

1-1-2012

Risk of road traffic accidents in patients discharged following treatment for psychotropic drug overdose: A self-controlled case series study in Australia

Tharaka L. Dassanayake
University of Newcastle

Alison L. Jones
University of Wollongong, alisonj@uow.edu.au

Patricia Michie
University of Newcastle

Gregory Carter
University of Newcastle

Patrick McElduff
University of Newcastle

See next page for additional authors

Follow this and additional works at: <https://ro.uow.edu.au/medpapers>



Part of the [Medicine and Health Sciences Commons](#)

Citation

Dassanayake, Tharaka L.; Jones, Alison L.; Michie, Patricia; Carter, Gregory; McElduff, Patrick; Stokes, Barrie J.; and Whyte, Ian, 2012, Risk of road traffic accidents in patients discharged following treatment for psychotropic drug overdose: A self-controlled case series study in Australia, 269-276.
<https://ro.uow.edu.au/medpapers/180>

Risk of road traffic accidents in patients discharged following treatment for psychotropic drug overdose: A self-controlled case series study in Australia

Abstract

Background: Use of psychotropic drugs is known to impair driving and increase the risk of road traffic accidents. They are also the most common drugs taken in overdose in hospital-treated episodes of self-poisoning. Most patients who take psychotropic drug overdoses are discharged within 48 hours, while they still have possible subclinical drug effects. **Objective:** Using a self-controlled case series design, we aimed to determine whether patients with psychotropic drug overdose are at a higher risk of a traffic accident in the period following discharge compared with a control period not associated with hospital-treated drug overdose. **Methodology:** Using the New South Wales (NSW) Admitted Patient Data Collection (APDC) as the primary source, we retrieved 40845 hospital separation records dated between 1 July 2000 and 30 June 2008 (8 years) in patients aged 18-80 years admitted to a hospital in NSW following an intentional self-poisoning with a psychotropic drug (coded X61 or X62 as the International Classification of Diseases, 10th Edition, [ICD-10] external cause of injury). Of these, 33 459 hospital separations (i.e. discharges, transfers and deaths) involving 24 284 patients were considered eligible as the patients were discharged directly into the community where they could have driven a motor vehicle. We selected three separate post-admission periods (3 days, 1 week and 4 weeks), subtracted the number of inpatient days from each and calculated three separate post-discharge periods (immediate, intermediate and extended, respectively) for each episode of overdose. The control period was the duration of the study period where the individual was aged 18 years or older, excluding the total person-days in the post-discharge period/s and the index inpatient period/s. The APDC dataset was linked to the NSW Roads and Traffic Authority CrashLink dataset to identify any accidents in which each patient was involved as a motor-vehicle driver during the followup period. Incidence rate ratio (IRR) for matched post-discharge and control periods was found using random effects Poisson regression. **Results:** Seventy-two percent of the subjects were discharged within 2 days following their admission with overdose. Compared with the corresponding control periods the risk of a traffic accident was 3.5 times higher (IRR= 3.49; 95% CI 1.66, 7.33; p = 0.001) during the immediate, 1.9 times higher (IRR = 1.88; 95% CI 1.09, 3.25; p=0.023) during the intermediate and 1.6 times higher (IRR= 1.65; 95% CI 1.27, 2.15; p=0.0002) during the extended post-discharge period. **Conclusions:** Self-poisoning with psychotropic drugs is associated with a markedly increased risk of a traffic accident during the first few days following discharge. These findings raise clinical and medico-legal implications concerning fitness-to-drive during this period. The risk reduces with time but remains significantly elevated after 4 weeks post-overdose. Further research is necessary to find out the factors contributing to this ongoing risk

Keywords

psychotropic, road, drug, overdose, self, controlled, case, series, study, australia, traffic, accidents, patients, discharged, following, treatment, risk

Disciplines

Medicine and Health Sciences

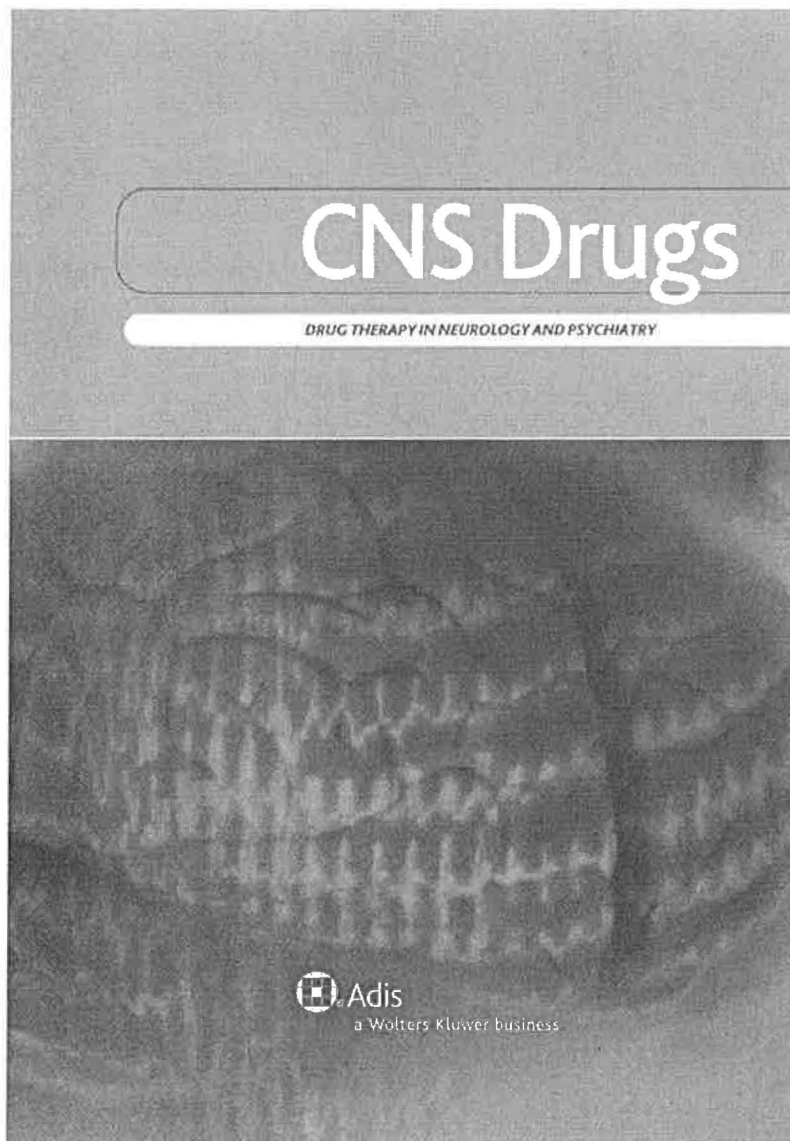
Publication Details

Dassanayake, T. L., Jones, A. L., Michie, P., Carter, G., McElduff, P., Stokes, B. J. & Whyte, I. (2012). Risk of road traffic accidents in patients discharged following treatment for psychotropic drug overdose: A self-controlled case series study in Australia. *CNS Drugs*, 26 (3), 269-276.

Authors

Tharaka L. Dassanayake, Alison L. Jones, Patricia Michie, Gregory Carter, Patrick McElduff, Barrie J.

**This material is the copyright of the original publisher.
Unauthorised copying and distribution is prohibited.**



Terms and Conditions for Use of PDF

The provision of PDFs for authors' personal use is subject to the following Terms & Conditions:

The PDF provided is protected by copyright. All rights not specifically granted in these Terms & Conditions are expressly reserved. Printing and storage is for scholarly research and educational and personal use. Any copyright or other notices or disclaimers must not be removed, obscured or modified. The PDF may not be posted on an open-access website (including personal and university sites).

The PDF may be used as follows:

- to make copies of the article for your own personal use, including for your own classroom teaching use (this includes posting on a closed website for exclusive use by course students);
- to make copies and distribute copies (including through e-mail) of the article to research colleagues, for the personal use by such colleagues (but not commercially or systematically, e.g. via an e-mail list or list serve);
- to present the article at a meeting or conference and to distribute copies of such paper or article to the delegates attending the meeting;
- to include the article in full or in part in a thesis or dissertation (provided that this is not to be published commercially).

Risk of Road Traffic Accidents in Patients Discharged Following Treatment for Psychotropic Drug Overdose

A Self-Controlled Case Series Study in Australia

Tharaka L. Dassanayake,^{1,2} Alison L. Jones,^{2,3} Patricia T. Michie,¹ Gregory L. Carter,^{4,5} Patrick McElduff,⁶ Barrie J. Stokes² and Ian M. Whyte^{2,7}

1 School of Psychology, The University of Newcastle, Newcastle, NSW, Australia

2 Discipline of Clinical Pharmacology and Toxicology, School of Medicine and Public Health, Faculty of Health, The University of Newcastle, Newcastle, NSW, Australia

3 Graduate School of Medicine, University of Wollongong, Wollongong, NSW, Australia

4 Department of Consultation-Liaison Psychiatry, Calvary Mater Newcastle, Newcastle, NSW, Australia

5 School of Medicine and Public Health, Faculty of Health, The University of Newcastle, Newcastle, NSW, Australia

6 Centre for Epidemiology and Biostatistics, School of Medicine and Public Health, Faculty of Health, The University of Newcastle, Newcastle, NSW, Australia

7 Department of Clinical Toxicology and Pharmacology, Calvary Mater Newcastle, Newcastle, NSW, Australia

Abstract

Background: Use of psychotropic drugs is known to impair driving and increase the risk of road traffic accidents. They are also the most common drugs taken in overdose in hospital-treated episodes of self-poisoning. Most patients who take psychotropic drug overdoses are discharged within 48 hours, while they still have possible subclinical drug effects.

Objective: Using a self-controlled case series design, we aimed to determine whether patients with psychotropic drug overdose are at a higher risk of a traffic accident in the period following discharge compared with a control period not associated with hospital-treated drug overdose.

Methodology: Using the New South Wales (NSW) Admitted Patient Data Collection (APDC) as the primary source, we retrieved 40 845 hospital separation records dated between 1 July 2000 and 30 June 2008 (8 years) in patients aged 18–80 years admitted to a hospital in NSW following an intentional self-poisoning with a psychotropic drug (coded X61 or X62 as the *International Classification of Diseases*, 10th Edition, [ICD-10] external cause of injury). Of these, 33 459 hospital separations (i.e. discharges, transfers and deaths) involving 24 284 patients were considered eligible as the patients were discharged directly into the community where they could have driven a motor vehicle. We selected three separate post-admission periods (3 days,

1 week and 4 weeks), subtracted the number of inpatient days from each and calculated three separate post-discharge periods (immediate, intermediate and extended, respectively) for each episode of overdose. The control period was the duration of the study period where the individual was aged 18 years or older, excluding the total person-days in the post-discharge period/s and the index inpatient period/s. The APDC dataset was linked to the NSW Roads and Traffic Authority CrashLink dataset to identify any accidents in which each patient was involved as a motor-vehicle driver during the follow-up period. Incidence rate ratio (IRR) for matched post-discharge and control periods was found using random effects Poisson regression.

Results: Seventy-two percent of the subjects were discharged within 2 days following their admission with overdose. Compared with the corresponding control periods the risk of a traffic accident was 3.5 times higher (IRR = 3.49; 95% CI 1.66, 7.33; $p = 0.001$) during the immediate, 1.9 times higher (IRR = 1.88; 95% CI 1.09, 3.25; $p = 0.023$) during the intermediate and 1.6 times higher (IRR = 1.65; 95% CI 1.27, 2.15; $p = 0.0002$) during the extended post-discharge period.

Conclusions: Self-poisoning with psychotropic drugs is associated with a markedly increased risk of a traffic accident during the first few days following discharge. These findings raise clinical and medico-legal implications concerning fitness-to-drive during this period. The risk reduces with time but remains significantly elevated after 4 weeks post-overdose. Further research is necessary to find out the factors contributing to this ongoing risk.

Background

Psychotropic drugs¹ could impair driving and be associated with increased risk of road traffic accidents.^[1-3] Pharmacoepidemiological studies in particular have focused on accident risk associated with therapeutic use of medications including benzodiazepines,^[4-9] antidepressants^[5,8-11] and opioids.^[5,8,11,12] However, psychotropic drugs are also among the most common substances taken in overdose, accounting for around 100 000 hospital-treated overdoses per year in the US (2006),^[13] 46 000 in the UK (mid-2009 to mid-2010)^[14] and 20 000 in Australia (mid-2007 to mid-2008).^[15] Most of these patients are discharged from hospitals relatively early with an average length of hospital stay of 1 day in the UK^[14] and 1–2 days

in Australia.^[15] Therefore, many patients who are deemed 'clinically' recovered might be returning to the community while still having residual effects of the drugs on which they overdosed.

However, no study so far has examined whether patients with psychotropic drug overdose are more prone to major adverse outcomes such as traffic accidents during the period following their discharge from hospital. In the present study, we aimed to assess whether patients treated in hospitals in New South Wales (NSW) for self-poisoning with psychotropic drugs are more prone to traffic accidents during the period following discharge from hospitals. Using a self-controlled case series approach,^[16,17] we compared the traffic accident rates of a group of patients overdosed with psychotropic drugs in the period following the

¹ Although opioids may not be classified under psychotropic drugs in a strict sense, they are included under the term 'psychotropic drugs' in the present paper to avoid verbosity. However, the distinction is made when necessary.

overdose with the rate in a control period where they were not affected by the overdose.

Methods

Data Sources

We used a record-linkage approach based on two population databases in NSW, Australia.

New South Wales Admitted Patient Data Collection

Admitted Patient Data Collection (APDC) includes records for all separations (i.e. discharges, transfers and deaths) in all NSW public and private hospitals and day procedure centres. The database records include a range of demographic data items (e.g. sex, date of birth, residential address), administrative items (e.g. admission and separation dates and times, mode of separation) and coded health information (e.g. principal diagnosis [*International Classification of Diseases*, 10th Edition, ICD-10 version 4]), external cause of injury (ICD-10 version 4) and any complications that occurred and procedures performed during the admission. ICD-10 coding is assigned routinely for all hospital admissions in NSW by Clinical Coders employed by the NSW Ministry of Health. The APDC does not record individual drugs taken in overdose.

New South Wales Roads and Traffic Authority Traffic Accident (CrashLink) Database

The CrashLink database held by the NSW Roads and Traffic Authority maintains the records of traffic accidents that occur in NSW. An accident is entered in the database if it (a) is reported to the police, (b) occurred on a road open to the public, (c) involved at least one moving road vehicle and (d) involved at least one person being killed or injured or at least one motor vehicle being towed away. Therefore, minor non-injurious accidents are generally not entered into the database.

The CrashLink database records a range of data items pertaining to each vehicle controller (i.e. drivers of motor vehicles including motor cycles) involved in an accident, including demographic data items (e.g. sex, date of birth, postcode of residence) and items related to the accident (e.g. date and time of accident, road conditions,

casualties). The CrashLink Dataset for the 8-year period from 1 July 2000 to 30 June 2008 consisted of 664 225 motor vehicle controller records.

Data Extraction and Linkage

Using the APDC as the primary data source, we retrieved all hospital separations following an intentional self-poisoning with a psychotropic drug [coded X61 (antiepileptic, sedative-hypnotic, antiparkinsonism and psychotropic drugs, not elsewhere classified) or X62 (narcotics and hallucinogens, not elsewhere classified) as the ICD-10 version 4 external cause of injury] from a NSW hospital during an 8-year period from 1 July 2000 to 30 June 2008 (i.e. the study period), where the patient was aged 18–80 years on the day of separation. This dataset consisted of 40 845 hospital separations and involved 27 087 patients. Of these, 7386 separations were either transfers to other inpatient institutions or in-hospital deaths and thus were excluded. The remaining 33 459 separations involved 24 284 individuals who were treated for intentional self-poisoning with psychotropic drugs and discharged to the community within the study period (figure 1). Using demographic data items, the APDC data for these eligible individuals were linked to the CrashLink database to retrieve the accident records (if any) for each individual within the study period.

Ethical Considerations

The primary APDC and CrashLink dataset linkage was conducted by the NSW Centre for Health Record Linkage (CHeReL), independently of the researchers. Personally identifiable data items were removed from APDC and CrashLink records in the process and researchers were provided with de-identified data where each subject was assigned with a project person number. Ethics clearance for the study was granted by the NSW Population and Health Services Research Ethics Committee.

Data Analysis

Because this was the first study of its kind, we did not have previous estimates for the period

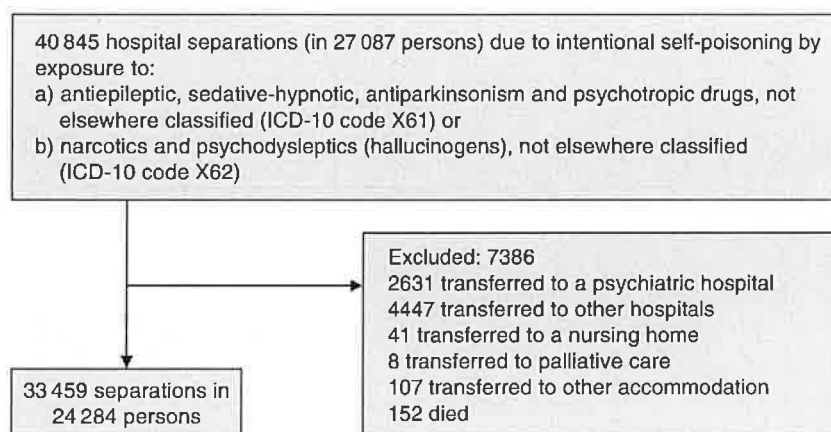


Fig. 1. Selection of the sample. ICD-10 = *International Classification of Diseases* (10th Edition).

where individuals could be at risk of driving impairment following a psychotropic drug overdose. Therefore, we defined three post-admission periods (3 days, 1 week and 4 weeks), subtracted the number of inpatient days (because the patients did not drive during this period) from each post-admission period and calculated three post-discharge risk periods (i.e. immediate, intermediate and extended, respectively) of different lengths for each episode of overdose. Given the wide variation of the half-lives (and the doses) of drugs taken by the patients in the study, we assumed it is biologically plausible that any effect of drug overdose could last for up to 3 days to 1 week, but not up to 4 weeks. When the same patient was hospitalized for psychotropic drug overdose more than once within the study period, the total person-days were calculated for each post-discharge period by adding the separate post-discharge periods (illustrated in figure 2). The control period for each subject was the total duration where the individual was aged 18 years or older during the follow-up period, excluding the total person-days included in the post-discharge period/s and the preceding inpatient days. The traffic accidents within each post-discharge period and corresponding control period were counted for each participant after combining the APDC and CrashLink datasets.

The data were analysed with random-effects Poisson regression models to calculate the incidence rate ratio (IRR) between each post-discharge period (i.e. immediate, intermediate and extended) and corresponding control period. For each analysis,

the records where length of hospital stay was longer than the defined post-admission period (i.e. 3 days, 1 week or 4 weeks) were excluded owing to the underlying assumption that a patient is no longer affected by drug exposure after the end of that period.

Because we defined three post-discharge periods and performed three IRR comparisons for the same cohort, we used a modified Bonferroni correction procedure – the step-wise Hochberg approach^[18] – to test statistical significance. The procedure ranks the p-values (three p-values in this study) and tests the first (lowest p-value) at 0.05/3. If it is significant the procedure then tests the next one at 0.05/2, and if it is significant the next one at 0.05/1. If one of the p-values is not significant, all those below it on the ranking are non-significant.

Data were analysed using STATA version 11 (StataCorp, College Station, TX, USA).

Results

Sixty percent of the subjects were female. The mean (SD) of age was 37.5 (13.3) years, and 75% of the subjects were aged 45 years or younger. Of the 33 459 hospital admissions 9175 were repeat admissions. Twenty percent of the patients were discharged on the same day, and 72% were discharged within 2 days following admission. There were 2825 traffic accidents where an individual in the group was involved as a driver during the study period.

The number of accidents and the computed IRRs for each post-discharge period versus control period are shown in table I. Numbers of subjects included in the analyses were different depending on the selected post-discharge period (table I, column 2), because those who were still inpatients at the end of the selected post-admission period (3 days, 1 week or 4 weeks) were excluded from the cohort eligible for that analysis. According to the Hochberg step-wise approach for multiple comparisons, the 4-week period that gave rise to the lowest p-value was tested first at 0.017, followed by the 3-day period at 0.025 and the 7-day period at the 0.05 cut-off. All three IRRs were significant in these comparisons. 18 381 patients were discharged within 3 days following admission. In this group the accident rate in the post-discharge period within first 3 days following admission was 3.5 times (IRR 3.49; 95% CI 1.66, 7.33; $p=0.001$) that in the corresponding control period. 21 751 patients were discharged in the first week following admission. The IRR of accidents between post-discharge and control periods in this group was 1.9 (IRR 1.88; 95% CI 1.09, 3.25; $p=0.023$). 23 940 patients were discharged within the first 4 weeks following admission and the accident risk remained significantly elevated² during the post-

discharge period within this 4-week period (IRR 1.65; 95% CI 1.27, 2.15, $p=0.0002$).

Discussion

To our knowledge, this is the first study that examined whether patients treated in hospital for intentional self-poisoning with psychotropic drugs are more prone to traffic accidents as motor vehicle drivers in the period following discharge from hospital. The results show that 72% of those patients are discharged within 2 days following admission. Their traffic accident risk during the first 1–3 days following discharge is 3.5 times their baseline accident risk. The risk reduces with time but remains significantly elevated after 4 weeks post-overdose.

Although our data are from mid-2000 to mid-2008, they are still clinically relevant, if not more so now than in 2008, because the length of hospital stay after an overdose has not changed and hospital admissions following psychotropic drug overdose have increased in Australia^[15] and other high-income countries.^[13,19] We obtained data from NSW population-wide databases and thus case selection was not affected by sampling biases. The records have been entered prospectively into each source database using standard disease



Fig. 2. Total post-discharge period and control period based on 1-week post-admission period in a hypothetical subject admitted twice during the study period, the first occurring on 1 July 2002 at the age of 19 years. When calculations are repeated for the same subject, (a) based on 3-day post-admission period: post-discharge period=3 days and control period=2550 days and (b) based on 4-week post-admission period: post-discharge period=53 days, control period=2500 days.

2 In order to eliminate the effect of accidents that occurred during the first 3 days on the risk calculated for the 4-week post-overdose period, we also defined a post-discharge period between 3 and 28 days (i.e. a period mutually exclusive from the 3-day post-overdose period) and recalculated the IRR. Fifty-one accidents occurred during this period and the IRR remained significantly elevated (IRR 1.53, 95% CI 1.16, 2.02, $p=0.003$) indicating that this is a genuine increase in accident risk, independent of the excess accidents occurred during the immediate post-discharge period.

Table 1. Incidence rate ratios for traffic accidents between post-discharge periods and control periods

Defined post-discharge period (duration post-admission)	Number of subjects included	Post-discharge period			Control period			IRR	95% CI	p-Value
		Crashes	Total person-days	Accidents/100 000 person-days	Crashes	Total person-days	Accidents/100 000 person-days			
Immediate (3 days)	18 381	7	44 176	15.8	2271	511 694 60	4.4	3.49	1.66, 7.33	0.001
Intermediate (1 week)	21 751	13	155 490	8.4	2617	605 658 32	4.3	1.88	1.09, 3.25	0.023
Extended (4 weeks)	23 940	58	824 606	7.0	2733	660 960 87	4.1	1.65	1.27, 2.15	0.0002

IRR = incidence rate ratios.

classification criteria and traffic accident definition criteria so that entries were not influenced by recall bias or other response bias. We eliminated confounding by unmeasured between-subject factors by using a self-controlled case-series design where each subject acted as their own control. Further, selection of a long control period increased the power of the study and eliminated the influence of random fluctuations of accident risk within the study period. We assumed that the risk of accidents did not change with time over the 8-year study period, which may not be the case in the presence of certain time-dependent intra-individual risk factors such as age and severity of any underlying psychiatric illnesses. However, the control period included both pre- and post-overdose periods within the study duration, thus minimising the influence of any time-variant risk factors. The linked dataset in the present study – particularly the accident counts – was too small to perform stratified subgroup analyses based on different demographic factors such as age and sex.

We did not have data on the percentage of drivers in the group or the driving habits of individual subjects. However, the accident rate in the study group during the control period (4.1–4.4 per 100 000 person-days, table I) was very similar to the rate in the general population in NSW: 664 225 reported accidents in NSW during the 8-year study period from an average population of 5 million^[20] people aged between 18 and 80 years is equivalent to an accident rate of 4.5 per 100 000 person-days. Eighty-three percent of the population aged older than 17 years held a driver's

licence in NSW in 2005.^[21] The above accident rates are an under-representation of all traffic accidents that occurred in NSW during the study period because an accident is reported to the NSW Roads and Traffic Authority and entered into the CrashLink database only if it fulfils all of the criteria listed above under Methods. For example, non-injurious accidents with minor property damage are not reported to the Roads and Traffic Authority.

As this is the first study that examined driving impairment following acute psychotropic drug overdose, and included overdoses with different drugs, we did not have an empirical basis to define a single 'at-risk' period for the individuals discharged from hospitals. Therefore, employing a more inclusive approach we defined three 'at-risk' periods post-overdose (3 days, 1 week and 4 weeks), and adjusted the level of statistical significance for multiple comparisons. Among the patients discharged within 3 days following admission, the accident risk within 1–3 days following discharge was 3.5 times that of their baseline risk. Given that the accident rate in the control period in the group is similar to that of the general population in NSW, the results signify a genuine increase in risk. A 3.5-fold rise in accident risk is equivalent to that associated with a blood alcohol level of 0.09 g/dL,^[22,23] nearly double the legal limit (0.05 g/dL) in NSW. The risk diminished with time as expected, but remained significantly elevated even after 4 weeks. The IRR of 1.65 observed after 4 weeks is equivalent to that observed with a blood alcohol level of 0.06^[23] to 0.07 g/dL,^[24] which is still above the

legal limit in NSW and other states in Australia and other countries.

A high accident risk observed in the first 3 days post-overdose seems compatible with drug effects. Although the APDC dataset does not specify the psychotropic drugs taken in overdose, the majority of the ingested drugs are expected to be CNS depressants (i.e. benzodiazepines, barbiturates, antipsychotics, opioids and sedating antidepressants) as they accounted for around 80% of the psychotropic drug overdoses in patients hospitalized from 1 July 2000 to 30 June 2008 in Australia.^[15] Increased accident risk at 4 weeks cannot be explained simply by acute effects of drugs taken in the overdose episode. Aggravation of underlying psychiatric illnesses, increased stress around the period following deliberate self-harm and/or change in psychiatric medications during post-overdose psychiatric consultations are some possible causes that could make these individuals more prone to traffic accidents, but we do not have data to test these speculations.

Some patient characteristics (e.g. tolerance due to chronic use/abuse of the drug taken in overdose), drug factors (e.g. drug class, dose, half-life of the drug) and their complex interactions can modify the severity and the duration of intoxication. Information on these factors was not available in the source databases of this study. Even when such meticulous documentation is available in a database, epidemiological modelling of an infrequent outcome like traffic accidents based on all these factors would require extensively large datasets to have reasonable statistical power.

Conclusions

Our findings suggest important clinical and medico-legal implications in relation to post-discharge management of patients with intentional self-poisoning of psychotropic drugs.

We believe that clinicians should warn those patients who are discharged within 1–2 days after overdose (which constitute 72% of these patients) that they are 3–4 times more likely to encounter a traffic accident if they drive during the first couple of days following discharge, and should advise

them not to drive during that period. Our results also suggest that the accident risk remains elevated at medico-legally significant levels even at 4 weeks after the day of admission. However, applying driving restrictions for this extended period for each patient with psychotropic drug overdose would be a rather contentious issue until more robust evidence identifies the specific factors that increase the 4-week accident risk in patients following psychotropic drug overdose. Future research should aim at larger population-based studies that enable such fine-grained analysis. At the same time it is worth exploring the feasibility of administering clinical tests of fitness-to-drive to patients at the time of discharge and perhaps before resuming driving, with the aim of assessing the risk on an individual basis.

Acknowledgements

This study was funded by the University of Newcastle Centre for Health Record Linkage (CHeReL) Committee with CheReL Data Linkage Credits. All stages of the study and manuscript preparation were independent of the funding body. We acknowledge NSW Department of Health for providing hospital separation data, NSW Roads and Traffic Authority (RTA) for providing traffic accident data and CHeReL for conducting primary APDC and CrashLink data linkage. We thank Jane Roberson and Catherine D'Este from the School of Medicine and Public Health of the University of Newcastle for their contribution in designing this study. The authors have no conflicts of interest to declare.

References

1. Dassanayake T, Michie P, Carter G, et al. Effects of benzodiazepines, antidepressants and opioids on driving: a systematic review and meta-analysis of epidemiological and experimental evidence. *Drug Saf* 2011; 34 (2): 125-56
2. Rapoport MJ, Lancot KL, Streiner DL, et al. Benzodiazepine use and driving: a meta-analysis. *J Clin Psychiatry* 2009; 70 (5): 663-73
3. Vermeeren A. Residual effects of hypnotics: epidemiology and clinical implications. *CNS Drugs* 2004; 18 (5): 297-328
4. Barbone F, McMahon AD, Davey PG, et al. Association of road-traffic accidents with benzodiazepine use. *Lancet* 1998; 352 (9137): 1331-6
5. Ray WA, Fought RL, Decker MD. Psychoactive drugs and the risk of injurious motor vehicle crashes in elderly drivers. *Am J Epidemiol* 1992 Oct 1; 136 (7): 873-83
6. Neutel CI. Risk of traffic accident injury after a prescription for a benzodiazepine. *Ann Epidemiol* 1995 May; 5 (3): 239-44
7. Engeland A, Skurtveit S, Morland J. Risk of road traffic accidents associated with the prescription of drugs: a

- registry-based cohort study. *Ann Epidemiol* 2007 Aug; 17 (8): 597-602
8. Leveille SG, Buchner DM, Koepsell TD, et al. Psychoactive medications and injurious motor vehicle collisions involving older drivers. *Epidemiology* 1994; 5 (6): 591-8
 9. Ravera S, van Rein N, de Gier JJ, et al. Road traffic accidents and psychotropic medication use in the Netherlands: a case-control study. *Br J Clin Pharmacol* 2011; 72 (3): 505-13
 10. Bramness JG, Skurtveit S, Neutel CI, et al. Minor increase in risk of road traffic accidents after prescriptions of antidepressants: a study of population registry data in Norway. *J Clin Psychiatry* 2008; 69 (7): 1099-103
 11. Gibson JE, Hubbard RB, Smith CJP, et al. Use of self-controlled analytical techniques to assess the association between use of prescription medications and the risk of motor vehicle crashes. *Am J Epidemiol* 2009; 169 (6): 761-8
 12. Bachs LC, Engeland A, Morland JG, et al. The risk of motor vehicle accidents involving drivers with prescriptions for codeine or tramadol. *Clin Pharmacol Ther* 2009; 85 (6): 596-9
 13. Coben JH, Davis SM, Furbie PM, et al. Hospitalizations for poisoning by prescription opioids, sedatives, and tranquilizers. *Am J Prev Med* 2010; 38 (5): 517-24
 14. National Institute of Health. Hospital episode statistics: primary diagnosis: 3 character 2009-10 [online]. Available from URL: <http://www.hesonline.nhs.uk/Ease/servlet/ContentServer?siteID=1937&categoryID=203> [Accessed 2011 Aug 29]
 15. Australian Institute of Health and Welfare National Hospital Morbidity Database. Separation, patient day and average length of stay statistics by principal diagnosis in ICD-10-AM, Australia, 1998-99 to 2007-08 [online]. Available from URL: <http://www.aihw.gov.au/hospitals-data-cube/?id=6442475319> [Accessed: 2011 Jun 9]
 16. Whitaker HJ, Farrington CP, Spiessens B, et al. Tutorial in biostatistics: the self-controlled case series method. *Stat Med* 2006; 25 (10): 1768-97
 17. Farrington CP. Relative incidence estimation from case series for vaccine safety evaluation. *Biometrics* 1995; 51 (1): 228-35
 18. Hochberg Y. A sharper Bonferroni procedure for multiple tests of significance. *Biometrika* 1988 Dec 1; 75 (4): 800-2
 19. National Institute of Health. Hospital episode statistics: inpatient data by external cause 2009-10 [online]. Available from URL: <http://www.hesonline.nhs.uk/Ease/servlet/ContentServer?siteID=1937&categoryID=211> [Accessed 2011 Dec 12]
 20. Australian Bureau of Statistics. Population estimates by age and sex, New South Wales by geographical classification [ASGC 2010], 2005 and 2010 [online]. Available from URL: <http://www.abs.gov.au/AUSSTATS/abs@.nsf/DetailsPage/3235.02010?OpenDocument> [Accessed 2011 Aug 30]
 21. NSW Roads and Traffic Authority. Road traffic crashes in New South Wales: statistical statement: year ended 31 December 2005 [online]. Available from URL: www.rta.nsw.gov.au/roadsafety/downloads/accidentstats2005.pdf [Accessed 2011 Aug 30]
 22. McLean AJ, Holubowycz OT, Sandow BL. Alcohol and crashes: identification of relevant factors in this association: Road Accident Research Unit: University of Adelaide; 1980 [online]. Available from URL: http://www.infrastructure.gov.au/roads/safety/publications/1980/Alcohol_1.aspx [Accessed 2011 Mar 12]
 23. Compton RP, Blomberg RD, Moskowitz H, et al. Crash risk of alcohol-impaired driving. In: Mayhew DR, Dussault C, editors. *Proceedings of the 16th International Conference on Alcohol, Drugs and Traffic Safety*; 2002 Aug 4-9; Montreal
 24. Borkenstein RF, Crowther RF, Shumate RP, et al. *The role of the drinking driver in traffic accidents*. Bloomington (IN): Department of Police Administration, Indiana University, 1964

Correspondence: Dr *Tharaka L. Dassanayake*, Department of Clinical Toxicology and Pharmacology, Calvary Mater Newcastle, Locked Bag 7, Hunter Region Mail Centre, Newcastle, NSW 2310, Australia.
E-mail: tharaka.dassanayake@uon.edu.au