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1

Characterising opportunity to use heroin reveals new avenues for intervention:

2

context, outcomes, and latency to initiation

3 Abstract

4 Preceding initiation, opportunity to use heroin is the earliest necessary condition for heroin 5 related outcomes to occur. This study aimed to characterise first heroin use opportunity (prior 6 to initiation), and to identify heroin-related outcomes associated with earlier age at first 7 opportunity. Structured interviews were conducted with 93 opiate substitution treatment 8 clients in UK drug and alcohol treatment clinics. The majority of participants (64.8%) 9 reported initiating heroin use on the same day as being first presented with the opportunity to 10 use heroin. Of those who reported early age at opportunity to use heroin, 77.4% reported this 11 came from friends/partner/family compared to 59.3% of those who reported later 12 opportunities. After adjustment, overdose was found to be more than twice as likely amongst those who reported first opportunity to use heroin at age 17 or under (AOR 2.82 95% CI 1.57 13 - 5.05). Findings indicate the early drug use environment is linked to later risk of overdose. 14 15 Greater consideration of context surrounding heroin use opportunity may indicate 16 mechanisms to disrupt or prevent initiation of heroin use and later drug-related harms. Given 17 short latency to initiation, focus should be placed on preventing initiation of heroin use through injecting. 18

19 Introduction

Dependence on heroin and other opioids accounts for the highest proportion of the illicit drug contribution to Disability Adjusted Life Years (Degenhardt, Whiteford, & Hall, 2014). This is despite low prevalence of use in general population samples (UNODC, 2014). Aside from dependence, heroin use is associated with a number of significant health risks. Overdose is the leading cause of mortality amongst those who use this drug (Degenhardt et al., 2011), whilst the administration of heroin through injection increases risks for blood borne virus
 transmission through syringe sharing (Strang et al., 1998).

3 These harms cannot occur amongst individuals who do not have the opportunity to use heroin 4 (Hines, Morley, Mackie, & Lynskey, 2015). The first stage of drug involvement is having the 5 opportunity to use a drug (regardless of whether the individual uses the drug or not). Having 6 the opportunity to use a drug is **distinct** from initiation of drug use, and has been previously 7 defined in the literature as an individual being offered a drug, or being present when others 8 were using so that an individual could have used it if they had wanted to (Storr, Wagner, 9 Chen, & Anthony, 2011). The first opportunity to use a drug forms an individual's earliest 10 necessary condition from which they are at risk of developing dependence (Wagner & 11 Anthony, 2002a), but having the opportunity to use a drug does not equate to an individual 12 initiating use. For example, research has identified a significant minority who report having 13 the opportunity to use cannabis, but do not report having used cannabis (Hines et al., 2016). 14 Following on from opportunity, an individual may initiate drug use, and can progress to subsequent use and regular drug use. 15

16 Research into drug use is increasingly exploring variation in drug opportunity to understand 17 the mechanisms underlying initiation of use and development of dependence (Burdzovic 18 Andreas & Bretteville-Jensen, 2017, 2018; Hines et al., 2016; Wagner & Anthony, 2002b). 19 Focus in this area can provide insight into the pathways through which drug use develops. Additionally, there is a need to understand the context of opportunities, such as the age at 20 which they occur and the people who are providing them, to inform interventions that target 21 22 the primary mechanisms progressing drug use (Fink, 2017). Considering the opportunity to use heroin (preceding initiation of use) and the context in which it occurs may help to inform 23 24 interventions to prevent initiation of use and the spread of injecting.

1 To date, no research has considered heroin opportunity as distinct from initiation of heroin 2 use. We know that initiation of drug use at earlier ages is commonly associated with 3 increased risks of substance use disorder development (Swift, Coffey, Carlin, Degenhardt, & 4 Patton, 2008), and that younger age of starting to use heroin is associated with increased rates 5 of non-fatal overdose (Lynskey & Hall, 1998). However, research has not established when 6 first opportunity to use heroin typically occurs, who provides those opportunities, and 7 whether the timing of heroin use opportunity (preceding initiation) is associated with greater 8 risk of harms once use has been initiated.

9 The low prevalence of heroin opportunity and use in longitudinal, general population samples 10 (Allen et al., 2017; Van Etten & Anthony, 1999) necessitates the use of populations in contact 11 with clinical services to study heroin use, which leads to low variation in dependence status 12 of the samples. However, using a treatment sample allows exploration of the latency from 13 heroin opportunity to initiation, networks through which heroin opportunity is provided, and 14 heroin-related harms associated with earlier opportunity (preceding initiation). To this end, a sample of individuals in treatment for their heroin use were recruited to address the following 15 16 aims:

Characterise first opportunity to use heroin (preceding initiation) in a treatment seeking sample

Identify relationship between timing of opportunity and latency of progression to
 initiation, injection onset and daily use.

- Identify demographic factors and heroin-use outcomes associated with age of
 opportunity to use heroin.
- 23
- 24 Methods
- 25 **Procedure**

1	Data collection took place in two UK drug and alcohol treatment services within the South
2	London and Maudsley NHS Foundation Trust (SLAM). In total, 93 participants were
3	recruited into the study; with a participant response rate of 89%. Participants provided
4	responses to a short structured quantitative interview administered by a researcher, and were
5	reimbursed £10 upon interview completion. All responses were provided through self-report.
6	Ethical approval
7	Ethical approval was granted by the NHS Research Ethics Committee (15 /LO/0705) and
8	SLAM Research and Development.
9	Measures
9 10	Measures Age of First Opportunity to Use Heroin
9 10 11	Measures Age of First Opportunity to Use Heroin Respondents were asked to specify the age (in years) at which they first had the opportunity
9 10 11 12	Measures Age of First Opportunity to Use Heroin Respondents were asked to specify the age (in years) at which they first had the opportunity to use heroin, whether or not they actually used heroin at that time. To improve
9 10 11 12 13	Measures Age of First Opportunity to Use Heroin Respondents were asked to specify the age (in years) at which they first had the opportunity to use heroin, whether or not they actually used heroin at that time. To improve understanding, participants were given the following prompt: "By an opportunity I mean
9 10 11 12 13 14	MeasuresAge of First Opportunity to Use HeroinRespondents were asked to specify the age (in years) at which they first had the opportunityto use heroin, whether or not they actually used heroin at that time. To improveunderstanding, participants were given the following prompt: "By an opportunity I meansomeone either offered you heroin, or you were present when others were using and you
9 10 11 12 13 14 15	MeasuresAge of First Opportunity to Use HeroinRespondents were asked to specify the age (in years) at which they first had the opportunityto use heroin, whether or not they actually used heroin at that time. To improveunderstanding, participants were given the following prompt: "By an opportunity I meansomeone either offered you heroin, or you were present when others were using and youcould have used if you wanted to" (Storr et al., 2011).

Due to the non-normal distribution of age of first opportunity to use heroin, the continuous age measure of this item was transformed into tertiles. Participants who were in the lowest tertile, reporting opportunity to use heroin at age 17 or under, were classified as experiencing early opportunity. Those aged 18 or over were classified as experiencing later opportunity to use heroin.

22 Heroin Outcomes

Participants self-reported whether they had ever experienced overdose. Information on the amount of heroin used was collected through the item "At your period of heaviest use, what amount of heroin/opiates were you using on a typical day?" Participants were asked to respond with an amount in grams and/or in pounds sterling (£). To combine response in £ and responses in grams, the continuous age measure of both these items was transformed into tertiles. Participants who were in the highest tertile for reported amount in grams or in £ were classified as reporting heroin heavy use.

8 Onset of Heroin Use Behaviours Following First Opportunity

Participants self-reported their age at initiation of heroin use, age at initiation of injecting
heroin, age at onset of daily heroin use, and the length of time between having the first
opportunity to use heroin (preceding initiation) and initiating heroin use. Participants
provided responses in days, weeks, months or years. These responses were coded to a
categorical variable of "initiated use same day", "initiated use within 1-7 days", "initiated use
between one week and one month following opportunity", "initiation within the same year as
opportunity" and "initiation more than a year after opportunity".

16 Contextual factors

Participants were asked who they were with when they first had the opportunity to use heroin.
Participants selected from the options spouse/partner/boyfriend/girlfriend, parent, step or
foster parent, sibling, other relative, friend, acquaintance, stranger; due to low group numbers
the variable was collapsed into stranger/acquaintance, friend/partner, or family. Participants
who spontaneously reported being alone at first opportunity (N=4) were coded as missing.

22 Demographic variables

Participants self-reported their gender, ethnicity (collapsed into the categories White British,
 Other White, and Black and Minority Ethnic (BME) Groups), highest level of education
 completed, and age at interview.

4 Analysis

5 Associations between age of first opportunity to use heroin (preceding initiation) and demographic, contextual and heroin outcome factors were initially assessed through t-test and 6 7 chi square analysis (or fishers exact test when group N <5). Associations between the 8 exposure age of opportunity to use heroin and heroin outcomes that were identified as 9 significant (P=<0.05) were further assessed through univariate logistic and linear regression (logistic regression for binary outcomes provides an Odds Ratio (OR) as measure of effect, 10 11 and linear regression for continuous outcomes provides a Beta coefficient (Beta) as measure 12 of effect). Multivariable regression adjusted for age at interview and age of initiation, serving 13 as a proxy for adjustment for duration of heroin use. The Huber-White estimator was applied 14 to all models to account for clustering of observations from the same clinic.

15 **Results**

16 Sample Description

17 This sample of participants in treatment for their heroin use were predominately male

18 (74.2%) and White British (55.9%), with a high school education or lower (67.8%). The

19 mean age of initiation of heroin use (following opportunity) was 22.6 (95% CI 21.1 - 24.1),

20 mean age of injecting onset was 26.1 (95% CI 24.3 - 27.9), and mean age at onset of daily

heroin use was 25 (95% CI 23.2 – 26.6). Lifetime heavy heroin use was reported by 36.4% of

the sample, and lifetime overdose reported by 54.8% of the sample. See Tables 1 and 2 for

23 complete data.

24 [Table 1 near here]

1 Characterising First Opportunity to use Heroin (preceding initiation)

2 The mean age of first opportunity to use heroin (preceding initiation of use) was 21.5 (SD = 3 7.08), with a range of 8-42 years. The majority of participants reported initiating heroin use 4 on the same day as having their first opportunity to use. Amongst those who did not immediately initiate use following this first opportunity, initiation of heroin use was most 5 6 commonly over a year later, or was within the 2-12 months following opportunity. Over half 7 of participants reported that their first opportunity to use heroin was provided by a 8 friend/partner, over a third reported that their first opportunity to use heroin was provided by 9 a stranger/acquaintance, and a minority reported their first opportunity to use heroin was provided by a family member. 10

11 [Table 2 near here]

12 Early Opportunity and Later Heroin Outcomes

Of those who reported their age of first opportunity to use heroin, 34.4% (N=31) reported 13 14 having their first opportunity at age 17 or under, and 65.6% (N=59) reported having their first opportunity to use heroin at age 18 or over. Between those reporting early and late 15 16 opportunity there were significant differences in report of overdose, mean age of initiation of 17 heroin use, mean age of injecting onset, and age of onset of daily heroin use. Between those reporting early opportunity to use heroin and those reporting later opportunity there were no 18 19 significant differences in gender, ethnicity, education, who was present at their first heroin 20 use opportunity (see Table 1), time from first opportunity to initiating heroin use, or heaviness of heroin use (see Table 2). However, it is notable that a much lower proportion of 21 22 those who had early opportunity to use heroin compared to later opportunity to use heroin 23 experienced this opportunity through strangers/acquaintances, indicating a trend towards 24 friends/partner and family providing earlier heroin use opportunities.

1 Identified associations between age of first opportunity to use heroin and heroin-related 2 outcomes were analysed through multivariable regression analysis, adjusting for age at 3 interview and reported age at initiation of heroin use to act as a proxy for duration of use. 4 After adjustment, early opportunity to use heroin was not associated with lower age of 5 injecting onset and lower age of onset of daily heroin use (see Table 3). However, those who 6 reported early opportunity to use heroin (preceding initiation) were more than twice as likely 7 to report having experienced overdose after adjustment for duration of heroin use (see Table 8 3).

9 [Table 3 near here]

10 Discussion

11 This study is the first to characterise opportunity to use heroin (being offered heroin or being 12 around individuals using the drug) as an event separate from and preceding the initiation of heroin use. Analysis of data collected from a treatment-seeking sample has identified 13 variation in the age at which individuals report having had their first opportunity to use 14 15 heroin. The majority of the sample reported initiating heroin use immediately following their 16 first opportunity, but a sizeable minority of individuals report a delay of over a year between 17 first having the opportunity to use heroin and initiating use. The majority of the sample report 18 that their opportunity to use came through friends or partners. Those who report first 19 opportunity to use heroin at age 17 and under have twice the likelihood of reporting overdose 20 during their heroin use career. This association remained after controlling for age of initiation 21 and duration of heroin use. After adjustment for age at initiation of use and duration of use, 22 earlier opportunity to use heroin was not associated with age of injection onset and age at 23 daily heroin use.

1 By collecting retrospective data on first opportunity to use heroin, this study has clearly 2 differentiated the opportunity to use heroin as distinct from initiation of use. The majority of 3 the sample reported initiating heroin use on the day of their first opportunity to use the drug 4 (and it is plausible to assume initiation immediately followed this first opportunity). However, a third of the sample report a delay of weeks, months or years between their first 5 6 opportunity to use heroin and initiating use. This study is the first to report variation in 7 latency between opportunity and initiation of heroin use. Further study of this area may 8 reveal prevention targets to disrupt progression from opportunity to initiation amongst those 9 who experience a delay. However, over half the sample report initiating use immediately 10 after having first opportunity to use; if this initiation is through injecting drug use, the 11 transition to daily heroin use will be especially rapid (Hines et al., 2017). This suggests the 12 most effective harm reduction approach would be policy level interventions to reduce uptake of injecting, such as altering policing to penalise the supply of injectable heroin whilst being 13 more tolerant of the supply of heroin that could only be smoked (Strang & King, 1997). 14

Opportunity to use heroin (distinct from initiation of heroin use) is a previously overlooked 15 mechanism for intervention. However, the present analyses suggest consideration of this 16 17 stage of drug use has utility for prevention; not only for disrupting heroin use initiation, but 18 also for reducing overdose. The association between earlier opportunity to use heroin and 19 increased likelihood of overdose - which remained after controlling for age of initiation and 20 duration of heroin use - parallels findings that younger age of heroin initiation is associated with overdose (Lynskey & Hall, 1998). In line with recent calls to expand the concept of 21 22 toxicity (Strang, Neale, McDonald, & Kalk, 2018), these findings suggest that the field may 23 benefit from expanding our concept beyond pharmacology to consider motivations and risk 24 behaviours underlying overdose. It is plausible that those who have earlier opportunity to use heroin are growing up in environments in which potentially dangerous drug use habits, such 25

as concomitant use of multiple drugs, will develop. Further exploring the mechanisms
 through which early drug use behaviours are linked to later drug use outcomes is a viable
 route to reveal overlooked targets for intervention.

4 Targeting prevention messages and interventions at the families and networks of those 5 involved in heroin use may be necessary to pre-emptively disrupt progression to initiation. It 6 is notable that a greater proportion of those who experience early heroin opportunity report 7 having this opportunity through friends/partner or their family, compared to 8 strangers/acquaintances. Knowledge of where opportunities are arising may act as a 9 mechanism to disrupt initiation of use (Fink, 2017). Previous qualitative research into friendship networks associated with heroin use has reported that these change as use develops 10 11 (Best, Manning, & Strang, 2007), but no existing quantitative research has considered the 12 effect of peers at the time of heroin exposure. Intervening with networks of people who inject 13 drugs to discourage initiation of others into injecting (Hunt, Stillwell, Taylor, & Griffiths, 14 1998) is one method through which this high-risk behaviour may be limited. 15 Limitations of this study must be considered when interpreting the results. Data were 16 collected on only a small number of potential covariates, and consequently detailed analysis 17 of what may underlie the relationship between age of opportunity to use heroin and overdose 18 cannot be conducted. The data were collected through self-report, which is unlikely to bias 19 results in samples of people who inject drugs when recall is short-term (Darke, 1998). 20 However, the use of retrospective self-report introduces the potential for recall bias to affect the results. Studies of cannabis, alcohol and tobacco have identified moderate reliability for 21 22 self-reported age of onset (Ensminger, Juon, & Green, 2007; Huerta, Chodick, Balicer, Davidovitch, & Grotto, 2005; Parra, O'Neill, & Sher, 2003; Shillington, Cottler, Mager, & 23 24 Compton III, 1995). The present findings would benefit from being replicated in prospective research, but this presents challenges given the low prevalence of heroin use in the general 25

population. The small sample size in this exploratory study may have led to limited power to detect significant associations, and precluded greater variation in the analysis of age of opportunity onset and time from opportunity to initiation. Additionally, the small sample precluded adjustment for potentially confounding variables beyond the continuous variables of age at heroin initiation and age at interview.

6 Conclusions

7 Considering opportunity to use heroin as an occurrence distinct from initiation of heroin use 8 has identified an association between earlier opportunity to use heroin and later overdose, and 9 has revealed that only a third of participants report a delay of weeks, months or years between opportunity and initiation. Two thirds of participants reported initiating heroin use 10 11 on the same day as having their first opportunity to use the drug. Efforts to disrupt 12 progression to heroin use initiation should focus on minimising drug use opportunity in high-13 risk environments. Given the short latency from opportunity to initiation, more focus should 14 be placed on preventing the initiation of heroin use through injecting routes to minimise harms. 15

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hosted by the Aurora Project Lambeth, for their feedback during the study design stage.

19 Declaration of interest

[redacted] is a researcher and clinician and has worked with a range of types of treatment and
rehabilitation service-providers. [redacted] 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. [redacted] employer ([redacted]) has registered intellectual

property on an innovative medication development with which [redacted] is involved, and
[redacted] has been named as inventor in a patent registration by a Pharma company for a
new medication. A fuller account of [redacted] interests is at [redacted]. [redacted] is also
supported by the National Institute for Health Research (NIHR) Biomedical Research Centre
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London.

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

8

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9	cocaine. Journal of Epidemiology, 918–925.
10	

1 <u>Table 1: Chi square analysis of relationship between demographic and contextual factors and</u>

2 age of first opportunity to use heroin

Variable		Whole sample	Early first	Later first	Chi square
			opportunity	opportunity to	P value
			to use heroin	use heroin (≥18)	
			(≤17)		
		% (N)	% (N)	% (N)	
Gender	Male	74 (69)	77 (24)	73 (43)	0.72
Ethnicity	White British	56 (52)	58 (18)	56 (33)	0.65
	Other white	23 (21)	26 (8)	20 (12)	
	BME	21 (20)	16 (5)	24 (14)	•
Education	Did not complete	41 (38)	42 (13)	39 (23)	0.96
	high school				
	High school	27 (25)	26 (8)	27 (16)	•
	Further/higher	32 (30)	32 (10)	34 (20)	-
	education				
Present at	Stranger/	35 (30)	23 (7)	41 (22)	0.10
first opportunity	acquaintance				
	Friend/partner	58 (50)	64 (20)	56 (30)	
	Family	7 (6)	13 (4)	4 (2)	

3

- 1 <u>Table 2: Chi square/t-test analysis of relationship between age of first opportunity to use</u>
- 2 <u>heroin and heroin-related outcomes</u>

Variable		Whole sample	Early first	Later first	Chi square P
		% (N)	opportunity to use	opportunity to use	value
		/0 (14)	heroin (≤17)	heroin (≥18)	
			% (N)	% (N)	
Time from	Same day	65 (57)	64 (20)	65 (37)	0.98
first opportunity	1-7 days	1 (1)	0 (0)	2 (1)	
to initiation	1 week – 1	3 (3)	3 (1)	3 (2)	
of use	month				
	Within a	11 (10)	13 (4)	10 (6)	-
	year				
	+1 year	19 (17)	19 (6)	19 (11)	-
Heavy heroin	n use	36 (32)	43 (12)	31 (18)	0.28
Overdose		55 (51)	74 (23)	46 (27)	0.01
		Whole sample	Early first	Later first	T-test P
		Mean (95% CI)	opportunity (≤17)	opportunity (≥18)	value
			Mean (95% CI)	Mean (95% CI)	
Age heroin u	se initiation	22.6	16.2	25.9	<0.001
		(21.1 – 24.1)	(14.5 – 18.0)	(24.2 – 27.6)	
Age injecting onset		26.1	22.3	28.8	<0.001
		(24.3 – 27.9)	(19.3 – 25.4)	(26.7 – 30.9)	
Age daily us	e onset	25.0	19.6	27.7	<0.001
		(23.3 – 26.6)	(17.3 – 21.9)	(25.9 – 29.6)	

Table 3: Regression coefficients (95% Confidence intervals) between age of first opportunity to use heroin and heroin-related outcomes

	Over	dose	Injecting	onset (≤24	Age of daily heroin use	
	N=51		N	= 25		
	Univariate	Multivariable ¹	Univariate	Multivariable ¹	Univariate	Multivariable ¹
	OR (95% CI)	AOR (95% CI)	OR (95% CI)	AOR (95% CI)	Beta (95% CI)	Beta (95% CI)
Later first opportunity to use	1.00	1.00	1.00	1.00	0	0
heroin (≥18)						
N = 59						
Early first opportunity to use	3.41**	2.58***	7.77***	0.81	-8.14*	1.42
heroin (≤17)	(2.64 – 4.39)	(1.40 – 4.76)	(6.08 - 9.92)	(0.29 – 2.22)	(-14.12.21)	(0.94 – 1.91)
N = 31						

¹Adjusted for age at interview and age at heroin use initiation

*P<0.05 **P<0.01 ***P<0.001