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The Relationship between Initial Route of Heroin Administration and Speed of Transition to Daily Heroin Use

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Running title: Injecting heroin linked to fast daily use onset

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## Abstract

**Introduction and Aims:** The effect of heroin administration route on speed of transition to regular use is unknown. This paper aims to determine whether the speed of transition from initiation of heroin use to daily heroin use differs by route of administration (injecting, chasing/inhaling or snorting).

**Design and Methods:** Privileged access interviewer survey of purposively selected sample of 395 current people who use heroin (both in and not in treatment) in London, UK (historical sample from 1991). Data on age and year of initiation, time from initiation to daily use, and routes of administration were collected by means of a structured questionnaire. Generalised ordered logistic models were used to test the relationship between route of initial administration of heroin and speed of transition to daily heroin use. Analyses were adjusted for gender, ethnicity, daily use of other drug(s) at time of initiation, year of initiation, and treatment status at interview.

**Results:** After adjustment, participants whose Initial Administration Route (IAR) was injecting had a 4.71 (95% CI 1.34 – 16.5) increase in likelihood of progressing to daily use within 1-3 weeks of initiation, compared to those whose IAR was non-injecting.

**Discussion and Conclusions:** The speed of transition from first use to daily heroin use is faster if the individual injects heroin at initiation of use. Those who initiate heroin use through injecting have a shorter time frame for intervention before drug use escalation.

**Key words:** Heroin, Drug Administration Routes, Heroin Abuse, Drug Addiction, Injecting Drug Use

## Introduction

Heroin use is associated with harms including dependence [1], blood borne viral infection transmission (when injected) [2] and unintentional overdose [3]. This drug can be delivered through multiple routes of administration [4]. Injection introduces heroin straight into the bloodstream, which provides a near instant effect and high bioavailability [5] which makes it the most efficient route of administration. In contrast, chasing (inhaling heroin vapour) and snorting (nasal administration) heroin result in slower absorption, lower bioavailability and a decreased onset of effect [5]. Injection is viewed as the most harmful route due to an increased likelihood of overdose [5] and increased risk of dependence and blood-borne virus transmission [1].

Understanding of drug use escalation and dependence benefits from examining the stages of drug use [6], which include opportunity to use, initiation, and escalation in frequency of use. Genetic and environmental factors are differentially associated with transition through these stages [6–12], and speed of transition is emerging as an important area in the study of drug use [13–18]. There is thought to be a short period after substance use initiation for implementation of prevention interventions [19], and identifying factors associated with more rapid transitions has implications for the timing of interventions. This may be especially true amongst people who use heroin, given that comparison of the speed of transition to monthly use amongst people inject drugs has identified that those using heroin have a faster progression to regular use, compared to those using methamphetamine [20].

To date, no comparisons have been made of the effect of heroin administration route on speed of transition to regular use. The timeframe available for indicated interventions is likely to differ depending on the route of initial administration, as there are important pharmacokinetic differences between injecting and other methods.

To investigate the role of Initial Administration Route (IAR) in speed of transition to daily use of heroin, we recruited a sample of London-based participants who initiated heroin through variable IAR methods. Prior to 1980, the predominant route of administration among London based people using heroin was injecting, but after 1980 chasing became more prevalent as a method of administration [21], meaning that our sample contained individuals who had initiated their heroin use by both major routes. This variation in the route of heroin administration allowed us to determine whether the speed of transition from heroin initiation to daily heroin use differs by the IAR.

## Methods

### Sample

The sample consisted of people who used heroin, recruited in the London area during 1991. All participants had used heroin in the month prior to interview. The sample was structured to include an even split of participants in contact with a treatment agency and participants who were not in treatment. A full description of the study has been provided previously [22].

Participants were interviewed by privileged access interviewers [23], and data were collected by means of an interviewer administered questionnaire on basic demographic data, current patterns of drug use, history of drug-using behaviour, transitions in route of administration, and social factors associated with transitions or non-transitions in route of administration.

## **Measures**

### **Independent variable**

*Initial Route of Administration* Participants were asked “thinking back to the first time you used heroin: 1) Did you inject it? 2) Did you chase it? 3) Other”. Of 408 participants, 231 reported chasing as their IAR and 106 reported injecting. ‘Other’ was reported by 63 participants, of which 58 reported snorting heroin, 3 reported smoking heroin and 2 reported oral administration. There were no differences between these groups in terms of gender ( $P=0.50$ ) or ethnicity ( $P=0.66$ ). Broader exploration of demographics within this sample has been previously described [22]. Data were missing for 8 participants.

The final analysis sample was comprised of the 395 participants who had reported IAR injecting (27%), chasing (58%) or snorting (15%). The IARs of injecting, chasing and snorting were included in the analyses, with smoking and oral excluded due to very low group numbers. Dummy variables were generated to test differences between IAR injecting and the other IARs, and between IAR chasing and the other IARs.

### **Dependent variable**

#### *Speed of transition to daily use*

Participants were asked “how long was it from your first use of heroin until it became something you used every day or most days?” Responses were provided in days, months or years, and were then recoded into the categories 1 to 3 weeks, 1 month to 11 months, 1 -2 years and 2 or more years.

Individuals who had not reported progressing to daily heroin use at time of interview ( $N = 34$ ) were not included in the variable of time to daily heroin use.

### **Covariates**

#### *Gender*

Data on gender were obtained through interviewer report. The sample was predominately male (61%).

#### *Ethnicity*

Participants reported being White, African/Caribbean, Asian, or Mixed. Due to low numbers of Black and Minority Ethnic participants this was coded as a binary White/Non-White variable. The sample was predominately white (90%).

#### *Regular drug use prior to heroin initiation*

Data were obtained through self-report to the item “when you used heroin for the first time, were you using any other drugs regularly (is every day or most days)?” The majority of the sample reported regular use of other drugs at heroin initiation (69%).

#### *Year of initiation of heroin use*

This was calculated from recorded year of interview, participant age at interview and age at initiation of heroin use. Responses ranged from 1954 – 1991.

#### *Current treatment*

Data were obtained through self-report of attending a drug clinic, a street agency, a needle exchange, or receiving treatment for a drug problem somewhere else at the time of interview. As a consequence of sampling method just over half the sample (58%) were receiving treatment at time of interview.

#### *Statistical analyses*

Initial tests of the association between IAR and speed of transition to daily heroin use were conducted using  $\chi^2$ . Regression analyses tested associations between IAR and speed of transition to daily use. The Dependent Variable (DV) of time to daily heroin use had more than two categorical levels which necessitated the use of an ordered logistic model, but under the proportional odds assumption the relationship with the Independent Variable (IV) must be the same for each level of the DV. This can be tested using likelihood ratio tests and the Brant test, with a significant result ( $P < 0.05$ ) indicating assumptions are violated. In the present data proportionality of odds assumption was violated for the dummy variable of IAR injecting (Likelihood ratio test  $P=0.02$ , Brant test  $P=0.01$ ), the dummy variable of IAR chasing (Likelihood ratio test  $P=0.05$ , Brant test  $P=0.05$ ), and year of heroin onset (Likelihood ratio test  $P=0.09$ , Brant test  $P=0.007$ ).

When the assumption is violated a generalised ordered logistic model can be used [24], which allows a different relationship between the IV and each level of the DV. This analysis produces multiple coefficients as the levels (J) of the DV are analysed equivalent to a series of binary logistic regressions where the categories (M) of the DV are combined. When  $M = 4$  (as in the present analysis), for  $J = 1$  category 1 is contrasted with categories 2, 3, and 4; for  $J = 2$  the contrast is between categories 1 and 2 versus 3 and 4; and for  $J = 3$ , it is categories 1, 2, and 3 versus category 4 [25]. The levels of the DV were 1 to 3 weeks, 1 month to within a year, 1 year, and more than 2 years. Coefficients (Odds Ratios) represent the likelihood of those who inject heroin being in a more rapid transition group compared to other IARs, or those who chase heroin being in a more rapid transition group compared to other IARs.

The regression model was adjusted for year of initiation (to account for known cohort effects resulting from a rise in smoking of heroin in the UK around 1980 [21]), gender, ethnicity, regular drug use prior to heroin initiation, and current treatment status (to account for sampling effects).

#### *Ethics*

Ethical approval was gained from the Joint Ethics Committee of the Institute of Psychiatry and the Bethlem & Maudsley NHS Trust (the former name of SLAM).

## Results

There were significant differences between the groups in the number of participants who did not progress to daily use (see Table 1): while only 1 individual (1%) who initiated injecting did not progress to daily heroin use, 9% of those who initiated through snorting and 12% of those who initiated through chasing did not progress to daily heroin use.

Differences in speed of transition to daily use between IAR injecting and the other two IAR groups can be seen in Figure 1, and Figure 1 Table 1 demonstrates differences were significant with 30% of those who initiated heroin use via injection reporting transition to daily use within 3 weeks of initiation compared with only 15% of those who initiated via chasing and 8% of those who initiated via snorting.

Table 2 shows the unadjusted and adjusted regression models for the transition from initiation to daily use. After adjustment, participants whose IAR was injecting were found to have a 4.71 (95% CI 1.34 – 16.5) increase in likelihood of progressing to daily use within 1-3 weeks of initiation compared to other IARs. There were not significant differences in transition speed between the non-injecting IARs. None of the covariates remained significantly associated with speed of transition after adjustment.

## Discussion

The sample utilised for exploring speed of transition to daily use was particularly appropriate as it was recruited during a time in which heroin initiation by both injecting and chasing were both common. In this study initial route of heroin administration was associated with differences in speed of transition to daily heroin use. Participants whose IAR was through injection (compared to those who initiated through chasing or snorting) were more than four times as likely to use daily within a month of initiation.

The data are based on retrospective self-report. This has been shown to be a valid method of data collection in drug using populations [26], and the findings support this as a viable method for studying transition speed. The results would benefit from replication in prospective cohorts, although given the low prevalence of heroin use in the general population there are feasibility issues. Existing research has identified differences between people who inject drugs and people who use drugs through non-injecting administration [27,28], and a limitation of the present study is the small number of covariates. The association between injecting IAR and speed of progression to daily heroin use would benefit from adjustment for further covariates, to ensure the true association is estimated. A final point to consider is that these findings would benefit from replication within a new cohort to ensure that the results are not an artefact of the drug market in the early 1990s [29].



Injection produces a high concentration of the drug in the bloodstream [30], and has higher bioavailability than smoking administration [5]. Injection is already known to be associated with greater likelihood of progressing to dependence as a result of the increased efficiency of drug delivery [1], and it is plausible that a similar mechanism is underlying the faster transition to daily use amongst participants initiating heroin use through injection. Consequently the findings in this paper are consistent with known pharmacology, which provides face validity for the results and supports the use of retrospective report as a viable method for the study of transition speeds.

Additionally, the observed consistency with the pharmacology of heroin administration methods suggests the methodology could be applied to assess the dependence potential of drugs. Although daily use is not necessary for drug use to be considered problematic, with heaviness of use over time proposed as a useful definition of drug use disorder [31], for many drugs speed of transition to daily use may prove a useful comparator of drug dependence potential. Given that methodology for assessing transition speed is non-invasive and low cost, this avenue warrants further investigation and may be of use for better understanding emerging novel psychoactive substances.

Our findings support the case for encouraging non-injection as a route of administration [4] as it was associated with slower progression to daily injecting. Further, the faster transition to daily use through injection has implications for drug treatment provision. The need for drug services to attract those whose treatment needs are less immediate, in order to encourage those already injecting to switch to non-injecting, has previously been suggested in the literature [1]. Focus may benefit from shifting to target those who have *recently* begun injecting, to provide encouragement to non-injecting administration (or indeed, heroin abstinence) [32]. However, intervening at the treatment service level could never be expected to reach the complete population of individuals who have recently initiated heroin use; this requires changes at the policy level. One idea that has previously been suggested is that of altering policing to penalise the supply of injectable heroin whilst being more tolerant of the supply of heroin that could only be smoked [33]. The findings of this study suggest that doing so has the potential to limit the harms of heroin use and reduce the prevalence of dependence by not only reducing the number of people who use heroin who progress to daily use, but also to allow a greater window for treatment services to reach people who use heroin before a daily habit has developed.

### Conclusions

The speed of transition to daily heroin use is faster if the individual injects heroin at initiation of use. These findings are in line with research that suggests advocating the non-injection administration of heroin over injection as a harm reduction strategy. Amongst those who initiate heroin use through injection there is a need for intervention and prevention efforts to begin very shortly after heroin initiation.

### Acknowledgements

JS is a researcher and clinician and has worked with a range of types of treatment and rehabilitation service-providers. He has also worked with pharmaceutical companies to seek to identify new or

improved treatments, and also with a range of governmental and non-governmental organisations. His employer (King's College London) has registered intellectual property on an innovative medication development with which JS is involved, and JS has been named as inventor in a patent registration by a Pharma company for a new medication. A fuller account of JS's interests is at <http://www.kcl.ac.uk/ioppn/depts/addictions/people/hod.aspx> . JS is also supported by the National Institute for Health Research (NIHR) Biomedical Research Centre for Mental Health at South London and Maudsley NHS Foundation Trust and King's College London.

There are no other declarations of interest from authors of this paper.

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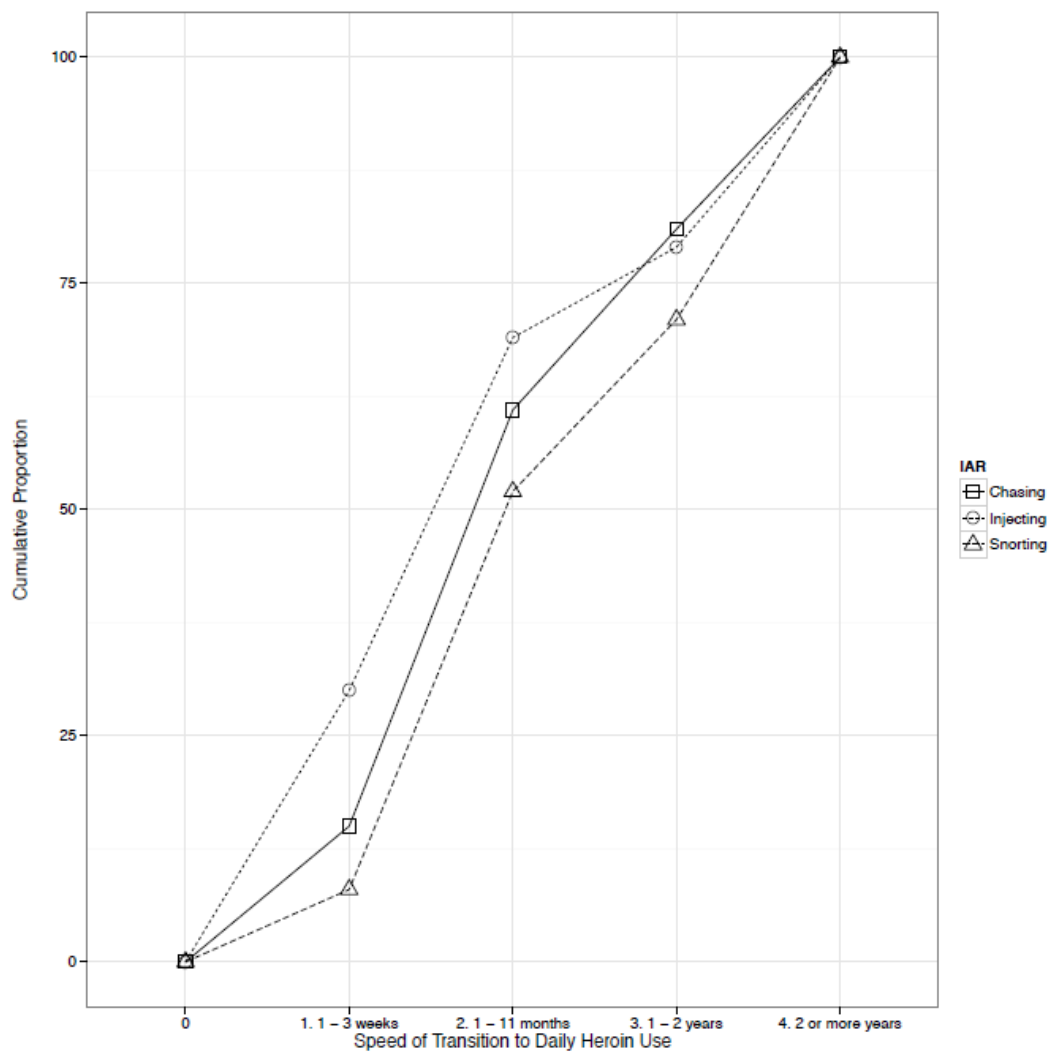
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**Table 1: Associations between initial administration route and: a) the prevalence (%) of daily heroin use and; b) speed of transition to daily use among those who report lifetime daily heroin use**

Variables		IAR			$\chi^2$ P value
		IAR injection N = 106 N (%)	IAR chasing N = 231 N (%)	IAR snorting N = 58 N(%)	
Did not progress to daily heroin use		1 (1)	28 (12)	5 (9)	<b>&lt;0.01</b>
Time from initiation to daily heroin use	1 to 3 weeks N=63	30 (30)	29 (15)	4 (8)	<b>&lt;0.01</b>
	1 month to 11 months N=153	40 (40)	90 (46)	23 (44)	
	1 -2 years N=60	10 (10.0)	40 (20)	10 (19)	
	2 or more years N=73	21 (21)	37 (19)	15 (29)	

**Figure 1: Speed of Transition to Daily Use by Initial Administration Route**

**Table 2: Generalised Ordered Logistic Model of the Association between Initial Administration Route and Speed of Transition to Daily Heroin Use**

IAR <sup>1</sup>	Transition speed group					
	1 to 3 weeks N=63		1 month to 11 months N=153		1 -2 years N=60	
	Unadjusted	Adjusted	Unadjusted	Adjusted	Unadjusted	Adjusted
Injecting v. non-injecting	<b>5.07**</b> (1.68 – 15.3)	<b>4.71*</b> (1.34 – 16.5)	2.09 (1.05 – 4.16)	1.01 (0.49 – 2.08)	1.54 (0.72 – 3.33)	1.00 (0.43 – 2.32)
Chasing v. non-chasing	2.08 (0.70 – 6.22)	1.93 (0.55 – 6.72)	1.43 (0.77 – 2.65)	0.89 (0.46 – 1.73)	1.74 (0.87 – 3.50)	1.00 (0.46 – 2.17)
Covariates						
Year of onset <sup>1</sup>	1.01 (0.97 – 1.05)	1.00 (1.00 – 1.00)	0.98 (0.95 – 1.01)	1.00 (1.00 – 1.00)	<b>0.94**</b> (0.90 – 0.98)	0.99 (0.95 – 1.03)
Non-white ethnicity	1.45 (0.79 – 2.68)	1.00 (0.52 – 1.90)	1.45 (0.79 – 2.68)	1.00 (0.52 – 1.90)	1.45 (0.79 – 2.68)	1.00 (0.52 – 1.90)
Regular drug use prior to heroin initiation	0.76 (0.50 – 1.14)	0.73 (0.47 – 1.13)	0.76 (0.50 – 1.14)	0.73 (0.47 – 1.13)	0.76 (0.50 – 1.14)	0.73 (0.47 – 1.13)
Female gender	1.26 (0.85 – 1.87)	1.00 (0.66 – 1.52)	1.26 (0.85 – 1.87)	1.00 (0.66 – 1.52)	1.26 (0.85 – 1.87)	1.00 (0.66 – 1.52)
In treatment at time of interview	1.20 (0.81 – 1.77)	1.00 (0.64 – 1.57)	1.20 (0.81 – 1.77)	1.00 (0.64 – 1.57)	1.20 (0.81 – 1.77)	1.00 (0.64 – 1.57)

\*P &lt; 0.05; \*\*P &lt; 0.01; \*\*\*P &lt; 0.001

<sup>1</sup> Variable did not meet the proportional odds assumption