ACSA
AGED & COMMUNITY SERVICES AUSTRALIA
ABN 65 070 261 871

23 January, 2013

The Secretary
Scheduling Secretariat
GPO Box 9848
Canberra ACT 2601

SMP@health.gov.au

Dear Sirs,

Notice inviting public submissions under Regulation 42ZCZK of the Therapeutic goods Regulations 1990

Please find attached our submission regarding the above and we thank you for the opportunity to provide our comments.

We look forward to hearing from you in due course.

Yours sincerely,
Aged & Community Services Australia

[redacted]

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TGA Proposal Feedback

About Aged and Community Services Australia (ACSA)

Aged and Community Services Australia (ACSA) is the national peak body for aged and community care providers; representing faith based, charitable and community-based organisations that provide residential and community care services, housing and accommodation to almost 1 million older persons, younger people with a disability, and their carers.

Introductory Comments

The Pharmacy Guild of Australia is currently preparing a submission to the Therapeutic Goods Administration (TGA) about a proposal to reschedule benzodiazepines from Schedule 4 (Prescription Only Medicines) to Schedule 8 (Controlled Drugs). ACSA has been given the opportunity to provide feedback on this proposal which is outlined in this submission.

ACSA Comments

Along with opioids, benzodiazepines are the prescription drugs most commonly associated with illicit drug use. Despite this, they are prescribed to treat a variety of conditions including insomnia, anxiety and panic disorders but also have other uses including, but not limited to, sedation for procedures and in intensive care units. ACSA has received an unusually high response from its membership to this proposal illustrating the sector's concern with the proposed changes.

Benzodiazepine's use is wide and varied and given the relevant size of the family of medicines, ACSA does not support the proposed re-scheduling from Schedule 4 to Schedule 8.

The areas of concern that have been raised by our members include:

1. Workload for staff
    a. Currently, this class of medication is able to be packed with other medications in such resources as Webster Packs.
    b. If however, the suggested re-scheduling were to come into effect, it would result in tighter regulatory requirements meaning that benzodiazepines would not be able to be packed in the current manner. As such, increases in the administrative process would result, placing an extra but unnecessary burden upon staff.
    c. Given the large size of this family of drugs, this resultant increase in administrative work would be very costly.
    d. Several examples of increased burden on staff have been highlighted by our members:
        i. Legislation states that Schedule 8 medications must be administered by two **qualified** staff members which would require extra staff to check every episode of administration.
        ii. Extra time would be needed to count and "check in" the delivered medications into the site's medication safe.

iii. Extra time would be needed to conduct the medication count of Schedule 8 medicines; a practice that is required at every shift change.
iv. There are some residents who are self-administering – if re-scheduling was to occur, not only residents who were not normally self-administering would require nurses to administer these medications but also those previously self-administering residents.

2. Staffing Requirements
    a. Given the extra workload and time commitments required if re-scheduling were to occur, many Aged Care facilities would need to employ extra qualified nursing staff.
    b. Not only would extra staff be required but given that these medications are mostly administered at night, it would require extra staff to be dedicated to the task at a peak work time of the day.
    c. Many facilities are already experiencing difficulties in attracting new staff members at the present time, let alone needing more staff in the future.
    d. If no extra staffing is obtained, it may have a negative impact on the quality of care given to other residents.
3. Storage Issues
    a. If re-scheduling were to occur, in order to comply with regulations regarding storage of Schedule 8 medications, many facilities would need to purchase additional cabinets or safes to ensure all medications can be stored according to legislated requirements.
    b. Staff would need to ensure that all medication from self-administering residents was collected and stored in appropriate safes. This would also add an extra burden on staff members and may cause confusion for the residents.
4. Increased Costs
    a. Obviously, given the possible changes required as a result of the proposal, costs for facilities to implement these changes would increase significantly. The two areas, staffing and storage as outlined previously, would be most affected.
    b. Staffing
        i. Wages
        ii. Additional staff
        iii. Skills development
    c. Storage
        i. Design
        ii. Installation
        iii. Maintenance

New South Wales Therapeutic Advisory Group Inc.

The Secretary
Scheduling Secretariat
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CANBERRA ACT 2601

Email:

Re: Invitation for public comment — ACMS and ACCS meeting, March 2013: Notice inviting public submission under regulation 42ZCZK of the Therapeutic Goods Regulation 1990.

The NSW Therapeutic Advisory Group is an independent not for profit association that promotes the Quality Use of Medicines (QUM) within and across the continuum of acute care. Our members are clinical pharmacologists, pharmacists, and other clinicians from each of the Drug and Therapeutics Committees in NSW public hospitals and Local Health Districts. Our goal is to promote QUM by sharing unbiased, evidence based information about drug therapy. Our objectives are to investigate and evaluate new initiatives in therapeutics, to support Drug and Therapeutics Committees and to promote rational, high quality, safe prescription, dispensing and administration of medicines in public hospitals and the wider community and hence the relevance of our position in putting forward this submission.

NSW TAG welcomes a review of benzodiazepine scheduling as a possible strategy to improve the health outcomes of consumers, who are taking or may take benzodiazepines and related substances in the future. The harms of benzodiazepines (BDZs), whilst reduced compared to the harms of previous therapies, are well known and pose significant morbidity and mortality risks, particularly in the older population (1). The challenge with BDZs is maintaining the right balance between the potential public health and social harm and the availability of effective medications for those who might benefit from them.

NSW TAG does not have the supporting documentation and evidence-base on which the rescheduling proposal has been based nor the criteria on which such a change would be based. The comments made in this submission are based on general QUM principles, feedback from our members and a literature search.

Overall, NSW TAG members' opinions differ on whether BDZ rescheduling to S8 would have the desired outcome, whether the potential benefits outweigh the burden associated with such a strategy, how the impact of such a strategy would best be measured and what outcome measure(s) should be used.

This submission is set out in 7 sections: the epidemiology of benzodiazepine use in Australia; the evidence for the impact of restricting the medication use by S8 rescheduling; evidence for the impact of rescheduling other addictive drugs; Australian guidelines and recommendations regarding the use of benzodiazepines; current BDZ monitoring and handling in NSW; the practical challenges posed by S8 rescheduling; and, the way forward.

Epidemiology of benzodiazepine use in Australia

Analysis of anxiolytic, hypnotic and sedative medication use (mainly BDZs) in Australia identified a slight increase in usage between 2002 and 2007 with 2.4% of the Australian population using a defined daily dose of these medications each day (2). Of particular concern

Promoting the quality use of medicines

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was the finding that the highest utilisation was in those aged 65 years and over, with peak use in the 85-89 years. There was also a trend for increasing use of alprazolam and zolpidem.

Other pertinent epidemiologic data include the significant use (3.2%) of tranquillisers or hypnotics for non-medical purposes by the Australians at some stage during their lifetime (3); the high use of BDZs (65%) in the polysubstance abuse community (4); and, the significant levels (20%) of positive urine testing for BDZs (along with other drug use) in detainees in police stations and watch houses (5).

Each year over 5 million Pharmaceutical Benefit Scheme (PBS) prescriptions for benzodiazepines are written accounting for up to 5% of general practice prescriptions (6). In 2012 diazepam was the 33rd most frequently prescribed medication on the PBS. General practitioners have been identified as the main source of supply (7). It is clear that there is significant nonmedical use, abuse and other harms from benzodiazepines in Australia, particularly in certain sub-populations.

Evidence for the impact of restricting BDZ medication use by S8 rescheduling

A 1991 paper by Shader and colleagues discusses the effects of the Triplicate Prescription Program (TPP) that was introduced into New York State in January 1989 (9). The TPP placed the same regulatory conditions on benzodiazepines as were on opiates, barbiturates and amphetamines. Copies of prescriptions were forwarded to the New York State Department of Health as well as copies being kept by the prescriber and dispensing pharmacist. In general, no repeats and no more than a 30-day supply could be prescribed. The medical and scientific community questioned the rationale of the TPP with concerns raised regarding the evidence for diversion, the unjustified restriction on supply in the majority of patients who were benefiting from their use and not displaying drug aberrant behaviours, and the lack of evidence that such a strategy would be beneficial without interrupting legitimate use. A reduction in BDZ prescribing was achieved with the TPP, (approximately one-half), and the New York State Department of Health believed this was due to a reduction in diversion and inappropriate prescribing. The deterrent effects of the procedure for prescribers, the potential stigma and professional harm associated with prescribing these agents, the patient's perception of stigma as 'a user of a regulated substance' and the effect of big brother involvement in the physician-patient relationship were postulated as reasons for the reduction.

Harms with the TPP were identified. These included the under-prescribing of a specific BDZ for certain epileptic conditions, the increased prescribing of alternative anxiolytics and hypnotics, some of which were likely to be more harmful, increased emergency room presentations for withdrawal syndromes or previously treated anxiety, and the under-treatment of anxiety and insomnia (9-11). Although BDZ overdoses declined, overdoses from other sedatives/hypnotics increased leading to no nett change (12). Furthermore certain patients groups such as those with mental health disorders felt victimised by the strategy. Shader et al. believed that the loss of appropriate access to the BDZs resulted in more harm than benefit and called for a consensus assessment of the scientific data and further study.

Simoni-Wastila et al compared the effect of the TPP in the New York Medicaid population suffering chronic mental health disorders with a control New Jersey Medicaid population suffering the same conditions (13). A reduction of BDZ use of approximately 50% was seen within 6 months in the New York population with no change in the New Jersey population. This change was sustained for the 7 years of follow-up. The greatest change was seen in those who had non-problematic BDZ use (those that did not exhibit high dose or pharmacy hopping).

Fisher and colleagues conducted a literature search of BDZ monitoring programs in 2010 (11). Despite a broad search strategy, all relevant articles (n=32) were based on the effects of the New York State TPP program and none had investigated the impact of the TPP since the mid

1990s. Fisher at al reported that the TPP did result in reduction in the use of BDZs but that there may have been unintended consequences and that these may have disproportionately affected a number of vulnerable populations. These populations included those with chronic psychiatric conditions (as above), those with chronic neurological conditions, and patients following cardiac hospitalisation and cancer patients as well as those at socioeconomic disadvantage. It is unclear whether the unintended consequences were maintained in these groups. These authors concluded that while BDZ use was reduced there was insufficient evidence to tell whether the TPP had promoted appropriate use of BDZs and called for further research to better understand the effect of such a program and their ability to achieve their goals of quality use of BDZs, reduced costs and reduced diversion, particularly in the long term. The article also provided information about existing prescription monitoring programs: as of July 2010, 27 US states and Saskatchewan in Canada were using PMPs for BDZs with an additional 7 US states and 5 Canadian states also monitoring opiates and stimulants.

A number of authors argue that the potential for BDZ abuse in the general population is low and that it is in the population of polysubstance abusers where BDZ use or abuse most frequently occurs (9,10). Reasons for this are unclear but may include induction or enhancement of the effects of other psychoactive drugs or the presence of other psychiatric co-morbidity. Although it is anecdotally suggested that abusers or misusers have 'favourite' BDZs, such as alprazolam or previously flunitrazepam, both potent BDZs, the statistics also suggest that other BDZs may be misused and it is unclear whether preference is due to differing pharmacologic effects or for other reasons. "Cherry-picking" with a regulatory strategy for some BDZs and not others is unlikely to be effective.

Evidence for the impact of rescheduling other addictive drugs

In New South Wales, ketamine was rescheduled from Schedule 4 to Schedule 8 in May 2005 when it became increasingly apparent that legitimate sources of ketamine were being diverted for recreational use leading to physical and psychological symptoms of ketamine dependence among users. Although a reduction in use was seen following this, it is unclear whether this was as a result of this action or due to other reasons such as an increased availability of ecstasy and whether this reduction has been sustained (4). Furthermore ketamine prescribing is tiny compared to that of the BDZs and thus the logistics of the rescheduling change was far less burdensome than that envisaged with and future S8 rescheduling of BDZs.

Australian guidelines and recommendations regarding the use of benzodiazepines

Despite the' proven efficacy of benzodiazepines as anxiolytics, sedatives and hypnotics as well as their antiepileptic, muscle relaxant and amnesic properties, their capacity for creating dependence means that they are not recommended therapy for the treatment of many of the disorders that may exhibit these symptoms. They are not recommended in the management of panic attack (14) and are only recommended in particular circumstances in post-traumatic stress disorder (15). Other authoritative texts advise their short term use as second line agents for insomnia (1, 16). This can be challenging for health care professionals given that the symptoms of anxiety and insomnia are often caused by disorders that are of longer duration. In the last 4 years, the Royal Australian College of General Practice (RACGP) have provided advice on the management of prescription drug abuse, substance abuse and post-traumatic stress disorder in their journal, Australian Family Physician (15,17,18).

In contrast to the opiates and other similar drugs such as cocaine and stimulants, the potential for harm from BDZs (adverse effects, misuse and abuse) is chiefly due to diversion, presumably through the lack of application of QUM principles (judicious selection of therapy and safe and effective use, including the monitoring of ongoing therapy) rather than the illicit production of these agents. Thus a case could be made that these are the areas that should be targeted in attempting to improve BDZ use in the Australian community and that implementation of clinical guidelines is a mandatory step in ensuring quality use of BDZs in the Australian community.

Although a number of guidelines and prescribing advice documents have been produced in Australia in the past, many are 5-10 years old and may not sufficiently reflect current evidence (1,16,19,20). The RACGP have acknowledged this and in response to a Coroners Court of Victoria recommendation (23) have undertaken to develop new guidelines and removed the 2000 guidelines from their website.

NSW TAG acknowledges the huge effort required in the development of guidelines and would advocate that appropriate support and resources be provided to RACGP guideline developers. However we wish to also highlight that the value of guidelines will not be realised without accompanying implementation programs that acknowledge the barriers and facilitators in local, state and national contexts. Numerous authors have identified barriers and facilitators to guidelines uptake (24-27). There is evidence that some in the medical community may not agree with guideline recommendations regarding BDZ use (28), that the guidelines or the potential harms of BDZ use do not apply to the person they are treating and that the alternative treatments are not easily available to them. These would include simple, affordable and readily available non-pharmacological therapies, and access to the necessary support and guidance for patients undergoing withdrawal syndromes.

Identification of facilitators for quality use of BDZs is also important. These may include assisted identification of those who may be misusing, abusing or at risk of harm from BDZs via real time prescription monitoring programs and other doctor shopping surveillance activities (29); greater roll-out of psychological services in areas of need; and, Home Medication Reviews in those identified as high or long term users.

NSW TAG notes the Parliament of Victoria Drugs and Crime Prevention Committee's (DCPC) Inquiry into the misuse and abuse of benzodiazepines and other pharmaceuticals drugs in December 2007 and the Victorian Government Response in May 2008 (30-31). The majority of recommendations covering the areas of education, research, prescription recording service, prescribing and packaging practices, treatment and management approaches, while supported, were supported *in principle* meaning that action to comply with the recommendation was contingent upon the the availability of resources, consideration of competing priorities or that an alternative action to achieve the recommended outcome was considered more appropriate. The status quo of fully supported recommendations or those that were supported *in principle* are unclear to NSW TAG and, if they have been implemented, whether or not the impact has been measured and shown to be successful. Nevertheless we recommend consideration of this Report and Response to the current TGA consultation. Of note, rescheduling of benzodiazepines to Schedule 8 in Recommendation 20 of the Report was not supported, acknowledging the practical difficulties, the risk of further harm and the lack of a rationale or evidence for such a step.

Current BDZ monitoring and handling in NSW

As indicated by the development of the QUM indicator 5.7 *Percentage of patients receiving sedatives at discharge that were not taking them at admission* (32), NSW TAG members and others have recognised the hospital's role in ensuring appropriate prescribing and safe and effective use of sedatives such as BDZs. However currently this indicator is under-utilised, probably for a variety of reasons and is not part of any mandated national or state indicator sets targeted at quality use of medicines (33). NSW TAG has a long association with strategies and projects to ensure the judicious, appropriate, safe and effective use of anxiolytics and sedatives in the hospital setting and across the continuum of care. These strategies and projects include:

- Development and publication of QUM indicators in Australian Hospitals that include the aforementioned Indicator 5.7 but also include other QUM indicators that may be applied to patients taking benzodiazepines;

- A current project developing QUM indicators for mental health funded by the Australian Commission on Safety and Quality in Health Care;
- The management of a repository for protocols and other resources regarding high risk medicines such as benzodiazepines that can be shared amongst members in order that individual members may be supported in the development and implementation of their organisation's policies and interventions. (members access only); and
- Input into safe prescribing of 'prn' medications in the design of the National Inpatient Medication Chart.

Benzodiazepines as a part of the sedative group of high risk medications are subject to the High Risk Medicines Management Policy PD 2012-003 in NSW public hospitals (34). This policy requires the mandatory development of a high risk medicines program which includes local protocols for their use within a public facility and patient monitoring (including adverse effects), and recommends strategies that mitigate risk and reporting of adverse incidents to the state-based Incident Information Management System.

In NSW, benzodiazepines are classified as Schedule 4 Appendix D medications (with the exception of flunitrazepam which is in Schedule 8) requiring special requirements for the supply, storage and administration of BDZs *in patient care areas* (but not pharmacies) in a manner similar to that of Schedule 8 medications and in recognition of their capacity to be misused or abused.. As well as the previously mentioned indications, benzodiazepines are also used as pre-medications prior to procedures and administration of cytotoxics in hospitals and outpatient clinics. Very small quantities of benzodiazepine may be also kept in emergency trolleys.

The practical challenges posed by S8 rescheduling of benzodiazepines

The rescheduling of BDZs to Schedule 8 would represent a significant challenge to hospital pharmacies and prescribers from compliance, storage, space, staffing and cost perspectives. S8 rescheduling would also place a significant burden on storage and dispensing requirements in community pharmacies with the likely need for the purchase of new safes. There is a possibility that the potential for overstocking of medications in safes, where space is already at a premium in both hospital and community pharmacy drug safes, could also lead to medication selection errors. The rescheduling to S8 classification would require a widespread and intensive education program throughout each hospital with consequent demands on time and staffing, as well as to the wider community of prescribers, pharmacists, nurses and consumers. The full costs of S8 rescheduling will require estimation and monetary subsidisation for small business owners should be considered by the Australian Government. Special dispensation for the storing of emergency supplies of BDZs on emergency trolleys would be required.

As outlined in the Victorian Government's Response to the Victorian DCPC *Inquiry into misuse and abuse of benzodiazepines and other pharmaceutical drugs*, S8 rescheduling would impose a significant burden on medical practitioners and may lead to increased use of less effective or more dangerous medicines in order to avoid this burden as well as underuse of BDZs where clinically indicated (31).

The way forward

Although NSW TAG members are strong advocates for consumers to have access to treatments, they have expressed concerns regarding the safe and appropriate use of BDZs and the need to have a clear plan for monitoring the quality use of these drugs.

Acknowledging that harm from BDZs will continue and that improvement in the quality use of BDZs should occur even if S8 rescheduling does or does not transpire, NSW TAG recommends consideration of the following:

- Greater research regarding BDZ use in Australian hospitals and the wider community including:
    - identifying the factors associated with and the patterns of BDZ misuse and abuse in Australia;
    - the incidence and prevalence of harms associated with BDZ use in Australia
    - identifying the facilitators and barriers to quality use of BDZs
    - identifying the impact of various strategies to improve quality use of BDZs prior to implementation of the strategy including any that involves increased regulatory surveillance of prescribing and supply
- Implementation of evidence-based strategies/programs and support for programs that neutralise the barriers to and facilitate the uptake of up-to-date evidence-based Australian guidelines regarding quality use of BDZs particularly judicious selection and monitoring for harm and efficacy. Such programs should be incorporated into the wider management of the conditions for which benzodiazepines are currently prescribed thereby optimising the overall care of sufferers of these conditions. Potential strategies include easier access to non-pharmacological therapies for anxiety and insomnia with Medicare reimbursement including cognitive behavioural therapy and relaxation therapies; feedback incorporating real time electronic prescription monitoring programs(PMPs) to identify doctor shopping and help health care professionals (HCPs) identify abuse and misuse; facilitated access to drug and alcohol clinics and sleep disorder units, which may require increased training of HCPs and increased numbers of clinics in areas of need; and, increased support for consumers withdrawing from BDZs. Community pharmacists may be useful in identifying those requiring sleep hygiene advice, delivering that advice and referral when required (35) as well as accredited pharmacists conducting Home Medicines Reviews. Consideration of all the recommendations of the Victorian DCPC Inquiry and their potential roll-out across Australia are recommended.
- Expansion of proven, feasible and cost-effective interventions given the limited resources to support patients and clinicians managing ever-increasing complex medication regimens. A multidisciplinary collaborative approach to the interventions is recommended. Interventions targeted at BDZ use involving clinical pharmacists have shown improved patients outcomes in acute and community health care sectors. For example, Westbury et al showed sustainable reduction in use and doses of BDZs taken by nursing home residents with pharmacist-led interventions (36-37). The implementation of such interventions, including building workforce capacity, can assist in improved patient outcomes but requires support from government, administrators and policymakers.
- Increased monitoring of quality use of BDZs and similar agents in all health care sectors.
- Measurement of the effect and outcomes of any implemented strategies/programs with the appropriate parameters identified prior to implementation of any strategy;
- Development and implementation of education programs for consumers of all ages (from adolescents to the older population)
- Increase the role of the media in conveying balanced information in an easily understood format that is readily available for patients, their carers and their HCP
- Acknowledging that the following strategies may need supporting evidence, consideration of whether strategies involving
    - a reduction in the pack sizes of BDZs may be one component of a successful intervention to improve quality use of BDZs. For example diazepam from 50 to 15-20 tablets with an authority required for increased quantities should be considered; and/or

- making all BDZ prescriptions authority only; and/or
- real time feedback to prescribers about their prescribing levels of BDZs as compared to their peers, particularly to the, say, top 20% of prescribers; and/or
- restricting initial prescriptions of certain benzodiazepines to specific specialists- with GPs able to write follow up prescriptions only for a limited time prior to follow-up review of the specific specialist; and/or
- removal of some less used BDZs from the PBS given that many have overlapping properties.

may reduce harm,misuse and abuse from BDZs..

Additionally if S8 rescheduling of BDZs does occur, NSW TAG recommends:

- Pilot testing this intervention prior to Australia-wide implementation to measure the impact and ensure the necessary measurements of positive and negative outcomes are undertaken (including morbidity and mortality due to withdrawal and use of substitutes as well as potentially vulnerable populations) and the additional components that will need to accompany the rescheduling strategy are identified and developed.
- Consideration regarding the substitutes that may be prescribed must be undertaken and targeted interventions to particular populations are also recommended. If it is correct that misuse and abuse is largely concentrated in the polysubstance abuse population, then is rescheduling of BDZs likely to reduce misuse in this population and could it lead to more harm in this population with the substitution of more harmful drugs? What are the proven interventions in this population?
- Education regarding the role of other drugs that might be regarded as substitutes will be necessary should BDZs be rescheduled to the S8 category. In this case, it would seem appropriate that the Z-drugs including zolpidem and zopiclone should also be rescheduled to S8. Increased utilisation of other substitutes, both prescription and over-the-counter, such as antipsychotics, tricyclic antidepressants, sedating antihistamines, chloral hydrate and melatonin could be expected given the New York State TPP experience and may not be as appropriate or as safe as the BDZs, particularly in older people. Complementary medications such as valerian and combination products must also be included as well as alcohol substitution in such a case. Monitoring of the use of these substitutes and associated adverse effects is recommended.
- Education to HCPs and consumers about what S8 rescheduling of BDZs will require of them.
- Ensuring that sudden withdrawal does not occur in dependent patients and that the appropriate supporting resources and personnel and accessible and available.

In summary, NSW TAG believes that arrange of strategies should be considered to improve the quality use of BDZs and that any strategies should be evidence-based. Consideration must be given to not only increasing the appropriate and safe use of these drugs but also to ensuring their continued availability to those who have a legitimate clinical need.

Date: 16th January 2013

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NSW GOVERNMENT Health
Northern Sydney
Local Health District

16 January 2013

The Secretary,
Scheduling Secretariat,
GPO Box 9848,
Canberra,
ACT 2601.

Dear Sir/Madam,

Re: Rescheduling all benzodiazepines from Schedule 4 to Schedule 8: TGA call for public submissions

Thank you for the opportunity to comment on the proposal to reclassify all benzodiazepines to Schedule 8 medications. After detailed discussion we do not support this proposal. Instead, we propose that alprazolam alone be transferred to Schedule 8, for the following reasons:

- Our clinical experience and our review of the literature support our opinion that not all benzodiazepines are equally problematic. Alprazolam currently stands out among the benzodiazepines, in terms of the risks of abuse, dependence and adverse effects.
- We believe that reclassifying **all** benzodiazepines as Schedule 8 medication will dilute recognition of the particular dangers of alprazolam.
- We note that having all opioid medications classified as Schedule 8 medications has done little to limit the problems with misuse of drugs such as oxycodone (such as Endone and Oxycontin).
- Unintended consequences are likely if all benzodiazepines are Schedule 8. Doctors will feel less comfortable prescribing benzodiazepines for anxiety and insomnia, and will be more likely to prescribe more toxic and more expensive Schedule 4 medications such as atypical antipsychotics and tricyclic antidepressants. In the addiction field, a number of residential rehabilitation services can operate cheaply as "Schedule 8 free" but still allow for the safe prescription of benzodiazepines. These will no longer be able to provide treatment for a complex and numerous patient group.
- Compliance costs will be significant for pharmacies, nursing homes and aged care facilities, where there will be new requirements for storage, paperwork and review if all benzodiazepines are Schedule 8.

Of course we share the general concern over abuse of benzodiazepines, but our view is that the most powerful single measure would be to provide real time reporting of prescribing practices to medical practitioners and pharmacists. This approach is professionally accepted and technically feasible. The current Prescription Shopping Information Service ("doctor shopping" helpline) is inadequate, with long delays in reporting and insufficient capture of actual prescribing practices including private prescriptions.

In summary, our opinion is that alprazolam should be singled out for Schedule 8 authority only prescribing, rather than all benzodiazepines as a group. We have summarised this view in a recent submission to Pharmaceutical Services in New South Wales (attached).

Many thanks for your consideration of these very important issues. We are happy to discuss this matter further and to provide any additional information you may require.

[redacted]

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NSW GOVERNMENT Health
Northern Sydney
Local Health District

3 May 2012.

Mr Bruce Battye, Chairperson
Mr Peter Gilfedder, Secretary
Poisons Advisory Committee
NSW Health
PO Box 103
Gladesville
NSW 1675

Dear Mr Battye and Mr Gilfedder,

Re: Strategies to Manage the Misuse of Alprazolam

We have written previously about our concerns in relation to the misuse of alprazolam, and the negative impact on many of our patients. We received a response in August 2011 indicating that the National Drugs and Poisons Scheduling Committee considered this matter at a meeting last year and concluded there was insufficient evidence to support a change in scheduling of alprazolam.

Our concerns continue to grow, and have been highlighted by the deaths of two of our patients on opioid substitution therapy. It appears these deaths are attributable to alprazolam overdose with other CNS depressants. Since our earlier correspondence, we have subsequently been able to access more recent information about the toxicity and misuse of alprazolam when compared with other benzodiazepines (attached).

Isbister GK et al 2004 conducted a review of benzodiazepine overdose admissions between January 1987 and October 2002 in the Hunter Area, Australia. Cases where patients had ingested two benzodiazepines were excluded (so that only single benzodiazepine overdoses were analysed), as were second and subsequent admissions. Data from 2003 single benzodiazepine overdose admissions were reviewed, which included:

- 131 alprazolam overdoses;
- 823 diazepam overdoses;
- 1109 other benzodiazepine overdoses (bromazepam, clobazam, flunitrazepam, lorazepam, nitrazepam, oxazepam, temazepam and triazolam).

Alprazolam was found to be significantly more toxic than other benzodiazepines in overdose, as follows:

- 22% of alprazolam overdoses were admitted to ICU, a rate 2.06

times more likely compared with other benzodiazepines after multivariate analysis adjusting for age, dose, gender, time to ingestion and co-ingested drugs;
- the median length of stay for alprazolam overdoses was 19 hours, which was 1.27 times longer than for other benzodiazepines;
- Flumazenil was administered to 14% of alprazolam patients and 16% were ventilated, significantly more than for other benzodiazepines (8% and 11% respectively);

The authors note that 85% of prescriptions for alprazolam are for panic disorder, anxiety, depression or mixed anxiety/depression states. They conclude that alprazolam is relatively more toxic than other benzodiazepines and this is due to the intrinsic toxicity of alprazolam. They also conclude that because suicide attempts are more prevalent in people with panic disorder than the general population, the use of alprazolam in this group needs to be reviewed and better controlled.

Jones K et al 2011 conducted 18 open-ended qualitative interviews with key experts from criminal justice, law enforcement, alcohol and drug treatment agencies and primary health care services. The interviews focused on the contribution of benzodiazepines to criminal activity. The concluded:

- most key experts were of the opinion that alprazolam was associated with more harm and criminal activity compared with other benzodiazepines;
- crimes committed during alprazolam intoxication were often described as "impulsive" and not well planned.

Nielsen S et al 2011 conducted a pilot study to look at the effects of alprazolam in combination with methadone, and alprazolam in combination with buprenorphine-naloxone. Of note are the findings in relation to methadone and alprazolam on memory. The methadone subjects had a mean age of 36.8 years, had been in current treatment for 9.1 months and were on a mean methadone dose of 61.3 mg. Subjects were given a memory test and the memory prose score recorded for immediate recall and delayed recall. Findings indicated:

- the methadone only subjects scored 7 for immediate recall. In contrast, the methadone + 2mg alprazolam subjects scored 4;
- the methadone only subjects scored 6 for delayed recall. In contrast, the methadone + 2mg alprazolam subjects scored 0 and recalled none of the information in the memory test.

Dore G et al 2012 in preparation: A study in our own service found that of 49 patients admitted for treatment of high dose benzodiazepine dependence, almost half of the group reported using more than 100mg diazepam equivalents daily. Of the total group, 84% reported misusing diazepam and 65% reported misusing alprazolam (Xanax in all cases). This is despite the limited indications for prescribing Xanax on an authority prescription, namely Panic disorder where other treatments have failed or are inappropriate. It's also of note given that diazepam is prescribed at 5 – 10 times the rate of alprazolam in Australia (Isbister et al 2004).

Alprazolam is currently a Schedule 4 Appendix D medication, and an authority prescription can be provided if the patient has Panic Disorder, where other treatments have failed or are inappropriate. This criterion has not stopped doctors writing private prescriptions for alprazolam, and has not deterred doctors in obtaining authority prescriptions for patients with substance use disorders. Our clinical experience also suggests that some doctors are writing authority prescriptions when there is no clear evidence of Panic Disorder.

Given the popularity of alprazolam as a drug of abuse, and the levels of morbidity and mortality as a consequence, we request a major change in the way alprazolam is currently prescribed.

Reclassification of alprazolam

We request that alprazolam be **reclassified as a Schedule 8 medication**, and that criteria for the prescribing of alprazolam be established along the lines of *"The Criteria for the Diagnosis and Management of ADHD in Adults"* established by NSW Health Pharmaceutical Services Branch (under The Poisons and Therapeutic Goods Act 1966).

Criteria for the Prescribing of Alprazolam could include the following:

1. That the prescribing of alprazolam is limited to patients with a diagnosis of **Panic Disorder where other treatments have failed or are inappropriate.**

2. That the assessment of the suitability of alprazolam as a treatment, and the initial prescribing of alprazolam be limited to **Psychiatrists who have been issued with an authority number** by Pharmaceutical Services Branch of the NSW Department of Health (similar to S28c for the prescription of psychostimulants for ADHD).

3. That an **application for an authority to prescribe** for an individual patient must be made where there is a history of **substance misuse or dependence.**

    - Where this is a history of substance misuse or dependence, applications for authority to prescribe must be supported in writing by a detailed second opinion from an independent psychiatrist (e.g. from a different practice). The application or second opinion should be from **a psychiatrist experienced in drug and alcohol issues**.

    - Applications may be referred to the Medical Committee, established under Section 30 of the Poisons and Therapeutic Goods Act, for its advice.

4. Applications may be accepted from the patient's General Practitioner or another treating practitioner after a minimum of 6 months with the treating Psychiatrist and with their approval. A letter from the Psychiatrist to this effect must accompany the application.

5. Applications from General Practitioners to increase the dose or change the drug must be accompanied by a report from the referring Psychiatrist supporting the change.

Many thanks for your consideration of these matters.

[redacted]

[redacted]

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Jones K, Nielsen S, Bruno R, Lubman D. A Pinch in Every Bottle: Expert perspectives of alprazolam use in relation to offending. Poster at APSAD conference, Hobart, 2011.

Nielsen S et al. Pharmacodynamic interactions of alprazolam in buprenorphine-naloxone and methadone patients. Turning Point Alcohol & Drug Centre, 2011.

Benzodiazepines

Alprazolam leaflet

Overdose:
(From Moylan 2012-06-21Alprazolam is a common drug in overdose incidents leading to emergency department admissions (Buukx et al., 2010; Substance Abuse and Mental Health Services Administration, 2010). Data from the US Substance Abuse and Mental Health Services Administration (SAMHSA) showed that alprazolam is the most common benzodiazepine involved in emergency overdose situations, both in isolation and mixed with alcohol and other substances (Substance Abuse and Mental Health Services Administration, 2010). These data also suggest the incidence of alprazolam events is increasing at a faster rate than other benzodiazepines, from approximately 46,000 in 2004 to 80,000 in 2008 (73% increase) (Substance Abuse and Mental Health Services Administration, 2010). This finding may relate to the fact that alprazolam is the most utilised benzodiazepine in the US population.

In an Australian study of emergency department visits, the majority of alprazolam used in overdose was obtained through doctor prescription (Bukx et al., 2010). This high use of alprazolam in overdose is noteworthy, as in such situations alprazolam has demonstrated greater toxicity than other benzodiazepines with patients in one study 2.06 times more likely to require treatment in an intensive care unit than other benzodiazepines after adjusting for age, dose, gender and co-administered drugs (Isbister et al., 2004). It should be noted, however, that in overdose alprazolam (like other benzodiazepines) may be safer than other medications utilised for PD (e.g. TCAs).

I've used DUSC script numbers to determine a PAS per m scripts.

Buykx	PAS		scripts 2004	PAS per m scripts
diaz		46	2,033,719	22.6
alpraz		26	494,998	52.5
temaz		20	2,915,242	6.9

Driving
The impact of benzodiazepines on driving ability is a controversial area. In a study testing driving ability of 20 health volunteers administered alprazolam 1 mg, six of the subjects demonstrated impairment to the point of unsafe driving (Verster et al., 2002). Acute administration of alprazolam 1 mg has been equated to a blood alcohol concentration of 0.15% (Verster and Volkerts, 2004), significantly higher than most country legal limits, although whether use is causally related to road traffic accidents is disputed (Barbone et al., 1998; Smink et al., 2010). Benzodiazepines are commonly found in blood samples taken from drivers involved in major trauma accidents in Australia (15.6%) (Ch'ng et al., 2007) or apprehended due to dangerous or erratic driving in Norway (46.2%) (Christophersen and Morland, 2008). Recent data from individuals involved in car accidents in Victoria (July 2009 to July 2010) found that all of those with alprazolam in their blood were responsible for the collision (Ogden et al., 2010).This data also demonstrated that alprazolam levels found in patients were well above those expected from therapeutic dosing, with the mean level 0.138 mg/L in the toxic range (Ogden et al., 2010). This probably indicates this group of patients were using alprazolam outside of normal prescribing patterns potentially indicative of an abuse pattern. Impairment of motor coordination occurs in a dose-dependent fashion and hence care should be undertaken with driving when changes or initiation of benzodiazepines has occurred.

Xxx THE RELATIONSHIP BETWEEN ACCIDENT CULPABILITY AND THE PRESENCE OF DRUGS IN BLOOD SAMPLES TAKEN FROM PEOPLE INJURED IN MOTOR VEHICLE COLLISIONS
Ogden EJDI (presenting), Morris C1, Frederiksen TI, Boorman M1'2, King R2, Stough CKK2
1 Victoria Police ' Swinburne University
email: edward.ogden@police.vic.gov.au

l4% of samples contained a benzodiazepine, most commonly diazepam. It would be tempting to consider the benzodiazepines as a group, but to do so would be quite misleading. The individual members of the group have distinctly different metabolism. For instance midazolam has a half-life of 2 hours compared with diazepam 24 to 72 hours. They also have different uses in therapeutics and different abuse potential.

Overall the odds ratio for collision was increased (OR:10.4) when diazepam was detected with a clear relationship between blood level and likelihood of being responsible for collision. Considering how commonly these drugs are prescribed, further analysis with larger numbers of subjects is required to clarify the risk when the drugs are taken in common clinical doses.

Alprazolam stood out in this family of drugs. All drivers who had aprazolam detected were responsible for the collision (n= 23).
Alprazolam has limited place in the treatment of panic disorder. Unfortunately it has become popular as a recreational drug and is taken in quantities in excess of the recommended dose. This is reflected in levels far above the expected therapeutic level. The average level detected was 0. 138 mg/L which is in toxic range.

Do minor tranquillisers (benzodiazepines) increase risk of collision in which the driver is injured?
EDWARD J. D. OGDEN1, CARLA MORRIS1, TANIA FREDERIKSEN1, CON STOUGH2, REBECCA KING2, JACQUELINE DONALD2
1Victoria Police, Melbourne, Victoria, Australia
2Brain Sciences Institute, Swinburne University of Technology, Hawthorn, Victoria, Australia
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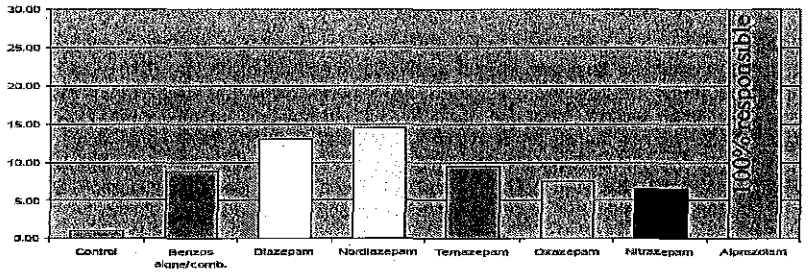
E-mail: edward.ogden@police.vic.gov.au

Chart 5: Comparison of odds ratios for individual benzodiazepines



NB. Calculations for categories include all drivers testing positive to the substance, not positive to *only* that substance.

Diazepam and alprazolam were the most common benzodiazepines detected in injured drivers (as well as nordiazepam, a metabolite of diazepam). They also carried a higher probability of being responsible for the collision.

Alprazolam

Table 4: Summary of responsibility for drivers testing positive to alprazolam

Group	Responsibility Analysis			Total
	Responsible	Contributory	Not Resp.	
Alprazolam (+/- other benzos only)	8	0	0	8
Alprazolam (+/- other drugs)	41	3	0	44
Low (<0.02mg/l)	5	1	0	6
Therapeutic (0.02-0.04mg/l)	9	1	0	10
High (0.041-0.075mg/l)	3	1	0	4
Toxic (>0.075mg/l)	24	0	0	24

Only 1 of the 44 alprazolam-positive drivers had a level of the drug considered low or therapeutic and had no other drugs in their system.

Alprazolam is of particular concern. Twenty four of the 44 drivers who tested positive (64%) had levels considered either high or toxic. In fact, only one driver had a level of alprazolam in the low-therapeutic range and no other substances. The only reasonable conclusion is that the other 43 drivers were taking the drug irresponsibly, recreationally, or in excess of the prescribed dose. All alprazolam-positive drivers were either responsible for, or contributed to the collision in which they were injured. The road safety implication is that alprazolam should be considered for special controls on prescription and supply.

APSAD 2012
PRESENTATION 3 – BENZODIAZEPINES AND RISK OF COLLISION

Issue: The contribution of prescribed and illicit benzodiazepines contribution to risk of collision.
Approach: A study of 184 injured drivers in Victoria.
Key Findings: While diazepam accounted for 51% of detected benzodiazepines, alprazolam at 11% had the most concerning contribution to collisions with 94% of those detected culpable. The contribution of alcohol in combination with benzodiazepines is significant, particularly in excess of the therapeutic range.
Implications: The implication that a zero blood alcohol concentration in combination with benzodiazepines should be discussed including rescheduling of alprazolam given that only one of 44 alprazolam drivers had no other drugs in their system or were in the therapeutic dose range.

Memory impairment

The level of memory impairment produced by benzodiazepines appears to be related to a higher relative lipid solubility and affinity at benzodiazepine receptor (Chouinard, 2004). Alprazolam exhibits both high relative lipid solubility and high binding affinity.

Chouinard G (2004) Issues in the clinical use of benzodiazepine: potency, withdrawal, and rebound. *Journal of Clinical Psychiatry* 65: 7–12.

Abuse potential

Abuse potential and non-clinical effects

Probably as a consequence of its high potency, rapid onset and short half-life (Chouinard, 2004; Mumford et al., 1995; Wolf and Griffiths, 1991), alprazolam has become a drug of abuse (Forrester, 2006; Substance Abuse and Mental Health Services Administration, 2010). Discussion regarding the potential for alprazolam to induce dependence is found earlier in the review. Some researchers suggest continuing use of alprazolam (Australian Bureau of Statistics, 2010; SDI/ Verispan, 2010) may represent ongoing clinical management of chronic conditions rather than drug dependence (Romach et al., 1991, 1992; Sellers et al., 1993). A qualitative investigation of youth attitudes concerning alprazolam revealed use was deemed common, the drug was highly addictive, difficult to cease and medical professionals were the greatest facilitators of use (Peters et al., 2007), indicating that at least a portion of ongoing use may relate to drug dependence.

Chouinard G (2004) Issues in the clinical use of benzodiazepine: potency, withdrawal, and rebound. *Journal of Clinical Psychiatry* 65: 7–12.

Forrester MB (2006) Alprazolam abuse in Texas, 1998–2004. *Journal of Toxicology and Environmental Health Part A* 69: 237–243.

Mumford G, Evans S, Fleishaker J, et al. (1995) Alprazolam absorption kinetics affects abuse liability. *Clinical Pharmacology and Therapeutics* 57: 356–365.

Peters RJ, Meshack A, Kelder S, et al. (2007) Alprazolam (Xanax) use among southern youth: beliefs and social norms concerning dangerous rides on 'handlebars'. *Journal of Drug Education* 37: 417–428.

Romach M, Busto U, Sobell L, et al. (1991) Long-term alprazolam use: abuse, dependence or treatment? *Psychopharmacology Bulletin* 27: 391–395.

Wolf B and Griffiths R (1991) Physical dependence on benzodiazepines: differences within the class. *Drug and Alcohol Dependence* 29: 153–156.

SAMHSA DAWN 2009, 2011
Substance Abuse and Mental Health Services Administration, Drug Abuse Warning Network, 2009: National Estimates of Drug-Related Emergency Department Visits. HHS Publication No. (SMA) 11-4659, DAWN Series D-35. Rockville, MD: Substance
Abuse and Mental Health Services Administration, 2011. Available from:
http://www.samhsa.gov/data/2k11/DAWN/2k9DAWNED/HTML/DAWN2k9ED.htm

In 2009, slightly over 120 million visits were made to EDs in general-purpose hospitals in the United States, and DAWN estimates that at least 4.5 million of these visits were drug related. Drug-related ED visits have increased by over 80 percent since 2004. This increase primarily reflects greater numbers of medical emergencies associated with adverse reactions, accidental drug ingestions, and misuse or abuse of prescription drugs and over-the-counter medications.

Overall Drug Misuse or Abuse
In 2009, DAWN estimates that about 2.1 million ED visits resulted from medical emergencies involving drug misuse or abuse, the equivalent of 674.4 ED visits per year per 100,000 population. For those aged 20 or younger, the rate is 473.3 visits; for those aged 21 or older, the rate is 754.8 visits.
Of the 2.1 million visits associated with drug misuse or abuse in 2009,
35.3 percent involved pharmaceuticals alone,
23.0 percent involved illicit drugs alone,
10.2 percent involved illicit drugs plus alcohol,
11.0 percent involved pharmaceuticals plus alcohol,
10.0 percent involved pharmaceuticals plus illicit drugs,
6.7 percent involved alcohol alone in patients aged 20 or younger, and
3.9 percent involved pharmaceuticals and illicit drugs plus alcohol.

Understanding that a visit may appear in more than one group, DAWN found that out of all drug misuse or abuse ED visits: 1,079,683 ED visits, or 52.1 percent, involved pharmaceuticals;

Although the overall number of ED visits attributable to drug misuse or abuse was stable from 2004 to 2009, increases were seen in ED visits involving nonmedical use of pharmaceuticals with no other drug involvement (117% increase), pharmaceuticals with illicit drugs (97%), pharmaceuticals with alcohol (63%), and pharmaceuticals combined with both illicit drugs and alcohol (76%).

Drugs and Alcohol Taken Together
Drugs for insomnia and anxiety were involved in 24.7 percent of visits, with the largest part of that being benzodiazepines (anti-anxiety drugs; 21.0%).

Nonmedical Use of Pharmaceuticals
Pain relievers were the most common type of drugs reported in the nonmedical use category of ED visits (47.8%). Among specific types of pain relievers, higher levels were seen for the narcotic pain relievers oxycodone, hydrocodone, and methadone (13.7%, 8.0%, and 5.8%, respectively). Drugs used to treat anxiety and insomnia were also seen frequently (33.6%) in visits related to nonmedical use of pharmaceuticals. Benzodiazepines were involved in 29.0 percent of such ED visits, with alprazolam (e.g., Xanax®), indicated in 10.4 percent of such visits.

Drug-Related Suicide Attempts
At 38.1 percent, pain relievers were the most commonly involved type of drug in drug-related suicide attempts. Benzodiazepines followed pain relievers at 28.7 percent, with alprazolam and clonazepam (e.g., Klonopin®) accounting for 11.7 percent and 8.1 percent of these visits, respectively. At 26.4 percent, psychotherapeutic drugs occurred at a level similar to benzodiazepines. Illicit drugs were involved in 17.9 percent of visits.
The number of drug-related suicide attempts has remained stable from 2004 to 2009. However, a significant rise was observed in the involvement of two pain relievers—hydrocodone and oxycodone—and three anti-anxiety drugs—alprazolam, clonazepam, and zolpidem (e.g., Ambien®).

Seeking Detox Services
The category of visits referred to as "seeking detox" includes nonemergency requests for admission for detoxification and visits to obtain medical clearance before entry to a detox program as well as acute emergencies in which an individual who is experiencing withdrawal symptoms is seeking detox.

As to the types of drugs involved, cocaine was observed in 29.2 percent of visits, heroin in 28.4 percent, marijuana in 18.3 percent, and stimulants in 5.4 percent. Among pharmaceuticals, narcotic pain relievers were observed in 38.2 percent of visits, including oxycodone at 22.2 percent. Benzodiazepines were observed in 23.7 percent of visits, with alprazolam at 13.6 percent.

Drugs (Abingdon Engl). 2012;19(2):144-155.
Patterns of prescription medication diversion among drug dealers.
Rigg KK, Kurtz SP, Surratt HL.
The type of medication most commonly sold by dealers was prescription opioid analgesics, and to a **lesser extent benzodiazepines such as alprazolam.**

"Xanax pills (2 mg), known as 'zanny bars' or 'footballs', were also a fairly common medication that dealers reported selling, but this comprised a much lower proportion of their overall sales in comparison to opioids."

IDRS (Vic)

Similarly, 71% of the sample reported recent use of benzodiazepines, although a much smaller proportion reported recent injection (2%). Illicit recent use of benzodiazepines (excluding alprazolam) was reported on a median of 10 days, whereas recent illicit use of alprazolam was reported on a median of 13 days. Sixty-nine percent of the sample reported recent use of illicit alprazolam, the highest single report in the Victorian IDRS of illicit use of a prescribed medication. Diazepam and alprazolam were the main benzodiazepines used by respondents.

As per 2010, the 2011 survey focused on the drug or drugs KE perceived to be 'most problematic' at the time of interview. A total of 17 responses were elicited in this area of questioning. The drugs named as most problematic by KE were most commonly prescription opiates (n=8), alprazolam (Xanax, a short-acting benzodiazepine) (n=3) and antipsychotics (n=3). Other drugs nominated by KE as problematic included heroin, crystal methamphetamine, dexamphetamine, steroids, Unisom and over the counter codeine.

Table 3

	Ever used %	Ever injected	Used last 6/12	Med days last 6/12
Alpraz licit	31	3	20	178
Alpraz illicit	81	11	63	9
Any form	88	14	69	13

4.7.3. Benzodiazepines
In 2011, participants were asked about alprazolam (trade name Xanax®) separately from other benzodiazepines. This survey change means that lifetime and recent use of alprazolam are now in a separate category, thus reducing reports in the general benzodiazepines category. In this section, other benzodiazepines are reported first and alprazolam is addressed second.

.....

Reports of lifetime use of alprazolam (88%) were only slightly less common than lifetime use of other benzodiazepines (92%), with a similar pattern evident for recent use (69% vs. 71% for alprazolam and other benzodiazepines respectively). Median reported days of use of alprazolam was 13 days, other benzodiazepines was also 13 days, whereas median days of use of any benzodiazepines including alprazolam was 96.
Compared to previous years, much fewer KE mentioned any form of benzodiazepine as being a particularly problematic drug. Three KE mentioned alprazolam as being a problematic drug; however, a number noted that while alprazolam use hadn't necessarily declined, the associated presenting problems had.
Illicit alprazolam use is reported by 69% of the sample; the single highest report of illicit use of a prescribed medication in this study. Given KE reports in previous years of behavioural issues associated with the use of alprazolam, data collected in the 2011 IDRS bears out the need to continue monitoring illicit use of this substance.

IDRS (Aust)

Stafford J, Burns L. Australian drug Trends 2011. Findings from the Illicit Drug Reporting System (IDRS). Australian drug Trends Series No. 73. National drug and alcohol Research Centre, University of New South Wales. Sydney, NSW, Australia 2012.

Sixty-two percent of the national sample reported using some form of alprazolam in their lifetime, with nearly half (46%) reported recently using any form of alprazolam on a median of 12 days.
• Three-quarters (75%) of the national sample had used another form of other benzodiazepines not including alprazolam in their lifetime. Over half (56%) reported recently using any form of other benzodiazepines on a median of 60 days. Small proportions reported recently injecting other benzodiazepines (5% or less).
• The majority (83%) of the national sample had reported the use of benzodiazepines (including alprazolam) at some stage in their lifetime. Sixty-nine percent reported the recent use of benzodiazepines on a median of 74 days. Only small numbers reported recently injecting benzodiazepines on a median of six days in the last six months. Eight percent reported recently injecting alprazolam.

Table 4: Forms of drugs used in the preceding six months, by jurisdiction, 2011 (continued)

Form of drug	National		NSW	ACT	VIC	TAS	SA	WA	NT	QLD
	N=902	N=868	n=150	n=98	n=150	n=100	n=100	n=70	n=98	N=102
	2010	2011								
Methamphetamine (%)										
Methamphetamine powder (speed)	41	44	30	46	49	67	36	43	43	40
Amphetamine liquid (oxblood)	3	6	3	7	3	8	15	1	4	6
Base methamphetamine (base/point/wax)	21	22	17	17	11	39	35	6	12	37
Crystalline methamphetamine (ice/crystal)	39	45	53	57	53	26	44	46	28	50
Prescription stimulants (%)										
Licit	2	1	1	7	1	0	0	0	1	0
Illicit	13	14	2	25	16	35	9	16	11	4
Cocaine (%)										
Powder	15	14	40	8	13	7	9	6	1	11
Crack	1	1	2	1	1	0	1	0	0	0
Rock	6	4	14	1	6	0	2	4	0	3
Hallucinogens (%)										
LSD	3	4	0	1	3	10	4	9	5	7
Mushrooms	2	4	0	9	4	6	3	1	2	4
Ecstasy (%)										
Pills	12	11	7	13	11	18	13	0	7	20
Powder	<1	1	0	0	1	2	2	0	2	0
Alprazolam (%)										
Licit	n.a	13	9	10	20	4	12	17	13	17
Illicit	n.a	39	37	27	63	40	23	27	36	40
Other Benzos^ (%)										
Licit	43	36	30	29	46	48	20	43	30	46
Illicit	40	35	35	34	47	61	19	23	24	33
Seroquel (%)										
Licit	n.a	9	9	8	15	9	2	17	3	10
Illicit	n.a	15	13	13	30	12	7	19	2	16
Cannabis (%)										
Hydro	68	70	76	76	79	72	59	67	63	75
Bush	44	43	39	59	31	59	54	49	21	40
Hashish (hash)	6	9	6	8	5	6	24	7	9	9
Hash oil	3	5	3	4	1	2	14	7	5	8

Source: IDRS participant interviews
Note: Percentages in each form may not total 100% as more than one form may have been used in the last six months
^ 'Other benzos' included Alprazolam in 2010.

Sixty-two percent of the national sample reported using some form of alprazolam in their lifetime, with nearly half (46%) reported recently using any form of alprazolam on a median of 12 days.
• Nearly three-quarters (75%) of the national sample had used another form of other benzodiazepines not including alprazolam in their lifetime. Over half (56%) reported recently using any form of other benzodiazepines on a median of 60 days. Small proportions reported recently injecting other benzodiazepines (5% or less).

The majority (83%) of the national sample had reported the use of benzodiazepines (including Alprazolam) at some stage in their lifetime. Sixty-nine percent reported the recent use of benzodiazepines on a median of 74 days. Only small numbers reported recently injecting benzodiazepines on a median of six days in the last six months. Eight percent reported recently injecting alprazolam.

4.7.3.1 Alprazolam

Sixty-two percent of the national sample reported using some form of alprazolam in their lifetime (23% licit and 53% illicit). Nearly half (46%) reported recently using any form of alprazolam on a median of 12 days in the last six months. Thirteen percent had recently used 'licit' alprazolam on a median of 172 days while 39% had recently used 'illicit' alprazolam on a median of seven days (Table 19).

A smaller proportion (15%) had injected alprazolam at some stage in their life (4% licit, 14% illicit), with 8% injecting any form of alprazolam (<1% licit, 8% illicit) in the last six months.

Table 19: Alprazolam use patterns, by jurisdiction, 2011

	National N=868	NSW n=150	ACT n=98	VIC n=150	TAS n=100	SA n=100	WA n=70	NT n=98	QLD n=102
	2011								
Recent use (%)									
Licit	13	9	10	20	4	12	17	13	17
Illicit	39	37	27	63	40	22	27	36	40
Any form (licit and/or illicit)	46	43	33	69	43	32	41	43	50
Median days used*									
Licit	172	180	180	178	95^	165	40	90	160
Illicit	7	24	5.5	9	6	3.5	4	6	7
Any form (licit and/or illicit)	12	48	10	13	6	4	6	10	22

Source: IDRS participant interviews

^ Medians based on small numbers (n<10); interpret with caution

* Among those who reported recent use or injection. Maximum number of days, i.e. daily use = 180. See page xiii for guide of days use/injection

Table 21: Main other benzodiazepine type used (excluding alprazolam) in the six months preceding interview, 2011

	Recent use among those who had recently used N=444	Recent injectors* N=52
Diazepam (%) *e.g. Antenex, Ducene, Valium, Valmpam*	84	79 (n=41)
Oxazepam (%) *e.g. Serepax*	7	12 (n=6)
Temazepam (%) *e.g. Normison, Temaze*	4	4 (n=2)
Clonazepam (%) *e.g. Rivotril*	2	0
Nitrazepam (%) *e.g. Alodorm, Mogadon*	<1	2 (n=1)
Flunitrazepam (%) *e.g. Hypnodorm*	<1	2 (n=1)

Source: IDRS participant interviews

* 96% (n=50) of recent benzodiazepine injectors also reported oral use; therefore, one cannot make the assumption that the main brand reported is being injected

Benzodiazepines

Table A3: Drug use history of the national sample, 2011 (continued)

	Ever used %	Ever injected %	Injected last six months %	Median days injected in last six months [a]	Ever smoked %	Smoked last six months %	Ever snorted %	Snorted last six months %	Ever swallowed[b] %	Swallowed last six months[b] %	Used last six months [c] %	Median days in treatment last six months [a, d]	Median days used last six months [a, e]
Speed powder	88	84	42	8	19	4	39	5	34	7	44	41	10
Base/paste/wax	48	44	21	5	7	3	4	1	10	3	22	43	6
Ice/ice/crystal	74	70	44	10	33	14	7	2	12	4	45	60	10
Methamphetamine liquid	25	21	8	5					0	0	8	56	4
Any methamphetamine*	94	92	66	10	43	16	42	6	41	41	66	60	19
Pharmaceutical stimulants (licit/prescribed)	8	3	<1	102^	<1	0	<1	0	7	1	1	60	25
Pharmaceutical stimulants (illicit/not prescribed)	34	20	10	3	<1	<1	<1	0	21	5	14	41	4
Any pharmaceutical stimulants	38	21	10	3	<1	<1	1	0	28	6	15	41	4
Cocaine	61	43	14	4.5	9	1	34	6	0	1	17	60	5
Hallucinogens	85	6	<1	3^	0	0	<1	43	82	8	8	60	2
Ecstasy	85	27	4	2	2	<1	8	1	58	12	14	60	2
Alprazolam (licit/prescribed)	23	4	1	12.5^	<1	<1	<1	<1	21	13	13	60	170
Alprazolam (illicit/not prescribed)	53	14	8	6	<1	<1	1	<1	46	35	39	60	6.5
Other benzodiazepines (licit/prescribed)	55	6	1	3^	1	<	1	<1	64	36	38	60	96
Other benzodiazepines (illicit/not prescribed)	53	7	2	4.5	<1	0	1	<1	51	33	35	60	7
Any benzodiazepines	83	21	10	6	2	<1	2	1	82	57	69	60	72
Seroquel (Licit/prescribed)	16	<1	<1	0	0	0	<1	<1	15	9	9	60	180
Seroquel (illicit/not prescribed)	31	<1	<1	0	0	0	0	0	29	15	15	60	3
Any Seroquel	41	1	<1	0	0	0	<1	<1	39	22	22	60	n.a.
Alcohol	95	5	<1	1^					94	65	65	60	24
Cannabis	97				97	80					78	60	180
Inhalants	24										3	60	2
Steroids	8	6	1	9	<1	0	0	0	2	1	2	60	12
Tobacco	97										94	60	180

Source: IDRS participant interviews
Note: Maximum number of days, i.e. daily use = 180. See page xiii for guide to days of use/injection
^ Small numbers commenting (n<10)
[a] Among those who had used/injected (as applicable).
[b] Refers to/includes sublingual administration of buprenorphine (trade name Subutex) and buprenorphine-naloxone (trade name Suboxone)
[c] Refers to any route of administration, i.e. includes use via injection, smoking, swallowing, and snorting
[d] Buprenorphine and buprenorphine-naloxone can be administered daily, every second day or three times per week
[e] Category includes speed powder, base, ice/crystal and amphetamine liquid (ox/blood). Prior to 2006, the 'methamphetamine' category also included pharmaceutical stimulants in this table. Pharmaceutical stimulants have comprised their own category since 2006
n.a. data not available

Bruno Ralmondo

Harms associated with recent 'illicit' (non-prescribed or IV) alprazolam use among injecting drug consumers (national, 2011, n=868)	No illicit alprazolam use (n=534) %	Illicit alprazolam use (n=334) %	OR
Male	67	65	0.88
Overdose *(last 6 months)*	7	12	1.89**
Daily injection	38	46	1.39*
Used pharmaceutical opioid *(yesterday)*	49	64	1.81***
Used opioid and benzodiazepine *(yesterday)*	15	37	3.36***
Arrested *(past year)*	29	47	2.26***
Engaged in crime *(past month)*	31	52	2.45***
High psychological distress *(K10 >30)*	26	34	1.47*
Minor IV harms *(scarring, bruising, problems with injecting)*	43	54	1.56**
Major IV harms *(abscess, thrombosis)*	11	12	1.10
Attended Emergency Department *(last month)*	12	16	1.44(*)
Attended a GP *(last month)*	59	66	1.31(*)
Attended psychotherapy *(last month)*	29	37	1.41*

Source: IDRS 2011

EDRS (Vic)
Nguyen P, Dietze P, Lloyd P. VICTORIAN TRENDS IN ECSTASY AND RELATED DRUG MARKETS 2011. Findings from the Ecstasy and related Drugs Reporting System (EDRS). Australian Drug Trends Series No. 85. National Drug and Alcohol Research Centre, University of New South Wales, Sydney, NSW 2052, Australia.

Half of the REU sample reported that drugs have impacted negatively on their sleep quality. Possibly in lieu of that, 44% of REU have reported taking sleep medication in the month prior to interview. Xanax (alprazolam) was the medication most reportedly used by REU, followed by Valium (diazepam) (see Table 49).
REU = regular ecstasy users

Table 49: Use of sleep medication in REU in the past month, 2011. VIC

How often taken sleep medication in past month (%)	**n=89**
Not in past month	56
Less than once a week	18
Once or twice a week	11
Three or more times a week	15
Medication used last time (%)	**N=39**
Valium (diazepam)	23
Other	21
Xanax (alprazolam	27
Temazepam (generic)	10

EDRS (Aust)
Sindicich N, Burns N. Australian trends in Australian drug markets 2011. Findings from the ecstasy and related drugs reporting system (ERDS). Australian Drug trend series No. 82. NDARC Sydney 2012.
Page 65
Licitly obtained (prescribed) benzodiazepines

Twenty -one percent of the 2011 (17% in 2010) sample reported having ever used licitly obtained benzodiazepines and 14% (10% in 2010) reported their use in the six months preceding interview. The mean age of first use was 22 years (median = 22, range=14-39 years). Licit benzodiazepines had been used on a median of 30 days (range=1-180 days) in the preceding six months. Twenty-three percent of recent users reported daily use (14% in 2010). Almost all (99%) of the recent licit benzodiazepine users reported swallowing in the preceding six month, with one report of injecting and two reports of smoking licit benzodiapine use.
The main type of benzodiazepine used by these users were: diazepam (63%; including brand names Valium and generic) and alprazolam (17%; including brand names Xanax).

Illicitly obtained (not prescribed) benzodiazepines.

Over half (58%) of the 2011 sample reported having ever used illicitly obtained benzodiazepines and one-third (33%) reported their use in the six months preceding interview (Table 26). The mean age of first use was 20 years (median = 19 years, range=12-38 years) in recent users. Illicit benzodiazepines had been used on a median of five days (range=1-180 days) in the preceding six months. Amongst recent users, the majority (89%) reported using illicit benzodiazepines less than monthly, six participants reported daily use. Swallowing was the most common ROA in the six months preceding interview (99%), though 7% (n=14) of recent users reported snorting and very few n<5 participants reported other means of consumption.

The main type of benzodiazepine used by these users were: diazepam (52%; including brand names Valium, Valpam and generic) and alprazolam (31%; including brand names Xanax and Alprax).

Table 26: Use of illicitly obtained benzodiazepines, by jurisdiction, 2010

(%)	National		NSW	ACT	VIC	TAS	SA	WA	NT	QLD
	2010 N=693	2011 N=574	n=100	n=80	n=101	n=75	n=76	n=28	n=11	n=103
Ever used	43	58	40	43	79	44	46	33	100	65
Used last 6 months	26	33	10	14	42	22	36	0	50	50
Median days use (n; range)*	3 (1-180)	5 (1-180)	6 (1-24)	3 (1-25)	10 (1-180)	5.5 (1-40)	6 (1-25)	2.5^ (1-7)	5^ (1-40)	3 (1-180)

Source: EDRS REU interviews
*Of those who had used illicit benzodiazepines in the past six months
^small numbers responded; interpret with caution

Forty-four percent of the national REU sample reported that drugs have impacted negatively on their sleep quality (see Table 132). Possibly in lieu of that, 30% of REU have reported taking sleep medication in the month prior to interview. Valium (diazepam) was the medication most reportedly used by REU, followed by other medications not included on the list such as St John's Worts and cold and flu medications, followed by Xanax (alprazolam) and Temazepam (Table 133). Vic

Table 133: Use of sleep medication in REU in the past month, 2011

How often taken sleep medication in past month (%)	N=537	n=98	n=79	n=89	n=75	n=76	n=26	n=11	n=83
Not in past month	70	78	75	55	73	68	77	73	68
Less than once a week	16	11	17	18	15	21	4	0	18
Once or twice a week	7	8	5	11	8	4	12	18	4
Three or more times a week	7	3	4	15	4	7	8	9	11
Medication used last time* (%)	**N=152**	**n=18**	**n=19**	**n=39**	**n=20**	**n=23**	**n=6^**	**n=3^**	**n=24**
Valium (diazepam)	29	11	32	23	50	39	33	33	21
Other	20	11	16	21	25	22	0	33	25
Xanax (alprazolam)	16	33	5	26	0	9	0	0	21
Temazepam (generic)	7	6	16	10	0	9	0	0	4

Source: EDRS REU interviews, 2011

DCPC (benzo)
Drugs and Crime Prevention Committee. Inquiry into the misuse/abuse of benzodiazepines and other forms of pharmaceutical drugs in Victoria Melbourne: Parliament of Victoria 2007.

A note on alprazolam (Xanax)
Throughout this chapter benzodiazepines have been discussed in a generic sense without very much differentiation between one type of drug within the class and another. This has been because as a general rule both the positive and negative aspects of the benzodiazepines could be viewed as being generally applicable to most drugs within the class. One possible exception to this rule however, is arguably the drug alprazolam, commonly known as Xanax.
Xanax is a benzodiazepine prescribed to alleviate anxiety and related conditions. It is a drug with a particularly high potency, short onset and longer duration of action, which makes it a preferred drug for recreational abuse.94 Whilst it is acknowledged as being a useful drug

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92 Submission of the Victorian Alcohol and Drug Association (VAADA) to the Drugs and Crime Prevention Committee Inquiry into the Misuse/Abuse of Benzodiazepines and other Forms of Pharmaceutical Drugs in Victoria, June 2007.
93 Submission of the Victorian Alcohol and Drug Association (VAADA) to the Drugs and Crime Prevention Committee, Inquiry into the Misuse/Abuse of Benzodiazepines and Other Forms of Pharmaceutical Drugs in Victoria, June 2007.
94 See comments of Joseph Rannazzisi made in a presentation to the Drugs and Crime Prevention Committee, Washington, July 2007 (Drug Enforcement Administration (DEA) 2007a).

in treating anxiety, concerns have been expressed by many witnesses who gave evidence to this Committee that Xanax, particularly when used for recreational purposes, or administered in the wrong way can be particularly dangerous.95 Experts in the field have also testified to its highly addictive qualities and the difficulties associated with withdrawing from the drug – even more so than with other forms of benzodiazepines. For example at a forum on prescription drug abuse in Bendigo, Ms Penny Buykx of the Faculty of Health Sciences, La Trobe University, stated to the Committee that:

> Xanax dependence is one of the most difficult to assist people with because of the halflife of the medication and the immediate drug effect. If a person is feeling quite jittery, Xanax is fantastic at fixing the symptoms immediately but it is quite difficult to deal with. It is also difficult if you are transferring someone from that medication to a longer acting medication in order to do a gradual withdrawal. It is harder to get an accurate equivalent. So I am interested in alprazolam and why it has become so popular, because it seems that some of the harms associated with it are more than amongst some of other benzodiazepines.96

Similar concerns have been expressed about Xanax in other rural areas of the state97including Swan Hill98 and Echuca.99

Dangers associated with inappropriate Xanax use are not restricted to rural Victoria. Reports of its abuse have also surfaced from urban Melbourne. For example, Dr Mark Stoové of Turning Point Alcohol and Drug Centre, drawing from Turning Point research, told the Committee that:

> Key informants are saying that Xanax is increasingly becoming popular both as a licit prescription amongst injecting drug users but also being used illicitly.100

Dr Stoové's colleague Mr Peter Muhleisen, senior pharmacist at Turning Point, added:

> What has happened is that whilst alprazolam has been promoted primarily for anxiety disorders, which it is appropriate for, drug-using populations have found that that is the drug that gets the effect that they like. Xanax has now become the hot new drug after they cannot get temazepam any more [due to a change in drug formulation].101

Of equal concern to some witnesses appearing before the Committee was that alprazolam appears to feature more prominently in crime related activity such as diversion and theft. For example in a submission to this Inquiry by the Pharmacy Board of Victoria, it was stated that it is not uncommon for Xanax tablets (100) to be prescribed and dispensed as private

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95 Alprazolam is a benzodiazepine in pill form which is not soluble in water. Injecting this drug therefore can result in major medical complications similar to those that have occurred when the benzodiazepine temazepam is injected (see discussion later in this chapter).
96 Ms Penny Buykx, Research Officer, Faculty of Health Sciences, La Trobe University, Bendigo, Evidence given to the Drugs and Crime Prevention Committee, Inquiry into the Misuse/Abuse of Benzodiazepines and Other Forms of Pharmaceutical Drugs in Victoria, Prescription Drug Forum, Bendigo, 30 May 2007.
97 And also particularly in rural areas of the United States such as the Appalachian states of Kentucky and West Virginia. See discussion in Chapter 4.1 and see also Leukefeld et al 2007; Havens, Leukefeld & Walker 2006. In this regard Joseph Rannazzisi of the United States DEA has presented statistics to this Committee detailing

that alprazolam was ranked third in the number of prescriptions for controlled substances in the USA from 2003 to 2006 inclusive and that it was ranked 7th for all sales of generic pharmaceuticals for those years (Drug Enforcement Administration 2007a).
98 See the Submission of Dr Mike Moynihan, President of the Rural Doctors Association (Victoria) to the Drugs and Crime Prevention Committee, Inquiry into the Misuse/Abuse of Benzodiazepines and Other Forms of Pharmaceutical Drugs in Victoria, May 2007.
99 See the Submission of Ms Dot Moon, Alcohol and Other Drugs Withdrawal Co-ordinator, Echuca Regional Health, to the Drugs and Crime Prevention Committee, Inquiry into the Misuse/Abuse of Benzodiazepines and Other Forms of Pharmaceutical Drugs in Victoria, May 2007.
100 Dr Mark Stoové, Research Fellow, Turning Point Alcohol and Drug Centre, Evidence given to the Drugs and Crime Prevention Committee, Inquiry into the Misuse/Abuse of Benzodiazepines and Other Forms of Pharmaceutical Drugs in Victoria, Public Hearings, Melbourne, 9 July 2007.
101 Mr Peter Muhleisen, Senior Pharmacist, Turning Point Alcohol and Drug Centre, Evidence given to the Drugs and Crime Prevention Committee, Inquiry into the Misuse/Abuse of Benzodiazepines and Other Forms of Pharmaceutical Drugs in Victoria, Public Hearings, Melbourne, 9 July 2007.

prescriptions and then on-sold on the street at $5.00 per tablet.102 A submission from Youth Projects, a Melbourne based provider of drug and alcohol services for young people, has even reported anecdotal evidence of the stronger formulations of benzodiazepines, particularly Xanax, being used as a 'date rape' drug and/or to facilitate robberies.103 Whilst such reports are disturbing there is insufficient evidence of this happening to constitute an established trend.

Given these concerns it is not surprising that in some quarters there have been calls for stronger regulation of the prescribing of Xanax. For example, a submission from a group of clinicians working in the Victorian public hospital sector noted that alprazolam (Xanax) is only listed at Schedule 4 despite the concerns of many clinicians:

> The overwhelming consensus among alcohol and drug clinicians is that alprazolam is one of the most widely abused of the benzodiazepines, and that management of withdrawal of patients using alprazolam is particularly difficult.
> While recognising that the scheduling of medications is currently administered at Commonwealth level, it is appropriate that the idea of rescheduling be raised in this document. Given the extent of abuse of alprazolam and the risks of withdrawal and overdose associated with this benzodiazepine, a change in schedule to S8 (alongside drugs like morphine and oxycodone) would be a positive public health measure. This change in regulation would increase the controls on alprazolam prescribing, may restrict duration of prescribing of this drug and could raise prescriber awareness of the risks of alprazolam.104

This is in fact a path that one state has gone down. In 2006 a review was conducted in relation to alprazolam prescribing in Tasmania. As a result of the review it was recommended that:

> • The prescribing of alprazolam will be required to be reported monthly by the dispensing pharmacist.
> • This reporting will be in a similar manner as the current reporting of dispensed schedule 8 medications.
> • Any prescribing of alprazolam for more than one month to persons receiving opioid analgesics will require an authority to prescribe.
> • Prescribers will be notified not to prescribe alprazolam if the patient is receiving opioid analgesics from another prescriber. (Currently persons declared as drug dependent cannot have S4 drugs prescribed by prescribers other than their authorised prescriber. However this is only detected when the prescribing comes to our attention through other ad hoc reports. The branch does not have access to PBS [Pharmaceutical Benefits Scheme] data in order to detect such prescribing.)
> • Patients receiving methadone or who are on the pharmacotherapy program will not be allowed to have alprazolam prescribed concurrently unless this is endorsed by the Director of Alcohol and Drug Services in accordance with the pharmacotherapy policy and guidelines.
> • Consultation with the Tasmanian Branch of the Royal Australian and New Zealand College of Psychiatrists will be sought in regard to these recommendations, along with their opinion in relation to the appropriate use of alprazolam given the concerns raised in this report.

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102 Submission of Pharmacy Board of Victoria to the Drugs and Crime Prevention Committee, Inquiry into the Misuse/Abuse of Benzodiazepines and Other Forms of Pharmaceutical Drugs in Victoria, June 2007. See also the submission of Dr Mike Moynihan, President of the Rural Doctors Association (Victoria) to the Drugs and Crime Prevention Committee, Inquiry into the Misuse/Abuse of Benzodiazepines and Other Forms of Pharmaceutical Drugs in Victoria, May 2007.
103 See submission of Youth Projects Inc to the Drugs and Crime Prevention Committee, Inquiry into the Misuse/Abuse of Benzodiazepines and Other Forms of Pharmaceutical Drugs in Victoria, May 2007.
104 Submission of the Interhospital Liaison Group to the Drugs and Crime Prevention Committee, Inquiry into the Misuse/Abuse of Benzodiazepines and Other Forms of Pharmaceutical Drugs in Victoria, May 2006.
• Medicare Australia will be consulted as to possible audits of prescribing of alprazolam outside their authority criteria.

• An education campaign be undertaken through the Division of General Practice to highlight the problems with alprazolam and give advice in relation to its prescribing and use.105

Many of these recommendations have now been implemented in Tasmania. In particular, the new state regulatory requirements came into effect on 1 September 2007. Prior to this date, an education campaign and information sessions were conducted under the auspices of the General Practice Divisions throughout Tasmania. Also, a clinical guideline sheet has been prepared in consultation with representatives of the Royal Australian College of Psychiatrists (RACP), the Royal Australian and New Zealand College of General Practice (RANZCGP) and the Pharmaceutical Services Branch of the Tasmanian Health Department that addresses the problem and the appropriate clinical use of alprazolam. This will be available to all medical practitioners in the state.

In their submission to this Inquiry Mr John Galloway and Ms Mary Sharpe state that increased monitoring of alprazolam will now achieve the following purposes:

- A clear picture of all prescribing, not just those prescriptions claimed on the PBS
- Ability to limit/prevent prescribing where there are concerns about safety
- Patients most at risk of misusing alprazolam will now only be able to have it prescribed under highly controlled circumstances
- Reduction in availability of alprazolam for illicit use and diversion.106

It may be that rescheduling of alprazolam to Schedule 8 is an appropriate strategy.107However, there is insufficient evidence as to whether or not this is a problem in Victoria to make conclusive findings in this area. Nonetheless, it may be appropriate as a first step to conduct a review with regard to the use and prescribing of this drug.

105 Review summarised in Submission of Mr John Galloway, Chief Pharmacist and Ms Mary Sharpe, Deputy Chief Pharmacist, Pharmaceutical Services Branch, Department of Health and Human Services, Tasmania, to the Drugs and Crime Prevention Committee, Inquiry into the Misuse/Abuse of Benzodiazepines and Other Forms of Pharmaceutical Drugs in Victoria, June 2007.
106 Submission of Mr John Galloway, Chief Pharmacist and Ms Mary Sharpe, Deputy Chief Pharmacist, Pharmaceutical Services Branch, Department of Health and Human Services, Tasmania, to the Drugs and Crime Prevention Committee, Inquiry into the Misuse/Abuse of Benzodiazepines and Other Forms of Pharmaceutical Drugs in Victoria, June 2007.
107 For further discussion of drug scheduling, see Chapter 3.1.

PARLIAMENT OF VICTORIA
DRUGS AND CRIME PREVENTION COMMITTEE

INQUIRY INTO THE MISUSE/ABUSE OF BENZODIAZEPINES AND OTHER FORMS OF PHARMACEUTICAL DRUGS IN VICTORIA

Final Report

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DCPC (female prisoners)
Drugs and Crime Prevention Committee. Inquiry into the Impact of Drug-related Offending on Female Prisoner Numbers - Interim Report. Melbourne: Parliament of Victoria, 2010

From page 40:

It is often assumed that substance addiction issues that lead to offending relate to the use of illicit substances such as amphetamines and methamphetamines. However, the use of prescription medications is also reported as being related in the same way to women's offending and imprisonment.73 The submission from Flat Out and CHRIP reported that women who had been in 'the system' felt that 'pills' presented a greater risk for offending than heroin. 74 The Committee was told that the legal and illegal use of Xanax and benzodiazepines was an issue. Moreover, anecdotal reports alleged there are certain health professionals allegedly well known to prescribe high doses of these and other highly addictive prescription drugs to dependent women on request.75 It was further reported that specific areas of Melbourne are well known for the sale and distribution of illegal benzodiazepines, including Richmond and Footscray where it is allegedly possible to purchase three Xanax off the street for $10.76 The Committee was also told that many of Flat Out's clients who had been in prison or police custody in the past six months reported that their offences had not been pre-planned and that they could not recollect their actions as a result of 'Xanax misuse blackouts'.77

See joint submission from Flat Out and CHRIP and submission from the Australian Community Support Organisation (ACSO) to the Drugs and Crime Prevention Committee, Inquiry into the Impact of Drug-related Offending on Female Prisoner Numbers, June 2010.
74 Joint submission from Flat Out and CHRIP to the Drugs and Crime Prevention Committee, Inquiry into the Impact of Drug-related Offending on Female Prisoner Numbers, June 2010.
75 Joint submission from Flat Out and CHRIP to the Drugs and Crime Prevention Committee, Inquiry into the Impact of Drug-related Offending on Female Prisoner Numbers, June 2010.
For an account of the problems associated with the abuse of prescription drugs such as Xanax and benzodiazepines, including a discussion of 'doctor shopping', see Drugs and Crime Prevention Committee 2007, *Inquiry into the misuse/abuse of benzodiazepines and other pharmaceutical drugs in Victoria – Final Report.*
76 Joint submission from Flat Out and CHRIP to the Drugs and Crime Prevention Committee, Inquiry into the Impact of Drug-related Offending on Female Prisoner Numbers, June 2010.
77 Joint submission from Flat Out and CHRIP to the Drugs and Crime Prevention Committee, Inquiry into the Impact of Drug-related Offending on Female Prisoner Numbers, June 2010.

Turning Point:
AOD presenters
Nielsen S, Bruno R, Carruthers S, Fischer J, Lintzeris N, Stoové M. INVESTIGATION OF PHARMACEUTICAL MISUSE AMONGST DRUG TREATMENT CLIENTS. FINAL REPORT 2008. Turning Point Alcohol and Drug Centre, Melbourne 2008.

A range of harms (including dependence, withdrawal, effects on memory and a range of injecting related harms) were experienced by participants, although only a minority of these harms resulted in a medical intervention. Among the benzodiazepines, alprazolam misuse was particularly associated with harmful experiences such as seizures, traffic accidents and crime related harm.

Monitoring harms associated with specific pharmaceuticals
Alprazolam appeared to be more problematic than other benzodiazepines with disproportionate harms associated with alprazolam use. Monitoring to establish the extent of alprazolam misuse and related harms is warranted to inform consideration of whether a specific and perhaps regulatory response is required.

Similar paradoxical responses have been reported about other benzodiazepines, such as alprazolam and diazepam (French, 1989; Rudorfer et al, 1989).

Patterns and nature of presentation to treatment
In all regional areas pharmaceutical opioids and benzodiazepines were mainly reported.
The most common pharmaceutical opioids noted were long acting morphine and oxycodone products. Diazepam and alprazolam were the most common benzodiazepines reported.

A range of harms (including dependence, withdrawal, effects on memory and a range of injecting related harms) were reported, although only a minority of these harms resulted in a medical intervention. Among the benzodiazepines, alprazolam was particularly associated with the experience of harmful outcomes.

Table 12 - Prescription opioid and benzodiazepine history of use in the 4 weeks before entering treatment (n = 305)

	Lifetime use			Use in four weeks prior to treatment entry (mean days reported for those that use in any the four weeks prior to treatment entry)					
	As prescribed %	Not as prescribed %	IV %	As prescribed %	Frequency (/28 days)	Not as prescribed %	Frequency (/28 days)	IV % Frequency (/28 days)	Any form % Frequency (/28 days)
Pharmaceutical opioids									
Methadone syrup	51	49	36	4	5	14	3	4	10
Physeptone tablets	9	25	18	1	2	13	3	3	6
Buprenorphine	37	43	38	3	3	13	4	5	8
Buprenorphine-naloxone	29	18	14	6	6	9	0	0	6
Morphine	27	73	64	4	1	41	8	12	13
Oxycodone	19	66	54	4	2	32	6	6	10
Tramadol	28	39	10	3	2	13	8	1	11
Panadeine Forte	27	22	2	6	5	10	11	0	16
Any prescription opioid	73	88	71	25	6	66	11	10	14
Benzodiazepines									
Oxazepam	41	66	8	10	6	27	11	0	14
Diazepam	73	80	16	30	9	55	12	0	18
Clonezepam	10	31	3	2	4	9	11	1	14
Temazepam	49	64	30	9	7	19	9	0	13
Alprazolam	30	69	17	9	4	38	9	1	12
Nitrazepam	30	44	3	4	5	16	8	0	11
Any benzodiazepine	79	88	42	42	11	69	14	1	21

While data indicates that diazepam was the main benzodiazepine used by the sample, a large proportion of individuals reporting seizures (55%), traffic accidents (50%), and crime (30%), while under the influence of benzodiazepines, identified that alprazolam was the main benzodiazepine involved (ahead of diazepam and other benzodiazepines). As such, there was a disproportionally high level of harm associated with alprazolam use.

It appears that rates of harms are broadly comparable with pharmaceutical opioids and benzodiazepines, though effects on memory and being arrested while intoxicated appeared more common with benzodiazepines. A disproportionate amount of harm was reported with the benzodiazepine alprazolam.

Monitoring harms associated with specific pharmaceuticals
The findings of this study, in agreement with the recommendation in the DCPC report (Drugs and Crime Prevention Committee, 2007) was that alprazolam was more problematic that other benzodiazepines. The finding of disproportionate harms associated with alprazolam use is significant. Monitoring to establish the extent of alprazolam misuse and related harms is warranted to inform consideration of whether a regulatory response is required.

French AP (1989) Dangerously aggressive behavior as a side effect of alprazolam. *The American Journal Of Psychiatry* **146**:276.

Rudorfer MV, Osman OT and Potter WZ (1989) Alprazolam and aggression. *The American Journal Of Psychiatry* **146**:949-950.

Verster JC and Volkerts ER (2004) Clinical Pharmacology, Clinical Efficacy, and Behavioral Toxicity of Alprazolam: A Review of the Literature. *CNS Drug Reviews* **10**:45-76.

Verster JC, Volkerts ER and Verbaten MN (2002) Effects of alprazolam on driving ability, memory functioning and psychomotor performance: a randomized, placebo-controlled study. *Neuropsychopharmacology* **27**:260-269.

Turning Point: benzodiazepines in crime.
Best D, Wilson A, Reed M et al. Understanding the Role of Benzodiazepine Use in Crime. Turning Point Alcohol and Drug Centre. Melbourne 2012.

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- : Alprazolam use has been associated primarily with property type crimes.
- The link between alprazolam use and crime requires further investigation due to gaps in the literature; including exploring individual traits predisposing users to crime, and the impact of drug treatment or criminal justice interventions on the BZD -crime relationship.

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- Professional perception of link between BZD use and a range of offending behaviours, and alprazolam use in particular associated with problematic and risky behaviours.
- Interviews with alprazolam users linked this to both memory loss and atypical behaviour that was not recognised afterwards.
- The key finding of quantitative data analysis is that the sample of BZD/alprazolam users comprised two populations: (1) polysubstance users engaged in treatment, largely involved in acquisitive crime and (2) dependent BZD users who were less engaged in polydrug use patterns and more problematic in terms of elevated levels of psychological distress and mental health diagnoses.

Conclusions and implications

- Alprazolam use is associated with significant memory loss and unpredictable and erratic behaviour, but is positively valued by users.

Alprazolam use in the day before offending was associated with greater drug use and drug treatment involvement but was not typically associated with high degrees of BZD dependence

- Acquisitive crime and BZD use was associated with complex polydrug users who often acquired alprazolam and other BZDs from the streets and where alprazolam use was part of a complex polydrug using pattern that did not seem to have been disrupted by treatment engagement.

Page 2

1. Alprazolam
    a. Alprazolam has a high potential for abuse;
    b. Anecdotal evidence suggests an increasing association with recreational misuse and criminal activity;
    c. Both animal and human studies have shown that alprazolam elevates aggression, social conflict and hostility and is connected to poor and risky decision making which may underscore its link to criminal behaviour.

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1.1.1 Alprazolam

Alprazolam (Xanax) is a potent, short acting BZD that is often prescribed for the treatment of severe anxiety disorders, panic attacks with or without agoraphobia, and depression (Vester & Volkerts, 2004). Alprazolam facilitates binding of gamma-aminobutyric acid (GABA; a major inhibitory neurotransmitter in the central nervous system) which induces general slowing of brain activity or sedation (Saddock, Kaplan, & Saddock, 2007). The pharmacokinetics and interactions of alprazolam with the CNS contribute to its clinical effectiveness and may have implications for addiction and negative side effects. Therefore, alprazolam has a relatively high potential for recreational misuse (Griffiths & Wolf, 1990).

Due to its high potency and potential for abuse, there has been much anecdotal suggestion that alprazolam use is associated with elevated aggression (Rapaport & Braff, 1985) and criminal activity. However, there is little empirical evidence to support this. Studies have shown that alprazolam use is connected to poor and risky decision making. Lane and colleagues (2005) found a dose-related effect on risky decision making in 16 dose naive adults administered varying doses of alprazolam. The highest dose was associated with a higher probability of consecutive risky responses as well as novelty seeking on personality scales.

Experimentally, alprazolam use has been associated with increased aggression to provocation in humans (Bond, Curran, Bruce, O'Sullivan, & Shine, 1995) and in social conflict between laboratory animals such as mice (Votava, Krsiak, Podhorna, & Miczek, 2001) and rats (de Almeida, et al., 2008). When alprazolam was combined with alcohol, this combination was found to increase aggressive behaviour in humans (Silvieri, 1993). Interestingly, immediately following the experiment, alprazolam use alone was found to decrease anxiety but not hostility in these subjects.

Very little information, if any, exists regarding the associations of alprazolam use and crime and any causal connections between the two. In fact, to date very little data is present showing the connection of alprazolam to crime.

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Almost all of the BZDs had been used illicitly with levels ranging from 84.4% for nitrazepam, to 97.4% for alprazolam. Diazepam and temazepam recorded the largest rates of prescribing, with 79.3% and 65.8%, respectively. These were considerably higher than the prescribing rate for alprazolam (38.5%). The BZDs were acquired both licitly and illicitly as shown in the table below: for BZDs sourced generally, in the last 6 months prior to crime and the source of alprazolam in the last 6 months prior to crime.

In the sample, thirty participants reported using alprazolam of which the majority reported using alprazolam both as prescribed and not as prescribed. Although some BZDs were sourced through prescription for the treatment of real symptoms, a large percentage was sourced illicitly; with much of the supply sourced through friends or the streets. Some participants had sought criminal means of obtaining BZDs, namely pharmacy theft (16.9%) and prescription fraud (22.9%). Alprazolam was mainly sourced from purchase on the streets (66.2%) or sourced through friends and partners (74.5%). Very little to no criminal activity, such as prescription fraud and pharmacy theft, was reported as used to obtain alprazolam.

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1. The drug-crime link
   This section examines drug use patterns a month and 24 hours prior to the index crime as well as analyses the various characteristics of participants (including mental health issues) and how these may serve as indicators for the drug-crime link.
2. Use of alprazolam on the day of the index offence
   This section investigates the pattern of alprazolam use prior to the index crime. Analysis also includes the relationship between alprazolam use and characteristic traits of users and non-users.
3. Alprazolam and the drug-crime link
   Qualitative thematic analysis of the in-depth interviews of alprazolam users is provided and compared to the information extracted from KE interviews.

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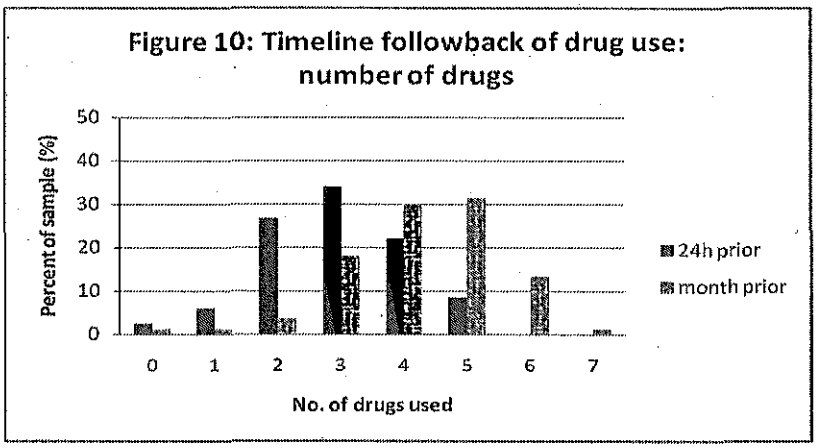
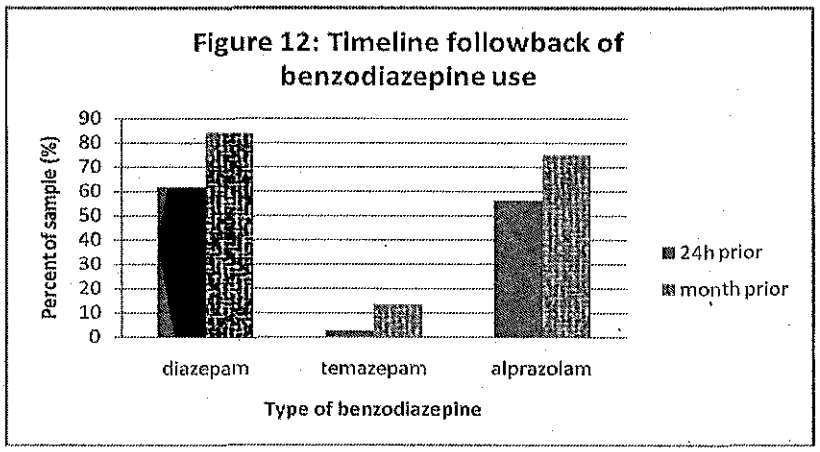
(i) Drug use and crime:

The following figure shows the pattern of drug use in the month and 24 hours prior to the crime event:



The drugs used most commonly in the month prior to the crime included: tobacco (95.2%), diazepam (84.1%), alprazolam (78%), cannabis (77.1%), heroin (75.6%) and alcohol (63.9%). In the 24 hours prior to the crime, the most common drugs used were: tobacco (87.5%), cannabis (61.7%), diazepam (61.7%), alprazolam (58.5%) and heroin (55.6%).

Diazepam and alprazolam were used by more of the sample both the month (including the previous 24 hours) and 24 hours prior to the crime event with diazepam levels at 84% for the month prior and 62% the day prior and alprazolam levels at 75% and 56% respectively (compared to 13% and 3% for temazepam).



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1.1.2 SUMMARY OF FINDINGS:

The data show:

1. Weak associations between alprazolam use and pattern and type of offending;
2. Mental health status had no effect on the alprazolam use and crime;
3. Street purchasing of alprazolam was much more strongly associated with alprazolam use around the time of the offence.

1.1.3 DISCUSSION

Of the 64 individuals who reported using alprazolam in the month before the index offence, 48 (75.0%) reported that they had used alprazolam in the 12-24 hours prior to the index offence. On average, participants reported using a mean of 13.2 mg (±20.1mg) on an average of 10.9 days (±11.0) in the month of the offence.

There was no relationship between the type of offence and the pattern of alprazolam use in the previous month – violent crime was slightly more common in those who had used in the month but not the previous day (25.0%) than those who had used in the previous 24 hours (16.7%) but this is not significant. However, while there was no relationship between the groups in terms of likelihood of receiving a prescription for alprazolam (fake or genuine symptoms) those who had not used in the previous month before the offence were much less likely to have bought alprazolam on the street (50.05% compared to 81.3% of both the last month and the last 24 hour groups; $\chi^2 = 7.20$, $p<0.05$). In other words, street purchasing of alprazolam was much more strongly associated with alprazolam use around the time of the offence.

Finally, there was no difference in the typical dose of alprazolam used between those who did and those who did not use it on the day before the offence.

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1.1.4 DATA:

In Table 14 below, alprazolam users are split into three groups on the basis of their use around the time of the index offence:

- People who had not used alprazolam either on the day before or in the month before the offence (no alpraz group)
- People who had used alprazolam in the month but not the day before the offence (no current alpraz group)
- People who had used alprazolam in the 24 hours before the offence (active alpraz group

Table 14: Relationship between alprazolam use at the time of the offence and key indicators

Variable	No alpraz group (n=18)	No current alpraz group (n=16)	Active alpraz group (n=48)	F significance
K10	33.6	37.9	33.7	0.39
HSUT total	7.7	12.8	7.3	1.21
UPPS total score	103.7	107.2	105.9	0.09
MH diagnoses	1.8	2.8	2.2	1.21
No drugs used in prior month	3.2	4.8	4.6	12.88***
No drugs used in 24 hours before	2.2	2.6	3.3	8.67***
No of treatment types	3.0	4.1	4.4	3.20*
SDS BZD	19.4	6.6	7.4	3.76*

Key= * significance $p < 0.05$, *** significance $p < 0.01$

1.2 Alprazolam and the drug-crime link

1.2.1 SUMMARY OF FINDINGS:

In summary:

1. Most alprazolam users are polydrug users, using alprazolam in combination with alcohol and other drugs.
2. The main reason for using alprazolam is for relief of symptoms of anxiety and depression and to assist with amphetamine withdrawal.
3. Many use alprazolam to improve the effects of heroin.
4. The negative effects of alprazolam are reported as memory loss, and seizures related to alprazolam withdrawal.
5. Shop theft appears to be the most commonly reported crime related to alprazolam use with crimes of violence reported less commonly.

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1.2.1.1 Reasons for taking alprazolam

For the majority, first use of alprazolam for this group of participants was non-prescribed. In some cases, alprazolam had been prescribed by a doctor for genuine symptoms of mental health conditions, however for this group, it was typically after trying alprazolam illicitly and recognising the benefits of use in regards to relief of symptoms.

"Yeah someone offered it to me and yeah I took it...I get anxiety and depression anyway and someone offered it to me and yeah I took it.....It didn't get me pilled or anything, but it took away the uncomfortable effects of the anxiety".

Anxiety was cited by 11 participants as reason for using alprazolam. Whether anxiety had been caused as a result of withdrawal from other drugs i.e. heroin or amphetamines or there was diagnosed post traumatic stress disorder (PTSD), depression or anxiety, alprazolam was reported as assisting with symptoms of these disorders or the effects of withdrawal.

"Because it's a pharmaceutical drug it did improve things for me. It made me stabilise emotionally and psychologically so it was beneficial, it was very beneficial".
"Yeah, it basically took away all the anxiety and stress."

According to KE's, anxiety was also cited as the most common condition for BZD use, both prescribed and not prescribed. And for those prescribed alprazolam in particular, good effectiveness for the management of anxiety was noted.

Sleeplessness in some cases was improved with the use of alprazolam and increased ability to sleep post amphetamine use was reported.

"And then I realised how beneficial they are to me because I've got a lot of anxiety, I've got a sleeping disorder, I turn my head like this and I can't sleep, I've had that all my life."

Some give an account of use of other BZDs, for example, Valium, Serepax or Rivotril and discovered that by using alprazolam they were able to relieve symptoms by taking fewer BZDs.

"Yeah, so after a couple of years it just stopped doing what it was doing and like something, instead of me using like five or 10 at a time, they started prescribing Xanax"

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12 of the 16 qualitative interview participants claimed that using alprazolam enhanced the effects of heroin. It was often cited that alprazolam would be taken prior to using heroin and this would improve the outcome; it was stated that it was cost effective to use heroin this way and the participant would get better value for their money. And that poorer quality heroin could be improved by using, for some as little as 1mg of alprazolam to increase the effect. For those obtaining their alprazolam with prescription, the cost could be as low as $5 per 50 tablets and if purchasing from the street, $5 per pill. This was confirmed by KE's stating that BZDs were used with heroin to supplement or enhance the effects or to deal with periods of withdrawal.

"Yeah, yeah so instead of buying four caps I can buy one and get the same result. "
"I have a few before I have a whack of heroin, I have a few before I have that because it makes me go on the nod more and yeah it makes me feel the heroin more"
"It increased the effects of the heroin basically so if I was using $300 worth I could use $50 or $100 and have a few Xanax and feel more of the effect"
"Yeah the heroin is not as strong as it used to be so that gives it a bit of a kick".
"..the gear [heroin] wasn't getting me stoned without the pills"
"I don't really like it [alprazolam], it just enhances the heroin"

Alprazolam, for this group of participants, was generally used to relieve the symptoms of anxiety and increase the effects of heroin.

1.2.1.2 Memory loss and crime

A definite recurring theme for this group is memory loss. Alprazolam used on its own in higher than usual doses or combined with other drugs or alcohol can cause memory loss ranging from hours to days, to not ever being able to recall situations according to participants.

This memory loss can be related to involvement in crime. Participants claimed they would do things that they would not ordinarily do, except when using alprazolam. They recounted becoming 'confident' or 'careless' about committing crime. The respondents appear genuine in their discussions about memory loss and crime. Although it seems common knowledge among this group that gaps in memory can be a frequent event when using alprazolam, in relation to their own stories, some seem surprised by their actions.

Often this group have a lack of insight into their involvement in crime, having 'blinkers on' and courage to commit crime in situations that may be precarious and without regard to the potential consequences of their actions.

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Interviewer: Have you had any total black outs?
"A whole night at one stage, this whole night that all this trouble happened we'd been on them for about four or five days yeah and it's just sort of..".
Interviewer: So is that when you did the burglary?
"Yeah because I remember the whole day but just, this is why I just don't remember it."
Interviewer: So you were helping your partner with the crime?

"Yeah I got charged for two burglaries and two thefts"
Interviewer: Over what period of time?
"Over 36 hours."
Interviewer: Have you ever gone that hard before?
"No, this has like scared me this time so I haven't used since, not anything."

Amnesia or memory loss was reported across almost all the KE interviews as an issue specifically associated with alprazolam. From this perspective, memory loss linked with alprazolam was often framed in a high dose picture.

"..the effects of having high doses of alprazolam are periods of forgetfulness" **(Addiction Medicine Specialist)**

The crime sometimes does not appear to be beneficial in terms of gains and odd things are taken from stores or supermarkets with little understanding as to why.
" I can't even remember to tell you the truth; I woke up in the morning and found stupid things in my bag, like how can I put it, like things that wouldn't mean anything, like I woke up one day with like 100 cups or something, stupid stuff."

Shop theft appears to be the most frequent crime committed whilst on alprazolam. Respondents claim loss of inhibitions and the feeling of 'being invisible' after alprazolam use which results in crime.

"No, no not that I'm aware of. I would have known. Oh actually, yes I did. One of the first times I took alprazolam I found myself with a bag full of shoplifting from a chemist which I couldn't recall. There we go, yep. Thanks for saying that one that reminded me".

Crime associated with violence was not commonly reported and this was confirmed by KE's. Violence following the use of BZDs was generally reported as the rare end of the spectrum. Minor fights were reported by KE's as unplanned, impulsive behaviour associated with intoxication. When violence was reported it was generally discussed in the context of disinhibition and sudden rage with memory loss.

"The other typical situation is like violent offending where someone has just randomly assaulted someone and again it is associated with 'I don't know what went on there it is to do with the pills that I took earlier'...cos sometimes there is no history of violence whatsoever in their background then this has happened and y'know it's random and unprovoked and it's weird" **(Lawyer)**

"Well I did, like a couple of times I might have like gotten really angry and punched the wall really hard and then hurt myself from it. So just certain things like that. I've never really been too violent but at a time when I took Rivotril and alprazolam together the next day I know my girlfriend at the time, I think she threw away my, the other Rivotril I had left over for the next day and that made me so angry that I trashed my own apartment and made a big fuss about it, the police were called and I was acting really irrationally and I ended up getting capsicum sprayed and arrested for the night. Luckily it was just for the night and they realised, I realised it was just a silly mistake that I made because I was on drugs and luckily I didn't get put in jail for any longer for that but yeah, I did get a one year CBO as a result from that sort of incident. So that was basically how I paid the price for the silly mistake I made with the irrational thinking and the aggression that it bought out afterwards."

"Yeah, it happened to me...I told you when I took the Alprazolam and I broke into the car all that, that caught up with me, I got charged with that and that night I was with another friend and I can't remember what happened with him and I woke up on the train in [train line], in the middle of nowhere in the last train and I got stranded in [suburb] yeah, I don't even know what I was doing on that train line...and yeah so."

"I was pretty run down and I was getting a haircut actually and the next minute I woke up on the ground and I smashed my head on the table, It may have been a seizure or something, but I was taking a lot of alprazolam at that time".

Interviewer: So why do you think that alprazolam is associated with crime, do you have any, well for a start do you think that it's true and do you have any opinion...?
"I spoke to one of my workers about this, it's weird 'cos I know some people take alprazolam that like they might abuse them too but they won't get up and go out and commit crime like for example, I was saying to my worker about it, just say I took five and my worker took five, he's not likely to go out and break into cars you know, I don't know if it's because, I don't know, it's weird. Yeah some people will take them and go home and watch telly and others will go out and commit crime or whatever, I don't know if that's because they think committing crime is like a familiar road...and yeah".

Both major and minor theft and shoplifting was consistently reported in connection with alprazolam intoxication across almost all KE and participant interviews. The theft was reported as opportunistic, impulsive and unplanned often associated with memory loss for the event and a lack of awareness of surroundings. It was often reported that items were stolen that were not needed (in comparison to pre-planned theft for money associated with heroin use).

1.2.1.3 Case studies

Case 1: Male, age 32
Unemployed in the month prior to the crime and his main source of income was criminal activity.

The participant was most recently charged with theft. He rates his memory as 2 on a scale of 0-10 (0 = very poor, 10= excellent) for memory or recall for this crime event.
"I got pulled over in a stolen car and I can't remember much of it.....I was that messy I wasn't my normal cautious self..... I can't even remember getting pulled over, I can't even remember getting interviewed until I looked at my interview tape".

The participant had taken heroin and alprazolam prior to this crime. In the month prior to being caught for this crime, he was committing daily property crime, dealing more than once per week and committing fraud less than once per week.

The participant first tried alprazolam at age 30. His reason for trying alprazolam was that he would try anything and everything. On this first occasion, he had 2mg of alprazolam combined with heroin describing a 'messy' effect. Elaborating on this 'messy' effect, he said he would become forgetful, commit crime and have no memory or care about anything. He feels alprazolam directly contributed to this due to having 'blinkers' on.

His preference when using alprazolam is to take 1mg with heroin to enhance the effect of the heroin.
The participant has never been prescribed alprazolam. He tried once to get it from his regular doctor, but as he was already being prescribed other BZDs, his GP refused to prescribe anything stronger. Consequently, alprazolam was always given by a friend or purchased off the street.

He claims there have been no physical or emotional benefits from taking alprazolam and no side effects from withdrawal.

His Kessler 10 score for psychological distress was rated as moderate mental disorder for the month prior to the crime. He has been diagnosed with depression, anxiety, attention deficit hyperactivity disorder and drug induced psychosis.

Although this participant has never previously had treatment for his alprazolam use, he considers the main reason for stopping as his most recent arrest, jail and the current court ordered treatment he is receiving. This participant has previously been treated for heroin use but never for his alprazolam use.

Case 2: Female, age 29
Unemployed in the month prior to the crime and main source of income pension

This participant's most recent crime was theft. She rates her memory of this crime as 0 on a scale of 0-10 (0 = very poor – 10 = excellent).
"I've got no recollection of it, only what the cops told me."
"Like we all say, there's a pinch or two in every bottle, because we don't know what we're doing and we can't remember, we think other people can't remember and they don't care"

In the 12 to 24 hours prior to the crime, the participant had taken, alprazolam, cannabis, heroin, Serepax, Valium and Methadone.In the month prior to this crime, the participant was committing property crime more than once per week.

The participant first used alprazolam aged 17. She was prescribed 8mg twice per day by her GP after hearing about the use of Kalma (alprazolam) to withdraw from Methadone. Alprazolam has also been prescribed for panic attacks and she says it helps her to cope, she feels "confident and normal".
She has doctor shopped when unable to obtain through her regular GP. She does not purchase from the street or obtain through other sources.

This participant will often take more than prescribed and has no memory of this until the next day when she realises that the bottle is empty. Memory loss is problematic for this participant and she feels it is related to high doses.

She mainly uses alprazolam in combination with other BZDs, but has combined with heroin, speed and alcohol.

The participant thinks there are benefits for her in terms of sleep and reducing anxiety. Withdrawal symptoms have included; anxiety, depression and seizures requiring overnight hospitalisation.

The Kessler 10 psychological distress score for this participant rated her as likely to have severe mental disorder.The participant reported previous diagnoses for bipolar, panic disorder and personality disorder.

She has had previous treatment for heroin use and on one occasion she attempted a detox for alprazolam and cannabis use but didn't complete the stay. The participant was caught using drugs in detox and was asked to leave.
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1.3 Key Findings:

- Professional perception of link between BZD use and a range of offending behaviours, and alprazolam use in particular associated with problematic and risky behaviours
- Interviews with alprazolam users linked this to both memory loss and atypical behaviour that was not recognised afterwards
- The key finding of quantitative data analysis is that the sample of BZD/alprazolam users comprised two populations: (1) polysubstance users engaged in treatment, largely involved in acquisitive crime and (2) dependent BZD users who were less engaged in polydrug use patterns and more problematic in terms of elevated levels of psychological distress and mental health diagnoses.

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The findings would indicate that the majority of the sample, particularly those involved in polydrug use, had access to both prescribed and illicit BZD, but that almost none of the sample used only BZD as prescribed. This would suggest the need to examine the street access and purchasing patterns of BZD as a step towards establishing control processes. This does not diminish the need to consider increased control of the prescription of BZD and the distribution, particularly around supervised consumption options for known polydrug users. More generically, it may be appropriate to consider greater awareness raising endeavours to primary care and specialist prescribers about the

diversion and misuse of BZDs, and their potential role in criminality. This is particularly true for populations with diagnosed psychosis for whom there may be significantly elevated risks of violent offending and treatment disruption through arrest and incarceration. Additional research may be required that assesses the pattern of alprazolam and general BZD use in primary mental health treatment populations and the associations with both acquisitive and violent offending.

MPBV Bulletin June 2009.
This item has been prepared by the Department of Human Services.
Recent evidence suggests that alprazolam is more subject to non-medical use, and causes a disproportionally higher level of serious harm, than other benzodiazepines.

Alprazolam is a drug with particularly high potency and short onset of action, which makes it a preferred drug for recreational abuse. As with other benzodiazepines, inappropriately high doses can cause anterograde amnesia. Anecdotal reports suggest that among the benzodiazepines, non-medical use is particularly associated with harmful experiences such as seizures, traffic accidents and crime-related harm. Alprazolam is now the most commonly reported benzodiazepine among Australian injecting drug users who report injection of benzodiazepines.

Many witnesses giving evidence to the Victorian Drugs and Crime Prevention Committee's *Inquiry into Benzodiazepines and other Pharmaceutical Drugs in Victoria* expressed concerns that alprazolam, when used for recreational purposes, can be particularly dangerous. They commented on its highly addictive qualities. The Senior Pharmacist at Turning Point Alcohol and Drug Centre commented that for the drug-using population, alprazolam provides the effect they want. Others commented that alprazolam appears to feature more prominently in crime-related activity such as diversion and theft.

The Pharmacy Board of Victoria stated that it was not uncommon for alprazolam (Xanax) tablets (100) to be prescribed and dispensed as private (non-PBS) prescriptions and then on-sold on the street for $5 per tablet.

The Victorian Interhospital Liaison Group expressed concern that alprazolam is one of the most widely abused of the benzodiazepines and that management of withdrawal was particularly difficult.

Most recently, alarming reports from several Needle Syringe Programs (NSPs) describe the effects of high-dose non-medical use of alprazolam by their clients causing problems of anger and aggression, as well as violent and threatening behaviour, which the users do not remember the next day. During these episodes it is not possible to reason with or calm individuals. Alprazolam tablets are also known as 'angry pills'. Some NSPs report that people affected by high doses will commit crimes such as shoplifting but will be unaware of their surroundings.

When they recover in the police cells they do not remember the actions that led to their arrest. When intoxicated they appear to be more at risk of either committing or being the subject of violence, as well as of falls and other injury as a result of intoxication. There has been particular concern in Tasmania about prescribing and non-medical use of alprazolam. A circular to pharmacists in that state noted that serious injury and death has resulted from the practice of injecting alprazolam alone, or with other drugs, to produce a heroin-like 'high'.

Alprazolam should only be prescribed when there is a clear indication for its use, after taking into account the risks to the patient and the burden of harm to the community. The recommendation of the Royal Australian and New Zealand College of Psychiatrists (RANZCP) is that alprazolam has a limited role in the treatment of panic disorder and anxiety. The initial approach should be psychological measures, such as cognitive behavioural therapy. First line drug therapy for panic disorder is stated to be the newer antidepressants, particularly paroxetine and sertraline. Benzodiazepines are listed as second line therapy along with tricyclic antidepressants and the MAOI's. This approach is supported by the PBS approval, which is 'for the treatment of panic disorders where other treatments have failed or are inappropriate'.

Horyniak

Jones

Jones K, Nielsen S, Bruno R, Lubman D. 'A pinch in every bottle': expert perspectives of alprazolam use and its relation to offending. Paper 181. APSAD 2011 Conference. Drug Alcohol Rev 2011;30 (Supplement 1);47. November 2011

'A PINCH IN EVERY BOTTLE': EXPERT PERSPECTIVES OF ALPRAZOLAM USE AND ITS RELATION TO OFFENDING

KATY JONES,[1,2] SUZANNE NIELSEN,[1,2] RAIMONDO BRUNO,[1,3] DAN LUBMAN[1,2]
[1]*Turning Point Alcohol and Drug Centre, Melbourne, Victoria, Australia,*
[2]*Monash University, Melbourne, Victoria, Australia,* [3]*University of Tasmania, Hobart, Tasmania, Australia*
Presenter's email address: suzinielsen@yahoo.com

Introduction and Aims: Concerning anecdotal reports have indicated a link between alprazolam (Xanax, Kalma) use and crime. Despite its clinical effectiveness as an anxiolytic, emerging evidence suggests that alprazolam may be associated with criminal activity such as theft, disinhibited behaviour, aggression and violence. This study aimed to understand the relationship between alprazolam use and crime and the gaps in treatment.
Design and Methods: Key experts (n = 20) in criminal justice, primary health and drug treatment sectors completed a qualitative interview, investigating two broad themes: impacts of benzodiazepines on treatment, and on offending. Alprazolam was of specific interest but discussion of other benzodiazepine use and harms was also of importance. Verbatim interviews were analysed using thematic analysis informed by previous literature.
Results: Alprazolam was perceived as causing more harm and having higher levels of abuse than other benzodiazepines due to its rapid onset and sedation effect in high doses. Alprazolam abuse was most commonly associated with shop theft and burglary, with some reports of violence, disinhibited and uncontrolled aggression. Alprazolam was reported to be associated with re-offending behaviour, unplanned crime and anterograde amnesia. Widespread availability and over-prescription of alprazolam were commonly reported. Workers across fields were concerned about the lack of specific benzodiazepine treatment, information and education.
Conclusions: Despite its clinical effectiveness for short term treatment of anxiety, alprazolam has a high abuse potential and its use may be problematic among those with existing alcohol or substance use disorders and criminal history. Crimes committed under the influence of alprazolam associated with memory loss and disinhibited behaviour present challenges for both sentencing and effective treatment.

alprazolam

Dr Malcolm Dobbin

Senior Medical Adviser (Alcohol & Drugs)

BZDs: useful properties

health

- Hypnotic
- Anxiolytic
- Amnesic
- Anti-convulsant

benzodiazepine treatment

health

Efficacy	**Selected**
Trials: short duration	• selected patients – exclude high risk • skilled practitioners • Hawthorn effect

benzodiazepine treatment

Efficacy Trials: short duration	**Selected** • selected patients – exclude high risk • skilled practitioners • Hawthorn effect
Effectiveness Real world practice	**Wide variability** • clinical skills • patient characteristics • drug-seeking, addiction

benzodiazepine treatment: recommendations

health

UK

Committee on Safety of Medicines, Chief Medical Officer (2004)

Themes: **short term use** (2-4 weeks) for severe or disabling anxiety or insomnia if extremely distressed

Interval dispensing

Australia

RANZCP, Therapeutic Guidelines: Psychotropic, Australian Medicines Handbook

Themes: **short term use** in broader treatment plan, caution in substance use disorder.

benzodiazepine treatment: adverse effects

health

- **Psychomotor impairment**

Ataxia, falls (hip #), confusion, memory loss,

- **Cognitive impairment**
- **Dependence**

Withdrawal syndrome – seizure

- **Caution**

Elderly, substance use disorder

Concerns about long-term treatment.

- **Dementia**

Current bzd users had increased risk of dementia (aOR = 2.71) & dementia risk reduced as the duration of discontinuation lengthened (Wu CS et al. Amer J Geriatr Psychiatry 2010).

- **Cognitive impairment**

Impairment different from acute administration. High dose long-term - poor visual-spatial ability and sustained attention. (Golobok S et al, Psychol Med 1988).

Discontinuation - improved psychomotor and cognitive functioning, particularly in elderly (Lader M et al. CNS drugs 2009).

Concerns about long-term treatment: mortality risk.

health

Belleville G.

Mortality hazard associated with anxiolytic and hypnotic drug use in the National Population Health Survey.

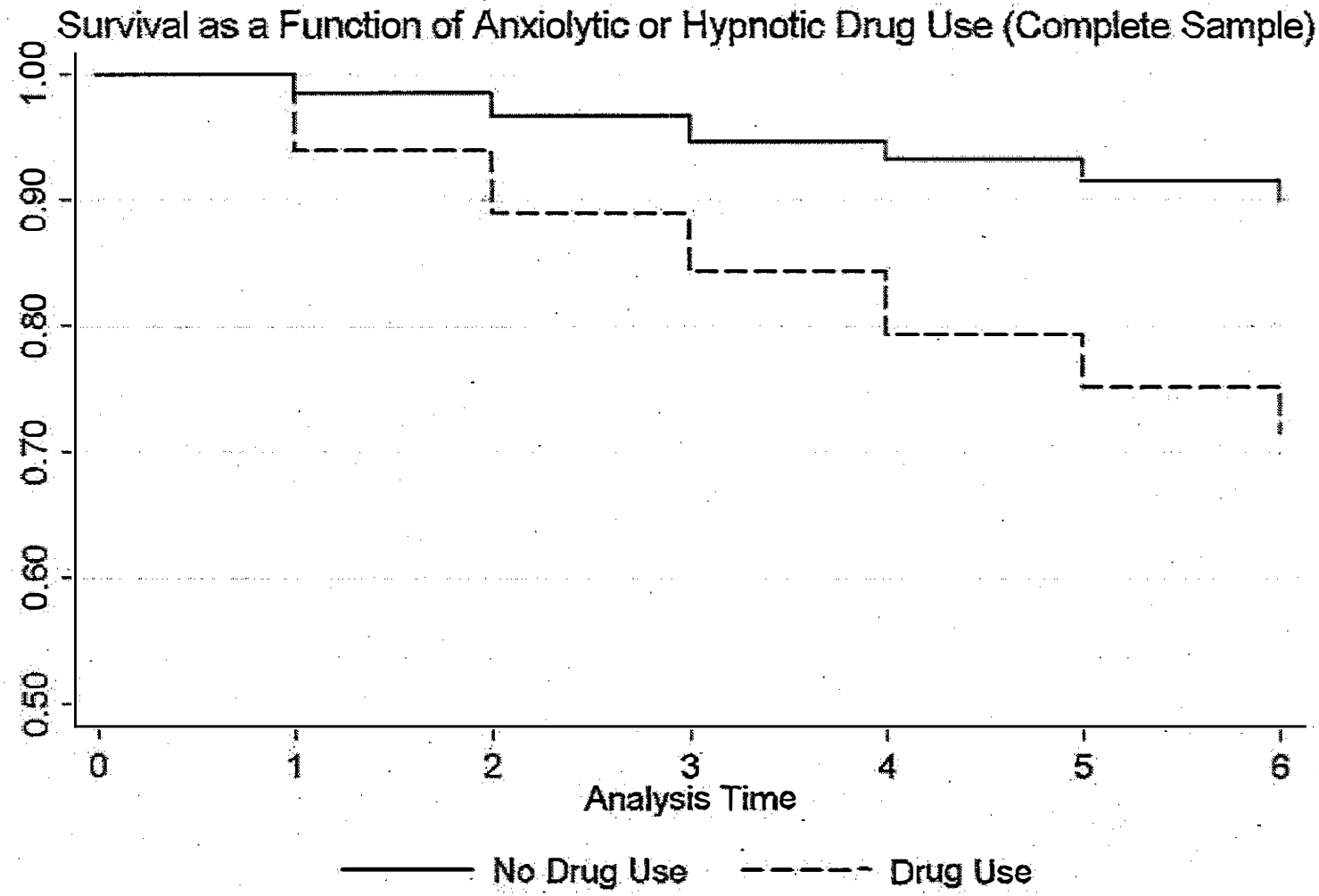
(Can J Psychiatry 2010;55:558-67).

Small but significant increase in mortality risk after adjustment (OR 1.36).

Kripke DF.

Chronic hypnotic use: deadly risks, doubtful benefits. Review article. Sleep Med Rev 2000;4:5-20.

Belleville G - survival

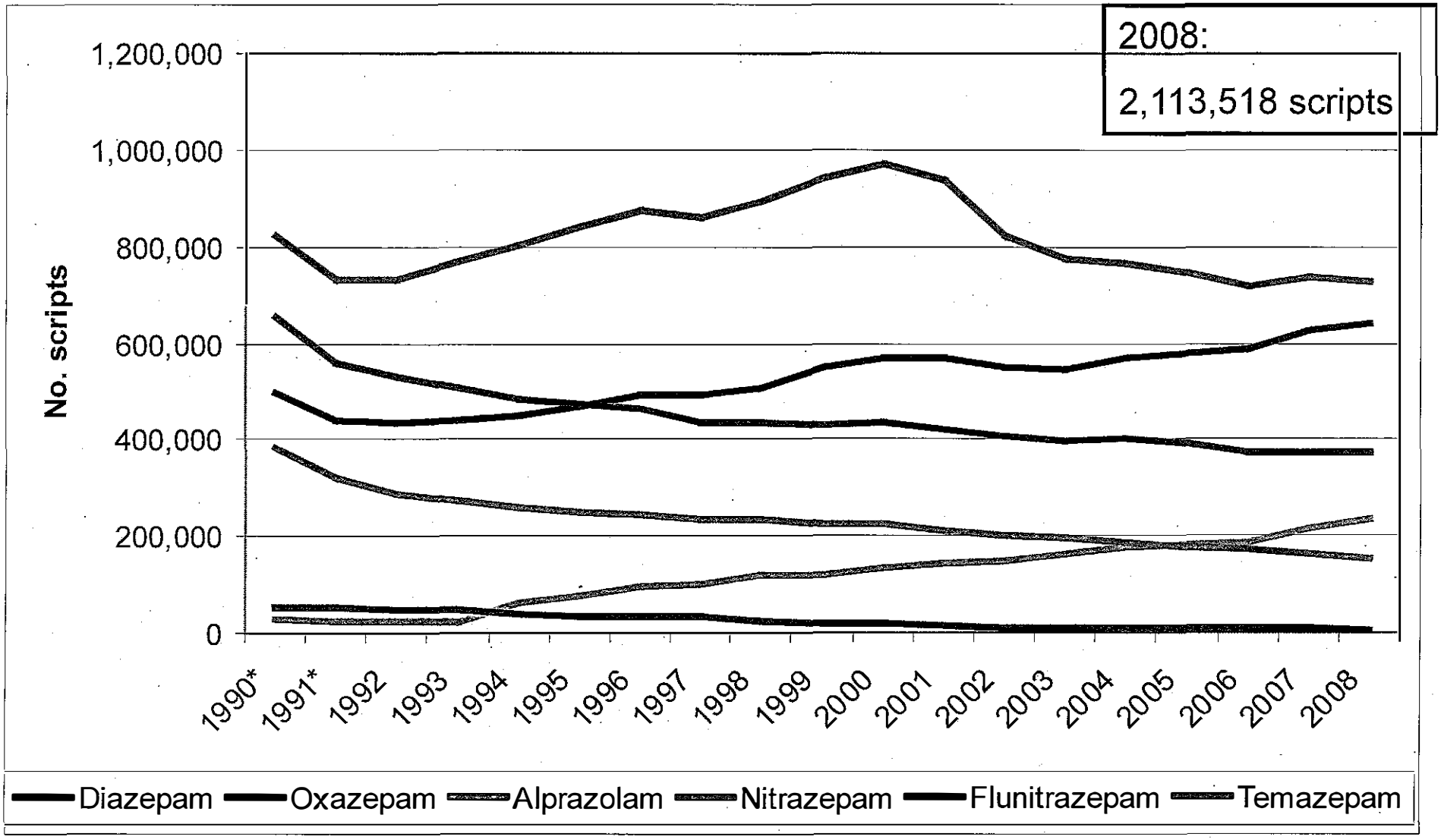


90%

~70%

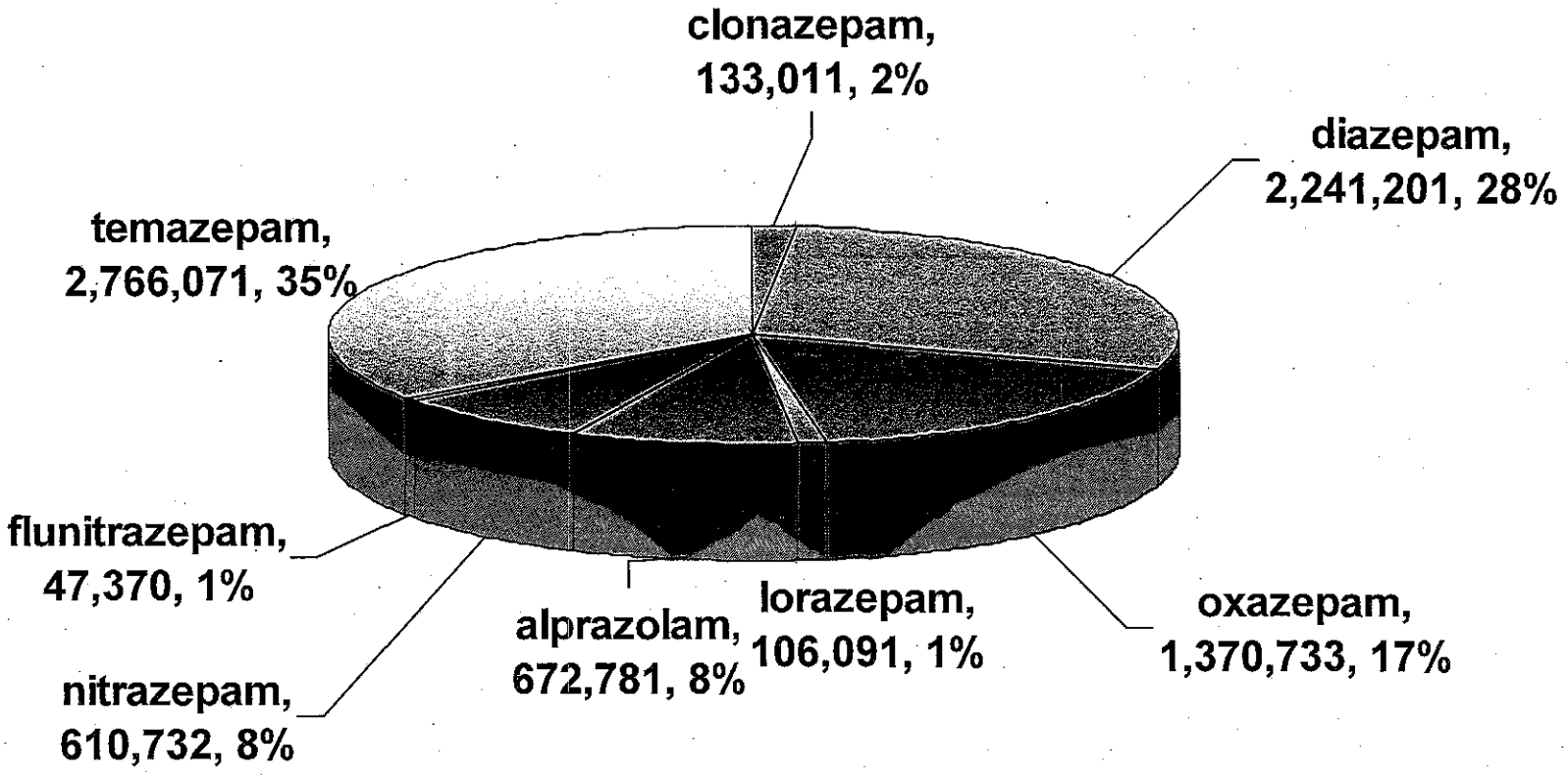
Benzodiazepine script supply: Victoria 1990-2008

health



Benzodiazepine prescriptions: Australia 2008

health

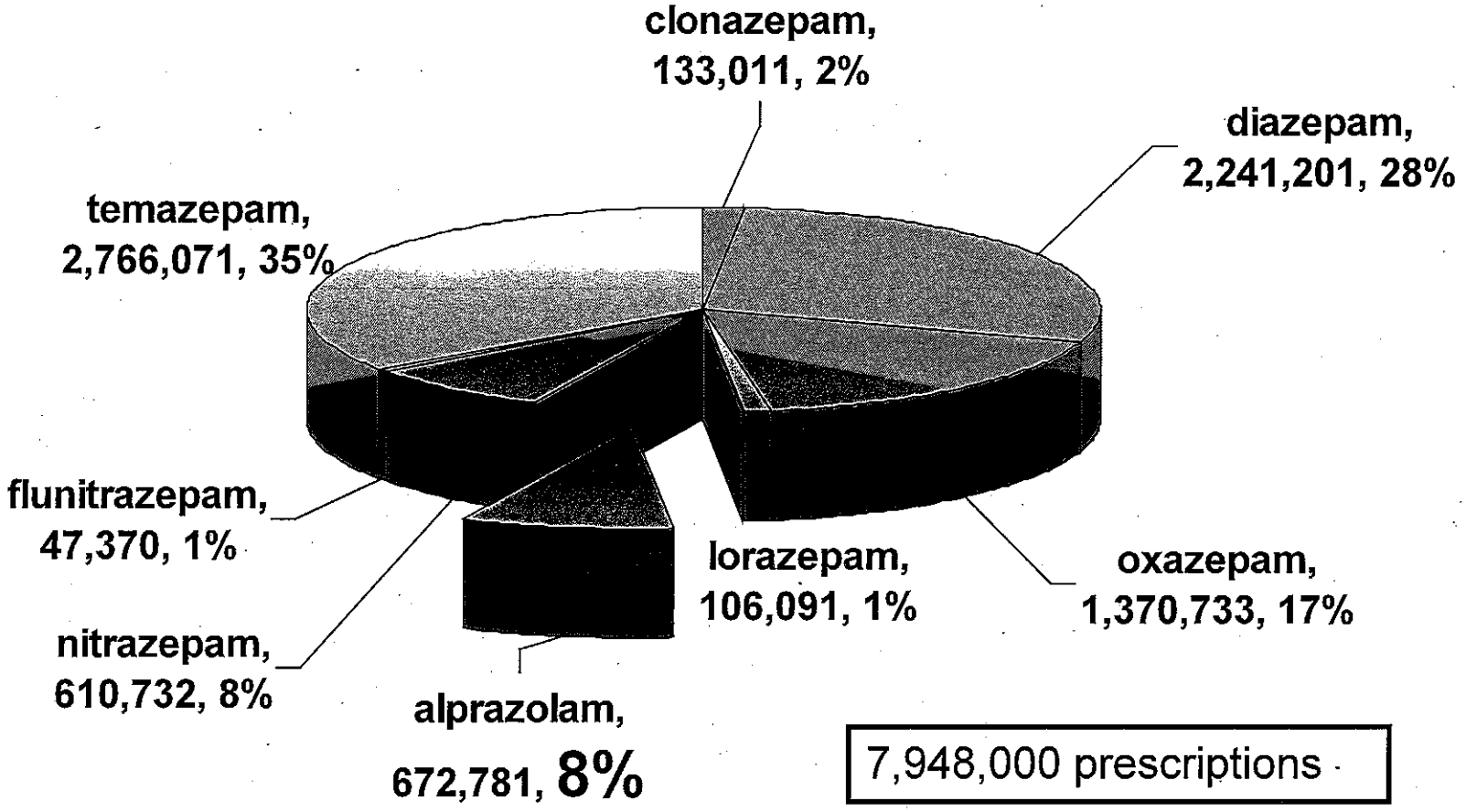


7,948,000 prescriptions

Australian Statistics on Medicines. DUSC, PBAC

Benzodiazepine prescriptions: Australia 2008

health

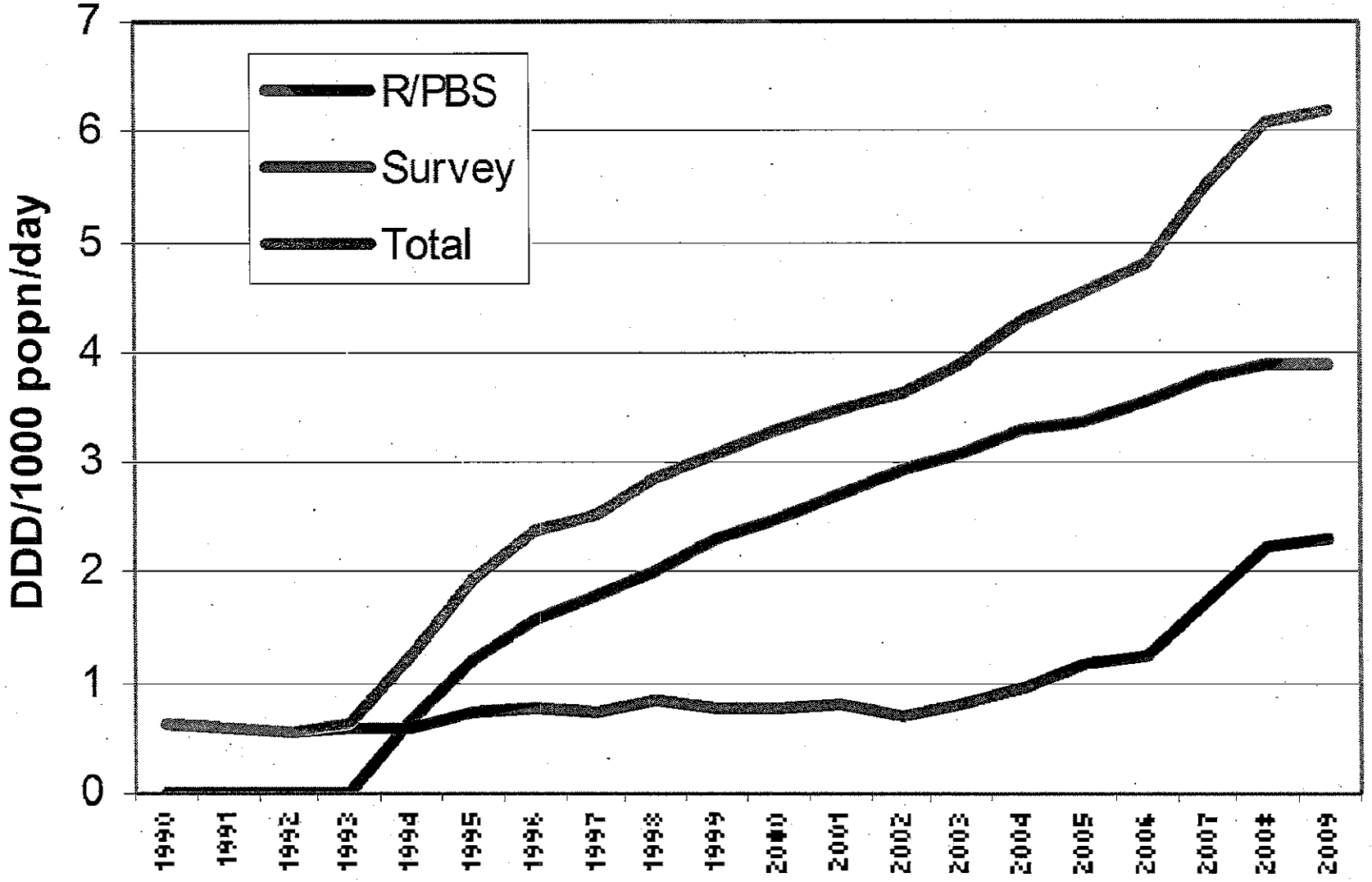


7,948,000 prescriptions

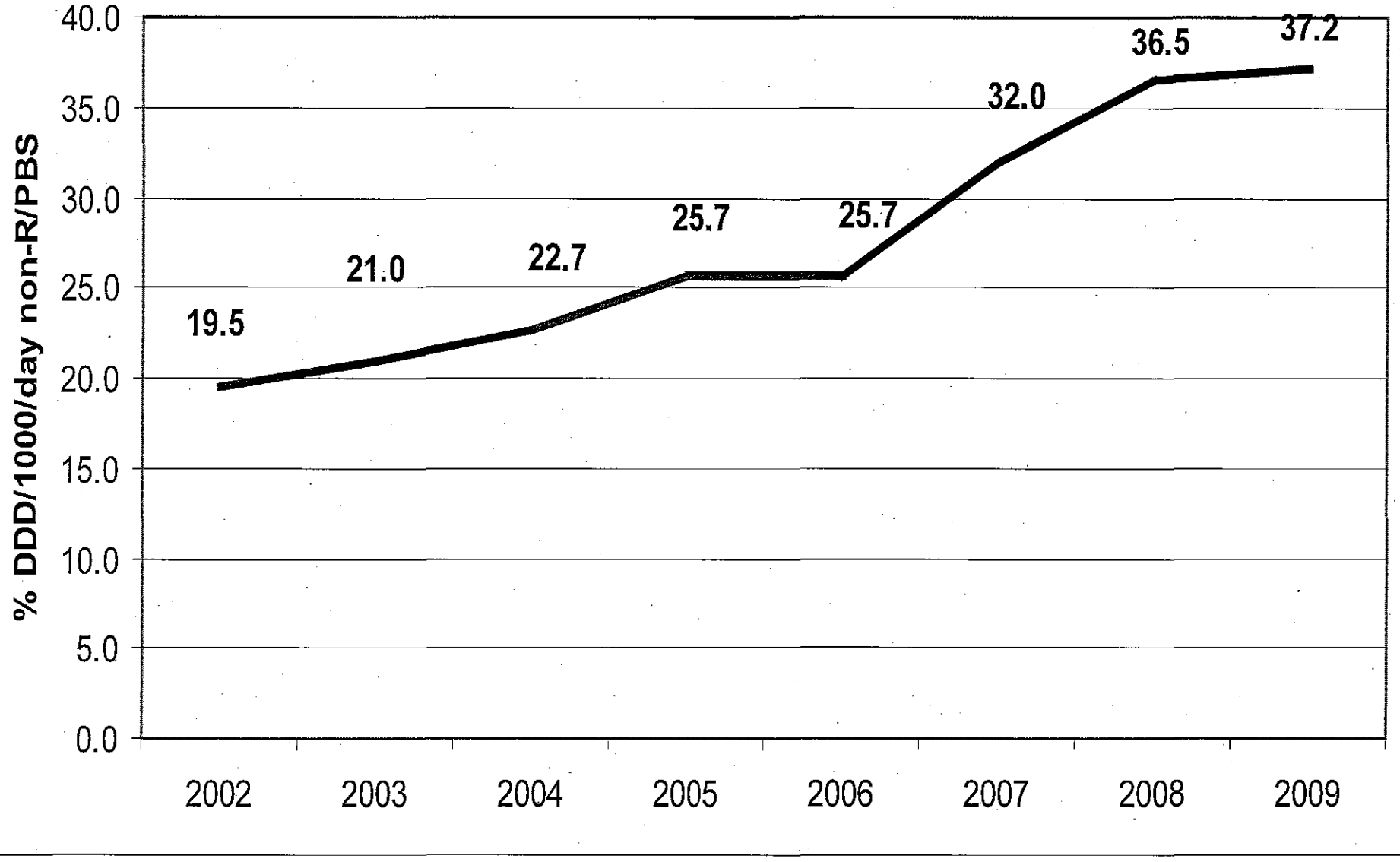
Australian Statistics on Medicines. DUSC, PBAC

Benzodiazepines

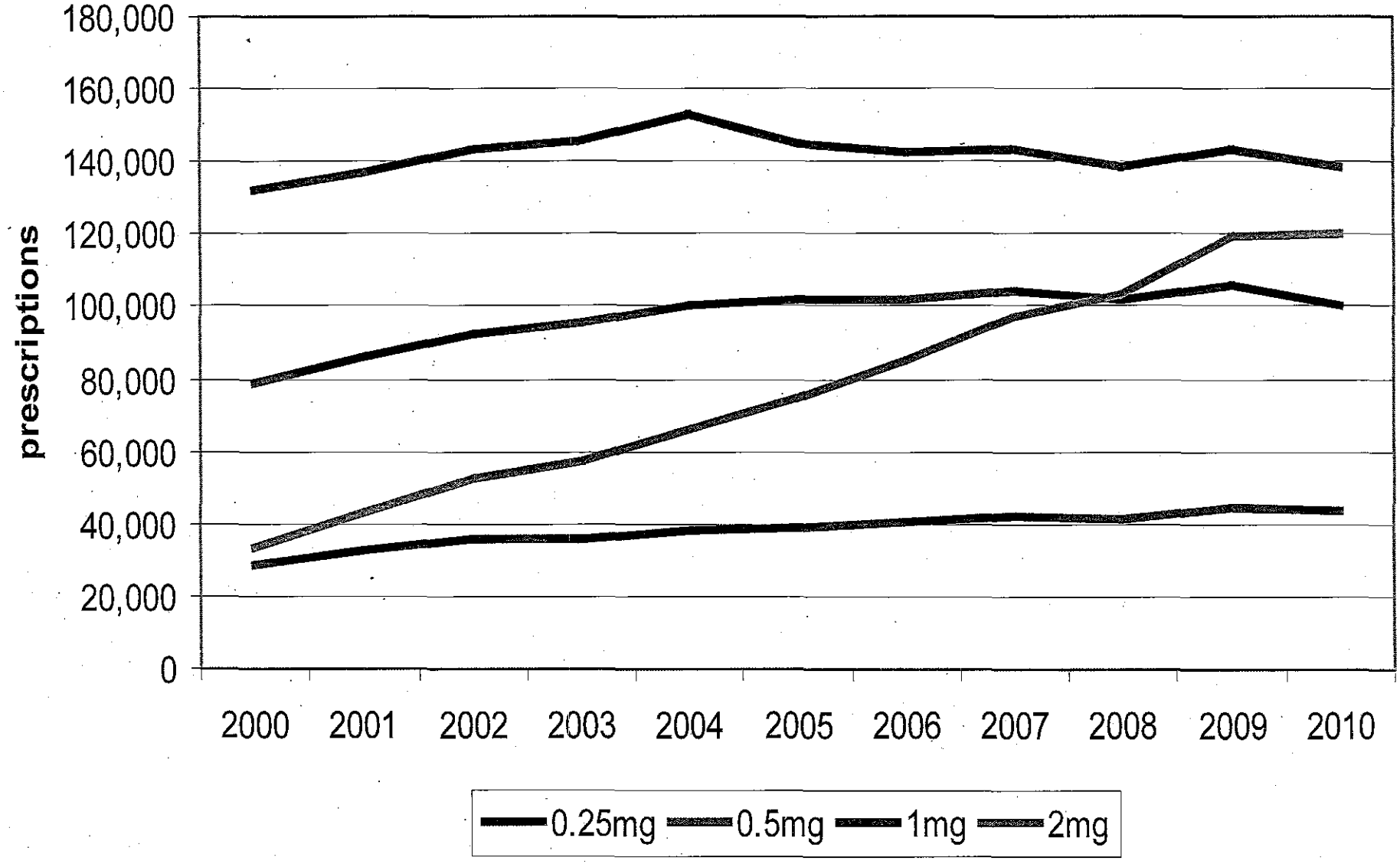
Alprazolam supply (DDD/1000 popn/day)



Proportion of alprazolam supply privately prescribed



PBS alprazolam supply: Australia 2000-2010



Alprazolam prescription rate: Victoria 1990-2010

health

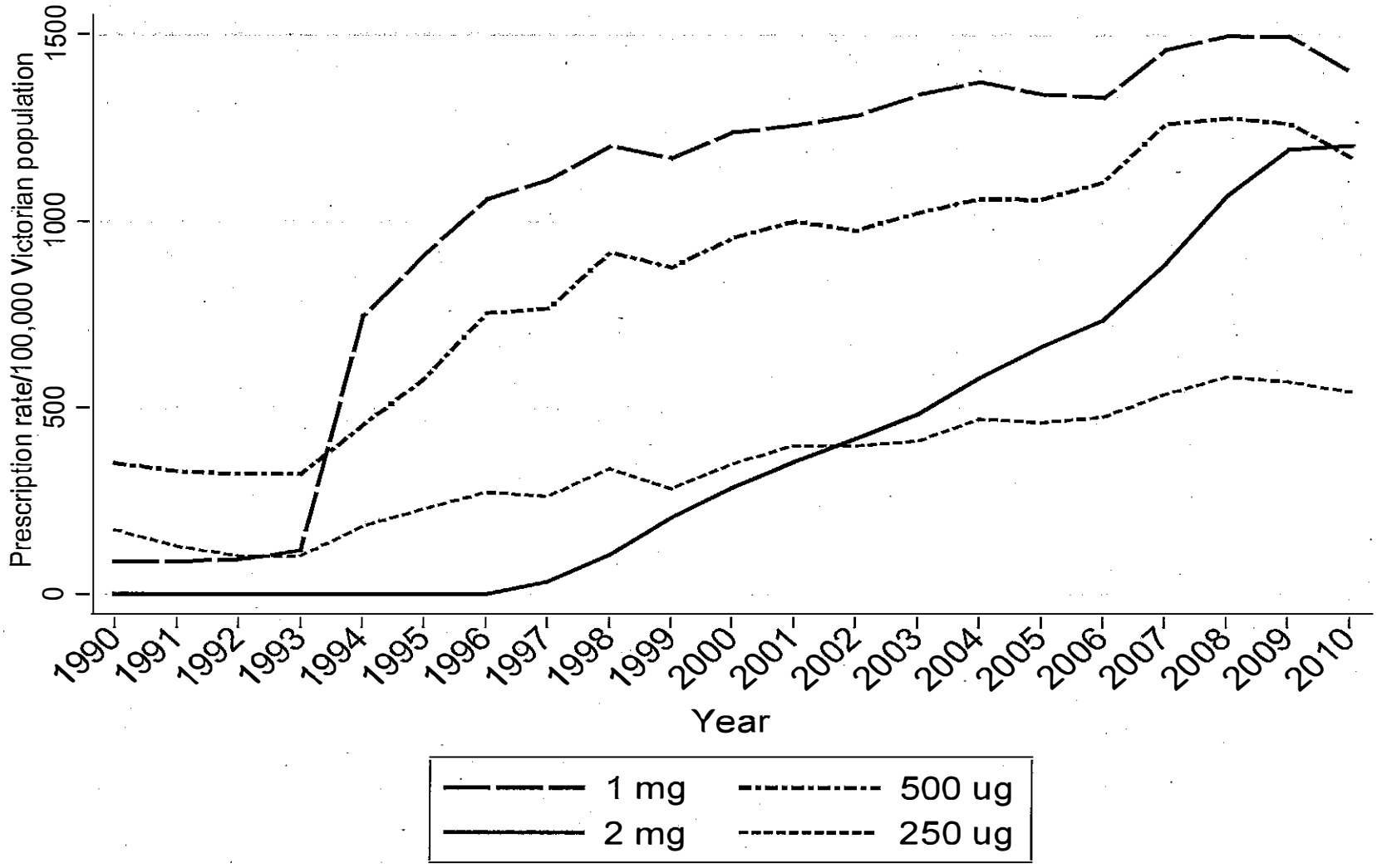
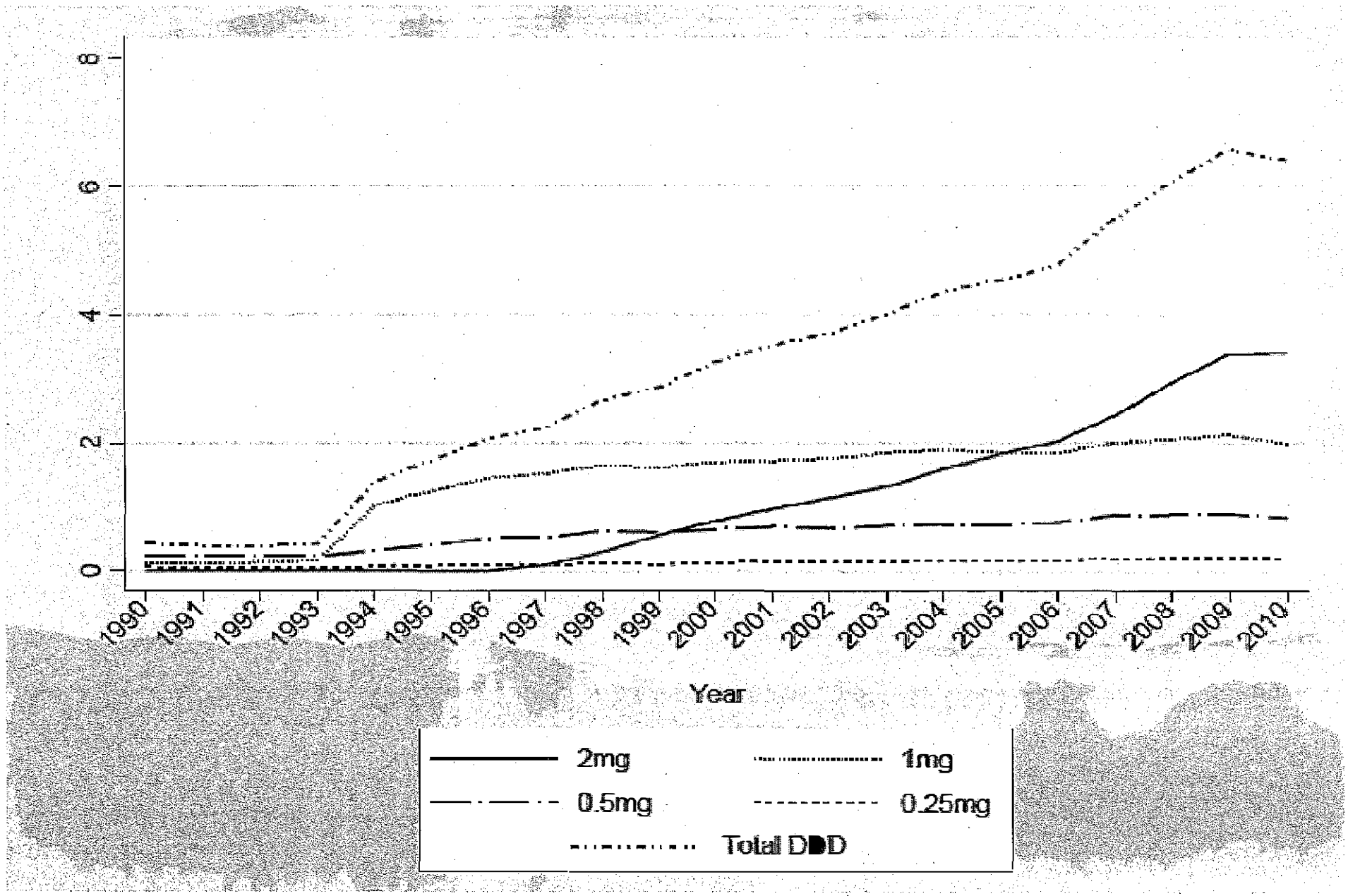


Figure 1: Estimated alprazolam DDD/1000/day by dose formulation, Victoria, 1990-2010



Harm

health

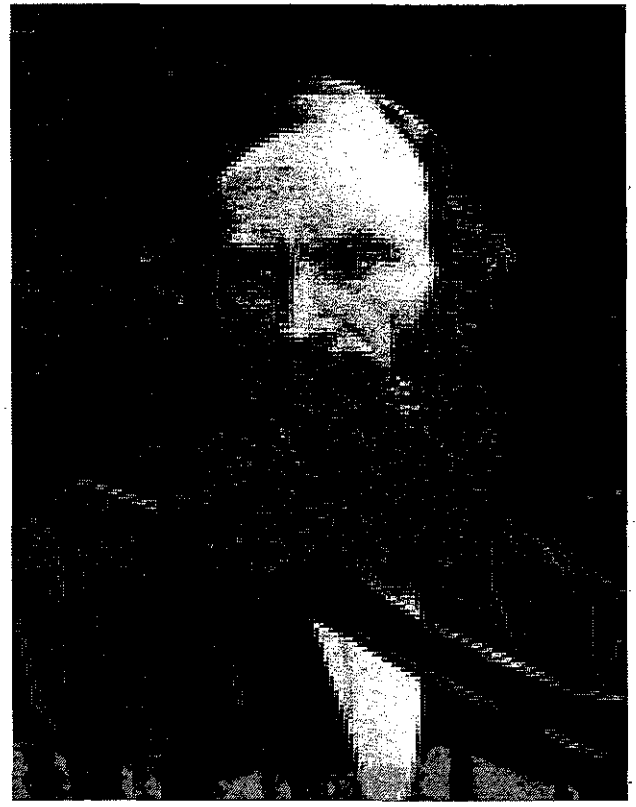
Department of Health

Quantification

health

"When you can measure what you are speaking about, and express it in numbers, you know something about it, when you cannot express it in numbers, your knowledge is of a meagre and unsatisfactory kind; it may be the beginning of knowledge, but you have scarcely, in your thoughts advanced to the stage of science."

Lord Kelvin, 1824-1907



Alprazolam harm

health

- Driving
- Misuse
- Crime
- Overdose
- Australian regulatory and other responses

Driving

health

Department of Health

Risk of road accident associated with the use of drugs: A systematic review and meta-analysis of evidence from epidemiological studies

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[a] Institute of Transport Economics, Gaustadalléen 21, NO-0349 Oslo, Norway
[b] Aalborg University, Department of Development and Planning, Fibigerstræde 13, DK-9220 Aalborg Ø, Denmark

Accident Analysis and Prevention xxx (2012) xxx–xxx

Harm	No. papers	Best estimate OR adjusted	95%n confidence interval
Fatal	10	2.30	(1.59, 3.32)
Injury	51	1.07	(0.98, 1.16)
property	4	1.35	(1.04, 1.76)

Verster et al: laboratory study

health

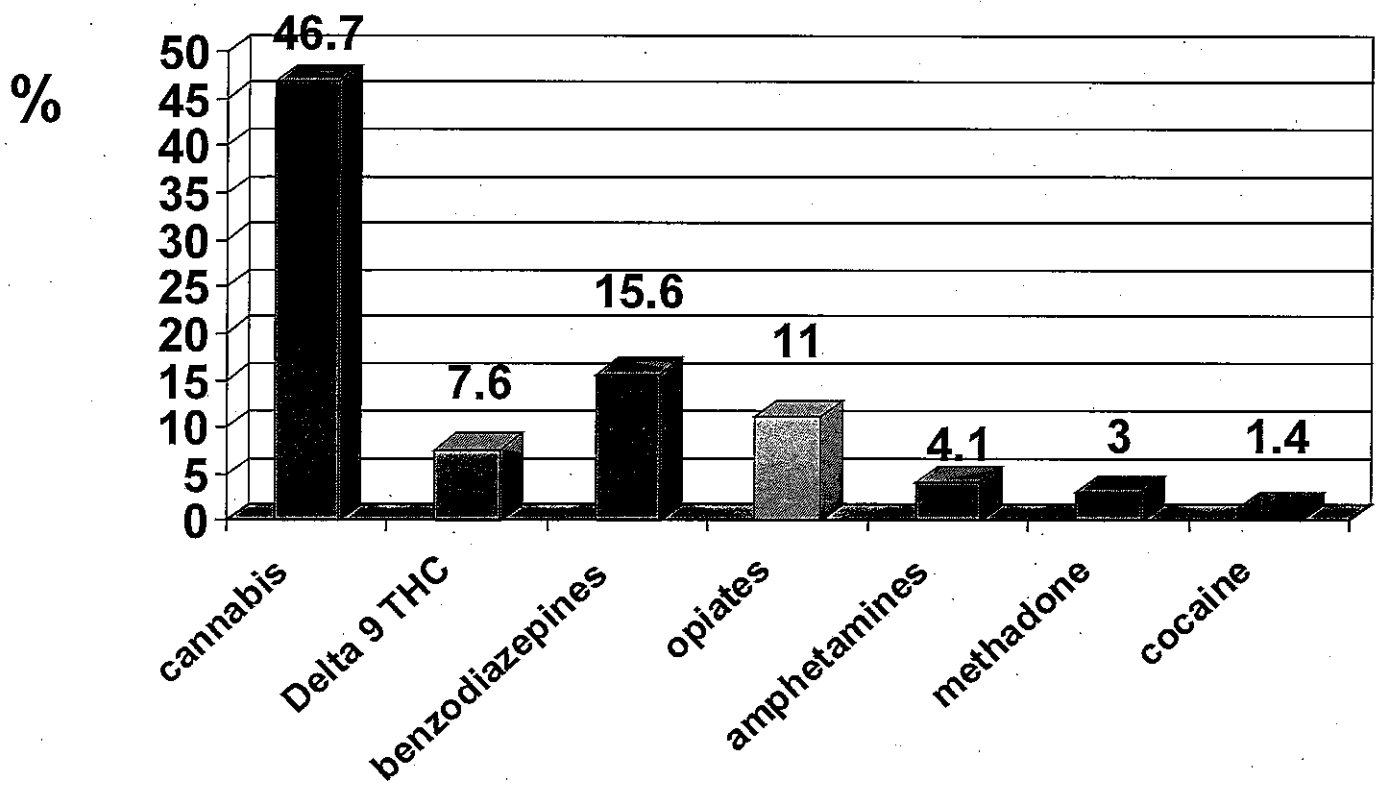
Impaired Standard deviation of lateral position:	*p <0.0001*
Impaired Standard deviation of speed:	*p <0.0001*
Impaired driving quality:	*p<0.001*
Decreased alertness:	*p<0.0001*
Decreased mental activation:	*p<0.03*
Increased mental effort during driving:	*p<0.0001*

In conclusion, alprazolam users must be warned not to drive an automobile or operate potentially dangerous machinery.

Verster JC et al. Effects of alprazolam on driving ability, memory functioning and psychomotor performance: A randomized, placebo controlled study. Neuropsychopharmacol 2002 27: 260-9

Blood samples Alfred Trauma Centre: drivers, non-fatal MVA.

health



Ch'ng CW et al. Drug use in motor vehicle drivers presenting to an Australian adult major trauma centre. Emerg Med Australas 2007;19:359-65.

Ogden EJD et al. Do minor tranquilisers (benzodiazepines) increase risk of collision in which the driver is injured?

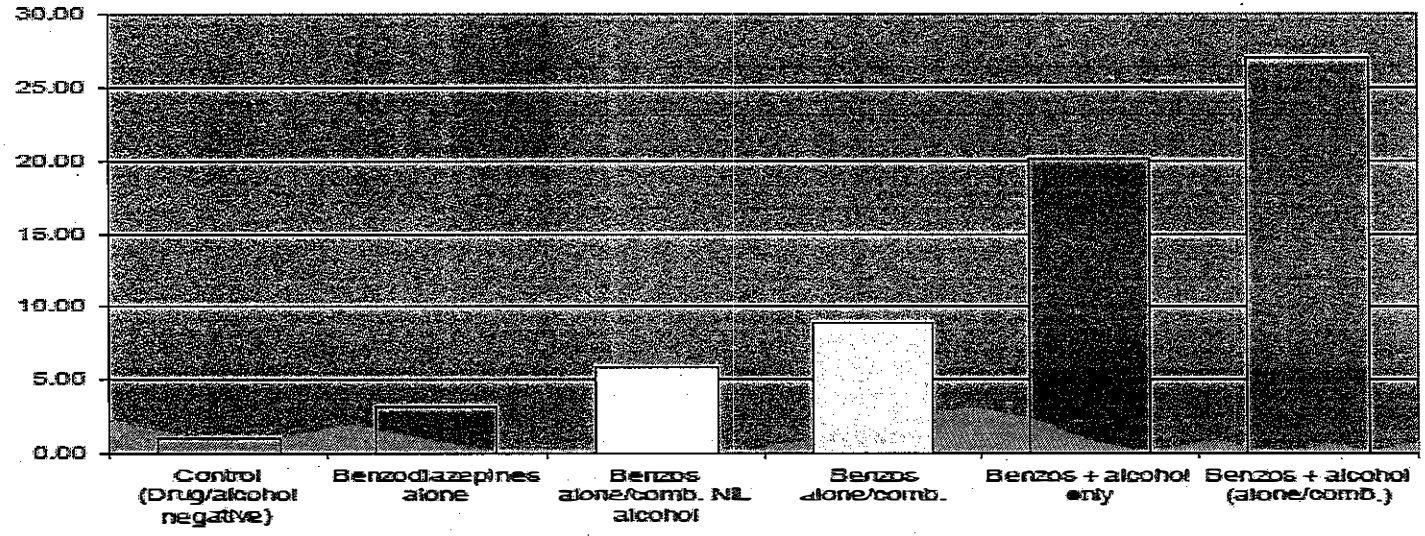
health

1802 samples

Alcohol - 96% responsibility

Benzodiazepines detected in 10.2%

Chart 4: Odds ratio of being responsible for collision by presence/absence of a BZD alone or in combination



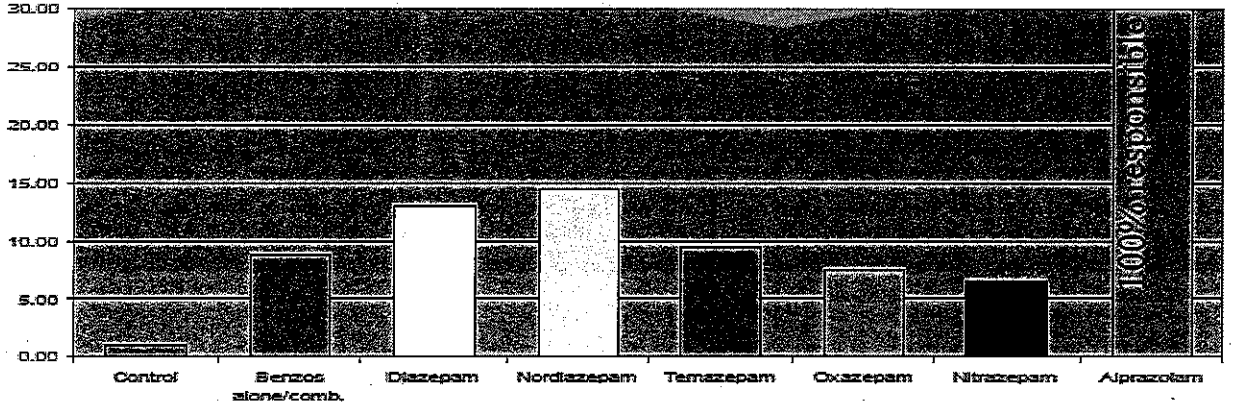
Ogden EJD et al. Do minor tranquilisers (benzodiazepines) increase risk of collision in which the driver is injured?

health

Table 4: Summary of responsibility for drivers testing positive to alprazolam

Group	Responsibility Analysis			Total
	Responsible	Contributory	Not Resp.	
Alprazolam (+/- other benzos only)	8	0	0	8
Alprazolam (+/- other drugs)	41	3	0	44
Low (<0.02mg/l)	5	1	0	6
Therapeutic (0.02-0.04mg/l)	9	1	0	10
High (0.041-0.075mg/l)	3	1	0	4
Toxic (>0.075mg/l)	24	0	0	24

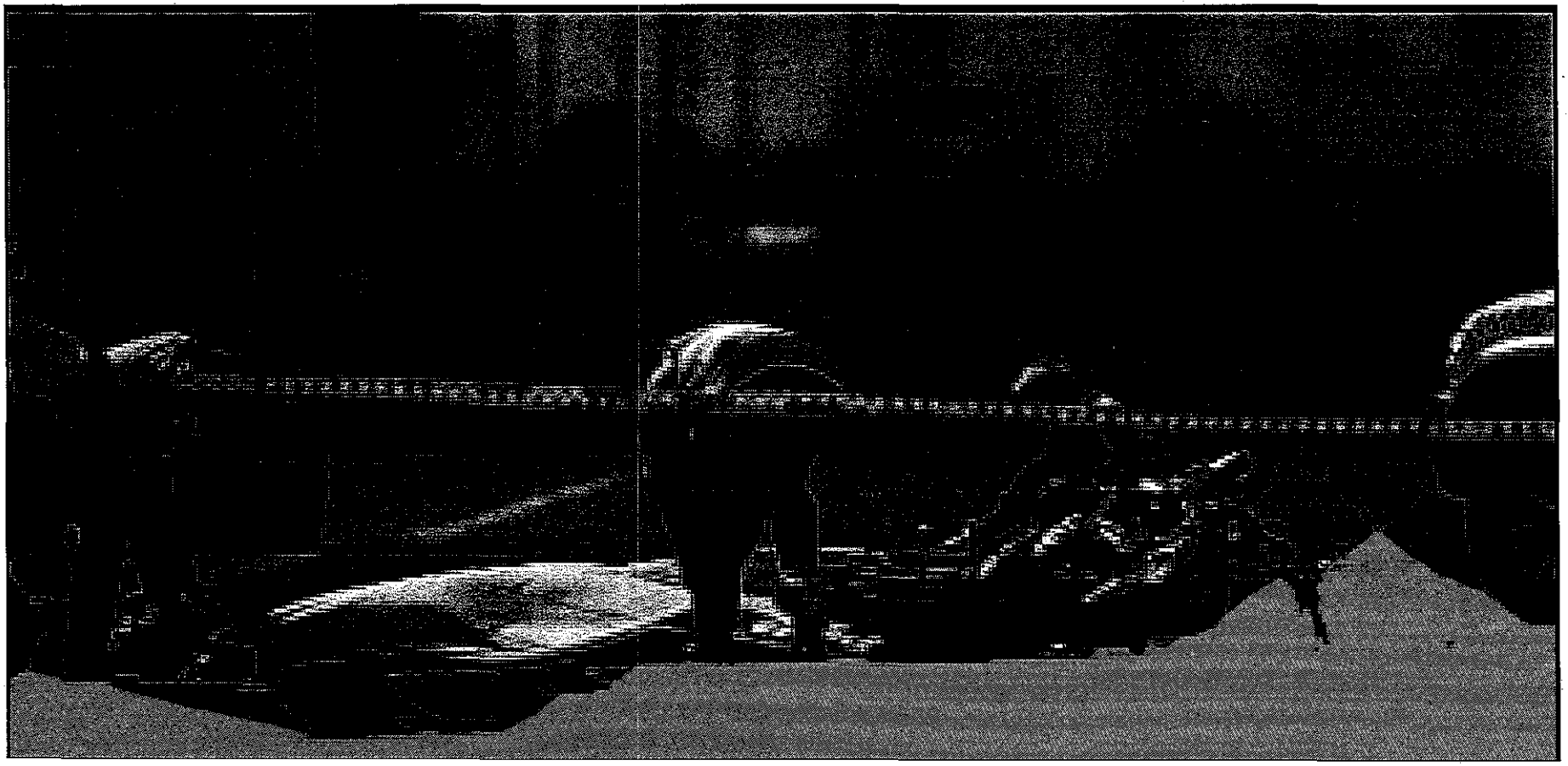
Chart 5: Comparison of odds ratios for individual benzodiazepines



Only 1 of the 44 alprazolam-positive drivers had a level of the drug considered low or therapeutic and had no other drugs in their system. Suggests taking drug irresponsibly, recreationally, or in excess of the prescribed dose.

Culpable driving

health



12 caps heroin, shot of speed 10 codeine tabs, 10 Xanax tabs

Misuse

health

Department of Health

alprazolam

health

- High potency
- Rapid onset
- Short half-life
- Discontinuation particularly difficult (serious rebound and withdrawal symptoms (Tesar GE 1990)

Chouinard G (2004) Issues in the clinical use of benzodiazepine: potency, withdrawal, and rebound. *Journal of Clinical Psychiatry* 65: 7–12.

Mumford G, Evans S, Fleishaker J, et al. (1995) Alprazolam absorption kinetics affects abuse liability. *Clinical Pharmacology and Therapeutics* 57: 356–365.

Tesar GE. High potency benzodiazepines for short-term management of panic disorder: The US experience. J Clin Psychiatry 1990;51 (suppl):4-10.

Wolf B and Griffiths R (1991) Physical dependence on benzodiazepines: differences within the class. *Drug and Alcohol Dependence* 29: 153–156.

BZD non-medical use

health

Unsanctioned use common

Heroin: 40 -100%

Alcohol: 59% (Australian ATOS)

Methadone & bup: 65-100%

Ecstasy and related drugs:29% recent use, 45% lifetime use

Preference for certain benzodiazepines

Benzodiazepine misuse harm

health

Cognitive impairment – confusion *

Amnesia – anterograde *

Contribution to poisoning ('overdose')

Aggression: paradoxical effect

Crime: 'Rambo' effect

Dependence, withdrawal

Withdrawal seizures

Diversion, trafficking

* Treatment implications

Youth beliefs

health

use was deemed common

the drug was highly addictive,

difficult to cease

medical professionals were the greatest facilitators of use

Peters RJ, Meshack A, Kelder S et al. (2007) Alprazolam (Xanax) use among southern youth: beliefs and social norms concerning dangerous rides on 'handlebars'. *Journal Drug Ed* 37: 417–428.

Vic Parliament: DCPC report 2007

health

PARLIAMENT OF VICTORIA
DRUGS AND CRIME PREVENTION COMMITTEE

INQUIRY INTO THE MISUSE/ABUSE OF BENZODIAZEPINES AND OTHER FORMS OF PHARMACEUTICAL DRUGS IN VICTORIA

Final Report

Ordered to be printed

December 2007

by Authority
Government Printer for the State of Victoria

Vic Parliament: DCPC report 2007

health

Concerns expressed by many witnesses about alprazolam

Highly addictive

Difficulty with withdrawal

More harms than with other bzds (Buykx)

Similar concerns (Swan Hill, Echuca)

Key informants: increasingly popular (Stoove)

Xanax hot new drug after removal of temazepam (Muhleisen)

Appears to feature more prominently in crime, including diversion and theft

Xanax commonly privately prescribed and dispensed and on-sold on street at $5 per tablet (Pharmacy Board Victoria)

Strong benzodiazepines particularly Xanax used for date-rape and to facilitate robberies (Youth Projects)

Vic Parliament: DCPC report 2007

health

The overwhelming consensus among alcohol and drug clinicians is that **alprazolam is one of the most widely abused of the benzodiazepines**, and that **management of withdrawal** of patients using alprazolam is **particularly difficult**.

While recognising that the scheduling of medications is currently administered at Commonwealth level, it is appropriate that the idea of **rescheduling** be raised in this document. Given the extent of abuse of alprazolam and the risks of withdrawal and overdose associated with this benzodiazepine, a change in schedule to S8 (alongside drugs like morphine and oxycodone) would be a positive public health measure. This change in regulation would increase the controls on alprazolam prescribing, may restrict duration of prescribing of this drug and could raise prescriber awareness of the risks of alprazolam.

VAILA submission 2006

DCPC inquiry female prisoners 2010

PARLIAMENT OF VICTORIA

DRUGS AND CRIME PREVENTION COMMITTEE

INQUIRY INTO THE IMPACT OF DRUG-RELATED OFFENDING ON FEMALE PRISONER NUMBERS

Interim Report

October 2010

Ordered to be printed

by Authority
Government Printer for State of Victoria

DCPC inquiry female prisoners 2010

health

Women in the system felt that 'pills' presented greater risk for offending than heroin

Legal and illegal use of Xanax and bzds was an issue

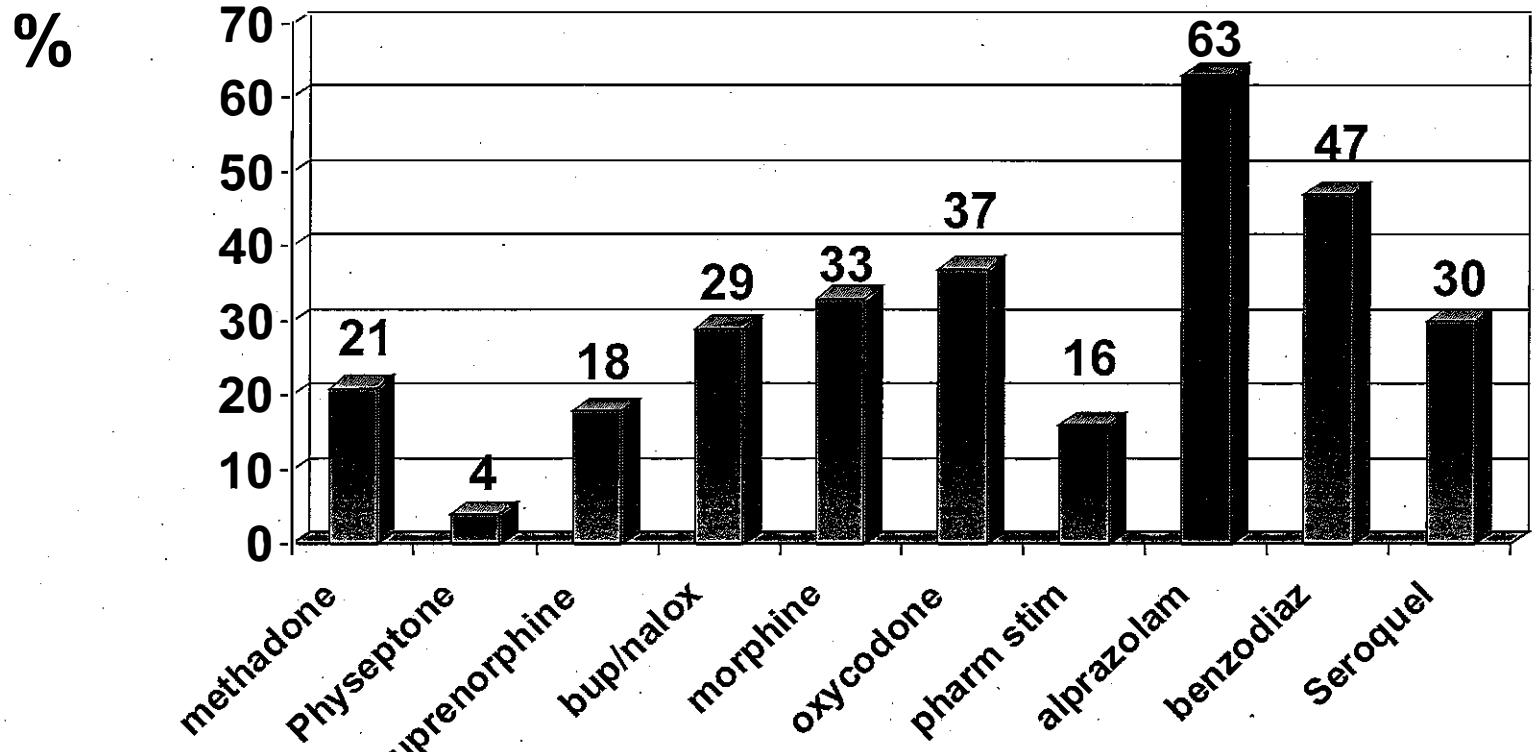
Certain health professionals well know to prescribe high doses to dependent women on request

Specific areas of Melbourne known for sale and distribution of illegal bzds (inc Richmond, Footscray)

Can purchase three Xanax off street for $10

Recent illicit use of pharmaceutical drugs: IDRS, Victoria, 2011

health



Illicit Drug Reporting System: Australia

health

Year	% recent use alprazolam	Most common injected
2003	3	diazepam
2004	4	diazepam
2005	5	diazepam
2006	6	diazepam
2007	11	alprazolam
2008	14	alprazolam
2009	17	alprazolam
2010	21	alprazolam
2011	46	alprazolam

Harms associated with recent 'illicit' (non-prescribed or IV) alprazolam use among injecting drug consumers (national, 2011, n=868)	No illicit alprazolam use (n=534) %	Illicit alprazolam use (n=334) %	OR
Male	67	65	0.88
Overdose *(last 6 months)*	7	12	1.89**
Daily Injection	38	46	1.39*
Used pharmaceutical opioid *(yesterday)*	49	64	1.81***
Used opioid and benzodiazepine *(yesterday)*	15	37	3.36***
Arrested *(past year)*	29	47	2.26***
Engaged in crime *(past month)*	31	52	2.45***
High psychological distress *(K10 >30)*	26	34	1.47*
Minor IV harms *(scarring, bruising, problems with injecting)*	43	54	1.56***
Major IV harms *(abscess, thrombosis)*	11	12	1.10
Attended Emergency Department *(last month)*	12	16	1.44(*)
Attended a GP *(last month)*	59	66	1.31(*)
Attended psychotherapy *(last month)*	29	37	1.41*

Source: IDRS 2011

Pharmaceutical misuse in drug treatment clients

health

305 interviewed in 4 States

lifetime non-med use

88% bzds, 66% alprazolam

Use in 4 weeks prior to treatment

69% bzds, 38% alprazolam

Last bzd used

diazepam 51%, alprazolam 16%

Mean SDS score 6.3 = dependent

Nielsen S et al. Investigation of pharmaceutical misuse amongst drug treatment clients. Final Report 2008. Turning Point Alcohol and Drug Centre, Melbourne 2008.

Pharmaceutical misuse in drug treatment clients: alprazolam harm

health

Seizures: 55%

Traffic accidents: 50%

Crime: 30%

(alprazolam main bzd causing harm)

Most injection-related harm: alprazolam

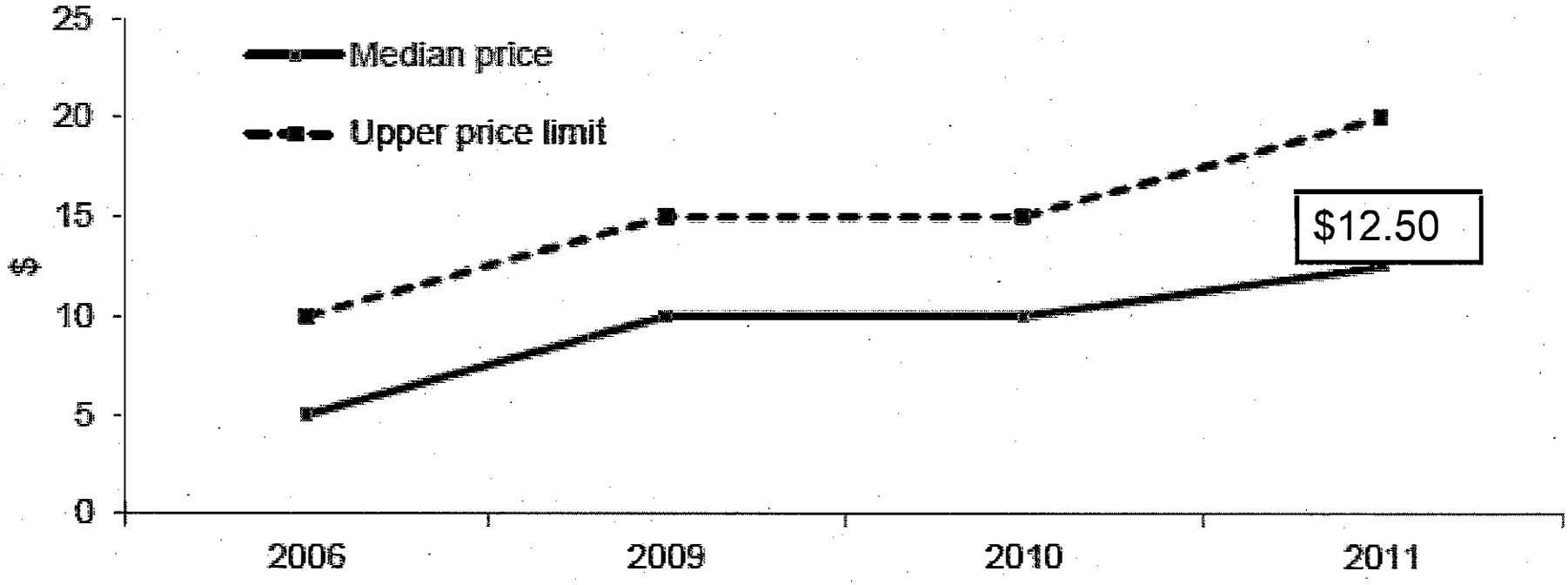
Disproportionally high level of harm from alprazolam

Nielsen S et al. Investigation of pharmaceutical misuse amongst drug treatment clients. Final Report 2008. Turning Point Alcohol and Drug Centre, Melbourne 2008.

IDRS Tasmania 2011

health

Figure 65: Median and upper limit of prices paid for 2mg alprazolam, 2006-2011*



Source: IDRS PWID interviews

* This data was not collected in the 2007-2008 surveys

Overdose and other harms

health

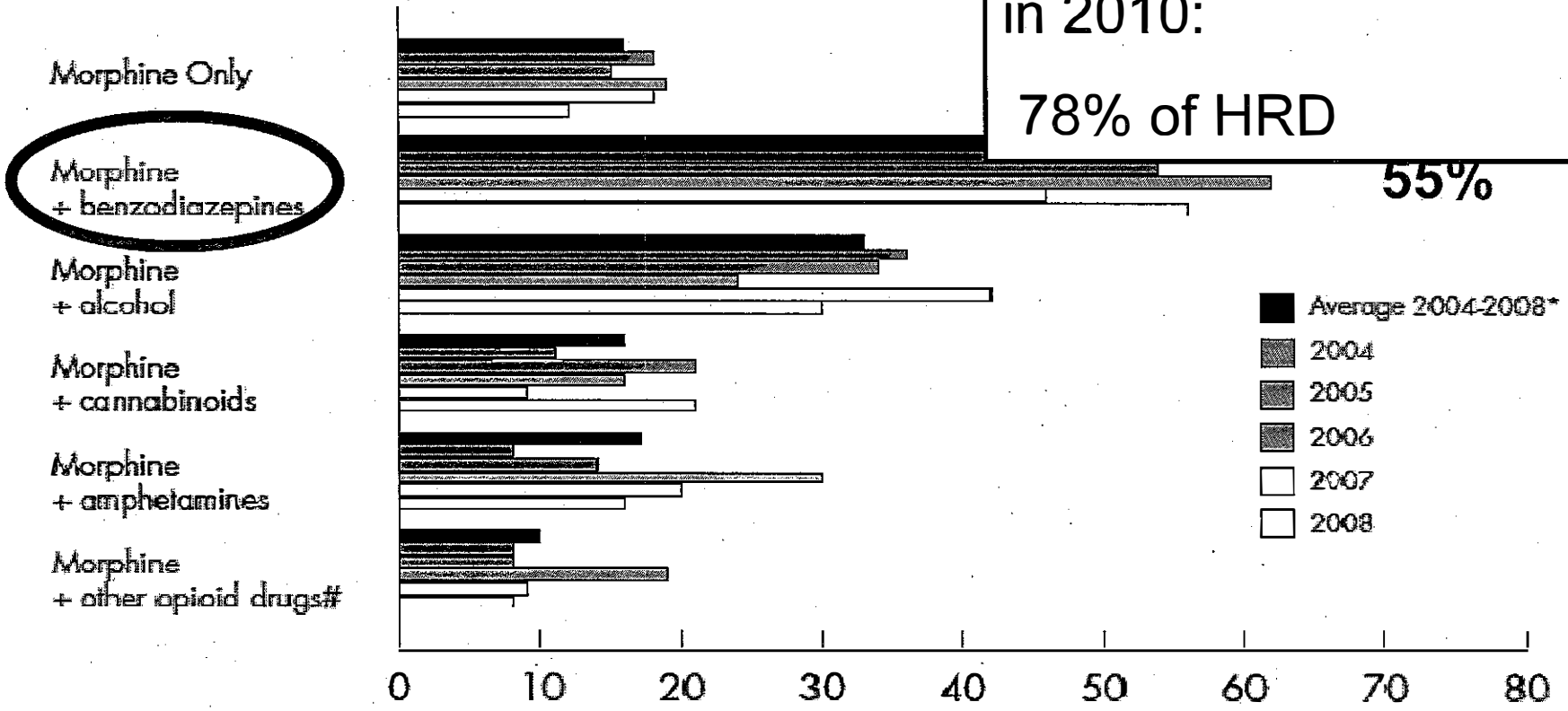
Victorian heroin-related deaths: other drugs, 2004-08

health

FIGURE 4 PRESENCE OF OTHER DRUG

BZD involvement highest in 2010:

78% of HRD



* Total percentage equals more than 100% as multiple combinations of other drugs may be present.
# i.e. methadone, propoxyphene, oxycodone, etc.

Overdose and other harms

- 28-times greater chance of heroin overdose if BZD used 12hrs prior (Dietze et al 2005)
- Alprazolam more toxic in overdose: 2.06 times more likely to require ICU admission than other benzodiazepines (Isbister et al 2004)

Overdose: inner city ED

health

Table 2: Specific benzodiazepines implicated in misuse or overdose.

Benzodiazepine	% PAS data[a] (n=213)	% Victorian prescription data 2004[b] (n=1,742,726)
Diazepam	46	27
Alprazolam	26	7
Temazepam	20	36
Nitrazepam	10	10
Oxazepam	6	20
Clonazepam	4	1
Flunitrazepam	3	<1
Bromazepam	1	<1
Lorazepam	1	0
Unspecified benzodiazepine	4	n/a

Notes: a) The total exceeds 100% because some individuals consumed more than one benzodiazepine type.

b) Source: Drugs and Crime Prevention Committee. (2007). Inquiry into Misuse/Abuse of Benzodiazepines and Other Pharmaceutical Drugs Final Report. Melbourne, Australia: DCPC, Parliament of Victoria.

Buykx P et al. Medications used in overdose and how they are acquired: an investigation of cases attending an inner city emergency department. Aust NZ J Public Health 2010;34:401-4.

Overdose: inner city ED

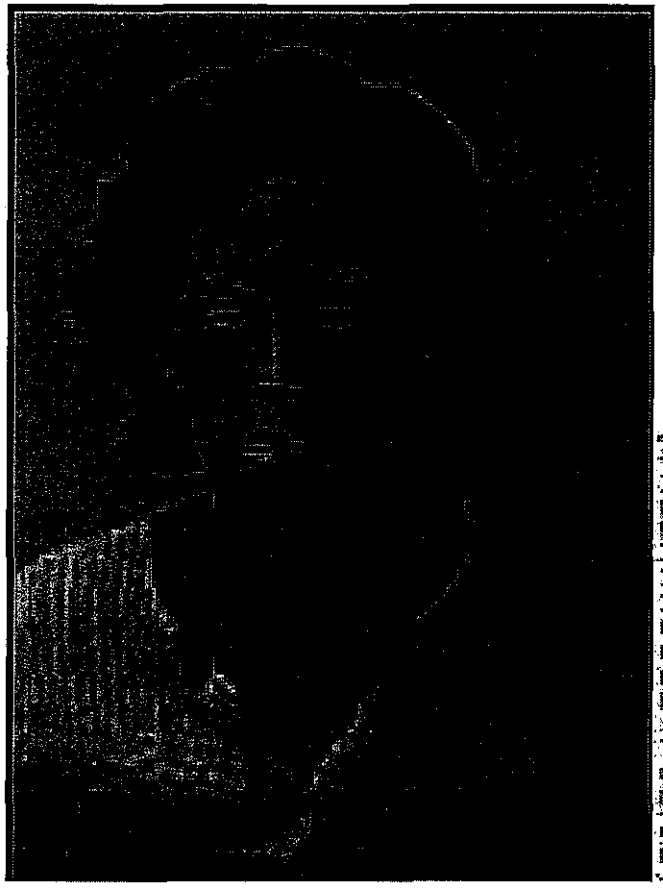
	Misuse or overdose cases	Prescriptions for 2004 (DUSC)	Cases per million prescriptions
diazepam	46	2,033,719	22.6
alprazolam	26	494,998	**52.5**
temazepam	20	2,915,242	6.9

Buykx P et al. Medications used in overdose and how they are acquired: an investigation of cases attending an inner city emergency department. Aust NZ J Public Health 2010;34:401-4.

US experience

- Alprazolam leading BZD for emergency department visits in US: 112,525 visits in 2009 (DAWN ED)
- > 1,800 robberies of U.S. pharmacies in past 3 yrs - most common targeted hydrocodone, oxycodone and Xanax
- At least 1 prescription for a sedative/hypnotic was a stronger risk factor for drug related death than an opioid prescription (Paulozzi L et al 2012)

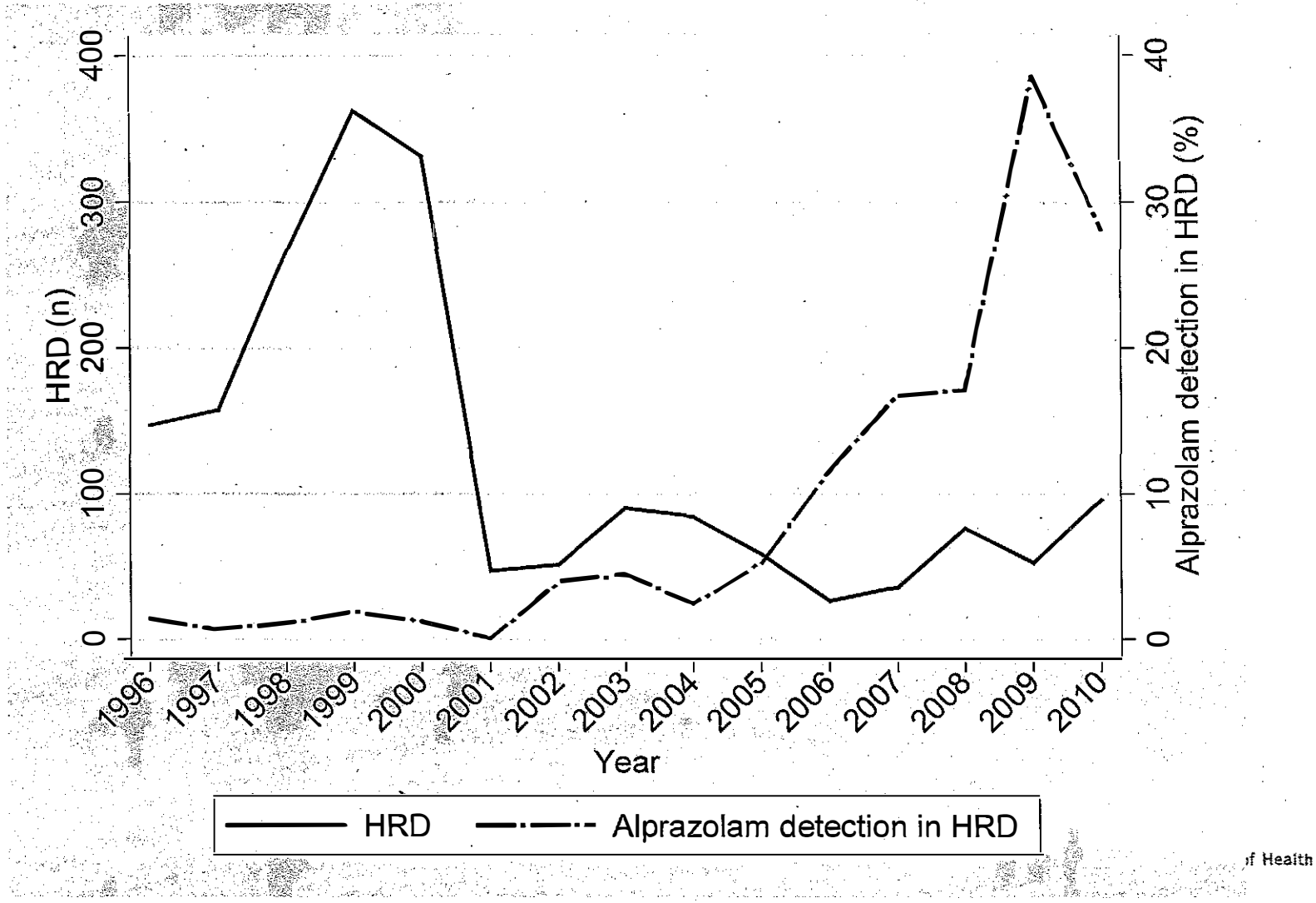
US experience: forged prescription Xanax



(TALLAHASSEE POLICE)

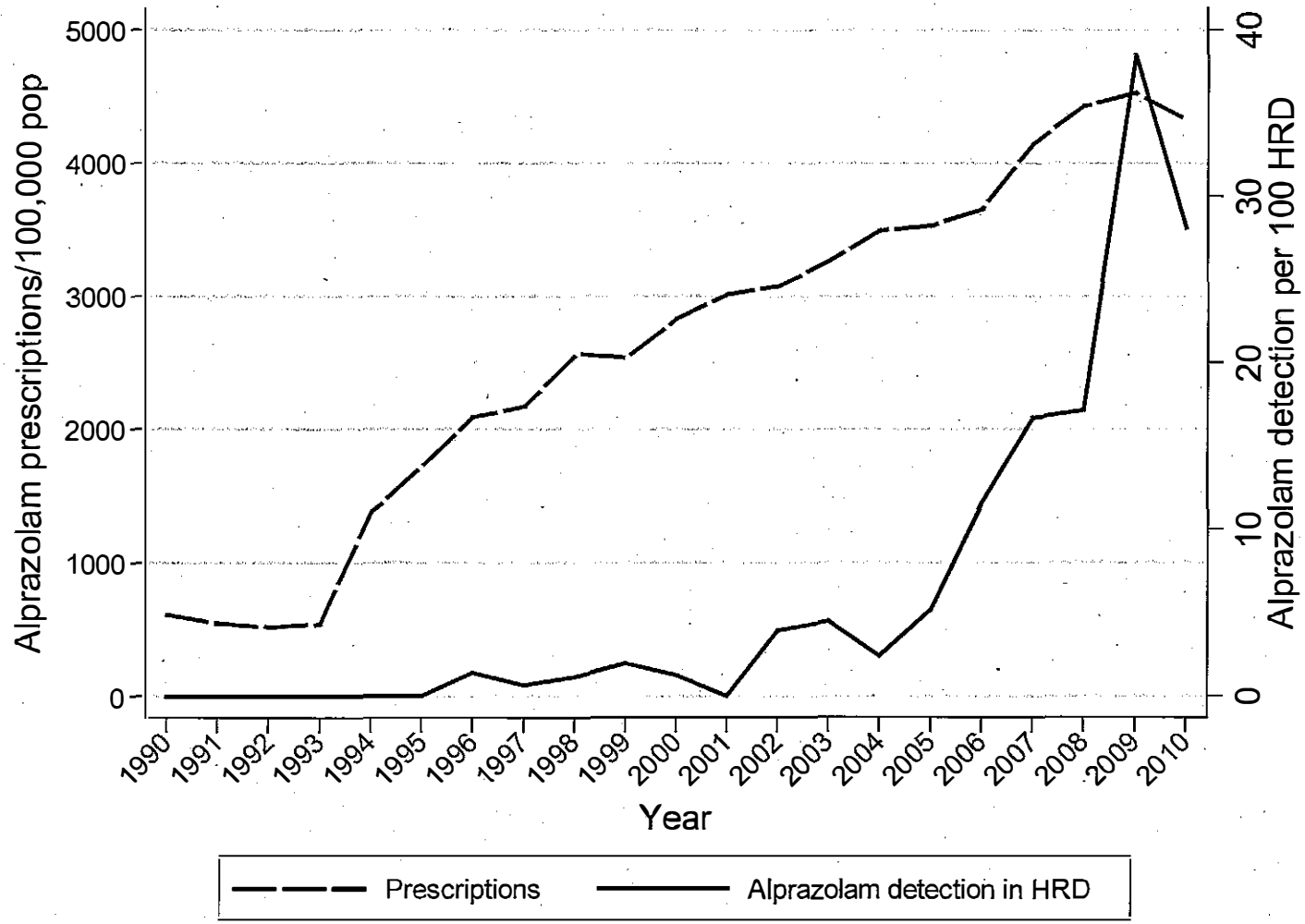
No. heroin related deaths & % where alprazolam detected: Victoria, 1996-2010

health



Alprazolam prescriptions and % detected in HRD: Victoria 1990-2010

health



Heath Ledger

health

"died as the result of acute intoxication by the combined effects of oxycodone, hydrocodone, diazepam, temazepam, alprazolam, and doxylamine."

Crime

health

Department of Health

Understanding role of benzodiazepine use in crime

health

- Expert informants: alprazolam associated with problematic risky behaviour and crime (drug court)
- Alprazolam users report memory loss and atypical behaviour not recognised later
- Two populations:

Polysubstance users in treatment – acquisitive crime

Dependent bzd users with psychological distress

- Acquisitive crime – polydrug users, acquired alprazolam on street
- Memory loss, seizures associated with withdrawal
- Shop theft most common

Best D et al. Understanding the role of benzodiazeine use in crime. Turning Point A&D Centre. Melbourne 2012

Australian regulatory and other responses

health

Australian and New Zealand clinical practice guidelines for the treatment of panic disorder and agoraphobia

Royal Australian and New Zealand College of Psychiatrists Clinical Practice Guidelines Team for Panic Disorder and Agoraphobia

Background: The Royal Australian and New Zealand College of Psychiatrists is co-ordinating the development of clinical practice guidelines (CPGs) in psychiatry, funded under the National Mental Health Strategy (Australia) and the New Zealand Health Funding Authority.
Method: For these guidelines, the CPG team reviewed the treatment outcome literature, consulted with practitioners and patients and conducted a meta-analysis of recent outcome research.
Treatment recommendations: Education for the patient and significant others covering: (i) the nature and course of panic disorder and agoraphobia; (ii) an explanation of the psychopathology of anxiety, panic and agoraphobia; (iii) rationale for the treatment, likelihood of a positive response, and expected time frame.
Cognitive behaviour therapy (CBT) is more effective and more cost-effective than medication. Tricyclic antidepressants (TCAs) and serotonin selective reuptake inhibitors are equal in efficacy and both are to be preferred to benzodiazepines. Treatment choice depends on the skill of the clinician and the patient's circumstances. Drug treatment should be complemented by behaviour therapy.
If the response to an adequate trial of a first-line treatment is poor, another evidence-based treatment should be used. A second opinion can be useful. The presence of severe agoraphobia is a negative prognostic indicator, whereas comorbid depression, if properly treated, has no consistent effect on outcome.
Key words: agoraphobia, panic disorder, treatment outcomes.

Australian and New Zealand Journal of Psychiatry 2003; 37:641–656

These guidelines, provided to promote good clinical care, are designed for mental health professionals trained to assess, diagnose and treat panic disorder (PD). Specialist clinicians should consider, but not be limited to, the treatments recommended. Panic disorder has been much studied in the past 30 years. The literature is extensive and there are numbers of systematic reviews of randomised controlled trials. There are aspects about which less is known and lower orders of evidence have been used. The levels of evidence can be used as a guide to the robustness of the evidence.

Definitions and main features

Anxiety is a normal emotion that can be adaptive and aid performance. We all suffer from uncomfortable levels of anxiety at some time. In fact, 40% of young *people have had at least one spontaneous panic attack* [1], although they will not have repeated attacks and do not meet the criteria for PD (Table 1).

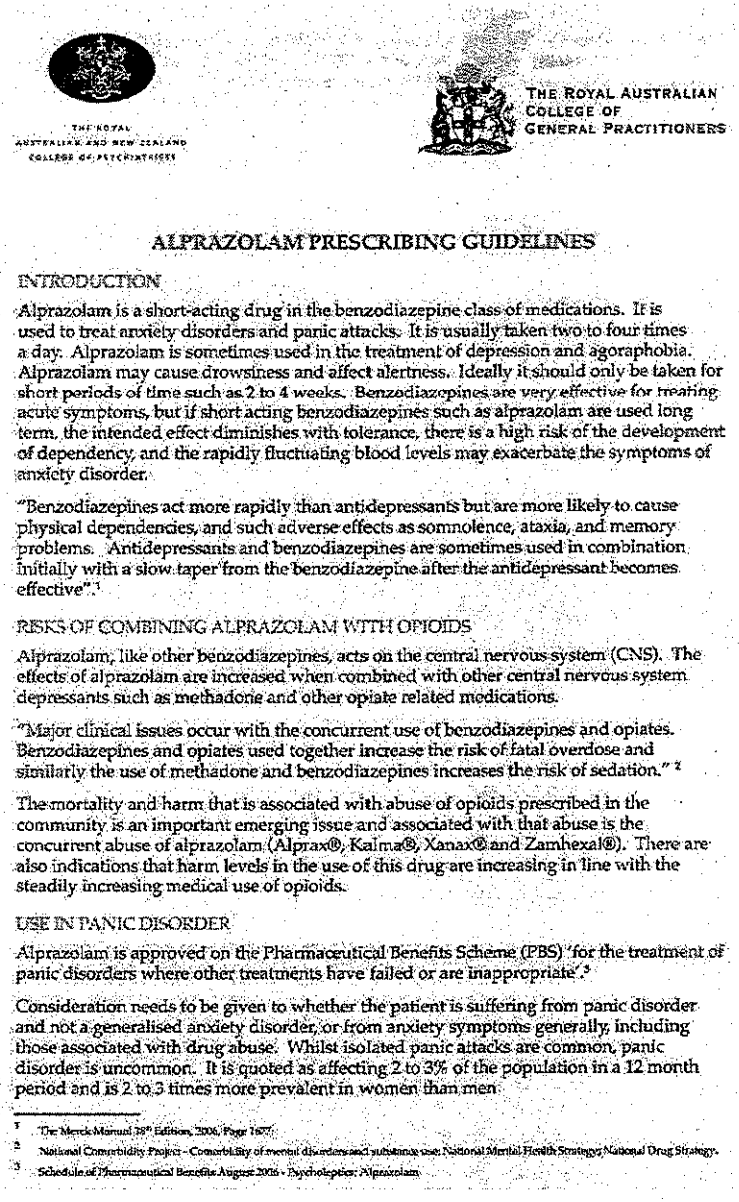
Gavin Andrews, Chair (Correspondence)

CPG Team for Panic and Agoraphobia, Clinical Research Unit for Anxiety Disorders, St Vincent's Hospital, 299 Forbes Street, Darlinghurst NSW 2010. Email: [illegible]

Received 27 November 2002; accepted 28 November 2002.

Australian regulatory and other responses: Tasmania 2007

health



THE ROYAL AUSTRALIAN AND NEW ZEALAND COLLEGE OF PSYCHIATRISTS

THE ROYAL AUSTRALIAN COLLEGE OF GENERAL PRACTITIONERS

ALPRAZOLAM PRESCRIBING GUIDELINES

INTRODUCTION

Alprazolam is a short-acting drug in the benzodiazepine class of medications. It is used to treat anxiety disorders and panic attacks. It is usually taken two to four times a day. Alprazolam is sometimes used in the treatment of depression and agoraphobia. Alprazolam may cause drowsiness and affect alertness. Ideally it should only be taken for short periods of time such as 2 to 4 weeks. Benzodiazepines are very effective for treating acute symptoms, but if short acting benzodiazepines such as alprazolam are used long term, the intended effect diminishes with tolerance, there is a high risk of the development of dependency, and the rapidly fluctuating blood levels may exacerbate the symptoms of anxiety disorder.

"Benzodiazepines act more rapidly than antidepressants but are more likely to cause physical dependencies, and such adverse effects as somnolence, ataxia, and memory problems. Antidepressants and benzodiazepines are sometimes used in combination initially with a slow taper from the benzodiazepine after the antidepressant becomes effective".[1]

RISKS OF COMBINING ALPRAZOLAM WITH OPIOIDS

Alprazolam, like other benzodiazepines, acts on the central nervous system (CNS). The effects of alprazolam are increased when combined with other central nervous system depressants such as methadone and other opiate related medications.

"Major clinical issues occur with the concurrent use of benzodiazepines and opiates. Benzodiazepines and opiates used together increase the risk of fatal overdose and similarly the use of methadone and benzodiazepines increases the risk of sedation." [2]

The mortality and harm that is associated with abuse of opioids prescribed in the community is an important emerging issue and associated with that abuse is the concurrent abuse of alprazolam (Alprax®, Kalma®, Xanax® and Zamhexal®). There are also indications that harm levels in the use of this drug are increasing in line with the steadily increasing medical use of opioids.

USE IN PANIC DISORDER

Alprazolam is approved on the Pharmaceutical Benefits Scheme (PBS) 'for the treatment of panic disorders where other treatments have failed or are inappropriate'.[3]

Consideration needs to be given to whether the patient is suffering from panic disorder and not a generalised anxiety disorder, or from anxiety symptoms generally, including those associated with drug abuse. Whilst isolated panic attacks are common, panic disorder is uncommon. It is quoted as affecting 2 to 3% of the population in a 12 month period and is 2 to 3 times more prevalent in women than men.

1 The Merck Manual 18th Edition, 2006, Page 1677.
2 National Comorbidity Project - Comorbidity of mental disorders and substance use; National Mental Health Strategy; National Drug Strategy.
3 Schedule of Pharmaceutical Benefits August 2006 - Psycholeptics: Alprazolam

- per capita prescription rate double that of national rate
- repeated cases of morbidity and mortality
- Working party RANZCP, RACGP, State govt 2006
- Education sessions to regions 2007
- Regulatory changes 2007:
  - Pharmacy monthly reporting
  - permit >4 weeks where opioids also prescribed
  - OST patients – require approval