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Reductions in heroin use are not associated with increases in other drug use: 2-year findings from the Australian Treatment Outcome Study

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Abstract

Aims: To determine whether reductions in frequency of heroin use were associated with reductions in the use of other drugs over a 24-month period.
Design: Longitudinal cohort, with follow-up at 3, 12 and 24 months.
Participants: Six hundred and fifteen heroin users recruited for the Australian Treatment Outcome Study.
Setting: New South Wales, Australia.
Findings: The proportion reporting weekly heroin use declined significantly at 3, 12 and 24 months. Reductions in heroin use were associated with longer periods in both residential rehabilitation (RR) and maintenance treatment (MT). Less frequent use of other opioids, cocaine, amphetamine, cannabis and benzodiazepines were noted over follow-up, with alcohol use remaining stable. Across follow-up, lower frequency heroin use was associated with reduced likelihood of frequent use of other opioids, cocaine, amphetamine and benzodiazepines. Alcohol and cannabis use were unrelated to heroin use. Longer periods spent in RR were associated with declines in the use of all other drug classes, with MT associated with declines in other opioid and alcohol use.
Conclusions: There was no evidence for drug substitution in the face of reduced heroin use in this cohort of treatment seekers. The fear that a successful reduction in heroin use amongst treatment seekers will precipitate an increase in the use of other drugs appears ill-founded.

Keywords: Heroin; Polydrug; Treatment; Cohort

1. Introduction

Heroin use typically occurs within the context of widespread polydrug use (Darke and Ross, 1997; Gossop et al., 2002; Hubbard et al., 1997). Importantly, such polydrug use is not merely episodic, with high proportions of heroin users meeting diagnostic criteria for dependence on other drugs (Darke and Ross, 1997; Dinwiddie et al., 1996; Kidorf et al., 1996; Ross and Darke, 2000). One clinical issue that arises from polydrug use is the association between heroin use and other drug use. More specifically, is there evidence that reduced heroin use is accompanied by substitutive increases in other drug use (Fairbank et al., 1993; Ward et al., 1998)? There is certainly evidence within the naturalistic setting for such substitution. In recent years an unparalleled, and sustained decrease in the availability of heroin in Australia was associated with substantial increases in cocaine and amphetamine use (Topp et al., 2003). While perhaps not surprising in the non-treatment setting, such substitution would have great clinical implications within the treatment setting, as polydrug use presents a range of additional clinical problems including poorer treatment outcome (DeMaria et al., 2000), increased risk of opioid overdose (Fugelstad et al., 2003; Warner-Smith et al., 2001), increased risk of suicide (Borges et al., 2000; Darke and Ross, 2002), and elevated psychiatric comorbidity (Darke and Ross, 1997).

Results to date are equivocal. Both maintenance therapies and inpatient drug free residential rehabilitation have been shown to substantially reduce heroin use (Darke et al., 2005; Gossop et al., 2002; Hubbard et al., 1997; Ward et al., 1998), with longer treatment exposure and greater treatment stability associated with improved outcome (Darke et al., 2005; Flynn et al., 2003; Hubbard et al., 1997; Gossop et al., 1999; Simpson et al., 1997; Ward et al., 1998). Global reductions in other substance use have

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also been noted (DeMaria et al., 2000; Fairbank et al., 1993; Gossop et al., 2002; Hubbard et al., 1997), though this is not always the case. Best et al. (2000) recently reported significant *increases* in cocaine, cannabis and non-prescribed methadone use among methadone maintenance patients. Variations in other drug use may also differ by drug class: a number of studies report no decline in alcohol use among treated heroin users (Fairbank et al., 1993; Gossop et al., 2002). There may also be differences between the effects of different treatment modalities upon other drug use. Hubbard et al. (1997), for example, reported that residential rehabilitation had more effect upon other drug use than did outpatient methadone maintenance.

To date, no study has specifically examined the relationship between frequency of heroin and other drug use. The current study aimed to determine whether reductions in the frequency of heroin use were associated with reductions in the use of other drugs, or the substitution of other drugs, over a 24-month period. Generalised estimating equations (GEE) (Liang and Zeger, 1986) were employed to specifically examine the relationship between heroin use and the frequency of other drug use. GEE offers important advantages, in that it enables examination of the relationship between variables at all time points, and allows the inclusion of subjects with incomplete data (Twisk, 2003). In addition, the study also examined the effects of cumulative exposure to different treatment modalities on frequency of other drug use.

2. Materials and methods

2.1. Procedure

The data were collected from the New South Wales component of the Australian Treatment Outcome Study (ATOS). ATOS is a longitudinal study of entrants to treatment for heroin dependence, recruited from randomly selected treatment agencies delivering maintenance treatment (MT), detoxification (DTX) or residential rehabilitation (RR). Baseline interviews were conducted between February 2001 and August 2002. 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. In Australia, enrolment in MT programmes is of unlimited duration. The RR agencies comprised two short-term programmes (approximately 1 month) and two long-term programmes (approximately 3–6 months). The DTX programmes were inpatient, and were approximately 7–10 days duration. In addition, a comparison group of heroin users not currently in treatment (NT) were recruited participants were interviewed at baseline, 3, 12 and 24 months. 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) aged over 17 years, and (v) fluent in English.

ATOS relies on self-reported drug use. Hair sampling, however, was conducted at 3-month follow-up on 61 randomly selected participants (10% of the baseline sample) as a biomarker for heroin use over the month preceding interview. Overall agreement between self-reported heroin use and morphine in the hair was 75% ($\kappa = 0.51$). In 15% of discrepancies heroin use was reported, but hair morphine not detected. In only 10% of cases was heroin use denied and morphine detected. Due to logistical constraints, no hair sampling was conducted at other times throughout follow-up.

2.2. Structured interviews

At baseline, participants were administered a structured interview that addressed demographics, treatment history, drug use, criminal behaviours and psychopathology. Full interview details are reported elsewhere (Darke et al., 2005). Drug use over the month preceding interview was measured using the opiate treatment index (OTI) (Darke et al., 1992). OTI drug use estimates are ratios based upon the three most recent use episodes, and are expressed as *Q* scores: 1.0 indicates an average of one use episode of a drug per day, greater than one indicates more than daily use, and scores smaller than one less than daily use. The methodology has been demonstrated to have a high degree of validity and reliability (Darke et al., 1991; Darke et al., 1992). Follow-up interviews were abbreviated forms of the baseline interview. Participants were asked how many times they had commenced treatment for heroin dependence since the most recent interview, modality, and the time spent in each treatment episode.

2.3. Statistical analyses

Multiple regression analyses, applying GEE were used to test and estimate the effect of weekly heroin use on weekly use of each other major drug classes (other opioids, cocaine, amphetamines, cannabis and benzodiazepines) across the study period, with odds ratios (OR) and 95% confidence intervals (CI) reported. The term "weekly use" refers to use on a weekly, or more frequent basis. Due to the high prevalence of alcohol use, daily, as opposed to weekly use was used in order to obtain a more accurate model. Variables entered into the equations were age, sex and weekly heroin use. As heroin use and treatment exposure were collinear (Darke et al., 2005), another set of GEE were conducted to address the effect of proportion of time between baseline and 24-month follow-up spent in each of the three major treatment modalities on weekly drug use. The results presented here are based on all the available data ($n = 615$), including cases in which information was not obtained at all follow-up points. All analyses were conducted using SAS Version 8.2 (SAS, 1999).

3. Results

3.1. Sample characteristics

The baseline sample consisted of 615 current heroin users: 201 entering MT, 201 entering DTX, 133 entering RR and 80 NT subjects. The mean age at baseline was 29.3 years (S.D. 7.8, range 18–56 years), and 66% were male. The cohort had completed a mean of 10.0 years of secondary education (S.D. 1.7, range 2–12 years), 29% had completed a trade/technical course, and 6% a university degree. Forty one percent had a prison history, and 55% reported criminal behaviours in the preceding month. A wage/salary was the main source of income for 18%. The mean age of first intoxication from any substance was 13.7 years (S.D. 3.3, range 2–34 years), with alcohol (52%) and cannabis (42%) the two most common substances. The mean age of first heroin use was 19.7 years (S.D. 5.3, range 9–43 years) and length of heroin use career was 9.6 years (S.D. 7.4, range <1–35 years). Eighty nine percent had previously been enrolled in a treatment program for opiate dependence, including 85% of the NT group. Follow-up rates at the three time points were: 3 months (89%, $n = 549$), 12 months (80%, $n = 495$) and 24 months (76%, $n = 469$). Comparisons of those re-interviewed with those lost to follow-up indicated there were no differences in age, heroin use, previous treatment enrolment, criminal involvement or global mental health.

3.2. Treatment exposure over 24 months

Almost all subjects (99%) followed-up at 24 months had received treatment for heroin dependence over the study period (Table 1). The cohort had commenced a median of three treatment episodes since baseline, with a median proportion of

Table 1
Treatment exposure over 24 months

	Males ($n = 300$)	Females ($n = 169$)	All ($n = 469$)
Received treatment	296 (99%)	168 (99%)	464 (99%)
Type of treatment received			
MT	193 (64%)	127 (75%)	320 (68%)
DTX	163 (54%)	69 (41%)	232 (49%)
RR	123 (41%)	52 (31%)	175 (37%)
Number of treatment episodes (median)	3	3	3
Proportion of time spent in treatment between baseline and 24-month follow-up	37%	48%	41%
Currently enrolled in a treatment programme	149 (50%)	106 (63%)	255 (54%)

follow-up time spent in treatment of 41%. At initial 3-month follow-up, 71% of the MT group and 28% of the RR group were still in index treatment. At 24 months, 54% of the cohort interviewed were currently in treatment.

3.3. Drug use over follow-up

Weekly heroin use declined at all follow-up points (Table 2). At 3 months there were significant declines in weekly use of other opioids, cocaine, amphetamines, cannabis, and benzodiazepines. At 12 months there were further declines in the use of other opioids and cocaine, with the use of other drug classes remaining stable. Apart from heroin, the only drug class to decline at 24 months was benzodiazepines. Due to the high prevalence of weekly alcohol use, daily use was used to obtain a more accurate model. Daily alcohol use did not significantly decline at any point.

3.4. Heroin and other drug use

Those who reported using heroin less than weekly over follow-up were significantly less likely to report weekly use of other opiates (OR 0.58, CI 0.39–0.88), cocaine (OR 0.33, CI 0.23–0.48), amphetamines (OR 0.49, CI 0.32–0.74) and benzodiazepines (OR 0.43, CI 0.33–0.56). There was no relationship between heroin use and cannabis ($p > 0.50$) or alcohol ($p > 0.90$).

3.5. Treatment and drug use over follow-up

Higher proportions of time spent in MT between baseline and 24-month follow-up were associated with reductions in weekly use of heroin, other opioids and daily alcohol use (Table 3). Higher proportions of time spent in RR were associated with reductions in weekly use of heroin, other opioids, cocaine, amphetamine, cannabis and benzodiazepines, and daily alcohol use. Proportion of time up spent in DTX was not related to reductions in the use of any drug.

4. Discussion

There were large declines in heroin use across the 24-month period, but no evidence of drug substitution. The only drug class where a decline in use did not occur was alcohol, but even this did not increase. The GEE analyses of heroin and other drug use were consistent with the global drug use patterns seen amongst the cohort. The lower frequency use of both heroin and other opioids was particularly illustrative. If substitution was to have been evident, the use of substitute opioids would have been the most likely scenario.

Larger proportions of time across follow-up spent in RR and MT were strongly associated with reduced heroin use. Consistent with Hubbard et al. (1997), there appeared to be differences between treatment modalities in their effects upon non-heroin use. Longer periods spent in RR were associated with declines in the use of all other drugs. By contrast, MT was associated with declines only in other opioid and alcohol use. These findings, in all probability, reflect the pharmacological focus of MT upon reductions in opioid use through stabilisation by a substitute opioid (Ward et al., 1998), whereas RR adopts a global abstinence oriented approach to all drugs. The reductions in alcohol use associated with MT were, however, in contrast to other non-opioids. In recent years, however, there have been a number

Table 2
Heroin and other drug use at baseline, 3, 12 and 24 months

Drug	Baseline ($n = 615$)	3 months ($n = 549$)	12 months ($n = 495$)	24 months ($n = 469$)
Weekly heroin use (OR, CI)[a]	584 (95%)	198 (36%) (0.05, 0.04–0.09)	139 (28%) (0.60, 0.47–0.78)	108 (23%) (0.71, 0.55–0.92)
Weekly other opioid use (OR, 95% CI)	123 (20%)	60 (11%) (0.63, 0.43–0.93)	35 (7%) (0.51, 0.33–0.79)	28 (6%) ns
Weekly cocaine use (OR, 95% CI)	154 (25%)	66 (12%) (0.85, 0.36–0.70)	25 (5%) (0.32, 0.21–0.48)	19 (4%) ns
Weekly amphetamine use (OR, 95% CI)	98 (16%)	38 (7%) (0.55, 0.36–0.86)	25 (5%) ns	33 (7%) ns
Weekly cannabis use (OR, 95% CI)	363 (59%)	220 (40%) (0.54, 0.43–0.68)	198 (40%) ns	183 (39%) ns
Weekly benzodiazepine use (OR, 95% CI)	252 (41%)	121 (22%) (0.51, 0.39–0.68)	94 (19%) ns	75 (16%) (0.72, 0.55–0.94)
Daily alcohol use (OR, 95% CI)	160 (26%)	104 (19%) ns	109 (22%) ns	113 (24%) ns

ns: not significant.
[a] Odds of use compared to previous interview point (GEE).

Table 3
GEE analyses of proportion of time in treatment modality and frequency of drug use

Drug	Analyses by treatment modality
Weekly heroin use	MT (OR 0.30, CI 0.22–0.42); RR (OR 0.06, CI 0.03–8.33); DTX ns
Weekly other opioid use	MT (OR 0.31, CI 0.18–0.52); RR (OR 0.04, CI 0.01–0.15); DTX ns
Weekly cocaine use	MT ns; RR (OR 0.09, CI 0.02–0.45); DTX ns
Weekly amphetamine use	MT ns; RR (OR 0.14, CI 0.04–0.51); DTX ns
Weekly cannabis use	MT ns; RR (OR 0.11, CI 0.06–0.19); DTX ns
Weekly benzodiazepine use	MT ns; RR (OR 0.18, CI 0.09–0.36); DTX ns
Daily alcohol use	MT (OR 0.70, CI 0.50–0.99); RR (OR 0.06, CI 0.02–0.15); DTX ns

ns: not significant; MT: maintenance; RR: residential rehabilitation; DTX: detoxification.

of campaigns emphasising the dangers of alcohol in increasing opioid overdose risk (McGregor et al., 2001), which may be reflected in these data. It is important to note that the proportion of time spent in DTX was not associated with reductions in the use of any drug.

Declines in use were marked for other opioids, cocaine and amphetamine. By contrast, cannabis and alcohol use remained common. Similar to previous studies (Fairbank et al., 1993; Gossop et al., 2002), no overall decline in alcohol use was observed. Encouragingly, there was evidence that more extensive exposure to RR and MT did reduce daily alcohol use, but it is clear that alcohol use is particularly resistant to change. This is cause for clinical concern, as a pattern of less frequent opioid use accompanied by alcohol consumption has been linked to fatal opioid overdose (Darke et al., 2002; Fugelstad et al., 2003), and alcohol use amongst a population with high levels of hepatitis C exposure risks exacerbating liver damage (Karch, 2002).

In interpreting these results, it should be borne in mind that biomarkers were only collected at 3-month follow-up. As such, caution needs to be exercised in interpreting reported drug use rates. Hair analyses, however, showed respectable concordance with self-reported heroin use, and most discordance was from reported use *not* being detected. Self-reported use also varied widely across drug classes, with no obvious global "halo effect". In extrapolating the results to other heroin users, it should be also noted that this was a cohort of active treatment seekers, with almost all having received treatment by 24-month follow-up. Indeed, despite the wide range of use careers, almost all had previously received treatment for opioid dependence. The extent to which such covariations are typical of untreated heroin users is unknown. The study also did not also examine the effects of length of use career upon substitution behaviours.

In summary, there was no evidence for drug substitution in the face of reduced heroin use. Rather, less frequent heroin use was generally associated with less frequent use of other drugs.

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References

Best, D., Harris, J., Gossop, M., Farrell, M., Finch, E., Noble, A., Strang, J., 2000. Use of non-prescribed methadone and other illicit drugs during methadone maintenance treatment. Drug Alcohol Rev. 19, 9–16.

Borges, G., Walters, E.E., Kessler, R.C., 2000. Associations of substance use, abuse, and dependence with subsequent suicidal behaviour. Am. J. Epidemiol. 151, 781–789.

Darke, S., Hall, W., Heather, N., Wodak, A., Ward, J., 1992. Development and validation of a multi-dimensional instrument for assessing outcome of treatment among opioid users: the opiate treatment index. Br. J. Addict. 87, 593–602.

Darke, S., Hall, W., Kaye, S., Ross, J., Duflou, J., 2002. Hair morphine concentrations of fatal heroin overdose cases and living heroin users. Addiction 97, 977–984.

Darke, S., Heather, N., Hall, W., Ward, J., Wodak, A., 1991. Estimating drug consumption in opioid users: reliability and validity of a "recent use" episodes method. Br. J. Addict. 86, 1311–1316.

Darke, S., Ross, J., 1997. Polydrug dependence and psychiatric comorbidity among heroin injectors. Drug Alcohol Depend. 48, 135–141.

Darke, S., Ross, J., 2002. Suicide among heroin users: rates, risk factors and methods. Addiction 97, 1383–1394.

Darke, S., Ross, J., Teesson, M., Ali, R., Cooke, R., Ritter, A., Lynskey, M., 2005. Factors associated with 12 months continuous heroin abstinence: findings from the Australian Treatment Outcome Study (ATOS). J. Subst. Abuse Treat. 28, 255–263.

DeMaria, P.A., Sterling, R., Weinstein, S.P., 2000. The effect of stimulant and sedative use on treatment outcome of patients admitted to methadone maintenance treatment. Am. J. Addict. 9, 145–153.

Dinwiddie, S.H., Cottler, L., Compton, W., Abdallah, A.B., 1996. Psychopathology and HIV risk behaviours among injection drug users in and out of treatment. Drug Alcohol Depend. 43, 1–11.

Fairbank, J.A., Dunteman, G.H., Condelli, W.S., 1993. Do methadone patients substitute other drugs for heroin? Predicting substance use at 1-year follow-up. Am. J. Drug Alcohol Abuse 19, 465–474.

Flynn, P.M., Joe, G.W., Broome, K.M., Simpson, D.D., Brown, B.S., 2003. Recovery from opioid addiction in DATOS. J. Subst. Abuse Treat. 25, 177–186.

Fugelstad, A., Ahlner, J., Brandt, L., Ceder, G., Eksborg, S., Rajs, J., Beck, O., 2003. Use of morphine and 6-monoacetylmorphine in blood for the evaluation of possible risk factors for sudden death in 192 heroin users. Addiction 98, 463–470.

Gossop, M., Marsden, J., Stewart, D., Rolfe, A., 1999. Treatment retention and 1 year outcomes for residential programmes in England. Drug Alcohol Depend. 57, 89–98.

Gossop, M., Marsden, J., Stewart, D., Treacy, S., 2002. Change and stability of change after treatment of drug misuse. Two-year outcomes from the National Treatment Outcome Research Study. Addict. Behav. 27, 155–166.

Hubbard, R.L., Craddock, S.G., Flynn, P.M., Anderson, J., Etheridge, R.M., 1997. Overview of 1 year follow-up outcomes in the Drug Abuse Treatment Outcome Study (DATOS). Psychol. Addict. Behav. 11, 261–278.

Karch, S.B., 2002. Karch's Pathology of Drug Abuse, 3rd ed. CRC Press, Boca Raton.

Kidorf, M., Brooner, R.K., King, V.L., Chutuape, M.A., Stitzer, M.L., 1996. Concurrent validity of cocaine and sedative dependence diagnoses in opioid-dependent outpatients. Drug Alcohol Depend. 42, 117–123.

Liang, K.-Y., Zeger, S.L., 1986. Longitudinal data analysis using generalize linear models. Biometrika 73, 13–22.

McGregor, C., Ali, R., Christie, P., Darke, S., 2001. Overdose among heroin users: evaluation of an intervention in South Australia. Addict. Res. 9, 481–501.

Ross, J., Darke, S., 2000. The nature of benzodiazepine dependence among heroin users in Sydney. Aust. Addict. 95, 1785–1793.

SAS Inc., 1999. SAS Version 8.2. SAS Inc., Carey.

Simpson, D.D., Joe, G.W., Brown, B.S., 1997. Treatment retention and follow-up outcomes. I. The Drug Abuse Treatment Outcome Study (DATOS). Psychol. Addict. Behav. 4, 294–307.

Topp, L., Day, C., Degenhardt, L., 2003. Changes in patterns of drug injection concurrent with a sustained reduction in the availability of heroin in Australia. Drug Alcohol Depend. 70, 275–286.

Twisk, J.W.R., 2003. Applied Longitudinal Data Analysis for Epidemiology. Cambridge University Press, Cambridge.

Ward, J., Mattick, R.P., Hall, W. (Eds.), 1998. Methadone Maintenance Treatment and Other Opioid Replacement Therapies. Harwood, Amsterdam.

Warner-Smith, M., Darke, S., Lynskey, M., Hall, W., 2001. Heroin overdose: causes and consequences. Addiction 96, 1113–1125.