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Title: Script in a Day (SCID) intervention for individuals who are injecting opioids: A feasibility randomised control trial

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Abstract
Opioid substitution treatment (OST) reduces the harm of injecting and opioid dependence. The SCID feasibility trial explored the processes of conducting a randomised control trial (RCT) with people who inject drugs (PWID) in a low threshold agency. Feasibility of the intervention investigated whether offering PWID immediate access to OST via specialist primary care increased numbers in OST at 3 months, compared to offering advice and case management.

Methods
Un-blinded RCT was conducted at Bristol Drugs Project needle exchange. A total of 311 individuals were eligible and 100 consented to participate. Trial process outcomes involved exploring OST status at 3 months; secondary outcomes were substance use and health related quality of life measures.

Results
Follow-up was 86%. At 3 months, 51% intervention and 47% of control participants were in OST (OR of success of intervention 1.17 (0.54-2.57). Opioid use reduced by 79% and 73% respectively (OR of intervention success 1.38 (0.5-3.7). Physical and mental health improved but there was little differences between groups.

Conclusions
The feasibility of conducting the trial was a success, but there was insufficient evidence of an effect compared to intensive case management. Further development and evaluation of case management approaches in low-threshold agencies is warranted.

Key Words: people who inject drugs, opioid substitution treatment, primary care

Word Count: Abstract-199 Manuscript-2,975

Introduction

Opioid substitution treatment (OST) reduces the harm of injecting and opioid dependence: reducing drug related mortality, the frequency of injecting, Hepatitis C Virus, HIV, and drug related crime (1-6). Prolonged treatment has a positive effect on overall survival and prevalence of blood borne viruses (7, 8). Promoting OST and reducing the time out of treatment, therefore, is a key goal in the prevention of drug related harm.

There is evidence that motivational interviewing and intensive case management can increase treatment onset (9, 10). Recent meta-analyses suggest that exposure to motivational interviewing or case management intervention increases the likelihood of entering treatment by 1.69 and 3 times respectively (9). However, generalising the studies to a UK population is problematic as all were US based, in contexts where treatment was not free at point of delivery. Furthermore, brief interventions and case management to encourage OST uptake are already in place in low threshold agencies in contact with people who inject drugs (PWID) in many sites in the UK. In designing the current trial, we involved PWID and drug workers and their favoured option was for the provision of immediate low threshold access to OST. This has already been developed in Amsterdam with mobile access to OST (11, 12). In many sites in the UK there is ready access to primary care , which delivers the majority of OST (13). Therefore, we designed an intervention "Script in a Day" (SCID) that would offer immediate access to OST through referral to a local specialist primary care centre (14). In this feasibility study we test whether PWID can be recruited and followed-up and whether we can evaluate if receiving SCID increases the number of patients in OST at 3 months after exposure compared to treatment as usual within a randomised control trial.

Methods

Study design

This feasibility trial explored the processes of conducting a small scale RCT. An un-blinded parallel-group trial tested the feasibility of the intervention which offered same day access to opioid substitution therapy (OST), described as "Script in a Day", compared with standard care with 3 month follow-up.

Recruitment

Recruitment took place on two days a week (when slots with the GP were available) at the Bristol Drugs Project (BDP) low threshold agency (also known as "direct access" in the UK) between October 2011 and September 2012 (Figure 1). Drug workers or volunteers approached potentially eligible adults who were accessing the needle syringe programme (NSP). Eligibility requirements were: living in Bristol; not prescribed OST in the last two weeks; and injecting opioids. Participants were given detailed information about the study, time to reflect whether they wished to participate and questions answered before being consented into the study. Participants completed baseline questionnaires with the assistance of the research staff before being randomised to the "Script in a Day" intervention or standard care. Data collected at baseline and 3 month follow-up included: the Treatment Outcomes Profile Measure (TOP) which is widely used in drug services and measures substance use; injecting risk behaviour and crime (15, 16); and two health related quality of life measures EQ-5D-5L (17) and the SF-12-v1 (18). Randomisation was a web-based allocation provided by Bristol Randomised Trial Collaboration (BRTC) using random sized blocks and stratifying by sex. Participants were invited to return the following day to receive £15. Participants also received £15 at the three month follow-up. Ethics approval was given by National Research Ethics Service, South West, [11/H0102/1].

Usual care was defined as offering participants advice and information about obtaining a script and if wished, help with making a telephone call to their general practitioner (GP) to initiate this process(9).

Script in a Day Intervention

The Script in a Day Intervention involved one GP practice agreeing to keep open appointment slots twice a week for intervention participants. Participant details were faxed to the intervention GP who requested a fax from the participant's GP prior to the appointment to avoid double scripting. Participants were offered the support of a peer support volunteer on the 15 minute walk to the GP

surgery. This is part of the volunteer role at BDP and we included this as part of the feasibility study. On arrival, participants provided a urine sample to check for the presence of opioids using Drug-Screen-Multi 5MB, and if screen positive and no other contra-indications, participants were initiated on 30-40ml of methadone, which was taken on the day. A further script for 6 days was issued and participants were asked to return on Day 7 and 21 for further scripts and if required adjustments between 10-20ml. From Day 21 participants were transferred to their GP practice and shared care worker when spaces became available.

Outcome measures

The feasibility outcomes were numbers recruited, randomised and outcome data collected at 3-months.Follow-up was conducted through self-report and data linkage via medical, BDP and other drug treatment agencies' records. At baseline and 3 months we assessed drug use (TOP), and quality of life (EQ-5D-5L and SF-12-v1) using questionnaires administered face-to-face. From these, we derived Quality Adjusted Life Years (QALYs). QALYs are a measure of health status whereby survival is weighted by quality of life.

Data were analysed using 95% confidence intervals (CI) for all outcome measures in preference to p values as this feasibility study was not powered for hypothesis testing. Confidence intervals for percentages were calculated using the exact binomial method. Effect sizes for the difference from baseline to 3 months were calculated using the standard deviation for a paired t-test and assumes that the distribution of the differences was normally distributed. Effect sizes for the effect of the intervention were calculated using a regression model controlling for baseline value and used the standard deviation associated with the test statistic for the coefficient. OST at 3 months post randomisation was investigated using a Kappa statistic to compare self-report with medical records checks. Health related quality of life (SF-12-v1) produced 8 domains with two aggregate measures: a physical and a mental component. Those reported here are standardised as scores out of 100 for direct comparison across domains and for comparison with the EQ-5D visual analogue score (VAS). Preference weights for the UK population were obtained at baseline and 3 months for the EQ-5D-5L using the cross-walk algorithm(19), and for the SF-6D (six domains derived from the SF-12) using Brazier's algoritm(20). Quality of life preference weights are country-specific and range from negative values for health states worse than death, zero for death and up to one for the "best imaginable health". Three month QALYs were derived calculating the area under the curve by treatment arm and adjusting for baseline scores (21) .

A nested qualitative study explored trial processes with a purposive sample of 20 participants that included both intervention (8) and control groups (12). Semi-structured interviews guided by a topic guide were conducted and data thematically analysed (for more detail see our companion paper (22).

Results

A total of 311/1,371 individuals assessed were eligible and 100/311 consented (Figure 2 Participant Flow Diagram). Reasons for declining included being too busy or not interested in receiving a script. The vast majority (881/1060 (83%)) of participants screened were excluded because they were already on a script. The remaining were either not on a script (n=35), not injecting opioids (n=111), not living in Bristol (n=13) or not recorded (n=20). The participants comprised 84 men and 16 women; 93.4% were white, 69% were registered with a GP, 26% had no fixed abode, and 90% had previously received OST (Table I). These characteristics are similar to people who inject drugs (PWID) attending local services (e.g. PWID attending needle syringe programme. Feasibility outcomes are shown in Table II. Forty nine participants were allocated to the intervention, of which 43 received a script, two did not arrive at the GP practice, three were already scripted and in one, no opioids were detected in the urine and so could not receive a prescription.

Most intervention arm participants chose to be accompanied to their GP appointment by a peer volunteer and appreciated the positive reinforcement and role model for recovery that this afforded (see box 1).

Box 1: quotes from participants about peer volunteers here

Overall, follow-up was 86% (84% intervention and 86% control) through interview, 90% through medical records (98% intervention and 80% control), and 95% (97% intervention and 92% control) from interview or medical records.

Table I and II here

Outcome measures

There was good agreement between the two methods of follow up for 79 participants with both self-report and medical records OST at 3 months (Kappa of 0.872). Self-report rates of OST at 3 months were slightly higher at 59.5% (47/79) than medical report rates 53.2% (42/79) with discrepancies occurring in a few individuals on OST sporadically over the follow up time. Combining the results suggested that there were 49 patients on OST at 3 months. The intention to treat analysis assumed that those lost to follow-up were not in OST at 3 months. Overall, 51% and 47% of the intervention and control participants were in OST (OR of success of intervention 1.17 95% CI 0.54 to 2.57, Table III).

Table III here

There were substantial reductions in self-reported opioid use in both the intervention and control population (33.3% and 22.7% not having used in the last 28 days) but insufficient evidence of any differences in effect between intervention and control (OR of intervention success 1.38 95% CI 0.5 to 3.7). Table IV shows the change in self-reported substance use between baseline and 3 months (expressed as standardised effect sizes corresponding to mean difference divided by the standard deviation of this difference). Effect sizes showed that being in the study had a large effect on both the number of days of opioid use and number of days injecting drug use, a moderate to strong effect on crack use, but little impact on alcohol or other drug use. Differences between the intervention and control group were less marked but there was a small difference in reduction of opioid use of 2 days, in contrast to overall average reduction in opioid use for all trial (control and intervention) participants of 14 days.

Table IV here

There were improvements in HRQL over the three months. These were medium effect sizes for both the EQ-5D and all the components of the SF-12. The intervention was associated with a small non-significant decrease in the overall HRQL score with the EQ-5D, but a positive medium sized effect for the mental health quality of life aggregate score for the SF-12, which was present in all the mental health domains. For participants completing both the EQ-5D and the SF-12, there was no evidence of incremental QALY gains between arms, -0.006 [95% CI -0.020 to 0.008] using the EQ-5D and 0.003 [95% CI -0.005 to 0.010] using the SF-6D (Table V). In this group the distribution of SF-6D scores displayed less variability and baseline imbalance than for the EQ-5D scores (Figure 3).

Table V & Figure 4 here

Qualitative interviews showed that completing the baseline questionnaires at recruitment appeared to enhance motivation for treatment for all participants. For some control participants, this motivation seemed to increase a sense of self-efficacy and cognitive dissonance generated between their current health state and own aspirations was resolved by seeking treatment from their GP (22).

Box 2 quotes from participants illustrating how taking part in the trial increased self-efficacy and motivation here.

DISCUSSION

Main findings

This feasibility trial of script in a day (SCID), whereby peer support volunteers facilitate ready access to opioid substitution treatment (OST) in primary care for opioid dependent people, could be considered a success. First, we demonstrated that opioid dependent people who inject drugs (PWID) could be recruited and randomised into the trial from a low threshold agency and followed-up successfully. Recruitment was generally ahead of schedule and the follow-up rate was 80-98%. Second, there was active involvement from users and practitioners' in the formulation of the hypothesis, development of the intervention and conduct of the trial. Individuals who had previously injected drugs agreed to be members of the Trial Steering Group and actively contributed at these meetings. They were also involved in the discussion of the results.

Third, a nested qualitative study reported that the intervention seemed acceptable both to participants and practitioners involved in the trial. Taking part in the trial enabled intervention arm participants to obtain treatment for their problematic drug use.

However, there was insufficient evidence of an intervention effect with similar outcomes for OST and reductions in substance use at 3 months between the intervention and control arm. Quality of life over the duration of the trial improved, but again there was insufficient evidence for any adjusted quality of life gains between the groups.

What is already known on this topic

People who inject drugs have poorer health and quality of life, are more likely to be engaging in crime thus, promoting OST and recovery from drug use is a key goal in the prevention of drug related harm.

What this study adds

The SCID feasibility trial demonstrates that it is possible to conduct an RCT, 3 month follow-up of a novel intervention suggested by patients/ users and peer workers to increase the uptake of OST for people who inject heroin. We also provide further evidence that health quality of life (HQoL) of PWID is poor compared to general population (7, 23). For example, the average HQoL of young adults (30-44) is near 1 whereas our sample of dependent opioid users/PWID reported average scores markedly lower at 0.6 (24). Within current policy, the key focus is upon recovery. Thus, whilst this feasibility study focused upon the uptake of OST and not recovery, we suggest that the findings contribute to drug treatment services in beginning the process to promoting recovery.

To our knowledge this study is the first to investigate an intervention such as SCID, with accelerated access to OST in primary care facilitated by peer support volunteers. The importance of peers in substance misuse treatment is well recognised (25). Low threshold access to methadone through a mobile bus was offered to PWID in Amsterdam at peak of HIV epidemic; and several trials have shown how intense case management can increase OST uptake (9, 11, 26). Bristol in contrast to other sites in the UK, has developed an extensive shared care network of OST delivered in primary care. The average wait for an appointment and initiation onto OST is 3-5 days following a first GP appointment, and a high proportion of PWID are in treatment (as shown by the high numbers and proportion of people attending the NSP who were ineligible for the trial because they were already in treatment). We believe this to be relatively rapid compared to other cities in UK and elsewhere, and therefore provides an ideal setting to test an intervention that offers immediate access to OST. It was important to conduct the feasibility trial in a site like Bristol with good access to OST so that any difference in the outcome could be attributed to the intervention rather than restrictions to OST. We show that an intervention like SCID may be unnecessary, but that further work on case management in low-threshold agencies to encourage OST uptake could be worthwhile.

There is limited information on health utilities or quality of life (HQoL) of PWID prior and during treatment, which can limit evaluations of cost effectiveness of interventions in this group (23, 27, 28). Several studies have shown that HQoL generally is depressed compared to general population (7). However, whilst some studies show HQoL improves during and after OST this may not be sustained in the longer term (29). Thus, the importance of psychological well-being and providing practical, social and environmental support should also be considered (30). We found that OST increased HQoL though it was still poor in contrast to the general population (24). We also suggest that the SF12 questionnaire may be preferable to obtain quality of life measurements in future studies in PWID and opioid dependent people due to less variability and its greater weight given to mental health domains.

Limitations

There is controversy over how feasibility studies should be used to guide future evaluations, especially if the decision is based on evidence of a small or clinically unimportant effect (31). However, at 100 participants, our study is as large as several other recent trials (32-35). Though the confidence interval of the intervention effect (0.54 to 2.57] was consistent with a decrease of nearly 50% or greater than 2.5 fold increase, the high number and proportion of the control in OST at 3

months suggests that there is little further improvement that could be made by the intervention, and that the specific intervention we developed may not be required to encourage PWID into OST.

Secondly, did the control receive treatment as usual? Participants who attended our recruitment site and were not in treatment were invited to make an appointment with their local general practitioner (GP) to initiate OST. Additionally, our control group were subject to an approximately hour long baseline interview where they gave consent for the study and follow-up , provided information on their current drug use and quality of life and were also compensated for their time. Our nested qualitative study suggests that this extra hour providing information may have inadvertently provided time for reflection that motivated these participants to seek treatment (22). This does not invalidate this feasibility trial, but does suggest that a new trial of enhanced case management which involves a more considered assessment of current drug use and quality of life informed by psychological theory may be warranted.

Conclusions

In conclusion, the feasibility aspects of the trial were successful as we demonstrate that PWID could be recruited into the trial and followed-up successfully. There was insufficient evidence of an effect for the intervention compared to intensive case management. Thus, further development and evaluation of case management approaches is warranted.

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The study sponsor had no role in study design, data collection, data analysis, data interpretation, writing of the report, no editorial direction or censorship.

Ethical Approval

Ethics approval was given by National Research Ethics Service, South West, [11/H0102/1]

Declaration of conflict of interest

No conflicts of interest have been declared.

Clinical trial Registration

This trial is registered with NIHR (UKCRN 10169) & International Standard Randomised Controlled Trial Number Register: SCript In a Day for injecting drug users: feasibility trial: ISRCTN16846554. http://www.controlledtrials.com/ISRCTN16846554/script+in+a+day

References

1. Amato L, Davoli M, Perucci CA, Ferri M, Faggiano F, Mattick RP. An overview of systematic reviews of the effectiveness of opiate maintenance therapies: available evidence to inform clinical practice and research. Journal of Substance Abuse Treatment. 2005;28(4):321-9.
2. Cornish R, Macleod J, Strang J, Vickerman P, Hickman M. Risk of death during and after opiate substitution treatment in primary care: prospective observational study in UK general practice research database. BMJ. 2010;341:c5475.
3. Gowing L, Farrell MF, Bornemann R, Sullivan LE, Ali R. Oral substitution treatment of injecting opioid users for prevention of HIV infection. Cochrane Database Syst Rev. 2011(8):CD004145.
4. Turner KM, Hutchinson S, Vickerman P, Hope V, Craine N, Palmateer N, et al. The impact of needle and syringe provision and opiate substitution therapy on the incidence of hepatitis C virus in injecting drug users: pooling of UK evidence. Addiction. 2011;106(11):1978-88.
5. MacArthur GJ, Minozzi S, Martin N, Vickerman P, Deren S, Bruneau J, et al. Opiate substitution treatment and HIV transmission in people who inject drugs: systematic review and meta-analysis. BMJ. 2012;345:e5945.
6. Godfrey C, Stewart D, Gossop M. Economic analysis of costs and consequences of the treatment of drug misuse: 2-year outcome data from the National Treatment Outcome Research Study (NTORS). Addiction. 2004;99(6):697-707.
7. Kimber J, Copeland L, Hickman M, Macleod J, McKenzie J, De AD, et al. Survival and cessation in injecting drug users: prospective observational study of outcomes and effect of opiate substitution treatment. BMJ. 2010;341:c3172.
8. Degenhardt L, Mathers B, Vickerman P, Rhodes T, Latkin C, Hickman M. Prevention of HIV infection for people who inject drugs: why individual, structural, and combination approaches are needed. Lancet. 2010;376(9737):285-301.
9. Roberts J, Annett H, Hickman M. A systematic review of interventions to increase the uptake of opiate substitution therapy in injecting drug users. J Public Health (Oxf). 2011;33(3):378-84.
10. Hesse M, Vanderplasschen W, Rapp R, Broekaert E, Fridell M. Case management for persons with substance use disorders. Cochrane Database Syst Rev. 2007;4(CD006265).
11. Langendam MW, van Brussel GH, Coutinho RA, van Ameijden EJ. The impact of harm-reduction-based methadone treatment on mortality among heroin users. AmJPublic Health. 2001;91(5):774-80.
12. Buning EC, van Brussel GH, Van SG. The 'methadone by bus' project in Amsterdam. BrJAddict. 1990;85(10):1247-50.
13. Strang J, Sheridan J, Hunt C, Kerr B, Gerada C, Pringle M. The prescribing of methadone and other opioids to addicts: national survey of GPs in England and Wales. British Journal of General Practice. 2005;55(515):444-51.
14. Practitioners RCoG. The Future Direction of General Practice: A road map. London: Royal College of General Practitioners.; 2007.
15. Marsden J, Eastwood B, Bradbury C, Dale-Perera A, Farrell M, Hammond P, et al. Effectiveness of community treatments for heroin and crack cocaine addiction in England: a prospective, in-treatment cohort study. Lancet. 2009;374(9697):1262-70.
16. Marsden J, Farrell M, Bradbury C, Dale-Perera A, Eastwood B, Roxburgh M, et al. Development of the Treatment Outcomes Profile. Addiction. 2008;103(9):1450-60.
17. van Agt HM, Essink-Bot ML, Krabbe PF, Bonsel GJ. Test-retest reliability of health state valuations collected with the EuroQol questionnaire. SocSciMed. 1994;39(11):1537-44.

18. Ware J, Jr., Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. Med Care. 1996;34(3):220-33.
19. Herdman M GC, Lloyd A, Janssen M, Kind P, Parkin D, et al. Qual Life Res. . Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). 2011;20(10):1727-36.
20. Brazier J, Roberts, JR,. Medical Care The estimation of a preference-based index from the SF-12. . 2004;42(9):851-9.
21. Manca A HN, Sculpher M Estimating mean QALYs in trial-based cost-effectiveness analysis: the importance of controlling for baseline utility. Health Econ. 2005;14 (5):487-96.
22. Ayres R, Ingram J, Rees A, Neale J, Beattie A, Telfer M. Enhancing motivation within a rapid opioid substitution treatment feasibility RCT: a nested qualitative study. Substance Abuse Treatment, Prevention and Policy. 2014;9(44):1-9.
23. Dietze P, Stoove M, Miller P, Kinner S, Bruno R, Alati R, et al. The self-reported personal wellbeing of a sample of Australian injecting drug users. Addiction. 2010;105(12):2141-8.
24. Kind PH, G; Macran, S. UK Population Norms for EQ-5D. Centre for Health Economics Discussion Paper, University of York. 1999:1-98.
25. Boisvert RM, L., Grosek, M. Claire, AJ. Effectiveness of a peer-support community in addiction recovery: participation as intervention. Occupational Therapy International 2008;15(4):205-20.
26. Plomp HN, Van Der Hek H, Ader HJ. The Amsterdam methadone dispensing circuit: genesis and effectiveness of a public health model for local drug policy. Addiction. 1996;91(5):711-21.
27. Martin NK, Vickerman P, Miners A, Foster GR, Hutchinson SJ, Goldberg DJ, et al. The cost-effectiveness of HCV antiviral treatment for injecting drug user populations. Hepatology. 2012;55(1):49-57.
28. McDonald SA, Hutchinson SJ, Palmateer NE, Allen E, Cameron SO, Goldberg DJ, et al. Decrease in health-related quality of life associated with awareness of hepatitis C virus infection among people who inject drugs in Scotland. J Hepatol. 2013;58(3):460-6.
29. Fingleton NM, C Jaffray, M. Changes in mental health during opiate replacement therapy: a systematic review. Drugs Education, Prevention and Policy. 2015;22(1):1-18.
30. De Mayer JV, W. Camfield, L. Vanheule, S. Sabbe, B. Broekaert, E. A good quality of life under the influence of methadone: a qualitative study among opiate-dependent individuals. International Journal of Nursing Studies. 2011;48:1244-57.
31. Arain M, Campbell M, Cooper C, Lancaster G. What is a pilot or feasibility study? A review of current practice and editorial policy. BMC Medical Research Methodology. 2010;10(1):67.
32. Borschmann R, Barrett B, Hellier JM, Byford S, Henderson C, Rose D, et al. Joint crisis plans for people with borderline personality disorder: feasibility and outcomes in a randomised controlled trial. The British Journal of Psychiatry. 2013;202(5):357-64.
33. Coffin PO, Santos GM, Das M, Santos DM, Huffaker S, Matheson T, et al. Aripiprazole for the treatment of methamphetamine dependence: a randomized, double-blind, placebo-controlled trial. Addiction. 2013;108(4):751-61.
34. Konstenius M, Jayaram-Lindstrom N, Guterstam J, Beck O, Philips B, Franck J. Methylphenidate for attention deficit hyperactivity disorder and drug relapse in criminal offenders with substance dependence: a 24-week randomized placebo-controlled trial. Addiction. 2013;109(3):440-9.
35. Levin FR, Mariani J, Brooks DJ, Pavlicova M, Nunes EV, Agosti V, et al. A randomized double-blind, placebo-controlled trial of venlafaxine-extended release for co-occurring cannabis dependence and depressive disorders. Addiction. 2013;108(6):1084-94.

Box 1: quotes from participants about peer volunteers

"He [peer support worker] explained to me about how it changed his life when he stops using heroin. Yeah I see how this guy's happy…and I'm thinking about this, I want to change my life" (participant #211; male; 37yr).

"With that support I didn't feel like turning back half way which, if I had been on my own, then I probably would have done" (participant #101; female; 36yr).

Box 2 quotes from participants illustrating how taking part in the trial increased self-efficacy and motivation.

"It made me think a lot actually about myself…I don't actually sit down and think about my overall day, usage or anything like that. But when I was going through the questionnaire I actually did think about "God … things aren't quite as good as I thought they were" (participant #219; Female; 28y).

" I suppose it made me get off me bum and go and get a script somewhere else" (participant #002; Male; 43y).

Figure 1. Script in a Day recruitment graph

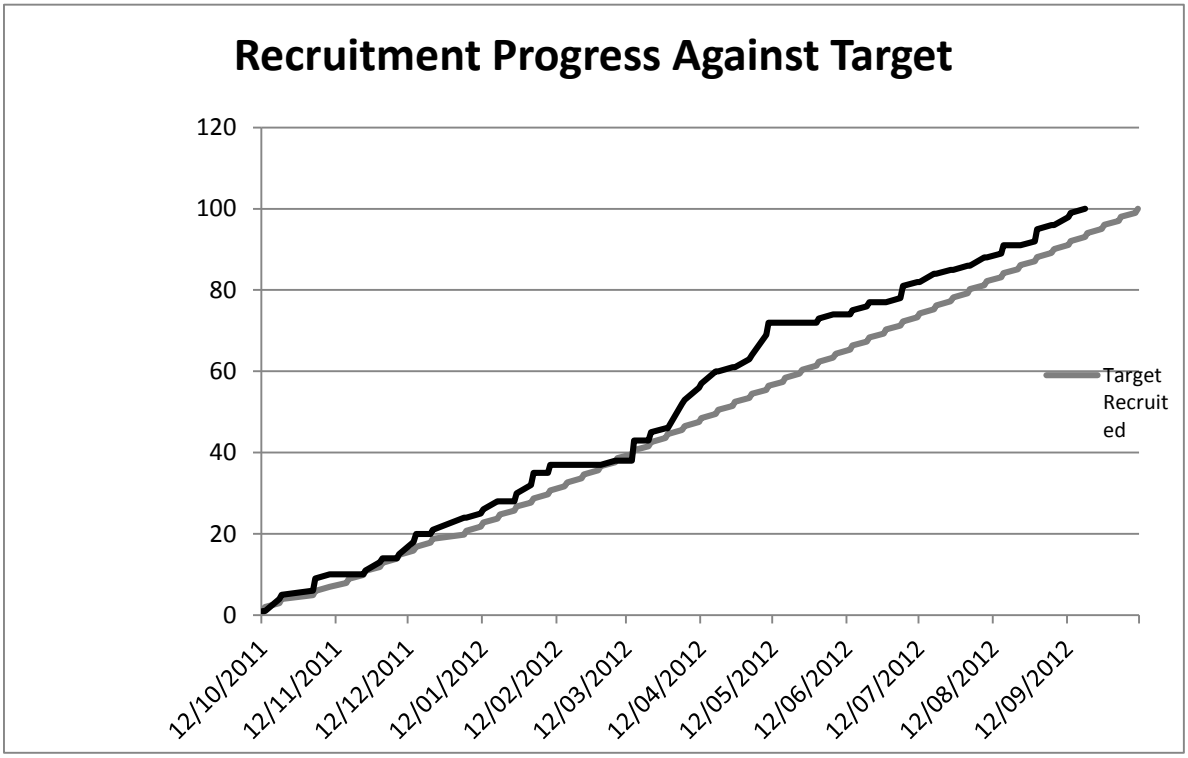

Figure 2 SCID flow diagram of participants recruited into the trial

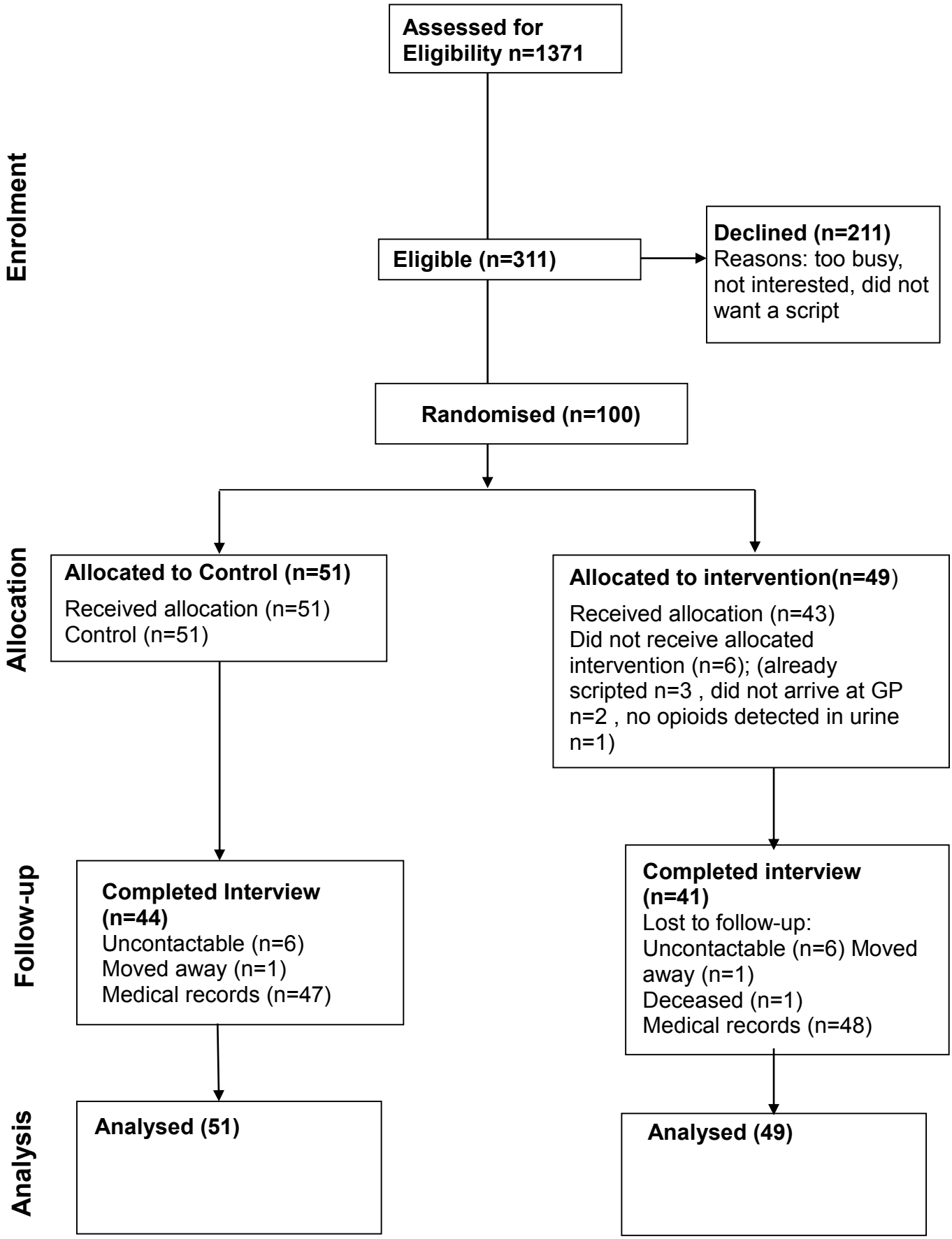

Figure 3. Evolution of quality of life preference scores for patients completing both the EQ-5D and the SF-12

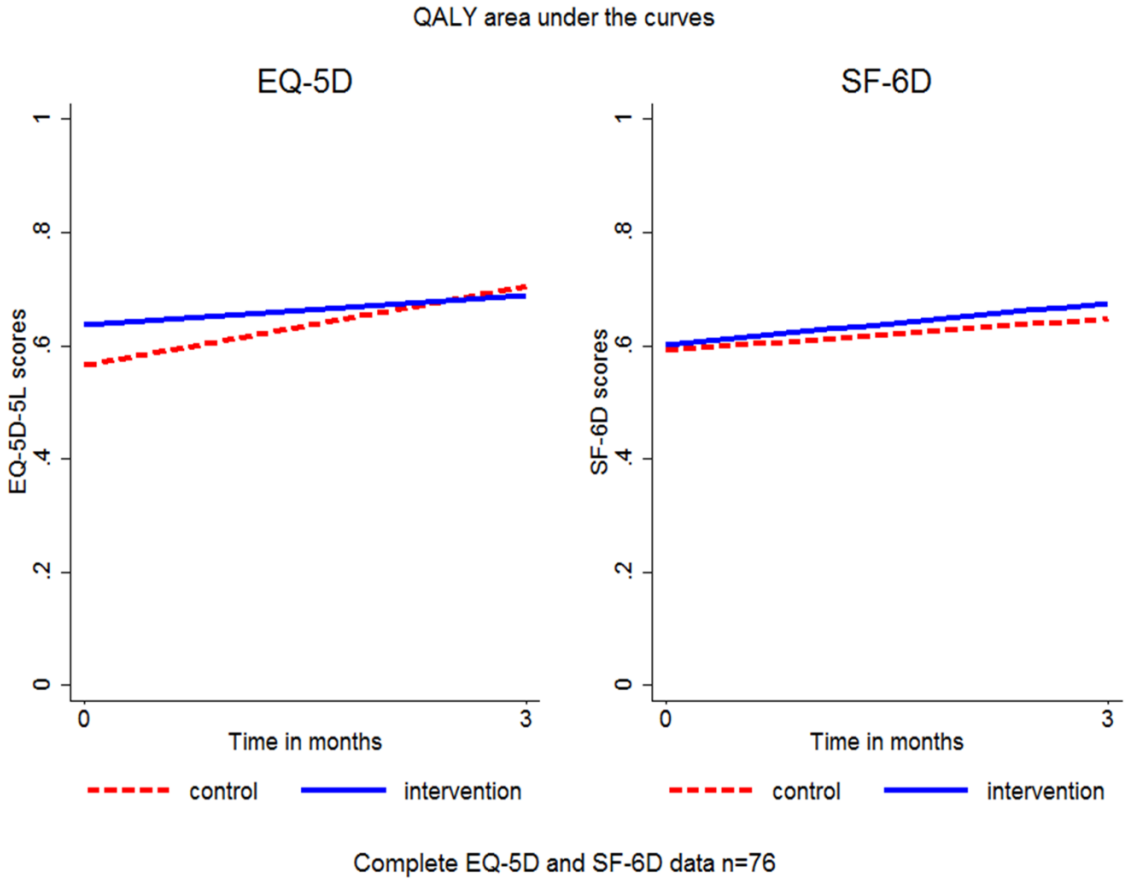

Table I Patients recruited and baseline characteristics (percentages with numbers or means with standard deviations in brackets).

Variable	Intervention sample	Control sample	Whole sample
Gender- female	14.3% (7/49)	17.6% (9/51)	16% (16/100)
White British/Irish/other	95.9% (47/49)	92.0% (46/50)	93.9% (93/99)
Caribbean, Asian, Other or Mixed race	4.1% (2/49)	8.0% (4/50)	6.1% (6/99)
Registered with a GP	71.4% (35/49)	66.7% (34/51)	69% (69/100)
Previous treatment for drug use.	89.8% (44/49)	90.2% (46/51)	90% (90/100)
Currently receiving support from mental health team	12.2% (6/41)	11.8% (6/51)	12% (12/100)
No fixed abode	20.4% (10/49)	31.4% (16/51)	26% (26/100)
TOP baseline data:			
No. of days using alcohol in last 28	10.8 (11.5)	11.2 (12.2)	11 (11.8)
No. of days using opiates in last 28	23.2 (6.7)	24.1 (6.6)	23.7 (6.6)
No of days using crack in last 28	16.2 (10.5)	16.7 (10.7)	16.4 (10.6)
No of days injecting drugs in last 28	22.8 (7.4)	24.7 (6)	23.8 (6.8)
Health related quality of life:			
EQ-5D score (SD) *(N)*	0.61 (0.24) *(49)*	0.54 (0.30) *(51)*	0.57 (0.28) *(100)*
EQ-5D VAS (0 to 100 scale)	51.0 (20.2)	49.0 (20.9)	50.0 (20.5)
SF-6D score (SD) *(N)*	0.59 (0.12) *(48)*	0.59 (0.12) *(47)*	0.59 (0.12) *(95)*
SF 12 physical HRQL score (0 to 100 scale)	44.1 (25.4)	43.1 (25.6)	43.6 (25.4)
SF 12 mental HRQL score (0 to 100 scale)	33.5 (21.5)	31.8 (21.6)	32.6 (21.5)

Table II Trial feasibility outcomes with 95% confidence intervals

Pilot Statistic	number	Rate/Percentage with 95% confidence interval
Average number of patients screened per session*	1371 screened from 90 sessions attended	15.2 [14.4, 16.1]
Percentage Eligible	311 / 1371	22.7% [20.5, 25.0]
Percentage Declined	211 / 311	67.8% [62.3, 73.0]
Average number of consented patients per session*	100 recruits from 90 sessions attended	1.1 [0.90, 1.35]
Recruitment percentage	100 / 311	32.2% [27.0, 37.7]
Percentage randomised to the intervention	49 / 100	49%
Face to face follow-up †	85 / 99	85.9% [77.4, 92.0]
Face to face follow-up: intervention group	41 / 49	83.7% [70.3, 92.7]
Face to face follow-up: control group	44 / 51	86.3% [73.7, 94.3]
Medical records follow-up†	88 / 99	88.9% [81.0, 94.3]
Medical records follow-up: intervention group	47 / 48	97.9% [88.9, 99.9]
Medical records follow-up: control group	41 / 51	80.4% [66.9, 90.2]
Attended GP appointment (intervention only)	47 / 49	95.9% [86.2, 99.5]
Received a same day script (intervention only)	43 / 49	87.8% [75.2, 95.4]

* Calculated using the exact Poisson method

† Deceased patient omitted from the denominator

Table III. Outcomes at 3 months as measured by OST, or days abstinence from opiates

Outcome measure	Percentage success at 3 months intervention	Percentage success at 3 months control	Odds ratio of success in intervention compared with control [95% confidence interval
Self-report OST at 3 months	57.1 (24/42)	54.5 (24/44)	1.11 [0.47, 2.60]
Medical records OST at 3 months	47.9 (23/48)	46.3 (19/41)	1.07 [0.46, 2.46]
OST at 3mth (self-report or medical records)	52.1 (25/48)	51.1 (24/47)	1.04 [0.466, 2.33]
ITT OST at 3mth – intention to treat (those with no medical records are included as not on OST at 3 months)	51.0 (25/49)	47.1 (24/51)	1.17 [0.54, 2.57]
Self-reported reduction in days using opiates in the last month compared with baseline	78.6 (33/42)	72.7 (32/44)	1.38 [0.51, 3.71]
No opiate use in the last 28 days	33.3 (14/42)	22.7 (10/44)	1.70 [0.66, 4.41]

Table IV: Change in self-reported substance use and quality of life from baseline to 3 months for those who completed the questionnaire at both time points (n=85)

	Mean (SD) baseline	Mean (SD) 3 months	Effect size for change at 3 months compared with baseline	Effect size for difference between intervention and control at 3 months
Substance Use	(number of days used in the last 28 days)			
Alcohol	11.1 (11.5)	9.1 (11.4)	0.20 [-0.02, 0.42]	-0.05 [-0.50, 0.39]
Opiates	23.5 (6.8)	9.9 (11.0)	1.15 [0.93, 1.36]	0.19 [-0.25, 0.63]
Crack	16.5 (10.6)	7.0 (9.4)	0.82 [0.60, 1.04]	0.07 [-0.37, 0.51]
Cocaine	0.16 (1.11)	0.14 (0.90)	0.06 [-0.15, 0.28]	-0.16 [-0.60, 0.28]
Amphetamine	0.86 (4.06)	0.46 (3.16)	0.09 [-0.13, 0.31]	0.13 [0.31, 0.57]
Cannabis	8.4 (10.4)	6.8 (10.2)	0.16 [-0.06, 0.37]	0.06 [-0.38, 0.50]
Other	4.6 (8.5)	3.0 (7.6)	0.17 [-0.05, 0.39]	0.39 [-0.06, 0.83]
Injecting	23.4 (38.5)	9.8 (11.4)	1.06 [0.85 1.28]	0.15 [-0.29, 0.59]
Health Related Quality of life				
EQ-5D VAS (0 to 100 scale)	49.8 (19.9)	60.0 (19.7)	0.45 [0.23, 0.67]	-0.06 (-0.50, -0.38)
SF 12 physical HRQL (0 to 100 scale)	43.0 (23.4)	57.0 (25.3)	0.53 [0.32, 0.75]	0.08 [-0.36, 0.52]
SF 12 mental HRQL (0 to 100 scale)	33.1 (21.2)	47.7 (25.3)	0.56 [0.35, 0.78]	0.43 [-0.01, 0.87]
8 domains of the SF-12 (0 to 100 scale)				
Physical health domains				
Physical functioning	65.9 (31.6)	80.9 (25.5)	0.43 [0.21, 0.65]	0.10 [-0.35, 0.56]
Role limitation physical	23.4 (38.5)	42.2 (45.2)	0.33 [0.10, 0.56]	0.15 [-0.31, 0.62]
Bodily Pain	53.6 (29.3)	68.1 (28.2)	0.45 [0.23, 0.66]	0.03 [-0.42, 0.47]
General Health	29.7 (20.6)	37.9 (25.8)	0.35 [0.13, 0.56]	0.02 [-0.46, 0.42]
Mental health domains				
Vitality	35.5 (20.2)	45.5 (26.6)	0.36 [0.14, 0.58]	0.51 [0.06, 0.95]
Role limitation emotional	20.6 (37.1)	44.4 (46.4)	0.48 [0.26, 0.71]	0.27 [-0.19, 0.72]
Mental health	38.7 (24.0)	50.7 (22.3)	0.46 [0.24, 0.68]	0.31 [-0.14, 0.75]
Social functioning	36.9 (28.9)	50.9 (30.2)	0.41 [0.20, 0.63]	0.21 [-0.23, 0.65]

Table V – Preference based scores and incremental QALY gains for patients completing both EQ-5D-5L and SF-12 measures (N=76)

	Mean baseline score	Mean 3m score
EQ-5D-5L		
Intervention (n=36) (SD)	0.637 (0.214)	0.688 (0.289)
Control (n=40) (SD)	0.565 (0.294)	0.705 (0.234)
QALY gain* [95% CI]		-0.006 [-0.020, 0.008]
SF-6D		
Intervention (n=36)	0.602 (0.112)	0.675 (0.183)
Control (n=40)	0.591 (0.121)	0.648 (0.093)
QALY gain* [95% CI]		0.003 [-0.005, 0.010]

* Adjusted for baseline score, robust standard errors