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#### **EXECUTIVE SUMMARY**

The current study examined the nature of benzodiazepine use among heroin users in Sydney with a particular focus on patterns of use, preferences and methods of procurement.

Of 329 heroin users two thirds (64%) had used benzodiazepines during the preceding six months and completed the structured face to face interview. All subjects were volunteers who had either been on a methadone programme or used heroin during the preceding three months. Using purposive sampling almost equal numbers of treatment and non-treatment subjects were recruited.

The median number of days on which benzodiazepines were used during the six months preceding interview was 19. However, 41% of the sample reported having used them more than once a week during that time. The most common reason given for having first used benzodiazepines related to their intoxicating effects (38%). In contrast, only 16% of subjects gave this as their reason for continuing to use benzodiazepines, with management of heroin withdrawal (23%) being the more common justification given.

A disturbingly high proportion of the sample (48%) had injected benzodiazepines, with a fifth (17%) having done so during the six months preceding interview. Diazepam and temazepam were equally the most commonly injected benzodiazepines. The parenteral use of benzodiazepine tablets, intended solely for oral administration, can lead to serious health effects such as thromboses and vascular morbidity.

Further cause for concern is the reported ease with which heroin users are able to procure benzodiazepines. The vast majority of subjects (86%) indicated that these drugs are easy or very easy to obtain. Over a half of the sample (58%) reported having given or sold benzodiazepines to someone in the preceding six months, with only a third (34%) having obtained them exclusively through a doctor. When asked which was the easiest benzodiazepine to procure a third of subjects (34%) specified diazepam and a fifth (19%) nominated oxazepam.

The sample exhibited distinct preferences for certain benzodiazepines. In preference ratings flunitrazepam and diazepam emerged as the two most favoured benzodiazepines. They were also reported to be among the most widely used. The reasons given for preferring these drugs related to their intoxicating effects.

The clear preferences that heroin users have for particular benzodiazepines should be borne in mind by clinicians when prescribing for this population. In this way the abuse potential and harms associated with benzodiazepine use may be lessened. Given the high prevalence of injecting of benzodiazepines among heroin users and the related health risks, further research into this practice is justified so that an appropriate intervention can be formulated.

## 1.0 INTRODUCTION

It is well documented both in Australia and overseas that benzodiazepines are widely used among regular injecting drug users (IDUs)<sup>1-8</sup>. In Australia the prevalence of current benzodiazepine use is reported to range upwards from a third of IDU, a finding that has been noted in relation to both primary heroin and amphetamine users<sup>4,5,9</sup>.

Several harms have been associated with the use of prescribed and non-prescribed benzodiazepines by IDUs. A consistent finding in the literature to date has been the relationship between benzodiazepine use and higher levels of needle sharing<sup>3-6,9-11</sup>. Such behaviour has obvious implications for the dissemination of HIV and other blood borne viruses. Benzodiazepine users have also been repeatedly found to have poorer levels of psychosocial functioning than other IDUs<sup>4,5,6</sup>. For instance, they are more likely to be currently engaged in criminal activity, to show signs of psychiatric morbidity, to be unemployed, to not have finished high school and to have engaged in prostitution<sup>4,5,6</sup>. It should be noted that this finding has been reported with regard to both heroin and amphetamine users who use benzodiazepines. Looking more extensively at the risks involved in benzodiazepine use, a tentative association has been established between the use of these drugs and both fatal and non-fatal heroin overdose<sup>6,12,13</sup>.

Recent studies indicate extensive injecting of benzodiazepines by IDUs in the United Kingdom<sup>14,15</sup>, a practice that carries serious health risks. The injecting of benzodiazepines can give rise to thromboses and has been associated with vascular morbidity and mortality among IDUs<sup>16,17</sup>. Given the high prevalence of current benzodiazepine use among Australian IDUs, the extent to which this is a problem in Australia clearly needs to be assessed.

Research in the United States and Europe has indicated that IDUs and other drug users may exhibit consistent preferences for particular types of benzodiazepines. For instance, among United States methadone maintenance clients diazepam, lorazepam and alprazolam have been rated significantly higher than other benzodiazepines<sup>18</sup>. Barnas et al<sup>2</sup> reported a preference for flunitrazepam and diazepam among Austrian methadone maintenance clients. As yet, the existence of such preferences among IDUs in Australia has not been investigated.

While benzodiazepine use among IDUs clearly represents a significant clinical and public health concern, surprisingly little is known about the nature of such use in Australia. Before interventions can be implemented to minimise the harm associated with the use of these drugs, there is a need to have a better understanding of the issues involved. The current study aimed to determine the patterns of benzodiazepine use, the availability and procurement of such drugs, and heroin users' familiarity with and preferences for various types of benzodiazepines.

## 1.1 Study Aims

The major aims of the present study were as follows:

- 1)To examine the extent and patterns of benzodiazepine use among heroin users.
- 2)To determine the availability of benzodiazepines to heroin users and the ways in which they were procured.
- 3)To ascertain whether preferences for different benzodiazepines exist among heroin users, and the reasons for such preferences.

### 2.0 METHOD

#### 2.1 Procedure

The current research was conducted in conjunction with another study which examined non-fatal heroin overdose <sup>19</sup>. Subjects participating in the overdose study who had used benzodiazepines during the six months preceding interview completed a module on benzodiazepines. Hence, the sample for the present study constitutes a sub-set of a larger cohort of heroin users. Two thirds (64%) of 329 heroin users interviewed for the overdose study met the criteria for entry to the benzodiazepine study and completed the structured face to face interview.

All subjects were volunteers who were paid A\$20 for their participation in the study. Recruitment took place from January to August of 1994, by means of advertisements placed in rock magazines, a users group magazine, needle exchanges, treatment agencies (methadone maintenance and drug free), 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 overdose study subjects had to either be on a methadone programme or have used heroin during the preceding three months, or both. Suitability for entry to the benzodiazepine study was determined at the time of interview when obtaining a drug use history from the subject. This form of screening has an advantage in that response bias, sometimes present when a subject is actively seeking entry into a study, is less likely to arise. As noted above, the entrance criterion was that benzodiazepines had been used by the subject at some time during the six months prior to interview.

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 in combination with the overdose interview module took between 45 and 60 minutes to complete.

#### 2.2 Structured Interview

A structured interview was devised that examined demographic characteristics, drug use history, patterns of benzodiazepine use, availability and procurement of benzodiazepines, and benzodiazepine familiarity and preference. The benzodiazepine module was pilot tested in December 1993 on 21 heroin users, and refinements were made on the basis of this. The areas covered by the interview are outlined in greater detail below (a copy of the questionnaire is available on request from the authors).

#### 2.2.1 Demographic characteristics

The demographic details obtained included: the subject's gender, age, suburb of residence, level of high school and tertiary education, employment status, current form of drug treatment, length of time in current treatment, whether they had a 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 some indication of overall drug use, subjects were asked which drug classes they had ever used, which ones they had ever injected, and which ones they had 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 regarding their age when they first used heroin, when they first used it regularly, when they first injected any drug and when they first injected any drug regularly. Subjects were also asked to indicate their main drug of choice.

#### 2.2.3 Heroin dependence

Heroin dependence was measured by giving subjects the Severity of Dependence Scale (SDS)<sup>20,21</sup> to complete. This is a 5 item scale which asks about psychological dependence in the preceding year. Questions include "Did you ever think your heroin use was out of control?" and "Did the prospect of missing a `shot' make you very anxious or worried?" SDS scores range from 0-15, with higher scores being indicative of greater heroin dependence.

#### 2.2.4 Injection related HIV risk taking behaviour

The HIV Risk-taking Behaviour Scale (HRBS), a component of the Opiate Treatment Index (OTI)<sup>22</sup>, was used in assessing injecting behaviours that placed subjects at risk of either contracting or transmitting the Human Immunodeficiency Virus (HIV).

#### 2.2.5 Patterns of benzodiazepine use

Information collected pertaining to subjects' use of benzodiazepines included: the age at which they had first used them regularly, the number of days since they had last used benzodiazepines, as well as the route of administration and type of benzodiazepine last used. Subjects were also questioned regarding their reasons for first using benzodiazepines and for continuing to do so, frequency and extent of benzodiazepine use during the preceding 6 months, poly drug use, efforts to stop using benzodiazepines, and route of benzodiazepine administration used in the last 6 months.

#### 2.2.6 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.

#### 2.2.7 Availability and procurement of benzodiazepines

Subjects were asked how easy they found it to acquire benzodiazepines, which were the easiest and most difficult to procure, the sources through which benzodiazepines had been acquired in the preceding 6 months, and whether or not they had sold or given benzodiazepines to anyone in the last 6 months. Several questions concerning their recent dealings with doctors in relation to benzodiazepines were also asked. It should be noted that subjects were asked to give the trade names rather than the generic names for the benzodiazepines. However, in reporting the results here the generic names are used (see Appendix 1 for a list of trade and generic names)

#### 2.2.8 Benzodiazepine familiarity and preferences

In order to determine how familiar subjects were with the variety of benzodiazepines and to gain some idea of their preferences, subjects were asked, having read a list of all the available benzodiazepines, to indicate which ones they had ever tried. They were then requested to report which ones they had ever injected, which ones they had used in the last 6 months, and which ones they had injected in the last 6 months. Using a `liking' scale of 0-10, where 0 meant that they did not like the drug at all and 10 indicated that they liked it a lot, subjects were asked to rate each of the benzodiazepines that they had ever tried. Finally, information was sought regarding which benzodiazepine subjects had used most in the last 6 months, which one they liked the best and why, what the best thing was about using benzodiazepines in general, and what the worst thing was about using benzodiazepines.

#### 2.3 Analyses

For continuous variables t-tests were employed. Categorical variables were analysed using chi<sup>2</sup>, with corresponding odds ratios (O.R.) and 95% confidence intervals (C.I.). Where distributions were highly skewed medians were reported. Highly skewed data were analysed using the Mann-Whitney U statistic, a non-parametric analogue of the t-test. In order to determine which factors were independently associated with levels of benzodiazepine dependence, simultaneous multiple regressions with backwards elimination were conducted. In this form of regression all variables are entered into the model simultaneously<sup>23</sup>. All analyses were conducted using SYSTAT<sup>24</sup>.

#### 3.0 RESULTS

#### 3.1 Sample Characteristics

The sample consisted of 210 subjects, of whom 65% were male. The mean age was 30 years but this differed significantly according to sex, with males being, on average,

3 years older than females (31 yrs v 28 yrs,  $t_{207}$  =-2.89, p<0.005). Subjects were recruited from all regions of Sydney (Table 1).

While the mean number of years of school education was 10 (SD 1.7; range 4-12), 38% of subjects had completed less than 10 years. Almost a third of the sample (31%) had completed 10 years of schooling and a quarter (25%) had completed 12 years. The majority of subjects (69%) had no tertiary education, with 20% having completed a trade or technical course and only 11% having acquired a university or college degree. Males were more likely than females to have completed some form of tertiary education (37% v 22%, O.R. 2.04, 95% C.I. 1.06-3.93).

The overwhelming majority of the sample was unemployed (77%), with only 7% in full-time and 12% in part-time/casual employment. A large proportion of the sample (41%) reported having a prison record, but this differed significantly according to sex. Males were more likely than females to report ever having been in gaol (46% v 31%, O.R. 1.86, 95% C.I. 1.02-3.37).

Half of the sample (51%) were not currently in treatment, and one third (33%) had never been in drug treatment. A significant age effect was noted, with the mean age of subjects presently in treatment being three years greater than that of those not in treatment (31.6 v 28.3 yrs,  $t_{207}$ =-3.74, p<0.001). Methadone maintenance was the most common modality for those currently in treatment (90/102).

**Table 1:** Demographic characteristics of 210 heroin/benzodiazepine users

N	<b>Male</b>	Female	Persons
	136	74	210
Age in years (mean) <sup>*</sup> (SD)	31	28	30
	7	6	7
Recruitment area (%): Inner City North South/South West	44	49	46
	23	15	20
	33	37	34
School Education (mean years)	10	10	10
Tertiary Education (%)*:			
No tertiary education	64	78	69
Trade/Technical	23	14	20
University/College	13	8	11
Trade & University	1	0	1
Employment Status (%):			
Unemployed Full-time Part-time/Casual Student Home duties	77 8 13 1	77 5 10 1 7	77 7 12 1 3
Prison Record (%)*:			
No	54	69	60
Yes	46	31	41
Treatment Status (%):			
Not in treatment	54	46	51
Methadone	40	49	43
Therapeutic community	6	4	5
Drug counselling	0	1	1
Regular IDU partner (%) <sup>*</sup> :			
No	58	24	46
Yes	42	76	54

Significant gender difference exists

## 3.2 Current Benzodiazepine Use

As stipulated by the entrance criteria for the study, all subjects had used benzodiazepines during the 6 months preceding interview. The median number of days on which benzodiazepines were used in the 6 months prior to interview was 19 (Table 2). A significant treatment effect was noted, with subjects currently in treatment having used benzodiazepines more frequently than those not in treatment (24 days v 14 days, U=4459.5, p<0.05). No gender effect was evident. A significant proportion of the sample (41%) had used benzodiazepines more than once a week during that time, including 15% who had used them daily. A notable minority of subjects (27%) reported sporadic use of these drugs, having used benzodiazepines less than monthly.

Subjects had last used benzodiazepines a median of 14 days prior to interview (range 1-180 days), with 45% having used them within the last 7 days. While the median number of benzodiazepine tablets taken on the last day of use was 3 (range 1-150), almost a fifth of subjects (17%) reported using 10 or more. Similarly, the median number of tablets reported to be typically taken on days when using benzodiazepines was 4 (range 1-50), with 17% of the sample indicating that they usually use 10 or more. When subjects were asked to indicate the greatest number of benzodiazepine tablets that they had ever taken in one day, the median number reported was 14 (range 1-200). However, a significant proportion of subjects (39%, 81/210) revealed that they had used more than 20 pills within a 24 hour period, with daily users of benzodiazepines being significantly more likely to have done so than less regular users (56% v 35%, O.R. 2.35, 95% C.I. 1.09-5.03).

Almost half (48%) of the sample had ever injected benzodiazepines, with approximately a fifth (17%) of subjects having done so at some stage during the 6 months preceding interview. No gender difference was apparent.

 Table 2:
 Benzodiazepine use of 210 heroin users

	Males	Females	Persons
N	136	74	210
Median number of days benzodiazepines were used in the last 6 months	15	24	19
Frequency of benzodiazepine use in the last 6 months (%):			
Less than monthly once a week or less More than once a week (but less than daily) Daily	32 27 25 15	18 41 27 15	27 32 26 15
Median number of days since last used benzodiazepines	14	14	14
Route of benzodiazepine administration used in the last 6 months (%):			
Swallowed &/or injected Swallowed only	18 82	15 85	17 83
% Ever injected benzodiazepines	46	47	48

### 3.3 Benzodiazepine Dependence

The mean SDS score for benzodiazepines was 3 (SD 4; range 0-15). As a measure of benzodiazepine dependence the SDS showed good psychometric properties based upon the current data. Cronbach's alpha was 0.95, 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 77% of the variance, with all items having loadings of 0.86 or greater. SDS scores were positively correlated with the number of days benzodiazepines were used in the preceding 6 months (r=0.57, p<0.001).

In a previous study which looked at amphetamine dependence an SDS cut-off mark of 4/5 was taken to be indicative of dependence<sup>9</sup>. Using a cut-off score of greater than 4, 28% of the current sample were classified as benzodiazepine dependent. As shown in Table 3, a linear relationship was found between frequency of benzodiazepine use and SDS scores, with daily users of benzodiazepines being significantly more likely to score greater than 4 on the SDS than less regular users (81% v 18%, O.R. 19.36, 95% C.I. 7.36-50.93)

**Table 3:** Benzodiazepine dependence by frequency of benzodiazepine use (N=58)

	Scored >4 on the SDS %
Frequency of benzodiazepine use:	
Daily > weekly < daily > monthly ≤ weekly ≤ Monthly	81 33 15 7

When asked to indicate their drug of choice only one subject nominated benzodiazepines, with the overwhelming majority (82%) favouring opiates.

In determining which factors were independently associated with levels of benzodiazepine dependence, simultaneous multiple regressions were conducted. The skewness of the dependent variable, the SDS, was 1.3, within recognised limits. The variables entered into the model were age, sex, route of administration used in the last 6 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 ( $F_{7,198}=18.14$ , p<0.001) and accounted for 37% of the

variance. Being female ( $\hat{a}$ =-0.991, p<0.05), greater frequency of benzodiazepine use during the preceding 6 months ( $\hat{a}$ =0.034, p<0.001), greater length of time since first trying benzodiazepines ( $\hat{a}$ =0.107, p<0.05) and being currently enrolled in treatment ( $\hat{a}$ =0.966, p<0.05) were independently associated with higher levels of benzodiazepine dependence.

The mean SDS score for benzodiazepines was 4 among subjects currently in treatment (SD 5; range 0-15) and 2 for those not in treatment (SD 3; range 0-15). Using the cut-off mark of greater than 4, over a third of treatment subjects (36%) could be classified as benzodiazepine dependent compared to approximately a fifth of non-treatment subjects (19%).

#### 3.4 Other Drug Use

As shown in Table 4, poly-drug use was common among the sample. All subjects had used heroin and 94% had done so in the last 6 months. Similarly, the majority of the sample (81%) had used other non-prescribed opiates, 51% during the 6 months preceding interview. Over a third of subjects (36%) reported having injected opiates other than heroin within that time.

The mean SDS score for heroin was 7.6 (SD 4.1; range 0-15). Using a cut-off mark of greater than 4, 69% were classified as heroin dependent. A significant gender effect was noted, with females being slightly more dependent than males (8.4 v 7.2,  $t_{208}$ =2.03, p<0.05).

It was almost universally reported that amphetamines (96%), hallucinogens (92%), alcohol (100%), cannabis (100%) and tobacco (99%) had been used at some stage. During the last 6 months, the use of amphetamines (48%) and hallucinogens (25%) were less commonly reported, while the majority of subjects reported using alcohol (83%), cannabis (89%) and tobacco (96%).

Most subjects (83%) had tried cocaine, with more than a quarter (28%) having used the drug in the last 6 months and a similar proportion (25%) having injected it during that time. While 73% of the sample reported having tried inhalants only 16% had done so in the 6 months preceding interview. A third of subjects (32%) indicated that they had tried barbiturates, but just 2% had used them in the last 6 months.

Including benzodiazepines, the mean number of drug classes ever used was 10 (SD 1.0, range 5-11), with a mean of 6 (SD 2.0, range 3-10) having been used in the last 6 months. The mean number of drug classes ever injected was 4 (SD 1.0, range 1-7), and 2 (SD 1.0, range 0-6) for the 6 months prior to interview. Current injectors of benzodiazepines reported using significantly more drug classes during the 6 months preceding interview than non-injectors (6 v 5,  $t_{208}$ =-4.45, p<0.001).

Table 4: Other drug use

(N=210)

Drug Class	Ever Used	Ever Injected	Used in Last 6 Months	Injected in Last 6 Months	Days Used in Last 6
	%	%	%	%	Months
Benzodiazepines	100	48	100	17	19
Heroin	100	100	94	94	72
Other Opiates	81	63	51	36	14
Amphetamines	96	91	48	44	5
Cocaine	83	75	28	25	3
Hallucinogens	92	28	25	3	2
Barbiturates	32	15	2	1	3
Alcohol	100	N/A	83	N/A	48
Cannabis	100	N/A	89	N/A	80
Inhalants	73	N/A	16	N/A	3
Tobacco	99	N/A	96	N/A	180
Poly-drug use⁺	10	4	6	2	-

<sup>\*</sup> Median number of days used in the last 6 months by those who had used the drug class in that period

<sup>\*</sup> Mean number of drug classes

### 3.5 History & Patterns of Benzodiazepine Use

#### **3.5.1** Initiation & continuation of benzodiazepine use

As shown in Table 5, the mean age of first benzodiazepine use was 19 years (SD 5.3; range 2-38) and 21 years (SD 6.2; range 10-42) for commencement of regular use (i.e. using once a month or more). The latter differed significantly according to sex, with females having commenced regular use at a younger age (20 v 22 years,  $t_{169}$ =-2.16). While 47% of the sample had used benzodiazepines prior to using heroin, over a third (38%) had used heroin before having tried benzodiazepines.

When asked the reason for first using benzodiazepines, a considerable number of subjects (38%) indicated that they had used them for the purpose of intoxication, that is, "to get out of it". In contrast, only 16% of the sample gave this as the reason for their continued use of benzodiazepines, with management of heroin withdrawal (23%) being the more common justification given.

Only a fifth (21%) of subjects reported first using benzodiazepines for insomnia or anxiety. While a greater proportion (33%) gave such reasons for continuing to use benzodiazepines, the inappropriate use of these drugs endured among the majority of the sample (66%).

When asked whether they had ever tried to stop using benzodiazepines 40% of the sample indicated that they had. Almost a fifth of the sample (18%) reported that they had attempted to stop while under the care of a doctor or drug and alcohol service. Of this 18%, almost two thirds (60%) had experienced convulsions when detoxing from benzodiazepines, representing 11% of the entire sample.

Withdrawal from benzodiazepines was significantly more likely to have been attempted by daily users of benzodiazepines than by less regular users (78% v 33%, O.R. 7.2, 95% C.I. 2.95-17.62). Daily benzodiazepine users were no more likely to have experienced convulsions when detoxing, but it should be noted that this finding is based upon a relatively small sample size (n=84). Those subjects who had tried to stop using benzodiazepines had used significantly more tablets on the last day of use than the rest of the sample (9.1 v 4.6,  $t_{90}$ =2.11, p<0.05)

 Table 5:
 Initiation & continuation of benzodiazepine use.

	Males	Females	Persons
N	136	74	210
Mean age when first used benzodiazepines	19	18	19
Mean age when first used benzodiazepines regularly (at least once a month) *	22	20	21
Reason for first using benzodiazepines (%):			
To get out of it Manage heroin withdrawal Sleep Anxiety Enhance heroin `stone' Manage amphetamine withdrawal Enhance methadone `stone' Other	37 19 14 5 2 4 1	41 10 14 11 7 3 0 16	38 16 14 7 4 4 1
Reason for continuing to use benzodiazepines (%):			
Manage heroin withdrawal Sleep To get out of it Anxiety Enhance heroin `stone' Manage amphetamine withdrawal Enhance methadone `stone' Other	22 24 16 8 5 4 2 19	24 16 16 15 4 1 3 20	23 22 16 11 5 3 2 20
Ever tried to stop using benzodiazepines (%): Yes No	37 63	46 54	40 60

<sup>\*</sup> Excludes those who have never used benzodiazepines regularly: Males n=106, Females n=65, Persons n=171

#### **3.5.2** Concurrent use of benzodiazepines and other drugs

A notable proportion of the sample (42%) reported that they had used more than one type of benzodiazepine simultaneously at some stage during the preceding 6 months, with a significant minority of subjects (11%) indicating that this had occurred at least half of the time (Table 6).

Benzodiazepines were commonly used at the same time as other drugs. The overwhelming majority (90%) of the sample reported that such concurrent use had occurred during the previous 6 months, with more than half (52%) declaring that they always used benzodiazepines with another drug. Daily users of benzodiazepines were significantly more likely to report *always* using benzodiazepines with another drug than less regular users (69% v 49%, O.R. 2.25, 95% C.I. 1.01-5.02).

Heroin was the most prevalent other drug used (29%), followed by other opiates (28%), alcohol (18%), and cannabis (9%). Over a third (36%) of subjects indicated that they tended to use benzodiazepines before the other drug, and the reverse order of use was reported by almost half of the sample (46%).

 Table 6:
 Concurrent use of benzodiazepines and other drugs

N=210

	%
	70
Frequency with which different types of benzodiazepines	
were used together in the preceding 6 months:	
All of the time	2
Most of the time	3 4
Half of the time	4
Some of the time	31
None of the time	59
Frequency with which benzodiazepines were used in	
conjunction with other drugs in the preceding 6 months:	
All of the time	52
Most of the time	9
Half of the time	11
Some of the time	18
None of the time	11
Other drug with which benzodiazepines were used most often	
in the preceding 6 months:	
Heroin	32
Other opiates	30
Alcohol	20
Cannabis	10
Other	8
Usual order of use:*	
Benzodiazepines first	36
Other drug first	46
Either drug first	8
Taken together	10

<sup>\*</sup> N=188, Excludes those subjects who had not used benzodiazepines in conjunction with other drugs in the preceding 6 months

#### 3.6 Availability & Procurement of Benzodiazepines

The vast majority of subjects (86%) reported that benzodiazepines were easy or very easy to obtain (Table 7). When asked which was the easiest type to procure, over a third (34%) specified diazepam, a fifth (19%) oxazepam, and a similar proportion (17%) indicated that they were all easy to acquire. When requested to designate which benzodiazepine was most difficult to obtain, more than half (52%) of subjects nominated flunitrazepam and over a quarter (28%) replied that none of them were difficult to procure.

During the preceding 6 months only a third (34%) of subjects had acquired their benzodiazepines solely through a doctor. Two thirds (66%) had obtained them from illicit sources at some stage during that period, including one fifth (18%) who had done so exclusively. While 64% of subjects reported acquiring their last benzodiazepines through a doctor, 36% had obtained them elsewhere. It was more common for subjects to have procured benzodiazepines from a friend (30%) the last time than through a sexual partner (4%). Over a half (58%) of the sample reported that they had sold or given benzodiazepines to someone else in the last 6 months.

**Table 7:** Availability & procurement of benzodiazepines

N=210

	1
	%
How easy is it to get benzodiazepines:	
Very easy	48
Easy	38
Difficult	12
Very difficult	1
Which is the easiest benzodiazepine to get:	
Diazepam	34
Oxazepam	19
All as easy as each other	17
Temazepam	13
Others	17
Which is the hardest benzodiazepine to get:	
Flunitrazepam	52
None	28
Oxazepam	3
Others	17
Where subjects have got benzodiazepines from in last 6 months:	
Doctors only	34
Doctors and others	47
Others only	19
Where subjects got benzodiazepines the last time:	-
, ,	
Doctor	
Partner	64
Friend	4
Other	30 2

#### 3.7 Procurement of Benzodiazepines through Doctors

Of those subjects who had been to a doctor for benzodiazepines in the last 6 months, the overwhelming majority (89%) reported being successful in obtaining them all or most of the time (Table 8).

When asked what they do when they fail to acquire benzodiazepines from a doctor 58% indicated that they go to another doctor. The median number of doctors attended for the procurement of benzodiazepines during the six months preceding interview was 3 (range 1-60). However, it should be noted that almost a fifth (19%) of these subjects reported visiting six or more doctors during that time.

A little over half (53%) of those subjects who had visited a doctor in order to obtain benzodiazepines in the preceding 6 months had done so less than once a month. A substantial minority (12%) had made such visits more than once a week, with over a third (36%) doing so between once a week and once a month.

 Table 8:
 Procurement of benzodiazepines through doctors

	%
How often subjects are successful when they go to doctors for benzodiazepines <sup>1</sup>	
All the time Most of the time 1/2 the time Sometimes	50 39 7 5
What subjects do when unsuccessful at getting benzodiazepines from a doctor <sup>2</sup>	
Find another Dr Get some heroin Try friends Try & get licit codeine Other	58 5 14 1 22
Number of doctors subjects have been to in order to get benzodiazepines during the 6 months preceding interview <sup>1</sup>	
1-2 3-5 6 or more	59 22 19
How often subjects have gone to doctors for benzodiazepines in last 6 months <sup>1</sup>	
< Once a month Once a week or less > Once a week Daily	53 36 11 1

<sup>&</sup>lt;sup>1</sup> N=170, excludes those who have not gone to doctors for benzodiazepines in the last 6 months

<sup>&</sup>lt;sup>2</sup> N=85, excludes those who have not gone to doctors and those who were always successful

When asked what symptoms they had cited during their consultations with doctors throughout the preceding 6 months, subjects most often reported insomnia (56%) and anxiety (42%) (Table 9). Almost a third (31%) indicated that they had referred to opiate dependence, 19% had complained of depression and 7% had mentioned benzodiazepine dependence.

**Table 9:** Symptoms that subjects described to doctors in order to obtain benzodiazepines

N=170

Symptom	% Yes
Insomnia	56
Anxiety	42
Opiate Dependence	31
Depression	19
Benzodiazepine Dependence	7
Speed Dependence	3
Other	32

NB: N=170, Excludes subjects who had not been to a Dr for benzodiazepines in the preceding 6 months

Subjects were permitted to give more than one response, so percentages do not add to 100

#### 3.8 Familiarity with Benzodiazepines

Subjects had used a wide range of benzodiazepines, with a median lifetime use of 5 (range 1-9) different types. A third of subjects (35%) had used 6 or more varieties of benzodiazepine. A median of 2 (range 1-6) types of benzodiazepine had been used in the preceding 6 months.

As can be seen in Table 10, the most widely used benzodiazepines were diazepam (92%), oxazepam (91%), flunitrazepam (84%) and temazepam (81%). These were also the four types most widely used in the preceding 6 months, with diazepam (66%) again being the most extensively used in that period. When asked to nominate the benzodiazepine that they had used most often in the preceding six months, diazepam was cited by 38% of subjects, with oxazepam (19%) the next most frequently nominated.

#### 3.9 The Injection of Benzodiazepines

The injection of benzodiazepines was widespread, with 48% of subjects having ever injected a benzodiazepine. Males (48%) and females (52%) were equally likely to have injected benzodiazepines. The median number of benzodiazepine varieties injected was 1 (range 1-7), with 10% of subjects having injected 2 or more types of benzodiazepine. Seventeen percent of subjects had injected a benzodiazepine in the preceding six months, with the median number of varieties injected again being 1 (range 1-6). Once more, males (15%) and females (17%) were equally likely to have injected benzodiazepines in this period. The parenteral use of benzodiazepines was unrelated to frequency of benzodiazepine use in the last six months.

As shown in Table 10, the most widely injected benzodiazepines were diazepam (25%) and temazepam (25%). Temazepam (9%) was the most commonly injected benzodiazepine in the preceding six months, with 5% of subjects having injected diazepam in that period.

 Table 10:
 Familiarity with benzodiazepines among heroin users

(N=210)

Benzodiazepine	Ever used	Ever injected	Used in last 6 months %	Injected in last 6 months
	%	%		%
Alprazolam	10	1	3	0
Bromazepam	2	0	0	0
Chlordiazepoxide	7	1	0	0
Clobazam	1	0	0	0
Clonazepam	33	2	16	1
Diazepam	92	25	66	5
Flunitrazepam	84	12	41	2
Flurazepam	1	1	0	0
Lorazepam	5	1	1	1
Midazolam	0	0	0	0
Nitrazepam	66	2	19	1
Oxazepam	91	14	51	2
Potassium Chlorazepate	2	0	1	0
Temazepam	81	25	41	9
Triazolam	10	1	4	1

#### 3.10 Preferences for Benzodiazepines

The benzodiazepine with the highest mean liking rating was flunitrazepam (Table 11). The mean rating for flunitrazepam was significantly higher than that of the next most liked drug, diazepam (6.5 v 5.7,  $t_{167}$ =2.3, p<.05). Diazepam was rated significantly higher than oxazepam (5.7 v 5.0,  $t_{178}$ =2.6, p<.05).

When independently asked to nominate their favourite benzodiazepine, flunitrazepam was overwhelmingly the most popular, being nominated by 42% of subjects. The next most popular type was diazepam, preferred by 24% of the sample.

When asked why they favoured flunitrazepam, the two most common responses related to intoxication: that it was the "strongest" benzodiazepine (50%), and that it gives a good "high" (22%).

 Table 11:
 Mean liking ratings of benzodiazepines among heroin users

Benzodiazepine	Mean rating <sup>*</sup>
Flunitrazepam	6.5 (3.4)
Diazepam	5.7 (3.0)
Oxazepam	5.0 (3.1)
Clonazepam	5.0 (3.5)
Temazepam	4.4 (2.9)
Alprazolam	4.3 (2.5)
Nitrazepam	3.9 (2.8)
Triazolam	3.1 (2.5)

<sup>\*</sup> Standard deviations in brackets

# 3.11 Comparisons of benzodiazepine using and non-benzodiazepine using heroin injectors

An advantage of conducting this research in conjunction with the heroin overdose study is that it allowed the following comparisons to be made between those heroin users who currently use benzodiazepines and those who do not.

## **3.11.1** Demographics

As with the benzodiazepine sample, 65% of the 119 non-benzodiazepine users were male. The two groups were also alike in terms of mean age (30 and 31 years respectively), mean number of years of school education (10 years), proportion currently in treatment (51% v 44%) and proportion in past treatment (67% v 65%). A similar percentage of subjects from each group reported having a prison record (41% v 40%). Current users of benzodiazepines were more likely to be unemployed (77% v 63%, O.R. 1.98, 95% C.I. 1.21-3.24).

#### **3.11.2** Drug use

While polydrug use was prevalent among both groups, benzodiazepine users appeared more severely drug entrenched. Excluding benzodiazepines, they had used more drug classes in the last six months (5 v 4,  $t_{327}$ =5.51, p<0.001), injected more drug classes during that time (2 v 1,  $t_{327}$ =5.03, p<0.001), used a greater number of drug classes in total (9 v 8,  $t_{327}$ =3.59, p<0.001) and injected a greater number of drug classes in total (4 v 3,  $t_{327}$ =3.65, p<0.001). Furthermore, during the preceding 6 months benzodiazepine users were significantly more likely to have used amphetamines (48% v 31%, O.R. 2.01, 95% C.I. 1.26-3.23), alcohol (83% v 69%, O.R. 2.26, 95% C.I. 1.33-3.84), cannabis (89% v 77%, O.R. 2.27 95% C.I. 1.24-4.16) and opiates other than heroin (36% v 26%, O.R. 2.95, 95% C.I. 1.81-4.82).

#### **3.11.3** Injection related HIV risk-taking behaviour

The benzodiazepine sample scored significantly higher on the HRBS injecting risk-taking sub-scale (4 v 3,  $t_{327}$ =3.52, p<0.001). As shown in Table 12, current users of benzodiazepines were more likely within the last 6 months to have injected a drug (89% v 79%, O.R. 2.06, 95% C.I. 1.12-3.8), borrowed a used needle (25% v 14%, O.R. 2.11, 95% C.I. 1.08-4.13), and lent a used needle (25% v 14%, O.R. 2.05, 95% C.I. 1.04-4.02). Defining sharing as having borrowed a used needle, lent a used needle or both, benzodiazepine users were also more likely to have shared (35% v 21%, O.R. 1.99, C.I. 1.11-3.55).

**Table 12:**A comparison of injection related HIV risk-taking behaviour among benzodiazepine and non-benzodiazepine using heroin IDU.

Behaviour during the month preceding interview	BZD users	Non-BZD users	Odds Ratio
preceding interview	(N=210)	(N=119)	
	%	%	(95% C.I.)
	70	70	
Injected a drug	89	79	$2.06^{*}$ $(1.12 \rightarrow 3.8)$
Borrowed a used needle	25	14	2.11 <sup>*</sup> (1.08 → 4.13)
Lent a used needle	25	14	2.05 <sup>*</sup> (1.04 → 4.02)
Shared a needle (either borrowed or lent)	35	21	1.99 <sup>*</sup> (1.11 → 3.55)

<sup>\*</sup> Significant group effect

## 4.0 DISCUSSION

#### 4.1 Major Findings of the Study

One of the major findings of the current study was the high prevalence of injecting of benzodiazepines among heroin users. Almost half of the sample (48%) reported having injected a benzodiazepine, with nearly one fifth having done so in the six months preceding interview. Given the associated risks of thromboses and vascular morbidity, the parenteral use of benzodiazepine tablets is serious cause for concern.

The second major finding was the ease with which heroin users are able to procure benzodiazepines. The overwhelming majority of subjects (86%) reported that these drugs are easy or very easy to obtain. Only a third of subjects (34%) had acquired their benzodiazepines exclusively through a doctor in the six months preceding interview. Furthermore, over half of the sample (58%) reported that they had sold or given benzodiazepines to someone else during that time. Doctors need to realise that they are, in effect, part of a chain of supply to IDUs with regard to benzodiazepines.

A third important finding was the existence of distinct preferences among heroin users for certain benzodiazepines. Subjects were familiar with a broad range of benzodiazepines, having used a median of 5 different types, yet when independently asked to nominate their favourite the responses showed significant concordance. Flunitrazepam was overwhelmingly the most popular benzodiazepine, being favoured by 42% of the sample. Given that the subjective effect of a drug is thought to be a key indicator of abuse liability<sup>25</sup>, such preferences should be borne in mind when prescribing benzodiazepines to this population.

#### 4.2 Data Validity and Sampling Bias

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 26-28. In a recent Australian study on primary heroin users for instance, self reported drug use showed respectable validity when assessed against collateral interviews and urinalysis results 29.

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, for example sex, age, and employment status, are in accordance with those reported by other studies of heroin users, both in Australia and overseas 30-32.

#### 4.3 Characteristics of Benzodiazepine Users

Demographically the sample used in this study appeared typical of other cohorts of heroin users, particularly in terms of mean age (30 years), number of years of school education (10 years), and proportion with a prison record (41%). Considering that the usual male to female ratio among a sample of heroin users seems to be approximately 2:1, the finding that two thirds of the current sample were male implies that male and female heroin users were equally likely to use benzodiazepines. This is in marked contrast to the situation in the general Australian population where significantly more females than males have been found to use benzodiazepines<sup>33</sup>.

The previously reported association between benzodiazepine use and injection related HIV risk-taking behaviour was confirmed by the current study. Benzodiazepine users were found to be significantly more likely than non-benzodiazepine users to have injected a drug in the preceding six months, and to have shared used injection equipment in the last month. They also reported greater levels of polydrug use. The exact nature of the relationship between HIV risk-taking behaviour and benzodiazepine use is yet to be illuminated. It is still unclear whether the effects of benzodiazepines simply appeal to those heroin users with a natural tendency to engage in risky behaviour, or whether the risky behaviour is a consequence of intoxication with benzodiazepines.

#### 4.4 History and Patterns of Benzodiazepine Use

While 47% of the sample had used benzodiazepines prior to using heroin, a significant proportion (38%) had used heroin before having tried benzodiazepines. The mean age of first use was 19 years for both benzodiazepines and heroin.

Of interest were the reasons that subjects gave for having first used benzodiazepines and for continuing to do so. The most common justification for initially trying benzodiazepines was 'to get out of it' (38%), that is, they were taken for their intoxicating effects. In contrast, only 16% of the sample gave this as their reason for continuing to use benzodiazepines, with management of heroin withdrawal being the more common rationale given (23%). The efficacy of such use on an outpatient basis is questionable given what is known about the associated HIV risk-taking behaviour among this group. There is obvious potential for the prescribing of benzodiazepines to be 'harm-inducing' rather than 'harm-reducing' given that almost a fifth of subjects (17%) reported having used ten or more tablets on the last day of use.

It should be noted that the clinical indications for the use of benzodiazepines are

anxiety disorders, anxiety symptoms with and without associated depression, insomnia, epilepsy, muscle spasm, terminal illness and acute alcohol withdrawal<sup>34</sup>. All of the benzodiazepines listed in MIMS specify "addiction prone" as a special precaution, that is, as a pre-existing condition that should be borne in mind when considering initiation of therapy.

Only a fifth of subjects reported first using benzodiazepines for insomnia or anxiety. While a greater proportion (33%) gave such reasons for continuing to use benzodiazepines, the inappropriate use of these drugs appears to have persisted among the majority of the sample (66%).

The discrepancy between the proportion of subjects who said that they continued to use benzodiazepines because of insomnia (22%), and those who had described insomnia to doctors in order to procure benzodiazepines (56%), suggests that some doctors are being deceived by their heroin using patients

A large proportion of subjects (41%) had used benzodiazepines more than once a week for the preceding six months, including 15% who had used them daily. 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 be avoided<sup>35</sup>. While it has been reported that the rate of daily use of benzodiazepines in the general practice population is also between 10 and 15%<sup>36</sup>, such regular use among IDUs has more serious implications.

A significant predictor of benzodiazepine dependence in the current study was frequency of use during the last six months, with higher levels of dependence being associated with a greater number of use days. SDS scores were recorded throughout the entire range of 0-15. While the mean SDS score was 3, 28% of the sample had scores of greater than 4 signifying dependence. Considering that only one person nominated benzodiazepines as their main drug of choice, it is noteworthy that such a high proportion of subjects showed signs of dependence. Given the nature of recruitment for this study it is not surprising that the majority of the sample (82%) indicated that they preferred opiates to any other drug class.

A cause for concern was the finding that current treatment status was a predictor of benzodiazepine dependence, with those currently in treatment for opiate dependence showing greater levels of benzodiazepine dependence. This may be accounted for by the finding that subjects currently in treatment had used benzodiazepines on significantly more days during the preceding six months than non-treatment subjects. It has been commonly documented in the literature that benzodiazepines are reported as enhancing the intoxicating effects of methadone<sup>2,7</sup>.

The fact that over a third of the subjects currently in treatment showed signs of benzodiazepine dependence may reflect a situation in which clients are not receiving sufficiently high dosage levels of methadone to sustain them. If this is the case, an increase in methadone dosage would be more appropriate than the continuation of benzodiazepine use. While the efficacy of methadone maintenance as a treatment for opioid dependence has been well established<sup>37</sup>, the usefulness of

benzodiazepines in such a situation remains doubtful given the serious harms associated with their use.

The use of benzodiazepines in conjunction with other drugs was extremely common among the sample, with 90% reporting that such co-use had occurred during the preceding six months. Heroin was the most prevalent other drug used (29%), followed by opiates other than heroin (28%) and alcohol (18%), all of which are central nervous system depressants. The non-fatal heroin overdose study<sup>19</sup> from which the current sample was drawn found that, of the people who had overdosed, 25% reported having used benzodiazepines at the time of their last overdose. It appears that heroin users are in need of education about the severe harm that may ensue from using benzodiazepines in combination with other drugs.

#### 4.5 Familiarity and Preferences

Subjects had a fair degree of familiarity with benzodiazepines, having used a median of 5 varieties during their lifetime. There appear to be differences in the patterns of use between heroin users and the general population. The types of benzodiazepines used most widely by subjects during the six months preceding interview were diazepam (66%), oxazepam (51%), flunitrazepam (41%) and temazepam (41%). The four benzodiazepines most widely prescribed in the Australian population are temazepam (2.87 million prescriptions), oxazepam (2.38), diazepam (1.74) and nitrazepam (1.35)<sup>35</sup>. Whereas flunitrazepam was the third most widely used benzodiazepine among heroin users, it is ranked a relatively distant fifth in overall prescriptions (310,100). Similarly, whereas diazepam ranks third in overall prescription, it is the most widely used drug by heroin users.

The sample exhibited a clear, consistent preference for flunitrazepam over other benzodiazepines. In preference ratings flunitrazepam was rated significantly higher than the next most desired drug, diazepam. This is consistent with other studies of injecting drug users<sup>2,38,39</sup>. The reasons for the

preference refer to intoxication, with nearly three quarters of those who preferred this drug giving responses relating to the strength of the drug effect, and its sought after "high". In terms of dose equivalence, subjects were correct when they said that flunitrazepam was the strongest of the benzodiazepines<sup>40</sup>. The next most preferred benzodiazepine, diazepam, shares with flunitrazepam the pharmacological characteristic of guick onset of effects.

#### 4.6 Availability and Procurement

The vast majority of subjects (86%) reported that benzodiazepines are easy or very easy to obtain. Given that diazepam was the second most preferred benzodiazepine among the sample, it is noteworthy that over one third of subjects (34%) indicated that diazepam was the easiest type of benzodiazepine to procure. While flunitrazepam, the most popular benzodiazepine among the subjects, was cited as the most difficult type obtain, a significant proportion of the sample (41%) had used this drug during the last six months. This figure is surprising considering that flunitrazepam requires an Authority to Prescribe under the Pharmaceutical Benefits Scheme.

Only a third of the sample had acquired benzodiazepines solely through a doctor during the preceding six months. The remainder had obtained benzodiazepines from an illicit source at some stage during that period, including a fifth of the sample who had done so exclusively. A large proportion of subjects (58%) reported having sold or given benzodiazepines to someone during the six months preceding interview. These findings suggest that doctors may be medicating far more people than they realise. This is a legitimate cause for concern given the serious harms that have been associated with the use of benzodiazepines among IDUs.

Given that a little over half (53%) of those subjects who had visited a doctor in order to obtain benzodiazepines in the preceding six months had done so less than once a month, it could be argued that a general practitioner would be most unlikely to be suspect them of being polydrug users. However, this problem has been addressed to some degree by the guidelines from the Royal Australian College of General Practitioners (RACGP) which advocate that doctors avoid prescribing for any patient that they do not know<sup>41</sup>.

Of those subjects who had been to a doctor for benzodiazepines during the six months prior to interview, the overwhelming majority (89%) reported having successfully obtained them all or most of the time. The most common response when subjects failed to obtain benzodiazepines from one doctor was to try another doctor (58%). While the median number of doctors seen for the procurement of benzodiazepines in the last six months was 3, approximately one fifth of the sample (19%) reported extensive `doctor shopping', having visited six or more doctors during that period.

While the symptoms that subjects most commonly reported describing to doctors were insomnia (56%) and anxiety (42%), almost a third indicated that they had mentioned their opiate dependence (31%). While it may be tempting for some doctors confronted with a patient who is in a state of heroin withdrawal to prescribe benzodiazepines, the evidence suggests that such practice is not in the patient's best interest.

#### 4.7 Injecting of Benzodiazepines

The current study indicates, as in the U.K., widespread injecting of benzodiazepines among Australian heroin users who use benzodiazepines. Nearly a half of subjects (48%) had injected benzodiazepines, with injecting being equally common in males and females. In the U.K., temazepam has been reported as the benzodiazepine most commonly injected 42-44. Among the current sample, however, diazepam and temazepam were equally the most commonly injected, with a quarter of subjects reporting having injected each of these drugs. Subjects 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. Only small proportions reported having injected other types of benzodiazepines. In the six months preceding interview temazepam was the most widely injected benzodiazepine. Overall, a broad pattern of benzodiazepine injecting appears to exist among Australian heroin users, rather than being restricted to gel preparations such as temazepam.

#### 4.8 Clinical Implications

The findings of this study have implications for the prescribing of benzodiazepines to heroin users. It has been reaffirmed that benzodiazepine use among this population is associated with harms such as greater prevalence of needle sharing, greater frequency of injecting, higher levels of poly drug use and unemployment. In addition, it was noted that over a quarter of the sample showed signs of benzodiazepine dependence. It is evident that the prescription of benzodiazepines to heroin users should be avoided when possible.

The current data suggest that despite declining prescribing<sup>35</sup> benzodiazepines are still far too readily available to this population. Based on the symptoms that subjects report having described to doctors, it appears that in some instances benzodiazepines are being prescribed inappropriately to IDUs. In cases where their use is necessary doctors should be discerning in the type of benzodiazepine prescribed. There appear to be meaningful differences in preferences for benzodiazepines, and in the likelihood of their being injected.

Flunitrazepam would appear to be a drug with great abuse liability for injecting heroin users. It would therefore be imprudent to prescribe flunitrazepam to this group. The fact that a substantial proportion of the sample (12%) had injected flunitrazepam tablets further reinforces this view. The widespread use, liking and injecting of diazepam would also appear to recommend a conservative approach in prescribing this drug to heroin users. While not a drug that heroin users rated highly, the widespread injection of temazepam indicates that prescribers should also exercise caution in the provision of this drug. The relatively low liking for nitrazepam, and the low levels of injecting of this drug indicate that it may be most suitable if benzodiazepines are to be prescribed.

While it may be argued that such preferences merely reflect the current trend in Sydney, it should be noted that flunitrazepam has also been reported to be the most favoured benzodiazepine internationally, in countries as diverse as Austria<sup>2</sup>, Spain<sup>38</sup>, Malaysia<sup>39</sup> and Portugal<sup>45</sup>. Diazepam, the current samples second most preferred benzodiazepine, is also popular overseas<sup>2,38</sup>. In double-blind trials conducted by Griffiths and colleagues diazepam and lorazepam were consistently preferred to oxazepam by subjects with sedative dependence histories<sup>46-48</sup>. Diazepam and lorazepam share with flunitrazepam the pharmacological characteristic of rapid onset of effects. In choice tests a placebo was never preferred to diazepam, whereas a placebo was preferred to oxazepam in 20% of tests. Such findings cannot be explained purely in terms of fashion.

#### 4.9 Research Implications

One of the most important findings of this study was the high incidence of benzodiazepine use by injection. As mentioned earlier, almost half of the sample (48%) had ever injected benzodiazepines and 17% had done so during the preceding six months. In view of the serious health ramifications that may result from the parenteral use of benzodiazepine tablets this is an area that warrants further investigation.

In order to fully appreciate the extent of the problem, greater detail is needed about how heroin users inject benzodiazepines. For instance, are filters used, how many tablets are injected at a time, how much water are the tablets mixed with and how does the procedure vary according to the benzodiazepine being used? Information concerning the prevalence of related health effects is also required. In addition, it would be useful to determine the reasons given by heroin users for their preference for particular routes of benzodiazepine administration, and for changing between different routes of administration. A knowledge of what motivates heroin users to inject benzodiazepines may enable the design and application of an appropriate intervention.

#### 4.10 Conclusions

The use of benzodiazepines was found to be widespread, with roughly two thirds of the heroin overdose sample meeting the criteria for participation in the current study. Such a high prevalence of use was not surprising considering the reported ease with which subjects were able to acquire benzodiazepines. The distinct preferences that heroin users in Sydney exhibit for certain benzodiazepines should be considered by clinicians when prescribing such drugs for this population. By withholding prescriptions for the preferred benzodiazepines such as flunitrazepam and diazepam, and the readily injectable temazepam, it is believed that the abuse potential and harms associated with benzodiazepine use could be minimised.

In addition to the problems that are generally associated with benzodiazepine use among injecting drug users, the parenteral use of benzodiazepines designed exclusively for oral administration carries inherent risks. The extent of the harm associated with such use has yet to be realised, and given the relatively high prevalence of benzodiazepine use by injection among Australian heroin users, it is an issue that merits further research.

The current study indicates that benzodiazepine use among heroin users in Sydney represents a significant public health problem that needs to be addressed from both a clinical and research perspective.

#### 5.0 REFERENCES

- 1. BALL, J.C., & ROSS, A. (1991). **The effectiveness of methadone treatment. Patients, programs, services and outcome.** New York: Springer-verlag.
- 2.BARNAS, C., ROSSMAN, M., ROESSLER, H., REIMER, Y., & FLEISCHHACKER, W. (1992). Benzodiazepines and other psychotropic drugs abused by patients in a methadone maintenance program. Journal of Clinical Pharmacology, 12, 397-402.
- 3.DARKE, S., HALL, W., & CARLESS, J. (1990). Drug use, injecting practices and sexual behaviour of opioid users in Sydney, Australia. British Journal of Addiction, 85, 1603-9.
- 4.DARKE, S., HALL, W., ROSS, M.W., & WODAK, A. (1992). Benzodiazepine use and HIV risk-taking behaviour among injecting drug users. **Drug & Alcohol Dependence**, 31, 31-6.
- 5.DARKE, S., SWIFT, W., HALL, W., & ROSS, M. (1993). Drug use, HIV risk-taking and psychosocial correlates of benzodiazepine use among methadone maintenance clients. **Drug & Alcohol Dependence**, 34, 67-70.
- 6.KLEE, H., FAUGIER, J., HAYES, C., BOULTON, T., & MORRIS, J. (1990) AIDS related risk behaviour, poly-drug use and temazepam. **British Journal of Addiction**, 85, 1125-32.
- 7.STITZER, M.L., GRIFFITHS, R.R., McLELLAN, A.T., GRABOWSKI, J., & HAWTHORNE, J.W. (1981). Diazepam use among methadone maintenance patients: Patterns and dosages. **Drug & Alcohol Dependence**, 8, 189-99.
- 8.DARKE, S. The use of benzodiazepines among injecting drug users. (1994). **Drug & Alcohol Review**, 13, 63-69.
- 9.DARKE, S., ROSS, J., & COHEN, J. (1994). The use of benzodiazepines among regular amphetamine users, **Addiction**, 89, 1683-1690.
- 10.DONOGHOE, M.C., DOLAN, K.A., & STIMSON, G.V. (1992). Life-style factors and social circumstances of syringe sharing in injecting drug users. **British Journal of Addiction**, 87, 993-1003.
- 11.METZGER, D., WOODY, G., De PHILIPIS, D., McLELLAN, A.T., O'BRIEN, C.P., PLATT, J.J. (1991). Risk factors for needle sharing among methadone treated patients. **American Journal of Psychiatry**, 48, 636-640.
- 12.WALSH, R.A. (1991). Opioid drug accidental deaths in the Newcastle area of New South Wales, 1970-1987. **Drug & Alcohol Review**, 10, 79-83.

- 13.GUTIÉREZ-CEBOLLADA, J., De La TORRE, R., ORTUÑO, J., GARCÉS, J., & CAMÍ, J. (1994). Psychotropic drug consumption and other factors associated with heroin overdose. **Drug & Alcohol Dependence**, 35, 169-174.
- 14.SEIVEWRIGHT, N., & DOUGAL, W. (1993). Withdrawal symptoms from high dose benzodiazepines in poly drug users. **Drug & Alcohol Dependence**, 32, 15-23.
- 15.RUBEN, S.M., & MORRISON, C.L. (1992). Temazepam misuse in a group of injecting drug users, **British Journal of Addiction**, 87, 1387-1392.
- 16.SCOTT, R.N., GOING, J., WOODBURN, K.R., GILMOUR, D.G., REID, D.B., LEIBERMAN, D.P. et al. (1992). Intra-arterial temazepam, **British Medical Journal**, 304, 1603.
- 17.VELLA, E.J., & EDWARDS, C.W. (1993). Death from pulmonary microembolism after intravenous injection of temazepam, **British Medical Journal**, 307, 26.
- 18.IGUCHI, M.Y., GRIFFITHS, R.R., BICKEL, W.K., HANDELSMAN, L., CHILDRESS, A.R., & McLELLAN, A.T. (1989). Relative abuse liability of benzodiazepines in methadone maintained populations in three cities. In L.S. Harris (Ed). Problems of Drug Dependence, NIDA Research Monograph 95, Rockville: NIDA, 1990.
- 19.DARKE, S., ROSS, J., COHEN, J., & HALL, W. (1994). Context and correlates of non-fatal overdose among heroin users in Sydney. NDARC monograph no.20, UNSW.
- 20.GOSSOP, M., GRIFFITHS, P., POWIS, B., & STRANG, J. (1992). Severity of dependence and route of administration of heroin, cocaine and amphetamines. **British Journal of Addiction**, 87, 1527-1536.
- 21.GOSSOP, M., DARKE, S., GRIFFITHS, P., POWIS, B., HALL, W., & STRANG, J. (In press). The severity of dependence Scale in English and Australian samples of heroin, cocaine and amphetamine users. **Addiction**.
- 22.DARKE, S., HALL, W., HEATHER, N., WARD, J., & WODAK, A. (1991). The reliability and validity of a scale to measure HIV risk-taking among intravenous drug users. **AIDS**, 5, 181-185.
- 23. COHEN, J., & COHEN, P. (1983). Applied multiple regression/correlation analysis for the behavioural sciences, 2nd edn (London, Lawrence Erlbaum Associates).
- 24.WILKINSON, L. (1987). **SYSTAT: The system for statistics.** SYSTAT Inc: Evanston II, Illinois.

- 25. STRANG, J., SEIVEWRIGHT, N., & FARRELL, M. (1993). Oral and intravenous abuse of benzodiazepines. In C. Hallström (Ed). **Benzodiazepine Dependence.** Oxford Medical Publications.
- 26. BALE, R.R., van STONE, W.W., ENGELSING, T.M.J., ZARCONE, V.P., & KULDAU, J.M. (1981). The validity of self reported heroin use. **International Journal of Addictions**, 16, 1387-1398.
- 27. BALL, J.C. (1967). The reliability and validity of interview data obtained from 59 narcotic drug addicts. **American Journal of Sociology**, 72, 650-654.
- 28. MAGURA, S., GOLDSMITH, D., CASRIEL, C., GOLDSTEIN, P.J., & LIPTON, D.S. (1987). The validity of methadone clients' self-reported drug use. **International Journal of Addictions**, 22, 727-749.
- 29.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. **British Journal of Addiction**, 87, 593-602.
- 30. CAPLEHORN, J.R.M. & SAUNDERS, J.B. (1993). Factors associated with heroin users' AIDS risk-taking behaviours. **Australian Journal of Public Health**, 17, 13-17.
- 31. HALL, W., BELL, J., & CARLESS, J. (1993). Crime and drug use among applicants for methadone maintenance. **Drug & Alcohol Dependence**, 31, 123-129.
- 32. GRIFFITHS, P., GOSSOP, M., POWIS, B., & STRANG, J. (1994). Transitions in patterns of heroin administration: a study of heroin chasers and heroin injectors. **Addiction**, 89, 301-309.
- 33. COMMONWEALTH DEPARTMENT OF HEALTH, HOUSING AND COMMUNITY SERVICES. (1992). Statistics on drug abuse in Australia. Australian Government Publishing Service: Canberra.
- 34. MIMS AUSTRALIA. (1994). MIMS February/March 1994. Promail Printing Group: NSW.
- 35. MANT, A., WHICKER, S.D., McMANUS, P., BIRKETT, D.J., EDMONDS, D., & DUMBRELL, D. (1993). Benzodiazepine utilisation in Australia: report from a new pharmacoepidemiological database. **Australian Journal of Public Health**, 17, 345-349.
- 36. MANT, A., WODAK, A., & DAY, R. (1987). Benzodiazepine dependence. Strategies for prevention and withdrawal. **Current Therapeutics**, February,

- 37. WARD, J., MATTICK, R., & HALL, W. (1992). Key issues in methadone maintenance treatment. Sydney, University of New South Wales Press.
- 38. SAN, L., TATO, J., TORRENS, M., CASTILLO, C., FARRÉ, M., & CAMÍ, J. (1993). Flunitrazepam consumption among heroin addicts admitted for in-patient detoxification. **Drug & Alcohol Dependence**, 32, 281- 286.
- 39. NAVARATANAM, V., & FOONG, K. (1990). Opiate dependence the role of benzodiazepines. **Current Medical Research & Opinion**, 11, 620-630.
- 40. Frank, L., & Pead, J. (1995). New concepts in drug withdrawal. A resource handbook. Services for Alcohol and Drug Withdrawal, Monograph No.4. The University of Melbourne.
- 41. THE ROYAL AUSTRALIAN COLLEGE OF GENERAL PRACTITIONERS. (1994). Guidelines for the rational use of benzodiazepines.
- 42.STRANG, J., GRIFFITHS, P., ABBEY, J., & GOSSOP, M. (1994). Survey of injected benzodiazepines among drug users in Britain. **British Medical Journal**, 308, 1082.
- 43. KEENE, J., STIMSON, G.V., JONES, S., & PARRY-LANGDON, N. (1993). Evaluation of syringe exchange for HIV prevention among injecting drug users in rural and urban areas of Wales. **Addiction**, 88, 1063-1070.
- 44. FORSYTH, A.J.M., FARQUHAR, D., GEMMELL, M., SHEWAN, D., & Davies, J.B. (1993). The dual use of opioids and temazepam by drug injectors in Glasgow (Scotland). **Drug & Alcohol Dependence**, 32, 277-280.
- 45. FERRIERA, L., OLIVIERRA, M.J., & HINDMARCH, I. (1983). Drug dependents' first choice benzodiazepines. International Congress and Symposium Series, 74, 105-109.
- 46. FUNDERBURK, F.R., GRIFFITHS, R.R., McLEOD, D.R., BIGELOW, G.E., Mackenzie, A., Liebson, I.A., & Nemeth-Coslett, R. (1988). Relative abuse liability of lorazepam and diazepam; an evaluation in recreational drug users. **Drug & Alcohol Dependence**, 22, 215-222.
- 47. GRIFFITHS, R.R., BIGELOW, G.E., & LIEBSON, I.A. (1979). Human drug self-administration: Double blind comparison of pentobarbital, diazepam, chlorpromazine and placebo. **Journal of Pharmacology & Experimental Therapeutics**, 210, 301-310.

48. GRIFFITHS, R.R., McLEOD, D.R., BIGELOW, G.E., LIEBSON, I.A., ROACHE, J.D., & NOWOWIESKI, P. (1984). Comparison of diazepam and oxazepam: Preference, liking and extent of abuse. **Journal of Pharmacology & Experimental Therapeutics**, 229, 501-508.

## **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.	SerepaxOxazepam (ANX)			
23.	TemazeTemazepam (SH)			
24.	TranxenePotassium Chlorazepate (ANX)			
25.	Valium Diazepam (ANX)			
26.	XanaxAlprazolam (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			