The sources of pharmaceuticals for problematic users of benzodiazepines and prescription opioids

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There are growing concerns in Australia and overseas about the increasing misuse of a range of pharmaceuticals, and associated harms.[1-4] This includes the problematic use of benzodiazepines and prescription opioids in Australia.

Clients of drug treatment services are commonly reported to use a range of pharmaceuticals.[5-7] For example, self-reported prevalence of benzodiazepine use among clients undergoing treatment for opioid use ranges from 66% to 100%,[5,7,8] and use confirmed by urine drug testing ranges from 51% to 70%.[8] Moreover, benzodiazepine use is associated with poorer treatment and health outcomes among opioid users.[9,10] In North America, prescription opioid-dependent clients outnumber heroin-dependent clients among those presenting for methadone maintenance treatment.[6,11] Given the considerable harms that have been linked to these pharmaceuticals, including overdose[12] and mortality,[13,14] understanding their use and sources is important for informing effective harm-reduction interventions.

To our knowledge, no studies examining the sources of pharmaceuticals used by problematic users in Australia have been published, but sources of prescription opioids have been described in the United States. Among recent methadone treatment entrants who reported prescription opioids as the primary problem drug, the most common sources were dealers (86%), friends and relatives (54%) and medical prescriptions (28%).[6] In contrast, the US National Survey on Drug Use and Health found most non-medical users sourced analgesics from a friend or relative for free (55%) or for payment (11%).[15] In both studies, the internet was rarely a cited source.[6,15]

The Australian Government recently announced the introduction of a real-time reporting system for prescription opioids that doctors can use to obtain an up-to-date prescrip-

tion history before prescribing drugs of addiction to any patient.[16] It is planned that the reporting system will monitor Schedule 8 (S8) medications, therefore it will only include benzodiazepines that are S8. One benzodiazepine, flunitrazepam, is currently S8. Alprazolam will be rescheduled to S8 in 2014. To gauge the potential usefulness of such a system, it is important to understand how often these medications are being sourced through medical practitioners.

We describe (i) the characteristics of pharmaceutical use by Australian clients of drug treatment services who reported regular and unsanctioned use of benzodiazepines and/or prescription opioids and (ii) the common sources of benzodiazepines and prescription opioids used by these clients.

Methods

Detailed methods are available elsewhere.[17] In brief, we recruited a con-

venience sample of 305 people entering treatment at private and public withdrawal (detoxification), residential rehabilitation and opioid substitution treatment services in Victoria, Western Australia, Queensland and Tasmania. They were recruited between January and July 2008 by referral from treatment service staff and using study flyers that were distributed from drug treatment services by the staff.

Treatment entrants were eligible to participate in the study if they: reported regular (an average of $\geqslant 4$ days per week) and unsanctioned use of benzodiazepines and/or prescription opioids over the 4 weeks before treatment entry; were 16 years or older; had entered treatment for drug or alcohol use in the previous 6 months; and had sufficient English language skills to provide informed consent and comprehend the study questions. Unsanctioned use was defined as using medication that was

Abstract

Objectives: To describe benzodiazepine and prescription opioid use by clients of drug treatment services and the sources of pharmaceuticals they use.

Design: Structured face-to-face interviews on unsanctioned use of benzodiazepines and prescription opioids were conducted between January and July 2008.

Participants: Convenience sample of treatment entrants who reported regular (an average of $\geqslant 4$ days per week) and unsanctioned use of benzodiazepines and/or prescription opioids over the 4 weeks before treatment entry.

Setting: Drug treatment services in Victoria, Queensland, Western Australia and Tasmania.

Main outcome measures: Participant demographics, characteristics of recent substance use, substance use trajectories, and sources of pharmaceuticals.

Results: Two hundred and four treatment entrants were interviewed. Prescription opioids were predominantly obtained from non-prescribed sources (78%, 84/108). In contrast, medical practitioners were the main source for benzodiazepines (78%, 113/144). Forging of prescriptions was extremely uncommon. A mean duration of 6.3 years (SD, 6.6 years) for benzodiazepines and 4.4 years (SD, 5.7 years) for prescription opioids was reported between first use and problematic use — a substantial window for intervention.

Conclusions: Medical practitioners are an important source of misused pharmaceuticals, but they are not the main source of prescription opioids. This has implications for prescription drug monitoring in Australia: current plans (to monitor only Schedule 8 benzodiazepines and prescription opioids) may have limited effects on prescription opioid users who use non-prescribed sources, and the omission of most benzodiazepines from monitoring programs may represent a lost opportunity for reducing unsanctioned use of benzodiazepines and associated harm.

not prescribed to the participant or using medication that was prescribed to the participant but in a way not intended by the prescriber (eg, taking a higher dose than prescribed, or injecting a drug that was intended as oral medication).

Structured face-to-face interviews of participants were conducted. They included questions on demographics (sex, age, ethnicity, employment, education level attained, current living arrangements), substance use (primary drug of concern at treatment entry, use in the 4 weeks before treatment entry, routes of administration), trajectories of substance use, and benzodiazepine and prescription opioid sources).

We used χ^2 and t tests to establish whether there were differences between participants who used benzodiazepines and those who used prescription opioids. Descriptive analyses were used to characterise benzodiazepine and prescription opioid initiation, use and sources.

The study was approved by institutional ethics committees in each jurisdiction — the Victorian Department of Human Services Human Research Ethics Committee, University of Tasmania Social Sciences Human Research Ethics Committee, Curtin University Human Research Ethics Committee and Prince Charles Hospital Human Research Ethics Committee.

Results

Characteristics of participants

A total of 204 people participated in the study; 107 had entered methadone and buprenorphine treatment programs, and the remainder had entered inpatient detoxification and residential rehabilitation programs (Box 1). One hundred and forty-two participants (70%) were seeking treatment for opioid dependence (heroin or pharmaceutical opioids), 19 (9%) were seeking treatment for benzodiazepine dependence, and 43 (21%) were seeking treatment for dependence on other substances (eg, alcohol, stimulants and cannabis). When asked about substance use in the 4 weeks before treatment entry, 144 participants reported regular and unsanctioned benzodiazepine use and 108 reported regular and unsanc-

tioned prescription opioid use; 48 reported regular and unsanctioned use of both drug classes.

The demographic characteristics of participants who used benzodiazepines only, prescription opioids only and both benzodiazepines and prescription opioids were similar — about 60% men, mean age about 33 years, and low levels of employment and education.

Of the 144 participants who met the criteria for regular unsanctioned benzodiazepine use (with or without prescription opioids), 18 (13%) reported benzodiazepines as their primary drug of concern, and 108 (75%) reported that their benzodiazepine use had become problematic. In contrast, more than half (56%, 60) of the 108 participants who met the criteria for regular unsanctioned prescription opioid use (with or without benzodiazepines) reported prescription opioids as their primary drug of concern, and 93 (86%) reported that their prescription opioid use had become problematic.

Pharmaceutical use in the 28 days before treatment entry

On average, benzodiazepines and prescription opioids were used almost daily (27 out of 28 days for both) (Box 2). The benzodiazepines most fre-

quently used as prescribed were diazepam (36%, 52/144), alprazolam (13%, 19/144) and oxazepam (13%, 18/144). For unsanctioned use, the benzodiazepines used most frequently were diazepam (80%, 115/144), alprazolam (58%, 84/144) and oxazepam (44%, 63/144). The prescription opioids most frequently used as prescribed were morphine preparations (10%, 11/108) and buprenorphine–naloxone tablets (8%, 9/108). For unsanctioned use, the prescrip-

1 Characteristics of the study participants ($n = 204$)

	Number (%)*
Men	126 (62%)
Mean (SD) age, years	32.6 (8.7)
Aboriginal or Torres Strait Islander	14 (7%)
Employed full time or part time	40 (20%)
Completed up to year 11 equivalent or less	126 (62%)
Living in unstable housing	59 (29%)
Current treatment	
Methadone	64 (31%)
Buprenorphine (with or without naloxone)	43 (21%)
Inpatient detoxification	49 (24%)
Residential rehabilitation	48 (24%)
Regular and unsanctioned substance use	
Benzodiazepines only	96 (47%)
Pharmaceutical opioids only	60 (29%)
Benzodiazepines and prescription opioids	48 (24%)

* Data are number (%) unless otherwise specified. ◆

2 Characteristics of benzodiazepine and prescription opioid use by study participants

	Benzodiazepine users ($n = 144$)	Prescription opioid users ($n = 108$)
Use in 28 days before treatment entry		
Mean (SD) period of prescribed use, days	12.5 (13.0)	7.5 (11.4)
Mean (SD) period of non-prescribed* oral use, days	20.9 (9.6)	16.3 (12.2)
Mean (SD) period of injected use, days	0.9 (4.2)	16.5 (12.0)
Mean (SD) period of use in any form, days	27.3 (2.3)	26.9 (2.8)
First-use occasion		
Medication prescribed on first-use occasion, number (%)	41 (28%)	27 (25%)
Trajectory of use[†]		
Mean (SD) age at first use, years	18.9 (6.9)	21.2 (8.1)
Mean (SD) age when first injected, years	22.7 (7.6)	22.7 (7.8)
Mean (SD) time from first use to monthly use, years	4.1 (5.9)	3.0 (5.1)
Mean (SD) time from first use to problematic use, years	6.3 (6.6)	4.4 (5.7)
Last use		
Medication used was drug of choice, number (%)	50 (35%)	71 (66%)
Medication used was not drug of choice, number (%)		
Seeking intoxication	29 (20%)	10 (9%)
Used to avoid or treat withdrawal symptoms	19 (13%)	1 (1%)
Used as substitute for heroin or other opioids	na	14 (13%)
Used for pain relief	na	4 (4%)

na = not applicable. * Refers to use where medication was not prescribed to the individual or where medications were used in a way other than prescribed. † Responses for questions on trajectory of use were incomplete; data presented here are based on the following numbers of responses for benzodiazepine use and prescription opioid use, respectively: 144 and 106 for age at first use, 70 and 91 for age when first injected, 134 and 105 for time from first use to monthly use, and 108 and 93 for time from first use to problematic use. ◆

3 Self-reported sources of pharmaceuticals used by study participants in the 28 days before treatment entry*

	A source	Usual source	Source for most recent unsanctioned use
Benzodiazepines			
n	144	123	139
Doctor — real symptom	104 (72%)	79 (64%)	—
Doctor — fake symptom	32 (22%)	9 (7%)	—
Any prescribed source	113 (78%)	88 (72%)	62 (45%)
Gift	63 (44%)	10 (8%)	50 (36%)
Swap	22 (15%)	1 (1%)	2 (1%)
Stolen	9 (6%)	3 (2%)	5 (4%)
Forged prescription	5 (3%)	0	2 (1%)
Bought from friend	28 (19%)	12 (10%)	11 (8%)
Buy from dealer	25 (17%)	9 (7%)	7 (5%)
Any non-prescribed source	80 (56%)	35 (28%)	77 (55%)
Both prescribed and non-prescribed	80 (56%)	—	—
Prescription opioids			
n	108	86	108
Doctor — real symptom	33 (31%)	20 (23%)	—
Doctor — fake symptom	13 (12%)	5 (6%)	—
Any prescribed source	36 (33%)	25 (29%)	33 (31%)
Gift	32 (30%)	10 (12%)	22 (20%)
Swap	16 (15%)	1 (1%)	1 (1%)
Stolen	4 (4%)	0	0
Forged prescription	1 (1%)	0	0
Bought from friend	42 (39%)	19 (22%)	21 (19%)
Buy from dealer	50 (46%)	30 (35%)	29 (27%)
Any non-prescribed source	84 (78%)	61 (71%)	75 (69%)
Both prescribed and non-prescribed	20 (19%)	—	—

* Data are number (%) unless otherwise specified. ◆

tion opioids used most frequently were morphine (65%, 70/108), oxycodone (50%, 54/108) and methadone liquid (29%, 31/108).

Injection of prescription opioids in the 28 days before treatment entry was reported by 81 participants (75%) in the prescription opioid group; on average, they reported injecting prescription opioids on 22 of the 28 days. In contrast, injection of benzodiazepines in the 28 days before treatment entry was reported by 12 of the participants (8%) in the benzodiazepine group; on average, they reported injecting benzodiazepines on 11 of the 28 days.

Initiation and trajectories of pharmaceutical use

On first-use occasions, both benzodiazepines and prescription opioids were most often not prescribed; 72% of participants in the benzodiazepine group and 75% of participants in the prescription opioid group reported using non-prescribed medication on the first-use occasion (Box 2). Benzodiazepine prescriptions for first-use occasions were most commonly reported to have been for anxiety (37%, 15/41) and sleep (22%, 9/41), and opioid prescriptions for first-use occasions were most commonly reported to have been for pain relief (81%, 22/27).

Mean age at initiation of pharmaceutical use was 19.1 years for benzodiazepines and 21.2 years for prescription opioids (Box 2). The mean length of time from benzodiazepine first use to monthly use was 4.1 years and to problematic use was 6.3 years. The mean length of time from prescription opioid first use to monthly use was 3.0 years, and to problematic use was 4.4 years.

Sources of pharmaceuticals

Most benzodiazepine users (78%, 113) reported a medical practitioner as a source of benzodiazepines in the 28 days before treatment entry (Box 3). Most also reported a medical practitioner as their usual benzodiazepine source (72%, 88), and most reported acquiring benzodiazepines for real symptoms. Of those reporting non-medical sources as their usual supply, access through friends or acquaintances (buying, swapping or gifts) were most common; only 7% reported buying from a dealer as their usual source.

In contrast, about half of prescription opioid users (46%, 50) reported buying from a dealer (Box 3). Most reported using non-prescribed sources (78%, 84), and most reported non-prescribed sources as their usual source (71%, 61).

Few participants reported stealing or using forged prescriptions to obtain benzodiazepines and prescription opioids (Box 3), and none reported using the internet as a source.

Discussion

Our results provide information on how benzodiazepines and prescription opioids are accessed and used by people who represent the more "severe" end of the spectrum of problematic pharmaceutical drug users — drug and alcohol treatment entrants reporting almost daily use of benzodiazepines or prescription opioids.

We found that pharmaceutical use was initiated early (at an average of about 20 years of age), and about three-quarters of participants reported that their initial use was via a non-medical source. On average, it took 3–6 years for participants to progress from first use to regular or problematic use, suggesting that there is a window of opportunity for providing interventions that could avert this progression.

There were clear differences between how the two drug classes were sourced. Prescription opioids were less commonly acquired from a doctor than benzodiazepines, and most prescription opioids were acquired from non-medical sources. This is consistent with previously reported source patterns for prescription opioids.[6,15] This common finding of sharing and onselling of prescription opioids has important implications for the medical profession. It highlights that while some individuals use opioids that were prescribed for other people, there may also be patients who do not use the opioids that are prescribed for them by their doctors. Most regular prescription

opioid users reported buying their opioids from others, highlighting that this prescription drug black market is an important area to better understand. Also, prescription opioids were more likely to be injected than benzodiazepines.

In contrast to prescription opioids, a medical practitioner was the main source of benzodiazepines. As such, there may be considerable opportunities for prescriber intervention to address benzodiazepine use. This finding, coupled with the serious harms associated with benzodiazepines (in terms of acute overdose, poorer health and poorer treatment outcomes[9,10,12,13]), is interesting in light of current plans to only monitor the prescribing of S8 benzodiazepines as part of the monitoring of all S8 class drugs in Australia — flunitrazepam and, from 2014, alprazolam.[16] This means that, despite the greater opportunity for prescribers to intervene in benzodiazepine supply, most benzodiazepines will not fall under the current plans for prescription drug monitoring. This also represents a missed opportunity for monitoring the impact of the planned rescheduling of alprazolam on the extent of use of other, unmonitored, benzodiazepines.

In contrast, monitoring opioid prescribing is unlikely to have a substantial impact on the behaviour of prescription opioid users, as they mostly acquire prescription opioids from non-medical sources. Also, it might give prescribers false confidence if they relied on the information from monitoring systems for the clinical assessment of drug-seeking behaviour alone, as opioids acquired from non-medical sources would not appear in such systems.

Other strategies — such as education of consumers and health professionals, and expansion of non-pharmaceutical evidence-based treatments for chronic pain and mental health disorders — are crucial. Approaches such as "universal precautions" with opioid prescribing have been recommended internationally[18] and in Australian policy,[19] but are yet to be established in practice.

Education for consumers on the harms associated with sharing medications is vital. Benzodiazepines are commonly implicated in non-fatal[12] and fatal[13,20] opioid overdose. We found that one-third of participants were given benzodiazepines as a gift for their most recent unsanctioned use. On first-use occasions, only one-quarter of benzodiazepines and prescription opioids were from a prescriber. Education about risks associated with self-diagnosis, peer diagnosis and self-medicating may help reduce medication sharing. Also, education initiatives for consumers could be used to challenge the perception that benzodiazepines are "less risky"[21] than illicit drugs.

Our study has strengths and weaknesses. Convenience sampling and collection of self-reported data are well recognised and valid methods for studying individuals who engage in unsanctioned substance use[22,23] and provide reliable answers in this context.[23] However, it is well recognised that these methods affect the accuracy and representativeness of the data collected, compared with prospectively collected and objectively validated data from random or more generalisable samples.

The participants of our study had similar demographic characteristics to participants in other studies of drug treatment clients in Australia conducted in Australia.[7,24] Although they may not represent most long-term problematic users of pharmaceuticals in the broader community, they represent a group who are more likely to experience acute harms from their pharmaceutical use and who use larger amounts of pharmaceuticals. As such, they are a priority when targeting strategies aimed at minimising pharmaceutical misuse.

These findings show that different approaches may be required to reduce unsanctioned use of different pharmaceuticals. Prescription drug monitoring programs need to ensure that the right substances are monitored. Current proposals may represent a significant lost opportunity with regard to the most benzodiazepines. Finally, developing guidelines and resources that help health professionals respond to pharmaceutical misuse identified through monitoring systems will maximise opportunities to reduce harm.

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