The extent of and factors associated with self-reported overdose and self-reported receipt of naloxone among people who inject drugs in England, Wales and Northern Ireland

# The extent of and factors associated with self-reported overdose and selfreported receipt of naloxone among people who inject drugs (PWID) in **England, Wales and Northern Ireland**

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Keywords: overdose; naloxone; people who inject drugs; harm reduction; heroin; United Kingdom.

### **Abstract**

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Background: Overdose is a major cause of death amongst PWID, and for opioid overdoses naloxone administration can reduce harm. However, globally there is limited national level data on the extent of non-fatal overdose and naloxone uptake. The first national level data on the extent of self-reported overdose and self-reported receipt of naloxone among UK PWID, providing a baseline to monitor the impact of the recent policy change regarding

naloxone availability, is presented.

Methods: Data on self-reported overdose and receipt of naloxone during the preceding year for 2013-2014 from a national survey of PWID was analysed. Participants who reported injecting during the preceding year were included.

Results: Participants (3,850) were predominantly male (75%); mean age was 36 years. The most commonly injected drugs were: heroin (91%), crack (45%) and amphetamine (29%). 15% (591) reported overdosing during the preceding year. There were no differences in the proportion reporting overdose by age or gender, but overdose was more common among those who: injected multiple drugs; recently ceased addiction treatment; injected with used needles/syringes; ever had transactional sex; had used a sexual health clinic or emergency department and lived in Wales or Northern Ireland. Among those reporting an overdose during the preceding year, a third reported two to four overdoses and 7.5% five or more overdoses; half reported receiving naloxone. Those reporting naloxone receipt in the preceding year were more likely to: live in Wales or Northern Ireland; ever received used needles/syringes; ever been imprisoned; and *less* likely to have injected two drug types.

<u>Conclusions:</u> These data provide a baseline for monitoring the impact of the 2015 UK policy change to improve take-home naloxone access. Interventions tackling overdose should

The extent of and factors associated with self-reported overdose and self-reported receipt of naloxone among people who inject drugs in England, Wales and Northern Ireland promote naloxone awareness and access, and target those who; are poly-drug injectors,

have ceased treatment, share needles/syringes and whose drug use links to sexual activity.

# Introduction

Overdose is a major cause of mortality among people who inject drugs (PWID), especially in those who inject opioids such as heroin (Pierce, Bird, Hickman, & Millar, 2015; Strang, 2015). The United Nations World Drug Report 2015 described the number of these premature deaths in drug users as "unacceptable" (United Nations Office on Drugs and Crime, 2015) because the majority are preventable through interventions such as long-term opioid substitution therapy and the use of opioid antagonists, such as naloxone.

In 2015, drug-induced overdose was the leading cause of injury-related death in the United States (US) (Hedegaard, Chen, & Warner, 2015), with the rate of fatal drug overdoses involving opioids doubling between 2000 to 2014 (Rudd, Aleshire, Zibbell, & Gladden, 2016) and the heroin overdose mortality rate nearly tripling between 2010 and 2013 (Hedegaard, et al., 2015). Reported overdose deaths have also been increasing in other countries such as Australia (Roxburgh & Burns, 2015), and Canada. In Ontario, Canada, drug related overdose is the third leading cause of accidental death (Carter & Graham, 2013) with the rate of opioid-related deaths doubling between 1991 and 2010 (Gomes, et al., 2014). The European Drug Report estimated that 3.4% of all deaths in Europeans aged 15-39 were due to drug

The extent of and factors associated with self-reported overdose and self-reported receipt of naloxone among people who inject drugs in England, Wales and Northern Ireland overdoses in 2013, and opioids were found in 82% of fatal overdoses in Europe in 2014 (European Monitoring Centre for Drugs and Drug Addiction, 2015, 2016).

In 2015, there were 3,288 registered drug-misuse deaths in the UK, with 81% (n=2,677) of these deaths mentioning an opioid. In recent years there been a marked increases in the number of drug-misuse deaths were an opioid is mentioned across the UK (with increases of 58% in England, 21% in Scotland, 23% in Wales and 47% in Northern Ireland between 2012 and 2015) (Advisory Council on the Misuse of Drugs, 2016). A national inquiry to investigate the causes of this rise concluded that the factors responsible were principally the availability and purity of heroin (Public Health England, 2016)

Naloxone is a powerful, yet relatively safe opioid-antagonist that temporarily blocks opioid receptors, thus reversing respiratory depression, sedation and hypotension caused by excess opioid ingestion (Hospira Inc., 2007; Strang & McDonald, 2016b).

In 2014 the World Health Organization (WHO) recommended that people likely to witness overdose (such as friends and family of people who use drugs, healthcare workers and police) should have access to naloxone and be trained in its administration (World Health Organization, 2014). A recent review of evaluations of Take-Home Naloxone (THN) programmes in the US, Canada, Germany and the UK, found that these significantly reduced heroin overdose mortality rates (Strang & McDonald, 2016a). As of September 2015, 43 US states had legalised naloxone access for peers (Davis & Carr, 2015), as well as New York state developing an opioid-overdose prevention and training program targeting all soon to be released inmates and parole officers (Zucker, Annucci, Stancliff, &

The extent of and factors associated with self-reported overdose and self-reported receipt of naloxone among people who inject drugs in England, Wales and Northern Ireland Catania, 2015). Australia has recently become the second country (after Italy in 1995) to approve naloxone as an over-the-counter (OTC) drug (Australian Government Department of Health, 2015; Lenton, Dietze, & Jauncey, 2016; Strang & McDonald, 2016b) and a number of US states have also proposed this (Beheshti, et al., 2015; Kim, Irwin, & Khoshnood, 2009).

In Scotland, as part of a National Naloxone Programme, THN kits have been provided to those at risk of overdose through Patient Group Direction (PGD) (Watt, et al., 2014) and this was associated with a 36% reduction in opioid-related deaths following prison release (Bird, McAuley, Perry, & Hunter, 2016), although recently there has been evidence to suggest a decline in day-to-day naloxone carriage among PWID in Scotland (McAuley, et al., 2016). In Wales, a national THN programme has issued over 10,500 THN kits since it was initiated in 2009, with one in ten reported to have been used in overdose events (Public Health Wales, 2016). In Northern Ireland, a THN programme has been available via drug treatment services from community addiction teams since 2012. Work is currently ongoing to extend the provision of naloxone to other services, for example community outreach teams (personal communication, L Jessop 2016).

In October 2015, UK regulations changed to allow naloxone to be supplied by drug treatment services (including prison and pharmacy based services) without a prescription. Previously it could only be prescribed either directly to a named patient or through a PGD. The supply of naloxone is not limited specifically to PWID at risk of overdose, and it can now be supplied to peers, friends and family of those at risk as well as people such as outreach workers (Public Health England, 2015b).

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In the UK, there is currently limited national data on the extent of recent self-reported overdose and receipt of naloxone among PWID. To assess the impact of the recent change in legislation, national baseline data on the extent of overdoses and receipt of naloxone is needed. Using new data from a national survey of PWID in the UK (excluding Scotland) we:

a) examine the extent of reported overdoses nationally among PWID, b) explore the factors associated with this, and c) examine the extent of naloxone uptake among those who had reported overdose.

### Material and Methods

#### Recruitment and data

PWID at sentinel locations have been recruited into a voluntary unlinked-anonymous monitoring system since 1990. Methodological details of this system, a series of annual cross-sectional surveys, have been published previously (Hope, et al., 2005; Sweeting, et al., 2009). Briefly, agencies providing services to PWID (e.g. needle and syringe programmes [NSPs] and providers of addiction services such as opioid substitution therapy [OST]) invite clients who have ever injected a psychoactive drug to participate in the survey each year. These sentinel sites are located throughout the UK, except Scotland, and are selected so as to reflect both the geographic distribution and range of services offered to PWID. Those who consent to participate provide a biological sample, currently a dried blood spot (DBS), and self-complete a short questionnaire. The DBS samples are tested for antibodies to HIV (anti-HIV), hepatitis C (anti-HCV) and the hepatitis B core anti-gen (anti-HBc) using published methods. The survey has received multi-site ethics approval.

The extent of and factors associated with self-reported overdose and self-reported receipt of naloxone among people who inject drugs in England, Wales and Northern Ireland In 2013, a question on self-reported overdoses and naloxone use was added to the survey questionnaire. Participants were asked: "In the last year (12 months), have you ever overdosed (OD-ed, gone over, gone-under) to the point where you have lost consciousness?" Those reporting 'yes' were then asked how many times they had overdosed in the preceding year, as well as, "In the last 12 months, did you receive naloxone (the heroin overdose antidote) when you overdosed?".

### Eligibility & analysis

Data from the first participations in the two survey waves undertaken during 2013 and 2014 were used in the analyses (i.e. those taking part in 2014 who reported having previously taken part in 2013 were excluded). Participants were included in the analyses if they reported injecting in the preceding year and answered the question on overdose.

Simple descriptive analyses and comparative analyses, using Pearson's Chi-squared test were performed to assess the bivariate association between the two outcome variables (overdosing to the point of unconsciousness in the preceding year and receiving naloxone in the preceding year when overdosed), and covariates (demographics, injecting practices, the drugs injected, sexual behaviour, and health services use). Where possible associations were found (p<0.10) with either of the outcomes, these were then further examined via binary logistic regression using the forward stepwise procedure to select variables for inclusion in the model, with selection based on the likelihood ratio test (p<0.05). All analyses were undertaken using SPSS 23.

### Results

#### Sample characteristics

During 2013 and 2014, there were 3,850 participants in the survey who reported injecting psychoactive drugs during the preceding year. Over half (56%, n=2,139) were aged 35 years or older (mean and median age both 36 years), the majority 75% (n=2,893) were male, and 6.4% (n=248) had been born outside of the UK. The most commonly injected drug in the past year was heroin (91%, n=3,508) followed by crack (45%, n=1,719), amphetamine (29%, n=1,096), cocaine (13%, n=499), mephedrone (8.2%, n=316), methadone (4.8%, n=186) and ketamine (4.8%, n=183). Almost one in 10 reported that they injected another drug (i.e. one that had not been specifically asked about, 9.0%, n=345); 38% reported injecting only one drug type, 37% reported injecting two drug types, 14% three drug types and 11% four or more drug types.

### Proportion reporting overdose

Overall, 15% (n=591) reported that they had overdosed to the point of unconsciousness in the preceding year. Of those who reported overdosing, 55% (n=323) reported overdosing only once in the preceding year, 34% (n=198) reported overdosing two to four times and 7.5% (n=44) reported overdosing five or more times (for 4.4% [n=26] frequency of overdose was not reported).

### Factors associated with self-reported overdose

The factors associated with having overdosed in the bivariate and multivariable analyses are shown in Table 1. In the multivariable analysis, self-reported overdose during the

The extent of and factors associated with self-reported overdose and self-reported receipt of naloxone among people who inject drugs in England, Wales and Northern Ireland preceding year was associated with injecting heroin and polydrug injection, (being most common) among those who had injected four or more drug types. Self-reported overdose was also more common among those who reported: previously being prescribed a detox or maintenance drug (compared to those who had never or were currently being prescribed); injecting with previously used works (needles/syringes); ever having transactional sex; using a sexual health clinic in the last 12 months; and using an emergency department in the last 12 months. Reporting overdose in the past year was also more common among those living in Wales and Northern Ireland, compared to those living in England.

#### [INSERT TABLE 1 NEAR HERE]

Survey participants were asked about oral use of selected drugs during the preceding month. Overall, 29% (1,118/3,850) reported that they had swallowed non-prescribed benzodiazepines. Oral use of benzodiazepines in the preceding month was more common among those reporting an overdose during the preceding year (p<0.0001, 40% [237/591] of those who reported an overdose had swallowed benzodiazepines, compared to 27% [881/3,259] of those not reporting an overdose).

### Extent of, and factors associated with, self-reported receipt of naloxone

Of the 591 participants reporting overdose in the past year, 477 were able to report whether they had received naloxone or not. Just under half (45%, 213/477) reported that they had received naloxone when they overdosed (the remaining 114 of those who had overdosed were not sure or didn't know if they had received naloxone).

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The factors associated with self-reported receipt of naloxone in the bivariate and
multivariable analyses are presented in Table 2. In the multivariable analysis, receiving
naloxone after overdosing was, as expected, more common among those who had injected
heroin in the past year. Self-reported receipt of naloxone was also more common in those
who reported: ever receiving previously used works (needles/syringes) from someone else;
and ever being imprisoned. Self-reported receipt of naloxone was also more common in
those living in Wales and Northern Ireland, compared to those living in England. Uptake
was less common among those injecting two drug types, compared to those injecting only

[INSERT TABLE 2 NEAR HERE]

### Discussion

one type.

### Overview of Findings

This is the first analyses to use national level data on overdose and naloxone use among PWID across England, Wales and Northern Ireland. Our data suggests that one in seven PWID report overdosing to the point of unconsciousness annually. One-third of these had reported an overdose on between two and four occasions, and one in 12 reported five or more overdoses during the preceding year. Previously, there has been limited national level data on the extent of non-fatal overdose among PWID, although studies suggest overdose is common and can be frequent, with some indicating frequencies of one to two overdoses a year (Bazazi, et al., 2015; Darke, et al., 2007; Grau, et al., 2009; Holloway, Bennett, &

The extent of and factors associated with self-reported overdose and self-reported receipt of naloxone among people who inject drugs in England, Wales and Northern Ireland Hills, 2016; Wagner, et al., 2015). Just under half of those who reported overdose reported that they had received naloxone, though many were unsure.

#### Factors associated with self-reported overdose

Self-reported overdose was two and a half times more common in those who reported injecting heroin in the past year compared to those who hadn't. This increased frequency of overdose in heroin injectors is most likely due to the physiological effects heroin has and the nature of a heroin overdose; there is often a fine line between acute respiratory suppression and when heroin dosage becomes toxic causing respiratory failure, hypoxia and potentially death (Jolley, Bell, Rafferty, Moxham, & Strang, 2015; White & Irvine, 1999). Batches of street heroin that have been linked to overdose risk have also been documented as being more popular among some groups of PWID due to the 'better' euphoric effects (Mars, et al., 2015; Singer, 2006). However, these effects are usually at the brink of overdose. Tolerance to respiratory depression in people who inject heroin can develop quickly with chronic use, but can be lost quickly in withdrawal, making the judgement of lethal doses hard to predict (Mars, et al., 2015; Strang, et al., 2003). Street heroin with variable purity levels and price due to the variances of supply, make it harder to identify a lethal dosage, particularly after heroin shortages when the 'normal' quality resumes (Darke, Hall, Weatherburn, & Lind, 1999; Travis, 2011; Unick, Rosenblum, Mars, & Ciccarone, 2014).

Self-reported overdose was also more common in those reporting polydrug injection, and was nearly two and a half times more common in those injecting four or more drug types compared to only one drug type. This finding is in line with other studies that show overdose and drug-related deaths are more common among polydrug-using PWID (Darke,

people who inject drugs in England, Wales and Northern Ireland 2003; Fairbairn, et al., 2008; Hickman, Carrivick, et al., 2007; Kaye & Darke, 2004; Petrushevska, Jakovski, Poposka, & Stefanovska, 2015; Powis, et al., 1999; Richer, Bertrand, Vandermeerschen, & Roy, 2013; Rossow & Lauritzen, 1999; Webb, et al., 2003). Co-use of opioids with other central nervous system depressant drugs such as methadone. which is often prescribed for opioid-dependence (Wunsch, Nuzzo, Behonick, Massello, & Walsh, 2013), can cause compounded depression of the respiratory system, potentiating the detrimental effects on breathing and heightening the risk of overdose (Coffin, et al., 2003; Ochoa, et al., 2005; Warner-Smith, Darke, Lynskey, & Hall, 2001). Two-thirds of our sample reported currently receiving prescribed treatment for their drug use suggesting many are or have been injecting on top of their opiate substitution therapy (which is typically methadone in the UK). Although our survey does not ask about injection of benzodiazepines (a depressant drug) as this is rare in the UK, with data from surveys undertaken in England using respondent driven sampling (Hope, Ncube, Parry, & Hickman, 2015) found only 1.5% reported injecting benzodiazepines during the preceding year (personal communication, V Hope 2016), self-reported overdose was also significantly more common among those who reported swallowing non-prescribed benzodiazepines in the past month. The use of stimulants and opiates at the same time, or "Speed/snowballing", can increase overdose risks, and in the UK heroin and crack-cocaine are common drug combination among PWID (Public Health England, 2015a; Turning Point, 2007). Co-use of heroin and cocaine, commonly used interchangeably compensate for depressant or stimulant withdrawal (Guzman & Ettenberg, 2004; Leri, Bruneau, & Stewart, 2003) may also cause an individual to be more at risk to opioid overdose (Fiala, et al., 1998; Zhang, et al., 1998) and can cause unpredictable respiratory depression if the stimulant effects mask the delayed effects of opioid overdose (Cattelle, 2015; Newcombe, 2007: Treatment4addiction).

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Currently being prescribed treatment for drug addiction was protective for self-reported overdose in our study, as this population was less likely to report overdose compared to those who had previously been prescribed treatment. Those who had previously been treated for addiction, but who have ceased therapy, have been documented as having a high mortality risk, and may represent a group of PWID that are harder to reach and target in harm reduction strategies (Davoli, et al., 1993; Seal, et al., 2001). The link between recent release from drug treatment programs and self-reported overdose is most likely due to lowered drug tolerance following periods of drug abstinence during detoxification (Strang, et al., 2003) or patients lost to follow up, and highlights the need for enhanced aftercare once a PWID has completed or prematurely left a drug treatment programme.

Those who reported injecting with previously used needles and syringes were also more likely to have reported overdose in the past year; with a quarter of those who had shared needles/syringes also reporting overdosing. This finding might reflect a group of more chaotic users with a range of risky injecting practises, but more research is needed.

Overdose, as would be expected, was commonly reported in those who had recently attended an emergency department, but was also more commonly reported among those who had attended a sexual health clinic in the preceding year. As the level of self-reported overdose was also elevated among those reporting transactional sex, this could indicate a vulnerable population in which chaotic or unsafe drug use is linked to increased sexual risks, as well as highlighting the opportunity to offer this population interventions in sexual healthcare settings. This link needs further exploration to determine how overdose is related to sexual activity.

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#### Factors associated with self-reported receipt of naloxone

Receipt of naloxone was reported in just under half of those who reported overdosing and injecting heroin during the past year, similar to that reported in previous small-scale studies (Holloway, et al., 2016). Since the majority of heroin injectors sampled did not report receiving naloxone when they overdosed, this could indicate a substantive need for improved provision and accessibility of naloxone. The recent UK legislative change allowing wider availability of naloxone could thus have the potential to positively impact on the harm from overdose.

Self-reported receipt of naloxone after overdose was significantly lower among those injecting two drug types, compared to those injecting only one drug type, or those injecting three drug types. This disparity in naloxone provision could be due to the injection of heroin and crack together being common in much of the UK (Hickman, Hope, et al., 2007; Public Health England, 2015a). The injection of these two drugs in combination has been associated with chaotic behaviour, which might impact on access to naloxone.

Those who reported ever being imprisoned were also one and a half times more likely to have reported receiving naloxone, but those who had ever been imprisoned were not more likely to have reported an overdose. This higher level of self-reported naloxone receipt among this group could be due to the recent N-ALIVE trial (Strang, Bird, & Parmar, 2013) where prisoners in England and Wales were given naloxone on prison release, or that PWID who have recently been released from prison are more likely to recognise their vulnerability to overdose.

Those in Wales and Northern Ireland were also twice as likely to report receiving naloxone when they overdosed compared to those in England. These variations may reflect varying

The extent of and factors associated with self-reported overdose and self-reported receipt of naloxone among people who inject drugs in England, Wales and Northern Ireland local approaches in naloxone provision, such as the THN programmes in Wales and Northern Ireland. However, this also may be due to a higher level of reported overdose in these areas; one in five individuals from Wales and Northern Ireland reported overdosing in the past year and they were one and a half times more likely to overdose compared to PWID England. This and the association of reporting ever receiving previously used works (needles/syringes) need further investigation.

#### Limitations

This study has several limitations. Firstly, the behavioural data used here is based on self-reports, the accuracy of which may be subject to recall bias. However, previous studies have demonstrated the reliability of self-report risk behaviours among people who inject drugs (Latkin, Vlahov, & Anthony, 1993). However, due to loss of the consciousness self-reports of overdose and naloxone receipt may be particularly affected by recall issues.

Secondly, the illicit and marginalised nature of injecting drug use makes the recruitment of a representative sample problematic. To maximise representativeness, this survey used the extensive provision of targeted services for people who inject drugs as a sampling frame. In the UK, the uptake and use of such targeted services is high, with very few of the people who inject drugs recruited through community based studies found not to be in contact with such services (Craine et al., 2010; Hickman et al., 2007).

Finally, it is possible that those who have received naloxone may not always be aware of this when they have lost consciousness, and so receipt of naloxone may be under reported. Considering these issues, caution should be used when generalising the findings presented here.

# Conclusions

Overdose has been recognised as a major cause of death in PWID, and previous overdose is a significant predictor of mortality (Darke, Mills, Ross, & Teesson, 2011). Interventions and harm reduction strategies should focus on reducing opioid overdoses in PWID by promoting naloxone uptake and targeting those most at risk; notably those who inject multiple drugs, those who have recently stopped treatment, and those whose drug use may be linked to sexual activity.

Our analysis presents baseline national data on the extent of self-reported overdose and self-reported receipt of naloxone among PWID in the UK from an ongoing survey programme. Data from future survey waves can be used to examine the impact of legislative changes allowing wider access to naloxone in the UK that came into effect in October 2015.

## References

- Advisory Council on the Misuse of Drugs. (2016). Reducing Opioid-Related Deaths in the UK. In.
- Australian Government Department of Health. (2015). Final decisions and reasons for decisions by a delegate of the Secretary to the Department of Health. In Therapeutic Goods Administration (Ed.). Australia: Australian Government Department of Health,.
- Bazazi, A. R., Zelenev, A., Fu, J. J., Yee, I., Kamarulzaman, A., & Altice, F. L. (2015). High prevalence of non-fatal overdose among people who inject drugs in Malaysia: Correlates of overdose and implications for overdose prevention from a cross-sectional study. *Int J Drug Policy*, *26*, 675-681.
- Beheshti, A., Lucas, L., Dunz, T., Haydash, M., Chiodi, H., Edmiston, B., Ford, C., Bohn, N., Stein, J. H., Berrett, A., Sobota, B., & Horzempa, J. (2015). An Evaluation of Naloxone Use for Opioid Overdoses in West Virginia: A Literature Review. *Am Med J*, *6*, 9-13.
- Bird, S. M., McAuley, A., Perry, S., & Hunter, C. (2016). Effectiveness of Scotland's National Naloxone Programme for reducing opioid-related deaths: a before (2006-10) versus after (2011-13) comparison. *Addiction*, *111*, 883-891.
- Carter, C., & Graham, B. (2013). Opioid Overdose Prevention & Response In Canada. In *Policy Brief Series*. Vancouver: Canadian Drug Policy Coalition / CDPC.
- Cattelle, B. Death Trap: The Dangers of SpeedBalling. Retrieved 24 June 2016 from <a href="http://lighthouserecoveryinstitute.com/dangers-of-speedballing/">http://lighthouserecoveryinstitute.com/dangers-of-speedballing/</a>. Coffin, P. O., Galea, S., Ahern, J., Leon, A. C., Vlahov, D., & Tardiff, K. (2003). Opiates,
- Coffin, P. O., Galea, S., Ahern, J., Leon, A. C., Vlahov, D., & Tardiff, K. (2003). Opiates, cocaine and alcohol combinations in accidental drug overdose deaths in New York City, 1990-98. *Addiction*, *98*, 739-747.
- Darke, S. (2003). Polydrug use and overdose: overthrowing old myths. *Addiction, 98*, 711.
  Darke, S., Hall, W., Weatherburn, D., & Lind, B. (1999). Fluctuations in heroin purity and the incidence of fatal heroin overdose. *Drug Alcohol Depend, 54*, 155-161.
  Darke, S., Mills, K. L., Ross, J., & Teesson, M. (2011). Rates and correlates of mortality
- Darke, S., Mills, K. L., Ross, J., & Teesson, M. (2011). Rates and correlates of mortality amongst heroin users: findings from the Australian Treatment Outcome Study (ATOS), 2001-2009. *Drug Alcohol Depend*, 115, 190-195.
- Darke, S., Williamson, A., Ross, J., Mills, K. L., Havard, A., & Teesson, M. (2007). Patterns of nonfatal heroin overdose over a 3-year period: findings from the Australian treatment outcome study. *J Urban Health*, *84*, 283-291.
- Davis, C. S., & Carr, D. (2015). Legal changes to increase access to naloxone for opioid overdose reversal in the United States. *Drug Alcohol Depend*, *157*, 112-120.
- Davoli, M., Perucci, C. A., Forastiere, F., Doyle, P., Rapiti, E., Zaccarelli, M., & Abeni, D. D. (1993). Risk factors for overdose mortality: a case-control study within a cohort of intravenous drug users. *Int J Epidemiol, 22*, 273-277.
- European Monitoring Centre for Drugs and Drug Addiction. European Drug Report 2015: Trends and Developments. from <a href="http://www.emcdda.europa.eu/publications/edr/trends-developments/2015">http://www.emcdda.europa.eu/publications/edr/trends-developments/2015</a>.
- European Monitoring Centre for Drugs and Drug Addiction. European Drug Report 2016: Trends and Developments.
- Fairbairn, N., Wood, E., Stoltz, J. A., Li, K., Montaner, J., & Kerr, T. (2008). Crystal methamphetamine use associated with non-fatal overdose among a cohort of injection drug users in Vancouver. *Public Health*, 122, 70-78.
- Fiala, M., Gan, X. H., Zhang, L., House, S. D., Newton, T., Graves, M. C., Shapshak, P., Stins, M., Kim, K. S., Witte, M., & Chang, S. L. (1998). Cocaine enhances monocyte migration across the blood-brain barrier. Cocaine's connection to AIDS dementia and vasculitis? *Adv Exp Med Biol, 437*, 199-205.

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- Gomes, T., Mamdani, M. M., Dhalla, I. A., Cornish, S., Paterson, J. M., & Juurlink, D. N. (2014). The burden of premature opioid-related mortality. *Addiction*, *109*, 1482-1488.
- Grau, L. E., Green, T. C., Torban, M., Blinnikova, K., Krupitsky, E., Ilyuk, R., Kozlov, A. P., & Heimer, R. (2009). Psychosocial and contextual correlates of opioid overdose risk among drug users in St. Petersburg, Russia. *Harm Reduct J, 6*, 17.
- Guzman, D., & Ettenberg, A. (2004). Heroin attenuates the negative consequences of cocaine in a runway model of self-administration. *Pharmacol Biochem Behav, 79*, 317-324.
- Hedegaard, H., Chen, L. H., & Warner, M. (2015). Drug-poisoning deaths involving heroin: United States, 2000-2013. *NCHS Data Brief*, 1-8.
- Hickman, M., Carrivick, S., Paterson, S., Hunt, N., Zador, D., Cusick, L., & Henry, J. (2007). London audit of drug-related overdose deaths: characteristics and typology, and implications for prevention and monitoring. *Addiction*, *102*, 317-323.
- Hickman, M., Hope, V., Brady, T., Madden, P., Jones, S., Honor, S., Holloway, G., Ncube, F., & Parry, J. (2007). Hepatitis C virus (HCV) prevalence, and injecting risk behaviour in multiple sites in England in 2004. *J Viral Hepat, 14*, 645-652.
- Holloway, K. R., Bennett, T. H., & Hills, R. (2016). Non-fatal overdose among opiate users in Wales: A national survey. *Journal of Substance Use, 21, 471-477.*
- Hope, V. D., Judd, A., Hickman, M., Sutton, A., Stimson, G. V., Parry, J. V., & Gill, O. N. (2005). HIV prevalence among injecting drug users in England and Wales 1990 to 2003: evidence for increased transmission in recent years. *AIDS*, *19*, 1207-1214.
- Hope, V. D., Ncube, F., Parry, J. V., & Hickman, M. (2015). Healthcare seeking and hospital admissions by people who inject drugs in response to symptoms of injection site infections or injuries in three urban areas of England. *Epidemiol Infect, 143*, 120-131.
- Hospira Inc. Naloxoné Hydrochloride [product insert]. Lake Forest, IL 60045 USA: Hospira, Inc.; 2007. from <a href="https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=8535cc84-ad4a-4d67-8480-fb5a2e3406f8">https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=8535cc84-ad4a-4d67-8480-fb5a2e3406f8</a>.
- Jolley, C. J., Bell, J., Rafferty, G. F., Moxham, J., & Strang, J. (2015). Understanding Heroin Overdose: A Study of the Acute Respiratory Depressant Effects of Injected Pharmaceutical Heroin. *PLoS One, 10*, e0140995.
- Kaye, S., & Darke, S. (2004). Non-fatal cocaine overdose among injecting and non-injecting cocaine users in Sydney, Australia. *Addiction, 99*, 1315-1322.
- Kim, D., Irwin, K. S., & Khoshnood, K. (2009). Expanded access to naloxone: options for critical response to the epidemic of opioid overdose mortality. *Am J Public Health*, 99, 402-407.
- Lenton, S. R., Dietze, P. M., & Jauncey, M. (2016). Australia reschedules naloxone for opioid overdose. *Med J Aust, 204*, 146-147.
- Leri, F., Bruneau, J., & Stewart, J. (2003). Understanding polydrug use: review of heroin and cocaine co-use. *Addiction*, *98*, 7-22.
- Mars, S. G., Fessel, J. N., Bourgois, P., Montero, F., Karandinos, G., & Ciccarone, D. (2015). Heroin-related overdose: The unexplored influences of markets, marketing and source-types in the United States. *Soc Sci Med, 140*, 44-53.
- McAuley, A., Munro, A., Bird, S. M., Hutchinson, S. J., Goldberg, D. J., & Taylor, A. (2016). Engagement in a National Naloxone Programme among people who inject drugs. *Drug Alcohol Depend, 162*, 236-240.
- Newcombe, R. Speed Ball Wake up Call. Retrieved 24 June 2016 from <a href="http://www.drugaidcymru.com/services/real-deal/speed-balling.aspx">http://www.drugaidcymru.com/services/real-deal/speed-balling.aspx</a>.
- Ochoa, K. C., Davidson, P. J., Evans, J. L., Hahn, J. A., Page-Shafer, K., & Moss, A. R. (2005). Heroin overdose among young injection drug users in San Francisco. *Drug Alcohol Depend*, 80, 297-302.
- Petrushevska, T., Jakovski, Z., Poposka, V., & Stefanovska, V. V. (2015). Drug-related deaths between 2002 and 2013 with accent to methadone and benzodiazepines. *J Forensic Leg Med, 31*, 12-18.
- Pierce, M., Bird, S. M., Hickman, M., & Millar, T. (2015). National record linkage study of mortality for a large cohort of opioid users ascertained by drug treatment or criminal justice sources in England, 2005-2009. *Drug Alcohol Depend, 146*, 17-23.

- The extent of and factors associated with self-reported overdose and self-reported receipt of naloxone among people who inject drugs in England, Wales and Northern Ireland
- Powis, B., Strang, J., Griffiths, P., Taylor, C., Williamson, S., Fountain, J., & Gossop, M. (1999). Self-reported overdose among injecting drug users in London: extent and nature of the problem. *Addiction*, *94*, 471-478.
- Public Health England. Shooting Up: Infections among people who inject drugs in the UK, 2014. from <a href="https://www.gov.uk/government/uploads/system/uploads/attachment\_data/file/47571">https://www.gov.uk/government/uploads/system/uploads/attachment\_data/file/47571</a> 2/Shooting Up 2015 FINAL.pdf.
- Public Health England. Take-home naloxone for opioid overdose in people who use drugs. from <a href="http://www.nta.nhs.uk/uploads/phetake-homenaloxoneforopioidoverdosefeb2015rev.pdf">http://www.nta.nhs.uk/uploads/phetake-homenaloxoneforopioidoverdosefeb2015rev.pdf</a>.
- Public Health England. Understanding and preventing drug-related deaths: The report of a national expert working group to investigate drug-related deaths in England. from <a href="http://www.nta.nhs.uk/uploads/phe-understanding-preventing-drds.pdf">http://www.nta.nhs.uk/uploads/phe-understanding-preventing-drds.pdf</a>.
- Public Health Wales. Harm Reduction Database Wales: Take Home Naloxone 2015-16. from <a href="https://www2.nphs.wales.nhs.uk/SubstanceMisuseDocs.nsf/0/73a04023c6b9bd9580257ee50049e202/\$FILE/FINAL%20Naloxone%20HRD%20report%202015-16.pdf">https://www2.nphs.wales.nhs.uk/SubstanceMisuseDocs.nsf/0/73a04023c6b9bd9580257ee50049e202/\$FILE/FINAL%20Naloxone%20HRD%20report%202015-16.pdf</a>.
- Richer, I., Bertrand, K., Vandermeerschen, J., & Roy, E. (2013). A prospective cohort study of non-fatal accidental overdose among street youth: the link with suicidal ideation. *Drug Alcohol Rev*, *32*, 398-404.
- Rossow, I., & Lauritzen, G. (1999). Balancing on the edge of death: suicide attempts and life-threatening overdoses among drug addicts. *Addiction*, *94*, 209-219.
- Roxburgh, A., & Burns, L. (2015). Accidental drug-induced deaths due to opioids in Australia, 2011. In *National Illicit Drug Indicatiors Project (NIDIP) Bulletins*. Sydney: University of New South Wales,.
- University of New South Wales,.
  Rudd, R. A., Aleshire, N., Zibbell, J. E., & Gladden, R. M. (2016). Increases in Drug and Opioid Overdose Deaths--United States, 2000-2014. MMWR Morb Mortal Wkly Rep, 64, 1378-1382.
- Seal, K. H., Kral, A. H., Gee, L., Moore, L. D., Bluthenthal, R. N., Lorvick, J., & Edlin, B. R. (2001). Predictors and prevention of nonfatal overdose among street-recruited injection heroin users in the San Francisco Bay Area, 1998-1999. *Am J Public Health*, *91*, 1842-1846.
- Singer, M. (2006). Something Dangerous Emergent and Changing Illicit Drug Use and Community Health. Long Grove, IL: Waveland Press.
- Strang, J. (2015). Death matters: understanding heroin/opiate overdose risk and testing potential to prevent deaths. *Addiction, 110 Suppl 2, 27-35.*
- Strang, J., Bird, S. M., & Parmar, M. K. (2013). Take-home emergency naloxone to prevent heroin overdose deaths after prison release: rationale and practicalities for the N-ALIVE randomized trial. *J Urban Health*, *90*, 983-996.
- Strang, J., McCambridge, J., Best, D., Beswick, T., Bearn, J., Rees, S., & Gossop, M. (2003). Loss of tolerance and overdose mortality after inpatient opiate detoxification: follow up study. *BMJ*, *326*, 959-960.
- Strang, J., & McDonald, R. (2016a). Are take-home naloxone programmes effective? Systematic review utilizing application of the Bradford Hill criteria. *Addiction, 111*, 1177-1187.
- Strang, J., & McDonald, R. Preventing opioid overdose deaths with take-home naloxone. from http://www.emcdda.europa.eu/system/files/publications/2089/TDXD15020ENN.pdf.
- Sweeting, M. J., Hope, V. D., Hickman, M., Parry, J. V., Ncube, F., Ramsay, M. E., & De Angelis, D. (2009). Hepatitis C infection among injecting drug users in England and Wales (1992-2006): there and back again? *Am J Epidemiol, 170*, 352-360.
- Travis, A. Drug overdose deaths highlight Britain's recent heroin shortage. from <a href="https://www.theguardian.com/society/2011/mar/15/heroin-shortage-britain-overdose-deaths">https://www.theguardian.com/society/2011/mar/15/heroin-shortage-britain-overdose-deaths</a>.
- Treatment4addiction. Speedballing. Retrieved 24 June 2016 from <a href="http://www.treatment4addiction.com/addiction/speedballing/">http://www.treatment4addiction.com/addiction/speedballing/</a>.

- The extent of and factors associated with self-reported overdose and self-reported receipt of naloxone among people who inject drugs in England, Wales and Northern Ireland
- Unick, G., Rosenblum, D., Mars, S., & Ciccarone, D. (2014). The relationship between US heroin market dynamics and heroin-related overdose, 1992-2008. *Addiction, 109*, 1889-1898.
- United Nations Office on Drugs and Crime. World Drug Report 2015. from <a href="http://www.unodc.org/documents/wdr2015/World\_Drug\_Report\_2015.pdf">http://www.unodc.org/documents/wdr2015/World\_Drug\_Report\_2015.pdf</a>.
- Wagner, K. D., Liu, L., Davidson, P. J., Cuevas-Mota, J., Armenta, R. F., & Garfein, R. S. (2015). Association between non-fatal opioid overdose and encounters with healthcare and criminal justice systems: Identifying opportunities for intervention. *Drug Alcohol Depend, 153*, 215-220.
- Warner-Smith, M., Darke, S., Lynskey, M., & Hall, W. (2001). Heroin overdose: causes and consequences. *Addiction*, *96*, 1113-1125.
- Watt, G., Jaquet, S., Ellison, S., Christie, I., Nicholson, J., & B., S. Service Evaluation of Scotland's National Take-Home Naloxone Programme. from <a href="http://www.gov.scot/Resource/0045/00451251.pdf">http://www.gov.scot/Resource/0045/00451251.pdf</a>.
- Webb, L., Oyefeso, A., Schifano, F., Cheeta, S., Pollard, M., & Ghodse, A. H. (2003). Cause and manner of death in drug-related fatality: an analysis of drug-related deaths recorded by coroners in England and Wales in 2000. *Drug Alcohol Depend,* 72, 67-74.
- White, J. M., & Irvine, R. J. (1999). Mechanisms of fatal opioid overdose. *Addiction, 94*, 961-972.
- World Health Organization. Community Management of Opioid Overdose. from <a href="http://www.who.int/substance\_abuse/publications/management\_opioid\_overdose/en/">http://www.who.int/substance\_abuse/publications/management\_opioid\_overdose/en/</a>
- Wunsch, M. J., Nuzzo, P. A., Behonick, G., Massello, W., & Walsh, S. L. (2013). Methadone-related overdose deaths in rural Virginia: 1997 to 2003. *J Addict Med, 7*, 223-229.
- Zhang, L., Looney, D., Taub, D., Chang, S. L., Way, D., Witte, M. H., Graves, M. C., & Fiala, M. (1998). Cocaine opens the blood-brain barrier to HIV-1 invasion. *J Neurovirol*, *4*, 619-626.
- Zucker, H., Annucci, A. J., Stancliff, S., & Catania, H. (2015). Overdose prevention for prisoners in New York: a novel program and collaboration. *Harm Reduct J*, *12*, 51.

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# Results Table 1

Table 1. Factors associated with self-reported overdose in the preceding year among PWID in England, Wales and N.Ireland: 2013-14.

Variable	Value	eding year among PWID in England, Wales and N.Ireland: 2013-14.  Self-reported overdose?*								
		<b>Yes</b> 15% (591)		<b>Total</b> 100% (3,850)		p - value	Adjusted Odds Ratio, with 95% confidence interval			
		%	n	%	n			· u.		
Ever been prescribed a detox or	Never/Not Reported	15%	93	100%	630		1.00			
maintenance drug regime (such as	Previously prescribed	22%	125	100%	580	<0.0001	1.17	0.85	-	1.61
opioid substitution therapy)?	Currently prescribed	14%	373	100%	2,640		0.72	0.55	-	0.94
Injected heroin?*	No	7.0%	24	100%	342	0.0004	1.00			
	Yes	16%	567	100%	3,508	<0.0001	2.26	1.43	-	3.56
	No	12%	262	100%	2,131					
Injected crack?*	Yes	19%	329	100%	1,719	<0.0001	†			
	No	15%	542	100%	3,667					
Injected ketamine?*	Yes	27%	49	100%	183	<0.0001	†			
	No	14%	468	100%	3,351					
Injected cocaine?*	Yes	25%	123	100%	499	<0.0001	†			
Injected mephedrone?*	No Voc	15%	517	100%	3,534	<0.0001	†			
,octouopou.oo.	Yes	23%	74	100%	316		•			
Injected other drugs?*  Polydrug injection use*‡	No	14%	503	100%	3,505	<0.0001	†			
	Yes	26%	88	100%	345	<0.0001	ı			
	Only 1 drug type/Not						1.00			
	Reported	10%	142	100%	1,477		1.00			
	2 drug types	17%	242	100%	1,419	< 0.0001	1.69	1.34	-	2.14
	3 drug types	18%	93	100%	530		1.42	1.06	-	1.92
	4 or more drug types	27%	114	100%	424		2.31	1.72	-	3.11
Had an abscess, sore or open wound	No/Not Reported	14%	398	100%	2,852	<0.0001	+			
at an injection site?*	Yes	19%	193	100%	998	<0.0001	†			
Injected with a needle/syringe that had already been used by someone else?*	No/Not Reported	14%	437	100%	3,235	<0.0001	1.00			
	Yes	25%	154	100%	615	<0.0001	1.60	1.26	-	2.03
Ever received used needles or	No/Not Reported	13%	254	100%	2,036	.0.0004	1.00			
syringes from anyone?	Yes	19%	337	100%	1,814	<0.0001	1.32	1.08	-	1.61
	No/Not Reported	13%	158	100%	1,199					
Had sex (vaginal or anal)?*	Yes	16%	433	100%	2,651	0.012	†			
	Never/Not Reported	14%	487	100%	3,409		1.00			
Ever received money, goods or drugs	Yes but not in last year	18%	42	100%	236	<0.0001	1.07	0.74	_	1.54
in exchange for sex?	Yes, in the last year	30%	62	100%	205	10.000	1.94	1.38	-	2.73
Used a Sexual Health, GUM or STI	No/Not Reported	14%	489	100%	3,449		1.00			
Clinic?*	Yes	25%	102	100%	401	<0.0001	1.66	1.27	-	2.16
Used an NHS Walk-In clinic?*	No/Not Reported	15%	458	100%	3,102	0.04	†			
	Yes	18%	133	100%	748		•			
Used an emergency department?*	No/Not Reported	11%	294	100%	2,676	<0.0001	1.00			
	Yes	25%	297	100%	1,174		2.62	2.17	-	3.15
Used none of the listed health services?*	No/Not Reported	16%	538	100%	3,386	0.012	+			
	Yes	11%	53	100%	464	0.012	†			
	South incl. London	18%	70	100%	399		1.00			
Region	Midlands & East of						0.92	0.67	_	1.26
	England	14%	207	100%	1,504	0.003				
	North England	15%	222	100%	1,500		1.04	0.76	-	1.42
	Wales & N. Ireland	21%	92	100%	447		1.48	1.02	-	2.13

There was no association in the bivariate analyses with: ever being in prison/young offenders institution in the last year; whether UK born; using a needle/syringe programme in the last year; whether injected speed or methadone in the last year; ever being vaccinated for hepatitis B; using a family planning clinic in the last year; or a GP/family doctor in the last year

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- \* in the last year
  † Entered in to the multivariable analysis, but not in final model
  ‡ Those injecting 2 or more drug types will include both those co-injecting drugs (i.e. using drug combinations) and those injecting several drugs separately

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# Results Table 2

Table 2. Factors associated with self-reported receipt of naloxone among PWID reporting overdose in the preceding year in England, Wales and N.Ireland: 2013-14.

Variable	Value	Reported receipt of naloxone when overdosed?*								
		<b>Yes</b> 45% (213)		<b>Total</b> 100% (477)		p - value	Adjusted Odds Ratio, with 95% confidence interval			
		%	n	%	n					
Injected heroin?*	No	12%	2	100%	17	0.005	1.00			
	Yes	46%	211	100%	460		8.47	1.83	-	39.26
Injected other drugs?*	No	43%	169	100%	398	0.031				
	Yes	56%	44	100%	79		†			
Polydrug injection use*	Only 1 drug type /Not Reported	47%	52	100%	110		1.00			
	2 drug types	37%	73	100%	197	0.024	0.58	0.35	-	0.96
	3 drug types	47%	35	100%	74		0.87	0.47	-	1.612
	4 or more drug types	55%	53	100%	96		1.20	0.67	-	2.123
Ever received used needles/syringes from anyone?	No/Not Reported	39%	78	100%	202	0.023	1.00			
	Yes	49%	135	100%	275		1.62	1.10	-	2.38
Used an emergency department?*	No/Not Reported	40%	95	100%	237	0.046				
	Yes	49%	118	100%	240		†			
Region	South incl. London	40%	25	100%	62		1.00			
	Midlands & East of England	46%	75	100%	165	0.053	1.30	0.70	-	2.428
	North England	40%	68	100%	172		0.94	0.50	-	1.749
	Wales & N. Ireland	58%	45	100%	78		2.04	1.007	-	4.152
Ever been in prison/young offenders institution?	No/Not Reported	38%	54	100%	144		1.00			
	Yes	48%	159	100%	333	0.039	1.59	1.04	_	2.44

There was no association in the bivariate analyses with: age; whether UK born; using a needle/syringe programme in the last year; being prescribed treatment for drug use; injecting crack, speed, ketamine, methadone, mephedrone or cocaine in the last year; having an abscess/sore or open wound at injection site in the last year; injecting with used works; having sex in the last year; ever having transactional sex; ever being vaccinated for hepatitis B; using a sexual health/GUM/STI clinic/family planning clinic/NHS walk-in clinic/GP/family doctor or none of these services in the last year.

\*in the last year

<sup>†</sup> Entered in to the multivariable analysis, but not in final model

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