James Shearer, Alex Wodak & Kate Dolan

The Prison Opiate Dependence Treatment Trial

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THE PRISON OPIATE DEPENDENCE TREATMENT TRIAL

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EXECUTIVE SUMMARY

The Prison Opiate Dependence Treatment Trial (the trial) examined the treatment history and treatment outcomes for 204 heroin users in NSW prisons between January 2002 and January 2004. The trial was commissioned by the New South Wales Corrections Health Service to evaluate the introduction of naltrexone, a long-acting opioid antagonist, through a controlled comparison with the two existing treatments for heroin users: methadone maintenance treatment (MMT) and drug-free counselling (AOD). The randomisation of subjects to each of the three treatment groups was not successful due to a number of factors outside the control of the researchers. Principal among these was the very poor uptake of naltrexone. Only 9 out 66 (14%) subjects assigned to naltrexone actually started naltrexone treatment and ultimately only 14 subjects out of 204 (7%) started naltrexone over the entire two year study period. An intention-to-treat analysis would be inappropriate when so few designated subjects received their experimental treatment. Secondly, the improved availability of MMT and the introduction of the mixed opioid agonist/antagonist buprenorphine meant that experimental control for methadone/buprenorphine was largely lost. Finally, the availability of heroin within NSW prisons declined in line with reduced supply in the general community (Day, Topp et al. 2003). Heroin use was a principal outcome for the study. Low levels of heroin use at baseline considerably reduced the likelihood of detecting any treatment effects. For these reasons the trial ceased recruitment in July 2003 but continued follow up until January 2004.

The trial was successful in recruiting and following up subjects with a 91% follow up achieved. Subjects were assessed for suitability, randomised and interviewed regarding their drug use history, prison history and other health and psychosocial outcomes. Subjects provided hair samples to be tested for opiate use and finger prick blood samples to be tested for HIV and hepatitis C antibodies. The subjects were re-interviewed at six months and provided further hair and blood samples. At twelve months, record checks were undertaken to examine treatment retention, compliance, concomitant medications and side-effects. For analytical purposes, subjects were divided into five mutually exclusive treatment exposure groups. Subjects who received naltrexone prior to their follow up interview were categorised as the naltrexone study group (n=9). Subjects who received buprenorphine were categorised as the buprenorphine group (n=39). Subjects who received MMT only were categorised as the MMT group (n=89). Subjects who received AOD counselling only were categorised as the AOD group (n=23) and finally subjects who did not receive any of these treatment were categorised as a No Treatment group (n=26).

The study found very poor induction and retention rates for oral naltrexone. Only seven percent of all subjects started naltrexone over the two year study period. Among those subjects, only seven percent were retained in treatment at six-months. Six-month retention was significantly lower in the 14 subjects who started naltrexone (7%) compared to the 12 subjects who started methadone (58%) (p=0.0007). Mean days in treatment were 59 (95% CI, 32-86) for naltrexone, 100 (95% CI, 70-130) for buprenorphine and 149 (95% CI, 117-181) for methadone. While compliance to daily doses was good when subjects were receiving naltrexone (98%), most ceased naltrexone once they were released from prison even when specific arrangements were made for community dosing at no cost to the patient. This was of particular concern as overdose risk is highest post-prison release and this may be further increased if subjects have recently ceased naltrexone. No deaths or serious adverse events were noted during the study. Few side effects were noted in those subjects who received naltrexone. Most side effects were minor, including dizziness, nausea, headache, sleep disturbance and loss of appetite which resolved or were

manageable. There were no other statistically significant differences in outcomes between the study groups although results were limited by the small sample sizes of the multiple comparison groups.

The experience of this study was consistent with other studies of oral naltrexone in Australia and overseas. The study did not replicate the success observed among prison parolees in the US or work release programs in Singapore. The most likely reason for this was that inmates were not subject to coercion or incentives to enter and stay on naltrexone maintenance. In the absence of such incentives, opioid dependent inmates showed a preference for agonist treatment including methadone maintenance and buprenorphine maintenance. Many inmates who achieved abstinence preferred no treatment or drug free counselling over naltrexone. The overall conclusion of the study was that poor patient acceptability and retention did not support oral naltrexone in this treatment group.

The study also found relatively poor retention in subjects who started buprenorphine (n=21) due to the high proportion (20%) who were discontinued due to diversion. Diverted buprenorphine was the second most injected illicit drug (11%) after heroin (14%) at follow up. Investigation of alternate dose formulations may be warranted. Half the trial subjects did not receive any AOD counselling, mostly because they declined to attend for AOD counselling (42%) or claimed that counselling was not offered (38%). Given that subjects who received AOD counselling had improved outcomes, the underlying reasons for failure to attend or be offered AOD counselling warrant further investigation. Subjects who received no treatment of any kind had the poorest outcomes on most measures. This group was characterised by shorter sentences. New forms of depot preparations and implantable devices for both naltrexone and buprenorphine may overcome the poor treatment retention experienced in this study: however such devices remain experimental. At the conclusion of recruitment for this study, CHS withdrew funding support for oral naltrexone. We conclude from this study that treatment of heroin dependence in correctional settings using oral naltrexone is relatively ineffective because of limited attraction and poor compliance and that compliance is superior for oral methadone which is also more attractive and more effective.

1. INTRODUCTION

Over 50% of male NSW inmates have a history of heroin injecting with half continuing heroin use in prison (Butler and Milner 2003). It has been estimated that 9% of heroin injectors start injecting while in prison (Gore, Bird et al. 1995; Dolan, Shearer et al. 2003). Imprisoned IDUs face a high risk of acquiring blood borne viral infections through sharing of syringes and injecting paraphernalia with multiple partners of unknown serostatus. The prevalence of hepatitis C in male NSW inmates has been estimated at 40% (Butler and Milner 2003). The prevalence of HIV in male NSW inmates is very low (<1%) (Butler and Milner 2003) although transmission in four cases has been confirmed (Dolan and Wodak 1999). The relative risk of fatal overdose in custody has been estimated at 19 times that in the community (Essential Equity 1999) while the risk of fatal heroin overdose is highest in the first 24 hours after prison release (Darke, Ross et al. 2000).

In 2001-2002 there was a daily average NSW inmate population of 7,667 (93% male) (Corrections Health Service 2002). There are approximately 25,000 inmate movements in and out of the NSW prison system, and 8,000 movements within the system every year (AOD HHPU 2001). Over 80 percent of inmates have a history of drug and alcohol problems and programs provided by the Corrections Health Service and the Department of Corrective Services provide important continuity of healthcare. The CHS Methadone Program was established in 1986 and is the largest program in NSW. On average, over 900 inmates are enrolled in the program at any one time. CHS also provides detoxification services and drug-free counselling is provided by the Alcohol and Other Drugs HIV Health Promotion Unit of the Department of Corrective Services. In 1998, the NSW prison methadone program was evaluated in a randomised controlled trial. Heroin use, measured by self-report and hair analysis, and self-reported drug injecting and syringe sharing in prison, all declined significantly in the treated group compared to a control group who were on a 4-month wait list (Dolan, Shearer et al. 2003; Dolan, Shearer et al. 2003). A four-year follow up study of the 382 participants enrolled in the original RCT examined longer term outcomes including mortality, re-incarceration, hepatitis C seroconversion and HIV seroconversion (Dolan, Shearer et al. 2004).

The New South Wales Drug Summit (May 1999) concluded that heroin use was a chronic relapsing condition for which several courses of treatment may be necessary before abstinence may be achieved. A key recommendation of the Drug Summit was to fund clinical trials of alternative pharmacotherapies within the New South Wales Prison System including this evaluation of naltrexone maintenance, methadone maintenance and drug-free counselling. The National Evaluation of Pharmacotherapies for Opioid Dependence (NEPOD), a national collaboration of 13 treatment outcome studies involving 1,425 patients, also found that patients may require different forms of treatment at different stages of their drug-use career and that new pharmacotherapies were associated with reductions in opioid-related harms (Mattick, Digiusto et al. in press). NEPOD accordingly recommended the promotion of diversity of treatment options including methadone, buprenorphine and naltrexone from the perspective both of treatment effectiveness and cost effectiveness. This trial increases the treatment options available to inmates particularly those unable to tolerate, accept or benefit from methadone. Despite evidence for methadone maintenance treatment (Ward, Mattick et al. 1998), uptake by

correctional authorities world wide has been poor. Prison authorities are likely to look more favourably on an antagonist drug. This was another rationale for the trial.

Naltrexone is an orally well absorbed, long acting opioid receptor antagonist with no agonist properties. It completely blocks the analgesic and euphoric affects of opiates through competitive binding of the opioid receptor sites. Naltrexone is notaddictive, produces no mood altering effects and has few side effects. It is prescribed for opioid dependent patients who have detoxified from all opiates and intend to remain abstinent (Tucker and Ritter 2000). Naltrexone cannot be used in patients who have used opiates, including methadone, heroin, morphine and high dose codeine, in the previous 7 days as this may precipitate a severe withdrawal. Patients who have ceased naltrexone are at particularly high risk of opioid overdose because naltrexone treatment substantially reduces tolerance to opiates.

Naltrexone has not been successful in the treatment of unselected opioid dependence, principally due to poor acceptance and retention rates (Capone, Brahen et al. 1986; Fram, Marmo et al. 1989; Zador, Adams et al. 1999). A recent systematic review of the efficacy of naltrexone maintenance found that there was no clinical evidence to support its use in heroin dependence (Kirchmayer, Davoli et al. 2002). Strategies to overcome induction problems have included rapid detoxification either under sedation (RODS) or full anaesthesia (RODA) and detoxification under a tapering buprenorphine regime (Collins, Whittington et al. 2002). However, regardless of the method of induction onto naltrexone maintenance, compliance to oral naltrexone in studies continues to be very poor. The National Evaluation of Pharmacotherapies for Opioid Dependence (NEPOD) (Mattick, Digiusto et al. in press) evaluated seven clinical trials involving naltrexone maintenance in 512 patients. Six-month retention rates varied between nil in heroin users inducted with conventional inpatient detoxification, 5% in already abstinent heroin users, and 9% after rapid detoxification in heroin users and methadone patients. A study in Adelaide which participated in the NEPOD evaluation, compared RODA and RODS in 101 equally randomised heroin users and found no difference in treatment retention at 6- or 12-months (McGregor, Ali et al. 2002). Only two participants completed 9 months of naltrexone treatment. Strategies to improve poor compliance to oral naltrexone may hold more promise. These include injectable depot preparations (Cromer, Collins et al. 2002) and implanted depot preparations (O'Neil and Hulse 2002; Carreno, Alvarez et al. 2003; Foster, Brewer et al. 2003; Hulse, O'Neil et al. 2003; Hulse and Tait 2003).

Adverse events including death have been reported during rapid opioid detoxification using naltrexone (Whittington, Collins et al. 2000; Hamilton, Olmedo et al. 2002) and post-naltrexone treatment when patients who resume heroin use are vulnerable to overdose (Bell, Young et al. 1999; Latt 1999; Thackway, Ward et al. 1999). The NEPOD study found that post-treatment overdoses in patients who received naltrexone were eight times the rate recorded for patients who left agonist treatments such as methadone, buprenorphine and LAAM (Diguisto, Shakeshaft et al. 2004). Forty-four percent of overdoses occurred within 2 weeks of stopping naltrexone. They recommended that clinicians alert naltrexone patients of the risk of heroin overdose after ceasing naltrexone. High overdose rates have been reported in two studies. Bell et al (Bell, Young et al. 1999) reported overdose rates of 10% in 30 subjects over 3 months (one fatal) and Miotti et al(Miotto, McCann et al. 1997) reported 16% in 81 subjects over 12 months (four fatal). An increased overdose rate if naltrexone is used intermittently and alternated with heroin is biologically plausible. Ritter (Ritter 2002) reviewed the literature regarding the relationship between naltrexone and depression as well as the risk of heroin overdose. She

concluded that there was no evidence of an association between naltrexone and depression but there was mounting evidence of increased risk of overdose particularly given high treatment drop-out rates.

The best results for naltrexone have been achieved in selected groups of well supported and motivated patients such as business executives, physicians, prison parolees and participants in prison work release programs. While the meta-analytic review, previously mentioned, found no evidence that naltrexone significantly improved treatment retention or opioid use, they did find that in conjunction with behavioural treatment, naltrexone significantly reduced the risk of re-incarceration (OR=0.3; 95% CI 0.12-0.76) compared to placebo(Kirchmayer, Davoli et al. 2002). They attributed this finding to the higher motivation of subjects in these studies to avoid re-incarceration. Brahen (Brahen, Wiechert et al. 1984) studied a work release program (1974-1984) for 691 inmates on Long Island, New York. No control group was used but prison officials and clients considered the program to be successful in the transition from prison to employment.

A study of parolees considered to be at high risk of relapse due to the increased opportunity to obtain heroin outside prison (Cornish, Metzger et al. 1997) examined the effect of naltrexone treatment on reducing the rate of re-arrest and opioid use. Fifty-one subjects were assigned at random in a 2:1 ratio to a six-month program of probation plus naltrexone and counselling (n=34) or to a control group of probation plus counselling alone. Fifty-two percent of the experimental group and 33% of the control group remained in treatment for six-months although this was a non-significant difference. Those treated were significantly less likely to test positive for opioids (8% vs 30%) and to have been re-incarcerated (26% vs 56%). In Singapore, Chan (Chan 1996) studied a cohort of 66 detained addicts between 1991 and 1993. The subjects participated in a community work release program where they were guaranteed employment and were allowed to return to their homes after working hours with curfews being enforced and electronic surveillance. The community program was combined with naltrexone in the first year and 76% of subjects had completed the program. Naltrexone, counselling and electronic tagging were withdrawn in the second year and program retention fell to 32%. Washton (Washton, Pottash et al. 1984) reported superior treatment 12 month retention rates in 114 business executives (64%) and 15 physicians (74%). Most subjects were at risk of job loss or deregistration if treatment failed.

Oral naltrexone maintenance for inmates with a history of heroin dependence was introduced into the NSW prison system in 2001. This study aimed to evaluate the effect of the introduction of naltrexone compared to other treatment interventions on: rates of treatment acceptance, retention, compliance and side effects; hepatitis C/HIV incidence and risk behaviours; heroin use, other drug use, heroin injecting, sharing of injecting equipment; and other health and psychosocial outcomes.

2. METHODS

2.1 Design

This study was an open, non-randomised pre-post trial. Two hundred and four inmates applying for heroin treatment, who satisfied eligibility criteria, were recruited over 18 months between January 2002 and July 2003. Recruitment took place in 14 prisons including remand, low, medium and high security prisons (See Appendix A). An attempt to randomise subjects into three treatment groups (naltrexone, methadone, drug free counselling) was unsuccessful. Naltrexone was only available to one in three subjects allocated to the naltrexone group because it was not available outside the study unlike methadone or buprenorphine treatment which were available to all subjects at baseline and through the study period. Most subjects were already enrolled in methadone (54%) or buprenorphine (17%) at baseline. At the same time, the uptake of naltrexone was poor (14%) partly due to the inability of subjects to detoxify from methadone within the six-month study period. All subjects were offered a referral to drug and alcohol counselling but many (51%) did not take up this offer. Thus the treatments received by each randomisation group were essentially uncontrolled and self-selected. Accordingly, subjects have been divided into five mutually exclusive treatment exposure groups. Subjects who received naltrexone prior to their six-month follow up interview were categorised as the naltrexone study group (n=9). Subjects who received buprenorphine were categorised as the buprenorphine group (n=39). Subjects who received MMT only, were categorised as the MMT group (n=89). Subjects who received AOD counselling only, were categorised as the AOD group (n=23) and finally subjects who did not receive any of these treatment were categorised as a No Treatment group (n=26).

2.2 Eligibility criteria

For an inmate to be eligible to participate in this trial it was essential to:

Be male

Have a history of heroin injecting

Have a prison sentence of at least six months

Be drug free or willing to undergo detoxification

Be willing to provide blood and hair samples when required

Be willing to give informed consent

Exclusion criteria were;

Being HIV positive

Active or unstable psychiatric or medical condition

Being female

Inmates who were HIV positive had immediate access to naltrexone. Previous research had indicated that wait list designs were not feasible among female inmates as the supply of

methadone places met demand from female inmates. Further, most female inmates served sentences of less than three months. A total of 776 inmates were assessed for the study and 572 were excluded (74%). Most exclusions were due to sentences being less than six months (44%) or inmates declining naltrexone (26%) (See Appendix B).

2.3 Study Procedures

2.3.1 Assessment

All inmates who applied for naltrexone were given a comprehensive drug and alcohol assessment by a trained Clinical Nurse Consultant (CNC) and, if they met study eligibility criteria, they were referred to the prescribing Medical Officer for further assessment. Inmates with a history of mental illness were referred to a Psychiatric Registrar. All participants were offered a referral to a drug and alcohol counsellor. Participants were also referred to the Public Health Unit for testing for blood borne viruses and vaccinations where appropriate. In addition to the normal intake procedures for the prison opiate dependence treatment program, the trial nurses explained the study, obtained informed consent and invited inmates to participate. Subjects were interviewed and a sample of hair and blood was collected. Study participants received a $10 postal order for each of the two study interviews they attended.

2.3.2 Treatment

Before starting naltrexone, inmates had to provide a negative urine result for opiates including methadone. They then underwent a two part naloxone challenge. If the first injection elicited a clinically observable or self-reported response, the inmate was asked to return at a later date. If it was negative, a second injection of naloxone was given and, if this challenge was negative, naltrexone treatment was started. Naltrexone was commenced at 25 mg/day for the first two days increasing to 50 mg/day. All doses were supervised. Side effects were systematically reviewed for one week using daily symptom checklists. All inmates commencing naltrexone treatment were inducted at their prison of residence. The Drug Free Wing at Parklea Prison was available during part of the study but was not used as all study participants chose to remain in their priosn of residence.

Failure to continue naltrexone after release was a particular concern as overdose risk is highest during the 2-weeks post-release and may even be higher if patients recently discontinued naltrexone. Free placement in community naltrexone programs was arranged for subjects who were receiving naltrexone and who were about to be released. Naltrexone is not subsidised under the Pharmaceutical Benefits Scheme (PBS) and the average monthly cost is approximately $375 including dispensing fees. This cost was borne by Corrections Health Service. Inmates received a triple dose on the day of release to protect them for the first three days post-release. Protocols were implemented requiring three post-release contacts. The clinical trial nurse contacted the community drug and alcohol specialist and dosing pharmacy within 1-2 days of release to confirm attendance. Those patients who did not attend for community doses were contacted by telephone and then two letters were sent.

All inmates treated with naltrexone were advised repeatedly of the high risk of overdose if this treatment was only taken intermittently and heroin consumed following a naltrexone treatment period.

2.3.3 Follow-up procedure

All subjects were scheduled for re-interview six months after their first interview. Trial nurses located inmates and conducted the follow-up interviews and collected hair and blood samples. Inmates who left the NSW prison system were not followed up. Inmates who left and then

returned to the NSW prison system were re- interviewed. All inmates enrolled in the study were offered naltrexone after the follow up interview. At 12 months, prison medical records were checked to collect further information on treatment uptake, compliance, retention, concomitant medications and side effects. All data were kept confidential and de-identified. Results of hair and blood assays were not made available to inmates, clinicians or prison authorities.

2.4 Outcome measures

2.4.1 Serology

Finger prick blood samples were collected with a single use lancet. Inmates' fingers were dabbed onto blotting cards filling three circles (1 cm in diameter). Samples were tested for antibodies to HIV and hepatitis C by the Centre for Immunology, St. Vincent's Hospital, Sydney. The samples were assayed using an algorithm that has a high correlation with assays of venous blood samples (NCCLS 1988). HIV antibody was detected using Genetic Systems HIV-1 ELISA tests, and if reactive twice, underwent Western blot confirmatory testing. Specimens were tested for HCV antibody using a modified third generation enzyme immunoassay (Abbott HCV 3.0, Chicago II). A modified cut-off value for optical density was calculated to capture greater than 95% of the seronegative population. Specimens were considered positive for anti-HCV if the optical density cut- off ratio was greater or equal to 1.0 on initial and subsequent testing.

2.4.2 Hair Analysis

Quantitative results for hair analysis (nanograms per mg of hair) were analysed. Over 50 hairs were cut approximately 2 mm from the scalp at the vertex. Hair samples were tested for morphine and the heroin metabolite 6-monoacetyl-morphine (6-MAM) by the Victorian Institute of Forensic Medicine. At baseline, two cm of hair cut from the root was analysed for morphine to assess heroin use in the previous two months. At follow-up the process was repeated. Results have been reported in terms of sample weight, calculated limit of detection (LOD) and concentration of morphine (ng/mg). Morphine concentrations greater than the calculated LOD for each individual sample were deemed presumptive of heroin use. For a sample weight of 10 milligrams the calculated LOD was1 nanogram per milligram of hair.

2.4.3 Interview Schedule

The baseline interview schedule covered demographic characteristics, prison history, drug use history both in the community and in prison, HIV/hepatitis C risk taking behaviour, drug treatment history and the results of recent HIV, hepatitis C and hepatitis B tests if any. Inmates were asked about drug use, injecting and sharing in the two months preceding interview while they were in prison. The Opiate Treatment Index (OTI) (Darke, Hall et al. 1992) was used to measure HIV/hepatitis C risk taking behaviour, physical, psychological and social functioning at baseline and follow up. At follow up, questions about drug use, were repeated. Questions about other risk behaviour including tattooing and sexual activity were also asked at follow up. Subjects were also asked questions about the treatments they received including pharmacotherapies and drug free counselling.

2.5 Data Analysis

Data were analysed using SPSS for Windows (version 11.0). Statistical tests were two-tailed using a 0.05 level of significance and 95% confidence intervals. T-tests and analysis of variance (ANOVA) were used for continuous variables. Medians and ranges were reported for skewed

data and analysed using Mann- Whitney U, Wilcoxon and Kruskal- Wallis tests. The chi-square statistic was used for categorical data. Retention data were analysed using the Kaplan-Meier Log Rank Test.

2.6 Ethical Approval and payment of subjects

Ethical approvals were obtained from the Committee on Experimental Procedures involving Human Subjects at the University of NSW, the Research Ethics Committee of St. Vincent's Hospital, the Research Ethics Committee of Corrections Health Service and the Institutional Ethics Committee of the NSW Department of Corrective Services. Subjects were remunerated $10 for each of two research interviews.

2.7 Steering Committee

A steering committee was constituted to oversee the project. The Committee comprised; Dr Alex Wodak (St. Vincent's Hospital), Dr Richard Matthews, Dr Gilbert Whitton, Sandy Ozols and Sharon Barton (Corrections Health Service), James Shearer and Dr Kate Dolan (National Drug and Alcohol Research Centre), and Paul Finlay (Alcohol and Other Drugs, HIV and Health Promotion Unit). An inmate representative from the Long Bay Prison Complex joined the Committee.

3. RESULTS

3.1 Sample Characteristics

Study participants had a mean age of 31 years (sd 7 years). Twenty one percent were of Aboriginal or Torres Strait Islander descent. They had been in prison an average of five times (sd 4). The most serious offence committed for which they had been presently sentenced was armed robbery (28%), break and enter (18%), robbery (15%) and assault (11%). Security classifications were 51% C (minimum), 15% B (medium), 14% A (maximum) and 19% E (escapee). Subjects had been in prison for a median of 76 weeks (R 1-780) and had median sentence lengths of 286 weeks (R: 20-1560). They started injecting at an average age of 18 (sd 4 years) and commenced daily injection at an average age of 20 (sd 5 years). Eighty-one percent reported a history of drug injecting while in prison, with nine percent reporting they had started injecting while in prison. Seventy-seven reported the results of their last hepatitis C status as positive. Baseline characteristics by treatment exposure group and follow up status appear in table 3.1.

Table 3.1 Baseline characteristics of subjects by treatment received and follow up status

Variable	*Naltrexone (n=9)*	*Buprenorphine (n=39)*	*MMT (n=89)*	*AOD (n=23)*	*No Treatment (n=26)*	*Lost to follow-up (n=18)*
Mean age (sd)	28 (5)	32 (6)	31 (7)	31 (8)	29 (6)	30 (5)
Aboriginal or Torres Strait Islander %	22%	31%	17%	22%	19%	17%
Mean times in prison (sd)	8 (13)	5 (4)	6 (4)	3 (2)	5 (3)	6 (5)
Most Serious Offence						
Armed Robbery	11%	36%	28%	22%	31%	28%
Robbery	22%	5%	16%	30%	15%	6%
Break & Enter	22%	10%	20%	22%	15%	17%
Assault	11%	8%	15%	4%	17%	6%
Security Classification						
A1	-	-	1%	-	4%	-
A2	11%	23%	10%	-	23%	6%
B	22%	10%	12%	22%	19%	22%
C1	11%	33%	34%	30%	15%	11%

C2	33%	21%	16%	22%	23%	33%
C3	-	8%	1%	4%	-	-
E1	-	3%	2%	-	4%	6%
E2	22%	3%	23%	22%	12%	17%
Median weeks in prison at baseline	60 (9-364)	114 (1-780)	72 (1-728)	61 (4-780)	56 (1-676)	50 (1-429)
Median sentence length weeks	384 (26-716)	416 (36-1560)	260 (30-1248)	312 (72-1248)	254 (36-1124)	260 (20-884)
Mean age first injection (sd)	18 (4)	17 (4)	17 (4)	18 (4)	19 (5)	20 (5)
Mean age daily injection (sd)	19 (3)	19 (5)	19 (5)	20 (6)	20 (5)	21 (5)
Ever shared syringes in community %	78%	69%	74%	61%	65%	61%
Mean weeks since shared syringes in community (sd)	173 (124)	267 (252)	254 (264)	166 (235)	168 (158)	250 (206)
Ever injected in prison %	78%	95%	81%	74%	75%	83%
Started injecting in prison %	14%	11%	7%	10%	5%	13%
Ever shared syringes in prison %	100%	90%	**65%***	**57%***	87%	78%
Mean weeks since shared syringes in	75 (68)	96 (131)	186 (258)	96 (182)	74 (126)	121 (163)

prison (sd)						
Self reported HCV prevalence %	67%	74%	74%	73%	74%	67%

*p=0.001

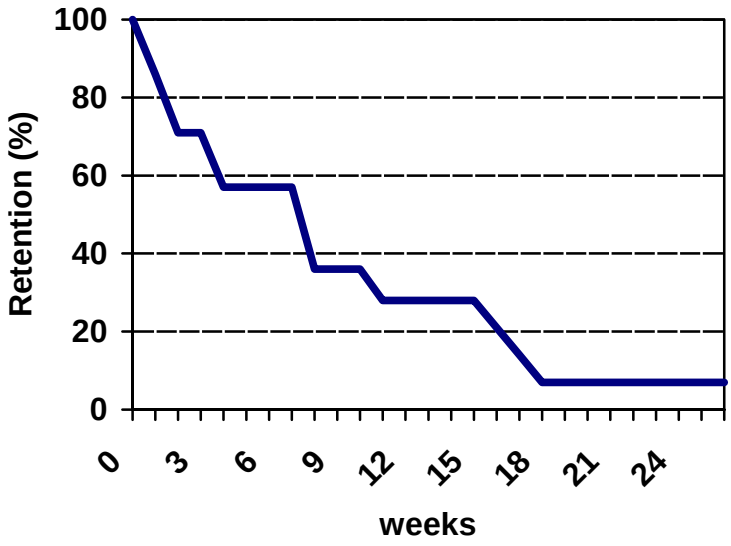
Differences in baseline demographics between exposure groups and follow up status were examined using one way ANOVA and Chi-Square with significance levels set at the 0.01 level to compensate for multiple group and variable comparisons. Subjects in the methadone and AOD counselling groups were less likely to report a history of syringe sharing in prison (p=0.001).
The aim of the study was to follow up subjects after six months. Follow up interviews were conducted with one hundred and eighty six subjects representing a 91% follow up rate. The mean duration of follow up was 29 weeks or under seven months (sd 14 weeks). Most subjects had not changed prisons since their baseline interview (62%) and very few had been released and re-incarcerated (4%).

3.2 Naltrexone Treatment

3.2.1 Retention

Sixty six subjects were randomised to naltrexone treatment, however, only nine subjects started naltrexone treatment (14%) with the remainder declining or failing to start naltrexone. A further five subjects commenced naltrexone after their follow up interview. Retention, compliance and side effect data were analysed for all 14 subjects who commenced naltrexone. Retention in naltrexone treatment over 26 weeks is illustrated in figure 3.1. Only one subject remained in treatment at the end of 26 weeks. Almost two thirds of subjects who started naltrexone had ceased after seven weeks of treatment. Release from prison was the most common reason for discontinuing naltrexone. Seven subjects were released from prison, five ceased naltrexone entirely and two ceased attending community pharmacy for naltrexone after 4 days and sixty days. Four subjects that were released on naltrexone subsequently returned to prison. Three subjects ceased due to reported side effects (see 3.2.3). Three ceased due to suspected diversion or prison movement.

Figure 3.1. Retention in naltrexone over 26 weeks (n=14)



3.2.2 Compliance

Compliance to daily naltrexone is an important aspect of naltrexone treatment. The risk of heroin overdose increases in subjects who fail to adhere to daily doses, as they lose their original opiate tolerance. Subjects may be tempted to miss doses if they believe that heroin may become available. Compliance while subjects were receiving naltrexone treatment in the study was extremely good. Compliance to daily doses ranged between 88% and 100%. Average compliance was 98% over a median treatment duration of 53 days (R 5-508). Ten out of 14 subjects attended for daily doses every day they were in naltrexone treatment.

3.2.3 Side effects and serious adverse events

Generally naltrexone has few side effects but these can sometimes be difficult to distinguish from late stage withdrawal symptoms (Foy, Sadler et al. 1998). The main side effects reported have been headaches, low mood, disturbed sleep and nausea. Our objective was always to minimise side effects attributable to opiate withdrawal by thorough induction screening for opiates. There were no deaths or other serious adverse events requiring hospitalisation. Most subjects reported no side effects (8 out of 14 cases). A small number of subjects (n=3) reported mild side effects during the induction phase such as dizziness, nausea, headache and loss of appetite which all resolved or were manageable. Three subjects ceased naltrexone treatment due to reported side effects including moderate headache, insomnia, lethargy and loss of appetite in one case, disturbed sleep in another case and depression in a third case. Many reported problems were not necessarily associated with naltrexone but pre-existing complaints or were prison related issues with other inmates, family or legal matters.

3.2.4 Treatment preferences

Table 3.2: Follow Up Treatment Status and Preferences: Subjects Originally Randomised to Naltrexone.

(n=63)	Treatment at Follow Up	Treatment Preference at Follow Up
Naltrexone	5%	18%
Methadone	44%	31%
Buprenorphine	8%	16%
AOD Counselling	14%	7%
No treatment	29%	24%

The follow up treatment status and treatment preferences of the 63 subjects who were randomised to naltrexone and followed up, is summarized in table 3.2. The main reason that subjects had not commenced naltrexone was that they had failed to detox from methadone or buprenorphine. A majority preferred to continue with agonist maintenance with a trend from methadone towards buprenorphine. Many subjects were opiate free and preferred not to accept daily medication or to rely solely on AOD drug fee counselling when needed.

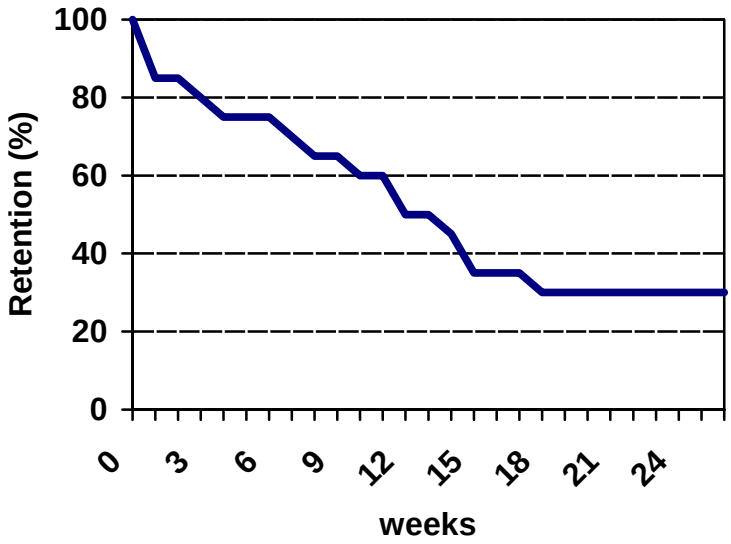
Of the 14 subjects who started naltrexone, at the end of the study, only one was still receiving naltrexone treatment. Out of the seven subjects released, three remained in the community while four had been re-incarcerated and three of these entered the prison methadone program. One subject was retreated and released and continued to collect naltrexone in the community. Another subject who had ceased due to a prison movement has requested to recommence naltrexone. His case will be considered after psychiatric review for depression. Four subjects remain in prison and have chosen not to receive any treatment. One subject who ceased due to side effects is currently enrolled in the prison buprenorphine program.

3.3 Buprenorphine Treatment

3.3.1 Retention

Thirty nine subjects received buprenorphine between baseline and follow up interview. They have been designated as the buprenorphine treatment exposure group. Retention data in figure 3.2 is for subjects who commenced buprenorphine during the study period but excludes subjects who were already on buprenorphine at baseline (n=13) and subjects who received a short period of buprenorphine for detoxification purposes (n=5). Main reasons for discontinuing buprenorphine were diversion (20%), return to methadone (15%), release (10%) or completion of program (10%).

Figure 3.2. Retention in buprenorphine over 26 weeks (n=21)



3.3.2 Compliance

Average compliance to daily doses was 98% (range 86%-100%) over a median treatment period of 72 days (R 2-182). Subjects received a median dose of 8 mg/day (R 4-24 mg). Side effect and concomitant medication data were not systematically collected outside the naltrexone group.

3.3.3 Treatment preferences

Table 3.3: Follow Up Treatment Status and Preferences: Subjects Who Received Buprenorphine.

(n=38)	Treatment at Follow Up	Treatment Preference at Follow Up
Naltrexone	-	8%
Methadone	18%	13%
Buprenorphine	58%	55%
AOD Counselling	5%	8%
No treatment	18%	13%

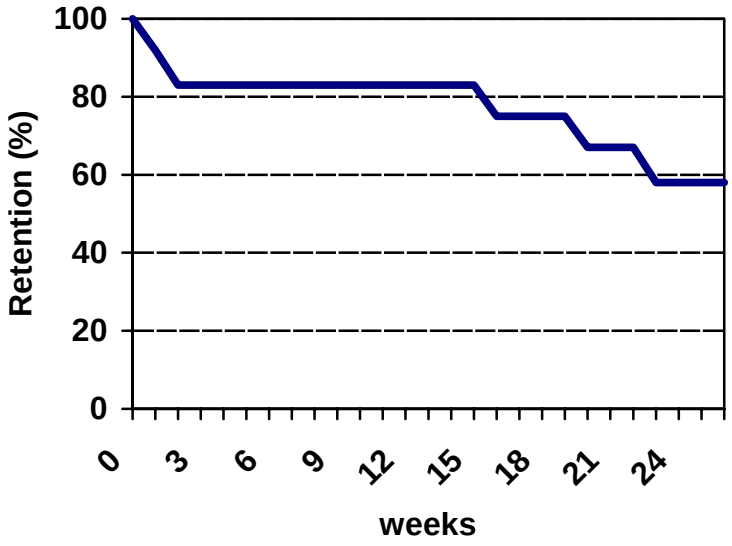
The follow up treatment status and treatment preferences of the 38 subjects who received buprenorphine and were followed up, is summarized in table 3.3. The majority preferred to remain on buprenorphine with equal small proportions choosing to return to methadone or receive no treatment. Naltrexone and drug free counseling were the least popular choices in this group.

3.4 Methadone Treatment

3.4.1 Retention

Eighty-nine subjects received only methadone between baseline and follow up interview. They have been designated as the methadone treatment exposure group. Retention data in figure 3.3 is for subjects who commenced methadone during the study period and excludes subjects who were already receiving methadone at baseline (n=77). Two subjects were released, two successfully completed the program and one gave no reason for discontinuing.

Figure 3.3. Retention in methadone over 26 weeks (n=12)



3.4.2 Compliance

All 12 subjects who started methadone during the study period had 100% compliance to daily doses over a median treatment period of 182 days (R 2-182). Subjects received a median dose of 60 mg/day (R 5-80 mg). Side effect and concomitant medication data were not systematically collected outside the naltrexone group.

3.4.3 Treatment preferences

Table 3.4: Follow Up Treatment Status and Preferences: Subjects Who Received Methadone Only.

(n=89)	Treatment at Follow Up	Treatment Preference at Follow Up
Naltrexone	-	11%
Methadone	75%	57%
Buprenorphine	-	6%
AOD Counselling	5%	6%
No treatment	20%	16%

The follow up treatment status and treatment preferences of the 89 subjects who received methadone only and were followed up, is summarised in table 3.4. While most elected to remain in methadone treatment, there were proportions who preferred no treatment or naltrexone. Very few subjects nominated buprenorphine or AOD counseling.

3.5 Comparison of treatment retention: methadone, buprenorphine and naltrexone.

Treatment retention in subjects who commenced naltrexone (n=14), buprenorphine (n=21) or methadone (n=12) during the study is presented in figure 3.4. There was a significant difference in treatment retention between the treatment groups (Log Rank Statistic =10.75, df=1, p=0.001). A comparison between groups found treatment retention was significantly higher in methadone compared to naltrexone (Log Rank Statistic = 11.52, df=1, p=0.0007). There were no statistically significant differences between buprenorphine and naltrexone (Log Rank Statistic = 3.27, df=1, p=0.07) or between buprenorphine and methadone (Log Rank Statistic = 3.09, df=1, p=0.08). Mean treatment retention by group is presented in figure 3.5.

Figure 3.4. Retention by Group over 26 weeks

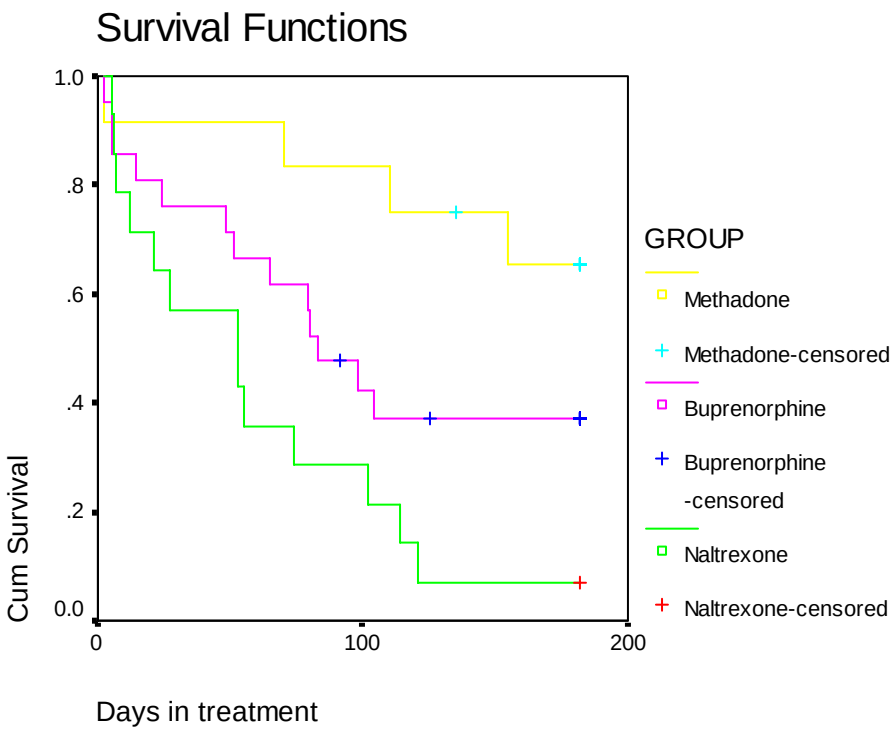
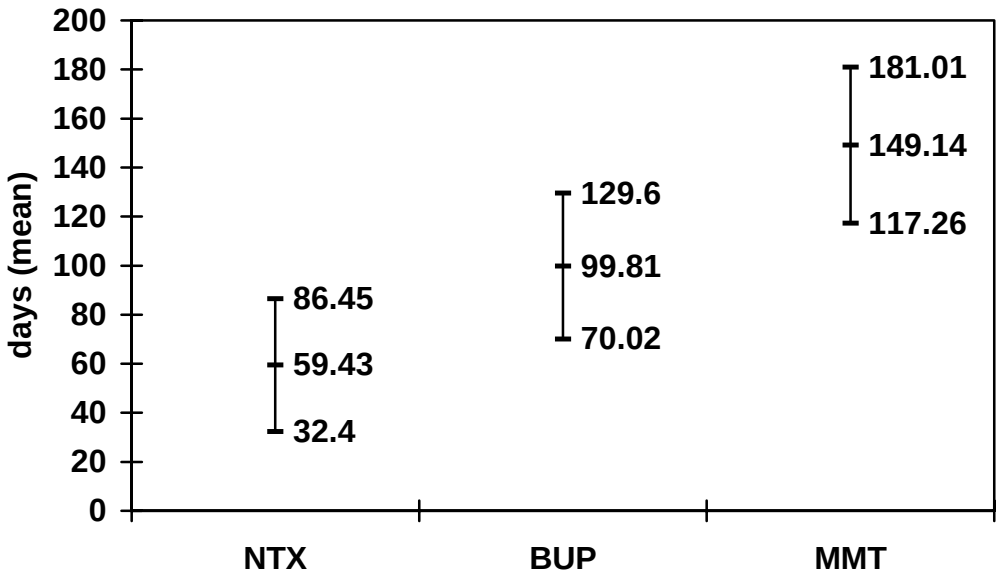


Figure 3.5: Mean days in treatment (95% CI) by group



3.6 AOD Counselling Treatment

All trial participants were offered a referral to drug and counsellors employed by the Alcohol and Other Drugs HIV and Health Promotion Unit of the Department of Corrective Services. The main objective of the unit is reduction of substance related harms and recidivism. This unit offered a range of short term and longer term drug and alcohol counselling programs delivered individually and, in some prisons, in groups. The unit employs over 90 AOD workers and conducts an intensive pre-release 12 week program at a therapeutic community known as Ngara Nura. In 2002-2003, alcohol and drug workers screened 4,612 inmates for alcohol or drug related needs, assessed 5,144 inmates to determine the extent of their alcohol and/or other drug problems, assisted in case management and provided counselling and group programs to 10,096 inmates. Additional education and programs on relapse prevention, healthy lifestyle and infection control were also conducted during this period (NSW Department of Corrective Services 2003). Policies and program availability tended to vary across prisons as drug and alcohol counsellors worked largely independently and resource availability also varied. For example, in some prisons referrals could not be accepted as inmates wishing to receive drug and alcohol counselling were expected to make appointments under their own initiative. The nature and availability of programs varied over the course of the study as programs were revised and new programs introduced. The uptake of AOD counselling is detailed in table 3.5.

Table 3.5: AOD Programs Attended by Subjects* (N=90)

Program	N (%)
One-to-one AOD counselling	41 (46%)
Relapse Prevention	24 (27%)
Harm Minimisation Program	18 (20%)
Short Term AOD Course	13 (14%)
One Day Health Information Course	10 (11%)
Anger Management	5 (6%)
Narcotics Anonymous	3 (3%)
Phoenix Program	3 (3%)
Ngara Nuru	2 (2%)
NET program	2 (2%)
Healing Addictions	2 (2%)
Other (1 attendance each)**	13 (14%)

*Multiple responses permitted

** Lifeskills, 12 step, stress management, breakout, conflict resolution, HIV awareness, VPP program, other AOD attendance not specified.

Almost half of subjects did not attend AOD counselling. During the study follow up it became apparent that many subjects were not attending or receiving counselling. A question was introduced to determine why subjects had not attended or received AOD counselling. The reasons for non-attendance are detailed in table 3.6. Missing data (not known) represents those subjects followed up prior to the introduction of this question.

Table 3.6: Reasons for non-attendance of AOD Programs (N=93)

Reason	N (%)
Declined/refused	22 (24%)
Not offered	20 (22%)
Previously attended	10 (11%)
Not known	41 (44%)

3.6.1 Treatment preferences

Table 3.7: Treatment Preferences: Subjects Who Received AOD Counselling Only or No Treatment.

	AOD counselling (n=23)	No Treatment (n=26)
Naltrexone	13%	19%
Methadone	4%	12%
Buprenorphine	9%	4%
AOD Counselling	35%	4%
No treatment	39%	62%

Among subjects who received only AOD counselling during the study, similar proportions preferred to continue drug free counselling or to have no treatment. Results are presented in tables 3.7. A small proportion was interested in naltrexone while very few were interested in either methadone or buprenorphine. Among subjects who did not participate in any treatment during the study, most did not wish to receive any further treatment.

3.7 Drug Use and Injecting

3.7.1 Baseline drug use

Subjects lost to follow up and those who did not accept any treatment were more likely to have used heroin in the two months prior to enrolling in the trial (p=0.01). Results are presented in tables 3.8. Most subjects in the buprenorphine and methadone groups were already receiving these treatments at baseline (46% and 87% respectively). Subjects in the AOD counselling group were significantly less likely to have been on methadone prior to study entry (p<0.001).

Table 3.8 Drug use in two months prior to baseline interview

Drug	*Naltrexone (n=9)*	*Buprenorphine (n=39)*	*MMT (n=89)*	*AOD (n=23)*	*No Treatment (n=26)*	*Lost to follow-up (n=18)*	*Total*
Heroin	11%	15%	15%	22%	**42%***	**44%***	22%
Prescribed naltrexone	-	3%	1%	-	-	-	1%
Prescribed Methadone	22%	44%	**87%****	**4%****	19%	50%	54%

Diverted Methadone	11%	5%	10%	9%	8%	17%	9%
Amphetamine	-	15%	10%	22%	19%	22%	14%
Cocaine	-	3%	3%	-	4%	11%	3%
Ecstasy	-	-	1%	8%	4%	-	2%
Tranquilisers	22%	5%	17%	4%	15%	11%	13%
Steroids	-	5%	1%	-	4%	-	2%
Cannabis	56%	46%	56%	70%	81%	61%	59%
Prescribed Buprenorphine	22%	**46%****	7%	9%	12%	22%	17%
Diverted buprenorphine	-	7%	17%	16%	7%	18%	13%

***p=0.01**
****p<0.001**

3.7.2 Baseline injecting behaviour

There were no significant baseline differences between exposure group or follow up status in drug injecting or syringe sharing. Results are presented in tables 3.9. Large variations in some measures were due to outlier reports of frequent injecting activity and small cell sizes.

Table 3.9 Drug injecting and syringe sharing in two months prior to baseline interview

	Naltrexone (n=9)	*Buprenorphine (n=39)*	*MMT (n=89)*	*AOD (n=23)*	*No Treatment (n=26)*	*Lost to follow-up (n=18)*
Any injecting	11%	23%	21%	30%	39%	50%
Mean times injected heroin (sd)	3 (-)	11 (14)	30 (67)	3 (2)	10 (14)	34 (50)
Median times injected heroin (R)	3 (-)	8 (1-35)	2 (1-240)	2 (1-6)	4 (1-42)	6 (1-120)
Mean times injected any drug (sd)	3 (-)	8 (12)	65 (213)	11 (13)	15 (21)	101 (222)
Median	3 (-)	2 (1-37)	7 (1-	4 (1-35)	6 (1-67)	12 (1-682)

times injected any drug (R)			940)			
Any sharing	100%	56%	74%	86%	90%	67%

3.7.3 Follow up drug use

The only significant between-group differences at the 0.01 level were in the use of prescribed naltrexone, methadone and buprenorphine in the respective treatment groups (see Table 3.10). Drug use overall declined across all categories except prescribed buprenorphine which increased (from 17% to 25%) while prescribed methadone declined (from 54% to 40%) as subjects detoxified in preparation for naltrexone or transferred to buprenorphine. Heroin use declined (from 22% to 14%) with the greatest decline achieved in the AOD group (from 22% to 9%) although injecting of buprenorphine increased in that group (from 16% to 22%). Declines in reported use of heroin also occurred in all other groups except the naltrexone group.

Table 3.10 Drug use in two months prior to follow up interview

Drug	*Naltrexone (n=9)*	*Buprenorphine (n=39)*	*MMT (n=89)*	*AOD (n=23)*	*No Treatment (n=26)*	*Total (n=186)*
Heroin	22%	10%	11%	9%	31%	14%
Prescribed naltrexone	**78%*** **	-	-	-	-	4%
Prescribed Methadone	-	31%	**70%*** **	-	-	40%
Diverted Methadone	11%	5%	6%	-	15%	7%
Amphetamine	-	8%	6%	9%	4%	6%
Cocaine	-	3%	1%	-	4%	2%
Ecstasy	-	**8%***	-	-	-	2%
Tranquilisers	33%	8%	8%	4%	19%	10%
Steroids	-	-	-	4%	-	1%
Cannabis	56%	41%	44%	52%	58%	47%
Prescribed Buprenorphine	11%	**69%*** **	8%	22%	27%	25%
Diverted buprenorphine	11%	8%	8%	22%	19%	11%

***p<0.05**
****p<0.01**
*****p<0.001**

3.7.3 Follow up injecting behaviour

There were no significant between-group differences in drug injecting and syringe sharing at follow up (Table 3.11). Large variations were due to outliers and small cell sizes. Drug injecting declined in subjects who received buprenorphine, AOD counselling and methadone but was stable in those who received no treatment and increased in the naltrexone group. The most commonly injected drugs were heroin, diverted buprenorphine and methadone.

Table 3.11 Drug injecting and syringe sharing in two months prior to follow up interview

Drug	*Naltrexone (n=9)*	*Buprenorphine (n=39)*	*MMT (n=89)*	*AOD (n=23)*	*No Treatment (n=26)*
Any injecting	33%	18%	18%	35%	39%
Mean times injected heroin (sd)	8 (9)	25 (46)	21 (46)	6 (5)	8 (11)
Median times injected heroin (R)	8 (2-14)	3 (1-94)	2 (1-145)	6 (2-9)	3 (2-30)
Mean times injected any drug (sd)	9 (6)	33 (64)	25 (41)	13 (25)	11 (13)
Median times injected any drug (R)	10 (2-14)	6 (1-178)	4 (1-150)	4 (1-75)	4 (1-34)
Any sharing	100%	36%	48%	67%	91%
If Yes time since last shared (weeks).	27 (48)	76 (42)	69 (45)	24 (43)	13 (29)
Any sharing of injecting equipment?	100%	36%	56%	100%	100%
If Yes time since last shared (weeks).	27 (48)	76 (42)	73 (43)	26 (42)	13 (29)

3.8 Opiate Treatment Index (OTI) Outcomes

OTI outcomes are summarised in Table 3.12 (baseline) and Table 3.13 (follow up). Overall there were no significant between-group differences on any OTI outcome domains at follow up. HIV risk scores for the groups at baseline ranged from low risk to below average risk categories since only 27% had injected drugs in the two months preceding baseline and there were only four reports of sexual activity. At follow up, HIV risk scores declined in all groups except the naltrexone group. Baseline Health scores ranged from better than average for IDU in the naltrexone and AOD groups to average for the other groups. All groups had improved by follow up. Psychological adjustment at baseline was in the average clinical range for all groups. This had improved to better than average at follow up. Social adjustment at baseline was in the above average clinical range for all groups although interpretation of this instrument is limited by the institutional context. As with the other OTI measures, social adjustment improved to well above average at follow up.

Table 3.12 Between group comparison on OTI outcomes at baseline

	Naltrexone (n=9)	*Buprenorphine (n=39)*	*MMT (n=89)*	*AOD (n=23)*	*No Treatment (n=26)*
HRBS	1.5	2.3	2.6	3.7	5.0
Health	6.7	11.6	10.9	9.0	9.5
GHQ	4.6	7.0	6.2	3.4	4.6
Social	16.0	13.3	16.2	13.5	14.7

Table 3.13 Between group comparison on OTI outcomes at follow up

	Naltrexone (n=9)	*Buprenorphine (n=39)*	*MMT (n=89)*	*AOD (n=23)*	*No Treatment (n=26)*
HRBS	4.3	2.0	1.5	3.6	4.5
Health	6.6	9.9	8.8	6.7	7.2
GHQ	1.7	5.7	4.7	4.0	2.6
Social	13.0	12.5	13.2	11.1	14.4

3.9 Other risk behaviour at follow up

3.9.1 Sex related risks

Table 3.14 Between group comparison self-reported sexual activity at follow up

	Naltrexone (n=9)	*Buprenorphine (n=39)*	*MMT (n=89)*	*AOD (n=23)*	*No Treatment (n=26)*	*Total (n=186)*
Any sex?	-	1 (3%)	1 (1%)	2 (9%)	-	4 (2%)
If Yes how many different partners?	-	1	1	1	-	1
How often were condoms used?	-	never = 1	never = 1	never = 2	-	never =1

Ninety-eight percent of subjects described their sexuality as "straight" at the baseline interview and four subjects described themselves as "bisexual". Results are presented in tables 3.14. Four subjects reported sexual contact while in prison, all with one partner only (two of these were with their wives). No-one reported the use of condoms.

3.9.2 Tattooing risk

Table 3.15 Between group comparison on self-reported tattooing activity at follow up

	Naltrexone (n=9)	*Buprenorphine (n=39)*	*MMT (n=89)*	*AOD (n=23)*	*No Treatment (n=26)*	*Total (n=186)*
Any tattoo?	33%	5%	8%	4%	12%	9%
If Yes how many?	4 (1)	2 (1)	3 (2)	6 (-)	2 (1)	3 (2)
If Yes did you share the needle?	-	-	-	-	33% (n=1)	6% (n=1)
If Yes did you clean the needle?	100%	33% (n=1)	33%	100% (n=1)	33%	50%
Did you share the ink?	33% (n=1)	-	-	-	-	7% (n=1)

Nine percent of the entire sample had received a prison tattoo since the baseline interview. Results are presented in tables 3.15. Those who were tattooed received an average of three different tattoos. Only one subject reported the sharing of tattoo needles or tattooing ink.

3.9.3 Blood contact related risks

Table 3.16 Between group comparison of self-reported other blood contact risk at follow up

	Naltrexone (n=9)	*Buprenorphine (n=39)*	*MMT (n=89)*	*AOD (n=23)*	*No Treatment (n=26)*	*Total (n=186)*
Any fights with broken skin/blood?	-	10%	21%	9%	12%	15%
If Yes how many fights?	-	2 (1)	2 (1)	3 (1)	1 (-)	2 (1)
Other blood contact?	11% (n=1)	15%	9%	9%	4% (n=1)	10%

Fights constituted another potential exposure for blood borne viruses. Results are presented in tables 3.16. Other blood contact includes clean up of blood spills, sports accidents and assisting inmates who had accidents or engaged in self-harm.

3.10 Adverse events

3.10.1 Overdose

One subject reported a heroin overdose while in prison since the baseline interview. The subject reported that he was resuscitated by his cell mates who walked him around until he was awake.

3.10.2 Medical attention and new medications

Seventy-eight percent of subjects reported requiring medical attention since the baseline interview (n=145). Of these, 20% required medical attention for an injury, 14% due to illness, 6% for an assault, one subject required attention due to a suicide attempt and two because of self-harm. Two-thirds reported "other" reasons. Sixty-three percent of subjects reported receiving new medication prescriptions. Of these, 33% were for pain relief (anti-inflammatory, paracetamol, codeine); 19% for antibiotics; 10% for anti-depressants; 7% for tranquilisers and 5% for anxiolotics. Further analysis by treatment exposure group was not informative. Refer to

3.2.3 for a more detailed assessment of adverse events and concurrent medications in subjects who received naltrexone.

3.11 Comparison of self-reported drug use to urinalysis and hair analysis

The only consistently applied measure of drug use in the study was self-reported drug use data collected at the baseline and follow up interviews. Hair samples were also collected at these interviews and it was planned that these samples would be tested for the presence of heroin metabolites. However, the unexpectedly low prevalence of heroin use in the sample, the considerable cost of hair analysis and previous experience of relatively lower sensitivity of hair analysis compared to self-report, led to a decision to cease testing hair samples for heroin metabolites. Two hundred and seven hair samples (baseline n=136; follow up n=71) were analysed prior to the decision to discontinue hair sample analysis. One hundred and eighteen subjects were tested as part of a random and targeted urinalysis while they were in the study. As hair and urine were not systematically collected and tested, these results are used to examine the reliability of self-report but had no value when comparing study groups.

3.11.1 Self-reported heroin use compared to hair analysis

Table 3.17 Agreement between self-reported heroin use and hair analysis results (baseline and follow up combined)

		Self Reported Heroin Use		Total
		Negative	Positive	
Hair Result	Negative	173 86% of hair results 94% of self-report	28 14% of hair 85% of self-report	201
	Positive	11 69% of hair results 6% of self-report	5 31% of hair 15% of self-report	16
		184	33	217

Agreement between self-reported heroin use and hair analysis results is summarised in table 3.17. Both measures estimated heroin use in the two months prior to interview. Agreement between negative self-report and hair results was high (86-94%) while agreement between positive self-report and hair results was low (31%-15%). The frequency of heroin injections in the past two months represented a continuous measure of self-reported heroin use. A logistic regression was performed to test the relationship between reported frequency of heroin injections and hair analysis result. Higher frequency of injections significantly increased the odds of a positive hair result (p=0.025). This analysis suggests that self-report was more sensitive than hair analysis in detecting heroin use at low frequencies typical of prison heroin use.

3.11.2 Self-reported heroin use compared to urinalysis

Table 3.18 Agreement between self-reported heroin use and prison urinalysis program results (follow up)

		Self Reported Heroin Use		Total
		Negative	Positive	
Urinalysis Result	Negative	87 86% of urinalysis results 95% of self-report	16 16% of urinalysis 84% of self-report	103
	Positive	5 63% of urinalysis results 5% of self-report	3 38% of urinalysis 16% of self-report	8
		92	19	111

Agreement between self-reported heroin use and urinalysis program results over the course of the study is summarised in table 3.18. As with the hair analysis comparison, agreement between negative self-report and urinalysis results was high (85-95%) while agreement between positive self-report and urinalysis results was low (38%-16%). Note that 17% of subjects who were asked to provide a urine sample under this program failed or refused at some time and were charged and punished as if they had provided a positive sample. It could be reasonably assumed that many, if not most, failures to provide samples were due to recent drug use and that the program therefore under estimates the prevalence of drug use.

Taken together, the comparisons with hair analysis and urinalysis indicate that self-report obtained through confidential clinical interviews detected twice as many positive cases of heroin use. It is also interesting that both objective measures detected under-reporting of heroin use of about the same magnitude (5-6%). These results also suggest that the sensitivity of hair analysis and a program of random and targeted urinalysis are broadly comparable although they have not been directly compared here, as only 71 follow up hair samples were analysed and urinalysis results were limited to the follow up period.

3.11.3 Random and targeted urinalysis program results

Over the study period 118 subjects (58%) provided 262 urine samples for testing by the random and targeted urinalysis program conducted by the Department of Corrective Services. The results are summarised in table 3.19. Note that urine samples were not tested for buprenorphine. Proportions add up to more than 100% due to multiple test results.

Table 3.19 Random and targeted urinalysis program results

Drug	% Positive (n=118 subjects)	No. of samples	% of all samples (n=262)
Drug Free	83%	169	65%
Cannabis	23%	40	15%
Refused	17%	27	10%
Morphine heroin	7%	9	3%
Tranquilisers (non-prescribed)	6%	9	3%
Amphetamine	3%	4	1.5%
Methadone (non-prescribed)	2.5%	3	1%
Other	1%	1	<1%

3.12 Comparison of self-reported hepatitis C status and baseline serology

The high baseline prevalence of hepatitis C (77% by self-report) indicated that the study would have insufficient statistical power to confidently detect any between group differences in hepatitis C incidence. Given the cost of serology and lack of analytical benefit, a decision was taken to cease testing blood samples for hepatitis C and HIV antibodies. Ninety-eight blood samples (baseline n=87; follow up n=11) were analysed prior to the decision to discontinue blood testing. Agreement between self-reported hepatitis C status and serology results at baseline is summarised in table 3.20.

Table 3.20 Agreement between self-reported hepatitis C status and blood serology results at baseline

		Self Reported Hepatitis C Status			Total
		Negative	Positive	No test/unknown	
Serology Result	Negative	12	3	4	19 (19%)
	Positive	6	57	5	68 (81%)
		18 (21%)	60 (69%)	9 (10%)	87

Agreement between negative self-report and serology was high (21-19%) while agreement between positive self-report and serology was lower (69%-81%). However, once subjects who were unsure about their hepatitis C status or had not been tested are excluded, the agreement between positive self-report and serology results was high (77-81%). It is a concern that one third of subjects who reported they were hepatitis C negative had positive serology results. Half of those who did not know their status also had positive serology results.

4. Discussion

4.1 Naltrexone

This evaluation of the introduction of oral naltrexone as an alternative treatment for heroin users in the NSW prison system is a negative report. Although findings are limited by the absence of an effective control condition, oral naltrexone was unattractive to imprisoned male heroin users (14 subjects out of 204 (7%) commenced naltrexone over 2 years). Among those who started naltrexone, the six-month treatment retention rate of 7% was significantly lower than the 58% among subjects who started methadone ($p<0.001$). These findings of poor patient acceptability and treatment retention are consistent with other reports in Australia (Zador, Adams et al. 1999; McGregor, Ali et al. 2002; Mattick, Digiusto et al. in press) and overseas (Capone, Brahen et al. 1986; Fram, Marmo et al. 1989). Unlike the positive reports among prison parolees in the United States (Cornish, Metzger et al. 1997) and prison work program participants in Singapore (Chan 1996), this population of Australian imprisoned heroin users were not subject to any penalties or incentives to commence or remain in naltrexone maintenance.

There were few side effects associated with oral naltrexone and most of these resolved or were manageable. Compliance while in treatment was good with an average of 98% compliance to daily doses. There were no other significant differences between those subjects who received naltrexone or any other treatment exposure with respect to any other outcome including heroin and other drug injecting, HIV and hepatitis C risk behaviours or any other health or psycho-social outcomes. These latter findings were limited due to small sample sizes, multiple comparison groups and subject self-selection into the comparison groups. At the conclusion of the study, the CHS withdrew funding support for naltrexone except in cases where new inmates entered the prison system while receiving naltrexone. Inmates were able to request naltrexone but it was no longer provided free of charge and the cost of $375 per month had to be met by the inmate. Naltrexone has not been requested by any inmate under these conditions.

It could be argued that subjects who were on methadone or buprenorphine when they enrolled in this study were not given an adequate opportunity to detoxify and commence naltrexone maintenance treatment. The main clinical objective was to minimise side effects attributable to opioid withdrawal and to avoid precipitated withdrawal by a thorough induction screening for opioids. Detoxification was based on a methadone tapering method with transfer to buprenorphine detoxification. The CHS did not have the resources or experience to conduct more rapid induction techniques. Further such techniques remain experimental and, thus far, have not shown any clinically meaningful advantage over conventional detoxification (McGregor, Ali et al. 2002). Many subjects did successfully detoxify from methadone over the study as demonstrated by an overall decline in methadone treatment from 54% at baseline to 40% at follow up but most of these transferred to buprenorphine maintenance. Ultimately, oral naltrexone was an unpopular option among opioid dependent inmates. They preferred agonist treatments. Abstinent inmates preferred no treatment or drug free counselling.

The viability of an oral naltrexone program was also undermined by the high proportion of subjects who were released and immediately discontinued naltrexone even though specific arrangements were made for them in community programs. The risk of heroin overdose is greatest in the 24 hours after release as heroin users have easier access to larger amounts of heroin and their tolerance is lowered. No overdoses or deaths were noted in the released group. This may have been partly due to the 'triple dose' of naltrexone administered on the day of

release, however, the reluctance of subjects to continue naltrexone post-release and the resources necessary to organise community doses and follow up makes prison-based oral naltrexone programs problematic.

4.2 Buprenorphine

Six-month treatment retention in buprenorphine (30%) was lower than methadone (59%) although this was not statistically significant. The main reason for differential attrition was program suspension due to attempted diversion of buprenorphine. Buprenorphine maintenance was introduced during this study and there was limited experience of appropriate supervision. Supervision of buprenorphine is more difficult than methadone as sublingual buprenorphine tablets need more time to dissolve. Further, buprenorphine was not tested in the random and targeted prison urinalysis program, and for this reason was reputedly highly sought after. This situation was further compounded by the dramatic reduction in the availability of heroin. Indeed, after cannabis (47%) and heroin (14%), the injection of diverted buprenorphine (11%) was the third most frequent illicit drug reported during the study. Inmates enrolled in buprenorphine treatment were sometimes targeted by other inmates (so-called "stand-overs") and were threatened or attacked if they did not divert buprenorphine. This situation has now improved as buprenorphine and detection of diversion has improved.

4.3 AOD counselling

Subjects who chose drug fee counselling as their only treatment (n=23) reported reduced drug use (heroin, amphetamine, cannabis) although drug injecting increased from 30% to 35% due to increased injecting of diverted buprenorphine. They also improved on OTI measures of health, psychological adjustment and social adjustment but not in HIV risk again due to no changes in injecting behaviour. None of these outcomes were statistically significant due to small sample size and multiple comparator groups. These findings are also limited by potential self-selection bias, for example their OTI scores at baseline were generally lower, and therefore better, than for all other groups, suggesting better pre-existing social and psychological functioning. Nevertheless, AOD counselling was no less beneficial than any other treatment for those inmates who took it up.

4.4 Methadone

Retention in subjects who started methadone during this study was better than buprenorphine and significantly better than naltrexone. There was a shift towards buprenorphine which appeared to stabilise towards the end of the study. Fifteen percent of new buprenorphine patients returned to methadone within the first six-months of treatment. By the conclusion of the study preference for buprenorphine was low (6%) in the methadone group suggesting that most inmates who were able to transfer had done so. Reported drug use and injecting was modestly lower between baseline and follow up although it should be recalled that 87% of this group were enrolled in methadone at baseline and so baseline heroin use rates were already effectively suppressed.

4.5 Sample characteristics

In comparison with our earlier study of prison methadone, this sample was much older (mean age of 31 years compared to 27 years) and were serving much longer prison sentences (median sentence of 286 weeks compared to 73 weeks). This certainly seems to be a much more criminally entrenched group although this may also have been an artefact of the recruitment criterion of a six-month sentence. Forty percent of inmates (229 inmates out of 572) otherwise eligible for the study were excluded due to their sentence being shorter than six months. Naltrexone may also have been of more interest to older inmates with longer histories of heroin use or methadone treatment.

4.6 No treatment group

The largest treatment exposure group after methadone and buprenorphine was the 'no treatment' group (n=26). This seemed to be a highly treatment refractory group which was characterised by significantly higher heroin use and drug injecting at baseline. This was a feature they shared with the lost to follow-up group. They were also younger and had the shortest sentence length but these did not reach statistical significance due to small sample size. In terms of outcomes, heroin use fell in this group but was still triple that reported in methadone, buprenorphine or AOD counselling. This group was also the largest user of diverted buprenorphine (19%) and diverted methadone (15%). This group also had the highest HIV risk as measured by the OTI.

4.7 Non-opiate drug use

Cannabis was the most commonly reported illicit drug used with 47% reporting use at the follow up interview compared to 59% at baseline. Amphetamine use at baseline (14%) declined at follow up (6%). Non-prescription tranquiliser use was steady at 13% at baseline and 10% at follow up. Levels of cocaine, ecstasy and steroid use were very low at both times (<3%).

4.8 Recommendations

The poor treatment acceptance and retention rates experienced in this study do not support oral naltrexone in this treatment population. Scarce prison health resources may be better directed towards treatments of proven efficacy including methadone maintenance, buprenorphine maintenance and AOD counselling. To overcome the central problem of poor treatment retention, a trial of implanted devices may be warranted (should these receive TGA approval in Australia) although interest among inmates may be limited. Careful and independent ethics review of the arrangements would be required to ensure prisoners were free to choose to accept a naltrexone implant.

Diversion of buprenorphine was identified in this trial as a problem and, although procedures to curtail diversion have since been implemented, the situation requires continued monitoring including implementing new testing technology for buprenorphine. Corrections Health Service may want to consider investigating alternative dose methods or formulations. The Suboxone formulation contains both buprenorphine and naloxone and may be less liable to parenteral abuse (Fudala, Bridge et al. 2003) although some studies have found no significant differences in their relative reinforcing effects (Strain, Stoller et al. 2000; Comer and Collins 2002).

While half of inmates received some form of counselling, most commonly face-to-face sessions with AOD workers, half did not receive any counselling at all. Given that there seem to be benefits from AOD counselling this is of concern. When questioned about their failure to attend AOD counselling only 19% of responded that they had previously attended courses. This left a large proportion of inmates who either declined counselling (42%) or claimed that they were not offered counselling (38%). The underlying reasons for refusal or failure to provide this service warrant further exploration.

APPENDIX A

1. Recruitment Status by Prison

Jail/complex	Security	Inmates	Recruited	Excluded
Junee	medium/minimum	578	41 (22%)	129 (23%)
Parklea	Medium	429	31 (16%)	57 (10%)
Cessnock	Minimum/maximum	438	27 (15%)	62 (11%)
Goulburn	maximum/minimum	499	22 (13%)	40 (7%)
Cooma	Minimum/medium	140	13 (8%)	29 (5%)
Lithgow	Maximum	325	18 (8%)	39 (7%)
Bathurst	Medium/minimum	391	12 (7%)	21 (4%)
Parramatta	Remand	324	10 (7%)	23 (4%)
John Moroney 2	Maximum/minimum	293	4 (2%)	26 (5%)
Long Bay	Maximum/minimum	1088	4 (2%)	68 (12%)
Silverwater	Minimum	427	7 (3%)	27 (5%)
Kirkconnell	Minimum	210	1 (1%)	2 (<1%)
MRRC	Maximum	886	0	10 (2%)
Grafton	medium/minimum	241	14 (7%)	28 (5%)
Prison not identified				11
TOTAL			204	572

APPENDIX B

Reasons for exclusions:

Sentence < 6 months	229	(44% of exclusions)
Declined	136	(26% of exclusions)
Other	54	(10% of exclusions)
Psychiatric illness	7	(1% of exclusions)
Other dependence	36	(7% of exclusions)
Physical illness (incl HIV+)	8	(1% of exclusions)
Not heroin users (HITS)	50	(9% of exclusions)
Parole/Appeal	20	(4% of exclusions)
Other	6	(1% of exclusions)
Prefer BUP detox	26	(5% of exclusions)
Total Excluded	572	

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