

PATTERNS OF DRUG PREFERENCE AND USE AMONG PEOPLE WHO INJECT DRUGS IN MELBOURNE, AUSTRALIA

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Running head: Patterns of drug preference and use.

Word count: 3850 excluding references, abstract, figure legends and appendices.

ACKNOWLEDGEMENTS

The authors gratefully acknowledge the contribution to this work of the Victorian Operational Infrastructure Support Program. The authors would like to thank Emma McBryde for feedback on the Markov Model. The Melbourne Injecting Drug User Cohort Study is funded through a variety of National Health and Medical Research Council grants and untied philanthropic contributions. The research reported in this paper has been funded by the National Drug Law Enforcement Research Fund. PD is the recipient of an Australian Research Council Future Fellowship. AR is a recipient of an NHMRC Research Fellowship.

ABSTRACT

Background: Understanding of substitution patterns in drug using careers is limited. Between 2009 and mid-2013 the purity-adjusted price of methamphetamine declined sharply in Melbourne in absolute terms and relative to the purity-adjusted price of heroin. We determine whether there were associated increases among people who inject drugs (PWID) in 1) use of methamphetamine and 2) citing methamphetamine as the drug of choice.

Method: Responses to 'drug of choice' and 'most used drug' were obtained from baseline and follow-up interviews of the 688 PWID enrolled in the Melbourne Injecting Drug User Cohort Study between April 2008 and August 2013, categorised as heroin, methamphetamine, cannabis, or other. Previous month heroin and methamphetamine use was reported at baseline by 82% and 41% of participants respectively, and 51% had completed three or more interviews in this period. A Markov model that included marginal effects for methamphetamine purity-adjusted price was used to calculate 1) transitions between drug of choice; and 2) conditional probabilities for most used drug. Parameters were determined by fitting multinomial logistic models to appropriate data subsets.

Results: At baseline the majority of participants reported heroin as both their preferred drug and the drug they used most. There were no significant increases in reports of methamphetamine as drug of choice, or as the most used drug.

Conclusion: In a cohort of PWID who reported a range of drug behaviours, there was little evidence of drug substitution into methamphetamine, despite substantial declines in its purity-adjusted price.

Keywords: Heroin, methamphetamine, drug substitution, purity-adjusted price, drug market, Markov model.

INTRODUCTION

Economists distinguish between demand and consumption. Demand reflects consumers' preference. Consumption results from the intersection of demand and supply, so it reflects both consumer preferences and market conditions (Caulkins & Nicosia, 2010; Gallet, 2014). In smoothly functioning markets for conventional goods, this distinction mostly plays out in terms of price. If someone prefers a steak to a hamburger, but the steak costs three times as much, that person might still eat hamburger, perhaps almost exclusively if money were tight. Price – or more accurately, purity-adjusted price – can likewise affect which drug is used. Changing patterns of use may also affect which drug is preferred, although the direction of the effect is ambiguous.

Economists also study how changes in the supply of one good affect consumption of another. For example, one would expect that a shortage of hamburger would lead to greater consumption of steak, since they are substitutes, but lower consumption of complements, such as ketchup and hamburger buns. There is a small but growing literature on so-called “cross price elasticities of demand” for illegal drugs measuring how a change in the price of one drug affects use of another substance (Jofre-Bonet & Petry, 2008; Petry, 2000; Petry & Bickel, 1998; Sumnall, Tyler, Wagstaff, & Cole, 2004). Many factors other than price can affect the types of drugs PWID consume. Over time, PWID may ‘mature-out’ (Winick, 1962) of injecting and favour different types of drugs, for example cannabis, and interventions such as Opioid Substitution Therapy (OST) have been shown to reduce (illicit) opioid consumption (Gowing, Farrell, Bornemann, Sullivan, & Ali, 2011). The supply of illicit drugs may also vary between individuals, for example due to periods of incarceration (Darke, Kaye, & Finlay-Jones, 1998; Dolan, Wodak, Hall, Gaughwin, & Rae, 1996; Victorian Auditor-General, 2013), or simply by geographic location due to the existence of sub-markets (Caulkins, 1995). This can likewise affect the types of drugs that are consumed.

Here we can neither estimate the cross-price elasticity of demand, nor formally untangle demand from consumption. But we can observe how a large sample of people who inject drugs (PWID) and who initially almost exclusively nominated heroin as their drug of choice reacted to a dramatic change in the supply of a potential substitute, namely methamphetamine, whose purity-adjusted price underwent a sustained and substantial decline in absolute terms and relative to the purity-adjusted price of heroin. Even if a-priori we may not expect heroin and methamphetamine to be close substitutes due to their different effects (heroin is a depressant while methamphetamine is a stimulant), given the paucity of data concerning natural experiments that create incentives for drug substitution, the response of a sample of PWID exposed to these changes is worth investigation.

The history of the Australian heroin market contains a similar natural experiment and recent drug market changes can be usefully be contrasted with an earlier period popularly referred to as the heroin “drought”. Following a period of highly available and high purity heroin in the 1990s (Dietze & Fitzgerald, 2002), a dramatic supply reduction in 2001 resulted in more expensive and lower purity heroin in Victoria (Miller, Fry, & Dietze, 2001). These less favourable market conditions were correlated with a decrease in heroin use and an increase in methamphetamine use among PWID (Dietze et al., 2004). In contrast, during the present study period, between 2009 and mid-2013, the heroin market was relatively stable (Cogger, Dietze, & Lloyd, 2014; Scott, Caulkins, Ritter, Quinn, & Dietze, 2014), but there was a considerable decline in the purity-adjusted price of methamphetamine (Scott, Caulkins, Ritter, Quinn, et al., 2014), possibly resulting from an increase in supply (Australian Crime Commission (ACC), 2014). In both cases methamphetamine became much more affordable relative to heroin, although in the first instance that was because heroin prices rose and in the more recent period it was because methamphetamine prices fell. We are interested in whether similar transitions in use occurred in this second instance.

Throughout the recent period of decreasing methamphetamine purity-adjusted price, the Melbourne Injecting Drug User Cohort Study (MIX) (Horyniak et al., 2013) has collected information on participants' preferences and use of a range of illicit substances. This allows us to contrast answers to the questions "what is your main illicit drug of choice" and "what illicit drug did you use most during the last month". While the drug research literature is not always careful to distinguish demand and consumption, these two questions can be used to draw insights concerning both, and can be used to detect correlations with market conditions. MIX participants report a high prevalence of polydrug use, so drug substitution when prices and availabilities vary is a plausible behavioural response. For example, although heroin was the drug of choice for the majority of the cohort at baseline, 93% had previously used methamphetamine, 41% had done so in the month prior to recruitment.

In this paper, we use a Markov model to investigate whether transitions in use similar to during the 2001 heroin shortage have recently occurred. More specifically, we ask whether between 2009 and mid-2013 there were any increases in 1) PWID citing methamphetamine as their drug of choice; and 2) methamphetamine use among PWID who prefer another drug, such as heroin, that may correlate with the decrease in methamphetamine purity-adjusted price.

METHODS

Data Source

We used data on drug preferences and use collected from 688 participants enrolled in the Melbourne Injecting Drug User Cohort Study (MIX). MIX is a prospective cohort study of young (≤ 30

years of age) PWID who were recruited into the study between April 2008 and January 2010 from three Melbourne neighbourhoods: Inner West (Footscray); Central (CBD, Fitzroy, St Kilda, Richmond, Collingwood); and Outer-Urban (Dandenong, Frankston). Experienced fieldworkers interview participants approximately annually in face-to-face interviews and as of 1 August 2013, 51% of participants had completed three or more interviews and a total of 2152 interviews had been conducted. Median dates for the baseline and the first three follow-up interview waves are July 2009 (Inter Quartile Range (IQR) March 2009 - October 2009), August 2010 (IQR April 2010 - December 2010), August 2011 (IQR April 2011 - December 2011) and August 2012 (IQR March 2012 - November 2012). Further details of the MIX cohort can be found elsewhere (Horyniak et al., 2013; Scott, Caulkins, Ritter, & Dietze, 2014b).

In each interview, individuals are asked “what drug did you use most during the last month?” and “what is your main illicit drug of choice (i.e. preferred or favourite drug)?” as well as a range of questions about demographic, injection frequency, OST utilisation and incarceration history. Interviewers record participant responses to drug used most as the one of the following: heroin, speed, methamphetamine base, crystal methamphetamine / ice, ecstasy, pharmaceutical stimulants, cocaine, LSD, ketamine, GHB-type substances, methadone, morphine, buprenorphine, suboxone, benzodiazepines, cannabis, inhalants, alcohol, other, don't know, refuse to answer or not applicable, and participant responses for illicit drug of choice as: heroin, methadone, buprenorphine, other opiates (e.g. codeine, morphine, opium), amphetamines, cocaine, hallucinogens (including LSD, peyote, mescaline, mushrooms), ecstasy, benzodiazepines, cannabis, inhalants, other, don't know, refuse to answer and not applicable. Responses to both questions were collapsed into four categories: heroin, methamphetamine, cannabis and other.

The date of each interview was matched with the purity and purchase-size adjusted methamphetamine price series (aggregate for Melbourne) from (Scott, Caulkins, Ritter, Quinn, et al., 2014) to create a methamphetamine purity-adjusted price variable.

Statistical and modelling methods

For each interview and location, the percentages of participants nominating each drug category as their main illicit drug of choice and as the drug they used most in the last month were calculated. To summarize transitions between drug of choice categories from one interview to the next, transition matrices listing the percentage of participants making each transition during the three between-interview periods (baseline – follow-up 1, follow-up 1 – follow-up 2, follow-up 2 – follow-up 3) were calculated. The percentage of participants nominating each drug as the one *used* most, conditional on their nominated drug of choice, were also calculated for the baseline and first three follow-up interviews. Both the transition matrices and conditional drug of choice matrices were determined for the whole cohort and stratified by location.

Hidden Markov Models are well suited to describe systems with an outcome dependent on a latent variable (Collins & Lanza, 2010; Lanza & Collins, 2008; Lanza, Patrick, & Maggs, 2010; Shirley, Small, Lynch, Maisto, & Oslin, 2010). For this analysis we constructed an analogous Markov model with most-used-drug considered logically dependent on the variable drug of choice. This differs to a Hidden Markov Model since we explicitly observe the latent variable drug of choice. Covariates were included for methamphetamine purity-adjusted price, OST status, injection frequency, geographic location and recent incarceration (Altman, 2007; Lanza, Collins, Lemmon, & Schafer, 2007), and the model was calculated as described below. Further details are provided in the appendix.

For heroin, methamphetamine, cannabis or other, the set of interviews where each drug was nominated as current drug of choice were considered separately. On each of these subsets of the data, two independent multinomial logistic models were used to determine 1) the likelihood of nominating heroin, methamphetamine, cannabis or other as the drug of choice in the following interview; and 2) the likelihood of nominating heroin, methamphetamine, cannabis or other as the drug used most. For example, where heroin was nominated as the drug of choice, the first model determines the likelihood of nominating heroin-heroin, heroin-methamphetamine, heroin-cannabis or heroin-other in consecutive interviews, and the second model determines the conditional likelihood of using each drug the most if a participants' current drug of choice was heroin. For the first models, all consecutive interviews were pooled so that only the current interview was used as input. To account for different numbers of observations from each participant (due to loss to follow up and differing times between interviews), standard errors were clustered on participant ID, relaxing the requirement that all observations be independent. Thus, variances and confidence intervals were measured across clusters (participants) rather than across all observations.

Each model was initially run with controls for methamphetamine purity-adjusted price, geographical location (Inner West, Central or Outer-Urban), whether a participant was on OST (the drug of choice models have four categories given by off/off, off/on, on/off, and on/on in the current and next interview, and the drug used most models have off or on), whether a participant was released from prison within the month prior to being interviewed and number of injections reported in the last week (assuming a linear relationship between number of injections and outcomes). Heroin dependence may be a confounder in this analysis. To account for this at least partially, a control variable for whether heroin was reported as drug of choice at baseline was included (no explicit drug dependence variables were captured in the data and the limited number of participants who

nominated non-heroin drug of choice categories at baseline meant that a stratified analysis was not possible).

The three different OST categories for the drug of choice models did not have significantly different outcomes and were replaced by a single category (whether a participant was on OST in one or more of the consecutive interviews). Incarceration status did not have any significant effects in the models and was removed (participants only reported recent incarceration in 6% of interviews). Categorised weekly injection frequencies (none, 1-6 times, 7-13 times, 14 or more times) were also tested: results were consistent with a linear assumption, however the addition of these parameters to models with low observation numbers made estimates substantially weaker, and so the linear estimate was retained.

As the purity-adjusted price of methamphetamine decreased steadily throughout the period of interest (from approximately \$2000 for one pure gram in the first quarter of 2009 to just under \$500 for one pure gram in mid-2013), the covariate methamphetamine price introduces a near linear relationship with time. For this reason no independent time variables are included, and time trends that occurred during this period are cautiously interpreted as associations with decreasing purity-adjusted methamphetamine price.

RESULTS

MIX participants were two thirds male (67%, n=459), and at baseline interviews had a mean age of 26.9 years; mean length of injecting career of 9.5 years; mean injection frequency of 8.9 times per week; 35% (n=242) were enrolled in OST; and 59% (n=407) had a history of incarceration. At baseline

interviews, 97% (n=665) and 93% (n=639) of participants reported lifetime heroin and methamphetamine use respectively; and 82% (n=569) and 41% (n=283) of participants reported using heroin and methamphetamine in the last month respectively.

Drug of choice and drug used most

Heroin was the drug of choice reported by the majority of the cohort, however over time this decreased and cannabis preference increased (Figure 1, top). At baseline, 72% (N=491), 12% (N=81), 7% (N=48) and 9% (N=61) of the cohort reported heroin, methamphetamine, cannabis and other as their drug of choice respectively, and at follow-up 3 this was 58% (N=194), 15% (N=51), 21% (N=69) and 7% (N=22) of the cohort respectively ($\chi^2(9)=57.8$, $p<0.001$). Drug of choice varied between geographic locations. Heroin preference was cited more frequently in the Inner West ($\chi^2(2)=68.8$, $p<0.001$), and methamphetamine preference was cited more frequently in Outer-Urban regions ($\chi^2(2)=48.1$, $p<0.001$).

Heroin was the drug used most by the majority of the cohort at baseline, however over time this decreased and cannabis use increased (Figure 1, bottom). At baseline, 61% (N=415), 6% (N=43), 19% (N=127) and 15% (N=101) of the cohort reported heroin, methamphetamine, cannabis and other as the drug they used most, and at follow-up 3 this was 31% (N=104), 9% (N=29), 37% (N=124) and 23% (N=75) respectively ($\chi^2(9)=129.3$, $p<0.001$). Drug used most varied between geographic locations. Heroin was more frequently used the most in the Inner West ($\chi^2(2)=174.5$, $p<0.001$), and other drugs were more frequently used the most in Outer-Urban regions ($\chi^2(2)=203.7$, $p<0.001$).

Over the first four interview waves, in 39% (N=733) of interviews the participants did not use their preferred drug the most in the last month. Where there was a disjunction between preference and use, cannabis was the drug used most 43% (312/733) of the time.

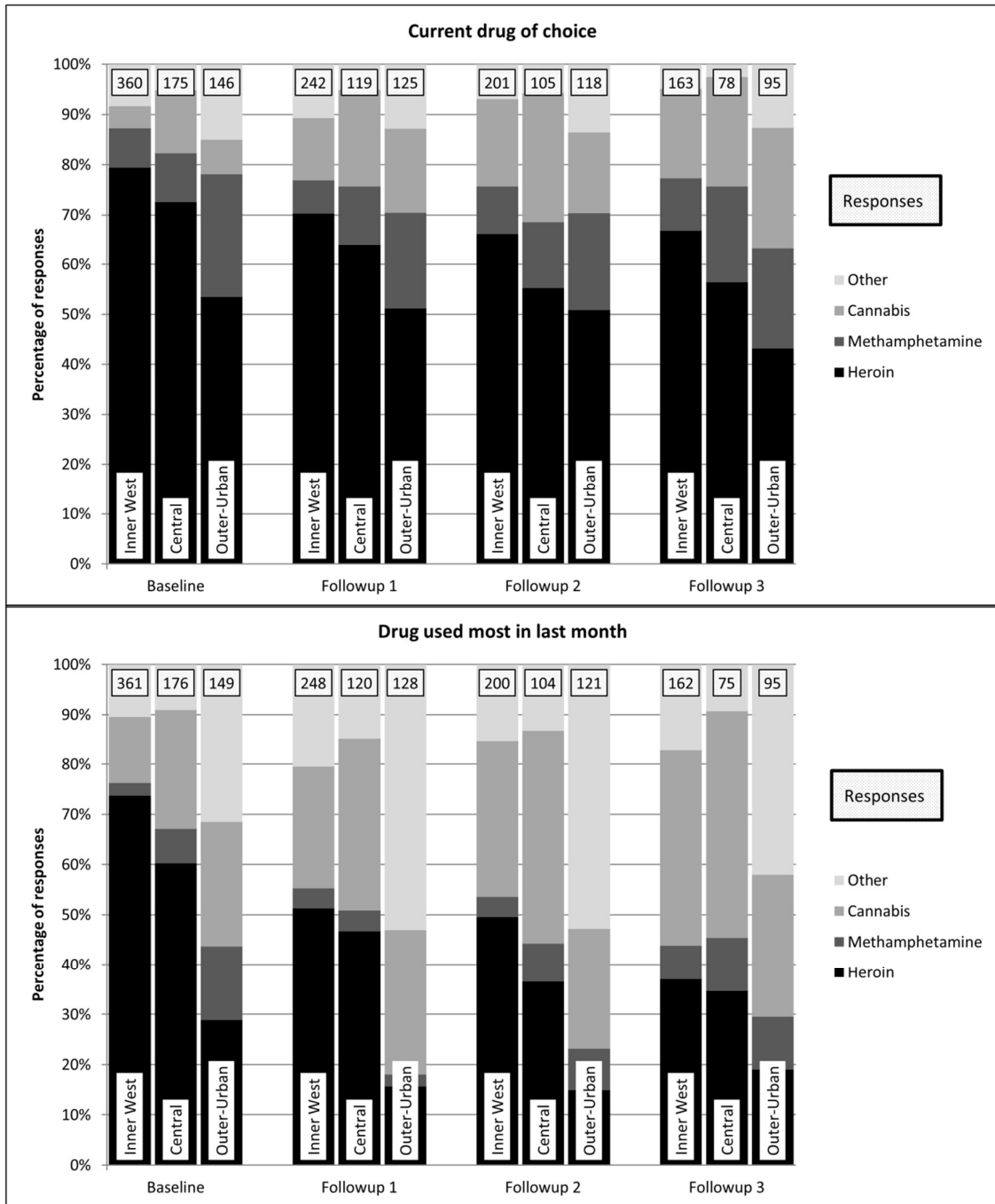


Figure 1: Distributions of main drug of choice and drug used most in the last month by interview and location, April 2008 – August 2013.

Figure 2 shows transition matrices for drug of choice and Figure 3 shows the percentage of participants nominating each drug as the one used most, conditional on their nominated drug of choice. Large diagonal entries in Figure 2 indicate a relative stability of drug preferences, more so for heroin than other drug types. Participants were most likely to use their preferred drug if it was cannabis (Figure 3, cannabis diagonals), and across all drug preferences, participants from Outer-Urban regions were more likely to use other drugs the most when compared to participants from the Inner West or Central (Figure 3). These observations may be affected by variables that will be controlled for in the Markov model.

All sites		Transition from baseline to follow up 1: Final drug of choice state				Transition from follow up 1 to follow up 2: Final drug of choice state				Transition from follow up 2 to follow up 3: Final drug of choice state			
		Heroin	Amph.	Cannabis	Other	Heroin	Amph.	Cannabis	Other	Heroin	Amph.	Cannabis	Other
Initial drug state	Heroin	77%	6%	10%	7%	79%	5%	10%	5%	80%	8%	10%	3%
	Amph.	25%	46%	19%	10%	23%	49%	19%	9%	28%	60%	5%	8%
	Cannabis	31%	5%	56%	8%	23%	13%	62%	2%	22%	8%	66%	5%
	Other	43%	7%	12%	38%	34%	20%	10%	37%	28%	24%	8%	40%
Inner West		Heroin	Amph.	Cannabis	Other	Heroin	Amph.	Cannabis	Other	Heroin	Amph.	Cannabis	Other
Initial drug state	Heroin	77%	5%	10%	8%	81%	4%	11%	4%	85%	7%	7%	2%
	Amph.	33%	40%	27%	0%	45%	27%	18%	9%	27%	73%	0%	0%
	Cannabis	55%	0%	36%	9%	23%	14%	64%	0%	25%	3%	66%	6%
	Other	43%	0%	14%	43%	35%	20%	10%	35%	44%	11%	0%	44%
Central		Heroin	Amph.	Cannabis	Other	Heroin	Amph.	Cannabis	Other	Heroin	Amph.	Cannabis	Other
Initial drug state	Heroin	82%	6%	11%	1%	81%	8%	10%	2%	80%	13%	8%	0%
	Amph.	18%	64%	9%	9%	8%	50%	25%	17%	45%	45%	9%	0%
	Cannabis	28%	0%	67%	6%	21%	5%	74%	0%	32%	16%	53%	0%
	Other	25%	25%	13%	38%	17%	17%	33%	33%	25%	25%	25%	25%
Outer-Urban		Heroin	Amph.	Cannabis	Other	Heroin	Amph.	Cannabis	Other	Heroin	Amph.	Cannabis	Other
Initial drug state	Heroin	72%	11%	8%	9%	72%	5%	10%	12%	70%	6%	18%	6%
	Amph.	24%	42%	18%	15%	20%	60%	15%	5%	17%	61%	6%	17%
	Cannabis	10%	20%	60%	10%	25%	20%	50%	5%	0%	8%	85%	8%
	Other	54%	8%	8%	31%	40%	20%	0%	40%	17%	33%	8%	42%

Figure 2: Transition matrices for drug of choice, by interview and recruitment site.

		Baseline				Follow-up 1				Follow-up 2				Follow-up 3			
All sites		Drug used most				Drug used most				Drug used most				Drug used most			
		Heroin	Meth.	Cannabis	Other	Heroin	Meth.	Cannabis	Other	Heroin	Meth.	Cannabis	Other	Heroin	Meth.	Cannabis	Other
Drug of choice	Heroin	75%	1%	14%	10%	59%	1%	19%	21%	53%	3%	22%	23%	53%	2%	26%	19%
	Meth.	15%	41%	21%	23%	16%	21%	33%	31%	14%	31%	21%	34%	8%	45%	23%	25%
	Cannabis	12%	2%	69%	17%	14%	1%	69%	16%	7%	1%	76%	16%	4%	3%	82%	12%
	Other	29%	1%	20%	49%	12%	2%	23%	63%	21%	3%	21%	56%	0%	8%	29%	63%
Inner West		Heroin	Meth.	Cannabis	Other	Heroin	Meth.	Cannabis	Other	Heroin	Meth.	Cannabis	Other	Heroin	Meth.	Cannabis	Other
Drug of choice	Heroin	81%	0%	12%	6%	67%	3%	16%	14%	60%	3%	22%	15%	53%	3%	27%	17%
	Meth.	31%	28%	22%	19%	30%	25%	35%	10%	35%	30%	20%	15%	17%	44%	28%	11%
	Cannabis	24%	5%	57%	14%	19%	0%	69%	13%	10%	3%	78%	10%	6%	3%	86%	6%
	Other	41%	0%	14%	46%	13%	3%	23%	60%	35%	0%	24%	41%	0%	22%	22%	56%
Central		Heroin	Meth.	Cannabis	Other	Heroin	Meth.	Cannabis	Other	Heroin	Meth.	Cannabis	Other	Heroin	Meth.	Cannabis	Other
Drug of choice	Heroin	79%	0%	14%	7%	69%	0%	22%	9%	62%	2%	22%	14%	62%	2%	28%	9%
	Meth.	6%	65%	12%	18%	8%	31%	46%	15%	7%	43%	21%	29%	7%	53%	33%	7%
	Cannabis	9%	0%	86%	5%	14%	5%	68%	14%	4%	0%	92%	4%	0%	0%	94%	6%
	Other	22%	0%	33%	44%	0%	0%	43%	57%	33%	0%	50%	17%	0%	0%	50%	50%
Outer-Urban		Heroin	Meth.	Cannabis	Other	Heroin	Meth.	Cannabis	Other	Heroin	Meth.	Cannabis	Other	Heroin	Meth.	Cannabis	Other
Drug of choice	Heroin	47%	6%	18%	29%	23%	0%	23%	54%	28%	3%	19%	50%	43%	0%	19%	38%
	Meth.	5%	42%	24%	29%	8%	12%	24%	56%	0%	25%	21%	54%	0%	40%	10%	50%
	Cannabis	0%	0%	63%	38%	7%	0%	70%	22%	5%	0%	55%	41%	4%	4%	68%	24%
	Other	13%	4%	26%	57%	13%	0%	13%	73%	0%	6%	6%	88%	0%	0%	31%	69%

Figure 3: Drug used most in the last month for a given drug of choice, by interview and recruitment site.

Estimates for changes to drug preferences

The predicted parameters and marginal effects for changes in drug preferences are shown in Figure 4. After controlling for baseline heroin preference, drug of choice categories were stable more than 50% of the time, regardless of drug. In the Inner West, with methamphetamine price at \$1000 per pure gram, participants not on OST who injected once weekly were estimated to consecutively nominate heroin, cannabis, methamphetamine or other as their drug of choice 52% (95%CI 38 – 66%), 55% (95%CI 34 – 77%), 68% (95%CI 47 – 88) and 58% (95%CI 29 – 88%) of the time respectively if they had not nominated heroin as their baseline drug of choice.

Participants with baseline drug of choice heroin were 29% (95%CI 15 – 42%) more likely to consecutively nominate heroin as drug of choice; 21% (95%CI 3 – 39%) less likely to change drug of

choice from heroin to cannabis; and 25% (95%CI 8 – 42%) more likely to change drug of choice from methamphetamine to heroin.

Injecting less frequently was associated with changing drug of choice from heroin to cannabis.

Participants from Central were less likely to change their drug of choice from heroin to other than participants from the Inner West. Every \$100 decrease in the purity-adjusted price of methamphetamine was associated with a 1.9% (95%CI 0.4 – 3.4%) decrease in the likelihood of changing drug of choice from methamphetamine to heroin, and a 1.1% (95%CI 0.1 – 2.2%) decrease in the likelihood of changing drug of choice from heroin to other.

Marginal effects (percentage changes with variables) (95% C.I.)	Constant (Where applicable measured at Inner West, Off/off OST and Meth=\$1000 for one pure gram)	Location (Compared to Inner West)		OST (Compared to remaining out of treatment)	Price (per \$100 decrease in the price of one pure gram)	Injection frequency (per week)	Baseline heroin preference (compared to no)	
		Central	Outer-Urban	In treatment	Meth.		Yes	
Main drug of choice (t+1)		Main drug of choice (t) = Heroin [P1 model] N=1000 who had a following interview						
Heroin N=795	p11	51.6 (37.7, 65.5)	3.0 (-9.6, 15.6)	-9.0 (-20.1, 2.1)	7.7 (-2.7, 18.0)	0.8 (-0.7, 2.3)	0.9* (0.1, 1.7)	28.5*** (14.7, 42.3)
Methamphetamine N=60	p12	9.9 (0.4, 19.5)	4.3 (-4.0, 12.5)	5.7 (-3.1, 14.5)	-6.5 (-13.6, 0.7)	0.4 (-0.6, 1.3)	0.2 (-0.1, 0.5)	2.1 (-5.3, 9.4)
Cannabis N=97	p13	26.6 (12.7, 40.6)	2.4 (-10.5, 15.2)	-2.7 (-13.7, 8.4)	3.0 (-7.8, 13.8)	0.0 (-1.6, 1.6)	-1.2* (-2.2, -0.3)	-21.1* (-39.0, -3.2)
Other N=48	p14	11.8 (2.4, 21.3)	-9.6* (-18.2, -0.9)	6.0 (-4.4, 16.3)	-4.2 (-11.3, 3.0)	-1.1* (-2.2, -0.1)	0.2 (-0.3, 0.6)	-9.5 (-23.2, 4.3)
Main drug of choice (t+1)		Main drug of choice (t) = Methamphetamine [P2 model] N=187 who had a following interview						
Heroin N=43	p21	18.1 (4.6, 31.6)	-8.2 (-20.9, 4.5)	-6.3 (-18.2, 5.7)	-3.1 (-15.1, 9.0)	-1.9* (-3.4, -0.4)	0.3 (-0.3, 0.8)	24.7** (7.7, 41.8)
Methamphetamine N=99	p22	55.3 (34.1, 76.5)	14.8 (-9.1, 38.7)	9.7 (-11.2, 30.6)	6.1 (-14.2, 26.4)	2.3 (0.0, 4.6)	-0.4 (-1.4, 0.6)	-22.8 (-48.0, 2.5)
Cannabis N=29	p23	25.1 (7.4, 42.7)	-9.7 (-29.2, 9.9)	-9.8 (-27.4, 7.8)	-3.7 (-21.1, 13.8)	-0.3 (-2.6, 2.0)	0.2 (-0.6, 0.9)	-3.3 (-26.5, 19.9)
Other N=16	p24	1.6 (-1.6, 4.7)	3.1 (-5.9, 12.1)	6.4 (-1.8, 14.5)	0.7 (-1.8, 3.1)	-0.1 (-0.4, 0.3)	0.0 (-0.1, 0.1)	1.3 (-2.9, 5.5)
Main drug of choice (t+1)		Main drug of choice (t) = Cannabis [P3 model] N=234 who had a following interview						
Heroin N=61	p31	14.1 (2.0, 26.2)	4.5 (-8.4, 17.4)	-7.1 (-18.3, 4.1)	14.6 (-1.6, 30.8)	-0.3 (-1.7, 1.0)	0.4 (-0.3, 1.0)	4.0 (-8.1, 16.1)
Methamphetamine N=21	p32	14.9 (-5.5, 35.2)	-5.2 (-26.2, 15.9)	7.6 (-14.4, 29.5)	-0.3 (-15.9, 15.3)	0.6 (-1.7, 2.8)	-0.5 (-2.2, 1.3)	-20.8 (-66.2, 24.6)
Cannabis N=140	p33	67.6 (47.3, 87.9)	2.8 (-18.9, 24.6)	-1.4 (-23.2, 20.5)	-16.5 (-35.9, 2.8)	0.0 (-2.4, 2.5)	0.1 (-1.5, 1.8)	20.1 (-17.7, 57.9)
Other N=12	p34	3.4 (-1.3, 8.2)	-2.2 (-6.8, 2.5)	0.9 (-5.3, 7.2)	2.2 (-8.3, 12.7)	-0.3 (-1.2, 0.7)	0.0 (-0.3, 0.3)	-3.2 (-13.3, 6.8)
Main drug of choice (t+1)		Main drug of choice (t) = Other [P4 model] N=131 who had a following interview						
Heroin N=47	p41	17.7 (-3.0, 38.5)	-6.3 (-26.1, 13.5)	-0.6 (-15.6, 14.5)	8.9 (-7.1, 24.9)	-1.4 (-3.1, 0.4)	0.4 (-0.3, 1.2)	12.1 (-1.7, 25.9)
Methamphetamine N=20	p42	6.6 (-4.8, 18.1)	12.5 (-10.0, 35.0)	9.0 (-8.0, 26.0)	5.0 (-5.9, 16.0)	0.7 (-1.0, 2.3)	0.2 (-0.1, 0.5)	1.1 (-7.8, 10.1)
Cannabis N=14	p43	17.3 (-0.4, 35.0)	11.6 (-17.7, 40.8)	-8.7 (-27.2, 9.8)	-8.7 (-22.8, 5.4)	-0.8 (-3.3, 1.7)	-0.4 (-1.6, 0.8)	4.4 (-18, 26.7)
Other N=50	p44	58.3 (28.8, 87.9)	-17.8 (-57.1, 21.5)	0.3 (-24.8, 25.4)	-5.2 (-29.2, 18.8)	1.6 (-1.5, 4.6)	-0.2 (-1.7, 1.2)	-17.6 (-44.9, 9.7)

* p<0.05, ** p<0.01, *** p<0.001

Figure 4: Modelled probabilities for transitions between main drug of choice categories, all interviews between April 2008 and August 2013.

Estimates for the relationship between which drugs are preferred and which drugs are used

The predicted parameters and marginal effects for the relationship between drug of choice and drug used the most are shown in Figure 5. Participants were more likely to use their preferred drug if it was cannabis than if it were any other choice. In the Inner West, with methamphetamine price at \$1000 per pure gram, participants not on OST who injected once weekly were estimated to use cannabis the most 68% (95%CI 53 – 82%) of the time if it was their preferred drug, and heroin, methamphetamine and other drugs the most 54% (95%CI 41 – 68%), 37% (95%CI 23 – 52%) and 51% (95%CI 30 – 72%) of the time respectively if they were their preferred drugs, after controlling for baseline heroin preference.

If the preferred drug was heroin or methamphetamine, injecting more frequently was associated with using heroin the most, and if the preferred drug was heroin, injecting less frequently was associated with using cannabis the most. Participants on OST were more likely to use other drugs the most if their preferred drug was heroin.

Participants from Outer-Urban regions were less likely to use heroin and more likely to use other drugs the most than participants from the Inner West, regardless of their drug of choice. Participants from Central were more likely to use cannabis the most if their preferred drug was cannabis or other, and were less likely to use heroin the most if their drug of choice was methamphetamine than participants from the Inner West.

Decreasing methamphetamine purity-adjusted price was associated with less heroin and more cannabis use among participants who preferred heroin, however this is interpreted as a correlation with time. Methamphetamine purity-adjusted price was not associated with any significant changes in reports of methamphetamine as the drug used most, regardless of preferred drug.

Marginal effects (percentage changes with variables) (95% C.I.)		Constant (Where applicable measured at Inner West, Off/off OST and Meth= \$1000 for one pure gram)	Location (Compared to Inner West)		OST (compared to remaining out of treatment)	Price (per \$100 decrease in the price of one pure gram)	Injection frequency (per week)	Baseline heroin preference (compared to no)
			Central	Outer-Urban				
Drug used most	Main drug of choice (t) = Heroin [Q1 model] N=1314							
Heroin N=832	q1/1	54.2 (40.6, 67.8)	-3.2 (-12.3, 5.8)	-26.5*** (-36.6, -16.4)	-5.1 (-12.9, 2.7)	-1.9*** (-2.8, -0.9)	1.8*** (1.1, 2.6)	9.2 (-4.8, 23.2)
Methamphetamine N=20	q1/2	0.5 (-0.5, 1.5)	-0.2 (-0.6, 0.2)	0.5 (-0.7, 1.6)	0.4 (-0.7, 1.5)	0.0 (-0.1, 0.1)	0.0 (-0.1, 0.0)	0.5 (0.0, 1.0)
Cannabis N=238	q1/3	33.1 (20.1, 46.1)	5.3 (-4.4, 15.0)	-0.5 (-12.2, 11.1)	-2.8 (-10.4, 4.7)	1.50** (0.5, 2.5)	-1.1** (-1.8, -0.3)	-9.7 (-24, 4.5.0)
Other N=224	q1/4	12.3 (5.1, 19.4)	-1.9 (-7.3, 3.6)	26.5*** (15.5, 37.6)	7.5** (2.2, 12.8)	0.3 (-0.2, 0.8)	-0.8 (-1.6, 0.1)	0.0 (-6.1, 6.2)
Drug used most	Main drug of choice (t) = Methamphetamine [Q2 model] N=252							
Heroin N=31	q2/1	20.8 (7.6, 34)	-18.3** (-32.0, -4.6)	-19.4** (-33.3, -5.5)	-10.4 (-27.9, 7.0)	-1.2 (-3.0, 0.6)	1.0* (0.2, 1.8)	-4.6 (-25, 15.9.0)
Methamphetamine N=84	q2/2	37.4 (22.8, 52.0)	16.9 (-1.6, 35.4)	2.1 (-16.0, 20.1)	10.6 (-4.4, 25.6)	0.5 (-1.3, 2.3)	-0.2 (-1.1, 0.7)	-1.5 (-20.1, 17.1)
Cannabis N=60	q2/3	29.9 (15.6, 44.1)	0.1 (-19.0, 19.1)	-8.5 (-25.2, 8.2)	0.5 (-15.1, 16.0)	0.7 (-1.0, 2.3)	-0.8 (-2.0, 0.4)	0.3 (-18.1, 18.6)
Other N=77	q2/4	12.0 (3.5, 20.5)	1.4 (-10.3, 13.1)	25.9** (10.1, 41.6)	-0.7 (-7.8, 6.4)	0.0 (-0.8, 0.8)	0.0 (-0.4, 0.5)	5.8 (-2.1, 13.7)
Drug used most	Main drug of choice (t) = Cannabis [Q3 model] N=300							
Heroin N=28	q3/1	19.0 (6.0, 32.1)	-11.5 (-26.3, 3.4)	-11.8 (-26.1, 2.5)	8.9 (-3.4, 21.2)	-0.3 (-2.2, 1.6)	0.5 (-0.5, 1.5)	-1.4 (-16.6, 13.8)
Methamphetamine N=5	q3/2	4.9 (-3.3, 13.1)	-3.3 (-11.1, 4.5)	-3.1 (-9.8, 3.6)	1.6 (-6.2, 9.3)	0.7 (-0.6, 2.0)	-0.1 (-0.6, 0.4)	-3.1 (-13.7, 7.6)
Cannabis N=220	q3/3	67.7 (53.0, 82.4)	17.6* (1.9, 33.4)	-0.5 (-18.6, 17.6)	-5.9 (-20.7, 8.8)	0.3 (-2.0, 2.5)	-0.4 (-1.7, 0.9)	6.5 (-9.7, 22.6)
Other N=47	q3/4	8.4 (1.2, 15.6)	-2.9 (-9.8, 4.1)	15.4* (1.5, 29.3)	-4.6 (-14.1, 5.0)	-0.7* (-1.3, 0.0)	0.0 (-0.4, 0.4)	-2.0 (-10.1, 6.2)
Drug used most	Main drug of choice (t) = Other [Q4 model] N=177							
Heroin N=31	q4/1	16.7 (1.1, 32.3)	-6.0 (-24.4, 12.4)	-12.2 (-27.7, 3.4)	4.7 (-6.7, 16.1)	-2.1** (-3.6, -0.5)	0.7 (-0.1, 1.5)	4.6 (-11.6, 20.8)
Methamphetamine N=4	q4/2	0 (0, 0)						
Cannabis N=38	q4/3	32.2 (11.1, 53.3)	24.5* (-1.3, 50.3)	-2.4 (-22.9, 18.2)	4.7 (-13.4, 22.8)	2.3 (-0.3, 4.9)	-1.1 (-2.2, 0.1)	-10.2 (-33.8, 13.4)
Other N=104	q4/4	51.1 (29.8, 72.4)	-18.5 (-40.8, 3.8)	14.5 (-6.1, 35.1)	-9.0 (-27.6, 9.6)	-0.2 (-2.8, 2.4)	0.3 (-1.0, 1.6)	5.6 (-14.7, 25.9)

* p<0.05, ** p<0.01, *** p<0.001

Figure 5: Modelled probabilities for drug used most in the last month conditional on drug of choice, all interviews between April 2008 and August 2013.

DISCUSSION

The overall pattern of findings reveal limited responsiveness to the sharply decreasing purity-adjusted price of methamphetamine evident in Melbourne over the period considered. This is in some respects surprising, given prior findings of substitution when methamphetamine became relatively cheaper because heroin prices rose (Dietze et al., 2004), but may reflect a status quo bias. Although in theory relative prices ought to drive drug choice and substitution, in practice absence of change in the prices of drugs currently consumed may translate into an absence of change in behaviour, and these respondents did display a strong bias towards using heroin, whose market was stable throughout this period. Unlike in 2001, when unfavourable heroin market conditions were correlated with decreases in heroin use and increases in methamphetamine use among PWID (Dietze et al., 2004), participants who preferred heroin were able to continue their use without disruption. This would be consistent with a hypothesis that unless it is imposed on them, PWID are unlikely to switch from heroin to methamphetamine use. It is logical that these drugs are not close substitutes given their different effects - heroin is a depressant while methamphetamine is a stimulant – however two very different circumstances in Melbourne suggest that such statements depend on context.

We observed that the drug preferences of PWID can change over time and do not always correspond with the drug used most. There was an overall shift from heroin to cannabis preference and a decline in heroin use consistent with participants 'maturing-out' of injecting drug use. Further, both trends were associated with injection frequency, which was decreasing within the cohort throughout this period (Scott, Caulkins, Ritter, & Dietze, 2014a). Over the first four interview waves, 39% of the time participants reported not using their preferred drug the most. As cannabis is much cheaper than heroin, methamphetamine or most other drugs (Cogger et al., 2014) it is not surprising that when there was a disjunction between preference and use, cannabis was the most frequently

reported drug used the most, accounting for 43% of cases. PWID with heroin preference at baseline were more likely to consecutively nominate heroin as their drug of choice than those who preferred any other drug types, which may reflect heroin dependence and may also explain their resistance to substituting methamphetamine, despite its decline in purity-adjusted price.

The consumption of various drug types varied significantly across different parts of Melbourne. In particular, participants from Outer-Urban regions were more likely to use other drugs rather than heroin, despite heroin being their drug of choice. This suggests that a sub-market may exist, and Outer-Urban regions may have either decreased heroin availability or increased availability of other drugs such as pharmaceutical opioids. Our data do not permit estimating purity-adjusted prices by submarket as purity data is only available in aggregate for the state, however there were no significant differences across regions in the (unadjusted for purity) prices paid for methamphetamine (Scott et al., 2014b).

There were some limitations to this study. Firstly, between 2009 and mid-2013 there were indications that methamphetamine consumption increased among existing methamphetamine users (Parliament of Victoria, 2014; Scott, Caulkins, Ritter, Quinn, et al., 2014), which may not be captured in our analysis. For example, participants who reported methamphetamine as their most used drug and increased their use would not be measured. For this reason we have focussed on transitions in use across drugs. Secondly, the literature suggests that price responsiveness may be small (Petry & Bickel, 1998), and our data doesn't specify how consumption fluctuates without passing threshold values to become the "most used". Given heroin and methamphetamine were not expected to be close substitutes, there may have been smaller consumption changes that we were unable to detect. And thirdly, these data do not come from a controlled trial. Although statistical methods were used

to compensate for participants who were lost to follow-up, it is unknown whether these participants were more or less susceptible to drug substitution than those who remained in the cohort. Further, among participants remaining in the cohort, regression to the mean (Barnett, van der Pols, & Dobson, 2005), rather than participants maturing-out, may be an alternative explanation for shifts away from a near exclusive preference for heroin. This implies that participants may mature-out more slowly than we have observed.

CONCLUSION

In a cohort of PWID who reported a range of drug behaviours, there was little evidence of changes in the popularity of methamphetamine as either a nominated drug of choice or most used drug, despite substantial declines in the purity-adjusted price of methamphetamine over time. Drug preferences of PWID can change over time and do not always correspond with the drug used most. In particular, two trends were observed: participants changing drug preference from heroin to cannabis; and a decrease in reports of heroin as the drug used most. Both trends were correlated with a lower injecting frequency and consistent with participants maturing out of high risk behaviours. Differences observed across regions suggest that sub-markets with differing drug availabilities may exist across Melbourne.

DECLARATION OF INTERESTS

The authors report no conflicts of interest.

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APPENDIX

Modelling drug of choice transitions and conditional drugs used most

Let $D = \{\text{heroin, methamphetamine, cannabis, other}\}$ be the set of possible values for both 1) drug of choice and 2) drug used most, with entries labelled 1 to 4. For each participant n and interview s , the nominated drug of choice $C_{(n,s)} \in D$ will be the underlying state and a predictor for the drug used most, $U_{(n,s)} \in D$. Define the probabilities of changing drug of choice from one interview to the next, and the conditional probabilities of using particular drugs the most as

$$p_{ij}(n, s) = \Pr(C_{(n,s+1)} = j | C_{(n,s)} = i), \quad i, j \in D$$

$$q_{ji}(n, s) = \Pr(U_{(n,s)} = j | C_{(n,s)} = i), \quad i, j \in D.$$

The Markov model is then summarised by the transition and outcome matrices $P_{n,s} = \{p_{ij}\}$ and $Q_{n,s} = \{q_{ji}\}$, along with a baseline drug of choice distribution.

Including covariates in the model

Since there are four possible drugs, there are sixteen p and sixteen q parameters. However, so far only 55% of the participants have been interviewed four or more times, so we generally only observe three transitions and four combinations of a drug-preference and a drug-used, not enough to estimate sixteen parameters for each individual. So instead of p and q parameters having fixed effects for each n and s (i.e. each individual and interview), we only estimate fixed effects for relevant covariates. For example: the effects of OST on q_{11} (using heroin the most if drug of choice is heroin) and p_{j1} (changing drug of choice from heroin) offer potential to measure the programs' ability to influence people's behaviour and desires; any dependence of the q_{ji} 's on location can

provide insight into market saturation throughout different regions; and any correlations with drug prices can provide insight to various aspects of price responsiveness.

Method for calculating model parameters and covariate effects

For each i , two independent multinomial logistic models were used to determine the sets of parameters $p_i = \{p_{ij} \mid j \in D\}$ and $q_i = \{q_{ji} \mid j \in D\}$ ¹ as described below. Each model was initially run with controls for methamphetamine purity-adjusted price (by matching interview date with the purity and purchase-size adjusted prices from (Scott, Caulkins, Ritter, Quinn, et al., 2014)) geographical location (Inner West, Central or Outer-Urban), whether a participant was on OST (p_i models have four categories given by off/off, off/on, on/off, and on/on in the current and next interview, and q_i models have off or on), whether a participant was released from prison within the month prior to being interviewed and number of injections reported in the last week.

The three different OST categories for the p_i models did not have significantly different outcomes and were replaced by a single category (whether a participant was on OST in one or more of the consecutive interviews). Incarceration status did not have any significant effects in the models and was removed (participants only reported recent incarceration in 6% of interviews).

For the dummy variables Central, Outer-Urban and OST define a vector of covariates:

¹ Where $\sum_j p_{ij}, \sum_j q_{ij} = 1$ for each i , as a category is required to be chosen. Those abstaining or not answering were minimal and removed: of all consecutive interviews, 70/1622 had an invalid response for drug of choice following a valid one, and 35/2078 interviews named a valid drug of choice and no drug used most.

$X = (1, \text{Central, Outer-Urban, OST, meth. price } (t), \text{ injections in the last week})$.

As the purity-adjusted price of methamphetamine decreased steadily throughout the period of interest (from approximately \$2000 for one pure gram in the first quarter of 2009 to just under \$500 for one pure gram in mid-2013), the covariate “meth. price (t)” in X introduces a near linear relationship with time. For this reason no independent time variables are included and time trends for the p_{ij} and q_{ji} during this period are cautiously interpreted as associations with decreasing purity-adjusted methamphetamine price.

For every $i, j \in D$, define β_{ij} and δ_{ij} to be vectors of unknown parameters of lengths equal to X . For each $i \in D$, STATA was used to best fit the parameters $\{\beta_{ij} | j \in D\}$ and $\{\delta_{ij} | j \in D\}$ by maximising the likelihood of the sets of equations

$$p_{ij}(t) = \frac{\exp(\beta_{ij} X^T)}{\sum_{k=1}^4 \exp(\beta_{ik} X^T)}, j \in D$$

and

$$q_{ji}(t) = \frac{\exp(\delta_{ij} X^T)}{\sum_{k=1}^4 \exp(\delta_{ik} X^T)}, j \in D$$

over the subset of interviews where the current drug of choice is drug i . In each case, other drugs were used as the base outcome (i.e. $\beta_{i4} = \delta_{i4} = 0$) to avoid over determination of equations and standard errors were clustered on participant to account for repeated measurements. Base probabilities were determined for each parameter p_{ij} and q_{ji} by evaluating at

$$X = (1, 0, 0, 0, \$1000 \text{ for one pure gram}, 1)$$

and the marginal effects ($\frac{\hat{\partial}p_{ij}}{\partial\text{Central}}$, $\frac{\hat{\partial}q_{ji}}{\partial\text{Central}}$, etc.) and 95% confidence intervals of covariates

were calculated.