



NOVA

University of Newcastle Research Online

nova.newcastle.edu.au

McKetin, Rebecca; Najman, Jake M.; Baker, Amanda L.; Lubman, Dan I.; Dawe, Sharon; Ali, Robert; Lee, Nicole K.; Mattick, Richard P.; Mamun, Abdullah, 'Evaluating the impact of community-based treatment options on methamphetamine use: findings from the Methamphetamine Treatment Evaluation Study (MATES)'. Originally published in *Addiction* Vol. 107, Issue 11, p. 1998-2008 (2012)

Available from: <http://dx.doi.org/10.1111/j.1360-0443.2012.03933.x>

The definitive version is available at wileyonlinelibrary.com

Accessed from: <http://hdl.handle.net/1959.13/1040789>

**Evaluating the impact of community-based treatment options on methamphetamine use:
findings from the Methamphetamine Treatment Evaluation Study (MATES)**

Rebecca McKetin^{1,2}, Jake M. Najman³, Amanda Baker⁴, Dan I. Lubman⁵, Sharon Dawe⁶,
Robert Ali⁷, Nicole K. Lee^{8,9}, Richard P. Mattick², and Abdullah Mamun³.

¹ *Centre for Research on Ageing, Health and Wellbeing, The Australian National University*

² *National Drug and Alcohol Research Centre, University of New South Wales*

³ *Queensland Alcohol and Drug Research and Education Centre, University of Queensland*

⁴ *Centre for Brain and Mental Health Research, University of Newcastle*

⁵ *Turning Point Alcohol and Drug Centre, Eastern Health and Monash University*

⁶ *School of Psychology, Griffith University*

⁷ *University of Adelaide*

⁸ *The National Centre for Education and Training on Addiction, Flinders University*

⁹ *National Drug Research Institute, Curtin University*

Running head: Methamphetamine use treatment outcomes

Word Count: 3,500

Declaration of interest: Dan Lubman has received speaker honoraria from Astra Zeneca and Janssen. Other authors have no interests to declare.

Key words: methamphetamine, amphetamine, treatment, outcomes, longitudinal, substance abuse, psychiatric comorbidity, HIV risk, crime

Corresponding author:

Dr. Rebecca McKetin

Centre for Mental Health Research

ANU College of Medicine, Biology and Environment

The Australian National University

ACT 0200 Australia

Ph. + 61 2 61258407

Fax. + 61 2 61250733

Email: Rebecca.mcketin@anu.edu.au

ABSTRACT

Aims: To evaluate the impact of community-based drug treatment on methamphetamine use using inverse-probability-of-treatment weighted (IPTW) estimators to derive treatment effects.

Design: A longitudinal prospective cohort study with follow-ups at 3 months, 1 year and 3 years. Treatment effects were derived by comparing groups at follow-up. IPTW estimators were used to adjust for pre-treatment differences between groups.

Setting: Sydney and Brisbane, Australia.

Participants: Participants were methamphetamine users entering community-based detoxification (n = 112) or residential rehabilitation (n = 248) services and a quasi-control group of methamphetamine users (n = 101) recruited from the community.

Measurements: Frequency of methamphetamine use between interviews (no use, less than weekly, 1-2 days per week, 3+ days per week), continuous abstinence from methamphetamine use, past month methamphetamine use, and methamphetamine dependence.

Findings: Detoxification did not reduce methamphetamine use at any follow-up relative to the quasi-control group. Relative to quasi-control and detoxification groups combined, residential rehabilitation produced large reductions in the frequency of methamphetamine use at 3 months (OR = 0.23, 95% CI 0.15-0.36, $p < 0.001$), with a marked attenuation of this effect at 1 year (OR 0.62, 95% CI 0.40-0.97, $p = 0.038$) and 3 years (OR = 0.71 95% CI 0.42-1.19, $p = 0.189$). The greatest impact was for abstinence: for every 100 residential rehabilitation clients there was a gain of 33 being continuously abstinent at 3 months, with this falling to 14 at 1 year and 6 at 3 years.

Conclusions: Community-based residential rehabilitation may produce a time-limited decrease in methamphetamine use, while detoxification alone does not appear to do so.

INTRODUCTION

Methamphetamine dependence is estimated to cost at least three-quarters as much as heroin dependence per person [1], yet there is a comparatively little evidence documenting treatment outcomes [2] and few specialized treatment options [3]. Notable is the lack of any evaluation of whether generic community-based drug treatment can reduce methamphetamine dependence. Existing studies in this area focus largely on opioids and/or alcohol [4-6]: this research finding support for community-based residential rehabilitation [4-6] but less for detoxification [4]. However, these findings may not apply to people who are dependent on methamphetamine, who have high rates of psychiatric comorbidity [7-10], and who have different treatment needs than people dependent on other drugs [11]. Given the scale of methamphetamine use internationally [12] and the severity of problems it can incur [2], it is critical to know whether existing drug treatment infrastructure can be used to treat methamphetamine dependence.

A broader issue is the lack of control groups in previous community-based treatment outcome studies [4-6], making it difficult to attribute changes in drug use to treatment (cf. natural remission from drug use or other secular changes). Even where comparison groups exist, their non-equivalence makes it difficult to infer treatment effects [4]. In other areas of public health, treatment effects have been derived from observation treatment trials using ‘propensity matching’ procedures. Propensity matching provides a method of adjusting for bias in quasi-experimental studies that is superior to conventional regression adjustment. This method involves deriving a composite ‘propensity score’ for each individual in the study, which reflects the probability that they would receive treatment based on their clinical characteristics [13]. Treatment effects reflect the difference in outcomes for participants in each group who have a similar propensity score. This difference is then averaged across the sample to derive an ‘average treatment effect’.

Recent statistical developments provide a more parsimonious solution to the non-equivalence of treatment groups by using inverse-probability-of-treatment weighted estimators (IPTW) [14]. Participants are weighted according to the inverse probability that they would receive treatment based on their observable characteristics (e.g., demographics, prior treatment history, severity of illness). This creates a pseudo-population of groups that are equivalent on their pre-existing characteristics. Their benefit over conventional matching procedures is that they provide treatment effects that are more amenable to interpretation, they eliminate residual confounding that arises from using a fixed number of strata to match clients, and they provide better adjustment for time-dependent confounders (e.g., heavier drug users seek more intensive treatment and are more likely to relapse) [14,15].

Although IPTW estimators have been increasingly applied in public health research to establish the efficacy of clinical protocols in-situ [16-18], this methodology has not yet been applied to drug treatment outcome studies. The aim of this study was to use IPTW estimators to determine the effect of community-based treatment (residential rehabilitation and detoxification) on methamphetamine use. Outcomes for these treatment modalities were compared to a quasi-control group of methamphetamine users recruited from the community. Data were taken from the Methamphetamine Treatment Evaluation Study (MATES): a longitudinal prospective cohort study of methamphetamine users.

METHOD

Participants and procedure

Treatment participants (n = 360) were recruited on entry to 15 residential rehabilitation facilities and 11 detoxification units located in Sydney (n = 19) and Brisbane (n = 7),

Australia. These agencies were selected from the Australian Minimum Dataset for Alcohol and Other Drug Treatment Services (MDS-AODTS) [19] which includes all publicly funded government and non-government drug and alcohol treatment agencies in Australia. Whether services provided detoxification or residential rehabilitation was based on how they were classified in the MDS-AODTS [19]. Being community-based drug treatment services, there were no constraints on the type of treatment provided within each treatment modality. Detoxification typically involved brief (e.g., 1 week) in-patient stays with medical support to manage withdrawal symptoms. Residential rehabilitation typically involved longer stays (e.g., several weeks to months) in a drug-free residential setting that provided an intensive program of integrated services and therapeutic activities (e.g., behavioural treatment approaches, recreational activities, social and community living skills, group work, relapse prevention) [19].

Inclusion criteria for treatment participants were: (a) methamphetamine or amphetamine recorded as the primary or secondary drug problem in the MDS-AODTS, (b) being 16+ years old, (c) willingness to participate in follow-up interviews, and (d) comprehension of English. Exclusion criteria were having received methamphetamine treatment or any inpatient drug treatment, or imprisonment, in the month prior to entering the study. These exclusion criteria were necessary to obtain a naturalistic level of drug use at the baseline interview. Ineligibility ($n = 195$) was mainly due to drug treatment (58%) or incarceration (28%) in the month prior to recruitment, while 10% declined participation. Differences between this treatment sample and all recorded methamphetamine treatment episodes in Australia were small (see Appendix S1, Supporting information).

The quasi-control group ($n = 101$) was recruited through community health services and needle and syringe programs from the greater Sydney region from January 2006 until May 2008. Inclusion and exclusion criteria were the same as for the treatment group. In addition,

quasi-control participants needed to have a minimum level of methamphetamine use to ensure they were comparable to the treatment group: either screening positive for methamphetamine dependence (a score of 4+ on the Severity of Dependence Scale [20,21]) or using 3+ days/week in the past month. Most ineligible quasi-control participants (n = 109) failed to meet the methamphetamine use inclusion criteria (43%) or had been in drug treatment in the past month (35%), while 16% declined participation.

Baseline interviews took 1.5 hours and were conducted face-to-face. Follow-up interviews (3 months, 1 year, 3 years) took 45 minutes and were conducted face-to-face or by telephone. Interviews were conducted at treatment centres or mutually convenient locations (e.g., cafes, parks, local health centres). All participants provided informed consent and were reimbursed (AU\$30 at 3 months and 1 year, and AU\$40 at 3 years). Additional informed consent and reimbursement (AU\$10) was provided for hair samples at 1 year.

Baseline interviews with treatment participants were conducted on a median of 6 days after treatment entry (inter-quartile range 2–10 days) and measures pertained to the month prior to treatment entry. Follow-up interviews occurred at 3 months (median 98 days, inter-quartile range 88-117), 1 year (median 378 days, inter-quartile range 361–400) and 3 years (median 1,136 days, inter-quartile range 921–1,299) after the baseline interview. The time to follow-up was shorter for the quasi-control condition than for the treatment conditions (Figure 1). However, there was no significant relationship between days to follow-up and methamphetamine use at any of the follow-up points.

Measures

Treatment exposure

The index treatment was defined as contiguous treatment from recruitment, allowing up to 7 days gap in treatment to accommodate for transfers between services. The duration of the index treatment was defined as the first to the last day of treatment, and was measured at the 3 month follow-up interview. For residential rehabilitation clients, the duration of treatment included any time spent in detoxification in preparation for residential rehabilitation (this occurred in 71% of cases). The number of treatment episodes initiated after the index treatment, and whether the participant received treatment for their methamphetamine use during each of these treatment episodes, was recorded at each follow-up interview.

Methamphetamine use

Self-reported frequency of use was measured in the year prior to entering the study and between each interview using the categories: no use, less than weekly, weekly, twice weekly, 3-4 days a week, 5+ days a week. Continuous abstinence was defined as no use of methamphetamine since the baseline interview. Past month methamphetamine use was assessed at each interview using the Opiate Treatment Index (OTI) [22]. Self-reported methamphetamine use in the past month was validated at follow-up in a sub-sample of 83 participants, and abstinence was confirmed in 94% of these cases (see Appendix S2 for details).

Other measures

Motivation to reduce methamphetamine use was measured at baseline using the Readiness to Change Questionnaire and participants were scored as being in the 'pre-contemplation', 'contemplation' or 'action' stage [23].

Polydrug use was defined as the total number of drug classes used in the past month (including heroin, other opioids, cocaine, ecstasy, hallucinogens, cannabis, alcohol, inhalants and tobacco).

The Composite International Diagnostic Interview (CIDI) [24] was used to make DSM-IV diagnoses of methamphetamine dependence and other Axis I psychiatric disorders. A DSM-IV diagnosis of conduct disorder was made using a modified version of the Diagnostic Interview Schedule [25].

Statistical analysis

Data were analysed using Stata Version 11.1. All tests were two-sided with significance set at $p < 0.05$. Medians and inter-quartile ranges are reported for skewed data. Unadjusted treatment effects were derived for detoxification and residential rehabilitation compared to the quasi-control group. Comparisons between groups were undertaken at each follow-up using logistic regression for dichotomous outcome measures and ordinal logistic regression for categorical outcome measures. Generalised ordinal logistic regression models were used where the assumption of proportional odds was breached. Subsequent analyses used IPTW estimators to compare the outcomes for the residential rehabilitation group to the quasi-control and detoxification groups combined ($n = 213$). These groups were combined to increase statistical power, because their outcomes were not significantly different. IPTW treatment effects were derived by applying probability weights that represented the inverse probability that the participant would have received treatment based on their baseline characteristics. Weights that were calculated according to the procedure described by Robins and colleagues [14] (see Appendix S3 for details). Confidence intervals were derived using robust standard errors to account for data clustering within treatment centres and the IPTW

weighting procedures. Missing data were imputed using multiple imputation by chained equations, implemented using the Stata 'ice' command (detailed in Appendix S4) [26].

RESULTS

Participant characteristics

Almost all participants (97%) met DSM-IV criteria for methamphetamine dependence at baseline; this did not differ significantly between treatment groups (Table 1). Most injected the drug, and the majority were unemployed single males (Table 1). Participants had used methamphetamine on a median of 16 days in the past four weeks (inter-quartile range 8-23 days) with 3% of participants not having used during this time. Other drug use in the past month consisted largely of tobacco (95%, 90% daily), cannabis (78%, 39% daily) and alcohol (71%, 15% daily), with a minority using heroin (26%, 3% daily) or cocaine (27%, <1% daily). In terms of readiness-to-change methamphetamine use, the majority of participants were in the action stage (55%). Most participants had an extensive history of drug treatment (Table 1). Treatment participants were typically voluntary admissions (85%) seeking complete abstinence (87%; 79% for detoxification and 91% for residential rehabilitation).

There were a number of differences between participants in the quasi-control group and those in the treatment groups, most notably that the quasi-control group used methamphetamine less often, were less severely dependent on the drug and were less motivated to reduce their methamphetamine use (Table 1).

Follow-up of the cohort

The follow-up rates were 80% at 3 months, 74% at 1 year and 66% at 3 years, with 88% of participants followed-up at least once; loss to follow-up included participants who were

incarcerated or deceased (Figure 1). The main predictors of attrition were low education and a prison history. Analyses presented below use imputed missing data. See Appendix S4 for details of attrition, the imputation procedure and results without data imputation.

[Table 1 and Figure 1 about here]

Treatment exposure

Sixty two per cent received residential rehabilitation (n = 248) and the remainder (28%, n = 112) received detoxification as their index treatment. The median duration of residential rehabilitation was 62 days (inter-quartile range 29-98) and detoxification 5 days (inter-quartile range 4-7). Most participants (83%) had left their index treatment by the 3 month follow-up.

Additional treatment during the follow-up period was common in all groups (Figure 2) with 47% of the sample receiving additional treatment, and 43% receiving additional treatment for methamphetamine use.

Treatment outcomes

Unadjusted outcomes

There was a reduction in the frequency of methamphetamine use over the 3 year follow-up period in both the quasi-control group and the treatment groups (Figure 3). There was no significant difference in frequency of methamphetamine use between the detoxification group and the quasi-control group at any follow-up (3 months: OR 0.96, 95% CI 0.56–1.63, p = 0.882; 1 year: OR 1.01, 95% CI 0.59–1.75, p = 0.967; 3 years: OR 0.79, 95% CI 0.44–1.40, p = 0.418). The residential rehabilitation group showed a large reduction in methamphetamine use relative to the quasi-control group at the 3 month follow-up (OR = 0.20, 95% CI 0.13–0.33, p < 0.001). This effect was attenuated but still significant at 1 year (OR 0.58, 95% CI

0.36–0.95, $p = 0.031$) and 3 years (OR = 0.57, 95% CI 0.33–0.99, $p = 0.045$). The residential rehabilitation group showed a similar pattern of results relative to the detoxification group, who were more similar in their baseline methamphetamine use (Figure 3), although the effect was not significant at 3 years (3 months: OR 0.24, 95% CI 0.15–0.40, $p < 0.001$; 1 year OR 0.59, 95% CI 0.36–0.97, $p = 0.038$; 3 years OR = 0.72, 95% CI 0.40–1.32, $p = 0.289$).

[Figures 1-3 about here]

IPTW treatment effects

When the residential rehabilitation group was compared with the quasi-control and detoxification groups combined ($n = 213$), unadjusted effects for residential rehabilitation remained significant at all follow-ups (Table 2). IPTW estimators were used to adjust for between group differences in the number of previous drug treatment episodes, previous treatment for methamphetamine use, severity of methamphetamine use prior to treatment entry, motivation to reduce methamphetamine use, polydrug use, unemployment and prison history (See Appendix S3 for details).

IPTW estimators reduced the magnitude of the treatment effects which were no longer significant at the 3 year follow-up (Table 2). The greatest change in methamphetamine use was seen for abstinence, with 34% more participants in the residential rehabilitation group reporting no use at the 3 month follow-up, this dropping to 9% and 6% at the 1 and 3 year follow-ups respectively (Table 2). Similar results were seen for dependence and past month use (see Appendix S5).

Continuous abstinence

A problem interpreting the above result is that that the residential rehabilitation group had higher rates of treatment exposure during the follow-up period (Figure 2), and this might

account for their lower levels of methamphetamine use. To isolate the impact of the index treatment episode, we used continuous abstinence (measured at each follow-up) as the outcome measure. This was not affected by additional treatment exposure during the follow-up period because participants typically did not seek further treatment until they had relapsed to use. A small number of participants did re-enter treatment during the follow-up period despite being continuously abstinent ($n = 19$). We censored data from these participants from the analysis at the point when they re-entered treatment because it would not be accurate to attribute their subsequent outcomes to their index episode of residential rehabilitation. Again, the detoxification and quasi-control group were combined because these groups did not differ in their rates of continuous abstinence ($p > 0.05$).

Unadjusted analyses showed that the residential rehabilitation group had higher rates of continuous abstinence than the combined quasi-control and detoxification comparison group at all three follow-up points (Table 2). Again, IPTW estimators reduced the magnitude of these treatment effects (Table 2). Residential rehabilitation produced a 33 percentage point increase in the number of participants who remained abstinent at 3 months compared to the quasi-control group, with this benefit dropping to 14 and 6 percentage points at 1 and 3 years respectively. These treatment effects were significant at 3 months and 1 year but not 3 years (Table 2).

[Table 2 about here]

DISCUSSION

Community-based residential rehabilitation produced a large but time-limited reduction in methamphetamine use. The largest gains were seen for abstinence at three months after treatment, with a 33 percentage point increase in continuous abstinence compared to participants who received no treatment or detoxification only. However, by 1 to 3 years after

treatment, the vast majority of residential rehabilitation clients reported similar methamphetamine use levels to the level that would be expected if they had not received treatment or had only received detoxification. Detoxification alone did not change methamphetamine use at any follow-up relative to no treatment. These findings should be applied cautiously to locations where methamphetamine use patterns and drug treatment differ from those seen in Australia.

These findings highlight chronic relapsing nature of methamphetamine dependence and the need for a treatment approach with a more sustained impact. Although residential rehabilitation facilities provide a structured drug-free environment to initiate abstinence, this approach may not address factors that are likely to trigger relapse once clients re-enter the community (e.g., cravings for the drug, socializing and living with drug users, conflict and stress). Further research is also needed to determine whether the time-limited benefits of residential rehabilitation outweigh their expensive running costs (which have been cited at US\$11,016 per person in the USA [27]). While existing research shows that residential rehabilitation is cost-effective [28], the lack of control groups in previous studies means that they may over-estimate the benefits of treatment [29].

Detoxification conveyed no benefit in reducing methamphetamine use at any follow-up relative to not receiving treatment. This is consistent with previous research [4] and suggests that detoxification should not be provided as a stand-alone service. We found that most detoxification clients were highly motivated to reduce their methamphetamine use and sought abstinence, indicating a need to educate detoxification clients that addressing physical withdrawal symptoms may not alleviate methamphetamine dependence in the longer term, and that further treatment is needed to address the broader psychosocial issues (e.g., coping and interpersonal skills), as well as ongoing cravings for the drug, and their role in precipitating relapse [30,31].

The time-limited benefit of residential rehabilitation is inconsistent with previous treatment outcome studies, which suggest more sustained reductions in drug use [4-6]. This discrepancy largely reflects the use of a quasi-control group in the current study, with earlier studies examining pre-treatment versus post-treatment changes in drug use. While we also saw sustained drops in methamphetamine use after treatment relative to pre-treatment levels, similar reductions occurred in the quasi-control condition, suggesting that they were attributable to factors other than the index treatment (e.g., maturation out of methamphetamine dependence, the impact of the study procedure itself, and reductions in methamphetamine availability that occurred over the study period [32]). IPTW estimators further attenuated treatment effects, suggesting that it was partly the characteristics of clients who entered residential rehabilitation (e.g., high levels of motivation) that drove post-treatment improvements. Our findings highlight the need for quasi-control groups in observational treatment outcome studies, and the importance of using IPTW or other matching procedures to derive treatment effects.

Methodological considerations

The capacity of IPTW estimators to produce unbiased treatment effects assumes that there are no unmeasured confounders [14,33]. We were able to adjust for treatment history, severity of methamphetamine use, motivation, psychiatric disorders and basic demographics, but there were undoubtedly factors that we did not measure that may have impacted on treatment outcomes. The application of IPTW estimators also provides treatment effects that would arise should both the treatment and the non-treatment group be provided with treatment. This approach may underestimate the benefit of treatment as it applies to those people who are inclined to seek treatment (e.g., highly motivated clients) rather than the non-treatment seeking control used herein.

Self-reported methamphetamine use in the past month was validated using hair toxicology in a sub-group of the sample and found to be accurate in the vast majority of cases. This is consistent with previous evidence that self-report is generally found to be a reliable and valid indicator of drug use [34]. Having said this, there were a number of limitations in our validation procedures: toxicology could not be obtained on a random sample of participants; variability in the rate of hair growth can affect the validity of results; and the concentrations of methamphetamine in hair are affected by exposure to detergents (hair washing) and other environmental factors [35,36].

Treatment outcomes reported herein are contingent on the follow-up times, which were often delayed due to the difficulty locating participants, particularly for the 3 year follow-up. This may have attenuated treatment effects in so far as these treatment effects decayed over time. Low rates of continuous abstinence at the 3 year follow-up also meant that we may not have had enough statistical power to detect a significant effect. Imputation of missing data would have reduced bias due to the high attrition rate at 3 years, but this procedure cannot eliminate bias when attrition is due to client outcomes (e.g., clients being lost to follow-up because they have relapsed) [26].

Conclusion

Community-based drug residential rehabilitation produced large short-term reductions in methamphetamine use relative to no treatment or detoxification alone, but there was no clear evidence that it conveyed a benefit at three years after starting treatment. Detoxification alone did not reduce methamphetamine use relative to no treatment. Improved treatment approaches are needed to produce long-term reductions in methamphetamine use.

Acknowledgements

The data reported in this paper were collected through the Methamphetamine Treatment Evaluation Study (MATES), which was conducted by the National Drug and Alcohol Research Centre, University of New South Wales, and was funded by the National Health and Medical Research Council and the Australian Government Department of Health and Ageing. The authors thank Joanne Ross, who was an investigator on the project, researchers working on the project (Erin Kelly, Shelley Cogger, Rachel Sutherland, Grace Ho, Cathie Sammut, Kate Hetherington, Sagari Sarkar, Julia Rosenfeld and Miriam Wyzenbeek), the participating treatment agencies and health services, and the participants.

References

1. Nicosia N, Liccardo Pacula R, Kilmer B, Lundberg R, Chiesa J. The economic cost of methamphetamine use in the United States, 2005. Los Angeles, CA: RAND Drug Policy Research Center, Rand Cooperation; 2009.
2. Colfax G, Santos G-M, Chu P, Vittinghoff E, Pluddemann A, Kumar S, *et al.* Amphetamine-group substances and HIV. *Lancet.* 2010;376:458-474.
3. Rawson RA, Marinelli-Casey P, Anglin MD, Dickow A, Frazier Y, Gallagher C, *et al.* A multi-site comparison of psychosocial approaches for the treatment of methamphetamine dependence. *Addiction.* 2004;99:708-717.
4. Teesson M, Mills K, Ross J, Darke S, Williamson A, Havard A. The impact of treatment on 3 years' outcome for heroin dependence: findings from the Australian Treatment Outcome Study (ATOS). *Addiction.* 2008;103:80-88.
5. Gossop M, Marsden J, Stewart D, Kidd T. The National Treatment Outcome Research Study (NTORS): 4-5 year follow-up results. *Addiction.* 2003;98:291-303.
6. Hubbard RL, Craddock SG, Anderson J. Overview of 5-year followup outcomes in the drug abuse treatment outcome studies (DATOS). *Journal of Substance Abuse Treatment.* 2003;25:125-134.
7. Zweben JE, Cohen JB, Christian D, Galloway GP, Salinardi M, Parent D, Iguchi M, *et al.* Psychiatric symptoms in methamphetamine users. *American Journal on Addictions.* 2004;13:181-190.
8. Glasner-Edwards S, Marinelli-Casey P, Hillhouse M, Ang A, Mooney LJ, Rawson R, Methamphetamine Treatment Project Corporate A. Depression among methamphetamine users: association with outcomes from the Methamphetamine Treatment Project at 3-year follow-up. *Journal of Nervous & Mental Disease.* 2009;197:225-231.
9. Glasner-Edwards S, Mooney LJ, Marinelli-Casey P, Hillhouse M, Ang A, Rawson R, Methamphetamine Treatment Project Corporate A. Clinical course and outcomes of

- methamphetamine-dependent adults with psychosis. *Journal of Substance Abuse Treatment*. 2008;35:445-450.
10. Glasner-Edwards S, Mooney LJ, Marinelli-Casey P, Hillhouse M, Ang A, Rawson R, Methamphetamine Treatment Project Corporate A. Anxiety disorders among methamphetamine dependent adults: association with post-treatment functioning. *American Journal on Addictions*. 2010;19:385-390.
 11. Wright S, Klee H, Reid P. Attitudes of amphetamine users towards treatment services. *Drugs: Education, Prevention and Policy*. 1999;6:71-86.
 12. United Nations Office on Drugs and Crime. *World Drug Report 2010*. New York: United Nations; 2010.
 13. Höfler M. Causal inference based on counterfactuals. *BMC Medical Research Methodology*. 2005;5:28.
 14. Robins J, Hernan M, Brumback B. Marginal structural models and causal inference in epidemiology. *Epidemiology*. 2000;11:550-560.
 15. Curtis LH, Hammill BG, Eisenstein EL, Kramer JM, Anstrom KJ. Using Inverse Probability-Weighted Estimators in comparative effectiveness analyses with observational databases. *Medical Care*. 2007;45:S103-S107.
 16. Lipkovich I, Adams DH, Mallinckrodt C, Faries D, Baron D, Houston JP. Evaluating dose response from flexible dose clinical trials. *BMC Psychiatry*. 2008;8:3.
 17. Lee S-W, Park S-W, Yun S-C, Kim Y-H, Park D-W, Kim W-J, *et al*. Triple antiplatelet therapy reduces ischemic events after drug-eluting stent implantation: Drug-Eluting stenting followed by Cilostazol treatment REduces Adverse Serious cardiac Events (DECREASE registry). *American Heart Journal*. 2010;159:284-291.e281.
 18. Nishida Y, Takahashi Y, Nakayama T, Soma M, Kitamura N, Asai S. Effect of candesartan monotherapy on lipid metabolism in patients with hypertension: a retrospective longitudinal survey using data from electronic medical records. *Cardiovascular Diabetology*. 2010;9:38.

19. Australian Institute of Health and Welfare. *Alcohol and Other Drug Treatment Services National Minimum Data Set 2011–12 Specifications and collection manual*. Canberra: Australian Institute of Health and Welfare; 2011:1-183.
20. Gossop M, Darke S, Griffiths P, Hando J, Powis B, Hall W, Strang J. The Severity of Dependence Scale (SDS) in English and Australian samples of heroin, cocaine and amphetamine users. *Addiction*. 1995;90:607-614.
21. Topp L, Mattick RP. Choosing a cut-off on the Severity of Dependence Scale (SDS) for amphetamine users. *Addiction*. 1997;92:839-845.
22. Darke S, Hall W, Wodak A, Heather N, Ward J. Development and validation of a multi-dimensional instrument for assessing outcome of treatment among opiate users: the Opiate Treatment Index. *British Journal of Addiction*. 1992;87:733-742.
23. Rollnick S, Heather N, Gold R, Hall W. Development of a short 'readiness to change' questionnaire for use in brief, opportunistic interventions among excessive drinkers. *British Journal of Addiction*. 1992;87:743-754.
24. Andrews G, Peters L. The psychometric properties of the Composite International Diagnostic Interview. *Social Psychiatry & Psychiatric Epidemiology*. 1998;33:80-88.
25. Robins LN, Helzer JE, Ratcliff KS, Seyfried W. Validity of the diagnostic interview schedule, version II: DSM-III diagnoses. *Psychological Medicine*. 1982;12:855-870.
26. Royston P. Multiple imputation of missing values: update. *The Stata Journal*. 2005;5:1-14.
27. Flynn PM, Kristiansen PL, Porto JV, Hubbard RL. Costs and benefits of treatment for cocaine addiction in DATOS. *Drug & Alcohol Dependence*. 1999;57:167-174.
28. Godfrey C, Stewart D, Gossop M. Economic analysis of costs and consequences of the treatment of drug misuse: 2-year outcome data from the National Treatment Outcome Research Study (NTORS). *Addiction*. 2004;99:697-707.
29. Cartwright WS. Cost-benefit analysis of drug treatment services: review of the literature. *Journal of mental health Policy and Economics*. 2000;3:11-26.

30. Hartz DT, Frederick-Osborne SL, Galloway GP. Craving predicts use during treatment for methamphetamine dependence: a prospective, repeated-measures, within-subject analysis. *Drug and Alcohol Dependence*. 2001;63:269-276.
31. Brecht ML, von Mayrhauser C, Anglin MD. Predictors of relapse after treatment for methamphetamine use. *Journal of Psychoactive Drugs*. 2000;32:211-220.
32. Phillips B, Burns L. NSW Drug Trends 2009: Findings from the Illicit Drug Reporting System (IDRS). Australian Drug Trend Series No. 38. Sydney (Australia): National Drug and Alcohol Research Centre, University of New South Wales; 2010.
33. Austin PC. The performance of different propensity-score methods for estimating differences in proportions (risk differences or absolute risk reductions) in observational studies. *Statistics in Medicine*. 2010;29:2137-2148.
34. Darke S. Self-report among injecting drug users: a review. *Drug & Alcohol Dependence*. 1998;51:253-263.
35. Miyaguchi H, Kakuta M, Iwata YT, Matsuda H, Tazawa H, Kimura H, *et al.* Development of a micropulverized extraction method for rapid toxicological analysis of methamphetamine in hair. *Journal of Chromatography*. 2007;A. 1163:43-48.
36. Wennig R. Potential problems with the interpretation of hair analysis results. *Forensic Science International*. 2000;107:5-12.

Supporting information

Appendix S1 A comparison of treatment participants with methamphetamine treatment clients in Australia.

Appendix S2. Details of hair toxicology

Appendix S3 Derivation of IPTW estimators

Appendix S4. Predictors of attrition and data imputation procedures

Appendix S5. Treatment effects for methamphetamine dependence and past month methamphetamine use

Table 1. Characteristics of participants by treatment modality

	Quasi-control (n = 101)	Detoxification (n = 112)	Residential rehabilitation (n = 248)
Methamphetamine use			
DSM-IV diagnosis of dependence (%)	94	96	98
Duration of use (mean years)	16.6	13.0**	12.1***
Severity of dependence (mean SDS score) ^a	7.6	9.1**	8.9**
Days used in the past month (median)	14	20***	16 [†]
Injecting methamphetamine (%)	86	73*	67***
Polydrug use (mean)	3.8	3.4*	3.6
Demographics			
Age (mean years)	35.3	31.7**	30.5***
Male (%)	67	72	77
Unemployed (%)	84	74	89 [†]
Immigrant (%)	13	12	15
Incomplete schooling ^b (%)	39	40	29 [†]
Tertiary qualification (%)	42	46	49
No fixed address (%)	5	13*	5 [†]
Prison history (%)	61	46*	38***
Ever had children (%)	53	52	50
Single (%)	72	79	72
Previous drug treatment (%)			
Nil	25	30	30
1-4 episodes	36	40	42
5+ episodes	40	29	28
Previous treatment for methamphetamine use (%)	20	42***	46***
Motivation (% , action stage)	30	54***	66*** [†]
Psychiatric disorders (%)			
Major depression ^c (%)	63	38***	40***
Social phobia ^c (%)	27	21	23
Panic disorder ^c (%)	33	15**	29 [†]
Schizophrenia or mania ^d (%)	15	8	13
Conduct disorder ^d (%)	73	71	80

*** p < 0.001, **p < 0.01, *p < 0.05, compared to the quasi-control group

[†] p < 0.05 compared to the detoxification group

^a Higher scores indicate more severe dependence

^b Completed less than 10 years of schooling

^c Past year diagnoses taken at baseline

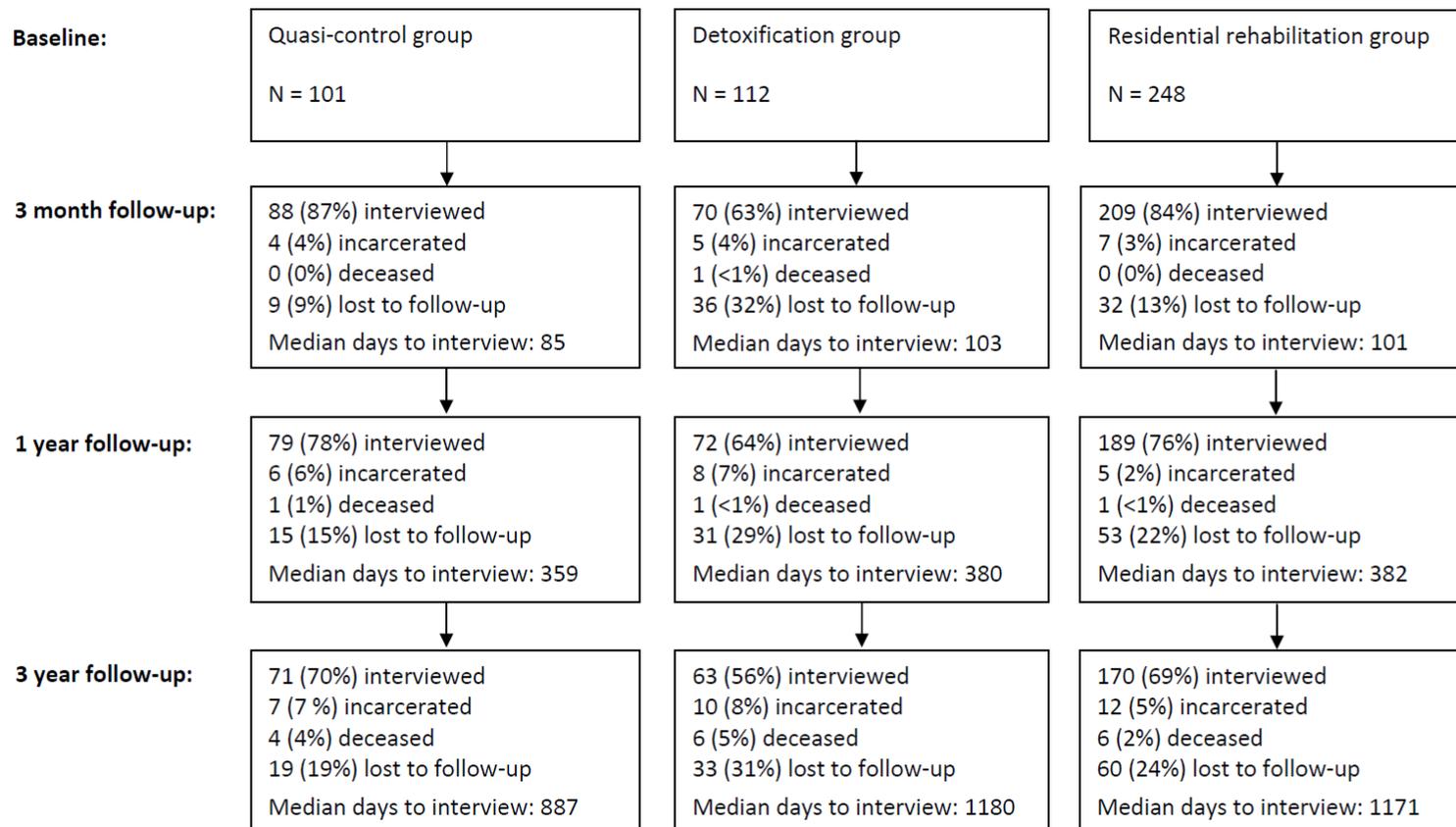
^d Lifetime diagnoses taken at follow-up

Table 2. Effect of residential rehabilitation (RR) on frequency of methamphetamine use and continuous abstinence from methamphetamine

	Unadjusted		IPTW							
	Odd ratio (95% CI)	P value	Predicted values (%)			Odd ratio (95% CI)	P value	Predicted values (%)		
			Control	RR	Absolute change			Control	RR	Absolute change
Frequency of use										
3 months	0.21 (0.14-0.32) ^a	< 0.001				0.23 (0.15-0.36) ^a	< 0.001			
No use			18	57	39			18	53	34
Less than weekly			34	24	-10			36	29	-7
1-2 days/week			27	12	-14			24	11	-13
3+ days per week			22	8	-14			22	7	-15
1 year										
No use	0.56 (0.38-0.81)	0.002	20	31	11	0.62 (0.40-0.97)	0.038	21	30	9
Less than weekly			41	43	2			44	45	1
1-2 days/week			19	14	-5			16	12	-4
3+ days per week			20	12	-8			19	13	-6
3 years										
No use	0.62 (0.42-0.91)	0.016	20	29	9	0.71 (0.42-1.30)	0.189	20	26	6
Less than weekly			47	48	1			49	50	1
1-2 days/week			19	14	-5			17	14	-3
3+ days per week			14	9	-5			14	11	-4
Continuous abstinence										
3 months	6.3 (3.8-10.4)	< 0.001	15	53	38	5.1 (2.8-9.3)	< 0.001	15	48	33
1 year	4.2 (1.9-9.7)	0.001	6	22	16	3.5 (1.3-9.8)	0.016	7	20	14
3 years	3.4 (1.2-9.4)	0.007	4	13	9	2.4 (0.7-7.6)	0.147	5	12	6

Note. Control: quasi-control and detoxification groups combined; RR: residential rehabilitation group

^aOdds of change differed across frequency of methamphetamine use. Unadjusted results: any use vs. abstinence OR 0.17, 95% CI 0.10-0.28; more than weekly vs. less than weekly OR 0.26, 95% CI 0.17-0.42; 3+ days vs. up to 1-2 days per week OR 0.29, 95% CI 0.14-0.58. IPTW results: any use vs. abstinence OR 0.20, 95% CI 0.11-0.37; more than weekly vs. less than weekly OR 0.26, 95% CI 0.16-0.44; 3+ days vs. up to 1-2 days per week OR 0.28, 95% CI 0.13-0.60.



Note. Incarcerated and deceased participants include only those that came to our attention when attempting to locate participants, and therefore these figures should not be taken to indicate true incarceration or death rates in the sample.

Figure 1. Follow-up of participants by group

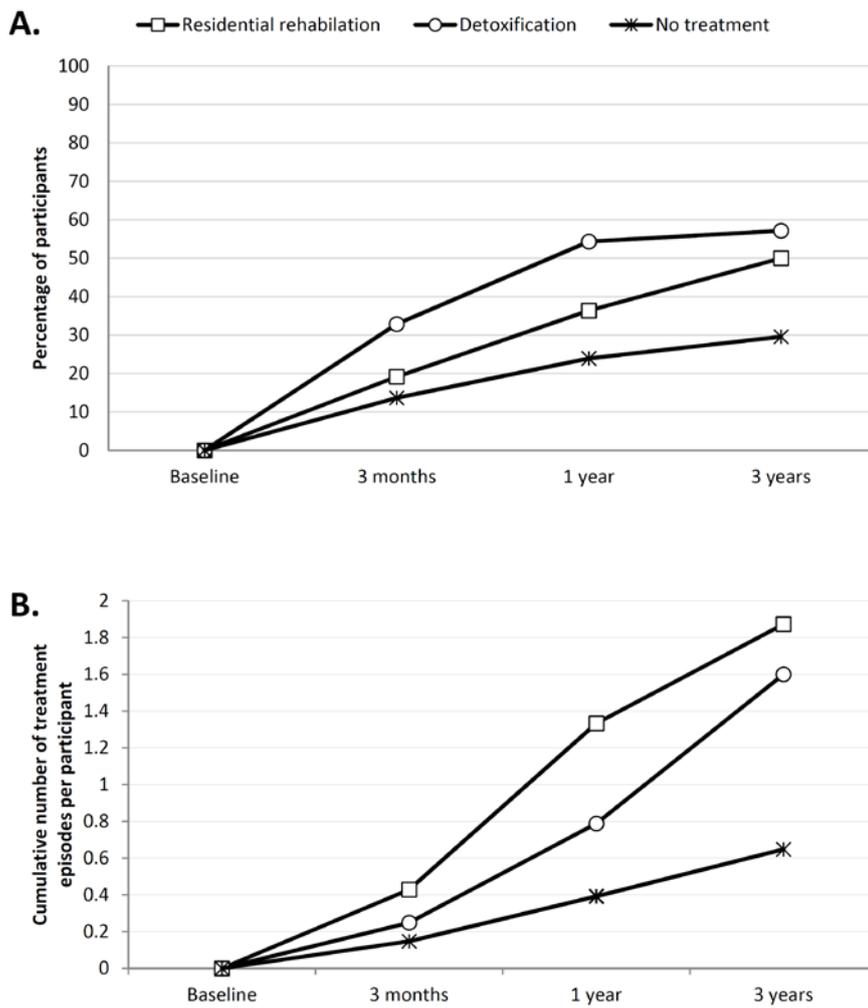


Figure 2. Exposure to drug treatment over the follow-up period (excluding the index treatment) by group: (A) the cumulative proportion of participants who received any drug treatment during the follow-up period; (B) the average cumulative number of treatment episodes initiated per participant during the follow-up period.

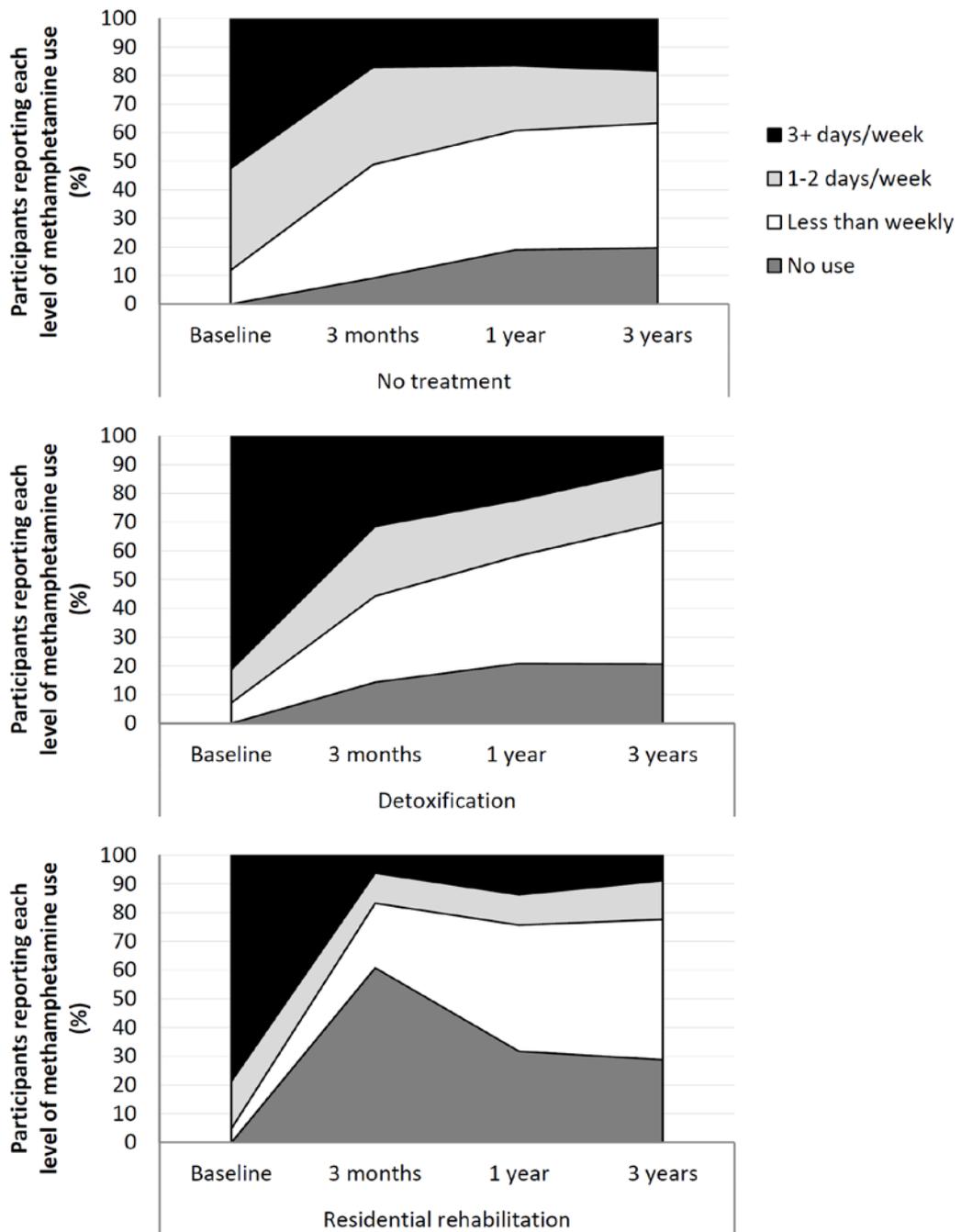


Figure 3. Frequency of methamphetamine use reported at each follow-up by group