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Can differences in the type, nature or amount of polysubstance use explain the increased risk of non-fatal overdose among psychologically distressed people who inject drugs?☆

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ABSTRACT

Background: This study investigates whether the *type*, *nature* or *amount* of polysubstance use can explain the increased risk of non-fatal overdose among people who inject drugs with severe psychological distress.
Methods: Data came from three years (2011–2013) of the Illicit Drug Reporting System (IDRS), an annual sentinel sample of injecting drug users across Australia ($n = 2673$). Structural Equation Modelling (SEM) was used on 14 drug types to construct five latent factors, each representing a type of polysubstance use. Tests of measurement invariance were carried out to determine if polysubstance use profiles differed between those with and without severe psychological distress. Next, we regressed non-fatal overdose on the polysubstance use factors with differences in the relationships tested between groups.
Findings: Among those with severe psychological distress a polysubstance use profile characterised by heroin, oxycodone, crystal methamphetamine and cocaine use was associated with greater risk of non-fatal overdose. Among those without severe psychological distress, two polysubstance use profiles, largely characterised by opioid substitution therapies and prescription drugs, were protective against non-fatal overdose.
Conclusion: The *types* of polysubstance use profiles did not differ between people who inject drugs with and without severe psychological distress. However, the *nature* of use of one particular polysubstance profile placed the former group at a strongly increased risk of non-fatal overdose, while the *nature* of polysubstance use involving opioid substitution therapies was protective only among the latter group. The findings identify polysubstance use profiles of importance to drug-related harms among individuals with psychological problems.

1. Introduction

Non-fatal overdose is common among people who inject drugs (PWID), with recent estimates from the UK and Australia finding approximately 30% of PWID had experienced a non-fatal overdose in the preceding 12-month period (Bennett and Higgins, 1999; Warner-Smith et al., 2002). Non-fatal overdose has received far less research attention compared with fatal overdose, yet the former has a greater prevalence and leads to a number of serious medical conditions including cardiovascular and pulmonary problems, cognitive-impairment and renal failure (Warner-Smith et al., 2001; Bartoli et al., 2014).

Risk factors for non-fatal overdose include injecting in public spaces and having recently been released from prison or terminating pharmacological treatment (Kerr et al., 2007; Fischer et al., 2004; Brugal et al., 2002; Strang et al., 2003; Dietze et al., 2005), older age, long-term dependent use and not being in treatment

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(Darke, 2014; Darke and Hall, 2003). Depression has also been found to increase the risk for non-fatal overdose (Bohnert et al., 2012; Pabayo et al., 2013; Wines et al., 2007), and a recent study found a number of psychiatric disorders led to similar increases in the risk of fatal overdose, suggesting the relationship may not be specific to depression (Bohnert et al., 2012). However existing studies offer little direct evidence concerning the mechanisms behind mental health problems and increased risk of non-fatal overdose (Bartoli et al., 2014). Some have speculated that either the types of drugs used, the nature of the use or the amount used may differ between those with and without mental health problems (Bohnert et al., 2012; Pabayo et al., 2013; Wines et al., 2007; Bartoli et al., 2014). Such speculation is supported by evidence that depressed individuals use a wider range of drug types than non-depressed individuals, suggesting the role of polysubstance use requires investigation (Connor et al., 2014).

In recent years, sophisticated statistical methods including mostly Latent Class Analysis (LCA) have been used to identify empirical polysubstance use profiles, and relate these to important risk factors or outcomes (Carter et al., 2013; Quek et al., 2013). A separate line of research has also highlighted the importance of polysubstance use to overdose risk, and identified specific drug combinations which elevate risk, including for example opioid use in combination with by benzodiazepines and alcohol (Martin et al., 2013; Darke, 2014; Pabayo et al., 2013; Jones et al., 2012; Dietze et al., 2005). Despite evidence for the prominent role of polysubstance use in the risk of overdose, no study has employed an empirical definition of polysubstance use to test associations with non-fatal overdose as far as the authors of this study are aware, marking an important area of further research (Conner et al., 2013; Dietze et al., 2005).

The limited available evidence suggests that mental health problems, polysubstance use and non-fatal overdose are interrelated, hence polysubstance use may be of central importance to explaining the relationship between mental health problems and non-fatal overdose via three distinct pathways: (i) the *type* of the polysubstance use profiles may differ between the two groups (those with and without mental health problems). To take an example from the literature, medications prescribed for mental health problems may increase the risk of overdose when combined with other substances (Bohnert et al., 2012); (ii) the *amount* of particular substances used (either the quantity and/or frequency of use) may increase among those with depression, perhaps as a means of self-medication (Bartoli et al., 2014; Wines et al., 2007); (iii) the *nature* of polysubstance use may differ among the two groups. The *nature* of the use refers to how the same substances may be used differently between those who do and do not have mental health problems in ways that lead to an increased risk of non-fatal overdose among the former group, independently of the type and overall amount used. For example, depression may inhibit the individual's ability to engage in self-maintenance behaviours thereby limiting their ability to take precautions when preparing and taking particular substances (Pabayo et al., 2013; Aldao et al., 2010). Lastly, it is important to consider how other risk factors associated with non-fatal overdose may be more common among people with mental health problems. Homelessness, recent incarceration and dropping out of treatment can increase the risk of non-fatal overdose by providing an insecure injecting environment and by decreasing tolerance, and are more common among those with mental health problems (Bohnert et al., 2012; Elkader et al., 2009).

In this study we examine whether differences in the *type*, *nature* or *amount* of polysubstance use between those with and without mental health problems (operationalised here as severe psychological distress) can explain the increased risk of non-fatal overdose among the distressed group. Person-centred techniques such as LCA have been favoured in a field of research keen to identify individuals as belonging to groups characterised by specific drug and alcohol usage patterns. However, for our situation a variable-centred approach is more powerful than LCA when aiming to determine *how* polysubstance use profiles effect non-fatal overdose risk. Specifically, we use multiple-group structural equation modelling to test three distinct hypotheses among a large sample of Australian PWID: (1) Do differences in the *type* of polysubstance use between the two groups explain differences in non-fatal overdose? This would be indicated by non-invariant polysubstance use profiles (i.e., profiles comprised of different types of drugs), which also differently relate to the outcome; (2) Do differences in the *amount* of polysubstance use between the two groups explain differences in the non-fatal overdose? This would be indicated by non-invariant polysubstance use means (i.e., latent factor means) of factors which are also associated with the outcome; and (3) Do differences in the *nature* of polysubstance use between the two groups explain differences in the non-fatal overdose? This would be indicated by non-invariant regression parameters of the relationships between the polysubstance use profiles and non-fatal overdose.

2. Methods

2.1. Sample

Since 2000, all Australia jurisdictions have participated in the Illicit Drug Reporting System (IDRS). A purposive convenience sampling method was used with participants recruited from needle and syringe programmes (NSPs), through advertisements, and peer referrals in the capital city of each jurisdiction. Eligible participants were those aged 16 years or older who had injected an illicit drug at least monthly in the previous six months, and had lived in the same area for 12 months. Each jurisdiction obtained ethics approval from relevant ethics committees. The interviewer-administered survey questions took approximately 45 min to complete and participants were reimbursed AU$40 for their time and travel expenses. More detailed descriptions of methods can be found in previous publications (Hando et al., 1998). Analysis were based on a total of 2673 participants drawn from the combined national samples of the three years 2011 (n = 868), 2012 (n = 922), and 2013 (n = 883).

2.2. Substance use

We included 14 categories of drugs, each of which was operationalised as a five-level ordinal variable representing the frequency of use over the past six months (*never/less than monthly/monthly/weekly/daily*). The drug categories included five illegal substances – heroin, three forms of methamphetamine (speed powder, base, crystal methamphetamine) and cocaine; three opioid substitution therapies – methadone, buprenorphine (Subutex) and buprenorphine-naloxone (Suboxone); and six prescription pharmaceuticals – morphine, oxycodone, other prescription opioids (e.g., fentanyl), alprazolam (i.e., Xanax and Kaima), other benzodiazepines (e.g., Valium, Serepax) and prescription stimulants (e.g., Ritalin). Due to the difficulties in characterising each drug category as illicit/licit and injected/not injected, we did not distinguish use by either the mode of administration (i.e., injection, oral administration, or otherwise) nor by the legality of use (e.g., methadone obtained via a physician or from the illicit drug market). In addition, measures of the average quantity of substance use were collected for some substances but were not used in the analyses because quantity and frequency were found to have a virtually one-to-one relationship (correlations of 0.99 for methadone and morphine and 0.95 for heroin and oxycodone), and thus the inclusion of quantity would add very little additional statistical information.

2.3. Non-fatal overdose and psychological distress

Psychological distress was measured with the Kessler Psychological Distress Scale (K10) (Kessler et al., 2002). The K10 includes ten questions concerning non-specific psychological distress answered on a five-point frequency scale, has good validity and reliability across a diverse range of general population and clinical settings, and correlates well with other similar scales including the General Health Questionnaire (GHQ) and the Short Form Health Survey (SF-12) (Andrews and Slade, 2001). The K10 questions concerned past month symptoms, and we used the established cut-off score of $\geq$30 out of 50 to represent severe psychological distress (Slade et al., 2011), resulting in 736 (29%) of the sample identified as having severe psychological distress. To assess non-fatal overdose participants were asked if they