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Three month outcomes for the treatment of
heroin dependence:
Findings from the Australian Treatment
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EXECUTIVE SUMMARY

Introduction
Heroin use, with its associated harms, represents a serious public health concern, and generates many challenges for treatment providers. In Australia, an estimated 74,000 individuals are thought to be heroin dependent, with more people treated for dependence on opioids than any other drug class. Despite this, little is known about how effective the main treatment options are in practice.

The Australian Treatment Outcome Study (ATOS) is the first large scale longitudinal study of treatment outcome for heroin dependence to be conducted in Australia. ATOS is coordinated by the National Drug and Alcohol Research Centre (NDARC), and is conducted in collaboration with the Drug and Alcohol Services Council (DASC) and Turning Point Alcohol and Drug Centre.

The aims of ATOS are:
1. To describe the characteristics of people seeking treatment for problems associated with heroin use in Australia;
2. To describe the treatment received; and
3. To examine treatment outcomes and costs at 3 and 12 months after commencement of treatment.
The current report presents data from the three month follow-up interview of subjects in the New South Wales arm of the study.

Method
Nineteen treatment agencies were randomly selected from within the three main treatment modalities (methadone/buprenorphine maintenance therapy; detoxification; residential rehabilitation) stratified by area health service. Five hundred and thirty five individuals entering treatment and 80 heroin users not seeking treatment were recruited into the study and interviewed by NDARC staff using a structured questionnaire. 89% of the treatment sample and 83% of the non-treatment sample were successfully recontacted and interviewed at three months. Data was collected on a variety of domains including: treatment experiences; heroin and other drug use, mental health and criminal activity.

Results
- 89% of the treatment sample and 83% of the non-treatment sample were successfully recontacted and interviewed three months after entering treatment. There were no differences between those re-interviewed and those lost to follow up in terms of heroin use at baseline.

- There were substantial reductions in heroin and other drug use across all three treatment samples. For example, the one month prevalence of heroin abstinence rose from 1% at baseline to 53% at three months across treatment modalities. While there was also an increase in one month abstinence in the non-treatment sample, this was considerably less marked than in the treatment samples (from 0% to 20%). The reduction in heroin use among the treatment samples was paralleled by reductions in the use of other drugs, suggesting that subjects were *not* simply substituting heroin use with the use of other drugs but were, in fact,

reducing their overall drug consumption. Confirmation of self-reported heroin use by means of hair analysis revealed excellent validity of self-report.

- Reductions in drug use were paralleled by improvements in both physical and mental health, assessed using the SF-12.

- There were notable reductions in the percentages of subjects reporting committing any crime or that their major source of income was from crime across the treatment samples.

Conclusion

The high rate of sample retention and subject participation attests to the feasibility of conducting longer term follow-up studies with groups of individuals entering treatment for heroin dependence. Three months after entering treatment there were substantial reductions in heroin use, other drug use, and in criminal activity. In addition, there were substantial improvements in mental and physical health. These results confirm, for the first time in a naturalistic Australian setting, the results of previous clinical trials and overseas research indicating that treatment for heroin dependence is associated with marked reductions in drug use, criminal activity and in substantial improvements in mental health in the short term. The twelve month follow-up results will be reported in future reports.

1. INTRODUCTION

Heroin use, with its associated harms, represents a serious public health concern, and generates many challenges for treatment providers. In Australia, an estimated 74,000 individuals are thought to be heroin dependent, with more people treated for dependence on opioids than any other drug class (Hall et al, 2000; Shand et al, 2001). Despite this, little is known about how effective the main treatment options are in practice. Recognition of the harms associated with heroin dependence and the chronic nature of this condition has lead to increased efforts to improve access to and availability of treatment in Australia, as well as to expand the range of treatment options available. Such an approach is supported by the results of numerous clinical trials establishing the efficacy of treatment for heroin dependence.

There is, however, an important though subtle difference between establishing the efficacy of an intervention within the context of an experimental trial and establishing the efficiency of that intervention delivered outside a research setting. Specifically, previous research has established that apparently positive treatment outcomes observed within the context of rigorously controlled clinical trials do not always translate into similar levels of success when the interventions are implemented on a larger scale (Wells, 1999).

For these reasons it is important to evaluate the effectiveness of "real world" treatments within the contexts and environments in which they are typically delivered. There have been a number of previous such naturalistic studies conducted overseas including: the California Drug and Alcohol Treatment Assessment (CALDATA; Gerstein et al, 1994; the Drug Abuse Reporting Program (DARP; Simpson et al, 1990); the Drug Abuse Treatment Outcome Study (DATOS; Hubbard et al, 1997; the National Treatment Outcome Research Study (NTORS; Gossop et al, 1997); and the Treatment Outcome Prospective Study (TOPS; Hubbard et al, 1989). We have previously summarized the major findings from these studies (Henderson et al, 2002), which have included:

     1. Recognition that it is indeed feasible to conduct large scale naturalistic treatment outcome studies with people entering treatment for opioid dependence. Specifically, retention rates in these studies have been in the region of 70 to 80 percent indicating that it is possible both to maintain contact and to obtain co-operation with this group.

     2. Confirmation of high rates of psychopathology and dysfunction in this group presenting to established services for treatment.

     3. Confirmation that standard treatments for opioid dependence, as delivered in non-research settings are effective in reducing drug use, rates of crime and are associated with generalized improvements in mental and physical health.

In recognition of the need to establish whether these generally positive outcomes of treatment of opioid dependence generalize to the situation in Australia, in 2000 the NH&MRC and the Commonwealth Department of Health and Aged Care funded the Australian Treatment Outcome Study (ATOS). ATOS is a naturalistic study of treatment outcome in a large cohort of heroin dependent individuals entering treatment who are to be interviewed at baseline (treatment entry), 3 months and 12 months. The study also contains data collection components in Victoria and South Australia and collection of data from a comparison group of heroin dependent individuals not seeking treatment.

This report represents the second in a series of reports detailing findings from the New South Wales component of the Australian Treatment Outcome Study. Extensive information on drug use, mental health and related factors were collected at time of treatment entry and where possible, all subjects will be re-interviewed at 3 and 12 months post treatment entry. We have previously detailed characteristics of the sample (Ross et al, 2003), including patterns of drug use, criminal activity and mental health. The specific aims of the current report are to describe patterns of drug use, mental health and related factors in the sample three months after entering treatment. The key findings have also been published in a bulletin (Appendix A).

2. METHODS

2.1 The ATOS (NSW) sample

Baseline data were collected between February 2001 and August 2002 as part of the New South Wales (NSW) component of ATOS. For a more detailed description of sample recruitment and the baseline questionnaire see Ross et al (2003). ATOS is a 12 month longitudinal study of entrants to treatment for heroin dependence, recruited from randomly selected treatment agencies, and a comparison group of non-treatment heroin users. Subjects were recruited from 19 agencies treating heroin dependence in the greater Sydney region, randomly selected from within treatment modality and stratified by regional health area. The agencies comprised ten methadone/ buprenorphine maintenance (MT) agencies, four drug free residential rehabilitation agencies (RR) and nine detoxification facilities (DTX). Four agencies provided both maintenance and detoxification services. In addition, a comparison group of heroin users not currently in treatment (NT) were recruited from needle exchange programs in the regional health areas from which treatment entrants were recruited.

Eligibility criteria were: i) no treatment for heroin dependence in the preceding month, ii) no imprisonment in the preceding month, iii) agreed to give contact details for follow-up interviews, iv.) had a good understanding of English, and v) were 18 years or older. Thus, no participant had been in treatment for the month prior to interview, the period over which health service utilisation was measured. A total of 1530 clients entering treatment were approached to participate in ATOS, of whom 694 were eligible for inclusion in the study (the majority (82%) of those not meeting eligibility criteria reported having been in treatment and/or prison within the preceding month). Five hundred and thirty five of those eligible were enrolled in the study.

The NT group consisted of 80 heroin using individuals not currently in any form of treatment. These individuals were selected after 434 individuals were screened for eligibility. Of these 434 clients of needle exchange programs who were approached, 213 (49%) did not meet eligibility criteria, with the principal reason for exclusion being that they had been in some form of treatment for heroin dependence within the preceding month (82% of those deemed ineligible). The participation rate among those eligible for the study was therefore 36.2%.

The total sample was thus 615 heroin users. All subjects were paid A$20 for completing the baseline interview, which took approximately 1 hour to complete. A brief description of the baseline interview is provided below. The conduct of this study was independently reviewed and approved by the ethics committees of the University of New

South Wales and each of the Area Health Boards responsible for the clinics included in the study.

2.2 Baseline interview

Subjects were administered a structured interview. Sections addressed:

2.2.1 Demographic characteristics

Age, gender, Aboriginal/Torres Strait Islander status, country of birth, level of school and tertiary education attained, main source of income in the preceding month, number of children under their care, usual form of accommodation, whether they have a prison history, and if so their longest period of incarceration and the length and recency of their last imprisonment.

2.2.2 Treatment history

Lifetime history of treatment for heroin dependence.

2.2.3 Drug use history

Participants were asked which drugs they had ever used, which ones they had ever injected, and which they had injected in the preceding six months. The number of days each drug was used in the preceding 6 months was also recorded. Drug use in the preceding month was assessed using the Opiate Treatment Index (OTI; Darke et al, 1992).

2.2.4 Heroin overdose history

Questions regarding lifetime history of non-fatal heroin overdose were based on earlier work conducted by the authors (Darke et al, 1996).

2.2.5 Injection-related risk-taking behaviour

The injecting sub-scale of the HIV Risk-Taking Behaviour Scale (HRBS), a component of the OTI, was used to measure current injection related risk behaviour (Darke et al, 1992).

2.2.6 Injection-related health

The injection-related sub-scale of the OTI health scale was used to assess injection-related health problems (Darke et al, 1992).

2.2.7 General health

The Short Form-12 (SF-12) is a standardised, internationally used instrument that provides a general measure of health status (Ware et al, 1996). The 12 items on the SF-12 are summarised in two weighted summary scales, and generate a mental health and a physical health score. Lower scores are indicative of more severe disability.

2.2.8 Criminal activity

Using the criminality scale of the OTI (Darke et al, 1992), participants were asked how frequently they had committed any property crime, dealing, fraud and/or violent crime in the preceding month.

2.2.9 Current Major Depression
Past month diagnoses of DSM-IV Major Depression were assessed using the version of the Composite International Diagnostic Interview (CIDI) used in the National Survey of Mental Health and Wellbeing (NSMHWB; Andrews et al, 1999).

2.2.10 Post Traumatic Stress Disorder
DSM-IV diagnoses of Post Traumatic Stress Disorder (PTSD) were obtained using the NSMHWB version of the CIDI (Andrews et al, 1999).

2.2.11 Anti-Social Personality Disorder
A modified version of the Diagnostic Interview Schedule (Robins et al, 1981) was used to obtain DSM-IV diagnoses of antisocial personality disorder (ASPD).

2.2.12 Borderline Personality Disorder
Participants were screened for potential ICD-10 diagnoses of Borderline Personality Disorder (BPD) using the NSMHWB version of the CIDI (Andrews et al, 1999).

2.2.13 Locator information
To facilitate follow-up at 3 and 12 months the following information was sought at baseline: full legal name, nicknames/street names, other surnames that had been used, height, distinguishing physical features, current address, name of person whose address this was, participant's phone number/s, where they expect to be living in 12 months time, name of a doctor or community health centre that would know how to reach the participant, the first person they would contact if arrested, where they would go if they could no longer stay at their current address, places where they spend time, where messages could be left for them, and the contact details of at least two friends, relatives or associates who could be contacted if needed to assist in locating the participant for follow-up.

2.3 Structured interview at three month follow-up

Three months after the baseline interview extensive efforts were made to recontact and re-interview all individuals who had participated in the baseline interview. If respondents were no longer at the same address as when they were enrolled in the study extensive locator information, including the names and addresses of at least three contact persons such as parents, siblings or best friends (see section above) was available. Multiple efforts were made to contact these persons. Once contacted, the purpose of the ongoing study was (re) explained to study participants and they were invited to participate in the follow-up interview at a time and location of their convenience. As for the baseline interview, participation in this follow-up phase of the study was conditional on the provision of signed, informed consent and all participants again received $20 to recompense them for costs associated with participating in the interview.

The three month interview was an abbreviated form of the baseline interview but questioning was restricted to events and behaviours that occurred in the intervening period between baseline and follow-up interviews. It included questioning on the following topics:

2.3.1 Treatment history
Participants were asked how many times they had commenced the various treatment options for heroin dependence since the baseline interview and how recently they had attended each type of treatment.

2.3.2 Drug use history
Drug use in the preceding month was assessed using the OTI.

2.3.3 Heroin overdose history
This questioning paralleled the questioning at baseline (see above) but was restricted to events occurring in the three months between interviews.

2.3.4 Injection-related risk-taking behaviour
The injecting sub-scale of the HRBS was used to measure current injection related risk behaviour. Questions paralleled those assessed at baseline.

2.3.5 Injection-related health
The injection-related sub-scale of the OTI health scale was used to assess injection-related health problems.

2.3.6 General health
The SF-12 was administered to participants.

2.3.7 Criminal activity
Using the criminality scale of the OTI.

2.3.8 Current Major Depression
The version of the Composite International Diagnostic Interview (CIDI) used in the National Survey of Mental Health and Wellbeing (NSMHWB; Andrews et al, 1999).

2.3.9 Locator information
To facilitate follow-up at 12 months, the locator information obtained at baseline (see above) was checked for accuracy and, where appropriate, updated.

2.4 Hair analysis
Eleven percent of the participants followed up at 3 months were randomly selected and asked to provide a hair sample as a biological measure of heroin use for the month preceding interview. The only exclusion criterion was having hair shorter than 3 cm in length. No participants refused to provide a sample when asked.

A sample of 50-100 hairs were taken from the posterior vertex (crown of head) of selected participants at the conclusion of the structured interview, with the hair being cut as close to the scalp as possible. Samples were stored in plastic bags at room temperature until sent for analysis at the Victorian Institute of Forensic Medicine. Hair analyses were conducted on the 1cm of hair closest to the scalp. Hair grows at a rate of approximately 1 cm per month (Tagliaro et al, 1998). The current study thus analysed heroin and other opiate use over the month preceding interview. The hair morphine concentrations obtained reflect the overall exposure to heroin in the month preceding interview.

Procedures followed by the Victorian Institute of Forensic Medicine for analysis of hair morphine concentrations were as follows. Pure standards of morphine and 6-mono-acetylmorphine were used. D3-morphine and D3-6-mono-acetylmorphine were also used as internal standards. All other chemicals and reagents were of HPCL analytical grade or better. Stock and working solutions of morphine and 6-mono-acetylmorphine were prepared in methanol, fresh for each assay, to give concentrations in acid ranging from 2.5 to 50ng/ml. The internal standards, D3-morphine and 6-mono-acetylmorphine were purchased as 0.1mg/ml solutions in methanol and acetonitrile respectively.

For each case 1cm from the root was analysed. All hair samples were decontaminated to remove any exogenous contaminants. The hair samples were washed with 5ml methanol, followed by 5ml 0.01M hydrochloric acid, and finally 5ml methanol before drying. The hair samples were weighed and cut into small (5mm or less) fragments. The weighed portions of hair were placed in a glass tube containing 2ml 0.25M hydrochloric acid and incubated overnight at 45EC. Standards, controls and hydrolysed hair samples were neutralised with 2ml borate buffer and 0.3ml 1M sodium hydroxide to achieve a pH of 8.3-8.5. The extraction method used was (briefly): Five millilitres of the extraction solvent (90:10, chloroform: isopropanol) was added and the tubes rotated for 30 minutes. Following centrifugation (3500rpm) for 10 minutes, the aqueous layer was aspirated. One millilitre of 0.1M sulphuric acid was added to the organic layer and the tubes rotated for 30 minutes. Following centrifugation (3500rpm) for 10 minutes, the organic layer was aspirated. The acid layer was neutralised with 1ml borate buffer and 0.8ml 0.1M sodium hydroxide to receive a pH of 8.3-8.5. Five millilitres of the extraction solvent (90:10, chloroform: isopropanol) was added and the tubes rotated for 30 minutes. After centrifugation (3500rpm) for 10 minutes the aqueous layer was aspirated and the organic layer was evaporated to dryness.

The dried extracts were derivatized with 50 ìl of pentaflouropropanol and 50 ìl pentaflouropropionic anhydride for 45 minutes at 75EC. The derivatised extracts were finally evaporated to dryness under nitrogen and reconstituted with 100 ìl ethyl acetate. 1 ìl was injected into a gas chromatograph-mass spectrometer. A Hewlett-Packard (Melbourne, Australia) Model 6890 gas chromatograph equipped with a Model 5973 mass-selective detector and a Model 7683 automatic liquid sampler was used. Injections (splitless) were performed on a Hewlett-Packard Ultra 2 (5% phenyl methyl siloxane) fused silica capillary column (25m x 0.2mm id., 0.33 ìm film thickness). Helium was used as the carrier gas at a flow rate of 1.4ml/min, in an EI mode. The operative temperatures were as follows: injector 250EC; column maintained at 70EC for 1 minute and programmed at 20EC/min to 300EC, the final temperature being held for 6 minutes.

Analyses of hair extracts were performed by monitoring the following ions: m/z 417, 580 (D3-Morphine) 414, 577, 430 (Morphine) 417, 476, (D3-6-mam) 414, 473, 361 (6-mam).

2.5   Statistical analyses

Where data were highly skewed medians were reported. Means were reported for non-skewed data. In order to determine factors independently associated with dichotomous variables, logistic regressions were conducted. Independent predictors of continuous variables were determined using linear regression. All analyses were conducted using SPSS for Windows, version 11.0 (SPSS Inc, 2001).

3. RESULTS

3.1 The ATOS sample at three months

A total of 549 individuals were re-interviewed at three month follow-up, representing 89% of the sample enrolled in the study at baseline. In order to determine factors associated with retention in the cohort at 3 months, a logistic regression was conducted. Variables entered into the model included index group, age, sex, previous treatment history, number of heroin use days in the month preceding baseline interview, suicide history, Major Depression at baseline, PTSD and presence/absence of a personality disorder. The overall model was significant ($\div^2$=21.0, df=11, p<.05). Importantly, there was only a slight difference between the treatment and non-treatment modalities in terms of sample retention. While participants in the RR group were more likely to be retained than those in the NT group (91% v 83%, OR=2.50, 95% CI: 1.03-6.10), this was not the case for the MT (92% v 83%, OR=2.21, 95% CI: 1.00-4.89) and DTX groups (88% v 83%, OR=1.62, 95% CI: 0.77-3.39). Gender was the only other factor associated with being followed up at 3 months, with males being less likely to be retained than females (87% v 95%, OR=0.34, 95% CI: 0.17-0.69).

Those re-interviewed and those lost to follow-up did not differ significantly from each other in terms of age (29.3 v 29.4 years, OR=1.01, 95% CI: 0.98-1.05), treatment history (89% v 92%, OR=0.59, 95% CI: 0.22-1.57), extent of heroin use (20.4 v 20.5 use days, OR= 1.00, 95% CI: 0.97-1.04), lifetime suicide attempt (33% v 39%, OR=0.61, 95% CI: 0.34-1.08), Major Depression (25% v 20%, OR=1.47, 95% CI: 0.74-2.93), PTSD (41% v 41%, OR=0.89, 95% CI: 0.50-1.58) and personality disorders (79% v 80%, OR=1.06, 95% CI: 0.53-2.11). Overall, this pattern of results suggests that the sample re-interviewed at three month follow-up was broadly representative of the initial sample of 615 enrolled in ATOS.

3.2 Treatment retention

Table 1 shows retention in the index treatment at three months and the percentage of each group (including NT) who were in any treatment at the time of the three month follow-up interview. Detoxification programs are generally no longer than 7 to 10 days duration, and two of the four RR units involved in ATOS offer 28 day programs. Thus, it is not surprising that treatment retention was highest in the MT group (72%), followed by the RR group (28%).

Table 1 also shows whether subjects were in any form of treatment (not just their index treatment) at three months. A large number of MT (88%) and RR (69%) clients were in some form of treatment at three months, with the most popular treatment modality among the latter group being residential rehabilitation. Similarly, just over half (54%) of those who had entered detoxification were receiving some form of treatment at the time of the three month follow-up. A fifth of the non-treatment group were also in some form of treatment at 3 month follow-up, with the most popular form of treatment being MT.

Table 1: Treatment involvement at three months by treatment modality at baseline

	MT (N=185)	DTX (N=177)	RR (N=121)	NT (N=66)	TOTAL (N=549)
Still in index treatment (%)	72	0	28	N/A	30 (35*)
Currently in treatment, but not the index treatment (%)	16	54	41	20	34
Current treatment - includes ongoing index treatment (%):					
None	13	46	31	80	36
Methadone maintenance	75	11	3	12	31
Outpatient detoxification	0	2	1	0	1
Inpatient detoxification	0	2	3	0	1
Residential rehabilitation	1	9	46	2	14
Buprenorphine maintenance	9	8	2	3	6
Outpatient counselling	0	7	4	2	4
Naltrexone maintenance	1	3	0	2	2
Other	2	11	9	0	6

* N=483, excludes NT group

3.3   Treatment experiences during the first three months of ATOS

While Table 1 shows the percentage of people in each index group who were in some form of treatment at three months, it is also the case that a number of people received additional treatment in the intervening three months. Details of all treatment experiences since the index treatment are summarized in Table 2. The majority (76%) of those who entered detoxification at baseline experienced some additional form of treatment in the intervening three months, as did 52% of those entering residential rehabilitation and 23% of those entering MT. Importantly, a third of the non-treatment group also entered some form of treatment in the three months between baseline and follow-up interviews.

Table 2: Treatment history between baseline and three month follow-up by treatment modality

	MT (N=185)	DTX (N=177)	RR (N=121)	NT (N=66)	TOTAL (N=549)
Any intervention since baseline interview - excludes index treatment (%)	23	76	52	33	48
Type of intervention since baseline interview (%):					
MT	11	15	4	14	11
Outpatient detoxification	1	9	5	6	5
Inpatient detoxification	2	22	13	11	12
Residential rehabilitation	1	24	26	3	14
Rapid opiate detoxification using naltrexone	1	1	1	2	1
Other maintenance therapy eg. buprenorphine, LAAM	1	2	1	5	2
Outpatient counselling	5	15	9	5	9
Naltrexone maintenance	1	6	1	2	3
Other	2	16	13	2	9
Mean treatment episodes since baseline interview (excludes index treatment)	0.32	1.31	0.83	0.63	0.79

3.4   Changes in heroin use from baseline to three months

At both the baseline and three month interview subjects were asked to describe their heroin use in the one month period preceding the interview (Table 3). There were dramatic changes in past month heroin use between baseline and three months. A reduction in heroin use was reported by 86% of treatment participants, with 53% reporting having been abstinent for the month preceding the three month follow-up interview. Heroin abstinence rates climbed dramatically in all three treatment modalities: from 3% to 54% in the MT group, from 0% to 42% in DTX and from 2% to 69% in RR. There were substantial reductions in the number of days heroin was used in the last month in all three treatment groups (Table 3). Heroin had been used on a mean of 2.6 days (SD 6.0, range 0-28) by the MT group, 3.1 days (SD 7.3, range 0-28) by the RR group and 8.2 days (SD 10.5, range 0-28) by the DTX group. There was a much smaller decline amongst the NT group, who had used on a mean of 14.8 days (SD 11.9, range 0-28). None of these subjects reported abstinence in the past month at baseline (a function of the NT inclusion/ exclusion criteria in the study), while 20% reported past month abstinence at three month follow-up.

Changes in the rates of abstinence from heroin were paralleled by a reduction in the median heroin OTI score: from a median of 2.0 (range 0-33, across all three treatment modalities) to a median of 0.0 (range: 0-12) at three month follow-up. These reductions are indicative of a marked reduction in heroin use in each of the treatment modalities. There was evidence of a less marked reduction among the NT group, from 2.0 (range 0.14-11) at baseline to 0.9 (range 0-12) at three month follow-up.

In order to examine the factors associated with the number of heroin use days at three months, a linear regression was conducted controlling for age, gender, index treatment status and baseline heroin use. The model was significant ($F_{4,543}$=26.6, p<.001) and accounted for 16% of the variance. While age and gender were not significant, having been in a treatment modality at baseline was independently associated with fewer heroin use days at three month follow-up (4.8 v 14.8, â=0.3, t=8.0, p<.001). A greater number of baseline heroin use days was also independently associated with more frequent heroin use at 3 months (â=0.2, t=5.6, p<.001).

A logistic regression was also conducted examining the effect of baseline treatment status on abstinence rates at three months, controlling for age, gender and abstinence at baseline ($\div^2$=29.9, df=4, p<.001). Baseline treatment status was the only significant factor, with the treatment modalities having higher rates of abstinence at three months than the non-treatment group (53% v 20%, OR=4.70, 95% CI: 2.49-8.87).

3.5   Changes in other drug use from baseline to three months

As shown in Table 3, there were notable reductions in the use of other drugs among all treatment modalities. These changes appeared most evident in the RR treatment group: the use of other opioids by this group declined from 23% at baseline to 12% at follow-up, use of amphetamines fell from 39% to 16%, use of cocaine fell from 36% to 7%; use of benzodiazepines fell from 50% to 16% and use of cannabis fell from 72% to 20%. Among the treatment modalities, the drug classes where there appeared to be little or no changes in levels of use between baseline and three months included antidepressants, alcohol and tobacco. While the non-treatment group also showed some reduction in other drug use, this reduction was less marked. In examining the number of drug classes used at 3 months (including heroin), a linear regression was conducted controlling for age, gender, index treatment status and the number of drugs used at baseline. The model was significant ($F_{4,544}$=18.9, p<.001) and accounted for 12% of the variance. Participants who had entered treatment at baseline had used significantly fewer drug classes at 3 months than the non-treatment group (3.3 v 4.4, â=0.2, t=4.3, p<.001). A higher level of baseline drug use was also independently associated with using a greater number of drug classes at 3 months (â=0.3, t=6.8, p<.001). There was no effect of age or gender.

Table 3: Comparison of drug use at baseline and three months by treatment modality

	MT (N=185)		DTX (N=177)		RR (N=121)		NT (N=66)	
	BL	3 mths	BL	3 mths	BL	3 mths	BL	3 mths
Median Heroin OTI score	1.50	0.00	2.00	0.07	1.50	0.00	2.00	1.00
Mean number of heroin use days in last month	19.3	2.6	23.2	8.2	16.8	3.1	22.2	14.8
Abstinent from heroin in preceding month (%)	3	54	0	42	2	69	0	20
Drugs used in last month (%):								
Heroin	97	47	100	58	98	31	100	80
Other opiates	36	19	28	17	23	12	36	26
Amphetamines	27	19	22	11	39	16	41	24
Cocaine	28	17	42	22	36	7	64	38
Hallucinogens	3	4	9	6	18	1	17	11
Benzodiazepines	48	34	49	28	50	16	42	36
Antidepressants	15	15	12	15	24	23	5	9
Alcohol	43	45	52	46	62	36	64	52
Cannabis	69	61	63	46	72	26	71	65
Inhalants	2	1	2	1	2	0	3	11
Tobacco	96	94	92	92	98	93	100	96
Mean no. of drug classes used last month	4.6	3.5	4.7	3.4	5.2	2.6	5.4	4.4

3.6   Heroin overdose

There were notable reductions in rates of non-fatal heroin overdose among treatment modalities for the preceding month (Table 4). In order to examine overdose experience between the baseline and 3 month interview, a logistic regression was conducted ($\div^2$=28.2, df=4, p<.001), controlling for age, gender, overdose experience in the three months preceding baseline interview, and index treatment status. Those participants who had overdosed prior to baseline were more likely than the remainder of the sample to have overdosed during the intervening months between baseline and 3 month follow-up (17% v 3%, OR 7.66, 95% CI: 3.33-17.64). Gender was barely significant, with males being slightly more likely than females to have overdosed in that time (6% v 3%, OR=2.66, 95% CI: 1.01-7.04). There was no significant effect of age, or baseline treatment status.

Table 4: Prevalence of heroin overdose

	MT (N=185)		DTX (N=177)		RR (N=121)		NT (N=66)	
	BL	3 mths	BL	3 mths	BL	3 mths	BL	3 mths
OD past 3 months (%)	10	1	14	7	25	7	6	3
OD past month (%)	4	0	10	3	18	5	5	3

3.7   General physical health

3.7.1   Physical health as assessed by the SF-12

The mean SF-12 physical health scores appeared to improve across all treatment modalities at three months and were closer to the general population norm than they were at baseline (Table 5). A linear regression examining physical health scores at 3 month follow-up was conducted controlling for age, gender, index treatment status and baseline SF-12 physical health score. The model was significant ($F_{4,542}$=21.3, p<.001), and accounted for 14% of the variance. Younger age (â=0.1, t=2.6, p<.01), higher baseline SF-12 scores (â=0.3, t=7.7, p<.001) and entering treatment at baseline (â=0.1, t=2.1, p<.05) were independently associated with higher physical SF-12 score (better health) at three month follow-up.

Table 5: SF-12 physical health component scores

	MT (N=185)		DTX (N=177)		RR (N=121)		NT (N=66)	
	BL	3 mths	BL	3 mths	BL	3 mths	BL	3 mths
SF-12 Physical health component score (mean)	43.6	47.3	43.8	48.8	44.1	50.5	43.7	46.0

3.7.2 Injection-related health

All treatment groups showed marked declines in the proportions injecting at least daily (Table 6). Less than 10% of the MT and RR groups were injecting at least daily at 3 months. A quarter of the DTX group were doing so, down from 82%. A much smaller decline was noted in the NT group, where a half were still injecting at least daily at follow-up. There were similar patterns of decline in the borrowing and lending of used needles among the treatment groups (Table 6).

In order to examine factors associated with daily (or more frequent) injecting at 3 month follow-up, a logistic regression controlling for age, gender, index treatment status and baseline frequency of injecting was conducted ($\div^2$=68.3, df=4, p<.001). Not entering treatment at baseline (50% v 14%, OR=6.28, 95% CI: 3.53-11.19), and injecting at least daily at baseline (23% v 3%, OR=8.78, 95% CI: 3.09-24.96) were independently associated with daily (or more frequent) injecting at three month follow-up. No age or gender effect was apparent.

Factors associated with having injection-related health problems in the month preceding the 3 month interview were also examined using a logistic regression ($\div^2$=55.6, df=4, p<.001). The variables entered into the model were age, gender, index treatment status and presence/absence of injection-related health problems at baseline. Not entering treatment at baseline (58% v 29%, OR=3.56, 95% CI: 2.05-6.20), and having injection-related health problems at baseline (39% v 13%, OR=4.22, 95% CI: 2.41-7.39), were independently associated with injection-related health problems at 3 months.

Table 6: Needle risk-taking behaviours at baseline and 3 months

	MT (N=185)		DTX (N=177)		RR (N=121)		NT (N=66)	
Behaviours/ problems in preceding month	BL %	3 mth %	BL %	3 mth %	BL %	3 mth %	BL %	3 mth %
Injecting at least daily	75	9	82	25	78	7	83	50
Borrowed needle	13	3	16	6	29	3	20	11
Lent needle	25	7	27	10	36	5	26	18
Injection-related health problems	71	29	84	23	73	33	80	58

3.8 Mental health

3.8.1 General mental health

All treatment groups showed striking differences in self reported mental health between the baseline and three month follow-up interviews (Table 7). A linear regression examining SF-12 mental health scores at 3 month follow-up was conducted ($F_{4,542}$=20.6, p<.001), controlling for age, gender, index treatment status and baseline SF-12 mental health score. The model accounted for 13% of the variance. Higher baseline SF-12

scores (â=0.4, t=8.8, p<.001), and entering treatment at baseline (â=0.1, t=2.7, p<.01), were independently associated with higher physical SF-12 score (better mental health) at three month follow-up.

3.8.2 Major Depression

Rates of current Major Depression dropped by over 50%: from 23% to 10% among those entering maintenance treatment, from 27% to 13% among those entering detoxification and from 31% to 10% among those entering residential rehabilitation. In contrast, rates of current Major Depression remained relatively stable in the non-treatment group. A similar pattern of results emerged for past month suicidal ideation and attempted suicide: rates of these behaviours fell dramatically in each of the three treatment groups, but remained relatively stable in the non-treatment group.

Using logistic regression, current Major Depression status at three months was examined controlling for age, gender, index treatment status and baseline depression status ($\div^2$=26.8, df=4, p<.001). Meeting DSM-IV criteria for Major Depression at baseline was the only factor significantly associated with Major Depression status at 3 month follow-up (OR=3.80, 95% CI: 2.21-6.55).

Table 7: Mental health at baseline and three months by treatment modality

	MT (N=185)		DTX (N=177)		RR (N=121)		NT (N=66)	
	BL	3 mth	BL	3 mth	BL	3 mth	BL	3 mth
SF-12 Mental health component score (mean)	33.3	43.2	30.3	38.2	28.0	40.4	36.7	38.9
Current Major Depression (%)	23	10	27	13	31	10	18	17
Thought a lot about committing suicide (%)	18	6	23	12	31	7	14	15
Made a suicide plan in past month (%)	11	4	16	8	17	4	6	8
Attempted suicide in preceding month (%)	3	1	7	2	7	1	2	3

3.9   Criminal activity and other sources of income

In parallel with the reductions in drug use and improvements in mental health, there were marked reductions between baseline and three month follow-up in the percentages of respondents who reported having committed crime in the one month preceding interview (Table 8). Specifically, self-reported involvement in any criminal activity in the past month fell from 47% to 24% among people in MT, from 57% to 3% among those who had entered detoxification and from 56% to 17% among those entering residential rehabilitation. In comparison, there was a less marked drop in crime among the non-treatment group, from 56% to 46%. Property crime and dealing remained the most common forms of crime reported at three months.

A linear regression examining factors associated with criminal activity at three months was conducted. Variables entered into the model were age, sex, index treatment status and OTI crime score at baseline. The model was significant ($F_{4,543}=24.6$, $p<.001$), and accounted for 15% of the variance. Not entering treatment at baseline ($\hat{a}=0.1$, $t=3.0$, $p<.005$), and greater baseline criminal involvement ($\hat{a}=0.3$, $t=8.2$, $p<.001$), were independently associated with greater criminal involvement at three months.

Table 8: Criminal activity at baseline and three months by treatment modality

	MT (N=185)		DTX (N=177)		RR (N=121)		NT (N=66)	
	BL	3 mth	BL	3 mth	BL	3 mth	BL	3 mth
Any crime in preceding mth (%)	47	24	57	30	56	17	56	46
Type of crime committed (%):								
Property	30	16	38	22	44	12	42	29
Dealing	20	8	27	12	21	7	38	15
Fraud	10	3	16	9	22	6	17	8
Violent	4	4	11	3	9	2	8	6

Reductions in self-reported criminal activity were paralleled by reductions in the percentages of respondents who reported criminal activity as their major source of income (Table 9). Specifically, the percentage of people reporting criminal activity as their main income source fell from 17% to 5% among those entering MT, from 24% to 8% among those entering detoxification and from 25% to 2% among those entering residential rehabilitation. In contrast, the reduction in the percentage of people in the non-treatment group who reported criminal activity as their primary income source was less marked: from 26% to 14%. It appears that the major changes in primary source of income for the treatment subjects came from a sharp increase in the percentage of people reporting government benefits as their primary source of income.

Table 9: Main source of income at baseline and three months by treatment modality

	MT (N=185)		DTX (N=177)		RR (N=121)		NT (N=66)	
	BL	3 mths	BL	3 mths	BL	3 mths	BL	3 mths
Main income past month (%):								
Gov benefit	53	74	45	61	39	87	47	53
Criminal activity	17	5	24	8	25	2	26	14
Wage/salary	17	16	19	22	20	8	15	18
Other	14	5	13	9	17	3	12	15
Living alone in past month (%)	14	11	20	14	25	7	27	24

3.10 Summary of changes in drug use, crime and mental health from baseline to three months.

In order to examine change over time in the major domains of drug use, crime, physical and mental health, a series of linear and logistic regressions were conducted using measures obtained at 3 months as the dependent variables (Table 10). Age, gender, treatment status at baseline and a baseline measure of the dependent variable were entered into all regression models. As mentioned earlier, males were less likely than females to be retained in the sample at 3 months, however, gender was not independently associated with any of the outcome measures. With the exclusion of current Major Depression, participants who had entered treatment at baseline showed significantly greater improvement in all areas than the non-treatment group. Controlling for baseline functioning, at three months the treatment group had fewer heroin use days in the preceding month, were more likely to be abstinent, had used fewer drug classes, had better general and injection-related health, better general mental health and were less criminally active than the non-treatment group. Poorer baseline functioning in terms of the number of heroin use days, polydrug use, injection-related health problems, general physical and mental health, current Major Depression and criminal involvement were also independently associated with poorer functioning in each of these areas at three months.

Table 10: Comparison of drug use, crime, physical and mental health at baseline and three months for the treatment and non treatment groups

	Treatment (N=483)		NT (N=66)		Comparisons
	BL	3 mth	BL	3 mth	
Drug Use Mean number of heroin use days	20.1	4.8	22.2	14.8	$F_{4,543}=26.6$, p<.001 (More heroin use days at baseline: â=0.2, t=5.6, p<.001; Non-treatment group: â=0.3, t=8.0, p<.001)
Abstinent from heroin in preceding month (%)	1	53	0	20	$\div^2=29.9$, df=4, p<.001 (Non-treatment group: OR=4.70, 95% CI 2.49-8.87)
Mean no. of drug classes used last month	4.8	3.3	5.4	4.4	$F_{4,544}=18.9$, p<.001 (Greater number of drugs used at baseline: â=0.3, t=6.8, p<.001; Non-treatment group: â=0.2, t=4.3, p<.001)
Physical Health SF-12 Physical health component score (mean)	43.8	48.6	43.7	46.0	$F_{4,542}=21.3$, p<.001 (Younger age: â=0.1, t=2.6, p<.01; Higher baseline SF-12 score: â=0.3, t=7.7, p<.001; Non-treatment group: â=0.1, t=2.1, p<.05)
Injection-related health problems in preceding month (%)	75	29	80	58	$\div^2=55.6$, df=4, p<.001 (Injection-related health problems at baseline: OR=4.22, 95% CI 2.41-7.39; Non-treatment group: OR=3.56, 95% CI 2.05-6.20)
Mental Health SF-12 Mental health component score (mean)	30.9	40.1	36.7	38.9	$F_{4,542}=20.6$, p<.001 (Higher baseline SF-12 score: â=0.4, t=8.8, p<.001; Non-treatment group: â=0.1, t=2.7, p<.01)
Current Major Depression (%)	26	11	18	17	$\div^2=26.8$, df=4, p<.001 (Current Major Depression at baseline: OR=3.80, 95% CI 2.21-6.55)
Crime Mean crime OTI score	2.2	0.7	2.6	1.5	$F_{4,543}=24.6$, p<.001 (Higher baseline OTI crime score: â=0.3, t=8.2, p<.001; Non-treatment group: â=0.1, t=3.0, p<.005)

3.11   Validation of self-reported drug use by analysis of hair samples.

The mean weight of hair samples (n=61) was 29.3mg (SD 11.2, range 11.1-74.1). There were significant correlations between OTI heroin use scores and hair morphine concentrations (rs=0.53), and between number of reported heroin use days in the preceding month and hair morphine concentrations (rs=0.52).

The overall agreement between any self-reported heroin use in the preceding month and the presence of morphine in hair was 75% (kappa=0.51). In 15% of cases heroin use was reported by participants, but morphine was not detected in their hair. In 6 of these 9 cases, self-reported heroin use was on 4 or fewer days over the preceding month. In only 10% of cases was heroin use in the preceding month denied, but morphine detected in hair samples.

The high rates of concordance are consistent with those reported in other studies of self-reported drug use among heroin users (Darke, 1998; Darke et al, 2002). In particular, the fact that the majority of disagreement between self-report and hair analysis was due to self-reported drug use not being detected by biomarkers is consistent with the broader literature on the validity of self-reported drug use (Darke, 1998).

4.   DISCUSSION

4.1   Major findings

The first major finding of this study concerned the feasibility of conducting longitudinal research within this population. The follow-up rate of 89% indicates that such research is eminently feasible. In terms of outcome, the major finding was that there were substantial reductions in heroin use across all three treatment modalities. Importantly, comparison of self-reported heroin use to analyses of hair samples revealed the self-report of ATOS participants to be *highly valid.* There were also substantial reductions in injection frequency, needle risk behaviours and heroin overdose. There were large declines in the levels of Major Depression in all treatment groups, and large improvements in general mental health. In contrast, there was comparatively little improvement among the non-treatment group. There were large declines in injection-related problems, and improvements in general health among all treatment groups. Much smaller improvements occurred amongst the non-treatment group. Finally, there were large declines in reported crime amongst all treatment groups, while levels of crime remained high among the non-treatment group.

4.2   Sample retention

At three month follow-up 89% of treatment entrants entering the ATOS study were successfully re-contacted and re-interviewed. This response rate exceeds those of other longitudinal studies of drug use populations conducted overseas (Gerstein et al, 1994; Simpson & Sells, 1990; Hubbard et al, 1989; Hubbard et al, 1997; Gossop et al, 1997), and indicates that, despite the often chaotic lifestyle of people entering treatment for opioid dependence, it remains feasible to conduct longitudinal studies of treatment outcomes in this group. The vast majority (83%) of the NT sample were also re-interviewed. Importantly, there appeared to be little difference between individuals re-interviewed at three months and those lost to follow-up, assessed on baseline characteristics. Most importantly, these two groups did not differ on levels of heroin use at baseline. While males were less likely to be followed up than females, gender was not

found to be a significant factor in any of the analyses assessing the various outcome domains.

4.3   Treatment retention and other treatment experiences

A strength of the ATOS study design was that comprehensive information on treatment experiences between baseline and follow-up was obtained. Analysis of this data indicated that in the MT group rates of treatment retention were relatively high, with 72% of people remaining in their index treatment at three month follow-up. Given that two of the residential rehabilitation services involved in ATOS offer 28 day programs, it is not surprising that the retention rate at three months was only 28% among the RR group. As expected in the DTX group, no individuals had remained in a single treatment episode for three months. Nonetheless, many of the individuals in these groups subsequently received some form of treatment: 27% of those entering MT, 83% of those entering DTX and 55% of those entering RR. Importantly, 33% of those in the non-treatment group also accessed some form of treatment for heroin dependence in the three months between study entry and follow-up interview. Access to treatment in this group may potentially explain some of the observed improvements in drug use and other outcomes and suggests that comparisons between treatment and non-treatment groups in this study may provide only a conservative estimate of the potential benefits of treatment for heroin dependence.

4.4   Heroin and other drug use

A pivotal finding to emerge from this study was that three months after entering treatment there had been a dramatic decline in levels of heroin use among those entering treatment. The vast majority of those entering treatment (86%) reported reducing their heroin use at three months while 53% reported that they were abstinent from heroin at three months. As has been repeatedly documented in drug research (Darke, 1998), the self-reported drug use of these heroin users was revealed by biomarkers to be of high validity.

In addition, there was no evidence to suggest a process of substitution whereby reduced heroin use was countered by an increase in the use of other drugs such as benzodiazepines. Indeed, it appeared that, overall, the use of other drugs also declined in the treatment group between baseline and three month interviews. In addition to the reductions in drug use among the treatment samples, there were also substantial reductions in injection frequency, and needle risk behaviours.

4.5   Mental health

Perhaps the most striking difference between baseline and three month follow-up concerned the change in general mental health. Ratings of general mental health improved markedly in the treatment groups, but remained relatively unchanged in the non-treatment group. There are a number of possible explanations for this pattern of results that need to be considered. Firstly, it may be that engagement with treatment services and access to care leads to a decrease in mental health problems – that is to say, that the reduction in rates of mental health problems represents a treatment effect. Alternatively, however, it could be that mental health problems act as a trigger to treatment seeking and that rates of these problems are therefore highest at the time that people enter treatment and may naturally decline thereafter. This interpretation is not entirely supported by the observation that, at baseline, rates of mental health problems are approximately equal in the treatment and non-treatment groups, but declined only in

the treatment groups. Although not traditionally considered the primary focus of treatment for heroin dependence, the potential for improvements in mental health during treatment is substantial. Future studies based on the ATOS cohort will more carefully examine issues surrounding improvements in mental health and, when future waves of data are available, will also be in a unique position to examine the extent to which such improvements may themselves act to promote and maintain reductions in heroin and other drug use.

A similar trend towards improvement was seen in relation to current Major Depression. However, baseline treatment status was not found to be significantly associated with having a major depressive disorder at three month follow-up.

4.6   Physical health

General physical health improved significantly across all treatment modalities, as did injection-related health. In contrast, a notable proportion of the non-treatment participants continued to have injection-related health problems at three months.

4.7   Criminal activity

Again, there were substantial reductions in self-reported criminal activity for the treatment groups between baseline and three month interviews. Such findings parallel the existing literature showing that successful engagement with treatment services is accompanied by substantial reductions in criminal activity. Such reductions can be considered as a major benefit of treatment and are typically attributed to a reduction in drug use.

4.8   Summary and conclusions

The majority of ATOS participants, in both the treatment and non-treatment modalities, were successfully located and re-interviewed at three months. Retention in the index treatment was highest among the MT group, but across all modalities (including the non-treatment sample) use of other treatment services was common. Comparison between baseline and three month characteristics revealed substantial improvements across a number of domains. While the non-treatment group showed apparent improvements across some domains, these improvements were less marked than among those entering treatment. Furthermore, the relatively high rate of treatment utilization by the "non-treatment" group during the intervening three months suggests that comparisons between treatment and non-treatment groups may provide only a conservative estimate of the potential benefits of treatment.

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APPENDIX A: ATOS THREE MONTH OUTCOMES BULLETIN