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ACKNOWLEDGMENTS

This research was funded by the Drug and Alcohol Directorate of New South Wales. The authors would like to thank the following organisations for their assistance in this study: Liverpool Hospital Drug and Alcohol Unit, Canterbury Hospital Drug and Alcohol Unit, Kullaroo Clinic, the Central Coast Needle Exchange, We Help Ourselves, St Mary's Needle Exchange and SWAP. In particular, we would like to thank Karen Becker, Jessica Darke, Mario Fantini, Bruce Flaherty, Anna Haining, Gayle Kennedy, Lisa Maher, Dorothy Oliphant, Suzanne van Opdorp, Helen Polkinghorn, Garth Popple and Sandra Sunjic.

EXECUTIVE SUMMARY

The current study examined transitions in routes of benzodiazepine administration among heroin users in Sydney. Of 312 heroin users, 94% had used benzodiazepines and 72% had used them in the six months prior to interview. Benzodiazepine injecting was fairly common, with 28% ever having injected these drugs and 13% having done so during the six months preceding interview. Males and females were equally likely to have injected benzodiazepines.

A transition to injecting benzodiazepines did not necessitate injection becoming the primary route of benzodiazepine administration. In this way a transition to injecting benzodiazepines differed markedly from a transition to injecting heroin or amphetamines. Nevertheless, the injection of tablets, intended exclusively for oral consumption, represents a serious health concern.

While there were clear harms associated with oral benzodiazepine use among the sample, these harms appeared to be exacerbated among subjects who had injected benzodiazepines. Current benzodiazepine injectors showed greater polydrug use, injection-related HIV risk-taking behaviour, criminal involvement, psychological distress, and injection related health problems, as well as poorer general health, and an increased risk of having overdosed than oral users of benzodiazepines.

Of clinical importance were the reasons given by ex-benzodiazepine injectors for having ceased injecting benzodiazepines. Concern for general health emerged as the most common rationale for having made a transition away from injecting, and for being likely to make such a transition.

The results of the present study suggest that heroin users can change their behaviour with regard to injecting benzodiazepines. Of those subjects who had ever injected benzodiazepines, 55% no longer did so. To enable heroin users to make better informed decisions about how they use benzodiazepines, they need to be advised of the risks associated with injecting these drugs. Staff in needle and syringe exchange programs and methadone clinics could play a pivotal role in the education process.

1.0 INTRODUCTION

Benzodiazepine use among injecting drug users (IDUs) has been repeatedly linked to higher rates of HIV risk-taking behaviour and psychopathology, poorer health, poorer social functioning, and greater risk of heroin overdose[1-6]. Despite a general decline in the prescribing of benzodiazepines[7], these drugs remain readily accessible to the injecting drug using population[8].

Recent studies have indicated extensive injecting of benzodiazepines by IDUs[9-11], a practice that has been associated with vascular morbidity, amputations and mortality among this group[12,13]. While benzodiazepine injecting has been widely documented in the United Kingdom, until relatively recently there were no published data on the practice in Australia. In a study of 301 regular amphetamine users in Sydney, 66% had used benzodiazepines, of whom 27% had injected them, with 15% having done so during the six months prior to interview[2]. In a sample of 329 heroin users, 64% reported being current benzodiazepine users, of whom 48% had injected them and 17% had done so in the preceding six months[9]. Clearly the injection of benzodiazepines is not a problem unique to the United Kingdom. A similar pattern of benzodiazepine use has emerged as a major problem in Australia.

In contrast to the United Kingdom where the injection of temazepam gel capsules predominates[11,14], a broader pattern of benzodiazepine injecting among heroin users in Sydney has been reported by the authors[9]. While 25% of current benzodiazepine using heroin injectors had injected temazepam, 25% reported having injected diazepam. Heroin users were thus as likely to be crushing diazepam tablets and injecting them as to be using the temazepam gel preparations. Oxazepam (14%) and flunitrazepam (12%) tablets had also been injected by substantial proportions of subjects. The potential health effects of injecting tablets meant for oral administration are the basis for serious concern.

If we are to minimise the harm caused by the parenteral use of benzodiazepines, a greater understanding of the correlates of benzodiazepine injecting is needed. Specifically, what are the factors associated with a change from swallowing to injecting these drugs? What factors are associated with the cessation of such injecting? What are the practices associated with benzodiazepine injecting? What health and psychiatric sequelae emerge over and above those associated with oral benzodiazepine use? What social dysfunction is associated with benzodiazepine injecting?

The current study aimed to address the questions raised above. The study was built upon work conducted by the authors into transitions in routes of amphetamine administration[15]. A knowledge of what motivates heroin users to inject benzodiazepines, and more importantly, to cease injecting benzodiazepines, may facilitate the design and application of appropriate interventions.

1.1 *Study Aims*

The major aims of the present study were as follows;

1) To examine the reasons given by subjects for preferring a particular route of benzodiazepine administration, and for changing routes of administration;

2)To examine the correlates of benzodiazepine injecting;

3) To examine benzodiazepine injecting procedures;

4) To examine problems associated with the injection of benzodiazepines.

2.0 METHOD

2.1 *Procedure*

All subjects were volunteers who were paid A$20 for their participation in the study. Recruitment took place from January to October of 1995, by means of advertisements placed in rock magazines, needle exchanges, methadone maintenance clinics and by word of mouth.

Subjects contacted the researchers, either by telephone or in person, and were screened for eligibility to be interviewed for the study. To be eligible for the study subjects had to either be in treatment for heroin dependence, or have used heroin during the preceding three months, or both.

Each interview was conducted in a location determined by the subject in an attempt to minimise any hesitation they might have about participating. Consequently, interview sites ranged from pubs, coffee shops, parks, shopping centres, to subjects' homes and the researchers' workplace (National Drug & Alcohol Research Centre). All subjects were guaranteed, both at the time of screening and interview, that any information they provided would be kept strictly confidential and anonymous. All interviews were conducted by one of the research team and took between 45 and 60 minutes to complete.

2.2 *Structured Interview*

A structured interview was devised that addressed the following areas: demographic characteristics, drug use history, heroin dependence, health, psychological functioning, heroin overdose, needle risk behaviours, criminal behaviours, benzodiazepine use history (including circumstances and reasons for changing between different routes of administration), benzodiazepine injecting procedures and the most recent benzodiazepine injection episode. The questionnaire was pilot tested on 10 heroin users, and refinements were made on the basis of this. The areas covered by the interview are outlined in detail below.

2.2.1 Demographic characteristics

The demographic details obtained included: the subject's gender, age, area of residence, level of high school and tertiary education, employment status, current treatment status, prison record and whether they had a regular sexual partner who was an injecting drug user.

2.2.2 Drug use history

In order to gain an indication of overall drug use, subjects were asked which drug classes they had ever used, which ones had they ever injected, and which ones had they injected in the last 6 months. An estimation of how many days they had used each of the drug classes during the 6 months preceding interview was also sought.

Further questions were asked about the first drug ever injected and how old they were when they first injected heroin.

2.2.3 Heroin dependence

Current dependence on heroin was measured using the Severity of Dependence Scale (SDS)[16,17]. This is a 5-item scale which asks about psychological dependence in the preceding year. SDS scores range from 0-15, with higher scores being indicative of greater heroin dependence.

2.2.4 Benzodiazepine use history

Information collected regarding subjects' use of benzodiazepines included: the age at which they first used benzodiazepines, the first route of administration used, the age at which they commenced regular (at least monthly) use of benzodiazepines, the age at which they had first injected benzodiazepines, the route of administration used during the 6 months preceding interview and the route of benzodiazepine administration used overall.

Those subjects who had never used benzodiazepines were asked to give their two main reasons why. Similarly, those subjects who had only ever swallowed benzodiazepines were asked why they had never injected them.

Subjects who had injected a benzodiazepine were asked questions relating to the circumstances surrounding the first injection. Data collected included the age at which subjects first injected benzodiazepines, the period of time that had elapsed between first trying and first injecting benzodiazepines, what proportion of their friends had been injecting these drugs, and whether they were living with someone who was injecting benzodiazepines at the time. Subjects were also asked how often they had injected benzodiazepines since the first time, and how injecting these drugs had affected their level of benzodiazepine and other drug use. In cases where benzodiazepines had been injected more than once, subjects were asked why they had continued to inject benzodiazepines. Current benzodiazepine injectors were asked how likely it was that they would stop injecting benzodiazepines. Those who said it was likely were asked to give the main reasons why.

2.2.5 Benzodiazepine dependence

Benzodiazepine dependence was assessed in the same way as heroin dependence. Subjects were again given the SDS to complete but this time the questions were related to their benzodiazepine use during the 12 months preceding interview.

2.2.6 Health

The Health Scale of the Opiate Treatment Index (OTI)[18] was used to gain some indication of the respondent's current state of health. This scale is divided into items addressing signs and symptoms in each of the major organ systems, with one

section specifically focusing on injection-related health problems. The higher the score obtained, the poorer the overall health of the subject.

Subjects who had injected benzodiazepines were also asked about specific health problems related to the injection of benzodiazepines, and whether they had consulted medical practitioners about these problems.

2.2.7 Psychological functioning

Psychological adjustment was assessed using the 28 item version of the GHQ[19]. This scale gives a global measure of non-psychotic psychopathology and is made up of the following 4 sub-scales: Somatic symptoms, Anxiety, Social dysfunction and Depression. Global scores range from 0-28, with 4/5 being the most commonly used cut-off point in determining the number of `cases' of psychopathology in a sample.

2.2.8 Heroin overdose

Subjects were asked how many times they had overdosed, how long since they had last overdosed and whether they had ever been administered naloxone.

2.2.9 Needle risk behaviours

The HIV Risk-taking Behaviour Scale (HRBS), a component of the OTI was used in assessing injecting behaviours in the month preceding interview that placed subjects at risk of either contracting or transmitting HIV and other blood borne viruses.

2.2.10 Criminal behaviours

Using the Criminality Scale of the OTI, a record was taken of any property crimes, drug dealing, fraud and violent crimes committed during the month preceding interview. Higher scores on the Criminality Scale denote greater criminal involvement. As in the OTI, subjects were also asked whether they were currently facing any charges. Subjects who had ever used benzodiazepines were asked whether they had ever committed either a property or violent crime while under the influence of these drugs. Those subjects who indicated that they had committed such a crime were asked why, and which type of benzodiazepine they were most likely to have used on such an occasion.

2.2.11 Benzodiazepine injecting procedures

Subjects were asked about the procedures they employed in injecting benzodiazepines. Information collected included the average number of tablets used in an injection, the greatest number of tablets injected in a day, the size of syringes used to inject benzodiazepines, how difficult they considered preparing benzodiazepines for injection to be, and who taught them how to inject these drugs.

2.2.12 Benzodiazepine familiarity and preferences among injectors

Having read a list of all the available benzodiazepines, subjects were asked to indicate which ones they had ever injected. They were then requested to indicate which benzodiazepine they found the easiest to inject, which one they preferred to inject and why. It should be noted that subjects were shown a list of the trade names rather than the generic names for the benzodiazepines. In reporting the results, however, generic names were used (see Appendix 1 for a list of trade and generic names).

2.2.13 Most recent benzodiazepine injection episode

Details of the most recent benzodiazepine injection were sought, including the length of time since the last injection, the type of benzodiazepine injected, the number of tablets used, whether the benzodiazepine tablets were mixed with water, the size of syringe used, and whether vein infusion sets were used. A vein infusion set consists of a needle attached to a length of plastic tubing, to which a syringe is attached. It may be occluded between injections to prevent blood loss through the inserted needle, and improves stability for the use of larger sized syringes. Subjects were also asked whether they mixed any other drug in the syringe with the benzodiazepine, whether they used a filter, and if so what type of filter.

2.3 *Analyses*

For continuous variables t-tests were employed. Categorical variables were analysed using chi^2, and corresponding odds ratios (O.R.) and 95% confidence intervals (C.I.) were calculated. Where distributions were highly skewed, medians were reported. Highly skewed continuous data were analysed using the Mann-Whitney U statistic. In order to determine which factors were independently associated with levels of benzodiazepine dependence, simultaneous multiple regressions with backwards elimination were conducted. The structure of the SDS was examined using a Principal Components Analysis.

Multiple logistic regressions were conducted in order to identify the factors associated with a change between routes of benzodiazepine administration. Backwards elimination of variables was used to select the most appropriate models.

Comparisons between current benzodiazepine injectors, oral users and the remainder of the sample were made using analyses of variance (ANOVA) for continuous variables and logistic regressions for categorical variables. "Current" use was defined as use within the six months preceding interview. All analyses were conducted using SYSTAT[20].

3.0 RESULTS

3.1 Sample characteristics

The sample consisted of 312 subjects, of whom 61% were male. The mean age of the sample was 28.8 years (SD 6.9, range 16-48) with males being significantly older than females (29.8 yrs v 27.3 yrs, t_{310}=3.1, p<.005). Subjects were recruited from all regions of Sydney (Table 1).

The mean number of years of school education was 9.7 (SD 1.5, range 3-12), with 45% having completed less than 10 years. Thirty eight percent of subjects had completed 10 years of schooling and 18% had completed 12 years. The majority of the sample (74%) had no tertiary qualifications, with 22% having attained a trade or technical certificate and 5% having gained a university or college degree.

The majority of the sample was unemployed (80%), with only 4% in full-time and 10% in casual or part-time employment. A large proportion reported having a prison record (45%), with males being more likely than females to report ever having been in gaol (55% v 30%, O.R.=2.8, 95% C.I. 1.7-4.5).

Approximately half of the sample (53%) were currently enrolled in treatment for opioid dependence, with females significantly more likely to be currently enrolled (66% v 46%, O.R. 2.4, 95% C.I. 1.5-3.9). A significant age effect was noted, with the mean age of subjects in treatment five years greater than that of those not in treatment (26.3 yrs v 31.0 yrs, t_{310}=-6.4, p<.001). The median length of time in current treatment was 24 months (range 1 day-12 years). Methadone maintenance was the most common modality utilised by those subjects currently in treatment (166/168). Two thirds (63%) of the sample had previously been enrolled in drug treatment.

The majority of the sample reported having a regular sexual partner (63%), but only 19% had a partner who was not an injecting drug user. Females were more likely than males to have a partner (71% v 57%, O.R. 1.9, 95% C.I. 1.1-3.0). Of those subjects with a regular partner, males were more likely to have a partner who did not inject drugs (38% v 20%, OR 2.5, 95% C.I. 1.3-4.8).

Table 1: Demographic characteristics of 312 heroin users

N	**Male** 190	**Female** 122	**Persons** 312
Age in years (mean)*	29.8	27.3	28.8
Recruitment area (%):			
North, Inner City/East/West	42	56	47
West, South West & South	58	44	53
School Education (mean years)	9.6	9.7	9.7
Tertiary Education (%):			
No tertiary education	75	73	74
Trade/Technical	22	21	22
University/College	3	4	4
Trade & University	0	2	1
Employment Status (%):			
Unemployed	83	75	80
Full-time	6	1	4
Part-time/Casual	11	9	10
Student	0	3	1
Home Duties	0	12	5
Prison Record (%)*:			
No	45	70	55
Yes	55	30	45
Currently in treatment (%):	46	66	54
Regular sexual partner (% yes)	57	71	63

* *Significant gender difference exists*

3.2 Benzodiazepine use

The majority of subjects (94%) had tried benzodiazepines, and 71% were current users, having used these drugs during the preceding 6 months. While 97% of those subjects who had ever tried benzodiazepines reported initially taking them orally, 3% indicated that they had administered them parenterally the first time. Current benzodiazepine users were on average, 4 years younger than the ex-users (27.8 yrs v 32.0 yrs, t_{291}=-4.8, p<.001), but the two groups did not differ significantly in terms of mean age of first benzodiazepine use (18.7 v 19.4) or mean age of first regular use (20.7 v 19.5).

Table 2 shows the history of benzodiazepine use among ***current*** benzodiazepine users. While the mean age of first use was 18.7 years (SD 5.2, range 2-37), this differed according to gender, with males being significantly older than females when they commenced using benzodiazepines (19.5 yrs v 17.6 yrs, t_{221}=2.8, p<.01). Similarly, the mean age reported for the commencement of regular benzodiazepine use was significantly greater for males (21.7 yrs v 19.5 yrs, t_{180}=2.8, p<.01). The mean length of time at interview since first benzodiazepine use was 9.1 years (SD 6.4, range 0-26). While 43% of current benzodiazepine users had used benzodiazepines prior to using heroin, 42% had used heroin before having tried benzodiazepines.

The median number of days on which benzodiazepines had been used during the 6 months preceding interview was 20 (range 1-180). Forty two percent of current benzodiazepine users reported having used these drugs more than once a week in the last 6 months, including 15% who indicated that they had used them daily.

When asked how they had used benzodiazepines over the last 6 months, 20% of current benzodiazepine injectors reported having administered benzodiazepines by injection on at least 50% of occasions. Current injectors had used benzodiazepines on significantly more days in the preceding 6 months than subjects who had only taken benzodiazepines orally in that period (55 v 14, U=4468.0, p<.05). Sixty three percent of injectors had used benzodiazepines more than once a week, including 13% who had used them daily.

Table 2: History of benzodiazepine use among current users

	Males	**Females**	**Persons**
N	131	92	223
Mean age when first used benzodiazepines (years)	19.5	17.6	18.7+
Mean age when first used benzodiazepines regularly *i.e. at least once a month* (years)*	21.7	19.5	20.0+
Mean length of time since first used benzodiazepines (years)	9.2	8.8	9.1
Median number of days benzodiazepines were used in the 6 months prior to interview	14	21	20

* *Excludes those subjects who have never used benzodiazepines regularly: Males n=104, Females n=78, Persons n=182.*

\+ *Statistically significant difference between males and females*

3.3 Benzodiazepine dependence

The mean SDS score for benzodiazepines among current users was 3 (SD 3.7, range 0-15). In a previous study which looked at amphetamine dependence an SDS cut-off mark of 4/5 was taken to be indicative of dependence[2]. Using a cut-off score of greater than 4, 21% of the sample showed signs of dependence. As a measure of benzodiazepine dependence the SDS showed good psychometric properties based on the current data. Cronbach's alpha was 0.90, indicating excellent internal reliability. The structure of the SDS was explored by submitting scores on the five items to principal components analysis. Dependence emerged as a one factor solution that accounted for 74% of the variance, with all items having loadings of 0.79 or greater.

In determining which factors were independently associated with levels of benzodiazepine dependence, simultaneous multiple regressions were conducted. The variables entered into the model were age, sex, route of administration used in the last six months (oral v parenteral), frequency of use during that period, length of time since first trying benzodiazepines, past imprisonment and current treatment status.

The final model was significant ($F_{1,220}$=123.0, p<.001) and accounted for 36% of the variance. The only variable significantly associated with dependence was

frequency of benzodiazepine use (β=0.04, p<.001), with greater use associated with higher levels of dependence.

3.4 Other drug use

As shown in table 3, poly-drug use was common among the sample. All subjects had used heroin and 86% had done so in the last 6 months. Similarly, the majority of the sample (82%) had used other non-prescribed opiates, with 40% having done so during the 6 months preceding interview. Twenty three percent of subjects reported having injected opiates other than heroin within that time.

The mean age of first heroin use was 18.5 years (SD 3.8, range 10-35). At the time of interview, the mean length of heroin use career was 10.3 years (SD 7.1, range <1-30yrs). Males had significantly longer heroin using careers than females (11.1 yrs v 9.0 yrs, t_{310}=2.6, p<.01). The mean SDS score for heroin was 7.9 (SD 4.5, range 0-15). Using a cut-off mark of greater than 4, 77% of subjects were classified as heroin dependent. Males and females were equally likely to be heroin dependent (7.7 v 8.2, t_{310}=-1.0, p>.05).

The vast majority of subjects reported having ever used amphetamines (97%), alcohol (99%), cannabis (99%), tobacco (98%) and hallucinogens (88%), with cocaine (75%) and inhalants (60%) having also been widely used. During the 6 months preceding interview the use of amphetamines (41%), cocaine (26%), hallucinogens (19%) and inhalants (13%) were less commonly reported, but the use of alcohol (75%), cannabis (80%), and tobacco (94%) remained pervasive.

While approximately a fifth of the sample (22%) reported having tried barbiturates, only 1% had done so in the last 6 months.

Including benzodiazepines the mean number of drug classes ever used was 9.2 (SD 1.5, range 3-11), with a mean of 5.5 (SD 2.1, range 1-11) having been used in the last 6 months. The mean number of drug classes ever injected was 3.8 (SD 1.4, range 1-7), and 1.8 (SD 1.2, range 0-6) for the 6 months prior to interview.

Table 3: Other drug use (N=312)

Drug Class	Ever Used %	Ever Injected %	Used in Last 6 Months %	Injected in Last 6 Months %	Days Used in Last 6 Months*
Benzodiazepines	94	28	71	13	20
Heroin	100	100	86	85	72
Other Opiates	82	66	40	23	7
Amphetamines	97	90	41	37	4
Cocaine	75	62	26	20	3
Hallucinogens	88	29	19	4	4
Barbiturates	22	8	1	0	2
Alcohol	99	N/A	75	N/A	14
Cannabis	99	N/A	80	N/A	90
Inhalants	60	N/A	13	N/A	3
Tobacco	98	N/A	94	N/A	180
Poly-drug use+	10	4	5	2	-

* Median number of days used in the last 6 months by those who had used the drug class in that period

+ Mean number of drug classes

3.5 Patterns of benzodiazepine administration

3.5.1 Injecting of benzodiazepines

Over a quarter of the sample (28%) had ever injected a benzodiazepine, and 13% had done so in the last 6 months. Males and females were equally likely to have ever injected a benzodiazepine (28% v 29%). The mean age of first benzodiazepine injection was 22.0 years (SD 5.3, range 12-38), but this differed according to sex, with males being significantly older than females when they first injected a benzodiazepine (23.1 v 20.4, t_{86}=-2.5, p<.05). A median of 2 years was reported to have elapsed between first trying benzodiazepines and first injecting them (range 0-22). While the majority of benzodiazepine injectors indicated that they had injected these drugs less than monthly since the first time, 11% (10/88) reported having injected them once a week or more.

Excluding those subjects who injected benzodiazepines on the first use occasion, 30% of benzodiazepine injectors reported using more benzodiazepines once they began injecting them and only 10% reported using less. The remainder (60%) reported no change in the quantity of benzodiazepines used. Of all the benzodiazepine injectors, almost a quarter (24%) reported using larger quantities of other drugs once they began injecting benzodiazepines, with 14% using less. The majority of subjects (64%) were not living with someone who was injecting benzodiazepines at the time of their first benzodiazepine injection, but 60% reported that injection had been the method of benzodiazepine administration used by half or more of their friends.

The overwhelming majority (88%) of subjects who had injected benzodiazepines, did so more than once (77/88). Those subjects who had injected benzodiazepines more than once were asked to give the two main reasons why they continued to do so (Table 4). The most popular response was that they obtained a better effect or `rush' from injecting (34%). The next two most common reasons given were that injecting resulted in a quicker onset of the drug (25%) and relieved heroin withdrawal (25%).

Table 4: Reasons why subjects continued to inject benzodiazepines

(n=77)

Reasons	**% Yes**
Better effect/rush	34
Quicker onset	25
Relieve heroin withdrawal	25
Needle fixation	13
Others doing it/recommended it	8
Cheap	5
Tolerance increased	4
Others	14

NB: Percentages do not sum to 100% as subjects were permitted to give 2 main reasons

Excludes those subjects who had only injected benzodiazepines once

Those subjects who had injected benzodiazepines in the preceding 6 months were asked how likely it was that they would stop injecting benzodiazepines. The majority (73%) stated that this was likely or very likely, and the main reason given was concern about their veins (25%). The next most common responses given were that injecting benzodiazepines did nothing for them (22%) and that they were concerned for their general health (13%). Interestingly, 9% reported that a transition away from injecting was likely because they were cutting down on their use of heroin.

In order to determine the factors associated with a change to injecting from swallowing benzodiazepines, multiple logistic regressions were performed. Those subjects who had never used benzodiazepines and those who had injected benzodiazepines on the first use occasion were excluded from the analysis. The first regression examined the association between demographic variables (age, sex, area of residence, education, age of first benzodiazepine use, employment status, and prison record) and a change to injecting. Area of residence and age of first benzodiazepine use were the only variables significantly associated with a change to injecting.

The second regression examined the relationship between psychosocial variables (benzodiazepine dependence, polydrug use, GHQ score, OTI health score, OTI criminality score and heroin dependence) and a change to injecting. Greater benzodiazepine dependence, greater number of drug classes ever used and

higher scores on the OTI criminality scale were significantly related to a change to injecting.

Those variables that were significant from the two regressions were entered into a model. Area of residence and age of first benzodiazepine use did not remain significant. Benzodiazepine dependence, polydrug use and the OTI criminality score remained significant and were entered into the final model (Table 5). The regression equation was significant (χ^2, 3df=37.9, p<.001), and had a reasonable fit (Hosmer-Lemeshow χ^2=4.8, p<.70).

Table 5: Multiple logistic regression predicting a change from swallowing to injecting benzodiazepines among heroin users.

(N=284)

Variable	O.R.	95% C.I.
Benzodiazepine SDS score	1.13	1.04-1.22
Poly-drug use	1.71	1.32-2.23
OTI Crime total	1.18	1.04-1.33

Hosmer-Lemeshow χ^2=4.8, p<.70

The results indicate that, after controlling for the effects of other variables in the model, each additional point scored on the on the SDS increased the odds of having made a change to injecting by 13%, each additional drug class ever tried by 71% and each additional point scored on the OTI criminality scale by 18%.

3.5.2 Cessation of benzodiazepine injecting

Of those subjects who had ever injected benzodiazepines (n=88), 55% reported not having done so in the last 6 months. While the majority of ex-benzodiazepine injectors had ceased all benzodiazepine use, 38% continued to use these drugs orally. The mean age of ex-benzodiazepine injectors at the time of their last benzodiazepine injection was 25.5 years (SD 6.0, range 15-45), representing a median of 2.5 years between last injection and interview. Only 10% of these subjects reported using more benzodiazepines once they stopped injecting, with 46% indicating that they used less and 44% using about the same amount as before. With regards to other drug use, 23% reported using more other drugs, 17% less other drugs and 60% the same amount of other drugs as before.

When asked how the cessation of benzodiazepine injecting had affected the route of administration used for other drugs, 15% of ex-benzodiazepine injectors indicated that they also stopped injecting other drugs. At the time that subjects

ceased injecting benzodiazepines over a third (38%) were living with someone who swallowed these drugs. However, 48% indicated that at least half of their friends were still injecting benzodiazepines at the time, including 29% who reported that the majority of their friends were doing so.

Subjects were asked for the main reasons why they abandoned benzodiazepine injecting (Table 6). The most popular response related to concerns about their health (27%), among which were a diverse range of problems including having experienced thrombosis, overdose, chest pain, a liver virus and endocarditis. The next most popular response was that the `rush' or intoxicating effect was not very good (13%). Those subjects who reported having made the transition away from injecting because they did not like the feeling from injecting (8%), typically referred to negative sensations experienced following the injection of benzodiazepines, such as feeling drugged rather than stoned or feeling very sick. A large proportion of the sample (40%) gave `other' reasons for having stopped injecting benzodiazepines but these varied considerably between subjects and included responses such as, "the heroin was getting better", "I stopped selling my methadone so wasn't hanging out so much", "I didn't want to end up with unnecessary track marks on my arms" and "I left the house of the people using them".

Table 6: Reasons why subjects ceased injecting benzodiazepines

(N=48)

Reasons	% Yes
General health concerns (eg. thrombosis, endocarditis)	27
Rush was not very good	13
Did not like the feeling from injecting	8
Too much hassle	8
Did not like the loss of control	8
Other	40

A multiple logistic regression was performed to determine the factors associated with a change to either cessation of benzodiazepine use or oral administration. The first regression examined the relationship between demographic variables (age, sex, area of residence, years of school education, age of first benzodiazepine use, employment status, and prison record) and the cessation of benzodiazepine injecting. Only employment status was significantly associated with the dependent variable.

A second regression analysis was conducted to assess the relationship between psychosocial variables (benzodiazepine dependence, polydrug use, GHQ score,

OTI health total, OTI criminality score and heroin dependence) and the cessation of benzodiazepine injecting. Being less heroin dependent, less criminally active and scoring lower on the OTI health scale, were significantly related to the cessation of injecting. The significant variables from the two regressions were entered into a third regression. Employment status was the only variable that did not retain significance. Heroin dependence, OTI criminality scores and OTI health scores were entered into the final model (Table 7). The regression equation was significant (χ^2, 3df=43.3, p<.001) and had a reasonable fit, Hosmer-Lemeshow χ^2=11.1, p<.20.

Table 7: Multiple logistic regression predicting the cessation of benzodiazepine injecting.

(N=88)

Variable	**O.R.**	**95% C.I.**
OTI health total	0.90	0.84-0.97
OTI criminality score	0.68	0.51-0.89
Heroin dependence score	0.80	0.68-0.94

Hosmer-Lemeshow χ^2=11.1, p<.20

The results indicate that after controlling for the effects of other variables in the model, each extra point scored on the OTI health scale reduced the odds of having stopped injecting benzodiazepines by 10%. Each extra point scored on the OTI criminality scale reduced the odds of having stopped injecting benzodiazepines by 32%, and each additional point on the heroin related SDS reduced the likelihood by 20%.

3.5.3 Oral use of benzodiazepines

Two thirds (66%) of the sample reported having used benzodiazepines by oral administration only. When asked their reasons for never having injected benzodiazepines the most common response was that they were concerned about their veins (28%), followed by being concerned for their general health (25%) (Table 8). Of those subjects who reported being too concerned for their health to inject benzodiazepines (n=51), 41% referred to fear of specific health complications such as ulcerations, loss of limbs, and organ damage. The remaining 59% were less specific, saying for example that they would worry about their health or that injecting benzodiazepines is `a good way of getting sick'.

Those reasons given by less than 7% of subjects were placed in the `other' category. Examples from this category include `tablets are not intended for injecting'(4%), `concern about overdose' (3%), and `fear of addiction' (1%).

Table 8: Reasons for never injecting benzodiazepines

(N=205)..... ....

Reason	% Yes
Concern for veins/Tablets `too chalky'	28
Concern for health	25
Did not know benzodiazepines could be injected/Never considered it	16
Could not be bothered	15
Do not like benzodiazepines	8
Good enough effect from swallowing	7
Others	33

NB: Percentages do not sum to 100% as subjects were permitted to give more than one reason

N=205, excludes those subjects who have never used benzodiazepines and those who have injected benzodiazepines

3.5.4 Cessation of benzodiazepine use

Of those subjects who had ever used benzodiazepines (n=293), 24% had not used these drugs in the preceding six months. With regards to the proportion who had stopped using benzodiazepines, there was no difference between those subjects who had only swallowed benzodiazepines and those who had injected them (25% v 21%).

The most popular reason given for stopping the use of benzodiazepines was that subjects did not like the negative consequences of their use (33%), such as having black-outs, losing control of their actions and committing crime (Table 9). The next most popular reasons given were that they had commenced methadone maintenance (14%), that the effect of benzodiazepines was not that good (13%) and that they had seen what benzodiazepines had done to other people around them (13%).

The responses placed in the other category were quite varied, examples of which include `the withdrawal from benzodiazepines is worse than that from heroin', `I had a son and had to settle down for his benefit', `I like heroin and it is dangerous to mix the two', and `I have got hepatitis C and they really knock me around'.

Table 9: Main reasons why ex-benzodiazepine users stopped using benzodiazepines

(N=70)

Reason	**% Yes**
Negative consequences e.g. black-outs, loss of control, crime	33
Commenced methadone maintenance	14
Effect of benzodiazepines was not that good	13
Seen what benzodiazepines have done to other people	13
Fear of addiction to benzodiazepines	6
Other	39

3.5.5 Never used benzodiazepines

A small proportion of the sample (6%) reported that they had never used benzodiazepines. The most common reason given for not doing so was that they had seen the effect of these drugs on other people (37%) (Table 10). The next most popular responses given were that they had not been aware of benzodiazepines (11%) or they thought that other drugs were better (11%). Once again, responses in the `other' category were varied, examples of which include `I work and so have the money to buy the drug I want', `I do not like tablets', and `I tried barbiturates years ago, and they either made me sleep or get aggressive, so I decided not to use pills'.

Table 10: Reasons for never having used benzodiazepines

(n=19)

Reasons	**% Yes**
Seen what they have done to other people	37
Was not aware of them	11
Other drugs are better	11
Like to be in control	5
Other	58

3.6 Preferences and practices of benzodiazepine injectors

3.6.1 Types of benzodiazepines used by injection

The most widely injected benzodiazepines were temazepam (68%) and diazepam (67%) (Table 11). Diazepam tablets had been injected by 49% of injectors, and liquid diazepam by 36%. The median number of benzodiazepine classes ever injected was 2 (range 1-8), with 44% of injectors having injected three or more classes of benzodiazepines. Those subjects who had injected more than one class of benzodiazepine (n=57) were asked to indicate which class they considered the easiest to inject. Temazepam (35%) and liquid diazepam (32%) were most commonly reported as being the easiest.

When subjects were asked to nominate the class of benzodiazepine they preferred to inject, temazepam (33%) emerged as the most popular, followed by liquid diazepam (30%) and flunitrazepam (12%). When asked why they preferred to inject temazepam, 42% of responses related to the nature of the formulation, referring to the fact that temazepam is a liquid (16%) and not `chalky' like other benzodiazepine tablets (26%). The next most popular reason given was that they liked the `stone' or intoxicating effect (37%) from injecting temazepam. Liquid diazepam was preferred for similar reasons, with 41% indicating that they liked the `stone' and 41% referring to the fact that it is a liquid. Of those subjects who nominated flunitrazepam as the benzodiazepine they preferred to inject, 71% indicated that it is the strongest and similarly, 29% stated that they like the `stone'.

Table 11: Classes of benzodiazepines used by injection

(n=88)

	%
Classes of benzodiazepines injected by more than 10% of injectors:	
Temazepam	68
Diazepam	67
Oxazepam	41
Flunitrazepam	34
Nitrazepam	26
Clonazepam	18
Number of benzodiazepine classes ever injected:	
1-2	56
3-5	35
6-8	9
Easiest benzodiazepine to inject:*	
Temazepam	35
Diazepam ampoules	32
All the same	12
Flunitrazepam	7
Oxazepam	7
Diazepam tablets	4
Temazepam & Oxazepam	2
Do not recall	2
Preferred benzodiazepine to inject:*	
Temazepam	33
Diazepam ampoules	30
Flunitrazepam	12
None	11
Nitrazepam	4
All the same	4
Diazepam tablets	2
Oxazepam	2
Alprazolam	2
Do not recall	2

* *NB: n=57, Excludes those subjects who have injected fewer than 2 classes of benzodiazepines*

3.6.2 Injecting practices

Those subjects who had ever injected a benzodiazepine tablet were asked how many tablets they used in an average injection (Table 12). While the median number of tablets reported was 4 (range 1-25), 20% indicated that they would generally use 10 or more. When asked to specify the maximum number of benzodiazepine tablets injected within a 24 hour period, a median of 10 was reported (range 1-75), with 21% having injected 25 tablets or more in one day.
The smaller sized syringes (1ml, 2ml & 5ml) were the most popular for injecting benzodiazepines, having been used by 66%, 38% and 25% of benzodiazepine injectors respectively. Although less popular, a notable proportion of subjects had used the larger 10 and 20 ml syringes for injecting benzodiazepine tablets.

The majority of injectors (63%) reported that benzodiazepines were either difficult or very difficult to inject, and most had been taught how to inject them by a friend (58%). A half of benzodiazepine injectors (45/88) reported having experienced a side effect or problem from injecting benzodiazepines. The most common problems encountered by these subjects were reported to be vascular damage (33%), thrombosis (11%), convulsions (9%) and nausea and vomiting (9%). While 51% of injectors reported experiencing problems related to injecting benzodiazepines, only 18% indicated that they had ever consulted a doctor in relation to any of these problems. Thrombosis (25%) and convulsions (19%) were the most common problems for which medical assistance was sought, followed by abscesses (13%) and hallucinations (13%).

Table 12: Benzodiazepine injection procedures

	Males N=53	**Females** N=35	**Persons** N=88
Number of tablets used in an average injection (Mdn)#	4	4	4
Maximum number of tablets ever injected (Mdn)#	10	10	10
Size of syringes ever used (%):*			
1 ml	66	66	66
2 ml	45	26	38
5 ml	28	20	25
10 ml	17	20	18
20 ml	17	17	17
How difficult is it to inject benzodiazepines?			
Very easy	8	6	7
Easy	26	37	31
Difficult	55	31	46
Very difficult	11	26	17
Who taught you how to inject benzodiazepines?			
Friend	56	57	58
Partner	4	14	8
No-one	32	23	28
Other	6	6	6
Ever experienced any side effects or problems from injecting benzodiazepines (% yes)	49	54	51
Ever been to a doctor because of problems arising from injecting benzodiazepines (% yes)	17	20	18

Excludes subjects who had only ever injected liquid diazepam: Males n=50, Females n=35, Persons n=85

* *Does not sum to 100% as subjects may have used more than one size of syringe*

3.6.3 Most recent benzodiazepine injecting episode

The median length of time since subjects last injected benzodiazepines was 8 months (range 1 day-15 years) (Table 13). The benzodiazepines most commonly injected on the last occasion were temazepam (40%) and diazepam (30%). While 17% of benzodiazepine injectors reported having last injected liquid diazepam, 13% indicated that they had injected diazepam tablets. The median number of tablets injected on the last occasion was 4 (range 1-25). The majority of subjects used a 1 or 2 ml syringe (72%), with only 16% using the larger 10 or 20 ml syringes. Vein infusion sets had been utilised by 15% of subjects at the time of their last benzodiazepine injection. Of this small group, 77% had used the infusion set with a 5, 10 or 20 ml syringe.

Excluding subjects who reported injecting temazepam or liquid diazepam on the last occasion, the majority (87%) of benzodiazepine injectors indicated that they had used a filter at the time of their last benzodiazepine injection. The most common filters used were cigarette butts (52%) and cotton swabs (39%). Thirty percent of injectors did not mix the benzodiazepine with water the last time, of whom 58% last injected temazepam and 42% last injected liquid valium. A small proportion of injectors (6%) reported having mixed either methadone or morphine with the last benzodiazepine that they injected.

Table 13: Details of most recent benzodiazepine injection

	Males N=53	**Females** N=35	**Persons** N=88
Median time since last injection (Mths)	18	4	8
Last benzodiazepine injected (%):			
Temazepam	42	37	40
Diazepam	32	29	30
Flunitrazepam	13	3	9
Oxazepam	2	20	9
Cannot remember	2	6	3
Others	10	6	8
Number of tablets injected (Mdn)[+]	4	4	4
Size of syringe last used (%):			
1ml	42	57	48
2ml	32	11	24
5ml	11	6	9
10ml	2	14	7
20ml	8	11	9
Cannot remember	6	0	3
Vein infusion set used (% yes)	9	23	15
Filter used[#]:			
Yes	81	94	87
No	19	6	13
Type of filter used[*]:			
Cigarette filter	53	50	52
Cotton swab	41	38	39
Other	6	12	9

[+] *Excludes those subjects who used liquid diazepam last time: Males n=42, Females n=28, Persons n=70*

[#] *Excludes those subjects who used liquid diazepam or temazepam last time: Males n=21, Females n=17, Persons n=38*

* *Excludes those subjects who had not used a filter: Males n=17, Females n=16, Persons n=33*

3.7 Criminal activity while under the influence of benzodiazepines

Of those subjects who had ever tried benzodiazepines (n=293), 47% reported having committed a property crime while under the influence of these drugs. The type of benzodiazepine reported to be most commonly used when committing property crime was oxazepam (45%), followed by flunitrazepam (33%) and diazepam (15%). When subjects were asked why they had committed property crime under the influence of benzodiazepines, the most common responses were that these drugs increased their confidence and made them feel invincible (34%), that they had no recollection of actually committing the crime but later realised what they had done (21%), that the benzodiazepines had made them feel invisible (19%), and that they simply needed money and would have committed the crime anyway (18%).

Of further concern is that 15% of those who had ever used benzodiazepines reported committing a violent crime under the influence of these drugs. Once again, oxazepam (45%) and flunitrazepam (41%) were the two benzodiazepines most commonly reported to have been used. When subjects were asked why they had committed the violent crime, the two most popular responses were that these drugs caused them to lose control and reduced their ability to suppress anger (39%), and that they increased their confidence and made them feel invincible (39%). Only 14% said that they would have committed the violent act regardless of whether or not they had used these drugs.

As measured by the OTI criminality scale, current benzodiazepine users reported significantly greater criminal involvement for the preceding month than ex-benzodiazepine users (1.88 v 0.94, t_{291}=3.2, p<.005). During that period current benzodiazepine users were significantly more likely to have committed a property crime (40% v 20%, O.R. 2.61, 95% C.I. 1.37-4.97), to have been involved in drug dealing (38% v 20%, O.R. 2.42, 95% C.I. 1.27-4.61) and at the time of interview were more than twice as likely to be facing criminal charges (21% v 10%, O.R. 2.34, 95% C.I. 1.0-5.45).

3.8 Factors associated with route of benzodiazepine administration

Comparisons were made between current injectors, oral users and the remainder of the sample in terms of demographics, drug use, health, criminal activity, psychological functioning, injection related HIV risk-taking behaviour, and heroin overdose (Table 14).

3.8.1 <u>Demographics</u>

While the mean age of subjects in the sample was 28.8 years (SD 6.9, range 16-48), this differed significantly according to current route of benzodiazepine administration ($F_{2,309}$=12.32, p<.001). Injectors were significantly younger than oral users of benzodiazepines (25.8 v 28.2, $F_{1,309}$= 4.12, p<.05), who in turn were significantly younger than non-users of benzodiazepines (28.2 v 31.5,

$F_{1,309}$=20.35, p<.001). No significant difference was apparent between the three groups with regard to the proportion of males, mean years of school education, and employment status.

3.8.2 Drug use

The extent of polydrug use varied significantly according to current route of benzodiazepine administration ($F_{2,309}$=41.06, p<.001). Excluding benzodiazepines, current injectors had used significantly more drug classes in the preceding six months than oral users (6.6 v 4.9, $F_{1,309}$=33.90, p<.001) who, in turn, had used significantly more drug classes in that time than non-users of benzodiazepines (4.9 v 3.7, $F_{1,309}$=28.38, p<.001).

Excluding benzodiazepines, the number of drug classes injected in the six months prior to interview also differed significantly according to current route of benzodiazepine administration ($F_{2,309}$=30.32, p<.001). Current injectors had injected significantly more drug classes than oral users (2.8 v 1.7, $F_{1,309}$=38.44, p<.001), who in turn had injected more drug classes than non-users of benzodiazepines (1.7 v 1.3, $F_{1,309}$=9.42, p<.005).

3.8.3 Health

As shown in figure 1, scores on the OTI health scale differed significantly according to current route of benzodiazepine administration ($F_{2,309}$=30.20, p<.001). Benzodiazepine injectors scored significantly higher than oral users (23.4 v 16.7, $F_{1,309}$=23.16, p<.001), indicating a poorer state of current health. Similarly, oral users scored significantly higher on the health scale than non-users of benzodiazepines (16.7 v 11.9, $F_{1,309}$=58.38, p<.001). A similar pattern was noted with regard to scores on the injection related sub-scale of the OTI ($F_{2,309}$=12.16, p<.001), with injectors scoring significantly higher than oral users (1.7 v 1.0, $F_{1,309}$=14.76, p<.001), indicating greater injection related health problems. Oral users scored significantly higher on the injection related sub-scale than non-users of benzodiazepines (1.0 v 0.8, $F_{1,309}$=4.29, p<.05).

3.8.4 Psychological functioning

Scores on the GHQ differed significantly according to current route of benzodiazepine administration ($F_{2,309}$=23.36, p<.001). As highlighted in figure 1, injectors reported higher levels of psychological distress than oral users (13.8 v 9.1, $F_{1,309}$=13.70, p<.001), who in turn showed greater psychological distress than non-users (9.1 v 4.7, $F_{1,309}$=21.88, p<.001). Similarly, the proportion of subjects who had scores over the diagnostic cut-off for `cases' of psychopathology varied significantly according to current route of benzodiazepine administration (χ^2 2df=28.41, p<.001), with injectors being more likely than oral users to score above the cut-off mark (80% v 63%, O.R. 2.31, 95% C.I. 1.01-5.30), and oral users being more likely than non-users to do so (63% v 36%, O.R. 3.08, 95% C.I. 1.82-5.23).

Figure 1: Factors associated with different routes of current benzodiazepine administration

3.8.5 Criminal activity

As measured by the OTI criminality scale, the degree of criminal activity for the month preceding interview differed significantly according to current route of benzodiazepine administration ($F_{2,309}$=23.49, p<.001). Figure 1 indicates that injectors scored higher on the criminality scale than oral users (3.5 v 1.5, $F_{1,309}$=33.06, p<.001), who in turn scored higher than non-users of benzodiazepines (1.5 v 0.9, $F_{1,309}$=4.96, p<.05). Injectors were more likely than oral users to report having committed any crime in the month prior to interview (90% v 50%, O.R. 9.10, 95% C.I. 3.11-26.61). Similarly, oral users were more likely than non-users of benzodiazepines to have committed any crime in that period (50% v 34%, O.R. 1.95, 95% C.I. 1.15-3.29).

3.8.6 Injection related HIV risk-taking behaviour

The likelihood of having borrowed used injection equipment in the month preceding interview differed significantly according to the current route of benzodiazepine administration (χ^2 2df=9.28, p<.05). Injectors were more likely to have borrowed a used needle than both oral users (25% v 11%, O.R. 2.72, 95%

C.I. 1.16-6.38) and non-users (25% v 6%, O.R. 5.6, 95% C.I. 1.77-17.71) of benzodiazepines. The likelihood of having lent used injection equipment during the preceding month also differed significantly according to the current route of benzodiazepine administration (χ^2 2df=11.89, p<.005). Both injectors (33% v 9%, O.R. 4.88, 95% C.I 1.82-13.02) and oral users (22% v 9%, O.R. 0.35, 95% C.I. 0.16-0.79) were more likely than non-users of benzodiazepines to have lent used injection equipment to someone during this period.

3.8.7 Overdose

As shown in figure 2, the likelihood of having overdosed during the six months prior to interview varied significantly according to current route of benzodiazepine administration (χ^2 2df=26.82, p<.001). Injectors were more likely to have overdosed during the six months prior to interview than both oral users (48% v 15%, O.R. 5.23, 95% C.I. 2.49-10.99) and non-users of benzodiazepines (48% v 8%, O.R. 10.60, 95% C.I. 3.94-28.53). Similarly, the likelihood of having been administered naloxone during the six months prior to interview also differed significantly according to current route of benzodiazepine administration (χ^2 2df=21.92, p<.001). Injectors were more likely to have been administered naloxone than both oral users (30% v 7%, O.R. 5.60, 95% C.I. 2.32-13.52) and non-users of benzodiazepines (30% v 2%, O.R. 18.64, 95% C.I. 3.93-88.36).

Figure 2: Proportion of current injectors, oral users and non-users of benzodiazepines who overdosed on heroin during the six months

Table 14: Factors associated with route of benzodiazepine administration.

	Current benzodiazepine injectors (N=40)	Current oral benzodiazepine users (N=183)	Other respondents (N=89)
Demographics			
Age (mean yrs)*	25.8	28.2	31.5
Sex (% male)	50	61	66
Education (mean yrs)	10.0	9.6	9.7
Unemployed (%)	90	79	78
Health			
OTI health total*	23.4	16.7	11.9
OTI injecting sub-total*	1.7	1.0	0.8
Needle risk (% in last month)			
Borrowed needles*	25	11	6
Lent needles*	33	22	9
Criminal behaviours (last month)			
OTI crime total*	3.5	1.5	0.9
Any crime (%)*	90	50	34
Psychological functioning			
GHQ total*	13.8	9.1	4.7
`Psychiatric' cases (%)*	80	63	36
Heroin overdose (% in last 6 months)			
Overdosed*	48	15	8
Naloxone administered*	30	7	2

* *Statistically significant difference exists between groups*

4.0 DISCUSSION

4.1 *Major findings*

The current study replicated earlier findings with regards to the prevalence of benzodiazepine use by injection among heroin users. In the 1994 study 32% of 329 heroin users had injected benzodiazepines[9], compared with 28% of the current sample. Clearly, the injection of benzodiazepines among heroin users is a common practice.

A major finding of the study was that a transition from swallowing to injecting benzodiazepines did not necessarily mean that injection became the primary route of benzodiazepine administration. Among current benzodiazepine injectors for instance, 80% had injected benzodiazepines on less than half of use occasions during the six months prior to interview. In this way, a transition to injecting benzodiazepines differs from either a transition to injecting amphetamines or heroin[15,27].

Of clinical significance were the reasons given by ex-benzodiazepine injectors for having stopped injecting benzodiazepines. The most popular reasons were concerns about a range of health problems, including having experienced thrombosis, chest pain, a liver virus or endocarditis. Anecdotal evidence suggests that many of these subjects were unaware of the health problems that could arise from injecting benzodiazepines until they experienced them first hand. It appears that an opportunity exists to educate heroin users about the harms associated with the parenteral use of benzodiazepines.

An important distinction made by the current study was the varying degree of harm associated with the different routes of benzodiazepine administration. While it has previously been reported that the use of benzodiazepines among IDUs is associated with poorer health, poorer social functioning, greater psychopathology, greater injection-related HIV risk-taking behaviour, and increased risk of heroin overdose[1-6], the current study demonstrates that injecting benzodiazepines exacerbates these problems. Given that 21% of those subjects who had injected benzodiazepines currently use these drugs solely by oral administration, it would appear that benzodiazepine injectors can change their behaviour and thereby reduce the harm associated with the injection of these drugs.

4.2 *Data validity and representativeness of the sample*

The findings of this study are derived from data based upon self-reported behaviour. Although the questions asked often required subjects to talk about their involvement in various illegal and socially stigmatised activities, efforts were made to ensure that valid data were obtained. Subjects were given strong assurances that any information they divulged would be treated as strictly

confidential and anonymous. Other research on illicit drug use has shown that when subjects are given such guarantees the information provided is reasonably valid and reliable[21-24].

In interpreting the results of the current study, it is appropriate to examine how representative the sample is of heroin users in general. Even though multiple recruitment methods were used in an attempt to access a broad spectrum of heroin users, the fact that the sample was self-selected implies that its characteristics should be borne in mind and care taken when generalising to other samples. At the same time, it is difficult to conceive how it would be known if a sample of heroin users was representative, given that the parameters of the population of heroin users are unknown. However, it is important to note that the characteristics of the sample are similar to those reported by other studies of heroin users, both in Australia and overseas[25-27].

4.3 *Benzodiazepine use and dependence*

The overwhelming majority of the sample had used benzodiazepines (94%) and 71% remained current benzodiazepine users. While the median number of days on which benzodiazepines had been used by current users during the six months prior to interview was 20, it is noteworthy that 42% used these drugs more than once a week, including 15% who used them daily.

The only significant predictor of benzodiazepine dependence among the current sample was frequency of use, with greater use being associated with higher levels of dependence. A fifth of current benzodiazepine users scored greater than 4 on the SDS, signifying some level of benzodiazepine dependence. In view of the withdrawal syndrome that has been associated with long term use in therapeutic doses, guidelines for the prescription of benzodiazepines generally advise that daily use for longer than four weeks should be avoided[7]. Such regular benzodiazepine use among IDUs has even more serious implications than it has for the more general population.

4.4 *Transitions: reasons and consequences*

While only 3% of those subjects who had ever tried benzodiazepines reported initially administering them by injection, a further 27% had since made a transition from swallowing to injecting benzodiazepines. A change to parenteral administration of benzodiazepines did not necessarily preclude oral administration remaining the primary route used. Among current benzodiazepine injectors, for instance, 80% had injected benzodiazepines on less than half of use occasions during the six months prior to interview.

Studies which have looked at transitions to injecting heroin[27] and amphetamines[15], indicate that injection generally becomes the primary route of administration for these drugs. Perhaps the fact that benzodiazepines are not usually the main drug of choice among IDUs[2,9], but are typically used as an

adjunct to either heroin or amphetamine use, partly explains why heroin users who begin to inject benzodiazepines do not feel compelled to exclusively use this route of administration. Nevertheless, the health risks of injecting benzodiazepine tablets intended for oral consumption cannot be overlooked. During the six months preceding interview 18% of current benzodiazepine users (13% of the sample) had injected benzodiazepines.

The factors found to be associated with a transition to injecting benzodiazepines were greater benzodiazepine dependence, higher levels of poly-drug use and higher scores on the OTI criminality scale. Males and females were equally likely to have injected a benzodiazepine. While the majority of subjects were not living with someone who was injecting benzodiazepines at the time of their first benzodiazepine injection, 60% indicated that injection had been the route of benzodiazepine administration used by half or more of their friends. Almost a third of those subjects who had injected benzodiazepines reported that they began to use more benzodiazepines following the change to injecting. While only a quarter reported using larger quantities of other drugs, it is noteworthy that polydrug use among current benzodiazepine injectors is significantly greater than that among oral users of benzodiazepines.

A significant proportion of those subjects who had injected benzodiazepines were no longer current benzodiazepine injectors (55%). Of these ex-benzodiazepine injectors, 38% continued to use benzodiazepines orally, indicating that even if heroin users do not want to give up benzodiazepines entirely, they can reduce the harm associated with their use by changing to a safer route of administration.

The factors that were associated with a transition away from injecting benzodiazepines were better general health, lower scores on the OTI criminality scale and less severe heroin dependence. Given that a quarter of those subjects who had injected benzodiazepines more than once had done so in order to manage heroin withdrawal, it is not surprising that being less heroin dependent is associated with the cessation of injecting benzodiazepines.

Almost half of those who formerly injected benzodiazepines indicated that at the time of their transition away from injecting benzodiazepines, at least half of their friends were still injecting these drugs. Peer influence does not appear to have been a major factor in the decision made by these subjects to cease injecting benzodiazepines. Concern for health emerges as the most common reason given for cessation of benzodiazepine injecting. Anecdotally, many subjects who gave this as a reason for having ceased injecting benzodiazepines, remarked that they had been unaware of the health problems that could result from this practice, until they experienced them personally. This suggests that heroin users are in need of greater education about the serious health consequences of injecting these drugs.

An interesting similarity exists between the key motivation of heroin users making a transition away from injecting benzodiazepines, and of amphetamine users making a transition away from injecting amphetamines. A study of amphetamine transitions conducted by the authors[15], revealed that concern for vascular health was the key motivation for making a transition away from injecting, suggesting a need for greater injection related health education among IDUs.

The second most popular reason given for having ceased injecting benzodiazepines was that the `rush' or intoxicating effect was inadequate. Similarly, of those current injectors who reported being likely to make a transition away from injecting benzodiazepines, 22% indicated that this was because benzodiazepines did nothing for them. It is ironic, therefore, that the main reason that subjects gave for initially continuing to inject benzodiazepines was that they were seeking a better effect or rush from these drugs.

Only 10% of ex-benzodiazepine injectors reported using more benzodiazepines once they ceased injecting them. This contrasts with the increase in benzodiazepine use reported by 30% of those subjects who had made a transition to injecting. With regard to other drug use, however, a change away from injecting benzodiazepines had a similar effect to that of a transition to injecting, with 23% of ex-injectors reporting an increase in other drug use following the cessation of benzodiazepine injecting.

4.5 *Classes of benzodiazepines used by injection*

The current study supports the earlier finding[9] that a broad pattern of benzodiazepine use exists among heroin users in Sydney. The median number of benzodiazepine classes ever injected was two, but 44% had injected three or more classes. Temazepam (68%) and diazepam (67%) were once again reported to be the most commonly injected benzodiazepines, unlike in the United Kingdom where the injection of temazepam predominates[28-30]. Almost half of the injectors had injected diazepam tablets and over a third had injected liquid diazepam. This latter finding raises the question of how heroin users gain access to ampoules of liquid diazepam.

Temazepam (33%) and liquid diazepam (30%) were the preferred benzodiazepines to inject, because they were liquid formulations and had a good intoxicating effect. While flunitrazepam tablets would need to be crushed in order to be injected, they were the third most preferred benzodiazepine to use by injection, primarily because they were considered the strongest. With regard to the last benzodiazepine injection occasion, temazepam (40%) and diazepam (30%) were again the most common benzodiazepines used. It is noteworthy, however, that while 17% had injected liquid diazepam, 13% had injected diazepam tablets.

4.6 *Benzodiazepine injecting procedures*

While the median number of benzodiazepine tablets used by injectors in a typical injection was four, a fifth of injectors reported that they would generally use ten or more tablets in an injection. The maximum number of benzodiazepine tablets used parenterally in a day was reported to be a median of 10, with a fifth of injectors having used 25 or more tablets. Given the known harms associated with benzodiazepine use among heroin users, this level of use would be worrying enough if it were by oral administration. The fact that this quantity of tablets was being used by injection heightens the seriousness of the situation, given the additional risks of vascular damage, thromboses and mortality.

The smaller sized syringes were the most popular for injecting benzodiazepines, but notable proportions had used the larger 10 and 20 ml syringes. The size of the syringe used is relevant, as it has been shown that the risk of passing on blood through needle sharing substantially increases as the size of the syringe increases[31]. Among current benzodiazepine injectors needle sharing was common, with a quarter of these subjects having borrowed a used needle in the month prior to interview, and a third having lent a used needle to someone in that time. With such high rates of needle sharing among benzodiazepine injectors, the use of large syringes is cause for concern.

The majority (66%) of injectors found it difficult to inject benzodiazepines and most had been taught how to inject them by a friend or partner (66%). Anecdotal evidence suggests that preparing benzodiazepine tablets for injection typically involves crushing the tablets between 2 spoons and mixing the crushed tablets with water. The solution in the spoon may be heated by a lighter before being drawn up through a cigarette filter or a cotton swab and injected. Not surprisingly, a half of benzodiazepine injectors reported having experienced problems or side effects from injecting benzodiazepines, yet only 18% had obtained medical advice in relation to any of these problems. Help was most commonly sought for serious problems such as thromboses (25%), convulsions (19%), hallucinations (13%) and abscesses (13%).

4.7 *Harms associated with benzodiazepine injecting*

While it has been well established in previous studies that IDUs who use benzodiazepines have poorer health and psychosocial functioning than their non-benzodiazepine using peers[1-6], the current study demonstrates that the degree of harm associated with benzodiazepine use is related to the route of administration used. Current benzodiazepine injectors showed greater polydrug use, criminal involvement, psychological distress, and injection related health problems, as well as poorer general health, and an increased likelihood of having overdosed on heroin, than oral users of benzodiazepines. In turn, those subjects who were not current benzodiazepine users faired significantly better on all these measures, excluding heroin overdose, than oral users of benzodiazepines. While both oral and parenteral use of benzodiazepines among

heroin users is associated with harm, the latter route of administration appears to exacerbate this harm. Again, heroin users need to be informed about the risks that they are taking when injecting benzodiazepines.

4.8 *Clinical implications*

The findings of the current study strongly suggest that the prescription of benzodiazepines to heroin users should be avoided whenever possible. A fifth of current benzodiazepine users in the sample exhibited some degree of dependence on these drugs. Furthermore, it was reaffirmed that the use of benzodiazepines among this population is associated with poorer health, poorer social functioning, greater psychopathology and greater injection-related HIV risk-taking behaviour. Among current benzodiazepine injectors, the use of benzodiazepines was also associated with an increased likelihood of having overdosed on heroin during the six months preceding interview. In cases where the use of benzodiazepines is considered necessary, clinicians should avoid prescribing the more commonly injected temazepam and diazepam.

Given that injecting benzodiazepines intensifies the harm associated with their use, it is cause for concern that 28% of the sample reported having injected these drugs. The reasons given by ex-injectors for ceasing to inject benzodiazepines imply that heroin users are concerned about their health. Unfortunately, anecdotal evidence suggests that awareness of health concerns is often not raised until problems are experienced first hand. While it would be naive to expect the behaviour of all heroin users to be influenced by education campaigns warning of the harms associated with injecting benzodiazepines, heroin users should be made fully aware of the risks involved. Given their close contact with clients, staff in needle and syringe exchange programs and treatment centres such as methadone clinics, are in the optimal position to educate heroin users in this regard.

4.9 *Conclusions*

In summary, the parenteral use of benzodiazepines was common among opioid injectors, with over a quarter of the current sample having injected a benzodiazepine at some stage. We know that the harms associated with this route of benzodiazepine administration are significantly greater than those associated with oral benzodiazepine use. We also know that heroin users can change from the parenteral use of benzodiazepines to exclusive oral consumption or even cease their use. It appears that when heroin users move away from injecting benzodiazepines the most common motivation for doing so is concern for their health.

Given this knowledge, an appropriate harm reduction approach to benzodiazepine use may be to educate heroin users about the severe health effects that may ensue from injecting benzodiazepines. Staff in HIV prevention units and methadone clinics could play a pivotal role in the education process,

facilitated by the provision to clients of pamphlets outlining the dangers of injecting benzodiazepines. The reality of the harms associated with this practice could be emphasised in the pamphlets, by including case histories of heroin users who have suffered negative health effects as a result of injecting benzodiazepines. Perhaps if heroin users are advised about the risks associated with injecting benzodiazepines, they need not experience the negative health effects first hand.

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APPENDIX 1

Trade and Generic names

1. Alepam .... *Oxazepam* (ANX)
2. Alodorm .... *Nitrazepam* (SH)
3. Antenex .... *Diazepam* (ANX)
4. Ativan .... *Lorazepam* (ANX)
5. Dalmane .... *Flurazepam* (SH)
6. Diazemuls .... *Diazepam* (ANX)
7. Ducene .... *Diazepam* (ANX)
8. Emoten .... *Lorazepam* (ANX)
9. Euhypnos .... *Temazepam* (SH)
10. Frisium .... *Clobazam* (ANX)
11. Halcion .... *Triazolam* (SH)
12. Hypnodorm .... *Flunitrazepam* (SH)
13. Hypnovel .... *Midazolam* (SH)
14. Lexotan .... *Bromazepam* (ANX)
15. Librax .... *Chlordiazepoxide* (ANX)
16. Librium .... *Chlordiazepoxide* (ANX)
17. Mogadon .... *Nitrazepam* (SH)
18. Murelax .... *Oxazepam* (ANX)
19. Normison .... *Temazepam* (SH)
20. Rohypnol .... *Flunitrazepam* (SH)
21. Rivotril .... *Clonazepam* (Anti-conv)

22. Serepax..... ..... *Oxazepam* (ANX)

23. Temaze .... *Temazepam* (SH)

24. Tranxene .... *Potassium Chlorazepate* (ANX)

25. Valium..... ..... *Diazepam* (ANX)

26. Xanax..... ..... *Alprazolam* (ANX)

Generic and Trade Names

1. *Alprazolam* (ANX)..... .....Xanax

2. *Bromazepam* (ANX) .... Lexotan

3. *Chlordiazepoxide* (ANX) ..... Librax, Librium

4. *Clobazam* (ANX)..... ..... Frisium

5. *Clonazepam* (Anti-conv) Rivotril

6. *Diazepam* (ANX)..... ..... Antenex, Diazemuls, Ducene, Valium

7. *Flunitrazepam* (SH) .... Hypnodorm, Rohypnol

8. *Flurazepam* (SH) .... Dalmane

9. *Lorazepam* (ANX)..... ..... Ativan, Emoten

10. *Midazolam* (SH) .... Hypnovel

11. *Nitrazepam* (SH)..... ..... Alodorn, Mogadon

12. *Oxazepam* (ANX) .... Alepam, Murelax, Serepax

13. *Potassium Chlorazepate* (ANX).... Tranxene

14. *Temazepam* (SH) .... Euhypnos, Normison, Temaze

15. *Triazolam* (SH)..... ..... Halcion

NB: (ANX) = Anxiolytic
(SH) = Sedative Hypnotic
(Anti-conv) = Anti-convulsant