BENZODIAZEPINE DEPENDENCE & PSYCHOPATHOLOGY AMONG HEROIN USERS IN SYDNEY

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EXECUTIVE SUMMARY

The current study examined the prevalence of benzodiazepine dependence and psychopathology among heroin users in Sydney. Using the Composite International Diagnostic Interview (CIDI), 222 heroin users were assessed for lifetime and current drug dependencies, anxiety and depressive disorders. Benzodiazepines had been used by 91% of the sample, of whom 26% met the criteria for a lifetime diagnosis of dependence. Two thirds of the sample had used benzodiazepines in the preceding 12 months, of whom 22% received a current diagnosis of dependence.

Those subjects who were diagnosed as ever having been benzodiazepine dependent were significantly more likely than other subjects to have ever had an anxiety (75% v 55%) or depressive disorder (65% v 33%). In the majority of cases, the anxiety or depressive disorder preceded the onset of regular benzodiazepine use. While this suggests that, to some extent, heroin users who use benzodiazepines are self-medicating pre-existing psychopathology, it does not rule out the possibility that benzodiazepine use then gives rise to further anxiety and/or depression.

Heroin users with a history of benzodiazepine dependence had also been dependent on a greater number of drugs (excluding benzodiazepines) than the remainder of the sample.

The Severity of Dependence Scale (SDS) was found to be an efficient measure of benzodiazepine dependence among the sample. An ROC analysis was performed, using DSM-III-R diagnoses of dependence as the criterion measure. The appropriate cut-off mark on the SDS was found to be 2, lower than that used when assessing heroin, cocaine or amphetamine dependence.

The high rate of benzodiazepine dependence among heroin users highlights the need for education for injecting drug users about the risk of benzodiazepine dependence, and the associated withdrawal syndrome. Doctors need to discuss these issues with their patients whenever they prescribe bezodiazepines, and should be mindful of the fact that heroin users who use benzodiazepines are at particularly high risk of becoming dependent. Regular use of benzodiazepines in conjunction with heroin also has serious implications for overdose.

Doctors should also be aware that many of the heroin users for whom they prescribe benzodiazepines are likely to have multiple drug dependencies, and co-existing anxiety and/or depressive

disorders. Treatment services, such as methadone clinics, need to be capable of managing clients who have multiple drug dependencies and co-existing anxiety and depressive disorders.

1.0 INTRODUCTION

When benzodiazepines were first introduced in the early 1960's they were thought to be "non-habit forming" (Lennane, 1986). By the end of the 1960's, it was even being suggested that non-medical personnel such as social workers should be permitted to prescribe benzodiazepines, as there were so few risks thought to be associated with them (Owen & Tyrer, 1983). While it is true that benzodiazepines, because of a lower risk of toxicity, represent a safer alternative to barbiturates, it is now firmly established that there is a withdrawal syndrome associated with their use (Mant et al, 1993).

Benzodiazepine use is widespread among heroin users (Navaratnam & Foong, 1990; Darke, 1994; Lennane, 1986; Ross, Darke & Hall, 1997), and previous studies suggest that approximately a quarter of those heroin users who use benzodiazepines exhibit some degree of benzodiazepine dependence, as determined by the Severity of Dependence Scale (SDS) (Ross, Darke & Hall, 1996; 1997). This is of particular concern given that benzodiazepine use is considered to play a significant role in heroin overdose fatalities, with benzodiazepines typically being detected in a quarter of overdose deaths (Zador, Sunjic & Darke, 1996; Darke, Zador & Sunjic, 1997). It should be acknowledged, however, that the SDS has yet to be validated for use in assessing benzodiazepine dependence. The studies that used the SDS as a measure of benzodiazepine dependence adopted the cut-off mark that has been found to be indicative of dependence when assessing heroin, cocaine and amphetamine dependence (Gossop et al., 1995; Topp & Mattick, 1997). It is possible that a different cut-off mark would be more appropriate when assessing benzodiazepine dependence. More importantly, no study to date has reported what proportion of heroin users meet the criteria for a clinical diagnosis of benzodiazepine dependence, as assessed by the American Psychiatric Association's Diagnostic and Statistical Manual (DSM).

A strong association between opioid use and psychopathology has been consistently identified in the literature (Limbeek, Wouters, Kaplan, Geerlings & Alem, 1992; Darke, Wodak, Hall, Heather, & Ward 1992; Rounsaville & Kleber, 1986), with higher rates of anxiety and depression being noted among those opioid users who use benzodiazepines (Darke et al., 1994; Ross et al., 1997). Heroin users who use benzodiazepines have been found to have higher levels of depression, anxiety and global psychopathology than other heroin users (Darke et al., 1994). Anxiety and depression have also been associated with route of benzodiazepine administration among heroin users (Ross et al., 1997), with injectors of

benzodiazepines exhibiting higher levels of psychological distress, as measured by the General Health Questionnaire (GHQ), than oral users. In turn, oral users exhibited greater psychological distress than non-users of benzodiazepines.

The exact nature of the relationship between benzodiazepine use and psychological disorders such as anxiety and depression remains unclear. It may be that heroin users who use benzodiazepines are self-medicating pre-existing anxiety and/or depression. Alternatively, it is possible that the increased psychological distress is a consequence of their benzodiazepine use. A third possibility is that these heroin users are using benzodiazepines to self-medicate pre-existing psychopathology, but through an erratic cycle of benzodiazepine use and withdrawal, the anxiety and/or depression becomes exacerbated. In terms of treatment, it would be useful to know which, if any, of these hypotheses is correct.

Benzodiazepine use among heroin users presents a serious treatment and public health concern. The current study aimed to determine to what extent heroin users meet the criteria for benzodiazepine dependence. If heroin injectors use benzodiazepines at levels sufficient to develop benzodiazepine dependence, they are likely to frequently be at greater risk of death from heroin overdose. The study also attempted to address the aetiological problem with regard to the onset of regular benzodiazepine use and the onset of anxiety and/or depression. A better understanding of the relationship between benzodiazepine use and psychopathology among heroin users may prove useful to health workers dealing with these clients in the treatment setting.

1.1 *Study Aims*

The major aims of the current study were as follows:

1) To assess the extent to which heroin users meet the criteria for a DSM-III-R diagnosis of benzodiazepine dependence;

2) To determine the predictors of benzodiazepine dependence;

3) To determine the lifetime prevalence of DSM-III-R diagnoses of anxiety and depression among heroin users;

4) To establish the extent to which the onset of anxiety and/or depressive disorders precede the onset of regular benzodiazepine use;

5) To determine an appropriate cut-off mark on the Severity of Dependence Scale for benzodiazepine dependence.

2.0 METHOD

2.1 *Procedure*

All subjects were volunteers who were paid A$30 for their participation in the study. Recruitment took place from April 1996 to February 1997, 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. Interview sites ranged from methadone clinics and needle exchanges, to pubs, coffee shops, parks, and shopping centres. 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 (JR) and took between 60 and 90 minutes to complete.

2.2 *Structured Interview*

A structured interview was devised that addressed the following areas: demographic characteristics, drug use history, heroin dependence, benzodiazepine dependence, benzodiazepine use history, and lifetime prevalence of anxiety and depressive disorders. 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, past treatment experience and prison record.

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, age of first use, which drugs they had ever injected, and which ones had they injected in the preceding 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. Using the Composite International Diagnostic Interview (CIDI) (World Health Organisation, 1993), all subjects were assessed for current and lifetime diagnoses of dependence or abuse on heroin, benzodiazepines, alcohol, cannabis, amphetamines, cocaine, inhalants and hallucinogens. The CIDI provides both lifetime and current DSM-III-R diagnoses, and gives an estimate of the onset and recency of each dependence disorder. It should be noted that a lifetime diagnosis means that the subject has had the diagnosis at some stage in their lives, not that they have been dependent all their lives.

2.2.3 Heroin dependence

Current dependence on heroin was measured using the Severity of Dependence Scale (SDS) (Gossop, Griffiths, Powis & Strang, 1992; Gossop et al., 1995). This is a 5-item scale which measures psychological dependence in the preceding year. SDS scores range from 0-15, with higher scores being indicative of greater heroin dependence.

As indicated earlier, diagnoses of heroin dependence and abuse were also obtained using the CIDI.

2.2.4 Benzodiazepine use history

Information collected regarding subjects' use of benzodiazepines included: the age at which they first used benzodiazepines, the age at which they commenced regular (at least monthly) use of benzodiazepines, the route of administration used during the 6 months preceding interview and the routes of benzodiazepine administration used overall. The CIDI also asked about the frequency of most regular benzodiazepine use, age of onset and recency of most regular use.

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. Benzodiazepine dependence and abuse diagnoses were also obtained using the CIDI.

2.2.6 Psychological functioning

All subjects were assessed for major depression, dysthymia, panic disorder, generalised anxiety disorder and phobic disorder using the CIDI. The CIDI provides an estimate of the age of onset and recency for each of these disorders.

2.3 *Analyses*

For continuous variables t-tests or pearson product correlations 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. Predictors of benzodiazepine dependence were also determined using multiple logistic regressions with backwards elimination. A receiver operating characteristic (ROC) analysis was conducted in order to determine the the most appropriate cut-off mark on the SDS for benzodiazepine dependence. All analyses were conducted using SYSTAT (Wilkinson, 1990).

3.0 RESULTS

3.1 Sample characteristics

The sample consisted of 222 subjects, of whom 59% were male. The mean age of the sample was 29.8 years (SD 7.2, range 17-50). Subjects were recruited from all regions of Sydney (Table 1).

The mean number of years of school education was 9.9 (SD 2.5, range 5-12), with 40% having completed less than 10 years. Thirty five percent of subjects had completed year ten and 25% had completed year 12. The majority of the sample (72%) had no tertiary qualifications, with 21% having attained a trade or technical certificate and 7% having gained a university or college degree.

The majority of the sample were unemployed (77%), with only 5% of subjects in full-time and 15% in part-time or casual employment. A large proportion reported having a prison record (44%), with males

being more likely than females to report ever having been imprisoned (55% v 29%, O.R.=2.9, 95% C.I. 1.64-5.10).

Approximately half of the sample (51%) were currently enrolled in methadone maintenance programmes and one subject was a member of a therapeutic community. The median length of time enrolled in current treatment was 16 months (range 1-156), with the median daily methadone dose being 50 mg (range 5-180).

Table 1: Demographic characteristics of 222 heroin users

	Male (n=130)	Female (n=92)	Persons (n=222)
Age in years (mean)	30.6	28.7	29.8
Region (%):			
Inner City/East/West	42	39	41
North	19	26	22
South/South West	19	21	19
West	21	14	18
School Education (mean years)	9.8	10.0	9.9
Tertiary Education (%):			
No tertiary education	71	74	72
Trade/Technical	21	22	21
University/College	8	4	6
Trade & University	1	0	1
Employment Status (%):			
Unemployed	76	78	77
Full-time	5	3	5
Part-time/Casual	17	13	15
Student	2	1	1
Home Duties	0	4	2
Prison Record (%)*:			
No	45	71	56
Yes	55	29	44
Currently enrolled in methadone maintenance (%)	46	59	51

**Significant gender difference exists*

3.2 Benzodiazepine use

The majority of subjects (91%) had used benzodiazepines, and 67% were current users (having used these drugs during the preceding 12 months). Current benzodiazepine users were on average, 3 years younger than the ex-benzodiazepine users (29.1 v 32.1, t_{200}=-2.6, p<.05), but the two groups did not differ significantly in terms of mean age of first benzodiazepine use (19.4 v 20.1) or mean age of first regular use (21.4 v 21.9).

Table 2 shows the history of benzodiazepine use among *current* benzodiazepine users. The mean age of first benzodiazepine use was 19.4 years (SD 6.1, range 6-40), and 21.1 years (SD 6.2, range 10-40) for the commencement of regular use. The mean length of time at interview since initial benzodiazepine use was 9.7 years (SD 7.2, range <1-28). While 43% of current benzodiazepine users had used benzodiazepines prior to trying heroin, 39% had used heroin first.

While the median number of days on which benzodiazepines had been used in the six months prior to interview was 11 (range 0-180), 37% had used them once a week or more, including 10% who had used them daily. Fourteen percent of current benzodiazepine users had injected benzodiazepines at some stage during the six months preceding interview.

Among current benzodiazepine users on methadone maintenance (n=58), there was a significant positive correlation between the number of days on which benzodiazepines had been used during the preceding six months and methadone dose (r=0.30, p<.05).

Subjects were asked to think back to the 12 month period when they were using benzodiazepines most frequently, and to recall how often they were using benzodiazepines during that period. Forty percent of current benzodiazepine users reported having had a 12 month period during which they used benzodiazepines almost every day. The mean age at commencement of their most regular benzodiazepine use was 22.2 years (SD 6.9, range 11-47), and the mean age when they last used benzodiazepines that regularly was 27.4 (SD 7.7, range 13-47). Benzodiazepine use by injection had been tried at some stage by 42% of current benzodiazepine users.

Table 2: History of benzodiazepine use among current users

	Males (n=87)	Females (n=61)	Persons (n=148)
Mean age when first used benzodiazepines (years)	19.8	18.8	19.4
Mean age when first used benzodiazepines regularly *ie. at least once a month* (years)*	21.8	20.7	21.4
Mean length of time since first used benzodiazepines (years)	10.1	9.0	9.7
Median number of days on which benzodiazepines were used in the six months prior to interview	10	12	11
Used benzodiazepines daily for the 6 months prior to interview (%)	8	12	10
Mean age at time of most regular use (years)	23.0	21.2	22.2
Frequency of most regular use (%):			
	44	44	44
Almost every day	5	13	8
3 or 4 days a week	20	13	17
1 or 2 days a week	15	18	16
1 to 3 days a month	17	12	15
Less than once a month			
Mean age when last used benzodiazepines that regularly (years)	28.4	26.0	27.4
Injected benzodiazepines (%)			
Ever	48	33	42

In preceding 6 months	15	12	14

3.3 Other drug use

Polydrug use was common among the sample (Table 3). Heroin, by definition, had been used by all subjects, with 87% having used it in the last 6 months. Similarly, the majority of the sample (82%) had used other non-prescribed opiates, with 40% having done so in the six months preceding interview. Twenty seven percent of subjects reported having injected opiates other than heroin in that time.

The mean age of subjects at the time of first heroin use was 19.5 years (SD 4.5, range 11-44). At the time of interview, the mean length of heroin use career was 10.4 years (SD 7.5, range <1-31). Males had significantly longer heroin using careers than females (11.3 yrs v 9.1 yrs, t_{220}=-2.12, p<.05). The mean SDS score for heroin was 7.0 (SD 4.4, range 0-15). Using a cut-off mark of greater than 4, 70% of subjects were classified as currently heroin dependent. Methadone clients scored significantly lower on the SDS for heroin dependence than the rest of the sample (6.1 v 7.9), and were significantly less likely to be identified as *heroin dependent* by the SDS (60% v 81%, O.R. 0.36, 95% C.I. 0.19-0.65).

The vast majority of subjects reported having ever used alcohol (100%), cannabis (99%), tobacco (98%), amphetamines (97%)and hallucinogens (88%), with cocaine (76%) and inhalants (69%) having also been widely used. In the six months prior to the most commonly used drugs were tobacco (95%), cannabis (83%), alcohol (73%) and amphetamines (51%).

Including benzodiazepines, the mean number of drug classes ever used was 9.0 (SD 1.2, range 4-10), with a mean of 5.3 (SD 1.9, range 0-10) having been used in the last six months. The mean number of drug classes ever injected was 3.8 (SD 1.3, range 1-6), and 1.8 (SD 1.1, range 0-6) in the six months prior to interview.

Table 3: Other drug use (N=222)

Drug Class	Ever Used %	Ever Injected %	Used in last 6 months %	Injected in last 6 months %	Days used in last 6 months*
Benzodiazepines	91	35	59	9	20
Heroin	100	100	87	87	64
Other Opiates	82	66	40	27	7
Amphetamines	97	92	51	38	4
Cocaine	76	61	21	14	2
Hallucinogens	88	28	23	3	3
Alcohol	100	N/A	73	N/A	48
Cannabis	99	N/A	83	N/A	100
Inhalants	69	N/A	11	N/A	3
Tobacco	98	N/A	95	N/A	180
Polydrug use#	9.0	3.8	5.3	1.8	-

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

Mean number of drug classes

3.4 Benzodiazepine dependence

According to the CIDI, 22% of current users were benzodiazepine dependent, 3% mildly so, 7% moderately and 12% severely dependent. Benzodiazepine abuse was identified in 6% of current benzodiazepine users. Among current benzodiazepine users, the median SDS score for benzodiazepines was 0 (range 0-15). Previous studies have shown that the appropriate cut-off mark for identifying dependence on cocaine, heroin or amphetamines using the SDS is 4/5 (Gossop et al., 1995; Topp et al., 1997). Using this cut-off mark, 18% of current

benzodiazepine users exhibited some degree of benzodiazepine dependence.

A quarter (26%) of those subjects who had ever used benzodiazepines had been dependent on them at some time. In order to determine which factors were independently associated with a lifetime DSM-III-R diagnosis of benzodiazepine dependence, a multiple logistic regression was conducted. The variables entered into the model were age, sex, years of school education, treatment status, routes of benzodiazepine administration ever used, frequency of most regular benzodiazepine use, age at initiation of injecting drug use, number of drug dependencies ever (excluding benzodiazepines), number of anxiety disorders ever and number of depressive disorders ever. The only significant predictors were frequency of most regular benzodiazepine use and the number of lifetime drug dependencies (Table 4). The regression equation was significant ($\div^2$, 2 df=94.4, $p<.001$), and had a good fit (Hosmer-Lemeshow $\div^2$=5.3, $p<.70$).

Table 4: Multiple logistic regression predicting a lifetime CIDI diagnosis of benzodiazepine dependence (N=202).

Variable	O.R.	95% C.I.
Frequency of most regular bezodiazepine use	3.68	2.21-6.13
Number of drug dependencies ever	2.56	1.67-3.92

Hosmer-Lemeshow $\div^2$=5.3, $p<.70$

The results indicate that, after controlling for the effects of other variables in the model, each categorical increase in the frequency of most regular benzodiazepine use, increases the odds of having been benzodiazepine dependent by more than three and a half times. Furthermore, each additional drug dependency ever experienced increases the likelihood of having been benzodiazepine dependent by two and a half times.

In order to determine the factors associated with severity of benzodiazepine dependence, a continuous variable consisting of the number of DSM-III-R criteria ever met for benzodiazepine dependence was created, simultaneous multiple regressions were

then performed. The variables entered into the model were the same as those used in the logistic regression. The final model was significant ($F_{2,199}$=81.8, p<.001) and accounted for 45% of the variance. Once again, the significant predictors of dependence were the frequency of most regular benzodiazepine use ($\hat{a}$=0.85, p<.001) and the number of lifetime drug dependencies ($\hat{a}$=0.90, p<.001).

3.5 Prevalence of DSM-III-R symptoms of benzodiazepine dependence

The most common DSM-III-R dependence symptom ever experienced by current benzodiazepine users were frequent intoxication/withdrawal when expected to fulfill obligations (36%), continued use despite social, physical or psychological problems (31%), and tolerance (24%) (Table 6).

To receive a lifetime diagnosis of benzodiazepine dependence, subjects had to report meeting at least three of the nine DSM-III-R symptoms. A quarter (26%) of current benzodiazepine users had ever been dependent, and these subjects had experienced a mean of 6.5 (SD 2.0, range 3-9) dependence symptoms. A fifth (22%) were diagnosed as currently benzodiazepine dependent, 3% mildly, 7% moderately and 12% severely dependent. The mean number of dependence symptoms experienced in the past 12 months by these subjects was 5.1 (SD 2.2, range 1-8). This represents 5 out of 8 criteria, as the CIDI does not obtain information about the recency of the sixth DSM-III-R criterion (continued use despite social, physical or psychological problems).

According to the CIDI, 6% of current benzodiazepine users met the criteria for current benzodiazepine abuse and 10% had ever abused these drugs.

DSM-IV reduced the number of dependence criteria from 9 to 7 (American Psychiatric Association, 1994). This involved the removal of frequent intoxication/withdrawal when expected to fulfill obligations; the removal of social problems from continued use despite social, physical or psychological problems; and the collapsing of withdrawal and withdrawal relief to form one criterion. When the CIDI data is reassessed to get an approximation of what proportion of current benzodiazepine users meet the criteria for a DSM-IV diagnosis of dependence, the lifetime prevalence is reduced slightly from 26% to 22%. It is noteworthy, however, that unlike DSM-III-R, DSM-IV specifies that three or more of the seven dependence criteria must be met "...at any time in *the same 12 month period*". As the CIDI does not obtain the age of onset for each dependence criterion, it is not possible to more accurately determine what proportion meet the DSM-IV criteria for a lifetime diagnosis of benzodizepine dependence.

Table 5: Prevalence of DSM-III-R benzodiazepine dependence symptoms among current benzodiazepine users

Dependence symptoms	Males (n=87) %	Females (n=61) %	Persons (n=148) %
Frequent intoxication/ withdrawal when expected to fulfill obligations	31	43	36
Continued use despite social, physical or psychological problems	31	31	31
Tolerance	23	25	24
Taken in larger quantities/for longer than intended	21	26	23
Withdrawal	20	28	23
Withdrawal relief	17	25	20
Persistent desire/unsuccessful efforts to cut down	15	23	18
A great deal of time spent acquiring/ using/recovering	16	16	16
Neglecting important activities	15	12	14
Withdrawal	20	28	23
Withdrawal relief	17	25	20

3.6 Determining an appropriate cut-off mark on the SDS for benzodiazepine dependence

An ROC analysis was conducted to determine the most appropriate cut-off mark on the SDS for assessing benzodiazepine dependence among heroin users. DSM-III-R diagnoses were used as the criterion measure. The area under the curve was 0.92 (Figure 1), suggesting that the SDS is a highly sensitive measure of benzodiazepine dependence among this population. The optimum cut-off mark is that which maximises the discrimination between the presence or absence of a disorder, a crude indication of which is given by the highest chi^2 value, as it gives equal weighting to sensitivity and specificity (Conigrave, Hall & Saunders, 1995). The highest chi^2 value was obtained for an SDS score of 3 (chi^2 value=76.5), suggesting that scores greater than or equal to three are indicative of benzodiazepine dependence.

Figure 1: Receiver Operating Characteristic (ROC) curve for the SDS in assessing benzodiazepine dependence among heroin users

The rates of misclassification, sensitivity and specificity are presented in Table 6. The misclassification rate refers to the proportion of false negatives and false positives among current benzodiazepine users. Sensitivity refers to the proportion of `cases' of dependence who are correctly identified, while specificity refers to the proportion of 'non-cases' correctly identified (Banks, 1983). Values for five different cut-off scores on the SDS are given in the table below.

Table 6: Validity of various cut-off scores on the SDS for assessing benzodiazepine dependence among heroin users

Cut-off score on SDS	Misclassification rate (%)	Sensitivity (%)	Specificity (%)
One	21.6	87.9	88.7
Two	11.5	81.8	91.3
Three	10.9	75.8	95.7
Four	8.9	66.7	95.7
Five	10.9	60.6	97.4

From the results presented above, it would appear that a cut-off mark of three on the SDS minimises the misclassification rate while maintaining adequate sensitivity and specificity. This concurs with the earlier finding that a cut-off mark of three yields the highest chi^2 value. Using a cut-off mark of greater than or equal to three, 25% of current benzodiazepine users were identified as currently dependent. As mentioned earlier, the CIDI identified 22% of current benzodiazepine users as benzodiazepine dependent.

3.7 Prevalence of anxiety and depressive disorders

Those subjects who were diagnosed by the CIDI as having ever been benzodiazepine dependent were significantly more likely than the remainder of the sample to have ever had either an anxiety (75% v 55%, O.R. 2.43, 95% C.I. 1.21-4.87) or depressive disorder (65% v 33%, O.R 3.85, 95% C.I. 2.00-7.40) (Table 7).

More specifically, subjects with a lifetime diagnosis of benzodiazepine dependence were more likely to have had panic attacks with agoraphobia (27% v 8%, O.R. 4.11, 95% C.I. 1.81-9.33), simple phobias (52% v 28%, O.R. 2.75, 95% C.I. 1.45-5.20), dysthymia (35% v 15%, O.R. 2.93, 95% C.I. 1.44-5.95) and major depression (54% v 27%, O.R. 3.14, 95% C.I. 1.66-5.97). With regard to social phobias, the difference between the two groups approached but did not attain significance (50% v 36%, O.R. 1.79, 95% C.I. 0.95-3.35).

Table 7: Lifetime prevalence of anxiety and depressive disorders among subjects with and without a lifetime diagnosis of benzodiazepine dependence.

Diagnosis	Lifetime benzodiazepine dependence (n=52) %	No benzodiazepine dependence (n=170) %	Total (n=222) %
Anxiety Disorders			
Social phobia	50	36	39
Simple phobia*	52	28	33
Agoraphobia	23	21	21
Panic attacks with agoraphobia *	27	8	12
Panic attacks	12	5	7
GAD	10	3	5
Depressive Disorders			
Dysthymia *	35	15	20
Major depression *	54	27	33
Any anxiety disorder *	75	55	60
Any depressive disorder*	65	33	41

* *Statistically significant difference exists between groups*

3.8 Order of onset of anxiety, depressive disorders and regular benzodiazepine use

Two thirds (66%) of regular benzodiazepine users had ever had an anxiety disorder, and a half (49%) had ever had a depressive disorder. Of those subjects identified as having had an anxiety disorder, 81% reported having had the disorder prior to the onset of regular benzodiazepine use (Table 8). This was particularly the case with regard to simple phobias (84%), social phobias (73%) and panic attacks with agoraphobia (71%).

Similarly, 61% of regular benzodiazepine users identified as having had a depressive disorder, reported having had such a disorder prior to the onset of regular benzodiazepine use. This was particularly true with regard to dysthymia (76%).

Table 8: Proportions of regular benzodiazepine users with anxiety or depressive disorders in which the diagnosis preceded the onset of regular benzodiazepine use

Diagnosis	Percent
Anxiety	
Simple phobia (n=57)	84
Social phobia (n=64)	73
Panic attacks with agoraphobia (n=24)	71
Panic attacks (n=12)	50
Agoraphobia (n=31)	32
Generalised Anxiety Disorder (n=8)	25
Any anxiety disorder (n=96)	81
Depression	
Dysthymia (n=33)	76
Major depression (n=60)	53
Any depressive disorder (n=71)	61

3.9 Prevalence of other substance dependence diagnoses

Excluding benzodiazepines, subjects with a lifetime diagnosis of benzodiazepine dependence had been dependent on a greater number of drugs in their lifetime than those subjects without a history of benzodiazepine dependence (3.8 v 2.5, t_{220}= -7.23, p<.001) (Table 9).

Subjects with a lifetime diagnosis of benzodiazepine dependence were significantly more likely than the remainder of the sample to have a lifetime diagnosis of alcohol dependence (83% v 60%, O.R. 3.19, 95% C.I. 1.46-6.96) and cocaine dependence (23% v 4%, O.R. 6.99, 95% C.I. 2.58-18.88).

Table 9: Lifetime prevalence of substance dependence diagnoses among subjects with and without a benzodiazepine dependence history

Substance dependence diagnosis	Lifetime diagnosis of benzodiazepine dependence (n=52) %	No history of benzodiazepine dependence (n=170) %	Total (n=222) %
Heroin	98	97	97
Alcohol[#]	83	60	65
Amphetamines	44	37	39
Cannabis	46	45	45
Cocaine[#]	23	4	9
Hallucinogens	10	4	5
Inhalants	2	1	1
Number of lifetime dependencies (mean)[#*]	3.8	2.5	2.8

 # Significant difference exists between groups

** Excludes benzodiazepine dependence*

4.0 DISCUSSION

4.1 *Major findings*

The major finding of the current study was that more than one in five of those heroin users who had used benzodiazepines in the 12 months prior to interview met the criteria for a current diagnosis of benzodiazepine dependence. This is of particular cause for concern given that benzodiazepines were not the primary drug of choice among this group.

Those heroin users who had a lifetime diagnosis of benzodiazepine dependence were significantly more likely than the rest of the sample to have had either an anxiety or depressive disorder. Among those subjects who were or had been regular benzodiazepine users, the onset of anxiety or depressive disorders appeared to precede the onset of regular benzodiazepine use in the majority of cases. This suggests that, to some extent, these subjects may be self-medicating pre-existing psychopathology.

The study also revealed that the SDS is a highly sensitive measure of benzodiazepine dependence among heroin users. The appropriate cut-off mark on the SDS for benzodiazepine dependence was found to be lower than that identified in previous studies of amphetamine, heroin and cocaine dependence.

4.2 *Benzodiazepine use*

As found in earlier studies, the use of benzodiazepines among the sample was widespread, with 91% having ever used them, and two thirds being current users. While the median number of days on which benzodiazepines had been used in the six months prior to interview was 11, over a third of current users had used them more than once a week, including 10% who used them daily. Surprisingly, when asked to recall the 12 month period during which they had used benzodiazepines most frequently, almost daily use was reported by 44% of current users. Such regular use can have serious implications, such as an increased risk of benzodiazepine dependence (Mant, Wodak & Day, 1987) and heroin overdose (Darke et al., 1997).

Of particular concern was the finding that 14% of current benzodiazepine users had injected these drugs during the preceding six months. Earlier work by the authors has shown that this route of benzodiazepine administration is associated with increased risk of heroin overdose, poorer health, poorer psychological functioning and increased criminal involvement (Ross et al., 1997).

4.3 *Benzodiazepine dependence*

A current DSM-III-R diagnosis of benzodiazepine dependence was received by 22% of current benzodiazepine users, with 12% being severely dependent. With an average of 5 dependence symptoms experienced in the preceding twelve months, it is clear that benzodiazepine dependence would be impacting significantly on the lives of these heroin users.

While only a fifth of current benzodiazepine users met the criteria for benzodiazepine dependence, it is noteworthy that approximately a third reported that in the preceding 12 months they had experienced frequent intoxication/withdrawal when expected to fulfil obligations or had continued to use benzodiazepines despite social, physical or psychological problems.

The only significant predictors of a lifetime diagnosis of benzodiazepine dependence were frequency of most regular benzodiazepine use and the number of drug dependencies ever experienced. Doctors and heroin users should be mindful of the fact that benzodiazepine dependence can occur after as little as 6 weeks of benzodiazepine use at therapeutic levels (Mant et al., 1987). As heroin users would very rarely nominate benzodiazepines as their preferred drug, and typically only use them as adjunct to heroin (Ross et al, 1996), it is highly unlikely that many of them would have considered whether or not they were at risk of becoming dependent on benzodiazepines. It is important that doctors take the time to ensure that their patients are fully informed of the risk of benzodiazepine dependence and the associated withdrawal syndrome.

4.4 *Use of the SDS for assessing benzodiazepine dependence among heroin users*

The current study suggests that the SDS represents an efficient way of assessing current benzodiazepine dependence among heroin users. While a cut-off mark of greater than four has been recommended for assessing heroin, cocaine or amphetamine dependence, a cut-off mark of greater than two appears more appropriate in assessing benzodiazepine dependence among heroin users. The lower cut-off point may, in part, be a reflection of the fact that benzodiazepines are not the primary drug of choice among this population. It is likely that the problems experienced as a consequence of benzodiazepine use are overshadowed by the problems associated with heroin use.

4.5 *Other drug use and dependencies*

Polydrug use was widespread among the sample, with a mean of nine drug classes having ever been used, and a mean of five used in the preceding six months. Excluding benzodiazepines, subjects with a lifetime diagnosis of benzodiazepine dependence had been dependent on significantly more drug classes in their lifetime than those without a history of benzodiazepine dependence. Alcohol use was particularly problematic, with 83% of those subjects who had a lifetime diagnosis of benzodiazepine dependence also having a lifetime diagnosis of alcohol dependence. This raises the question whether benzodiazepine users merely represent a subset of injecting drug users who take greater risks (which includes using a broader variety of drugs), or whether the greater risk-taking is a consequence of their benzodiazepine use. This question should not be considered in isolation from that other commonly asked question: are heroin users who use benzodiazepines self-medicating pre-existing anxiety and depression, or is the higher rate of anxiety and depression seen among this population a consequence of their benzodiazepine use? It is possible that those subjects who have a lifetime diagnosis of benzodiazepine dependence are self-medicating pre-existing psychopathology to a greater extent than their non-benzodiazepine using peers. The self-medication process may have involved the use of a greater number of other drugs at levels sufficient enough to make them dependent.

4.6 *Diagnoses of anxiety and depression*

While there was a high lifetime prevalence of anxiety and depression among the overall sample, subjects with a lifetime diagnosis of benzodiazepine dependence were more than twice as likely to meet the criteria for a lifetime DSM-III-R diagnosis of anxiety, and more than three and a half times as likely to meet the criteria for a depressive disorder. While over a third of the sample were given a lifetime diagnosis of social phobia, a half of subjects with a history of benzodiazepine dependence received the diagnosis. Those with a lifetime diagnosis of benzodiazepine dependence were significantly more likely to have had panic attacks with agoraphobia, and to have had simple phobias, than the remainder of the sample. These subjects were also more than three times as likely to receive a lifetime diagnosis of major depression, and more than two and a half times as likely to receive a diagnosis of dysthymia.

Given that benzodiazepines are prescribed for anxiety, it may not be considered surprising that subjects with a history of benzodiazepine dependence are more likely to have had an anxiety disorder. However, as benzodiazepines are commonly used among heroin users to manage symptoms of heroin withdrawal or to enhance the effects of heroin, it should not be assumed that the anxiety disorder is a precursor rather than a consequence of benzodiazepine use. Such high rates of anxiety and depression have implications for the treatment of drug use. Not only do treatment services need to be capable of managing clients who have multiple drug dependencies, they also need to cope with co-existing anxiety and depressive disorders.

4.7 *The onset of psychiatric disorders and regular benzodiazepine use*

While it is true that only a longitudinal study would provide irrefutable evidence regarding the order of onset of psychiatric disorders and regular benzodiazepine use, the CIDI provides an estimate of the age of onset by asking the respondent how old they were when they first experienced some of the symptoms of the various disorders. Among those subjects who have ever used benzodiazepines regularly, the onset of anxiety and depressive disorders appears to have preceded the onset of regular benzodiazepine use in the majority of cases (81% and 61% respectively). This was particularly true for simple phobias (84%), social phobias (73%), panic attacks with agoraphobia (71%) and dysthymia (76%). While this would appear to support the self medication theory, it does not rule out the possibility that an erratic pattern of benzodiazepine use results in the exacerbation of any pre-existing psychopathology.

4.8 *Implications*

With more than one in five of current benzodiazepine using heroin injectors meeting the criteria for a DSM-III-R diagnosis of benzodiazepine dependence, it is clear that heroin users need to be educated about the risks of benzodiazepine dependence and withdrawal. This could be achieved through doctors discussing these issues with their patients whenever they prescribe benzodiazepines, and through staff in methadone clinics and needle exchanges raising these problems with their clients.

Doctors should be aware that their heroin using patients, in many cases, have multiple drug dependencies and co-existing anxiety and/or depressive disorders. A lifetime diagnosis of alcohol

dependence was extremely common among the sample, particularly among those subjects with a lifetime diagnosis of benzodiazepine dependence. When prescribing benzodiazepines to patients whom doctors know to be heroin users, the dangers of polydrug use in relation to heroin overdose should be borne in mind. The high rate of current benzodiazepine dependence among the sample also highlights the need for adequate access to inpatient detoxification centres.

The pattern of benzodiazepine use among heroin users is different from that of other benzodiazepine users in the broader community. Their reasons for using benzodiazepines, and the route of administration that they use, give rise to risks associated with benzodiazepine use that are distinctly different for this population (Ross et al, 1997). While the risk of benzodiazepine dependence and withdrawal is shared by all users of benzodiazepines, the polydrug using nature of heroin users makes it probable that they could easily overlook the risk of benzodiazepine dependence.

4.9 Conclusions

Benzodiazepine use remains widespread among heroin users, the result being a high rate of benzodiazepine dependence among this population. The SDS represents a quick and efficient means by which health workers and researchers can assess heroin users for benzodiazepine dependence. It is hoped that, through education about the risk of benzodiazepine dependence and the associated withdrawal syndrome, heroin users will adopt a more cautious approach to benzodiazepine use. Doctors have a crucial role to play in the education process when issuing prescriptions for benzodiazepines. Those subjects with a history of benzodiazepine dependence were found to have a higher lifetime prevalence of other drug dependencies, anxiety and depressive disorders than the remainder of the sample, indicating that benzodiazepine users are a particularly at risk sub-set of heroin users.

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