The Use of Antidepressants Among Injecting Drug Users

Shane Darke & Joanne Ross

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EXECUTIVE SUMMARY

A sample of 201 Sydney injecting drug users (IDU) were interviewed about their use of antidepressants. The prevalence of both lifetime and recent antidepressant use was high. Forty percent of subjects had used antidepressants, 21% in the preceding 6 months.

The use of both SSRIs and tricyclic antidepressants was common. Similar proportions of subjects had ever used tricyclics (26%) and SSRIs (24%), with 8% reporting use of a MAOI. While lifetime exposure to the two major antidepressant classes were almost identical, recent use favoured the SSRIs. SSRIs were the class last used by 50% of current users, and were the antidepressants most often used by 48% of this group. Despite the predominance of SSRIs among current users, tricyclics were still widely used. Nearly a half (45%) of current antidepressant users had used tricyclics during the preceding six months.

The use of antidepressants appeared to be sporadic. The longest continuous use of antidepressants reported by subjects was one month, with females reporting longer maximum use (3 mths v 19 days). Current antidepressant users reported a median of 25 days continuous use in the preceding six months. Seventeen percent of subjects who had been prescribed antidepressants reported that they had exceeded the prescribed dosage on the last use occasion. The injection of antidepressants was rare, with only 3 subjects reporting ever having injected the drugs.

Ninety three percent of current antidepressant users had used other drugs in combination with antidepressants in the preceding six months, and a half had always combined the antidepressants with other drugs. The main drugs used in combination were heroin, methadone, benzodiazepines and alcohol, all CNS depressants.

Procurement of antidepressants was not solely through medical practitioners, with only 52% of current antidepressant users reporting having always obtained these drugs through doctors in the preceding six months. Only 46% of those who continued antidepressant use nominated depression as the main reason for doing so, with 12% reporting that they used the drugs for intoxication.

Antidepressant use was associated with higher levels of polydrug use, poorer health higher levels of psychiatric distress, and a greater risk of heroin overdose. The excess risk of overdose was specifically associated with tricyclics, rather than SSRIs.

1.0 INTRODUCTION

The oral and parenteral misuse of pharmaceutical products by Australian injecting drug users (IDU) is widespread[1-7]. The most common pharmaceutical products used by IDU in Australia are benzodiazepines and opioid preparations[1-7]. For instance, Australian studies repeatedly indicate that a third of IDU will have used benzodiazepines in any one month, two thirds within a six month period[1,2,7]. Approximately a third of IDU will have injected benzodiazepine tablets[3].

The misuse of pharmaceutical products such as benzodiazepines by IDU is of clinical importance as it is associated with a poorer clinical profile[1,2,7]. The use of benzodiazepines has been associated with factors such as higher levels of needle risk-taking, higher prevalence of heroin overdose, higher levels of psychopathology and more criminal involvement[1,2,7]. Similarly, the injection of methadone syrup has similar factors, as well as being associated with abscesses/infections in injection sites, having been diagnosed with a venous thrombosis[3].

There is recent evidence to indicate that the use of antidepressants may be common among IDU in Sydney[5,6,8]. In 1997 the Illicit Drug Reporting System (IDRS) asked IDU for the first time about the use of antidepressants[5]. Lifetime use of antidepressants was reported by 24% of subjects, with 14% reporting use in the preceding six months. The use of antidepressants was not restricted to Sydney, with widespread use among IDU also reported in South Australia[9] and Victoria[10]. The results of the 1998 IDRS confirmed the high prevalence of antidepressant use among Sydney IDU[6].

A recent study of all heroin related fatalities that occurred in south western Sydney between 1992 and 1996 reported that in 9% of cases toxicological analyses revealed the presence of antidepressants[8]. Antidepressants were detected in cases from all five years of the study period. In 13 of these 16 cases the drug detected was a

tricyclic antidepressant. The most commonly detected antidepressant was dothiepin.

The presence of antidepressants among heroin overdose fatalities is not solely a Sydney phenomenon, with a more recent study reporting that antidepressant were detected in 7% of all NSW cases between 1992 and 1996[11]. In 73% of these cases, tricyclics were the class of antidepressant detected. Again, dothiepin was the most commonly detected antidepressant.

The widespread use of antidepressants among IDU has potential clinical implications. The use of antidepressant drugs in combination with CNS depressants such as heroin, alcohol and benzodiazepines may increase the risk of an overdose[12-14]. The use of antidepressants in conjunction with opioid drugs, for example, is known to potentiate the effects of opioids[13,15]. This concern is particularly relevant to the older tricyclic antidepressants, which have been demonstrated to have a higher degree of toxicity than the newer selective serotonin reuptake inhibitors (SSRIs), with monoamine oxidase inhibitors (MAOIs) being of intermediate toxicity[16-21]. Major toxic effects of tricyclic drugs in overdose include coma, convulsions respiratory depression and cardiac arrest[20,22,23].

Given that antidepressants are being used by IDU, and in view of the potential harms associated with such use, it is important to gain a better understanding of the nature of antidepressant use among this population. To date, there has been no study examining factors such as the classes of antidepressants being used by IDU, routes of administration, dose compliance, and the patterns of use of these drugs. The current study was designed to ascertain the prevalence of the use of these drugs, the patterns of their use and any associated harm.

1.1 *Study Aims*

The major aims of the study were as follows:

1. To ascertain the prevalence and patterns of antidepressant use among IDU in Sydney;
2. To determine the types of antidepressants used and preferred by IDU in Sydney;
3. To determine any harm associated with antidepressant use.

2.0 METHOD

2.1 *Procedure*

All respondents were volunteers who were paid A$20 for their participation in the study. Recruitment took place from April to October of 1998, by means of advertisements placed in rock magazines, needle exchanges, and by word of mouth.

Respondents 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 respondents have injected a drug at least six times in the preceding six months, with at least one use occasion having occurred in the preceding two months.

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, and shopping centres, to the researchers' workplace (National Drug & Alcohol Research Centre). All respondents were guaranteed, both at the time of screening and interview, that any information they provided would be kept strictly confidential and anonymous. All interviews were conducted by one of the research team and took between 30 and 45 minutes to complete.

2.2 *Structured Interview*

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, drug treatment history and prison record.

2.2.2 Drug use history

In order to gain an indication of overall drug use, respondents were asked which drug classes they had ever used, which ones had they ever injected, and which ones had they injected in the last 6 months. An estimation of how many days they had

used each of the drug classes during the 6 months preceding interview was also sought. Further questions were asked about their main drug of choice, the first drug ever injected and how old they were when they first injected.

2.2.3 Needle risk behaviours

The needle risk component of the Opiate Treatment Index (OTI)[24] was used in assessing injecting behaviours in the month preceding interview that placed respondents at risk of either contracting or transmitting blood borne viruses.

2.2.4 Heroin overdose

Those subjects who had ever used heroin were asked how many times they had overdosed, how long since they had last overdosed, whether they had ever been administered naloxone, whether they had witnessed another person overdose and how long since they had witnessed an overdose.

2.2.5 Health

The Health Scale of the OTI was used to gain an indication of the respondent's current state of health. This scale is divided into items addressing signs and symptoms in each of the major organ systems, with one section specifically focusing on injection-related health problems. Scores range from 0-52. The higher the score obtained, the poorer the overall health of the subject.

2.2.6 Social functioning

The Social Functioning scale of the OTI was administered. The scale measures social adjustment, social support and drug culture involvement over the preceding six months. The scale ranges from 0-48. Higher scores indicate poorer social functioning.

2.2.7 Psychological functioning

Psychological adjustment was assessed using the 28 item version of the GHQ[25]. This scale gives a global measure of non-psychotic psychopathology and is made up of the following 4 sub-scales: Somatic symptoms, Anxiety, Social dysfunction and Depression. Global scores range from 0-28, with 4/5 being the most commonly used cut-off point in determining the number of 'cases' of psychopathology in a sample.

2.2.8 Antidepressant use

Subjects were asked about the use of antidepressants, including: age of onset, time since last use, number of antidepressant tablets taken, reasons for use and frequency of use. Subjects were also asked whether they had used specific brands of antidepressants, whether they had injected them, and whether they had used them in the preceding six months. For the purposes of analyses, brand names were reclassified into generic antidepressants types, based upon MIMS[26] classifications. Subjects were shown a list of the various antidepressant trade names to prevent confusion with benzodiazepines.

In order to ascertain preferences for different types of antidepressants, the methodology employed by Darke et al[2] in relation to benzodiazepines was employed. Subjects were asked to rate each antidepressant they had used on a 1-10 liking scale, higher scores indicating higher liking. For analyses, trade names were re-organised into the major antidepressant drug classes. For drug categories with more than one trade name, the highest liking score for the category was entered into the analyses. The highest liking score was employed as a measure of a generic drug's highest potential abuse liability. Group mean liking scores were calculated for those antidepressants that had been used by 10% or more of subjects.

2.3 *Statistical Analyses*

T-tests were used for continuous data. Where distributions were highly skewed, medians were reported, and were analysed using the Mann-Whitney U statistic. For

dichotomous categorical variables, Odds Ratios (OR) and 95% Confidence Intervals (95% CI) were reported. The chi-square statistic was reported for other categorical data. Wilcoxon rank sum tests were used to analyse antidepressant preference data.

All analyses were conducted using SYSTAT[27].

3.0 RESULTS

3.1 *Sample Characteristics*

The sample consisted of 201 regular IDU, recruited from all areas of Sydney. The mean age of subjects was 28.9 years (SD 7.5, range 18-52), with 73% being male (Table 1).

The mean years of formal school education was 10.0 (SD 1.9, range 0-12). Twenty eight percent of subjects had completed a trade or technical course, and 6% had completed a university course. The majority of subjects (79%) were currently unemployed, with 8% in full-time employment, and a further 11% in part-time/casual employment.

Thirty percent of subjects were currently enrolled in a drug treatment programme, having been so for a median length of 24 months (range 1-288 months). The overwhelming majority of these (55/60) were enrolled in methadone maintenance programs, with the median dose being 70 mg (range 15-300 mgs).

Forty one percent of subjects reported a history of imprisonment. Males were significantly more likely than females to report a history of imprisonment (50% v 15%, OR 5.83, 95% CI 2.57-13.20).

Table 1: Demographic characteristics of the sample

Variable	Males (N=147)	Females (N=54)	Total (N=201)
Age (mean yrs)	29.5	27.5	28.9
School education (mean yrs)	9.9	10.2	10.0
Tertiary education:			
University	4	11	6
Trade/technical	26	35	28
None	70	54	66
Employment (%):			
Unemployed	82	69	79
Full time	9	6	8
Part time	8	20	11
Student	1	4	2
Hone duties	0	2	1
In drug treatment (%)	27	37	30
Prison record (%)	50	15	41

3.2 *Drug Use History*

The mean age of first injection was 19.1 yrs (SD 4.7, range 8-41), with females first injecting at an earlier mean age (17.8 v 19.6 yrs, $t_{199}=2.5$, $p<.05$). Heroin was the drug first injected by 49% of subjects, with 39% having first injected amphetamines, 5% other opiates and 3% cocaine. Heroin was the current drug of choice of 76% of the sample, with 14% preferring amphetamines, 6% cocaine, and 4% other opioids.

The sample engaged in a wide variety of polydrug use (Table 2). The mean number of drug classes ever used was 8.8 (SD 2.0, range 3-11), with 5.9 (SD 1.9, range 2-11)

classes having been used in the last six months. A mean of 3.5 (SD 1.5, range 1-7) classes had been injected, 2.3 (SD 1.0, range 1-5) classes in the preceding six months.

The most commonly used drug classes over the preceding six months were tobacco (91%), heroin (88%), cannabis (74%), benzodiazepines (66%), cocaine (64%), alcohol (64%) and amphetamines (52%).

Table 2: Drug use history

Class	Ever used	Drug Ever Injected	Used lst 6 mths	Injected lst 6 mths	Days used lst 6 mths*
Heroin	97	96	88	87	128
Other opiates	60	44	36	20	10
Amphetamines	85	80	52	49	8
Cocaine	88	78	64	57	7
Hallucinogens	79	23	23	6	3
Benzodiazepines	86	30	66	14	10
Antidepressants	40	2	21	0	39
Alcohol	95	n/a	64	n/a	24
Cannabis	96	n/a	74	n/a	72
Inhalants	58	n/a	16	n/a	3
Tobacco	96	n/a	91	n/a	180
Mean no. drug classes	8.8	3.5	5.9	2.3	n/a

* *Median days used among those who used drug in last six months*

3.3 *Risk-Taking Behaviours*

The majority (57%) of the sample had injected on a daily basis over the preceding month, with a third (34%) reporting weekly use and 10% less frequent use (Table 3). Males were significantly more likely than females to have injected on a daily basis over the preceding month (60% v 45%, OR 1.90, 95% CI 1.01-3.56).

Nearly a quarter (22%) of subjects reported having injected with a borrowed used syringe in the preceding month, with females significantly more likely to have done so (33% v 18%, OR 4.66, 95% CI 1.06-4.32). Twenty two percent of subjects reported having passed on their used injecting equipment during the preceding month, with no difference in the proportions of males and females reporting having done so.

Over a half (54%) of subjects who had ever used heroin reported having experienced an overdose, 24% in the preceding year. Forty one percent reported having been administered the opioid antagonist naloxone, 20% in the preceding year. There were no gender differences in the prevalence of overdoses.

Table 3: Risk-taking behaviours

Variable	Males (N=147) %	Females (N=54) %	Total (N=201) %
Frequency of injection (last month):			
Once a week or less	9	11	10
More than once a week	29	44	34
Daily	60	45	57
Borrowed used needle (last month)	18	33	22
Lent used needle (last month)	20	28	22
*Heroin overdose**:			
Ever	56	51	54
Last year	25	21	24
Administered naloxone (ever)	43	34	41
Naloxone in last year	19	21	18

** % of those who had ever used heroin (n=195)*

3.4 *Antidepressant Use History*

The lifetime prevalence of antidepressant use among the sample was 40%, with no significant difference between males and females in lifetime exposure (38% v 46%) (Table 4). A fifth (21%) of subjects had used antidepressants during the preceding six months, with females being more than twice as likely to have done so (31% v 17%, OR 2.24, 95% CI 1.09-4.60). There were no significant differences between the ages of those who had ever used antidepressants and other subjects (30.0 yrs v 28.5 yrs) or between current users and other subjects (30.0 yrs v 28.7 yrs). Current antidepressant users were, however, significantly more likely to be enrolled in a drug treatment programme than other subjects (48% v 25%, OR 2.70, 95% CI 1.34-5.47).

Significantly more primary heroin users had used antidepressants compared to primary amphetamine users (43% v 21%, OR 2.71, 95% CI 1.04-7.06). While a larger proportion of primary heroin users than primary amphetamine users had used antidepressants in the preceding six months (20% v 14%), this difference was not significant.

The mean age of initial antidepressant use was 23.5 years, approximately four years after the onset of injecting drug use. Regular use of antidepressants (ie. at least monthly use) at some time was reported by 25% of subjects, with females being more likely to report such use (35% v 21%, OR 2.03, 95% CI 1.02-4.03). The mean age at which regular use commenced was 25.7 years, two years subsequent to initial use.

Subjects who had used antidepressants reported that the longest median period of continuous use of antidepressants was one month (range 1day-48mths), with females reporting a longer maximum period (3 mths v 19 days, U=887.5, p=.05). The median number of antidepressants pills taken on the last use occasion was 2 (range 0.5-19). Seventeen percent of those subjects who used antidepressants that

were prescribed for them on the last occasion reported exceeding the prescribed dose. A further 27% of antidepressant users had used tablets that were not prescribed for them on the last occasion. The maximum median number of pills taken in a day was 3 (range 1-60).

Table 4: Antidepressant use history

Variable	Males (N=146)	Females (N=55)	Total (N=201)
Prevalence of use (%):			
Ever used	38	46	40
Last 6 months	17	31	21
Past 12 months	21	37	26
Mean age first used antidepressants	23.4	23.6	23.5
Ever used antidepressants regularly	21%	35%	25%
Mean age first used antidepressants regularly (ie. at least monthly) *	24.7	27.2	25.7
Longest period continuously used antidepressants (median) #	19 days	3 mths	1 mth
Use:			
No. of pills taken on last occasion (median)#	2	2	2
Exceeded prescribed dose ⁋	17%	16%	17%
Most pills taken in a day (median)#	3	4	3

* *Total N=51, as excludes subjects who had not used antidepressants regularly*

\# *Total N=81, as excludes those subjects who had never used antidepressants*

⁋ *Total N=52, as excludes subjects for whom antidepressants had not been prescribed*

Depression was the most common reason given for commencement of antidepressant use, but was nominated by less than a half of subjects (42%) (Table

5). It should be noted that 12% reported that they first used the drugs to become intoxicated. Males were significantly less likely than females to nominate depression as their main reason for commencing antidepressant use (32% v 64%, OR 0.27, 95% CI 0.10-0.72), and were more likely to nominate other reasons. While 20% of males reported initiating use to become intoxicated, no females reported doing so. Antidepressant users also gave a wide variety of other reasons for initiating use, including curiosity, that they were withdrawing from heroin and for headaches.

Reasons for continued use reflected those given for initial use, with depression being the most common reason (46%), and 12% reporting intoxication as their main reason for continued use. Again males were significantly less likely than females to nominate depression as the main reason for having continued antidepressant use (36% v 67%, 95% CI 0.09-0.82). While 18% of males nominated intoxication as their main reason, no female did so. As with initial use, a wide variety of other reasons were given by antidepressant users, including management of heroin withdrawal, boredom and withdrawal from benzodiazepine use. Fifteen subjects had used antidepressants on only the one occasion.

Table 5: Reasons for initial and continued antidepressant use

Reason	**First use (%) (N=81)**	**Continued use (%) (N=66)**
Depression	42	46
Sleep	16	11
For anxiety	10	9
Intoxication	12	12
Other	20	23

Over a half (57%) of those subjects who had used antidepressants reported that they had experienced negative effects from their use. The negative effects nominated included drowsiness, nausea, dizziness, lethargy and vomiting. Nine percent reported that they had at some time attempted to stop using antidepressants, but could not.

3.5 *Antidepressant Familiarity and Preferences*

Lifetime use of tricyclic antidepressants was reported by 26% of subjects (range 1-4 tricyclic classes), with 24% reporting lifetime use of SSRIs (1-3 classes) (Table 6). Lifetime use of MAOIs (8%), tetracyclics (1%), and selective noradrenaline and serotonin reuptake inhibitors (SNRIs) (6%) were reported by small proportions of subjects. The injection of antidepressants was rare, with 1% of subjects having injected a tricyclic, 1% an SSRI, and 1.5% (3 subjects) having injected any antidepressant. No subject reported having injected antidepressants in the six months preceding interview.

The most common antidepressants that subjects had ever used were amitriptyline (17% of all subjects), fluoxetine (15%) and sertraline (15%). The three most common brands ever used were Tryptanol (15%), Prozac (15%) and Zoloft (15%) (Table 7).

The most widely used antidepressant drugs in the preceding six months were SSRIs (12% of all subjects) (range 1-3 SSRI classes), with 10% having used tricyclics (range 1-2 classes). Only 4% of subjects had used MAOIs, 3% SNRIs, and 1% tetracyclics.

The most common antidepressants that had been used by the sample in the preceding six months were sertraline (8%), amitriptyline (4%), fluoxetine (4%), moclobemide (4%) and paroxetine (4%). The most common brands used in the preceding six months were Zoloft (8%), Tryptanol (4%), Prozac (4%), Aropax (4%) and Aurorix (4%).

The mean liking score for SSRIs (4.8) was not significantly higher by the Wilcoxon test than that of tricyclics (4.6) for the 25 subjects who had used both types of antidepressants. No analyses were conducted on other antidepressants, as the prevalence of use did not exceed 10%.

Table 6: Antidepressant use history (Generic names)

Generic (N=201)	Ever used	Ever injected	Used lst 6 mths	Injected lst 6 mths	Liking score*
Amitriptyline	17	1	4	0	
Clomipramine	1	0	0	0	
Desipramide	1	0	0	0	
Dothiepin	9	0	3	0	
Doxepin	10	1	3	0	
Fluoxetine	15	0	4	0	
Fluvoxamine	1	0	1	0	
Imipramine	1	0	0	0	
Mianserin	1	0	1	0	
Moclobemide	7	0	4	0	
Nefazodone	4	0	2	0	
Nortriptyline	1	0	0	0	
Paroxetine	11	1	4	0	
Phenelzine	1	0	0	0	
Sertraline	15	1	8	0	
Tranylcypromine	1	0	0	0	
Trimipramine	1	0	1	0	
Venlafaxine	3	0	2	0	
Classes of antidepressants					
Any Tricyclic	26	1	10	0	4.6
Any SSRI	24	1	12	0	4.8
Any MAOI	8	0	4	0	4.4
Any SNRI	6	0	3	0	5.1
Any Tetracyclic	1	0	1	0	1.0

* *Mean liking score among those subjects who had used this class of drug*

Table 7: Antidepressant use history (Brand names)

Brand (N=201)	Ever used	Ever injected	Used lst 6 mths	Injected lst 6 mths
Allegron	1	0	0	0
Amitrol	1	0	0	0
Anafranil	1	0	0	0
Arima	0	0	0	0
Aropax	11	1	4	0
Aurorox	7	0	4	0
Deptran	5	1	0	0
Dothep	2	0	2	0
Efexor	3	0	2	0
Endep	2	0	1	0
Erocap	1	0	0	0
Lovan	1	0	1	0
Lerivon	0	0	0	0
Lumin	1	0	1	0
Luvox	1	0	1	0
Melipramine	0	0	0	0
Mutobon D	0	0	0	0
Nardil	1	0	0	0
Parnate	1	0	0	0
Pertofran	1	0	0	0
Placil	0	0	0	0
Prothiaden	9	0	2	0
Prozac	15	0	4	0
Serzone	4	0	2	0
Sinequan	7	0	3	0
Surmontil	1	0	1	0
Tofranil	1	0	0	0
Tolvon	1	0	0	0

Brand (N=201)	Ever used	Ever injected	Used lst 6 mths	Injected lst 6 mths
Tryptanol	15	1	4	0
Tryptine	1	0	0	0
Zactin	1	0	0	0
Zoloft	15	1	8	0

3.6 *Current Antidepressant Use*

The antidepressant use patterns of those subjects who had used these drugs in the preceding six months ("current use") was examined in detail (Table 8). Antidepressant use was sporadic over the preceding six months, having been used continuously on a median of 25 days (range 1-180), with only 21% of current users reporting daily use. While the median number of tablets taken on the last use occasion was 2 (range 0.5-8), 16% of those for whom antidepressants had been prescribed exceeded the prescribed dosage on that occasion. A further 24% of current antidepressant users had used antidepressants that were not prescribed for them on the last occasion.

In the six months preceding interview, SSRIs had been used by 57% of current antidedpressant users, and tricyclics by 45%. Similarly, the class of antidepressants most commonly used on the last occasion was the SSRIs (50%), with 36% of current users having last used a tricyclic. When asked to indicate which antidepressant they had used most often in the preceding six months, 48% of current users nominated an SSRI, and 36% a tricyclic. The brands of antidepressants most commonly used on the last occasion were Zoloft (31%), Tryptanol (12%) and Sinequan (12%). Similarly the brands used most often in the preceding six months were Zoloft (26%), Aropax (12%), Tryptanol (12%) and Sinequan (12%).

Antidepressants had been used in conjunction with other drugs in the preceding six months by 93% of current users, with 52% having always used antidepressants with other drugs. The most common drugs used in conjunction with antidepressants were

heroin (64%), methadone (52%) and benzodiazepines (50%). It should be noted that 88% of current antidepressant users were also current benzodiazepine users.

Table 8: Current antidepressant use

Variable	Males (N=25)	Females (N=17)	Total (N=42)
Frequency of use (%):			
<Monthly	24	18	21
Weekly or less	28	18	24
More than weekly	36	29	33
Daily	12	35	21
Length of use in preceding 6 months			
No. days used (mdn days)	21	60	39
Continuous use (mdn days)	21	60	25
Quantity of use:			
No. pills taken on last occasion (mdn)	2	2	2
Exceeded dose (%) *	18	13	16
Antidepressant last used (%):			
SSRI	44	59	50
Tricyclic	36	35	36
SNRI	12	6	10
MAOI	8	0	5
Tetracyclic	0	0	0
Antidepressants used most often in preceding 6mths (%):			
SSRIs	40	59	48
Tricyclics	40	30	36
SNRI	12	6	10
MAOIs	8	6	7
Tetracyclics	0	0	0
Antidepressant types used in preceding 6 months (%):			
SSRIs	48	71	57
Tricyclics	48	41	45
MAOIs	16	18	17
SNRIs	12	18	14
Tetracyclics	4	0	2
Antidepressants used in combination with other drugs (%):			
Always	56	47	52
Sometimes	36	47	41
Never	8	6	7
Types of drugs consumed in combination with antidepressants (%):			
Heroin	60	71	64
Methadone	44	65	52
Benzodiazepines	36	71	50
Alcohol	44	18	33
Amphetamines	16	53	31
Cocaine	28	35	31
Other opioids	20	18	19

* *Total N=32, as excludes subjects for whom antidepressants were not prescribed*

3.7 *Procurement of Antidepressants*

Current antidepressant users were questioned regarding the procurement of antidepressants during the preceding six months (Table 9). Procurement was estimated to be easy by 88% of current antidepressant users. Antidepressants were obtained through doctors by 76% of current users on the last occasion, with 16% obtaining them through friends or a partners. Nearly a third (31%) had obtained antidepressants from friends in the preceding six months. Only 62% of current users had *always* obtained their antidepressants through doctors in the preceding six months, with 19% *never* having done so. Higher proportions of females than males reported having last obtained their antidepressants through a doctor (88% v 68%), while more males reported having done so through friends (20% v 6%).

The median number of doctors seen for antidepressants in the preceding six months was 1 (range 1-5). Attendance at doctors was sporadic, with 57% reporting less than monthly attendance at doctors to obtain antidepressants, and only 2% reporting more than weekly attendance.

A third (36%) of current antidepressant users reported having gone to a doctor asking for benzodiazepines and having been prescribed antidepressants in their place. A fifth (21%) had sold or passed on their antidepressants during the preceding six months.

Table 9: Procurement of antidepressants among current antidepressant users during the preceding six months

Variable	Males (N=25)	Females (N=17)	Total (N=42)
Ease of procurement (%):			
Easy	84	94	88
Difficult	16	6	12
Where antidepressants were last procured (%):			
Doctor	68	88	76
Friend	20	6	14
Partner	0	6	2
Dealer	4	0	2
Other	8	0	5
Where antidepressants have been procured (%):			
Doctor	72	94	81
Friend	40	18	31
Partner	4	6	5
Dealer	8	0	5
Other	8	0	5
Frequency of procurement through doctors (%):			
Always	52	77	62
Sometimes	20	17	19
Never	28	6	19
Frequency of attendance at doctors for antidepressants (%):			
<Monthly	52	65	57
Weekly or less	20	24	21
More than weekly	0	6	2
Not procured through doctors	28	6	19
Number of doctors seen for antidepressants (mdn)	1	1	1
Given antidepressants instead of benzodiazepines (%)	36	35	36
Sold/given antidepressants to someone (%)	20	24	21

3.8 *Comparisons of Antidepressant Users with Other IDU*

Subjects who had ever used antidepressants had used significantly more different drug classes (excluding antidepressants) than other subjects (9.2 v 7.8, t_{199}=5.9, p<.001) (Table 10). Similarly, current antidepressant users had used significantly more different drug classes in the preceding six months than other subjects (6.4 v 5.6, t_{199}=2.8, p<.01).

Current antidepressant users were in significantly poorer health than other subjects, as measured by the OTI health scale (23.2 v 16.8, t_{199}=4.5, p<.001) and also had significantly higher GHQ scores, indicating higher levels of psychological distress (13.8 v 9.8, t_{199}=3.0, p<.01). Current antidepressant users scored significantly higher on the somatisation (3.4 v 2.2, t_{199}=3.0, p<.005), anxiety (3.8 v 2.7, t_{199}=2.7, p<.01) and depression (3.4 v 2.3, t_{199}=2.5, p<.05) sub-scales of the GHQ, but not on social functioning (3.2 v 2.5). Significantly more current antidepressant users exceeded the 4/5 cut-off for "caseness" on the GHQ (88% v 70%, OR 3.20, 95% CI 1.19-8.64).

There was no significant difference between the OTI social functioning scores of current antidepressant users and other subjects (20.3 v 20.9).

Amongst those subjects who had ever used heroin (n=195), a significantly higher proportion of those who had ever used antidepressants reported having had a heroin overdose than other subjects (65% v 47%, OR 2.1, 95% CI 1.17-3.78). A higher proportion of current antidepressant users reported having experienced a heroin overdose in the preceding six months (28% v 14%), but this narrowly failed to attain statistical significance.

There were no significant differences in the proportions of current antidepressant users and other subjects who had injected with a borrowed used syringe (26% v

21%) or had passed on their used injecting equipment (17% v 24%) in the preceding month.

Table 10: Comparisons of current antidepressant users with other IDU

Variable	**Antidepressant users (N=42)**	**Other IDU (N=159)**
Polydrug use		
Ever#	9.2	7.8*
Last 6 mths	6.4	5.6*
OTI health	23.2	16.8*
GHQ total	13.8	9.8*
% "cases"	88	70*
Sub-scales:		
Somatatisation	3.4	2.2*
Anxiety	3.8	2.7*
Depression	3.4	2.3*
Social functioning	3.2	2.5
OTI social functioning	20.3	20.9
Heroin overdose (%)⁋:		
Ever#	65	47*
6 mths	28	14
Borrowed used injecting equipment (last mth) (%)	26	21
Lent used injecting equipment (last mth) (%)	17	24

* *Statistically significant difference between groups*
\# *Lifetime use*
⁋ *Excludes those subjects who had not used heroin*

In order to examine the role of the major antidepressant classes in heroin overdose, comparisons of heroin users with no history of antidepressant use were made with those who had used tricyclics and those who had used SSRIs. A lifetime history of

tricyclic use was associated with significantly greater odds of having had a heroin overdose (68% v 47%, OR 2.39, 95% CI 1.21-4.74), with tricyclic use within the preceding six months also being associated with an overdose in that period (44% v 14%, OR 4.67, 95% CI 1.56-13.95). The use of SSRIs was not significantly associated with either a lifetime or recent history of heroin overdose. It is important to note that there were no significant differences in the ages of these groups. This is important as increasing age has been associated with the probability of overdose[28].

Table 11: History of heroin overdose by antidepressant use history

	Overdosed %	**OR**	**95% CI**
Lifetime			
No antidepressant use*	47	1.00	-
SSRI use	63	1.88	0.94-3.75
Tricyclic use	68	2.39	1.21-4.74
Six months			
No antidepressant use*	14	1.00	-
SSRI use	27	2.25	0.79-6.44
Tricyclic use	44	4.67	1.56-13.95

* *Reference group*

4.0 DISCUSSION

4.1 *Major Findings of the Study*

The major finding of the study was the high prevalence of both lifetime and recent antidepressant use among this sample of Sydney IDU. Nearly a half (40%) of subjects had used antidepressants, a quarter in the preceding year. The study confirms recent studies indicating widespread use of antidepressants among IDU.

The use of both SSRIs and tricyclic antidepressants was common. Similar proportions of subjects had ever used tricyclic (26%) and SSRIs (24%), with 8% reporting use of a MAOI. Procurement of these drugs was not solely through medical practitioners, with only 62% of current antidepressant users reporting having always obtained their antidepressants through doctors in the preceding six months.

Antidepressant use was associated with higher levels of polydrug use, poorer health, higher levels of psychiatric distress, and a greater risk of heroin overdose. Tricyclic drugs, in particular, were associated with a higher risk of overdose.

4.2 *Prevalence of Antidepressant Use*

The study confirmed that, like other pharmaceutical products, the use of antidepressants was common among IDU in Sydney. Nearly a half (40%) of the sample had used antidepressants at some stage, a fifth had used them in the preceding six months, and a quarter in the preceding year. The use of antidepressants was much more common among primary heroin users than primary amphetamines users.

While the lifetime exposure of antidepressants was equal for males and females, females were more than twice as likely to be currently using them. This stands in contrast to the use of benzodiazepines among IDU, where both lifetime and current use has repeatedly been shown to be equally common among both sexes[1,3,7]. A

lifetime history of regular antidepressant use was reported by a quarter of the sample. Females were also more likely to have reported regular use of antidepressants.

There were no differences in the ages of antidepressant users and other subjects. Antidepressant use commenced, on average, in the early twenties, approximately four years after the commencement of injecting drugs, with regular use commencing two years subsequently.

There was a strong association with current antidepressant use and enrolment in drug treatment. Most of those enrolled in treatment were enrolled in methadone maintenance. While not specifically asked about, it may be that these subjects are being prescribed antidepressants as a part of their overall treatment intervention.

4.3 *Types of Antidepressants Used*

Similar proportions of subjects had used tricyclics (26%) and SSRIs (24%). The lifetime use of other types of antidepressants was less common.

While lifetime exposure to the two major antidepressant classes were almost identical, recent use favoured the SSRIs. SSRIs were the drug last used by 50% of current users, and were the antidepressants most often used by 48% of this group. Despite the predominance of SSRIs among current users, tricyclics were still widely used. Nearly a half (45%) of current antidepressant users had used tricyclics during the preceding six months. Estimates of the aggregate community use of prescriptions for antidepressants during 1997 suggest that tricyclics (48%) and SSRIs (37%) are also the most commonly prescribed antidepressants in Australia[29].

There was no significant difference between the liking ratings given by subjects for SSRIs and tricyclics. This stands in contrast to preferences for benzodiazepines among IDU, where there is a marked preference for quick onset drugs such as

flunitrazepam and diazepam[2]. The preference for particular types of benzodiazepines makes it difficult to prescribe benzodiazepines that may be less popular, and have a lower abuse potential. This would not appear to be a problem with antidepressants, where no clear preference seems to exist among this population.

4.4 *Patterns of Antidepressant Use*

The use of antidepressants appeared sporadic. The longest period of continuous use of antidepressants reported by subjects was one month, with females reporting longer maximum use (3 mths v 19 days). Current antidepressant users reported a median of 25 days continuous use in the preceding six months, although again females reported a longer period of continuous use (60 v 21 days). Given that antidepressants require a period of 2-4 weeks daily use for their maximum effectiveness to be realised[26], it would appear that users of these drugs, and particularly males, may not be achieving the maximum therapeutic effects. Non-compliance with antidepressant therapy is not a problem unique to the injecting drug using population. In a study conducted in the United States[30], 28% of patients prescribed antidepressants in a primary care setting ceased using their antidepressant within the first month of therapy, and 44% had stopped taking them by the third month of therapy. Patients were more likely to have complied during the first month of therapy if they had been informed of the following by their physician: that it is important to take the medication daily, that they will need to take the medication for two to four weeks before an effect will be noticed, that the medication should be continued even if they are feeling better, that they should not cease the medication without consulting their doctor, and what to do if they have any questions regarding their antidepressant therapy.

It is important to note that nearly a fifth of subjects who had been prescribed antidepressants reported that they had exceeded the prescribed dosage on the last use occasion. It is common for IDU to exceed the prescribed dosage of drugs such as

benzodiazepines[7]. The same pattern appears to exist in relation to antidepressants. Excessive dosages may well increase the chances of antidepressant overdose, or an overdose in combination with other drugs.

While depression was the main reason given for using antidepressants, this reason was given by less than a half of subjects who had used antidepressants. Only 46% nominated depression as the main reason for continued use of antidepressants. While not common, 12% of antidepressant users reported that they used these drugs for intoxication. Other subjects reported using the drugs for reasons as diverse as sleep, anxiety, management of heroin withdrawal and to reduce benzodiazepine use. Like benzodiazepines, it is clear that antidepressants are used by IDU for a variety of reasons not associated with depression *per se*.

The injection of antidepressants was extremely rare, with only three subjects reporting ever having injected the drugs. These figures stand in stark contrast to those reported from studies examining injection of oral benzodiazepines and methadone syrup among Australian IDU[2,3]. These have reported a lifetime injecting prevalence of approximately a third of IDU for benzodiazepines and a half of heroin users for methadone syrup[2,3].

The regular combination of antidepressants with other drugs is cause for concern. Ninety three percent of current antidepressant users had used other drugs in combination with antidepressants in the preceding six months, and a half had always combined the antidepressants with other drugs. The main drugs used in combination with antidepressants were heroin, methadone, benzodiazepines and alcohol, all CNS depressants. There are clear risks of overdose in such combinations, particularly in conjunction with tricyclic antidepressant use[13,15].

4.5 *Procurement of Antidepressants*

Obtaining antidepressants was considered easy by the overwhelming majority of current antidepressant users. As has been demonstrated with benzodiazepines[7], IDU reported that the procurement of antidepressants was not restricted to doctors. Amongst current users of antidepressants, only 62% had always obtained antidepressants through doctors in the preceding six months. The second major source of antidepressants was through friends. In fact, a fifth of current antidepressant users had not obtained antidepressants through doctors at all in the preceding six months. It is clear, as with benzodiazepines, that when prescribing to IDU, doctors are medicating more people than the person to who they have prescribed the drug. This is emphasised by the fact that a fifth of current users had sold or passed on antidepressants in the preceding six months.

A third of current antidepressant users reported that they had asked a doctor to prescribe benzodiazepines, and had been prescribed antidepressants instead. As has been noted previously, benzodiazepine use is particularly widespread among IDU. In recent years there has been a great deal of research and clinical focus on the harms associated with such use. It is possible that due to the publicity surrounding benzodiazepines, that doctors are prescribing antidepressants in their place to some IDU.

4.6 *Harms Associated with Antidepressant Use*

Antidepressant users reported higher levels of overall psychological distress, reflected in higher GHQ scores. It is important to note that whilst current antidepressant users had higher depression scores than other subjects, they also had higher anxiety and somatatisation sub-scale scores. The distress these subjects were reporting was thus not specifically related to depression.

The higher depression sub-scale scores of current antidepressant users raises several possible interpretations. Firstly, it could be argued that the data indicate

that current users of antidepressants are indeed more depressed, and require medication. However, it also could be argued that the higher depression scores reflect poor treatment compliance by IDU. As noted previously, use of antidepressants was sporadic. Current antidepressant users had used antidepressants continuously for a median of 25 days. This would be insufficient in many cases to achieve optimal effects of antidepressants. Whilst it may be appropriate to provide antidepressant mediation to some IDU, close case management to maximise compliance would appear necessary.

Antidepressant users had not engaged in more recent needle risk-taking behaviours than other IDU. This is in contrast to the repeated findings of excess risk-taking among benzodiazepines users[1,2,7]. Higher rates of needle sharing related to benzodiazepine use has been suggested to be due to factors such as short-term memory impairment whilst intoxicated with benzodiazepines, or the disinhibitory effects of these drugs[1]. These would not appear to be factors related to the use of antidepressants. It would appear that it is not the risky use of pharmaceuticals per se by IDU that is related to needle sharing, but the type of pharmaceutical being used.

Antidepressant users had a higher level of polydrug use than other IDU (excluding antidepressants). As noted above, there was a high degree of concomitant use of antidepressants and other drugs, particularly CNS depressants. Clinicians need to be aware that antidepressant users are likely to be even more entrenched in polydrug use than other IDU.

The most important finding of antidepressant-related harms from this study was the association between the use of antidepressants and the prevalence of heroin overdose. This association appears to be attributable to the use of tricyclics, rather than SSRIs. Heroin users who had used tricyclics had a greater risk of having experienced a heroin overdose than those who had not used them, and current users

were more likely to have overdosed in the preceding six months. Conversely, there was no significant effect on the prevalence of overdose from the use of SSRIs. These data are consistent with the profile of tricyclics as being of greater toxicity than SSRIs, and with the data from fatal heroin overdose cases[11]. The association was not attributable to age, as there were no significant differences in the ages of tricyclic users and other subjects. It would appear that the combination of heroin and tricyclics is particularly risky.

4.7 *Conclusions and Implications*

The study confirmed the widespread use of antidepressants among IDU, and heroin users in particular. Doctors need to be aware of the high prevalence of use, and the poor treatment compliance of subjects. Whilst antidepressants do not appear to be associated with the general chaotic picture associated with the use of benzodiazepines, there are reasons for concern about such common use. It should be borne in mind that only a minority of the antidepressant users in this study took them for depression.

The prescription of tricyclics to heroin users would appear to increase their risk of overdose. If it is considered appropriate to prescribe antidepressants to heroin users, it would appear safer to prescribe SSRIs. The fact that such high proportions of IDU combined their use of antidepressants with drugs such as alcohol, benzodiazepines and heroin reinforces this point. As with all pharmaceuticals, caution should be exercised when prescribing to IDU.

The treatment compliance of IDU appeared poor. While use of the drugs was sporadic, many users exceeded their prescribed dose on the days they did use antidepressants. If antidepressants are prescribed to IDU, close case management to ensure compliance is necessary. This would be most feasible for those subjects who were enrolled in a regular drug treatment programme.

Finally, doctors need to be aware that there is substantial leakage of prescribed antidepressants to IDU other than the patients prescribed for. As with all pharmaceuticals prescribed to IDU, doctors are medicating a wider range of people than their patient.

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Brand name	Generic	Type
Sinequan	Doxepin	Tricyclic
Surmontil	Trimipramine	Tricyclic
Tofranil	Imipramine	Tricyclic
Tolvon	Mianserin	Tetracyclic
Tryptanol	Amitriptyline	Tricyclic
Tryptine	Amitriptyline	Tricyclic
Zactin	Fluoxetine	SSRI
Zoloft	Sertraline	SSRI

Abbreviations

MAOI Monoamine oxidase inhibitor

SNRI Selective noradrenaline and serotonin re-uptake inhibitor

SSRI Selective serotonin re-uptake inhibitor

ANTIDEPRESSANT GENERIC AND BRAND NAMES

Generic	Brand	Type
Amitriptyline	Amitrol, Mutabon-D, Endep, Tryptanol, Tryptine	Tricyclic
Clomipramine	Anafranil, Placil	Tricyclic
Desipramine	Pertofran	Tricyclic
Dothiepin	Dothep, Prothiaden	Tricyclic
Doxepin	Deptran, Sinequan	Tricyclic
Fluoxetine	Erocap, Lovan, Prozac, Zactin	SSRI
Imipramine	Melipramine, Tofranil	Tricyclic
Mianserin	Lerivon, Lumin, Tolvon	Tetracyclic
Moclobemide	Arima, Aurorix	MAOI
Nefazodone	Serzone	SNRI
Nortriptyline	Allegron	Tricyclic
Paroxetine	Aropax	SSRI
Phenelzine	Nardil	MAOI
Sertraline	Zoloft	SSRI
Tranylcypromine	Parnate	MAOI
Trimipramine	Surmontil	Tricyclic
Venlafaxine	Efexor	SNRI