

## Patterns of smoking and injecting methamphetamine and their association with health and social outcomes

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### Abstract

**Introduction** We examine how smoking and injecting methamphetamine change over time and correlate with specific health and social outcomes. **Methods.** Panel data from a longitudinal cohort dependent on methamphetamine ( $N = 444$ ; 891 months). Random effects regression models examined the relationship between smoking and/or injecting methamphetamine and past month outcomes (substance use,  $\geq$ daily injection, needle/syringe sharing, psychological distress, poor mental and physical health, sexual behaviour, psychotic symptoms, violent behaviour and crime). Effects were adjusted for between-group differences at baseline. **Results.** At baseline, 56% of participants only injected methamphetamine in the past month, 18% only smoked and 26% both injected and smoked (concurrent injecting and smoking). Compared to injecting only, concurrent injecting and smoking was associated with more days of methamphetamine use ( $b = 1.3$ ,  $P < 0.001$ ; adjusted [A]  $b = 1.2$ ,  $P < 0.001$ ), more frequent injection [odds ratio (OR) 1.8,  $P = 0.013$ ; adjusted OR (AOR) 1.6,  $P = 0.042$ ], violent behaviour (OR 2.1,  $P = 0.001$ ; AOR 1.8,  $P = 0.013$ ) and crime (OR 3.1,  $P < 0.001$ ; AOR 2.5,  $P < 0.001$ ). Non-injecting related outcomes did not differ significantly for only smoking versus only injecting. There was no significant transition from injecting methamphetamine at baseline to non-injecting methamphetamine use at follow up, or from exclusively smoking methamphetamine at baseline to any methamphetamine injection at follow up. **Discussion and Conclusion.** Efforts are needed to address heavier methamphetamine use, more frequent drug injection and elevated violent behaviour and crime among people who concurrently smoke and inject methamphetamine. [McKetin R, Sutherland R, Peacock A, Farrell M, Degenhardt L. Patterns of smoking and injecting methamphetamine and their association with health and social outcomes. *Drug Alcohol Rev* 2021;40:1256–1265]

**Key words:** methamphetamine, injecting, smoking, harm, amphetamine.

### Introduction

Methamphetamine use is a growing global concern [1–3] associated with elevated mortality, increased HIV and hepatitis C incidence, cardiovascular events and poor mental health (suicidality, psychosis, depression and violence) [3,4]. Within this context, there has been debate about the relative harms associated with smoking versus injecting stimulants [5,6]. There is particular uncertainty about the implications of the co-occurrence of smoking stimulant drugs (crack cocaine and crystal methamphetamine) and injecting stimulant drugs amongst people who inject drugs. This phenomenon has been observed in several contexts. For example, in Canada, one study found that 63% of people

who were actively injecting drugs reported the concurrent smoking of crack cocaine [7]. In Australia, a similar phenomenon has been seen with the co-occurrence of smoking and injecting methamphetamine amongst people entering treatment for methamphetamine use [8], amongst community samples of people who inject methamphetamine [9] and people who inject drugs more broadly [10]. There has also been a substantial increase in methamphetamine use among people seeking treatment for heroin use in the USA which is characterised by both smoking and injecting the drug [11], although the overlap in routes of administration in this context have not been explored [12].

Evidence regarding the potential health and social consequences of this pattern of concurrent smoking

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and injecting of stimulants, or the relative harms associated with smoking versus injecting stimulants, is limited and inconsistent [8,13,14]. Although non-injecting routes of administration generally confer a lower risk of harm than injecting [15,16], there is conversely evidence that suggests smoking of stimulants affords a rapid and intense drug effect [17] that is associated with a high risk of compulsive use and dependence [14,18,19] and other harms (e.g. sexual risk behaviour), particularly if co-occurring with injecting methamphetamine use (e.g. involvement in crime) [8]. Smoking stimulant drugs is also a risk factor for transition to injecting drug use [20]. Conversely, smoking the drug could substitute for injection, reducing blood-borne virus risk (e.g. 'Now stems are more available, I have stopped my injection use' [13]).

We use data from a longitudinal cohort of people who were dependent on methamphetamine to investigate patterns of smoking and injecting methamphetamine. Our previous analysis of the baseline data from this cohort found that smoking and injecting methamphetamine were associated with different demographics and drug use patterns but similar harms [8]. In this study, we use three subsequent waves of data collection from the Methamphetamine Treatment Evaluation Study (MATES) cohort to investigate how the co-occurrence of smoking and injecting methamphetamine (cf. either only injecting or only smoking methamphetamine) relates to other substance use patterns and various health and social outcomes (injecting behaviour, sexual behaviour, disability due to poor physical and mental health, psychological distress, violent behaviour, psychosis and crime). We also examine changes in route of methamphetamine administration in the cohort from baseline to follow up.

## Methods

### *Participants and procedure*

Participants ( $N = 444$ ) were selected from a larger study, the MATES cohort [21]; they met Diagnostic and Statistical Manual of Mental Disorders, fourth edition criteria for past year methamphetamine dependence (according to the Composite International Diagnostic Interview [22]), and either smoked or injected methamphetamine, on entry to the MATES study. The MATES cohort included 400 people entering community-based drug treatment services in Sydney and Brisbane, Australia, for methamphetamine use, and 101 people who use methamphetamine from Sydney who were not in treatment but who screened positive for dependence on methamphetamine (a score of 4+ on the Severity of Dependence Scale [23] or using

3+ days/week in the past month). Other inclusion criteria for MATES were being at least 16 years old, comprehension of English, being willing to participate in follow-up interviews, and not having been in methamphetamine treatment, other inpatient drug treatment or in prison in the month prior to entering the study. Recruitment of the cohort and the baseline structured interview took place in 2006 and 2007, and follow-up interviews (3 months, 1 year, 3 years) spanned from 2006 to 2010. Interviews were conducted face-to-face or by phone. All participants provided informed consent, were volunteers and were reimbursed for their time and travel expenses (up to AUD40 per interview).

For the current study, participants were excluded from the MATES cohort if, at baseline, they did not meet Diagnostic and Statistical Manual of Mental Disorders, fourth edition criteria for methamphetamine dependence ( $n = 17$ ), if they had not used methamphetamine in the past month ( $n = 14$ ) or if they neither smoked nor injected methamphetamine (i.e. they only swallowed or snorted the drug,  $n = 19$ ). This gave the final sample of 444 participants who were re-interviewed at 3 months (80%,  $n = 356$ ), 12 months (75%,  $n = 335$ ) and 3 years (67%,  $n = 296$ ) after entry to the cohort. The current study used only data where the participants used methamphetamine in the past month, giving 891 months of data. Correlates of attrition in the MATES cohort (see online supplementary material in McKetin *et al.* 2012 [21]) were not significantly correlated with smoking methamphetamine in the past month ( $P > 0.05$ ).

### *Measures*

*Baseline variables.* Demographic information collected at baseline included age, sex, completed years of schooling, tertiary qualifications (none vs. trade or university), prison history, marital status (single vs. married/de facto, separated, divorced, widowed), employment status (unemployed vs. casual/part-time, full-time, student, home duties), country of birth (Australia vs. other), main language spoken at home (English vs. other) and housing (public housing, privately rented dwelling, privately owned dwelling, parent's home, drug treatment centre, boarding house/shelter or refuge, no fixed address or other). The latter variable was used to identify where participants were living in unstable accommodation, defined as living in a boarding house/shelter or refuge, no fixed address or 'other' (which included caravans, sheds or temporary accommodation with friends). Drug use history variables included age when first injected drugs and age when first used methamphetamine. Sexual identity

(including gay, bisexual or other) was available for a subgroup of participants ( $n = 355$ , 733 months) who participated in the 12-month follow-up interview.

*Time-varying measures.* All time-varying measures were taken for the past month at each time point.

**Substance use:** All routes of methamphetamine administration in the past month (injected, smoked, swallowed and snorted) were recorded. The Opiate Treatment Index (OTI) [24] was used to measure days of use in the past month for methamphetamine use and other drug classes. High polysubstance use was defined as using more than the median number of drug classes (heroin, other opioids, cocaine, ecstasy, hallucinogens, cannabis, alcohol, inhalants and tobacco).

**Psychological distress:** Psychological distress was defined as a score of 17 or greater on the Kessler psychological distress scale (K10) [25].

**Disability from poor physical and mental health:** Disability from poor physical and mental health was defined as a score below 40 (i.e. more than 1 SD below the normative mean) on the physical and mental component scales of the Short Form 12 respectively [26].

**Psychotic symptoms and violent behaviour:** Psychotic symptoms were defined as a score of four or greater on any of the Brief Psychiatric Rating Scale items of suspiciousness, unusual thought content or hallucinations [26], and violent behaviour as a score of 6 or 7 on the Brief Psychiatric Rating Scale hostility item (corresponding to overt acts of hostility) [27]; inter-rater agreement for both psychotic symptoms and violent behaviour in this sample was good (kappa of 0.86 [26,27]).

**Crime:** The OTI Criminality Scale [24] was used to measure criminal involvement, which was coded as whether or not the participant committed drug dealing, property crime, fraud or violent crime in the past month.

**HIV risk behaviour:** HIV risk behaviour data were derived from responses to items in the OTI HIV Risk-taking Behaviour Scale [24], including frequency of injecting (categorised as less than daily vs. daily or more often), needle sharing (used a needle after someone else had used it in the past month) and, if participants were sexually active, whether they had unprotected sex with a casual partner in the past month.

*Design and statistical analysis.* Data were analysed using Stata SE version 16.0 (StataCorp LLC, College

Station, TX, USA). All tests were two-sided with significance set at  $P < 0.05$ .

The baseline characteristics of participants who only smoked methamphetamine in the past month, and those who concurrently smoked and injected methamphetamine in the past month, were compared to participants who only injected the drug in the past month. Group comparisons were made using  $t$ -tests for continuous data, Pearson's  $\chi^2$  tests for categorical data, and a median comparisons test for skewed continuous data, where medians and interquartile ranges are presented.

To examine the relationship between route of methamphetamine administration and each outcome, we undertook a series of random effects regression models using time-varying data from all four time points. These models included a random intercept for individual level data to account for the clustering of data on repeated measures. In all analyses, the predictor variable was the time varying route of methamphetamine administration which compared whether the participant had: (i) only injected methamphetamine in the past month (reference category, 561 months); (ii) concurrently smoked and injected methamphetamine in the past month (201 months); or (iii) only smoked methamphetamine in the past month (119 months). Months that involved only snorting or swallowing methamphetamine ( $n = 10$ ) were excluded from this analysis. Adjusted analyses included baseline variables that differed significantly between these three groups (i.e. age, sex, either being born outside Australia or being from a non-English speaking background, prison history, duration of methamphetamine use, heavy polysubstance use).

To examine transitions between routes of methamphetamine administration, we compared the route of administration recorded at baseline (injecting only, concurrent injecting and smoking, and smoking only) with the routes recorded across the three follow-up assessments (3 months, 1 year and 3 years). The route of administration across the three follow ups was coded as: (i) injecting only, if injection was recorded as a route of administration at any of the three follow ups, but there were no assessments when the person reported concurrent injection and smoking; (ii) injection and smoking if concurrent injection and smoking was recorded at any of the three follow-up assessments; (iii) 'smoking only', if smoking but no injecting was recorded at any of the three interviews; and (iv) snorting or swallowing only, if this was the only route of administration recorded at any of the three assessments. We collapsed the data across the three assessments because the pattern of results was similar at each assessment, with few participants changing route of administration (see Supporting Information for data at each follow up). The final analysis was restricted to months where methamphetamine use was

**Table 1.** Characteristics of participants at baseline by whether they smoked, injected or both smoked and injected methamphetamine

	Inject only (reference) ( <i>n</i> = 250)	Concurrent injecting and smoking ( <i>n</i> = 116)	<i>P</i> value	Smoke only ( <i>n</i> = 78)	<i>P</i> value	Total sample ( <i>N</i> = 444)
<i>Demographics</i>						
Age, mean years	33.4	31.2	0.013	26.9	<0.001	31.7
Male, %	79	72	0.107	62	0.002	74
Identified as heterosexual <sup>a</sup> , %	88	79	0.027	90	0.730	88
Single, %	73	76	0.535	69	0.540	73
Unemployed, %	84	84	0.996	77	0.180	82
Income in the past fortnight, median AUD	451	480	0.095	427	0.790	460
Schooling, median years	10	10	0.327	10	0.184	10
Tertiary qualification, %	48	49	0.839	41	0.281	47
Immigrant, %	12	10	0.723	22	0.024	13
Non-English-speaking background, %	3	3	0.735	9	0.019	4
Had children, %	50	53	0.697	46	0.513	50
Unstable housing, %	27	22	0.248	18	0.099	24
Prison history, %	46	58	0.043	23	<0.001	45
<i>Substance use at baseline</i>						
Ever injected a drug, %	100	100	NA	35	<0.001	89
Age when first injected any drug, mean years <sup>b</sup>	19.5	19.6	0.834	19.6	0.936	19.5
Duration of methamphetamine use, median years	14.8	13.4	0.100	8.9	<0.001	13.4
Days used methamphetamine in the past 4 weeks, median	16	16	0.747	16	0.915	16
Heavy polysubstance <sup>c</sup> use in the past month, median	51	67	0.003	45	0.361	54
Opioid use in the past month, <i>n</i> (%)						
Heroin use	29	34	0.393	5	<0.001	26
Other opioid use	33	28	0.404	5	<0.001	27
Any opioid use	43	46	0.655	10	<0.001	38
Recruited from drug treatment, <i>n</i> (%)	76	78	0.606	91	0.004	79

Comparisons were relative to participants who injected only. <sup>a</sup>Based on sub-sample of 733 participants, as data on sexual orientation was only collected at the 12 month follow-up interview. <sup>b</sup>Only for those who have ever injected a drug. <sup>c</sup>Four or more other drug classes used. NA, not applicable.

reported, and based on data from 182 participants at the 3-month follow up, 156 participants at the 1-year follow up and 109 participants at the 3-year follow up.

We used a McNemar test to determine whether there was a statistically significant change from injecting methamphetamine use at baseline to non-injecting methamphetamine use at follow up. To do this, we compared a binary variable for injecting versus non-injecting methamphetamine use [injecting only (1), injecting and smoking (1) vs. smoking only (0) or other non-injecting routes of administration (0)] at baseline and follow up.

## Results

### Baseline characteristics of the sample

The majority of participants were male (74%), heterosexual (88%), single (73%) and unemployed (82%).

They had used methamphetamine for a mean of 13.4 years (SD 7.9 years). In the month prior to recruitment, participants had used methamphetamine on a median 16 days (interquartile range 10–24 days) and most (86%) used crystalline methamphetamine. Thirty-eight percent of the sample had used opioids in the past month (26% for heroin, 27% for other opioids).

### Characteristics associated with smoking and injecting methamphetamine at baseline

At the baseline interview, 250 participants (56%) had only injected methamphetamine in the previous month, 116 (26%) had both injected and smoked methamphetamine (i.e. co-occurring smoking and injecting) and 78 (18%) had only smoked the drug. Participants who reported co-occurring injection and

**Table 2.** Methamphetamine use and harms during months of smoking and/or injecting methamphetamine

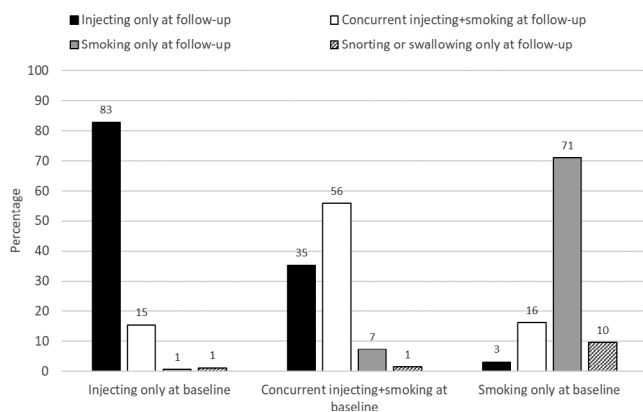
		Unadjusted		Adjusted <sup>b</sup>	
		OR (95% CI)	P value	OR (95% CI)	P value
<i>Injecting daily or more often, n (%)</i>					
Injection only (reference)	400 (71)				
Concurrent injecting and smoking	162 (81)	1.8 (1.1–2.8)	0.013	1.6 (1.0–2.5)	0.042
<i>Shared a needle/syringe, n (%)</i>					
Injection only (reference)	130 (23)				
Concurrent injecting and smoking	61 (30)	1.6 (0.9–2.7)	0.078	1.3 (0.8–2.1)	0.353
<i>Days of methamphetamine use, mean (SD)<sup>a</sup></i>					
Injection only (reference)	10.9 (8.8)				
Concurrent injecting and smoking	14.1 (8.6)	1.3 (1.2–1.4)	<0.001	1.2 (1.1–1.3)	<0.001
Smoking only	12.8 (9.7)	1.1 (1.0–1.3)	0.101	1.1 (0.9–1.0)	0.286
<i>OTI score, mean (SD)<sup>a</sup></i>					
Injection only (reference)	1.2 (1.7)				
Concurrent injecting and smoking	2.0 (2.0)	1.7 (1.5–2.1)	<0.001	1.6 (1.4–2.0)	<0.001
Smoking only	3.2 (5.0)	2.6 (2.1–3.1)	<0.001	2.3 (1.8–2.9)	<0.001
<i>Sexually active, n (%)</i>					
Injection only (reference)	368 (66)				
Concurrent injecting and smoking	147 (74)	1.5 (0.9–2.7)	0.145	1.3 (0.7–2.3)	0.346
Smoking only	91 (77)	1.9 (0.9–4.1)	0.110	1.5 (0.7–3.5)	0.324
<i>Unprotected casual sex, n (%)</i>					
Injection only (reference)	90 (16)				
Concurrent injecting and smoking	40 (20)	1.3 (0.7–2.4)	0.335	1.1 (0.6–1.9)	0.820
Smoking only	30 (25)	2.1 (1.0–4.3)	0.050	1.4 (0.7–3.1)	0.353
<i>Psychological distress, n (%)</i>					
Injection only (reference)	486 (87)				
Concurrent injecting and smoking	185 (93)	2.4 (1.1–5.0)	0.023	1.9 (0.9–4.1)	0.094
Smoking only	109 (92)	2.1 (0.8–5.4)	0.128	1.5 (0.5–4.1)	0.449
<i>Disability due to poor mental health (SF 12), n (%)</i>					
Injection only (reference)	397 (71)				
Concurrent injecting and smoking	144 (72)	1.3 (0.8–2.2)	0.295	1.0 (0.6–1.7)	0.989
Smoking only	83 (70)	1.0 (0.5–1.8)	0.965	0.7 (0.4–1.3)	0.259
<i>Disability due to poor physical health (SF 12), n (%)</i>					
Injection only (reference)	135 (24)				
Concurrent injecting and smoking	51 (26)	1.1 (0.7–1.8)	0.734	1.0 (0.6–1.7)	0.941
Smoking only	24 (20)	0.8 (0.4–1.6)	0.496	1.1 (0.5–2.2)	0.847
<i>Psychotic symptoms (BPRS), n (%)</i>					
Injection only (reference)	212 (38)				
Concurrent injecting and smoking	91 (45)	1.5 (0.9–2.4)	0.086	1.4 (0.9–2.1)	0.195
Smoking only	50 (42)	1.3 (0.7–2.4)	0.340	1.1 (0.6–2.0)	0.839
<i>Violent behaviour (BPRS), n (%)</i>					
Injection only (reference)	149 (27)				
Concurrent injecting and smoking	78 (39)	2.1 (1.3–3.3)	0.001	1.8 (1.1–2.8)	0.013
Smoking only	37 (31)	1.3 (0.7–2.4)	0.325	1.3 (0.7–2.5)	0.353
<i>Any crime in the past month, n (%)</i>					
Injection only (reference)	282 (51)				
Concurrent injecting and smoking	145 (72)	3.1 (1.9–5.1)	<0.001	2.5 (1.5–4.2)	<0.001
Smoking only	67 (58)	1.4 (0.8–2.5)	0.284	1.3 (0.8–2.7)	0.272

<sup>a</sup>Poisson regression. Other analyses comprised linear regression (continuous data) or logistic regression (dichotomous data).

<sup>b</sup>Adjusted for age, sex, prison history, being either immigrant or from a non-English-speaking background, duration of methamphetamine use, recruited through treatment services, any opioid use and heavy polysubstance use. BPRS, Brief Psychiatric Rating Scale; CI, confidence interval; OR, odds ratio; OTI, Opiate Treatment Index; SF 12, 12-Item Short Form Health Survey.

smoking had similar demographics to participants who only injected the drug, except that they were significantly younger, less likely to identify as heterosexual and more likely to have a prison history (Table 1).

In contrast, participants who only smoked methamphetamine (cf. participants who only injected) were significantly younger, significantly more likely to be female and significantly more likely to have been born



**Figure 1.** Routes of administration at follow up by route of administration at baseline.

outside Australia and not speak English as their first language; they had not used methamphetamine for long, they were significantly less likely to use opioids and they were significantly less likely to have a prison history (Table 1). Participants who exclusively smoked were also significantly more likely to be recruited via drug treatment services (Table 1). Of participants who only smoked methamphetamine in the previous month, 35% had a history of injecting drugs (32% had previously injected methamphetamine).

#### *Relationship with substance use and other health and social outcomes*

Table 2 shows health and social outcomes for months when participants concurrently smoked and injected methamphetamine (201 months), and months when they only smoked (119 months), compared to months when they only injected (561 months). Adjustment was made for variables that differed between these groups at baseline.

Compared to months when participants only injected methamphetamine, during months when participants concurrently smoked and injected methamphetamine they used methamphetamine more often (more days of use and on more occasions per day), they were more likely to inject daily or more often and they were more likely to be involved in crime and report violent behaviour (Table 2). The greater psychological distress associated with concurrent smoking and injecting methamphetamine (vs. injecting only) was not statistically significant after adjustment for baseline differences between groups.

There were no significant differences for health and social harms between months that involved only smoking methamphetamine and those that involved only injecting (aside from injection-related harms

being specific to months that involved injection), although months of smoking were associated with more methamphetamine use occasions per day (i.e. OTI score of 3.2 vs. 1.2) (Table 2). Months that involved only smoking methamphetamine usually did not involve any other injecting drug use (only 4% involved injecting drugs other than methamphetamine).

#### *Changes in route of administration at follow up*

There was no significant transition from injecting methamphetamine use at baseline to non-injecting methamphetamine use at follow up (or conversely from non-injecting methamphetamine use at baseline to injecting methamphetamine use at follow up; McNemar's  $\chi^2_{df=1} = 0.60, P = 0.439$ ), with 96% of participants who injected methamphetamine at baseline also injecting methamphetamine at follow up. The remainder exclusively smoked (3%) or used only other non-injecting routes of administration (1%) at follow up. Twenty-seven percent of participants who injected at follow up concurrently smoked methamphetamine (Figure 1). For participants who only smoked at methamphetamine at baseline, 19% injected at follow up (6 of 31 participants) although this change was not significant (as noted above); amongst participants with no history of injecting drug use this was 18% (4 of 22 participants).

#### **Discussion**

These findings suggest that the pattern of concurrently smoking and injecting methamphetamine may be associated with more frequent methamphetamine use and more frequent injecting drug use than either smoking or injecting alone. This pattern of concurrent smoking and injecting of methamphetamine was also associated with a higher likelihood of violent behaviour and involvement in crime than only injecting the drug. We did not find any significant association between routes of methamphetamine administration and the other health and social outcomes that we assessed. Nor did we find any significant transition between smoking and injecting methamphetamine.

Our findings suggest caution in assuming that the uptake of smoking stimulants amongst people who already inject stimulants will lead to a reduction in injecting drug use. Instead, our results suggest that people may adopt smoking as a complement to their injecting drug use, rather than as a replacement for injecting use, resulting in an increased frequency of methamphetamine use. This interpretation of the data

is consistent with anecdotal reports that methamphetamine smoking is an incidental pattern of substance use created by social demands (e.g. visiting friends who do not inject or at parties where people are sharing an ice pipe). An alternative explanation is that during periods when people are using methamphetamine very heavily, they resort to non-injecting routes of administration because these are more accessible and socially acceptable (e.g. smoking versus injecting in public location) or in an attempt to reduce the risks associated with injecting more often. Qualitative methods would help to elucidate the reasons behind this pattern of concurrent smoking and injecting methamphetamine and its consequences. We did not see a significant increase in needle/syringe-sharing associated with this increased frequency of injection, however, other injection-related harms (e.g. abscesses, thrombosis), which we did not assess, may be elevated.

We found that concurrently smoking and injecting methamphetamine was a risk marker for violent behaviour and crime amongst people who use methamphetamine. Both violent behaviour and crime are important social harms associated with methamphetamine use [4,28], with crime contributing substantially to the social costs attached to methamphetamine use [29,30]. Elevated violent behaviour and crime is likely to be related to the more frequent methamphetamine use seen amongst people who both inject and smoke methamphetamine. More frequent methamphetamine use is associated with an increased risk of both violent behaviour and crime [27,28,31], even after adjusting for demographics and polysubstance use [27,28,31], and has been found to be temporally related to periods of heavy methamphetamine use [27]. However, it is also possible that people who both smoke and inject methamphetamine have a predisposition to violent behaviour and crime. Early conduct problems predict both heavier substance use and involvement in crime in adulthood [32,33], and this involvement is influenced by deviant peer affiliations [34], indicating the importance of social context on the development of these adverse outcomes.

While motivations for concurrent methamphetamine injection and smoking were not explicitly explored in this study, some of our findings may elucidate this issue. Specifically, we found that smoking methamphetamine was associated with taking methamphetamine on more occasions per day than injecting methamphetamine. This is because when people smoke methamphetamine, they smoke a small quantity of the drug on a single occasion and allow the remaining crystal methamphetamine to cool so it can be smoked later, resulting in smaller doses being taken at more regular intervals than when compared to injecting (where a full dose is usually injected on a single occasion) [19]. Therefore, the greater number of use occasions per day

amongst people who smoked methamphetamine does not necessarily equate to a greater quantity of the drug being consumed. These different use patterns suggest that smoking and injecting methamphetamine may be complementary. Specifically, although the half-life of methamphetamine is long (~12 h) [17], acute behavioural tolerance results in a rapid reduction in the perceived drug effect, or 'high' [35]. Smoking the drug thereafter may reinstate the drug high, as it provides a similarly rapid and intense drug effect to injection [17], allowing a person to 'top-up' their high at regular intervals after they inject the drug.

Our findings also identify a need to address non-injection-related harms both among people who smoke and people who inject stimulants. Poor mental health was seen for both smoking and injecting (e.g. over 70% of the sample experienced disability related to poor mental health) and the majority of people in both groups were involved in crime. These harms are likely to result in poor life quality and contribute to the health and social costs associated with methamphetamine use. Many of these harms could be ameliorated by providing effective treatment. Current best evidence for stimulant treatment supports the use of contingency management over other psychosocial treatments [3,36–38], although this has not been widely implemented [3]. Low threshold interventions that address these harms directly may be a more immediate response option (e.g. improving access to care for co-occurring mental health disorders, for which there is good evidence of effectiveness, referral to which could be integrated with existing harm reduction services such as needle and syringe programs and peer-outreach [3]). Efforts are also needed to ensure good access to harm reduction services for people who use stimulants to reduce blood-borne and sexually transmitted infections, including providing pre-exposure prophylaxis to high-risk populations for HIV transmission [3,39]. This is particularly important because of the elevated risk of HIV and transmission amongst people who use stimulants [3] and the impact of stimulant use on HIV progression [40].

One observation was the relative stability of routes of administration across the course of the study. Importantly, we saw little evidence of people transitioning from injecting methamphetamine to the exclusive use of non-injecting routes of administration. This is consistent with previous evidence [41] and suggests that once injecting stimulant use is established, it is likely to remain the preferred route of administration. However, we did find evidence of some people transitioning from smoking to injecting use (19% of people who exclusively smoked methamphetamine at baseline transitioned to injecting at follow up). This shift was not statistically significant, but this null effect could be due to the small sample of people who

exclusively smoked methamphetamine and the short follow-up time. There are few other estimates of transition rates from smoking to injecting crystalline methamphetamine; however, our estimates are not greatly dissimilar to the 36-month hazard of initiating injecting drug use found among a Canadian sample of street youth who had used crystalline methamphetamine (32%) [20]. This potential transition from smoking to injecting methamphetamine is a concern because it may lead to an expansion of injecting drug use populations in regions where crystalline methamphetamine use has become popular. Given the high risk of blood-borne virus transmission associated with stimulant injection [3], this potential finding needs to be more accurately assessed and monitored.

### *Limitations and considerations*

These findings are based on a naturalistic study of people who were dependent on methamphetamine on recruitment and most of whom had a history of injecting drug use. They may not generalise to other settings, especially where people are seeking to reduce their injecting drug use by smoking the drug instead of injecting. Nor may findings generalise to stimulant use patterns seen in conjunction with the recent opioid epidemic in the USA, where concurrent opioid use may impact on stimulant use patterns, routes of administration and related harms. The lack of a significant transition between injecting and non-injecting routes of administration is likely to be related to the nature of the sample (being dependent on methamphetamine with most participants having a long history of injecting substance use). The findings are also specific to methamphetamine use and do not necessarily apply to smoking crack cocaine, where the shorter half-life may affect people's propensity to transition between routes of administration.

Although we showed that periods of concurrent smoking and injecting methamphetamine were associated with more frequent substance use and specific harms compared to injecting alone, we cannot infer the direction of this effect (i.e. whether using methamphetamine more often leads to taking methamphetamine via different routes of administration, or whether the route of administration leads to more use). Our examination of transitions between routes of administration was limited by relying on 1-month snapshots of use over a 3-year period (cf. continuous observation over the 3-year period). Although our approach provides some information on the stability of routes of administration, we were unable to estimate the incidence rate for the transition from smoking to injecting or vice-versa. There may be factors that we did not measure that influenced health and social

outcomes, including sexual identity, which was not included in the regression analyses because it was not assessed in the full sample.

Importantly, our results do not provide information about whether making more pipes available may dissuade the uptake of injecting amongst people who do not inject drugs. Nor do they suggest that providing safer smoking kits may not reduce the risk of blood-borne virus transmission or other harms potentially associated with smoking methamphetamine. Because we assessed harms during 1-month periods, we were unable to assess some of the less prevalent but more serious adverse health outcomes associated with methamphetamine use (e.g. overdose and mortality).

### **Conclusion**

Our results suggest that the concurrent smoking and injecting of methamphetamine has the potential to be associated with more harm than either solely injecting or solely smoking the drug. The level of harm associated with both smoking and injecting indicate a need for harm reduction efforts to focus on both routes of administration, and include not only blood-borne virus prevention but also strategies to address other adverse health and social outcomes. Further research is needed to accurately estimate the transition from smoking methamphetamine to injecting the drug. Harm reduction efforts need to target people who concurrently smoke and inject methamphetamine because they are at elevated risk of injecting-related harms. Efforts are also needed to better understand what is driving high levels of violence and crime in this sub-population so these adverse social outcomes can be ameliorated.

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## Conflicts of Interest

LD and MF have received investigator-initiated untied educational grants for studies of opioid medications in Australia from Indivior, Mundipharma and Seqirus. AP has received investigator-initiated untied educational grants for studies of opioid medications in Australia from Mundipharma and Seqirus. RS has received investigator-initiated untied educational grants for studies of opioid medications in Australia from Seqirus. RM has nothing to disclose.

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### Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher's website:

**Figure S1.** Routes of administration at each follow-up by route of administration at baseline.