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BRIEF REPORT

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Real or fake? Sourcing and marketing of non-prescribed benzodiazepines amongst two samples of people who regularly use illicit drugs in Australia

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Abstract

Introduction: There is concern around non-prescribed benzodiazepine use, particularly with increasing detections of counterfeit products containing high-risk novel compounds. The aims of this study were to investigate how and which non-prescribed benzodiazepines are being sourced; forms, appearance and packaging; and awareness of risks associated with non-prescribed benzodiazepines.

Methods: Data were collected from a sample of Australians who inject drugs or use ecstasy and/or other illicit stimulants on a monthly or more frequent basis, and who reported past 6-month use of non-prescribed benzodiazepines ($n = 235$ and $n = 250$, respectively). Data were collected on source, diversion from a known/trusted prescription, product name and aesthetic characteristics for the last non-prescribed benzodiazepine obtained.

Results: Amongst participants who injected drugs, 71% reported that their last non-prescribed benzodiazepines were diverted from a known/trusted prescription, compared to 59% of participants who used ecstasy/other stimulants. Sourcing via cryptomarkets was rare. Across both samples, the majority reported last obtaining substances sold/marketed as diazepam or alprazolam. Participants sourcing via non-diverted means were twice as likely to obtain alprazolam. Known sourcing of novel compounds was rare. Amongst participants who used ecstasy/other stimulants, 36% reported confidence in the content/dose of non-prescribed benzodiazepines even when the source is unknown.

Discussion and Conclusions: Most participants obtained substances sold as classic/registered benzodiazepines, mostly via diverted prescriptions, with a substantial minority potentially unaware of counterfeits circulating. While diverted use undeniably presents risks, tightening of prescriptions in Australia could inadvertently lead to greater supply of novel benzodiazepines as seen internationally, reinforcing prioritisation of demand and harm reduction strategies.

KEYWORDS
benzodiazepine, counterfeit medicines, cryptomarkets, diversion, new psychoactive substances

Key Points

- Most participants last obtained non-prescribed benzodiazepines sold as diazepam and alprazolam, mostly via diverted prescriptions.
- Those obtaining via non-diverted means were twice as likely to obtain alprazolam, which is unsurprising given its reclassification by the Therapeutic Goods Administration as a Schedule 8 poison.
- A substantial minority (36%) of those who had used ecstasy/other stimulants reported confidence in the content and dose of non-prescribed benzodiazepines even when the source is unknown, which is concerning given increasing detection of high-risk counterfeit products in Australia.
- Overall, these findings reinforce the need for ongoing monitoring and increased awareness of the risk environment for non-prescribed benzodiazepines.

1 | INTRODUCTION

Benzodiazepines are a group of central nervous system (CNS) depressants which induce sedation (anxiolysis) and sleep, and can therefore serve numerous therapeutic functions [1]. However, there are a variety of well-established health risks, including dependence, withdrawal [2] and overdose [3], particularly when used with other depressants like opioids and alcohol [1]. There is also some evidence linking long-term use with cognitive decline [4].

With increasing recognition of these risks, there have been shifts in prescribing in multiple countries (e.g., [5–8]). In Australia, alprazolam was up-scheduled by the Therapeutic Goods Administration in 2014 and restricted through the Pharmaceutical Benefits Scheme in 2017 [8]. More recently, safer prescribing guidelines and real-time prescription monitoring systems have been introduced targeting higher-risk psychoactive medicines, including all benzodiazepines [9]. Consequently, the Pharmaceutical Benefits Scheme data suggest that between 2012 and 2020 the rate of benzodiazepines dispensed steadily declined [10]. Despite these shifts, benzodiazepine-related harms have increased in Australia [3] and elsewhere (e.g., [11]). While sole benzodiazepine exposure is seldom the cause of death, drug-induced deaths involving benzodiazepines increased four-fold between 2004 and 2018 in Australia, making them the second most common drug type implicated in drug-induced deaths [3].

While it is unclear to what extent non-prescribed use is contributing to benzodiazepine-related harms, non-prescribed use is a growing concern. Self-reported use of non-medical/non-prescribed benzodiazepines has increased in Australian household surveys [12] and sentinel samples of people who use illicit drugs [13]. Risk of harm is exacerbated by increasing detection of counterfeits (fake or imitation products which may contain unexpected compounds and/or dose of compounds) in Australia, with multiple alerts issued for products containing multiple high-risk novel benzodiazepines [14, 15] and some with entirely different classes of drugs [16, 17]. Indeed, novel benzodiazepines (and opioids) are increasingly detected globally [18] and are driving overdose deaths in some countries (e.g., [5, 19]). While this does not appear to be the situation currently in Australia, there is evidence of novel benzodiazepines contributing to at least 40 fatal drug poisonings since 2015; whether consumption was unwitting is unknown [20]. Thus, there is a need to closely monitor the situation to inform policy and harm reduction strategies.

Currently, little is known about the non-prescribed benzodiazepine market in Australia, including how and which benzodiazepines are being sourced (e.g., classic/registered or novel/unregistered benzodiazepines). While some people seek out these more potent novel compounds—made increasingly available with the emergence of cryptomarkets [21]—those seeking non-prescribed classic/registered pharmaceutical benzodiazepines are at risk of being sold more dangerous counterfeits. Further, while public health warnings are emerging [14], it remains unclear to what extent people are aware of the complex risk environment associated with the non-prescribed benzodiazepine market. Thus, amongst two sentinel samples of people who regularly use illicit drugs in Australia, this paper aims to investigate: (i) how and which non-prescribed benzodiazepines are being sourced, and whether the type of benzodiazepine differs according to the source; (ii) aesthetic characteristics of non-prescribed benzodiazepines being sourced; and (iii) awareness of risks associated with non-prescribed benzodiazepine use (e.g., unknown content and/or dose).

2 | METHODS

2.1 | Study design and participants

The Ecstasy and Related Drugs Reporting System (EDRS) and Illicit Drug Reporting System (IDRS) are Australian illicit drug monitoring systems that include annual interviews with non-representative sentinel samples of people who regularly use illicit drugs recruited from all Australian capital cities. In 2021, eligibility criteria comprised: aged ≥18 years; used ecstasy and/or other illicit stimulants ≥6 times (EDRS) or injected illicit drugs ≥6 times (IDRS) in the preceding 6 months; and residence in the capital city of recruitment for 10 of the preceding 12 months. In 2021, interviews took approximately 45–60 min and were conducted face-to-face or via telephone (EDRS $N = 774$; IDRS $N = 888$). All information disclosed was anonymous, with participants reimbursed AU$40 for their time. Ethical approval for the EDRS was granted by the UNSW Human Research Ethics Committee (HREC; HC12086) and jurisdictional HRECs; IDRS approval was granted by the South Eastern Sydney Local Health District HREC (2020/ETHO2734) and jurisdictional HRECs.

2.2 | Measures

Participants were asked questions on non-prescribed benzodiazepines, including pharmaceutically manufactured products not directly prescribed to the person and/or illicitly manufactured products which may contain classic/registered and/or novel/unregistered benzodiazepines. For research aim 1, participants who had used any non-prescribed benzodiazepines in the past 6 months were asked questions relating to the last benzodiazepine they obtained, including: the source (e.g., friend, dealer), whether they were diverted from a known or trusted prescription and the product name (i.e., what they were sold/marketed as). For aim 2, those who did not source via a known/trusted prescription were asked questions about aesthetic characteristics (e.g., form, imprints and packaging). For aim 3, participants were asked their level of agreement (5-point Likert scale) with the statement 'I can be confident in the content and dose of drugs sold as benzodiazepines, because they are pharmaceuticals, even if I don't know the source' (EDRS only). See Figures S1 and S2, Supporting Information, for the full modules.

2.3 | Data analyses

Analyses were conducted using SPSS version 26. Of the 774 (EDRS) and 888 (IDRS) participants in 2021, 272 (35%) and 253 (29%) respectively reported recent non-prescribed benzodiazepine use, of which 250 (missing = 13; skipped/refused = 9) and 235 (missing = 2; skipped/refused = 16) completed the subsequent benzodiazepine questions. This subset comprises the focus of the current paper. We calculated valid percentages for categorical data, means for normally distributed continuous variables and medians for continuous data with significant positive skew and/or kurtosis. Binary logistic regression was performed (odds ratio and 95% confidence interval reported) to investigate the association between source (diverted or not) and last obtaining alprazolam or diazepam. Results were considered significant if $p < 0.05$.

3 | RESULTS

3.1 | Sample characteristics of those who reported non-prescribed benzodiazepine use

The median age of EDRS respondents ($n = 250$) was 25 years (interquartile range 21–29) and 63% were male. IDRS respondents ($n = 235$) were older with a mean age of 42 years (SD = 10) and 66% were male. See Table S1, Supporting Information, for full demographic statistics.

3.2 | Source of non-prescribed benzodiazepines last obtained

In both samples, almost three-quarters last obtained non-prescribed benzodiazepines through a friend, relative or partner (Table 1). A nominal per cent reported sourcing through cryptomarkets or surface websites. Almost three-fifths (59%) of EDRS respondents reported last obtaining via a diverted prescription, compared to 71% of IDRS respondents.

3.3 | Type of non-prescribed benzodiazepines last obtained and aesthetic characteristics

Amongst both samples, branded diazepam was the most commonly reported benzodiazepine last obtained, followed by branded alprazolam and then generic and street versions of these compounds (Table 2). Few participants ($n \leq 5$) reported last sourcing novel benzodiazepines. When aggregating responses into three categories (alprazolam; diazepam; other), respondents who did not source via a diverted prescription were at double the odds of buying alprazolam relative to diazepam (odds ratio 2.22;

TABLE 1 Source of non-prescribed benzodiazepines last obtained, EDRS/IDRS 2021.

	EDRS		IDRS	
Variable	***N* = 250**	**%**	***N* = 235**	**%**
Source[a]	$n = 247$		$n = 232$	
Friend/relative/partner	184	74.5	165	71.1
Known dealer	34	13.8	25	10.8
Unknown dealer/street dealer/mobile dealer/social media dealer	12	4.9	25	10.8
Acquaintance/workmate	9	3.6	12	5.2
Online cryptomarkets/surface websites	–	–	–	–
Other	–	–	–	–
Do not know	–	–	–	–
Known or trusted prescription (i.e., diverted prescription)[b]	$n = 246$		$n = 232$	
Yes	144	58.5	164	70.7
No	79	32.1	40	17.2
Do not know	23	9.3	28	12.1

Note: Skip responses have been excluded.

Abbreviations: EDRS, Ecstasy and Related Drugs Reporting System; IDRS, Illicit Drug Reporting System.

[a]Responses have been aggregated into a smaller number of more meaningful categories.

[b]There were instances where a reportedly diverted product was not available for prescription in Australia ever (clonazolam; diclazepam; 'street Xanax'; 'street valium'; each $n \leq 5$) or at the time of data collection (Xanax, $n = 46$; Ducene, $n \leq 5$). It is unclear whether these were prescribed in another country, at an earlier time, and/or were inaccurately marketed or understood as being diverted from a prescription source. Values suppressed due to small cell size ($n \leq 5$ but not 0). See Figures S1 and S2 for the original item response lists.

confidence interval 1.36–3.62; $p = 0.001$). Amongst respondents not sourcing via a diverted prescription, the vast majority reported receiving tablets featuring imprint codes/markings, mostly without original packaging/labelling (Table 2).

3.4 | Level of confidence in content and dose of non-prescribed benzodiazepines with unknown source

Amongst EDRS participants who responded ($n = 240$), approximately half 'disagreed' or 'strongly disagreed' (20% and 33%, respectively) with the statement 'I can be confident in the content and dose ... even if I don't know the source', 11% were neutral, and 36% 'agreed' or 'strongly agreed' (29% and 8%, respectively).

4 | DISCUSSION

Despite a decline in dispensing rates in Australia [10], most respondents in these samples (about two-in-three) self-reported last obtaining non-prescribed benzodiazepines through diverted prescriptions from people close to them (friends/relatives/partners). While use without clinical oversight undeniably presents health risks, it nevertheless avoids risks associated with the unregulated market, such as counterfeit products containing higher potency novel compounds [14]. In Scotland and the US, greater restrictions on benzodiazepine prescribing in the absence of increased demand reduction efforts has resulted in markets being dominated by higher toxicity novel benzodiazepines and increased rates of overdose, with health experts now advocating for safer supply/prescribing [5]. Findings of the current study and experiences internationally suggest responses in Australia should focus on expanding harm and demand reduction strategies, such as education (e.g., on risks and non-pharmacotherapy alternatives), enhanced rapid and precise surveillance/alert systems, drug checking featuring brief interventions and safe consumption rooms.

Despite the emergence of newer, more potent benzodiazepines, products marketed as classic pharmaceutical benzodiazepines were almost exclusively sought/sourced in this study. The vast majority of participants reported being sold branded forms of diazepam and alprazolam, followed by generic versions. These findings are consistent with cryptomarket studies which suggest benzodiazepines marketed/sold as classic diazepam and alprazolam

TABLE 2 Type of non-prescribed benzodiazepines last obtained and aesthetic characteristics, EDRS/IDRS 2021.

	EDRS		IDRS	
Variable	***N* = 250**	**%**	***N* = 235**	**%**
Sold/marketed as (name)[a]	*n* = 248		*n* = 232	
Diazepam (branded)[b]	92	37.1	93	37.1
Alprazolam (branded)[c]	56	22.6	51	20.3
Diazepam (generic)	27	10.9	21	8.4
Alprazolam (generic)	14	5.6	9	3.6
Oxazepam (branded)[d]	–	–	17	6.8
Alprazolam (street/pressed)	12	4.8	–	–
Diazepam (street/pressed)	6	2.4	6	2.4
Clonazepam (generic)	6	2.4	–	–
Clonazepam (branded)[e]	–	–	6	2.4
Any novel benzodiazepine[f]	–	–	–	–
Other	6	2.4	–	–
Do not know[g]	23	8.9	14	5.6
Among those who did not obtain through a diverted prescription and responded[h]				
Form product sold as	*n* = 79		*n* = 38	
Tablet/s	49	62.0	31	81.6
Pressed tablet/s[i]	28	35.4	7	18.4
Other	–	–	0	0.0
Imprint code or marking	*n* = 59		*n* = 34	
Yes	52	88.1	27	79.4
No	7	11.9	7	20.6
Packaging product sold in	*n* = 76		*n* = 36	
No packaging/baggie/unlabelled bottle	49	64.5	18	50.0
Labelled bottle	14	18.4	8	22.2
Blister pack with imprinted brand/drug	12	15.8	9	25.0
Other	–	–	–	–

Note: Benzodiazepine name response options with 0% have been excluded from this table and individual names have been aggregated into branded, generic or street versions of the compound. Skip responses have been excluded. Values suppressed due to small cell size ($n \leq 5$ but not 0).

Abbreviations: EDRS, Ecstasy and Related Drugs Reporting System; IDRS, Illicit Drug Reporting System.

[a]There were instances where a reportedly diverted product was not available for prescription in Australia ever (clonazolam; diclazepam; 'street Xanax'; 'street valium'; each $n \leq 5$) or at the time of data collection (Xanax, $n = 46$; Ducene, $n \leq 5$). It is unclear whether these were prescribed in another country, at an earlier time, and/or were inaccurately marketed or understood as being diverted from a prescription source.

[b]Combined EDRS/IDRS brands = Valium (96%); Antenex (3%); Ducene (1%).

[c]Combined EDRS/IDRS brands = Xanax (84%), Kalma (15%); Mylan (<1%).

[d]Combined EDRS/IDRS brands = Serapax (94%); Alepam (6%).

[e]Combined EDRS/IDRS brands = Rivotrol (75%), Paxam (25%).

[f]Combined EDRS/IDRS brands = Clonazolam (50%); Diclazepam (33%); Etizolam (17%).

[g]'Do not know' responses were aggregated with responses for unknown brand.

[h]'Do not know' responses were excluded.

[i]Limitation is that participants may not have understood that 'pressed tablet/s' refer to illicit presses.

remain the most commonly procured [21]. We also found those who did not report sourcing through a diverted prescription were twice as likely to obtain alprazolam relative to diazepam. This is unsurprising given alprazolam was reclassified as a Schedule 8 poison ('controlled drug') in Australia in 2014 [8], while most other benzodiazepines (including diazepam) remain Schedule 4 ('prescription only medicine'); however, it is concerning given alprazolam's high risk profile [8] and tendency to be counterfeited [14]. Indeed, most counterfeit benzodiazepine

products in Australia appear to be being sold/marketed as alprazolam (e.g., [17]), placing people who use non-prescribed alprazolam at particular risk of consuming something unexpected. Most respondents who did not source via a diverted prescription reported observing features resembling pharmaceuticals (e.g., imprint codes), however it is unknown whether these products were real or counterfeit since most were received without original packaging/labelling and analyses of counterfeit products have found that they typically feature brand markings [17]. While it is reassuring that many EDRS respondents (53%) indicated a lack of trust/confidence in the content/dose of benzodiazepines when the source is unknown, the results suggest warnings are not reaching all consumers and that further efforts are needed to raise awareness of risks.

4.1 | Limitations

Some key limitations should be noted. First, given the sampling methods, the findings cannot be generalised to the wider population of people who use benzodiazepines. Second, while self-report methods amongst people who use drugs have been shown to be sufficiently reliable and valid [22], we cannot verify responses (e.g., whether products were genuine diverted prescriptions or pharmaceutically manufactured products) and the data are subject to recall bias. Finally, it was beyond the scope of this brief report to examine differences in sourcing and awareness of risks between people who inject drugs and people who use ecstasy/other stimulants, but this remains a potentially important topic of investigation for future research.

5 | CONCLUSIONS

The most commonly reported source for non-prescribed benzodiazepines in these samples was diverted prescriptions, and most products were marketed/sold as diazepam and alprazolam. While one policy reaction might be to tighten prescription regulations, this could inadvertently increase risk by shifting the market towards more potent novel compounds. Rather, any potential responses should be multifaceted, focusing on expanding demand and harm reduction strategies (e.g., education, drug checking, safe consumption rooms), as well as enhancing surveillance.

DECLARATION OF COMPETING INTERESTS

Rachel Sutherland has received untied educational funds from Seqirus. Amy Peacock has received untied educational grants from Seqirus and Mundipharma for study of opioid medications. Simon Lenton has served as an unpaid member of an Advisory Board for Mundipharma. Funding from this organisation has now ceased, funding was for work unrelated to this project, and the funding bodies had no role in study design, analysis and reporting.

AUTHOR CONTRIBUTIONS

Jodie Grigg led manuscript conception, design, data analysis, writing and revising, and contributed to data collection. Amy Peacock, Simon Lenton, Caroline Salom, Natalie Thomas and Rachel Sutherland contributed to conception, design, data collection, data analysis, and writing and revising the manuscript. Seraina Agramunt and Tom Lyons contributed to conception, design, writing and revising the manuscript. Each author certifies that their contribution to this work meets the standards of the International Committee of Medical Journal Editors.

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CONFLICT OF INTEREST STATEMENT

All other authors have no conflicts of interest to declare.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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