made up 3.5% (£557 million), comprising inpatient care, mental health services, primary care, infectious diseases and social care.

Opioid agonist treatment (OAT) is recognised in the National Institute for Health and Care Excellence (NICE) guidelines as effective and cost-effective in the treatment of heroin use disorder. (5, 6) The effectiveness of pharmacological approaches to heroin dependence is, however, constrained by high attrition associated with relapse into illicit drug use. Contingency management (CM) is a behavioural intervention which uses incentives to promote positive behaviour change such as drug abstinence or treatment attendance. NICE guidelines have recommended CM as an adjunct to OAT (7) but, despite evidence of effectiveness, CM has not been adopted into practice in England.

A major barrier to implementing a potentially promising intervention has been the lack of evidence for cost-effectiveness and evidence that CM is value for money. Our systematic review of economic evaluations of CM programs identified nine studies that reported both costs and outcomes. (8) These were all conducted by specialists in CM in US treatment settings and were not generalisable to routine treatment services in the UK. This paper evaluates the cost-effectiveness of two 12-week CM schedules that used praise and financial vouchers to incentivise heroin users starting OAT for on-time attendance to weekly keyworker appointments and opiate abstinence or on-time attendance at weekly appointments only, compared to weekly keyworker appointments without CM.

Methods

This study was a within-trial cost-effectiveness analysis conducted alongside a cluster randomised controlled trial (RCT).

Participants, setting and randomisation

The participants were individuals with heroin use disorder starting OAT at 34 drug treatment clinics in England provided either by the National Health Service (NHS) or by non-government organisations and social enterprises (referred hereon in as non-NHS treatment clinics). All clinics provided OAT (both buprenorphine and methadone) and weekly specialist drug and alcohol keyworker

appointments. Clusters were assigned to treatments using random permuted blocks within type of service provider strata (NHS or non-NHS) using a block length of 3 in a 1:1:1 allocation ratio.

Interventions

Each cluster (treatment clinic) provided usual treatment (TAU), consisting of OAT plus twelve weekly appointments with a specialist drug and alcohol keyworker. Each cluster was randomly assigned to additionally provide either: i) positive reinforcement in the form of a £10 voucher given to participants at each weekly appointment for both on-time attendance and abstinence from opiates using an instant cup test (CM Abstinence group); ii) positive reinforcement in the form of a £10 voucher given at each weekly appointment for on-time attendance only (CM Attendance group); or no CM. The main clinical results (9) and design details (10) are reported elsewhere.

Perspective and time horizon

The economic analysis was conducted from a societal perspective including the health and social care perspective plus the impact on the criminal justice sector and on productivity (time off work due to illness), as heroin dependence significantly impacts many aspects of individuals' lives beyond health. (11) Since NHS providers in England compete with non-NHS providers to secure contracts to provide local drug and alcohol services, the health and social care perspective was not limited to statutory provision by the NHS and Local Authorities, but additionally included non-statutory services, such as charitable and private sector provision. NICE has acknowledged that reductions in crime as a result of drug treatment programmes are an appropriate extension to the recommended NHS personal social services perspective. (12) Costs and effects were estimated over a 24-week follow-up period, with data collected at baseline, 12 and 24-weeks post-randomisation.

Outcomes

The primary economic analysis was based on the primary clinical outcome of heroin-abstinence confirmed by laboratory tested urine drug screens expressed as the number of opiate-negative urines out of four in the 4 weeks prior to each follow-up period. This differed from the primary clinical analysis which used log odds of a heroin-free urine sample because differences in log odds are problematic to value in monetary terms. A heroin-negative weekly urine result suggests up to one week of heroin abstinence and therefore one week of heroin related crime avoided which, from a societal perspective, could be valued up to £767 based on the average weekly cost of crimes committed by individuals using heroin or crack use in England and Wales in 2003/2004. (3,8) A secondary cost-utility analysis was undertaken where outcomes were expressed as quality-adjusted life-years (QALYs), as preferred by NICE. (12) QALYs were calculated using the EQ-5D-3L (13) measure of health-related quality of life, measured at baseline, 12 and 24-week follow-up. The EQ-5D-3L has been found to be valid in the evaluation of chronic, heroin-dependent populations. (14) The health states generated by the EQ-5D-3L were given a utility score using responses from a representative sample of adults in the UK. (15) From these, QALYs were calculated using the area under the curve approach as defined by the utility values at baseline and each follow-up. It was assumed that changes in utility score over time followed a linear path. (16) QALYs were valued at the NICE willingness-to-pay threshold of £20,000 to £30,000 per QALY.

Resources

Throughout treatment, clinical staff recorded details of attendance at weekly appointments, voucher incentives and urine drug screens for each study participant and these were used as the basis for the calculation of the total cost of the intervention. They also asked participants about other drug clinic contacts for the post-treatment period between the 12 and 24-week follow-up assessments. Data on

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participant use of all other health and social care services were collected using the Adult Service Use Schedule (AD-SUS), previously modified for application to substance misusing populations. (11) The AD-SUS was also used to collect information about crimes committed by and against (victims of crime) participants. Information about time off work due to illness (absenteeism) was collected by researchers alongside the AD-SUS using the productivity questions of the World Health Organisation Work and Performance Questionnaire. (17) The AD-SUS was completed in interview with a research assessor at baseline and at the 12 and 24-week follow-up assessments. At baseline, information covered the previous twelve weeks. At follow-up, information covered the period since previous interview. Resource use by study participants was reported as means (standard deviation) by group and as a percentage of the group who had at least one contact. Differences in the use of services between randomised groups were reported descriptively but were not compared statistically to avoid problems associated with multiple testing and because the focus of the analysis was on cost and cost-effectiveness, rather than the resource use components that contribute to costs.

Costs

A unit cost was applied to each resource used by participants to calculate the total cost per participant (Table S1 in the online supplement). All unit costs were for the financial year 2014/15 (the last full year data were collected), uprated where necessary using the Hospital and Community Health Services Index. (18) Medication costs were calculated using daily dose information, the cost of the generic drug and controlled drug dispensing costs as per the NHS Business Services Authority. (19) Nationally applicable unit costs were applied to hospital services, NHS primary care services and social workers and support workers. (18) Absenteeism due to drug use was valued using the human capital approach based on the national gross average wage. (20)

The approach developed by the Personal Social Services Research Unit (PSSRU) at the University of Kent (21) was used for the calculation of the unit cost of keyworker sessions (Table S2 in the online supplement). At each site, employer's national insurance, superannuation contributions and overheads were added to the average clinical staff salary. A ratio of direct to indirect time of 1:0.47 for the time clinical staff spend conducting face-to-face appointments (direct) and the indirect time they spend on other activities, like receiving or providing CM related supervision, was estimated by our group in a previous study with a similar population. (22)

Costs of crime

The costs of crime and victim costs were valued using Home Office estimates which included costs in anticipation of crime (security, insurance), consequences of crime (victim costs, health services, property losses) and response to crime (criminal justice costs) (Table S3 in the online supplement). (23,24) Costs for crimes without direct victims, such as drug offences and soliciting, were not available and have been "zero-rated".

Analyses

The primary economic analysis was composed of two separate comparisons: 1) CM Abstinence + TAU versus TAU alone; and 2) CM Attendance + TAU versus TAU alone at the 24-week follow-up point. All analyses were based on pre-specified health economic and statistical analysis plans. (8) Cost-effectiveness was reported in terms of cost per additional heroin-negative urine sample collected each week in the 4 weeks preceding each follow up interview. The secondary cost-utility analysis was reported in terms of cost per QALY calculated from the EQ-5D-3L.

Costs and outcomes were compared between groups using generalised linear modelling (gamma family, identity link) as recommended to account for the highly skewed nature of cost data. (25) All analyses were adjusted for baseline costs or outcomes, as relevant, the stratification variable (NHS/Non-NHS), study site (as an indicator variable to account for clustering) and two baseline variables (social functioning, supported accommodation) identified as predictors of missingness at the 24-week follow-up reported in Table S8 in the online supplement.

Initially, incremental cost-effectiveness ratios (ICERs) were calculated, which are the difference in mean cost between an intervention and a control group divided by the difference in mean effects. (20) Missing cost and outcome data were imputed by multiple imputation using chained equations (MICE) based on the stratification variable (NHS/non-NHS), baseline total costs, baseline utility and study site (as an indicator variable to account for clustering). (26, 27) The number of multiple imputation datasets (m) was set to be equal to the fraction of non-responders (40%; m = 40) at the 24-week follow-up, as recommended by White and colleagues. (26) We set the number of bootstrap replications to 1000 for each of the 40 multiple imputation datasets (40 000 bootstrap replications). (28)

Repeat re-sampling (bootstrapping) from the cost and outcome data was used to generate a distribution of mean costs and effects for heroin-negative urine results and QALYs. (29) These distributions were used to calculate the probability that each of the treatments is the optimal choice, subject to a range of possible maximum values (the ceiling ratio, λ) that a decision-maker might be willing to pay for a unit improvement in outcome. To explore the uncertainty that exists around estimates of mean costs and effects and uncertainty regarding the maximum value of λ, cost-effectiveness acceptability curves (CEACs) are presented by plotting these probabilities for a range of possible values of the ceiling ratio (λ). (30) CEACs show the probability that one intervention is cost-effective compared to a comparator for different values of λ.

Sensitivity analyses

Sensitivity analyses were carried out to test the impact of varying methods and assumptions on the relative cost-effectiveness of the two CM schedules compared with TAU alone. There were two planned sensitivity analyses: i) a narrower economic perspective limiting costs to NHS/Personal Social Services (PSS) costs as recommended by NICE (31) where PSS refers to a range of public health and social care services provided or commissioned by local authorities in England to vulnerable people including drug and alcohol prevention and treatment; and ii) a complete case analysis for comparison with the results that used multiple imputation for missing data. A 12-week time horizon was added as a third sensitivity analysis after the analytical time horizon of the primary clinical analysis was changed from 24-weeks to 12-weeks. (9) A fourth sensitivity analysis was added after data analysis began, following detection of a potential bias that suggested that a number of clinics with large homeless caseloads had been randomised by chance into the CM Abstinence group. In order to address this potential source of bias, a sensitivity analysis was carried out which excluded the cost of accommodation.

Results

Participants

Participants (n=552) were enrolled from 34 clusters (drug treatment clinics) in England between November 2012 and October 2015. Thirty-four drug treatment clinics (clusters) were randomised to

the three treatments. The majority of these clinics were NHS (62%) and just under one half were within London (47%). Across 34 clusters, 789 patients were screened for eligibility, of whom 552 (70%) were consented, enrolled and allocated by cluster to receive CM Attendance (n=205), CM Abstinence (n=174) or TAU (n=173). Study participants were broadly representative of patients entering OAT in England. They were mostly male (n=404; 73%), white (n=435; 79%) with a mean age of 38.2 years [SD 8.8]. Over half had been in prison (n=291; 53%). A full description of the sample is available in the main clinical paper. (7) At 24 weeks follow-up, full service use data for the entire follow-up was available for 124 participants in the CM Abstinence group (60%), 109 in the CM Attendance group (63%), and 89 in TAU (51%) which was 58% of the total number randomised.

Resource use

Resource use over the 24-week follow-up period is reported in Table S4 in the online supplement. Patients in the CM Attendance group attended more weekly appointments than the other groups (mean 7.9 appointments per participant versus 6.6 in the CM Abstinence group and 5.2 in TAU), although the proportions attending at least one were similar (range 88.4% to 91.2%). Patients in the CM Attendance group earned more vouchers than the CM Abstinence group (mean £69 versus £42). The use of secondary and primary health care and social care services was broadly similar across the three randomised groups over 24-week follow-up. However, the CM Abstinence group spent substantially more time in supported accommodation than the other groups (mean 18.9 weeks versus 2.4 CM Attendance and 6.7 TAU) and reported more criminal offences (mean 12.2 offences versus 4.6 CM Attendance and 7.1 TAU). There were no differences in absence from work with around 16-17% of participants reporting days off work due to illness or drug use over the 24-week follow-up period. Similar proportions of all groups received similar doses of either methadone or buprenorphine.

Costs

Table S5 in the online supplement reports the disaggregated, complete case costs per participant from the primary societal perspective (NHS/PSS costs, productivity losses and criminal justice costs) and the NHS/PSS perspective (limited to NHS/PSS costs) at the 24-week follow-up period. Table 1 reports mean costs by group and imputed and adjusted cost differences from the societal perspective (primary economic perspective) and the NHS/PSS perspective (pre-specified sensitivity analysis), at both the 12-week follow-up (secondary economic follow-up point) and the 24-week follow-up (primary economic follow-up point). Imputed and adjusted costs were significantly higher in the CM Abstinence group compared to TAU (mean difference of £2562, SE £1188, 95% CI £32 to £5092, p=0.047) characterised by higher supported accommodation costs and higher costs of crime (Table S5 in the online supplement).

Table 1 about here

Outcomes

Outcome measures for the primary economic analysis (mean number of weekly heroin negative urine results over 4 weeks prior to the 24-week follow-up) and the secondary economic analysis (EQ-5D-3L health state utilities) are presented in Table S6 in the online supplement based on the complete data. Table 2 reports mean outcomes imputed and adjusted outcome differences at the 12- and 24-week follow-up. There were no statistically significant differences in the primary or secondary economic outcome at the 24-week follow-up, although CM Attendance had statistically

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significantly more heroin-negative urine samples at 9-12 weeks than TAU (adjusted and imputed mean difference 0.203, SE 0.095 95% CI 0.002 to 0.405, p=0.048).

Table 2 about here

Cost-effectiveness

The cost-effectiveness results, taking the societal perspective (the primary perspective) and based on imputed data, are summarised in Table 3. In terms of both the primary clinical outcome (heroin-negative urine samples) and the secondary outcome (QALYs), societal costs were higher and outcomes better in the CM Abstinence group and the CM Attendance group compared to TAU at the 24-week follow-up. These relationships are illustrated in the cost-effectiveness planes reproduced in the online supplement (Figures S1 to S4).

Table 3 about here

The CEACs for each CM intervention compared to TAU based on the primary economic outcome (heroin-negative weekly urine samples) appear in Figure 1. The CEAC for CM Abstinence compared to TAU in Figure 1 shows that the probability of CM Abstinence being cost-effective compared to TAU ranged from 1% to 3.5% as the societal willingness-to-pay for a weekly heroin free urine sample increased from £0 to £767 as described under Methods. Using the same societal willingness-to-pay thresholds for a heroin-free urine, the CEAC for CM Attendance versus TAU showed that CM Attendance had a 32% to 36% probability of being cost effective.

Figure 1 about here

The CEACs for each CM intervention compared to TAU based on the secondary economic outcome (QALYs) appear in Figure 2. The results were similar to the primary economic analysis. The CEAC for CM Abstinence versus TAU showed only a 4 to 6% probability of cost-effectiveness using the NICE willingness-to-pay thresholds of £20,000 to £30,000 per QALY with an ICER of £167,358. Using the same NICE threshold, the CEAC for CM Attendance versus TAU showed a 39.5% to 43% probability that CM Attendance was cost-effective with an ICER of £51,400.

Figure 2 about here

Sensitivity analysis

Table S7 in the online supplement summarises the results when the parameters and structure of the primary (or base case) economic analysis were varied in sensitivity analyses. The cost per additional heroin-negative urine result for the CM Abstinence arm remained well above the willingness-to-pay threshold of £767 in all scenarios. In two scenarios, the CM Attendance arm dominated TAU (societal perspective at 12-week follow-up and NHS/PSS perspective at 24-week follow-up), achieving more heroin-negative urine samples at a lower cost. The scatter plots of bootstrapped differences in imputed heroin-negative urine samples and costs at 12-week follow-up for both CM groups compared with TAU are presented in the online supplement (Figures S5 & S6) along with the associated CEACs (Figure S7). The CEACs show that the probabilities of cost-effectiveness of CM Abstinence or CM Attendance compared to TAU were 8.6% and 88.4%, respectively, at the societal willingness-to-pay for a weekly heroin free urine sample of £767 described in the Methods section.

Discussion

Our clinical report (9) found that CM in addition to TAU (OAT plus 12 weekly specialist drug and alcohol keyworker sessions) only achieved a statistically significant difference in heroin use compared to TAU alone in the CM Attendance group at the 12-week follow-up, which was not sustained at the 24-week follow-up after incentives were withdrawn. CM targeted at attendance and abstinence (CM Abstinence) failed to achieve statistically significant reductions in heroin use compared to TAU at either follow-up.

The results of the economic analysis conducted alongside the clinical trial were consistent with the clinical findings. CM targeted at abstinence from heroin confirmed by urinalysis and attendance at weekly appointments (CM Abstinence) was not cost-effective compared with TAU at either the 12-week or 24-week follow-up. CM targeted at attendance to weekly appointments only (CM Attendance) had a higher probability of being cost-effective compared to TAU at the 12-week follow-up, when attendance was incentivised by modest, fixed financial incentives, but there was no evidence to suggest that CM Attendance was cost-effective compared to TAU at the 24-week follow-up. The results of the cost-utility analysis using QALYs were broadly similar.

The relative cost-effectiveness of CM Attendance compared to TAU was sensitive to the follow-up time period and the chosen perspective, with CM Attendance dominating TAU at the 12-week follow-up point taking the societal perspective (primary perspective) and at the 24-week follow-up point taking the NHS/PSS perspective (secondary perspective). This was not the case for CM Abstinence, which remained cost-ineffective compared to TAU for all scenarios.

The results of this economic evaluation have several implications for the treatment of heroin use disorder in England. Firstly, they indicate that incentivising individuals to stop using heroin (CM Abstinence) appears not to add anything to TAU in terms of heroin abstinence; it is not a cost-effective use of limited public funds particularly in the context of reduced funding for drug treatment in England since 2013. (32) Secondly, incentivising individuals with heroin use disorders with modest or small incentives to engage with heroin treatment services (CM Attendance) may be cost-effective, but only while patients are being provided with the financial incentives to attend. These results also suggest the need for further research into the cost-effectiveness of longer-term CM interventions, such as an incentives maintenance model. (33) Given these results suggest that it may be more feasible to incentivise treatment engagement rather than directly targeting opiate abstinence, it is possible that enhanced treatment engagement may eventually lead to reduced heroin use and the associated negative economic sequelae compared to treatment as usual.

The interpretation of the results is subject to several limitations. From a clinical point of view, the results may have limited generalisability in contexts where addiction services and the types of opioids used are very different to those in England. The results are also based on data collected between 2012 and 2015 and thus may not reflect more recent developments in illicit opioid use such as the surge in fentanyl, a potent synthetic opioid. (34) In addition, more frequent, escalating incentive schedules have been shown to be more effective than the fixed voucher incentives used in this study. (35) However, escalating values were judged not to be feasible given the resource constrained budgets faced by English drug treatment services. Our clinical report could not conclude whether the absence of benefits after the 12-week follow-up was due to the withdrawal of financial incentives or the cessation of the weekly appointments. In England, weekly appointments are considered good practice in the first 12 weeks of a new treatment episode, (36) but weekly appointments are not routinely offered beyond this point. Considering the economic burden of heroin use on the health system and the wider community, and the relatively low cost of the

incentives used in our study, further research into different treatment and incentive schedules extending beyond 12 weeks may be indicated.

In terms of data, full follow-up data for the economic evaluation were available for only 58% (322/552) of the sample at the final 24-week follow-up which introduced additional uncertainty. The results were additionally adjusted for two potentially influential baseline predictors of missingness at the 24-week follow-up (supported accommodation, social functioning) although this made no material difference to the analysis. Finally, the complete case analysis and multiple imputation analysis produced similar findings, thus giving greater confidence in the results.

Resource use data collection (other than the trial-based treatments) was limited by the self-report nature of the data, which is subject to inaccuracies due to difficulties with recall. Accuracy could be improved by using routine data however this would not have included the important areas of criminal activity and supported accommodation. Of particular concern is the self-reporting of criminal activity. The Home Office has estimated that ninety percent of costs associated with Class A drug misuse are due to crime mostly committed to fund illicit drug use. (3) Accordingly, NICE methodological guidelines have specifically recognised that reductions in criminal activity due to drug treatment programmes should be included in any assessments of cost-effectiveness. (31) There may be ethical and reporting concerns in relying on self-reported data on criminal activity but there is also evidence of good agreement between self- reported criminal justice contacts and criminal justice records in drug users. (37,38) Additionally, data on criminal justice contacts (for example, with police, courts and prisons) or data on cautions, arrests or prosecutions, will not accurately reflect the cost of crimes committed, since many crimes go unreported or unsolved, and therefore would not capture the differential impact of interventions on criminal activity.

In terms of study design and analysis, the allocation of several treatment services with high homeless caseloads to the CM Abstinence group may have contributed to higher supported accommodation costs and costs of crime in this group. The imbalance in accommodation may have been caused by the cluster randomised design which was adopted to avoid contamination from offering the different treatments to patients attending the same clinic. However, the exclusion of supported accommodation costs in sensitivity analysis, and the exclusion of crime costs when taking the NHS/PSS perspective, did not materially change the base case results. Short time horizons are a further limitation of trial-based economic evaluations and this can be particularly problematic for drug treatment interventions where treatment discontinuation and relapse to heroin use carry a high risk of mortality. Future evaluations could benefit from economic modelling to extend the range of observed costs and outcomes. Additionally, the generalised linear modelling (GLM) used in the cost effectiveness analysis may have underestimated variation and uncertainty in data as recently demonstrated for ordinary least squares (OLS) methods compared to multi-level modelling (MLM). (39)

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Table 1: Mean costs and differences in imputed and adjusted costs (£) by follow-up period and perspective

	CM Abstinence	CM Attendance	TAU	CM Abstinence versus TAU			CM Attendance versus TAU		
Perspective	Mean (SD)	Mean (SD)	Mean (SD)	Mean diff (SE)*	95% CI*	P*	Mean diff (SE)*	95%CI*	P*
12 weeks									
NHS/PSS	£2280 (£3700)	£1212 (£2264)	£1382 (£3378)	£1019 (£840)	-£752 to £2791	0.241	-£90 (£292)	-£708 to £527	0.760
Societal	£3946 (£13070)	£1539 (£3066)	£2544 (£10743)	£1945 (£1386)	-£1044 to £4933	0.184	-£514 (£659)	-£1964 to £935	0.451
24 weeks									
NHS/PSS	£3685 (£6315)	£1618 (£2808)	£2091 (£4760)	£1076 (£873)	-£775 to £2928	0.236	-£207 (£416)	-£1085 to £669	0.624
Societal	£8268 (£19489)	£3369 (£5356)	£4247 (£6337)	£2562 (£1188)	£32 to £5092	0.047	£317 (£565)	-£882 to £1518	0.582

*Based on imputed and adjusted data

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Table 2: Mean outcomes and differences in imputed outcomes by follow-up period

	CM Abstinence	CM Attendance	TAU	CM Abstinence versus TAU			CM Attendance versus TAU		
Perspective	Mean (SD)	Mean (SD)	Mean (SD)	Mean diff (SE)*	95%CI*	P*	Mean diff (SE)*	95%CI*	P*
12 weeks									
Urinalysis**	1.851	2.071	1.525	0.118 (0.258)	-0.425 to 0.661	0.652	0.203 (0.095)	0.002 to 0.405	0.048
	(1.374)	(1.264)	(1.324)						
QALYs	0.162	0.154	0.145	0.007 (0.012)	-0.017 to 0.030	0.566	-0.005 (0.005)	-0.015 to 0.016	0.383
	(0.064)	(0.068)	(0.064)						
24 weeks									
Urinalysis***	1.466	1.496	1.231	0.252 (0.305)	-0.397 to 0.901	0.421	0.089 (0.147)	-0.223 to 0.402	0.552
	(1.337)	(1.291)	(1.367)						
QALYs	0.335	0.321	0.305	0.017 (0.015)	-0.015 to 0.049	0.289	0.005 (0.007)	-0.010 to 0.019	0.497
	(0.116)	(0.117)	(0.124)						

*Based on imputed and adjusted data; **Difference in the number of weekly heroin negative urine results in weeks 9, 10, 11 &12; ***Difference in the number of weekly heroin negative urine results in weeks 21, 22, 23 & 24

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Table 3: Summary of primary cost-effectiveness and cost-utility analyses at 24-weeks

	CM Abstinence versus TAU			CM Attendance versus TAU		
	Mean difference in societal costs (£)	Mean difference in outcomes	ICER	Mean difference in societal costs (£)	Mean difference in outcomes	ICER
Primary cost-effectiveness analysis	2562	0.252	£10,167 per heroin-negative urine	317	0.089	£3,562 per heroin-negative urine
Secondary cost-utility analysis	2786	0.017	£163,882 per QALY	257	0.005	£51,400 per QALY

ICER=incremental cost-effectiveness ratio

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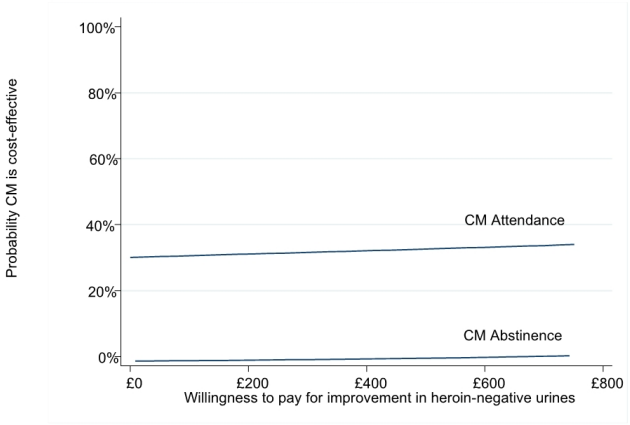

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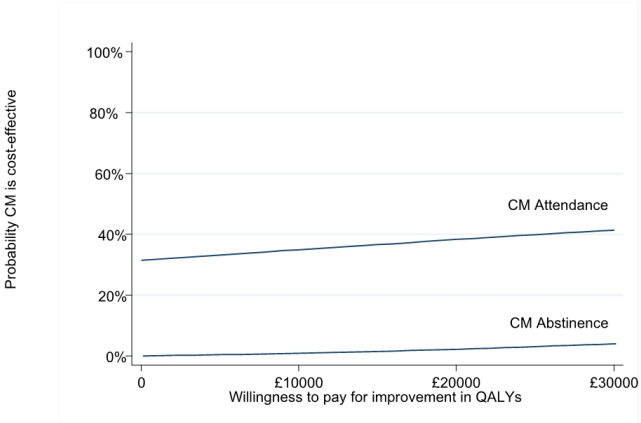

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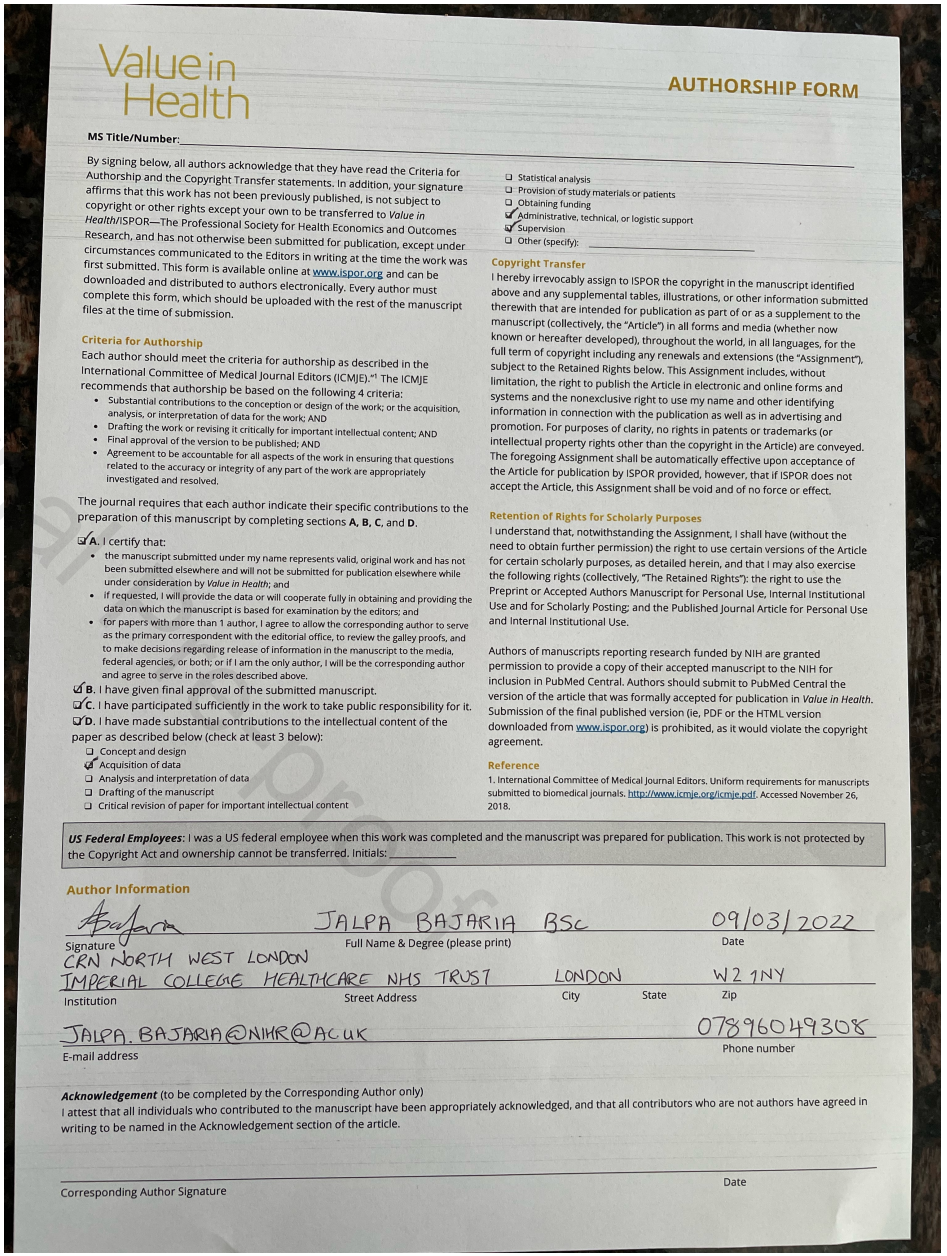

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