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Review

The source and diversion of pharmaceutical drugs for non-medical use: A systematic review and meta-analysis

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ABSTRACT

Background: The non-medical use (NMU) of pharmaceutical drugs is an increasing public health concern. This systematic review consolidates current knowledge about how pharmaceutical drugs are obtained for NMU and the processes and people involved in diversion.

Methods: Peer-reviewed and grey literature databases were searched for empirical studies published between 1996 and 2017 that examined the source or diversion of pharmaceutical opioids, sedatives or stimulants for NMU in countries with reported misuse problems. Pooled prevalence meta-analyses using random effects models were used to estimate the prevalence of medical and non-medical sourcing reported by end-users, and gifting, selling and trading by various populations.

Results: This review synthesizes the findings of 54 cross-sectional studies via meta-analyses, with a remaining 95 studies examined through narrative review. Pharmaceutical drugs are primarily sourced for NMU from friends and family (57%, 95% CI 53%–62%, I^2 = 98.5, n = 30) and despite perceptions of healthcare professionals to the contrary, illegitimate practices such as doctor shopping are uncommon (7%, 95% CI 6%–10%, I^2 = 97.4, n = 29). Those at risk of diversion include patients displaying aberrant medication behaviors, people with substance use issues and students in fraternity/sorority environments. Sourcing via dealers is also common (32%, 95% CI 23%–41%, I^2 = 99.8, n = 25) and particularly so among people who use illicit drugs (47%, 95% CI 35%–60%, I^2 = 99.1, n = 15). There is little to no organized criminal involvement in the pharmaceutical black market.

Conclusion: Pharmaceutical drugs for NMU are primarily sourced by end-users through social networks. Future research should examine how dealers source pharmaceutical drugs.

1. Introduction

Pharmaceutical non-medical use (NMU) involves the consumption of a prescription or over-the-counter (OTC) drug for non-therapeutic purposes or other than directed by a healthcare professional (HCP) (Barrett et al., 2008; Larance et al., 2011b; Nielsen et al., 2008; Sembower et al., 2013). The prevalence of pharmaceutical NMU now rivals the use of illicit drugs in many developed countries around the world. For instance, general population surveys conducted in the United States (US), Canada and Australia have found that the NMU of pharmaceutical opioids is second only to the illicit use of cannabis (Australian Institute of Health and Welfare (AIHW), 2017; Center for Behavioral Health Statistics and Quality, 2015; Health Canada, 2012; Office of National Drug Control Policy, 2011).

The health, social and economic costs of the NMU of pharmaceutical drugs are well documented. The health risks range from fatal and non-fatal overdose to intoxication and dependence (Kaye and Darke, 2012; Olfson et al., 2015; Saha et al., 2016). In addition, poly drug use − the misuse of pharmaceutical drugs in combination with alcohol or other drugs − can magnify these problems and result in an increased risk of serious adverse consequences such as death (McCabe et al., 2006a; UNODC, 2017). Recent data indicates that pharmaceutical opioid-related deaths are increasing in Australia (Australian Bureau of Statistics, 2017), Canada (Canadian Institute of Health Information, 2017), the US (UNODC, 2017) and the UK (Office for National Statistics, 2017). In the US, the NMU of pharmaceutical opioids has been estimated to cost over

Abbreviations: ADHD, attention deficit hyperactivity disorder; AIHW, Australian Institute of Health and Welfare; HCP, healthcare professional; NCJRS, National Criminal Justice Reference Service (US); NMU, non-medical use; OST, opioid substitution therapy; PMP, prescription monitoring programs; PWUD, people who use drugs; UK, United Kingdom; UNODC, United Nations Office of Drugs and Crime; US, United States

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$70 billion annually (Florence et al., 2016). The harms related to the NMU of sedative and stimulant drugs are also well documented and include dependence, hospitalization and death (Australian Bureau of Statistics, 2017; Australian Institute of Health and Welfare (AIHW), 2017; National Institute on Drug Abuse, 2017; Sussman et al., 2006).

Pharmaceutical drugs for NMU may be sourced directly from medical sources via a prescription or OTC from a pharmacy, or from non-medical sources such as friends, relatives, a dealer or online (Substance Abuse and Mental Health Services Administration, 2017). The process of accessing pharmaceutical drugs for NMU involves diversion, whereby pharmaceuticals are channeled from legal sources to the illicit marketplace for NMU (Inciardi et al., 2007b). There is a large evidence base concerning the diversion of pharmaceutical drugs. Diversion is believed to occur through a number of mechanisms such as doctor or pharmacy shopping, prescription forgery, illegal sale, theft, internet sales, sharing among family and friends, and over-prescribing by HCP (Ford and Lacerenza, 2011; Fountain et al., 1997; Inciardi and Cicero, 2009; Inciardi et al., 2009b; Inciardi et al., 2007b; Parran and Grey, 2000; Rodwell et al., 2010). In light of the prominence of pharmaceutical NMU and the associated costs, it is timely to consolidate what is known about sourcing and diversion. This is critical for informing the development of effective prevention, treatment and law enforcement interventions (Ritter, 2005).

To date, reviews of this topic have canvassed issues related to the demand for pharmaceutical drugs without examining source and diversion (Lofwall and Walsh, 2014; Mounteney et al., 2015) or focused on one particular drug class (Kaye and Darke, 2012; Manchikanti et al., 2010) or diversion mechanism (Nielsen and Barratt, 2009). Further, most of the reviews have examined the problem as it occurs only in the US (Fischer et al., 2010; Inciardi and Cicero, 2009; Inciardi et al., 2009b), despite increasing concerns elsewhere. In order to carve a path for future research and policy efforts, this review seeks to consolidate what is known about the source and diversion of pharmaceutical drugs for NMU in Australia, Canada, Europe, the UK and the US.

2. Method

This review was undertaken using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist (PRISMA Statement, 2015).

2.1. Search strategy

With the assistance of a librarian trained in systematic review methodologies, searches were conducted in seven peer-reviewed and grey literature databases: MEDLINE, EMBASE, PsycINFO, CINCH, Criminal Justice Abstracts, Drug database: DRUG and the US National Criminal Justice Reference Service (NCJRS). The detailed search strategy used for each of these databases is provided in Appendix A of the supplementary . Three groups of search terms were developed and Boolean operators were used to separate each term (OR) and each group (AND):

1 Pharmaceuticals, medication, prescri* (-ption, -bed), prescription drug, therapeutic drug, non-prescription drugs, over-the-counter, opioid, analgesic, stimulant, benzodiazepine, barbiturate, sedative, tranquiliser/zer; (AND)
2 Supply chain, supply, supplier, diversion, drug diversion, sourcing routes, source, drug market, drug trade, drug trafficking, Dark Web, Dark Net, Internet, doctor shopping, pharmacy shopping, drug dealing, on-selling, over-prescribing, theft, fraud; (AND)
3 Non-medical use, misuse, illicit use, recreational use, abuse, poly drug use.

For MEDLINE, EMBASE, PsycINFO and Drug database: DRUG, the search terms were mapped to the associated subject headings, in addition to keyword searches for specific phrases. For CINCH, Criminal Justice Abstracts and the NCJRS, keyword searches only were used.

Additionally, a number of selected websites were searched for relevant grey literature. International websites included: UNODC, the Center for Disease Control and the World Health Organization. Australian websites included: Australian Policy Online, Australian Institute of Criminology, NSW Bureau of Crime Statistics and Research, AIHW, Australian Criminal Intelligence Commission and the National Drug and Alcohol Research Centre.

Reference lists in retrieved articles were also scanned to identify any relevant studies not captured. Citations were managed using the bibliographic software EndNote with duplicates removed manually.

2.2. Study selection

Inclusion and exclusion criteria were developed, with a focus on including empirical quantitative and qualitative studies that contained content relating to the source or diversion of pharmaceutical drugs that are most often subject to NMU, namely pharmaceutical opioids (full agonists like oxycodone and partial agonists like buprenorphine), sedatives (barbiturates, benzodiazepines and benzodiazepine-like drugs or ‘z-drugs’) and stimulants.

The searches were limited to ‘humans’ and the English language, and published between 1996 and 2017 (22 years). The lower cut-off was chosen because it aligns with the increased prescribing and misuse of pharmaceutical opioids in the US (King et al., 2014), and to focus on results in the past two decades so that findings are most relevant to current policy and practice. For comparability, studies from Australia, Canada, Europe, the UK and the US were included in the review. Although challenges relating to the NMU of pharmaceuticals in developing countries are equally important, the supply issues experienced are different and warrant separate analysis that is outside the scope of this review.

Literature was also excluded if it focused on the supply of illicit drugs (e.g., marijuana, cocaine, heroin) with no mention of pharmaceuticals; or focused only on the trends or prevalence of NMU, in the absence of any focus on source or diversion. Reviews, editorials, commentaries, letters or notes, opinion pieces and media articles were also excluded.

2.3. Data extraction and quality assessment

A standardized coding form was developed to ensure that consistent information was extracted from each study, including: author, year, country of origin, methodology, study design, sample size, target population, prescription drug class and key findings relating to the source and diversion of pharmaceutical drugs.

A modified version of the Checklist for the Evaluation of Research Articles (Parts V and VI) developed by DuRant (1994) was used to assess the quality of the cross-sectional studies included in the meta-analyses (Pont et al., 2009). A score of 1 was given for ‘YES’ responses and 0 for ‘NO’, thus a higher score indicates better methodological quality. Studies with a high score were strong in their sample description, including detailed inclusion criteria and demographic characteristics of the sample and had sample sizes of greater than 100. Stronger studies also employed validity or reliability testing of the survey instruments and achieved a response rate of greater than 80%, indicating lower risk of bias. The statistical procedures employed in the higher quality studies were clearly described and involved multivariate analyses. The modified appraisal tool and detailed scoring for each study is provided in Appendices B and C.

2.4. Data synthesis

To synthesize the findings of the cross-sectional studies that examined the source of pharmaceutical drugs for NMU, several meta-