

Four-year follow-up of imprisoned male heroin users and methadone treatment: mortality, re-incarceration and hepatitis C infection

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ABSTRACT

Aims To examine the long-term impact of methadone maintenance treatment (MMT) on mortality, re-incarceration and hepatitis C seroconversion in imprisoned male heroin users.

Design, setting and participants The study cohort comprised 382 imprisoned male heroin users who had participated in a randomized controlled trial of prison-based MMT in 1997/98. Subjects were followed-up between 1998 and 2002 either in the general community or in prison.

Measurements All-cause mortality, re-incarceration, hepatitis C and HIV serostatus and MMT retention.

Findings There were no deaths recorded while subjects were enrolled in MMT. Seventeen subjects died while out of MMT, representing an untreated mortality rate of 2.0 per 100 person-years (95% CI, 1.2–3.2). Re-incarceration risk was lowest during MMT episodes of 8 months or longer (adjusted hazard ratio 0.3 (95% CI, 0.2–0.5; $P < 0.001$), although MMT periods 2 months or less were associated with greatest risk of re-incarceration ($P < 0.001$). Increased risk of hepatitis C seroconversion was significantly associated with prison sentences of less than 2 months [adjusted hazard ratio 20 (95% CI, 5–76; $P = 0.001$)] and MMT episodes less than 5 months [adjusted hazard ratio 4.2 (95% CI, 1.4–12.6; $P = 0.01$)]. Subjects were at greatest risk of MMT dropout during short prison sentences of 1 month or less (adjusted hazard ratio 10.4 (95% CI, 7.0–15.7; $P < 0.001$). HIV incidence was 0.3 per 100 person-years (95% CI, 0.03–0.99).

Conclusions Retention in MMT was associated with reduced mortality, re-incarceration rates and hepatitis C infection. Prison-based MMT programmes are integral to the continuity of treatment needed to ensure optimal outcomes for individual and public health.

KEYWORDS Cohort study, methadone, mortality and hepatitis C, prisons.

INTRODUCTION

Methadone maintenance treatment (MMT) for heroin users has been shown to reduce heroin use and rates of imprisonment [1–4], mortality [5–7], HIV risk behaviour

[8] and HIV infection [9–11]. MMT is rarely offered in prison settings although imprisonment is a common event in the lives of heroin users [12]. Prison populations are growing faster than general populations in many countries. The US jail and prison population grew 71%

between 1990 and 2001–1.96 million [13] with growth rates of 47% between 1993 and 1998 in England [14] to 65 300 and 45% between 1992 and 2002 in Australia [15] to 22 500. Hepatitis C prevalence in prisoners ranged from 30 to 40% in US prison inmates [13,16], 50% in European prisons [17] and between 30 and 40% in Australian prisons [18]. Hepatitis C incidence in prisoners ranged from 1.1. per 100 person-years in male prisoners in Maryland [19], 25 per 100 person-years in Danish prisons [20] and 38 per 100 person-years in prisoners in Victoria, Australia [21] who had been released and re-incarcerated.

Prison-based substitution treatment programmes have been documented in New York [22], New South Wales [23,24], France [25] and Baltimore [26]. Magura and colleagues [22] found that the Rikers Island MMT programme in New York significantly facilitated entry (85%) and retention at 6 months (27%) in post-release treatment compared to inmates enrolled in detoxification programmes (37% enrolled, 9% retained). Bellin and colleagues (1999) [27] demonstrated a 14% reduction in re-incarceration risk (adjusted for age, race and gender) for inmates in the Rikers Island prison programme who received high-dose methadone (≥ 60 mg) ($n = 1423$) compared to those who received low-dose methadone ($n = 1371$) ($P < 0.002$). A retrospective study [25] of 420 inmates in French correctional facilities found re-incarceration was significantly less likely among those inmates who had received maintenance therapy while incarcerated ($n = 89$) compared to those who had not ($n = 331$).

The New South Wales (NSW) prison methadone programme commenced in 1986. In 1997 the methadone programme treated a daily average of 685 inmates, representing approximately 9% of the state prison population. Dolan and colleagues evaluated the NSW prison methadone programme in a randomized controlled trial (RCT) [23,24]. Between 1997 and 1998, 382 eligible, consecutive applicants for drug treatment in the NSW prison system were randomized to methadone ($n = 191$) or a waiting list control group ($n = 191$). Subjects were interviewed at baseline and 5 months later about their drug use, injecting and syringe sharing and also provided finger-prick blood samples for testing for HIV and hepatitis C and hair samples for testing for heroin use. At 5 months, all subjects were offered methadone through the prison-based methadone treatment programme. Released subjects who had been treated through the prison methadone programme were offered the opportunity to transfer to local community methadone programmes. 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 the control group. This 4-year follow-up study of the 382 participants enrolled in the original RCT allowed examination of longer-term outcomes including mortality, re-incarceration, hepatitis C seroconversion and HIV seroconversion.

METHODS

The aim of this follow-up study of the 382 participants in the original prison methadone RCT was to examine further the possible effect of MMT on hepatitis C and HIV sero-incidence, mortality and re-incarceration. Mortality was assessed through the Australian Institute of Health and Welfare, Australian National Death Index (NDI) in July, 2002. Cohort data was matched to the NDI using multiple passes which grouped the data based on different characteristics such as date of birth and name. Cause of death was assigned based on *International Classification of Diseases* version 10 (ICD)-10 codes. Imprisonment data were obtained from the NSW Department of Corrective Services as of May 2002 and the relevant government departments in the other Australian states and territories (November 2001–August 2002). Methadone treatment data were obtained from the Pharmaceutical Services Branch of the NSW Department of Health as of May 2002. Data were not collected systematically on discharge policies, adjunctive psychosocial support and urinalysis programmes, which varied between individual prison-based and community-based MMT programmes. Participants in the original RCT were located via methadone clinics, probation and parole offices and letters sent to their last known address and contacted between September 2000 and December 2002 and interviewed. Interviewed subjects were also asked to provide finger-prick blood samples which were tested for HIV and HCV using techniques described previously [23]. The date of seroconversion was taken as the midpoint between the last negative and first positive antibody tests. Serology was conducted by the Centre for Immunology, St Vincent's Hospital, Sydney, Australia.

Recruitment and ethical approvals

Subjects were compensated for time and travel involved in study participation. They received AUD\$10 if interviewed in prison and AUD\$50 if interviewed in the community. Informed consent was obtained for all subjects who were interviewed. Four Ethics Committees constituted by the University of New South Wales, NSW Corrections Health Service, NSW Department of Corrective Services and the Australian Institute of Health and Welfare approved the study.

Data analysis

Descriptive statistics were reported for cohort characteristics and follow-up status; *t*-tests for continuous variables and χ^2 tests for categorical variables were conducted to examine differences on these variables between current MMT and imprisonment status. All statistical tests were two-tailed with a 0.05 level of significance. Prevalence and univariate analysis was conducted using SPSS for Windows (version 11.0) and incidence, survival and multivariate data were analysed using STATA (Stata Statistical Software, intercooled version 8.0 for Windows). Person-time methods using

Cox regression models with time-dependent covariates were used to examine predictors of time to event outcomes including death, re-incarceration, hepatitis C seroconversion and MMT dropout [28]. Variables that could vary within an individual over time such as imprisonment, methadone treatment or age were treated as time-dependent variables. Individuals could contribute multiple time-dependent variables without replication. Data for deceased subjects were included in each survival analysis up to their date of death. Time in prison and MMT were analysed by quartile, grouped according to exposure time. Quartile cut-off values varied due to differences in the subjects at risk in each analysis.

Table 1 Characteristics of the cohort at baseline.

Characteristic	(<i>n</i> = 382)
Mean years of age (SD)	27 (6)
Aboriginal or Torres Strait Islander (%)	24
Mean age (years) at first imprisonment (SD)	20 (4)
Most serious offence	
Robbery (%)	31
Break and enter (%)	22
Assault (%)	19
First prison term (%)	12
Sentence length (months) median (range)	18 (3–130)
Mean age (years) at first injection (SD)	17 (4)
Mean age (years) began daily injection (SD)	19 (4)
Started injecting prison (%)	10
Ever injected in prison (%)	85
Ever shared syringes in prison (%)	75

RESULTS

Follow-up and demographic characteristics

The demographic characteristics of the cohort at baseline appear in Table 1. Other demographic characteristics of the cohort have been described in detail previously [23,24]. The follow-up status of the cohort is summarized in Fig. 1. All subjects were recruited initially in prison. Median time between follow-up and initial interview was 4.2 years (range 3.4–4.7 years). Complete record checks were possible for nearly all subjects for mortality (100%), prison history (97%) and MMT history (93%) since the original RCT. Some prison data were unavailable due to the security classification of some prisoners that protected their identity. Seventeen (4%) subjects had died

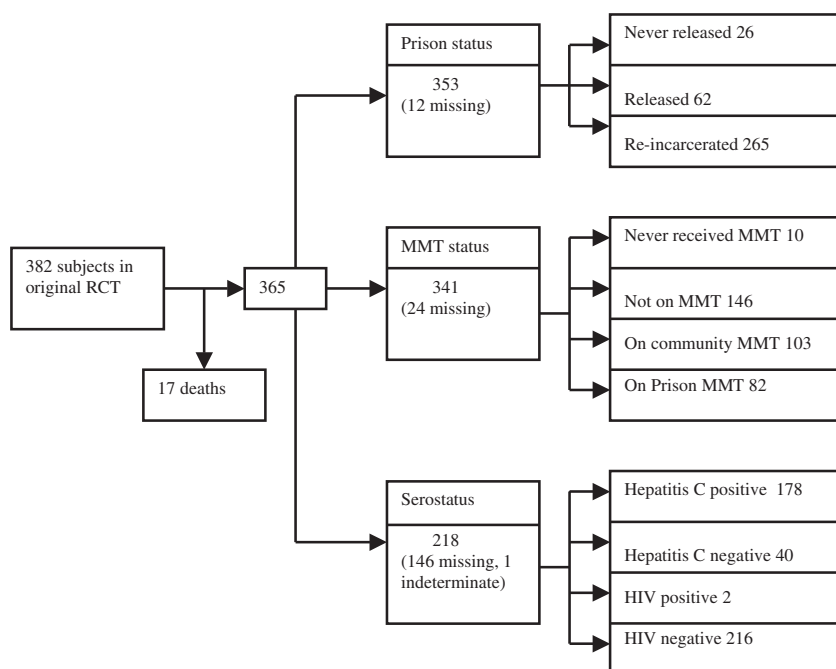


Figure 1 Mortality, prison, MMT and serostatus of cohort at follow-up

since the RCT. Almost all subjects (97%) had received MMT at some time either during or since the original RCT. Mean maximum dose reported at follow-up was 69 mg/day. Only 20% had been retained in MMT from commencement—most (77%) had received a median of two MMT treatment episodes with an average treatment episode duration of 41 weeks. One hundred and fifty-two subjects (43%) were in prison according to record checks as of May 2002, of whom 82 (54%) were enrolled in prison-based methadone programmes. Most subjects (93%) had been released since the RCT, but most (78%) had also been subsequently re-incarcerated on a median of three occasions for custodial periods of almost 6 months on each occasion.

Two hundred and thirty-six subjects (65%) were re-interviewed either in prison ($n=201$) or in the community ($n=35$), of whom 219 provided blood samples (60%). Ten (2.7%) declined a follow-up interview. Subjects who were re-interviewed ($n=236$) were comparable to those who were not re-interviewed ($n=129$) in terms of age (mean 30 ± 6 years), current MMT status (54% : 45%), original study treatment group allocation (50% : 51%) and baseline hepatitis C negative status (30% : 23%). Re-interviewed subjects were significantly more likely to be currently in prison compared to subjects who were lost to follow-up ($P < 0.001$) and have more post-RCT re-incarcerations ($P = 0.03$). Re-interviewed subjects also started drug injecting at a younger age ($P = 0.01$), started daily injecting at a younger age ($P = 0.03$) and were imprisoned at an earlier age ($P < 0.001$).

All-cause mortality

All-cause mortality was examined from the date of first interview to death record check in May 2002. Seventeen of 382 participants in the original RCT died during this period representing a mortality rate of 1.1 per 100 person-years (CI 0.68–1.75). All deaths occurred while subjects were not in MMT, representing an untreated mortality rate of 2.0 per 100 person-years (CI 1.2–3.2). There were eight drug-related overdoses, two suicides, one murder, four accidents and two deaths from chronic disease (cancer and renal failure). Among the eight fatal drug overdoses, four had never received methadone and four had ceased methadone prior to release from prison. There were no significant differences in mortality risk between original study group allocation, age and aboriginality. Mortality risk was 16 times higher outside prison compared to inside prison ($P < 0.001$); however, this result should be treated with caution, as the confidence interval is wide and no adjustment for MMT status could be made as no subjects died while enrolled in MMT. Relative risks for MMT status could not be calculated. Predictors of all cause mortality are summarized in Table 2.

Time to re-incarceration after first release

Re-incarceration and methadone treatment data for 342 subjects were included in this analysis. Forty subjects were excluded as they had not been released from prison ($n=26$), data were missing ($n=12$) or they died while in

Table 2 All-cause mortality rate predictors.

Variable	No. of deaths	Person-years at risk	Rate per 100 person-years	Adjusted hazard ratio (95% CI) (95% CI)*	P
Age					
30 years +	6	634	0.9 (0.4–2.1)	1.1 (0.3–4.0)	0.5
25–29 years	7	540	1.2 (0.6–2.7)	1.5 (0.4–5.2)	0.8
<25 years	4	389	1.0 (0.3–2.7)	1.0	
RCT group					
Treatment	6	789	0.8 (0.3–1.7)	1.7 (0.6–4.6)	0.3
Control	11	774	1.4 (0.7–2.6)	1.0	
Aboriginal					
Non-aboriginal	13	1192	1.0 (0.6–1.9)	1.2 (0.4–3.6)	0.9
Aboriginal	4	371	1.1 (0.4–2.9)	1.0	
Prison status					
Not in prison	15	640	2.3 (1.4–3.9)	16.5 (3.7–74.7)	<0.001
In prison	2	923	0.2 (0.1–0.8)	1.0	
MMT status					
Not in MMT	17	863	2.0 (1.2–3.2)	nc	nc
In MMT	0	700	0		

*Univariate rates unadjusted.
nc = not calculated

prison ($n = 2$), and therefore were not at risk of re-incarceration. Subjects who died after release contributed data until their date of death. Two hundred and eighty of the 342 released subjects were re-incarcerated representing an overall re-incarceration rate of 87.7 per 100 person-year. When analysed by quartile there was a trend for risk of re-incarceration after first release to decrease as MMT retention increased. Compared to periods of no treatment, the risk of re-incarceration was reduced by 70% during MMT periods 8 months or longer ($P < 0.001$). Age less than 25 was also associated with increased risk of re-incarceration ($P = 0.03$). Predictors of re-incarceration from first release are summarized in Table 3.

Hepatitis C seroconversion

Thirty-nine of 95 hepatitis C negative subjects from the original RCT seroconverted between enrolment in 1997 and 1998 and follow-up interview between September 2000 and December 2002, representing an incidence rate of 21.3 per 100 person-years (95% CI 15.6–29.2). In contrast, HIV incidence was very low (two cases or 0.276 per 100 person-years, 95% CI: 0.033, 0.996). There were no significant differences in hepatitis C incidence rates between original study groups, age or aboriginality. The adjusted risk of hepatitis C seroconversion during short prison sentences of less than 2 months was 20 times greater than when subjects were not in prison. In the final model (Table 4) periods of imprisonment of less than 2 months ($P \leq 0.001$) and MMT periods of less than 5 months ($P = 0.01$) were both significantly associated with increased risk of hepatitis C seroconversion. Note

that follow-up time for MMT less than 46 days was too limited to support statistical significance.

Retention in first MMT episode

Two hundred and seventy-five of 341 subjects dropped out of their first methadone treatment episode over 436 person-years at risk, representing an overall attrition rate of 63.1 (CI 56.1–71.0) per 100 person-years. MMT drop-out risk was 10 times higher during short prison sentences (1 month or less) compared to when subjects were in the community ($P < 0.001$), although after 4 months imprisonment was significantly protective for MMT drop-out (Table 5). No other variables were associated with increased risk.

DISCUSSION

This 4-year follow-up study of imprisoned male Australian heroin users found that improved outcomes were associated with longer periods of methadone treatment. Methadone treatment was associated with reduced mortality irrespective of treatment duration. This finding is consistent with previous findings of lower mortality in patients enrolled in MMT [5–7]. MMT treatment episodes of 8 months or longer significantly reduced re-incarceration risk compared to periods of no treatment. Longer, and by implication uninterrupted, periods of MMT significantly delayed re-incarceration, reflecting reduced criminal activity in released subjects. The findings of this prospective longitudinal study support previous reports

Table 3 First re-incarceration rate predictors.

Variable	No. of first re-incarcerations	Person-years at risk	Rate per 100 person-years (95% CI)*	Adjusted hazard ratio (95% CI)	P
Age					
25 + years	189	254	74 (65–93)	1.0	
<25 years	91	65	140 (106–163)	1.3 (1.0–1.7)	0.03
RCT group					
Treatment	143	142	107 (85–119)	1.0	
Control	137	177	77 (65–91)	0.8 (0.7–1.0)	0.1
Aboriginal					
Non-aboriginal	215	257	84 (73–96)	1.0	
Aboriginal	65	62	105 (82–133)	0.8 (0.6–1.0)	0.09
MMT status					
Not in MMT	197	204	97 (84–111)	1.0	
<18 days	12	1.2	973 (553–1714)	8.4 (4.4–15.9)	<0.001
19–73 days	21	6.7	315 (206–484)	2.7 (1.7–4.3)	<0.001
74–235 days	30	20.7	145 (101–207)	1.5 (0.99–2.2)	0.05
>237 days	20	86.7	23 (15–36)	0.3 (0.2–0.5)	<0.001

*Univariate rates unadjusted.

Table 4 Hepatitis C seroconversion rate predictors.

Variable	No. of HCV seroconversions	Person-years at risk	Rate per 100 person-years (95% CI)*ratio	Adjusted hazard (95% CI)	P
Age					
<24 years	23	105	21 (13–33)	1.0	
25 years +	16	78	22 (15–33)	1.0 (0.5–2.0)	>0.99
RCT group					
Treatment	16	99	16 (10–26)	1.0	
Control	23	84	27 (18–41)	2.0 (0.9–4.2)	0.08
Aboriginal					
Aboriginal	11	53	21 (11–37)	1.0	
Non-aboriginal	28	130	22 (15–31)	0.9 (0.5–2.0)	0.9
Prison status					
Not in prison	9	50	18 (9–34)	1.0	
<52 days	7	3	254 (121–533)	20 (5–76)	<0.001
53–129 days	7	13	54 (26–114)	3 (0.99–9.3)	0.05
130–287 days	6	28	22 (10–48)	1.6 (0.6–4.8)	0.4
>288 days	10	89	11 (6–21)	0.9 (0.4–2.4)	0.9
MMT status					
Not in MMT	23	107	22 (14–32)	1.0	
<46 days	2	2	127 (32–509)	1.6 (0.3–9.7)	0.6
47–146 days	6	6	97 (43–215)	4.2 (1.4–12.6)	0.01
147–376 days	4	17	23 (9–62)	1.1 (0.4–3.3)	0.8
>377 days	4	51	8 (3–21)	0.4 (0.1–1.2)	0.09

*Univariate rates unadjusted.

Table 5 MMT retention rate predictors.

Variable	No. of dropouts	Person-years at risk	Rate per 100 person-years (95% CI)*	Adjusted hazard ratio (95% CI)	P
Age					
< 25 years	80	108	74 (59–92)	1.0	
25–34 years	152	246	62 (53–72)	1.0 (0.8–1.3)	0.9
35 years +	43	81	53 (39–72)	1.0 (0.7–1.5)	0.9
RCT group					
Treatment	152	256	59 (50–69)	1.0	
Control	123	180	68 (57–82)	1.2 (0.9–1.6)	0.1
Aboriginal					
Non-aboriginal	206	326	63 (55–72)	1.0	
Aboriginal	69	110	63 (50–79)	1.2 (0.9–1.6)	0.2
Prison status					
Not in prison	105	144	73 (60–88)	1.0	
< 36 days	49	4	1169 (884–1547)	10.4 (7.0–15.7)	<0.001
36–133 days	50	25	196 (149–259)	1.7 (1.1–2.4)	0.01
134–294 days	37	63	58 (42–80)	0.5 (0.4–0.8)	0.002
>295 days	34	199	17 (12–24)	0.2 (0.1–0.3)	<0.001

*Univariate rates unadjusted.

of the benefits of prison-based medicated substitution treatment in reducing subsequent re-incarceration rates [25,27].

Short periods of imprisonment (less than 2 months) were significantly associated with greater risk of hepatitis

C infection. Short MMT episodes (less than 5 months) were also significantly associated with greater risk of hepatitis C. This finding is consistent with studies of HIV seroconversion in injecting drug users (IDUs) which found that HIV infection was highly correlated with duration

and stability of MMT participation [11]. These results also suggest that hepatitis C transmission occurs in prisons at a high rate, particularly in IDUs serving shorter sentences. The significantly greater risk of hepatitis C infection associated with short MMT duration underlines the importance of increasing retention in treatment, particularly during short prison sentences when MMT dropout was greatest.

This study has several limitations. Although this study began as a randomized trial the long-term follow-up sought to investigate factors beyond the original randomized assignment of immediate versus delayed methadone treatment. An inherent limitation of this long-term investigation is the potential for confounding that can influence the results of cohort studies. To address this issue the study used multivariate regression methods, combined with person-time analyses to account for differences in follow-up time.

Person-time methods were used to characterize and divide follow-up time into unexposed and exposed time grouped into quartiles, which were treated as distinct subjects in the analysis. The validity of such an approach assumes that the transfer from one exposure to another is independent of any subsequent failure event (i.e. death, re-incarceration or hepatitis C seroconversion) [29]. A form of selection bias may occur where the shifts between exposures is related to the failure event. For example, re-incarceration rates may be higher for younger, more chaotic or dysfunctional heroin users who also experience poorer treatment retention. The bias was controlled by estimating effects for subjects who were in the same age group or exposure groups in the case of imprisonment and MMT. The outcomes were adjusted further for other variables, such as age and aboriginality, which also independently influenced re-incarceration and other outcomes.

The analysis was limited to predictor and outcome variables where longitudinal data were available. Drug use data, both self-report and hair analysis, were limited to short-term outcomes measured at each follow-up point. Systematic records of psychosocial support were not available. Treatment history prior to enrolment in the original RCT was not recorded. Psychosocial support was provided as part of prison drug treatment programmes, but these were limited. Psychosocial support provided in community MMT programmes was not documented as the nature and extent of these programmes varied considerably. The findings of this follow-up study extended the findings of the earlier RCT and were consistent with earlier studies of community-based MMT. Therefore, the likelihood that factors other than MMT were responsible for the observed outcomes was remote.

Hepatitis C seroconversion data were limited to those who provided blood samples at the follow-up interview

and results may be subject to attrition bias. Subjects currently in prison were over-represented, possibly reflecting the greater likelihood of locating imprisoned subjects, particularly those with long sentences. This bias did not affect outcomes based on record checks including mortality, re-incarceration and MMT status. Importantly, there was no difference in follow-up of subjects who had hepatitis C negative results at baseline. HIV incidence was too rare to conduct meaningful analyses.

Absence of methadone dose data was another shortcoming in data collection. Records provided duration of treatment episodes in days and the minimum and maximum permitted dose ranges, but gave no indication of what maximum or average dose was achieved in any given treatment episode. Subjects were asked what dose they were currently receiving at the follow-up interview, but this was not a substitute for systematic time-series data. Therefore, the mean methadone dose between the different durations of treatment could not be estimated. Original study group allocation was included in all analyses, although all subjects were offered MMT at the conclusion of the RCT. It is doubtful whether any treatment group effect persisted after the initial 5-month RCT period, after which control subjects were offered MMT. Finally, the impact of time in prison-based MMT was not examined as an independent predictor as it was dependent on sentence length.

Notwithstanding these limitations, the results indicate that when subjects cycled through short periods of imprisonment or short periods of methadone treatment they were at significantly greater risk of hepatitis C seroconversion than at other times. These findings have important implications for clinical practice and public policy. Taken together with the findings relating to mortality, re-incarceration and MMT retention, strategies are needed to increase continuity in methadone treatment of heroin users as they move between the community and prison systems. Prisoners are provided explicit and peer-based education about blood-borne viruses (including hepatitis C), but the extent to which this reduces hepatitis C incidence is unknown. Bleach is available in NSW prisons, but there are no prison-based needle syringe programmes in Australia [30]. Further research is needed to identify other predictors of treatment failure, such as inadequate methadone dose, untreated mental illness, social stigma, institutional impediments and inadequate ancillary psycho-social support. The results also suggest that methadone treatment either in prison or the community may be a superior alternative to imposing short prison sentences, certainly in terms of reduced blood-borne virus transmission, mortality and re-incarceration (and antecedent crime). This study and the earlier RCT demonstrated that medicated drug treatment for heroin users, in this case based on methadone, is viable and

effective in prison-based programmes and reduces mortality, re-incarceration and hepatitis C incidence. Methadone programmes should be introduced in prison systems wherever community programmes exist both to ensure continuity of care between community and prison-based programmes and to initiate heroin users into treatment as early as possible in their drug using and prison careers.

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