

Exploring mortality among drug treatment clients: The relationship between treatment type and mortality

LLOYD, Belinda, ZAHNOW, Renee, BARRATT, Monica J., BEST, David <<http://orcid.org/0000-0002-6792-916X>>, LUBMAN, Dan I. and FERRIS, Jason

Available from Sheffield Hallam University Research Archive (SHURA) at:
<http://shura.shu.ac.uk/16728/>

This document is the author deposited version. You are advised to consult the publisher's version if you wish to cite from it.

Published version

LLOYD, Belinda, ZAHNOW, Renee, BARRATT, Monica J., BEST, David, LUBMAN, Dan I. and FERRIS, Jason (2017). Exploring mortality among drug treatment clients: The relationship between treatment type and mortality. *Journal of Substance Abuse Treatment*, 82, 22-28.

Copyright and re-use policy

See <http://shura.shu.ac.uk/information.html>

Accepted Manuscript

Exploring mortality among drug treatment clients: The relationship between treatment type and mortality

Belinda Lloyd, Renee Zahnow, Monica J. Barratt, David Best, Dan I. Lubman, Jason Ferris



PII: S0740-5472(17)30138-1
DOI: doi: [10.1016/j.jsat.2017.09.001](https://doi.org/10.1016/j.jsat.2017.09.001)
Reference: SAT 7630

To appear in:

Received date: 21 March 2017
Revised date: 30 August 2017
Accepted date: 1 September 2017

Please cite this article as: Belinda Lloyd, Renee Zahnow, Monica J. Barratt, David Best, Dan I. Lubman, Jason Ferris , Exploring mortality among drug treatment clients: The relationship between treatment type and mortality, (2017), doi: [10.1016/j.jsat.2017.09.001](https://doi.org/10.1016/j.jsat.2017.09.001)

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

TITLE: Exploring mortality among drug treatment clients: the relationship between treatment type and mortality

Running title: Drug treatment type and mortality

Author names and affiliations

Belinda Lloyd BA (Hons), PhD. Associate Professor^{1,2}
Renee Zahnow BA (Hons), PhD. Research Fellow³,
Monica J. Barratt BSc (Psych)(Hons), PhD, Research Fellow^{4,5,6},
David Best BA Hons, MSc, PhD, Ch Psychol, FRSA, Professor of Criminology^{1,7},
Dan I. Lubman MB ChB PhD FRANZCP FChAM, Director & Professor of
Addiction Studies and Services^{1,2}
Jason Ferris BPsych (Hons), MBIostats, PhD, Senior Research Fellow³

¹Turning Point, Eastern Health, 54-62 Gertrude Street, Fitzroy, 3065, Victoria, Australia.

²Eastern Health Clinical School, Monash University, Victoria, Australia.

³ Institute for Social Science Research, University of Queensland, St Lucia, Queensland, Australia

⁴Drug Policy Modelling Program, National Drug and Alcohol Research Centre, UNSW, Sydney, NSW, Australia

⁵National Drug Research Institute, Faculty of Health Sciences, Curtin University, Perth, WA, Australia

⁶Behaviours and Health Risks Program, Burnet Institute, Melbourne, VIC, Australia

⁷Department of Law and Criminology, Sheffield Hallam University, Sheffield, England.

Corresponding Author:

Dr Jason Ferris
Senior Research Fellow
Institute for Social Science Research
University of Queensland
St Lucia, Queensland, 4072
j.ferris@uq.edu.au
(Ph) 07 3365 6070
(Fax) 07 3346 7646

Word count: 2999

Abstract:

Aims: Studies consistently identify substance treatment populations as more likely to die prematurely compared with age-matched general population, with mortality risk higher out-of-treatment than in-treatment. While opioid-using pharmacotherapy cohorts have been studied extensively, less evidence exists regarding effects of other treatment types, and clients in treatment for other drugs. This paper examines mortality during and following treatment across treatment modalities.

Methods: A retrospective seven-year cohort was utilised to examine mortality during and in the two years following treatment among clients from Victoria, Australia, recorded on the Alcohol and Drug Information Service database by linking with National Death Index. 18,686 clients over a 12-month period were included. Crude (CMRs) and standardised mortality rates (SMRs) were analysed in terms of treatment modality, and time in or out of treatment.

Results: Higher risk of premature death was associated with residential withdrawal as the last type of treatment engagement, while mortality following counselling was significantly lower than all other treatment types in the year post-treatment. Both CMRs and SMRs were significantly higher in-treatment than post-treatment.

Conclusion: Better understanding of factors contributing to elevated mortality risk for clients engaged in, and following treatment, is needed to ensure that treatment systems provide optimal outcomes during and after treatment.

Keywords: mortality, treatment, cohort, linkage, drug

1 Introduction

In 2011/12, it is estimated that between 202, 168 and 232, 419 Australians received alcohol and other drug treatment (AOD) (Chalmers, Ritter, & Berends, 2016). Alcohol and other drug treatments take various forms (e.g. pharmacological detoxification, psychosocial interventions) and are delivered through a range of public and private service providers (Chalmers et al., 2016). While supporting evidence varies across modalities, there is widespread agreement that individuals who engage with treatment services are more likely to significantly reduce or cease drug use and remain drug free than those who do not undertake treatment (Corsi, Lehman, & Booth, 2009; Madras et al., 2009; Maremmani, Pani, Pacini, & Perugi, 2007; World Health Organisation, 2008). Drug use cessation is associated with improvements in general health, mental health and social functioning (Corsi et al., 2009; Department of Health (England), 2007; Kimber et al., 2010; Madras et al., 2009). Yet, there is also risk associated with treatment engagement and drug use cessation. Evidence suggests that among opioid, heroin and alcohol treatment attendees in particular, mortality rates peak within the first four weeks following treatment cessation (Buster, Brussel, & Brink, 2002; Cousins et al., 2011; Degenhardt et al., 2009; Strang et al., 2003). Examination of mortality outcomes for drug users indicates that treatment engagement is protective against premature mortality; that is mortality rates are lower when users are in treatment than prior to or indeed following treatment cessation (Darke, Mills, Ross, & Teesson, 2011; Degenhardt et al., 2009). The period immediately after discharge from residential detoxification (Strang et al., 2003) or following incarceration (Farrell & Marsden, 2008; Ødegård, Amundsen, Kielland, & Kristoffersen, 2010; Seaman, Brettle, & Gore, 1998), has been associated with sharply elevated overdose fatality risk. Indeed, clients whose drugs of choice are

central nervous system CNS depressants (alcohol or heroin) prior to entry into detoxification treatment have higher mortality risk following treatment, when compared with clients whose primary drugs are stimulants (Saitz et al., 2007).

Relapse after detoxification represents a specific risk due to a sharp reduction in tolerance.

Opioid-using cohorts receiving pharmacotherapy are the most extensively studied group in regards to post-treatment mortality. For instance, Degenhardt (2009) found that opioid pharmacotherapy clients had an in-treatment crude mortality rate (CMR) of 6.0 (95% CI: 5.7–6.4) per 1000 PY compared with an out-of-treatment rate of 11.5 (95% CI: 11.1–12.0) per 1000 PY. Similarly, Ledberg (2017) reported mortality rates in a sample of opiate users undergoing methadone maintenance treatment was significantly increased compared to the general population, both during periods of treatment and when not in treatment. While mortality risk is higher among opioid pharmacotherapy clients in the first two to four weeks following treatment cessation (Clausen, Anchersen, & Waal, 2008; Cousins et al., 2011; Degenhardt et al., 2009) the initial four weeks of pharmacotherapy induction is also a time of elevated risk compared with remaining time in treatment. Similar patterns of elevated mortality risk immediately following treatment cessation have been noted in other drug using cohorts.

In a cohort study of over 10,000 heroin users, mortality was measured across multiple treatment modalities, including methadone maintenance, therapeutic communities, pharmacological detoxification and treatment, and psychosocial treatments, finding most deaths occurred out of treatment, with the highest rate of death occurring in the first month out of treatment (Davoli et al., 2007). Similarly, when the effect of medication-free inpatient treatment (detoxification) was assessed among a Norwegian

group of drug users followed for eight years after treatment cessation, elevated risk of death was experienced in the first month following treatment discharge (Ravndal & Amundsen, 2010).

For clients seeking treatment for alcohol use problems, both short- and long-term mortality risks have been identified following treatment cessation (Costello, 2006; Lloyd, Barratt, Ferris, Best, & Lubman, 2013; Saitz et al., 2007). Acute alcohol-related contributors to causes of death (e.g. overdose and fatal injuries) influence short-term survival following treatment, while chronic conditions (e.g. cancers and liver disease) contribute significantly to increased mortality rates among clients followed up over longer periods (Costello, 2006). Ongoing engagement with support services, and identification of groups at elevated risk have been identified as important to reduce post-treatment mortality for such populations (Costello, 2006; Timko, DeBenedetti, Moos, & Moos, 2006).

While opioid-using cohorts receiving pharmacotherapy have been studied extensively, there is less evidence about mortality risks during and following other types of treatment and for groups of clients in treatment with drugs of concern (DoCs) other than opioids. This study examines mortality outcomes for clients engaged in treatment for alcohol, opioids and other drugs across a range of treatment modalities other than primary pharmacotherapy, and assesses mortality both during treatment and for the 2 years following discharge. Concerns about safety of treatment can compromise acceptance of treatment in the community and discourage engagement by drug users. By identifying periods of elevated risk, when heightened support may be required,

associated with different types of drug and alcohol treatment the results of this study can inform safer clinical practices.

2 METHODS

This study integrates client data from the Australian Alcohol and Drug Information System (ADIS) database (including detailed information regarding all specialist treatment) with the National Death Index (NDI; which includes detailed information regarding cause of death for all deaths occurring in Australia) to examine mortality outcomes among a cohort of Alcohol and Other Drug treatment service clients from Victoria, Australia. The two databases were linked based on partial client identifiers.

2.1 Cohort

ADIS is a register of government-funded, specialist Alcohol and Other Drug (AOD) treatment services (for a full list of services please see Table 1). The cohort used for the current study were selected based on three criteria: completion of one or more courses of AOD treatment (for example, counselling, residential withdrawal) in the 12-month period between 1 July 2000 and 30 June 2001, with first course of treatment (COT) starting on or after 1 January 2000; records had to include a valid date of birth (required for linkage purposes) and; records had to include a start date of first COT. After applying these criteria the final cohort included 18,686 clients. To enable data linkage, a unique identifier was created for each individual by combining partial name identifiers (second two letters of first name and first two letters and last letter of surname), date of birth and gender (for example John Doe, 17/01/1969, male would be ohdoe170169m).

2.2 Data sources

2.2.1 ADIS

To ensure full capture of sequential, overlapping and/or embedded COTs we matched cohort codes across eight years of ADIS data. This data captured all COTs that terminated between 1 July 2000 and 30 June 2008. Multiple COTs were common among the cohort with the median of 2 (IQR 1-5) COTs. COTs could be continuous, indicating a change of treatment type, agency or DoC.

The total number of COTs for this cohort was 89,764. A number of steps were taken to clean and prepare the data for analyses. COTs were excluded if they started before 1 January 2000 or after 1 January 2007 and overlapping COTs and consecutive COTs were recoded. Specifically, overlapping courses of treatment were amended so that the first one finished on the day the subsequent one started; both records were retained. Where two or more treatments started on the same day the longest running treatment remained for the analysis and the other treatments were removed. Data cleaning resulted in the removal of approximately 15% of records; a total of 76,342 COTs were retained for the final analysis.

2.2.2 National Death Index (NDI)

Data linkage, between the ADIS cohort and NDI, was conducted by the Australian Institute of Health and Welfare (AIHW). The first of three linkage passes used an exact match unique identifier. This process was repeated matching only on month and year of birth. The final pass identified cases within ADIS where the client was recorded as deceased where death occurred after the last ADIS contact date.

Ninety-four percent of deaths (N=532) were matched with NDI during the first pass; 10 cases (2%) were matched in the second pass; the final 23 (4%) cases were matched in the third pass.

2.3 Data Analysis

Data were examined using survival analysis. All analyses were conducted using Stata 11.

2.3.1 Predictor variables

Demographic, drug and treatment variables available in ADIS were included as predictors in survival time analysis. Sex, country of birth (born in Australia or not) and indigenous status were included as time constant predictors. Age, employment status (employed or not employed), living status (alone or with family/others), temporary or homeless accommodation status, and current involvement in the justice system (through community based orders, parole, bail, custody, etc.) were included as time-varying covariates. Other covariates in the models included primary DoC and injecting drug use at the start of each COT and medical and psychiatric comorbidities.

We included an indicator of polydrug use. This was computed using the reported DoCs for multiple COTs. Individuals who recorded different primary DoCs across multiple COTs were classified as polydrug users. This measure may underestimate polydrug use in the cohort but it has utility in identifying clients with multiple DoCs requiring treatment.

Within the ADIS database AOD treatment is classified as one of 11 types: counselling; residential withdrawal; other withdrawal; brokerage; outreach; specialist pharmacotherapy; other services; supported accommodation; aboriginal services; residential rehabilitation; post-withdrawal linkage. Treatment type classifications are defined in Table 1. We included variables to capture type of treatment received, number of COTs per client and reason for treatment termination.

2.3.2 *Crude mortality rates (CMR) and standardised mortality ratios SMR)*

All-cause CMRs are presented per 1000 person-years (PY) and were computed as the total number of deaths divided by the equivalent sum of person years of observation. Indirect all-cause SMRs for 10-year age groups were computed based on death rates of the Victorian population in the year 2000. To calculate CMRs and SMRs, time at risk (in person-years) was calculated from date of first COT (between 1 January 2000 and 30 June 2001) to the earliest of date of death, or two years after the last COT ended, or 31 December 2006. Two-sided 95% confidence intervals (95% CI) were based on Poisson distribution.

2.3.3 *Factors predicting mortality*

Time-at-risk following treatment was calculated from the date of termination of last COT to death or censorship. Censorship occurred at the earliest of two years after last COT ended or 31 December 2006. The median survival time was two years. In-treatment deaths were examined according to duration of treatment engagement for that COT.

Bivariate relationship between covariates and time-to-death were assessed using cox proportional hazards models. Variables that did not meet the proportional hazards assumption (Hosmer & Lemeshow, 1999) were split into two distinct hazard ratios (for year 1 and year 2) by creating ‘heaviside’ functions of the specific covariates: then modelled as an extended cox proportional hazards model (Kleinbaum & Klein, 2005). When heaviside functions are used, fixed hazard ratios for specified time intervals are generated (Kleinbaum & Klein, 2005). In this instance, an estimate of the hazard ratio is calculated for the indicator variable at year 1 and year 2; that is two distinct hazard ratios are concurrently modelled against time to death (Hosmer & Lemeshow, 1999). Reassessment of the proportional hazards assumptions using these time-interacted variables demonstrated all models were well-specified.

Only covariates with p-values <0.05 in univariate models were included as controls in the series of multivariate Cox proportional hazards models. These models controlled for age, sex, not being employed, living alone, psychiatric comorbidity, recent injecting and total number of COTs received. As the primary DoC may also impact which type of treatment an individual may seek (or be referred to) the primary DoC was also including in the multivariate models. As there were 10 primary DoCs reported (see Table 2) and a number of these had less than 1000 cases, the primary DoC was recoded into 5 categories when included in the multivariate models: heroin and other opioids; alcohol; cannabis; amphetamine; benzodiazepines, sedatives and other hypnotics; and other. Unadjusted and adjusted models were run separately for each treatment type, with the reference group defined as all other cases.

The Victorian Department of Human Services HREC and the AIHW Ethics Committee reviewed and approved all aspects of the project.

3 RESULTS

Treatment data of 18,686 individuals was analysed, representing 69,270 person-years over 89,764 COT. Two thirds (65%) of the cohort were male and median age at start was 28 years (IQR 21–36).

Table 1

Counselling was the most commonly received treatment type (Table 1). Residential withdrawal, other withdrawal and brokerage (case managed assessment, referral and linkage) services were also common. The median number of COTs per client was 2 (IQR 1–6) and median length of each COT was 31 days (IQR 10–74), although clients spent much longer in treatment overall – with a median of 115 days in treatment (IQR 36–295). Substantially more time was spent out of treatment: the median time out of treatment was 794 days (IQR 731–1575) or 2.2 years (IQR 2.0–4.3).

Table 2

The primary DoC varied across treatment types, with heroin and other opioids, alcohol and cannabis most commonly cited. While heroin and other opioids were commonly noted as the primary DoC for residential withdrawal, other withdrawal and residential rehabilitation (45%, 34% and 48% respectively), alcohol (33%, 36% and

34% respectively) and cannabis (12%, 17% and 8% respectively) constituted sizable proportions of COTs (Table 2).

Table 3

Table 3 highlights that the overall in-treatment CMR (12.4; 95% CI: 10.5–14.5) was significantly higher than the overall out-of-treatment (post-treatment) CMR (7.4; 95% CI: 6.7–8.1). This pattern was also reflected in SMRs: overall in-treatment SMR (10.7; 95% CI: 9.12–12.6) overall out-of-treatment SMR (6.1; 95% CI: 5.5–6.7). However, this difference was not as clear when comparing CMR and SMR in-treatment and out-of-treatment rates at particular treatment durations. For example, Z-tests and overlapping confidence intervals indicate that CMR estimates in treatment at the first month and second month of treatment did not significantly differ from CMR estimates out-of-treatment at the first month and the second month (Payton, Greenstone, & Schenker, 2003; Schenker & Gentleman, 2001). When divided further by treatment time, risk of death was not significantly different in the first two months after leaving treatment compared with any of the in-treatment time periods examined.

Table 4 and Figure 1 and Figure 2

The unadjusted hazard of death for clients discharged from residential withdrawal was two and a half times the rate of all other clients (148% increase – 95% CIs: 94%-217%). While there was some diminution of effect in adjusted analyses, rate of death for clients who were discharged from residential withdrawal remained significantly

elevated – at more than double the rate of all other clients (a 118% increase – 95% CIs: 68–185%).

After adjustment, clients whose last COT was counselling experienced a significantly lower hazard of death in the first year of follow-up compared with all other cases (42% decrease – 95% CIs: 25–55%) (Table 4 and Figure 1). However, there was no significant protective effect found for counselling in the second year following treatment cessation. There were no other statistical differences between the remaining treatment modalities (Table 4 and Figure 2).

4 DISCUSSION

While the benefits of AOD treatments are evident, studies also show that drug users experience elevated mortality risk within the four weeks immediately following treatment cessation (Clausen et al., 2008; Cousins et al., 2011; Degenhardt et al., 2009). To date research on this phenomenon has largely focussed on opioid-users engaged in pharmacotherapy (Clausen et al., 2008; Davoli et al., 2007; Degenhardt et al., 2009). As concerns about treatment safety may discourage engagement by drug users, identifying periods of elevated risk and providing extra support during these periods is an important public health endeavour. Here we extend on previous studies by presenting CMRs and SMRs for a cohort of specialist alcohol and other drug treatment clients who experienced problems with a wide range of drug types, and have sought treatment across several modalities. By focussing on a range of AOD treatment services and drug types our study identifies key differences in risk across drug types and treatment modalities. We summarize the results in three key findings.

First, we find that the overall CMRs and SMRs for clients whilst in treatment and clients in the first two months after treatment cessation were significantly greater than the overall rate. While previous studies have identified risk of death as being more elevated out-of-treatment (Davoli et al., 2007; Degenhardt et al., 2009; Ledberg, 2017), most indicate greatest risk of death is in the first month following treatment cessation (Clausen et al., 2008). Our results support these findings, with the highest risk of death in the first month following treatment cessation when examining all treatment types combined (Davoli et al., 2007; Degenhardt et al., 2009). Yet, our finding that CMRs and SMRs for clients in treatment were significantly higher than for clients who had ceased treatment when combining all time periods was in contrast to previous research. While most previous studies have focused primarily on populations of heroin users, and have largely drawn on opioid pharmacotherapy cohorts to examine relationships between treatment and mortality risk, our sample is diverse in both treatment modalities and drug types. Studies on opioid users engaged in substitution pharmacotherapy have noted an elevation in risk at transition periods, in the early stages of treatment and immediately following treatment cessation (Buster et al., 2002; Degenhardt et al., 2009). This is likely owing to the nature of opioid substitution therapy (OST), which can be considered a maintenance treatment or temporary approach to managing physiological withdrawal symptoms during detoxification (Amato, Minozzi, Davoli, & Vecchi, 2011). If abstinence is desired by a client undergoing OST, typically psycho-social based treatments are employed while OST is tapered and eventually eliminated. These psycho-social treatments include behavioral treatments such as counselling and family therapy (Amato et al., 2011 & Vecchi, 2011). Thus, the elevated risk period immediately following treatment cessation that has been identified in previous research may indeed point to

elevated risk *during* post-OST abstinence-based treatments. Our findings demonstrate a need to consider time in-treatment as also being characterised by increased mortality risk. We suggest more research is required to fully understand mortality risk during this period.

Second, we find that clients discharged from residential withdrawal were at increased risk of death in the first year out of treatment compared with all other clients in cohort. This is supported by prior research (Ravndal & Amundsen, 2010; Strang et al., 2003). However, the magnitude of the finding raises questions regarding what factors might drive such an elevation in risk of death, and although the analyses controlled for a range of covariates, unmeasured aspects of severity of substance issues and complexity of treatment pathways may contribute to these results. Further, as death risk has been calculated based on last treatment type, we are unable to discern from this study whether clients who transition from residential withdrawal to another treatment modality, such as community-based support, have better outcomes. Further research is needed to examine treatment and client trajectories in terms of suites of treatment and support, and also client profiles of severity, complexity, risk and support.

Third, clients discharged from counselling experienced a decreased risk of death in the first year out of treatment compared with all other clients. This significant finding may indicate protective effects of the most commonly used treatment type in the treatment system, or may reflect a client population experiencing fewer barriers to recovery. The severity of substance use issues experienced by clients in the cohort is

likely to vary significantly and this finding may reflect a propensity for counselling clients to present with less complex cases than those clients diverted to other treatments such as residential programs. Still, these findings are promising and highlight the potential importance of facilitating clients' engagement with counselling services both as a primary treatment modality and following detoxification.

Understanding protective and risk factors in relation to treatment options across diverse populations is essential, and is highlighted by the high proportions of clients accessing AOD treatment services for drugs other than opioids – with alcohol and cannabis representing primary DoCs for the majority of COT in Australia (Australian Institute of Health and Welfare, 2015). This study offers insight into diverse AOD treatment populations and is a significant new contribution to evidence in an Australian context. The findings presented here have significant policy and practice implications for assessment and support of people seeking AOD treatment regarding a need for enhanced engagement and support following treatment cessation, and emphasise a need for an evidence-based approach to treatment provision and delivery that incorporates an outcome monitoring framework.

4.1 Limitations

Despite adopting a robust linkage process that yielded a sufficiently large cohort for analysis, the findings presented here may underestimate mortality by missing ADIS clients who had incomplete data and were unable to be matched to NDI. We acknowledge that the data used here is somewhat dated, however, we also note continuity in AOD treatment services in Australia in the intervening years (Australian Institute of Health and Welfare, 2016). While the National Drug Strategy 2004-2009

was reviewed in 2009, funding structures for AOD treatment services were continued in the National Drug Strategy 2010-2015. The types of AOD treatment services utilised in Australia have remained relatively unchanged over the last decade thus we do not anticipate the age of the data to impact the relevance of the findings (Australian Institute of Health and Welfare, 2016).

A limitation of the data worth noting is that key indicators of the severity and complexity of the client's substance use issues were not recorded in ADIS; these factors are likely to influence the survival of drug treatment clients. For example, age of first drug use and first injection are important covariates for mortality (Bird & Hutchinson, 2010). Lifestyle factors and engagement with other agencies including mental health services and the criminal justice system are also likely to play a significant role in mortality risk; this information was not available in ADIS. More data regarding client journeys through treatment over time would be useful in determining patterns of treatment engagement that influence client outcomes. A final limitation relates to ADIS coding practices; treatment classification is interpreted by the treating agency thus some discrepancies across services may exist. Furthermore, coding practices for predictor variables may have changed systematically over the period examined resulting from policy changes – e.g., additional DoCs, and different categories of DoCs, have been adopted during this time. To minimise the impact on results, only complete and consistently accurate variables were included in analyses.

4.2 Conclusion

Survival following engagement in AOD specialist treatment is greatest following counselling treatment, whilst residential withdrawal represented the treatment

modality with poorest survival outcomes for clients where this was their last treatment type – which may reflect a lack of sufficient aftercare, or the comparative complexity of this client group. There is a need to explore the role of individual, treatment and social factors that may contribute to mortality following treatment, and opportunities to enhance support for AOD clients during and following treatment to improve outcomes. Through implementation of evidence-based strategies that enhance existing treatment modalities, and engage clients throughout the recovery process, there is great capacity to improve health of individuals, success of treatment, and reduce the impact of drug use on the community. There is an urgent need to better understand specific risks and factors contributing to elevated mortality risk, including causes of death for clients while engaged in treatment, and also following treatment, to ensure that the AOD system provides the best outcomes for its client populations.

5 ACKNOWLEDGMENTS

The authors would like to acknowledge and kindly thank the Australian Institute of Health and Welfare for access to NDI data, and the Victorian Department of Health for access to ADIS data. The authors would also like to acknowledge and thank Sharon Matthews for her support and assistance.

Funding acknowledgement

This project was funded by the Victorian Department of Health. M.J.B. is supported by a fellowship from the NHMRC (APP1070140). The National Drug and Alcohol Research Centre and the National Drug Research Institute are supported by funding from the Australian Government under the Substance Misuse Prevention and Service Improvement Grants Fund. We also acknowledge the contribution of the Victorian Operational Infrastructure Support Program received by the Burnet Institute.

Declaration of interest

Prof. Dan Lubman has received speaking honorarium for Astra Zeneca and Janssen, as well as travel support from Lundbeck.

ACCEPTED MANUSCRIPT

References

- Amato, L., Minozzi, S., Davoli, M., & Vecchi, S. (2011). Psychosocial and pharmacological treatments versus pharmacological treatments for opioid detoxification. *Cochrane Database of Systematic Reviews*(9). doi:10.1002/14651858.CD005031.pub4
- Australian Institute of Health and Welfare. (2015). *Policy related to methylamphetamine in Australia between 2003–04 and 2013–14*. Retrieved from <http://www.aihw.gov.au/publication-detail/?id=60129552818>
- Australian Institute of Health and Welfare. (2016). *Trends in alcohol availability, use and treatment 2003–04 to 2014–15*. Retrieved from Canberra: Australia: <http://www.aihw.gov.au/publication-detail/?id=60129557147>
- Bird, S. M., & Hutchinson, S. J. (2010). Over 1200 drugs-related deaths and 190,000 opiate-user-years of follow-up: relative risks by sex and age-group. *Addiction Research and Theory*, 18(2), 194-207.
- Buster, M. C. A., Brussel, G. H. A. v., & Brink, W. v. d. (2002). An increase in overdose mortality during the first 2 weeks after entering or re-entering methadone treatment in Amsterdam. *Addiction*, 97(8), 993-1001. doi:10.1046/j.1360-0443.2002.00179.x
- Chalmers, J., Ritter, A., & Berends, L. (2016). Estimating met demand for alcohol and other drug treatment in Australia. *Addiction*, 111(11), 2041-2049. doi:10.1111/add.13473
- Clausen, T., Anchersen, K., & Waal, H. (2008). Mortality prior to, during and after opioid maintenance treatment (OMT): A national prospective cross-registry study. *Drug and Alcohol Dependence*, 94(1–3), 151-157. doi:<http://dx.doi.org/10.1016/j.drugalcdep.2007.11.003>

- Corsi, K. F., Lehman, W. K., & Booth, R. E. (2009). The effect of methadone maintenance on positive outcomes for opiate injection drug users. *Journal of Substance Abuse Treatment, 37*(2), 120-126. doi:10.1016/j.jsat.2008.11.004
- Costello, R. (2006). Long-term mortality from alcoholism: a descriptive analysis. *Journal of Studies on Alcohol and Drugs, 67*(5), 694-699.
- Cousins, G., Teljeur, C., Motterlini, N., McCowan, C., Dimitrov, B. D., & Fahey, T. (2011). Risk of drug-related mortality during periods of transition in methadone maintenance treatment: A cohort study. *Journal of Substance Abuse Treatment, 41*(3), 252-260. doi:http://dx.doi.org/10.1016/j.jsat.2011.05.001
- Darke, S., Mills, K. L., Ross, J., & Teesson, M. (2011). Rates and correlates of mortality amongst heroin users: Findings from the Australian Treatment Outcome Study (ATOS), 2001–2009. *Drug and Alcohol Dependence, 115*(3), 190-195. doi:http://dx.doi.org/10.1016/j.drugalcdep.2010.10.021
- Davoli, M., Bargagli, A. M., Perucci, C. A., Schifano, P., Belleudi, V., Hickman, M., . . . for the, V. S. G. (2007). Risk of fatal overdose during and after specialist drug treatment: the VEdeTTE study, a national multi-site prospective cohort study. *Addiction, 102*(12), 1954-1959. doi:10.1111/j.1360-0443.2007.02025.x
- Degenhardt, L., Randall, D., Hall, W., Law, M., Butler, T., & Burns, L. (2009). Mortality among clients of a state-wide opioid pharmacotherapy program over 20 years: Risk factors and lives saved. *Drug and Alcohol Dependence, 105*(1–2), 9-15. doi:http://dx.doi.org/10.1016/j.drugalcdep.2009.05.021
- Department of Health (England). (2007). *Drug Misuse and Dependence: UK Guidelines on Clinical Management*. Retrieved from London: http://www.nta.nhs.uk/uploads/clinical_guidelines_2007.pdf

- Farrell, M., & Marsden, J. (2008). Acute risk of drug-related death among newly released prisoners in England and Wales. *Addiction, 103*(2), 251-255.
doi:10.1111/j.1360-0443.2007.02081.x
- Hosmer, D. W., & Lemeshow, S. (1999). *Applied Survival Analysis: Regression modelling of time to event data*. New York: John Wiley and Sons.
- Kimber, J., Copeland, L., Hickman, M., Macleod, J., McKenzie, J., De Angelis, D., & Robertson, J. R. (2010). Survival and cessation in injecting drug users: prospective observational study of outcomes and effect of opiate substitution treatment. *BMJ, 341*. doi:10.1136/bmj.c3172
- Kleinbaum, D. G., & Klein, M. (2005). *Survival Analysis: A self-learning text* (2nd ed.). New York: Springer.
- Ledberg, A. (2017). Mortality related to methadone maintenance treatment in Stockholm, Sweden, during 2006–2013. *Journal of Substance Abuse Treatment, 74*, 35-41. doi:10.1016/j.jsat.2016.12.005
- Lloyd, B., Barratt, M. J., Ferris, J., Best, D., & Lubman, D. I. (2013). Factors influencing mortality among alcohol and drug treatment clients in Victoria, Australia: The role of demographic and substance use characteristics. *Australian & New Zealand Journal of Psychiatry, 47*(9), 859-867.
doi:10.1177/0004867413491155
- Madras, B. K., Compton, W. M., Avula, D., Stegbauer, T., Stein, J. B., & Clark, H. W. (2009). Screening, brief interventions, referral to treatment (SBIRT) for illicit drug and alcohol use at multiple healthcare sites: Comparison at intake and 6 months later. *Drug and Alcohol Dependence, 99*(1–3), 280-295.
doi:http://dx.doi.org/10.1016/j.drugalcdep.2008.08.003

- Maremmanni, I., Pani, P. P., Pacini, M., & Perugi, G. (2007). Substance use and quality of life over 12 months among buprenorphine maintenance-treated and methadone maintenance-treated heroin-addicted patients. *Journal of Substance Abuse Treatment*, *33*(1), 91-98. doi:10.1016/j.jsat.2006.11.009
- Ødegård, E., Amundsen, E. J., Kielland, K. B., & Kristoffersen, R. (2010). The contribution of imprisonment and release to fatal overdose among a cohort of Norwegian drug abusers. *Addiction Research & Theory*, *18*(1), 51-58. doi:10.3109/16066350902818851
- Payton, M., Greenstone, M., & Schenker, N. (2003). Overlapping confidence intervals or standard error intervals: What do they mean in terms of statistical significance? *Journal of Insect Science*, *3*(34), 6.
- Ravndal, E., & Amundsen, E. J. (2010). Mortality among drug users after discharge from inpatient treatment: An 8-year prospective study. *Drug and Alcohol Dependence*, *108*(1-2), 65-69. doi:http://dx.doi.org/10.1016/j.drugalcdep.2009.11.008
- Saitz, R., Gaeta, J., Cheng, D. M., Richardson, J. M., Larson, M. J., & Samet, J. H. (2007). Risk of Mortality during Four Years after Substance Detoxification in Urban Adults. *Journal of Urban Health*, *84*(2), 272-282. doi:10.1007/s11524-006-9149-z
- Schenker, N., & Gentleman, J. F. (2001). On judging the significance of differences by examining the overlap between confidence intervals. *American Statistician*, *55*(3), 182-186. doi:Doi 10.1198/000313001317097960
- Seaman, S. R., Brettle, R. P., & Gore, S. M. (1998). Mortality from overdose among injecting drug users recently released from prison: database linkage study. *BMJ*, *316*(7129), 426-428. doi:10.1136/bmj.316.7129.426

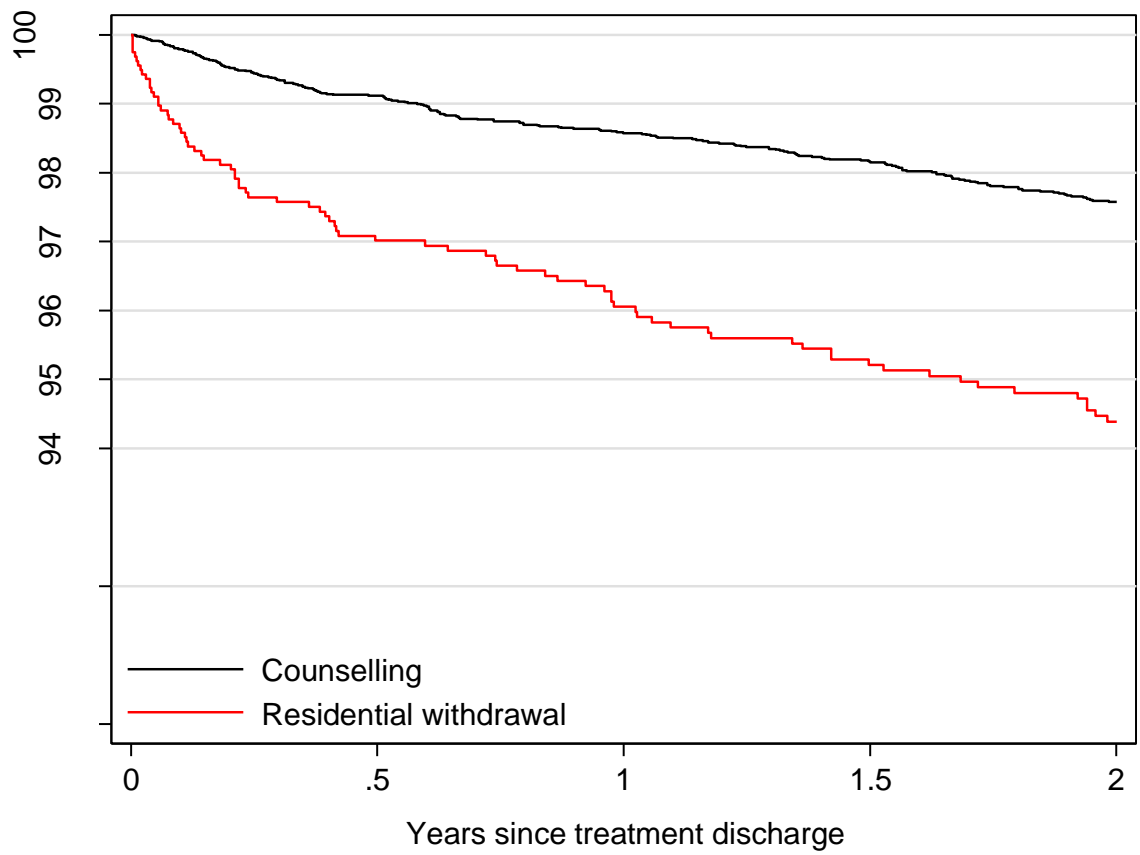
Strang, J., McCambridge, J., Best, D., Beswick, T., Bearn, J., Rees, S., & Gossop, M.

(2003). Loss of tolerance and overdose mortality after inpatient opiate detoxification: follow up study. *BMJ : British Medical Journal*, 326(7396), 959-960.

Timko, C., DeBenedetti, A., Moos, B. S., & Moos, R. H. (2006). Predictors of 16-Year Mortality Among Individuals Initiating Help-Seeking for an Alcoholic Use Disorder. *Alcoholism: Clinical and Experimental Research*, 30(10), 1711-1720. doi:10.1111/j.1530-0277.2006.00206.x

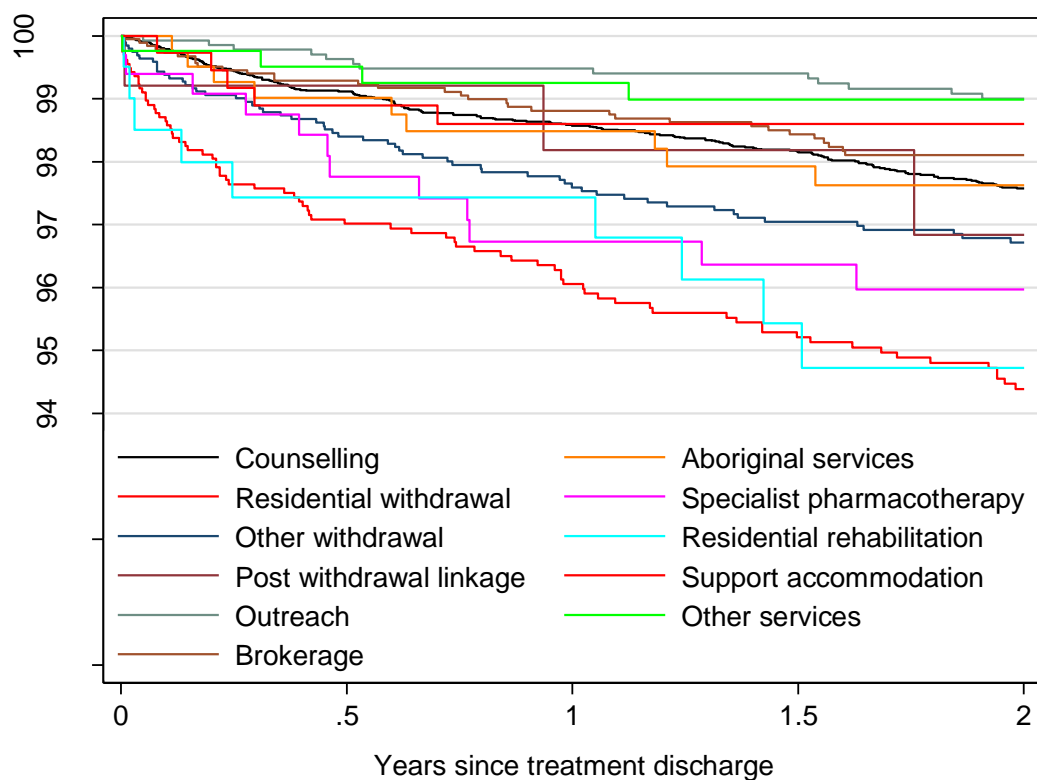
World Health Organisation. (2008). *The Effectiveness of a Brief Intervention for Illicit Drugs Linked to the Alcohol, Smoking and Substance Involvement Screening Test (ASSIST) in Primary Health Care Settings: A Technical Report of Phase III Findings of the WHO ASSIST Randomized Control Trial*. Retrieved from Geneva, Switzerland:
http://www.who.int/substance_abuse/activities/assist_technicalreport_phase3_final.pdf

Figure 1: Kaplan-Meier estimates by selected treatment types: Counselling and residential withdrawal



ACCEPTED

Figure 2: Kaplan-Meier estimates by selected treatment types: Counselling and residential withdrawal



ACCEPTED

Table 1: Treatment types received by 18,686 clients over 69,270 person-years

| Types of treatment | Definition | Frequency | % of total | % of known |
|----------------------------|--|-----------|------------|------------|
| Counselling | Counselling includes cognitive behaviour therapy, brief intervention, relapse intervention and motivational interviewing which can be individual, group or family therapy, or a combination. | 35,806 | 39.9 | 40.0 |
| Residential Withdrawal | Residential withdrawal treatment programs refers to treatment within an inpatient withdrawal unit or hospital with access to medical staff, medications and continuous monitoring. | 12,796 | 14.3 | 14.3 |
| Other Withdrawal | Other withdrawal programs are withdrawal management/support programs for individuals who no longer, or do not require inpatient withdrawal management. | 10,734 | 12.0 | 12.0 |
| Brokerage | Brokerage treatment models are case management based and seek to identify the client's needs and refer clients to appropriate treatment; does not usually include ongoing monitoring. | 9,545 | 10.6 | 10.7 |
| Outreach | Outreach treatment occurs in an outreach environment, such as any private or public location, excluding a client's home or usual place of residence | 8,198 | 9.1 | 9.1 |
| Specialist Pharmacotherapy | Specialist pharmacotherapy refers to the administration of agnostic medications, such as methadone and buprenorphine, used as maintenance therapies or relapse prevention. | 2,569 | 2.9 | 2.9 |
| Supported Accommodation | Supported accommodation refers to services primarily concerned with providing accommodation; some support may be available such as an agency worker who can be called for emotional support. | 2,404 | 2.7 | 2.7 |
| Aboriginal Services | Aboriginal services refers to a range of treatment interventions for Aboriginal and Torres Strait Islander peoples, including: evidence-based mainstream intervention that have had culturally specific practice integrated into them. | 2,067 | 2.3 | 2.3 |
| Residential | Residential rehabilitation refers to intensive treatment programs | 1,636 | 1.8 | 1.8 |

| | | | | |
|-------------------------|--|--------|-------|-------|
| Rehabilitation | conducted in a residential setting typically offering a mixture of one-on-one, group work, peer support and team/community building processes. | | | |
| Post Withdrawal Linkage | Post withdrawal linkage services provide withdrawal care planning, including relapse prevention and linkages to external support networks designed to address the client's psychosocial needs. | 1,325 | 1.5 | 1.5 |
| Other Services | | 2,541 | 2.8 | 2.8 |
| Total known | | 89,621 | 99.8 | 100.0 |
| Unknown | | 143 | 0.2 | |
| Total | | 89,764 | 100.0 | |

NOTES: Definitions sourced from Australian Institute of Health and Welfare (2014).

Table 2: Primary drug of concern across treatment types

| Types of treatment % | Heroin and other opioids | Alcohol | Cannabis | Amphetamine | Other psychostimulants and hallucinogens | Benzo-diazepines, sedative and hypnotics | Nicotine | Volatile substances | Other | Unknown | Total N |
|----------------------------|--------------------------|---------|----------|-------------|--|--|----------|---------------------|-------|---------|---------|
| Counselling | 36.6 | 36.1 | 15.3 | 5.3 | 0.4 | 2.7 | 0.6 | 0.6 | 1.2 | 1.0 | 35,806 |
| Residential withdrawal | 45.2 | 33.4 | 12.2 | 3.9 | 0.3 | 3.8 | 0.1 | 0.8 | 0.3 | 0.0 | 12,796 |
| Other withdrawal | 34.3 | 35.7 | 17.0 | 5.1 | 0.4 | 5.5 | 0.3 | 0.4 | 0.5 | 0.8 | 10,734 |
| Post withdrawal linkage | 48.2 | 26.9 | 15.0 | 6.3 | 0.7 | 1.6 | 0.0 | 0.2 | 0.5 | 0.7 | 9,545 |
| Outreach | 50.2 | 11.5 | 24.2 | 4.8 | 0.9 | 1.6 | 0.8 | 3.1 | 1.3 | 1.6 | 8,198 |
| Brokerage | 90.3 | 3.1 | 1.0 | 1.4 | 0.1 | 1.9 | 0.0 | 0.0 | 1.3 | 0.8 | 2,569 |
| Aboriginal services | 47.2 | 29.8 | 13.1 | 3.5 | 0.4 | 1.8 | 0.4 | 1.0 | 0.9 | 1.9 | 2,541 |
| Specialist pharmacotherapy | 51.9 | 23.5 | 14.8 | 6.6 | 0.2 | 1.6 | 0.2 | 0.2 | 0.5 | 0.5 | 2,404 |
| Residential rehabilitation | 10.4 | 69.5 | 9.5 | 4.4 | 0.1 | 1.1 | 0.6 | 2.6 | 1.0 | 0.7 | 2,067 |
| Supported accommodation | 48.3 | 34.4 | 7.9 | 7.6 | 0.3 | 1.0 | 0.0 | 0.1 | 0.1 | 0.3 | 1,636 |
| Other services | 26.4 | 46.4 | 17.9 | 5.0 | 0.5 | 2.6 | 0.1 | 0.2 | 0.6 | 0.2 | 1,325 |
| Unknown | 30.1 | 33.6 | 25.2 | 8.4 | 2.8 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 143 |
| Total N | 37,456 | 28,596 | 13,603 | 4,541 | 414 | 2,538 | 355 | 741 | 775 | 745 | 89,764 |

Table 3: Crude mortality rates and standardised mortality ratios by year, in-treatment and out-of-treatment (N = 18,686)

| | CMR | | | | | SMR | | | |
|--|--------------|-----------------|------|-----------|----------------------|-----------------|------|-----------|----------------------|
| | Person-years | Observed deaths | Rate | 95% CI | In vs Out treatment† | Expected deaths | Rate | 95% CI | In vs Out treatment† |
| Year of follow-up | | | | | | | | | |
| 2000 | 4,806 | 69 | 14.4 | 11.3–18.2 | | 5 | 12.9 | 10.2–16.3 | |
| 2001 | 17,282 | 123 | 7.1 | 6.0–8.5 | | 20 | 6.1 | 5.1–7.3 | |
| 2002 | 17,400 | 126 | 7.2 | 6.1–8.6 | | 21 | 5.9 | 5.0–7.0 | |
| 2003 | 10,642 | 80 | 7.5 | 6.0–9.4 | | 13 | 6.2 | 5.0–7.7 | |
| 2004 | 7,707 | 65 | 8.4 | 6.6–10.8 | | 9 | 7.0 | 5.5–8.9 | |
| 2005 | 6,364 | 60 | 9.4 | 7.3–12.1 | | 8 | 7.6 | 5.9–9.8 | |
| 2006 | 5,068 | 47 | 9.3 | 7.0–12.3 | | 6 | 7.2 | 5.4–9.6 | |
| Overall in treatment | 11,898 | 147 | 12.4 | 10.5–14.5 | Pr(z =4.612) <0.001 | 14 | 10.7 | 9.1–12.6 | Pr(z =4.639) <0.001 |
| First month in course of treatment | 4,401 | 52 | 11.8 | 9.0–15.5 | Pr(z =0.957) =0.830 | 5 | 10.4 | 7.9–13.6 | Pr(z =0.799) =0.788 |
| Second month in course of treatment | 2,516 | 29 | 11.5 | 8.0–16.6 | Pr(z =0.137) =0.554 | 3 | 9.9 | 6.9–14.3 | Pr(z =0.155) =0.562 |
| Remaining time in course of treatment | 4,982 | 66 | 13.2 | 10.4–16.9 | * | 6 | 11.4 | 9.0–14.5 | |
| Overall out of treatment | 57,372 | 423 | 7.4 | 6.7–8.1 | | 70 | 6.1 | 5.5–6.7 | |
| First month out of treatment | 4,088 | 58 | 14.2 | 11.0–18.4 | | 5 | 12.2 | 9.5–15.8 | |
| Second month out of treatment | 3,357 | 40 | 11.9 | 8.7–16.2 | | 4 | 10.3 | 7.6–14.1 | |
| Third to twelve month out of treatment | 24,412 | 186 | 7.6 | 6.6–8.8 | | 29 | 6.4 | 5.6–7.4 | |
| Remaining time out of treatment | 25,515 | 139 | 5.4 | 4.6–6.4 | | 32 | 4.3 | 3.7–5.1 | |
| Overall cohort | 69,270 | 570 | 8.2 | 7.6–8.9 | | 83 | 6.8 | 6.3–7.4 | |

Note. All rates per 1,000 person-years. † Z-test: $(IR_1 - IR_2) / \left(\sqrt{(\sqrt{IR_1/Exposure_1})^2 + (\sqrt{IR_2/Exposure_2})^2} \right)$. * Comparison between in treatment and out treatment for 'remaining time in course of treatment' is not compared due to different time periods.

Table 4: Most recent treatment type and associated risk of death

| Treatment type | Per cent | Unadjusted hazard ratio (N=17,820) | 95% CI | Adjusted hazard ratio ^a (N=14,880) | 95% CI |
|-------------------------------------|----------|------------------------------------|-----------|---|-----------|
| Counselling ^b | 52 | | | | |
| In Year 1 | 28 | 0.72 ** | 0.57–0.91 | 0.58 *** | 0.45–0.75 |
| In Year 2 | 24 | 1.12 | 0.80–1.56 | 0.93 | 0.64–1.37 |
| Residential withdrawal ^b | 9 | 2.48 *** | 1.94–3.17 | 2.12 *** | 1.62–2.79 |
| Other withdrawal | 11 | 1.31 | 1.00–1.73 | 1.17 | 0.86–1.59 |
| Post withdrawal linkage | 1 | 1.13 | 0.36–3.50 | 0.75 | 0.24–2.34 |
| Outreach | 8 | 0.35 *** | 0.20–0.61 | 0.92 | 0.52–1.63 |
| Brokerage | 11 | 0.69 * | 0.48–0.99 | 0.90 | 0.59–1.35 |
| Aboriginal services | 2 | 0.91 | 0.47–1.75 | 1.02 | 0.50–2.09 |
| Specialist pharmacotherapy | 2 | 1.60 | 0.90–2.84 | 1.13 | 0.57–2.23 |
| Residential rehabilitation | 1 | 2.11 * | 1.09–4.08 | 1.73 | 0.88–3.37 |
| Supported accommodation | 2 | 0.56 | 0.23–1.36 | 0.62 | 0.26–1.50 |
| Other services | 2 | 0.39 | 0.14–1.03 | 0.57 | 0.21–1.53 |

Note. * $p < .05$, ** $p < .01$, *** $p < .001$. ^a Complete-case analysis adjusted for age, gender, not employed, lives alone, psychiatric comorbidity, recent drug injection, total courses of treatment and primary drug of concern (heroin and other opioids; alcohol; cannabis; amphetamines; benzodiazepines, sedatives and hypnotics; and other). ^b Variables that did not meet the proportional hazards assumption were stratified by follow-up year using heaviside functions.

Highlights

- This study examines crude (CMR) and standardised mortality rates (SMR) in sample of alcohol and drug treatment clients.
- CMRs and SMRs were highest in treatment and in first two months after treatment cessation.
- Clients discharged from residential withdrawal were at increased risk of death in the first year out of treatment compared to the cohort.
- Clients discharged from counselling experienced lower risk of death in the first year out of treatment compared to the cohort.

ACCEPTED MANUSCRIPT