

Short Report

Risk of fentanyl overdose among clients of the Sydney Medically Supervised Injecting Centre



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ABSTRACT

Background: Fentanyl is a powerful analgesic, the prescription of which has increased markedly in recent years. The emergence of the drug at the Sydney Medically Supervised Injecting Centre (MSIC) warranted a retrospective clinical audit to assess the risk of fentanyl overdose in comparison with other opioids, in the context of a drug consumption room.

Method: Heroin, fentanyl or other prescription opioids (PO) injections resulting in overdose were audited (September 1, 2012 and August 31, 2015). Rates of overdose per 1000 injections and relative risks (RR) of overdose were calculated.

Results: In the audit period 189,203 injections by 4177 individuals occurred, with fentanyl injections increasing by 1000%, heroin injections increasing by 70% and, inversely, a sharp decline in other PO injections. Fentanyl injections had approximately four and half times the risk of resulting in overdose than heroin or other PO injections combined (RR = 4.6); and, had two times the risk of heroin injections, and eight times the risk of resulting in overdose than other PO injections (RR = 2.2 and RR = 7.9).

Conclusion: Findings from a drug consumption room, such as the Sydney MSIC can effectively inform harm reduction services and emergency services of the increased use of, and therefore risk of, fentanyl overdose relative to other opioids. The dynamic nature of drug markets mean that services such as MSIC are uniquely placed to provide not only real-time data on drug use trends, but also safer injecting advice to those engaging in new practices.

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Background

Fentanyl, a rapid acting, short duration synthetic opioid, is a powerful analgesic approximately 100 times more potent than morphine (Chodoff & Domino, 1965). Listed on Australia's Pharmaceutical Benefits Scheme in 2006 for the treatment of persistent non-cancer pain, fentanyl is available in several formulations including a transdermal patch, prescription of which has increased markedly in recent years both in Australia (Roxburgh et al., 2013) and North America (Compton & Volkow, 2006).

In the United States (US), increased rates of fentanyl prescription corresponded with increased fentanyl-related Emergency Department presentations (Compton & Volkow, 2006). People who inject drugs (PWID) find extraction of fentanyl from transdermal patches relatively easy (Firestone, Goldman, & Fischer, 2009), and fentanyl-related fatalities among PWID have occurred both internationally (Kronstrand, Druid, Holmgren, & Rajs, 1997; Tharp,

Winecker, & Winston, 2004) and in Australia (Reeves & Ginifer, 2002; Roxburgh et al., 2013). Concerns that increased fentanyl-related overdose deaths foreshadowed an emerging public health problem (Amlani et al., 2015; Canadian Centre on Substance Abuse, 2015; Centres for Disease Control and Prevention, 2008, 2013) were reinforced in March 2015 when the US Drug Enforcement Administration (DEA) released a nationwide alert in response to a surge in overdose deaths from fentanyl-laced heroin, noting a “significant threat to public health and safety”, with seizures of illicit drugs containing fentanyl tripling between 2013 and 2014 (Drug Enforcement Administration (DEA), 2015).

The Australian fentanyl experience differs somewhat from the US and North America in that there have been no recorded seizures of illicit drugs containing fentanyl to date. Fentanyl that is used in Australia comes in the form of a transdermal patch, which is then prepared for injection. The popularity of fentanyl use amongst PWID has increased significantly since the reformulation of Oxycontin in April 2014 but awareness of the required dosage remained unclear, with little information or educational resources available at the time. There is also cause for concern with regards to the preparation of fentanyl for injection, as the extraction process

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is complicated, time-consuming and lacking in clarification. The outcome being that while some PWID can successfully extract a suitable dose of fentanyl from the patch, there are others that are unable to do so.

Operational since May 2001, the Sydney Medically Supervised Injecting Centre (MSIC) is a safe injecting facility (SIF) where clients can inject drugs, including prescription opioids (PO), under the supervision of trained health professionals. MSIC has approximately 15,000 registered clients and, as at May 2015, had supervised more than 930,000 injections (41% PO; 38% heroin; 10% cocaine; 6% meth/amphetamines) and successfully managed almost 6,000 opioid overdoses. Collecting routine self-reported data on drug type injected, MSIC is a unique source of real-time drug trend information. Prior to 2012, presentations to inject fentanyl were infrequent and sporadic; systematic recording of fentanyl began in September of that year and its use has been exclusive via the preparation of transdermal patches of varying sizes and strength for injection. Although fentanyl accounts for a small minority of PO injections at MSIC, the drug's potency and comparative overdose risk (Chodoff & Domino, 1965) was deemed to warrant the conduct of a retrospective clinical audit to delineate the absolute and relative risk of fentanyl overdose in comparison with other opioids injected by MSIC clients.

This paper aims to present the results of the retrospective clinical audit of overdoses occurring onsite at the Sydney MSIC from 2012 to 2015 to determine the absolute and relative risk of overdose from fentanyl, as compared to heroin and PO individually and combined.

Methodology

All MSIC visits between September 1, 2012 and August 31, 2015 were audited to identify cases where heroin, fentanyl or 'other PO' (including all formulations of oxycodone and morphine but excluding methadone and buprenorphine) were reported as the cause of an onsite opioid overdose. Drug type is self-reported post overdose to MSIC clinical staff. It should be noted that MSIC clients are assessed for intoxication on presentation to use the service and those clients deemed to be intoxicated are excluded

and asked to re-present at a later time. The service's clinical indicators for opioid overdose are: a decrease in level of consciousness as measured by the Glasgow Coma Scale (GCS), decreased respiratory effort, pinpoint pupils and oxygen saturation of (SpO₂) less than 95% as measured by pulse oximetry. Any client with a SpO₂ reading of <95% is administered oxygen. Anyone with significantly reduced respiratory effort or apnoea is treated with Bag-Valve-Mask airway management; others are managed with supplemented O₂ via nasal prongs or Hudson mask. If required, naloxone is administered after five minutes of oxygen and airway management.

Data analysis

For each MSIC client visit, a clinical database records which drug the client intends to inject, and other events that occur during the visit, including the nature and management of onsite overdoses. Absolute risks of overdose were calculated as the proportion of injections of each drug type resulting in overdose. Relative risks (RR) were calculated as the rate of overdose among all fentanyl injections divided by rate of overdose among all other opioid injections (that is, heroin and other PO combined). RR were also calculated for rate of overdose following fentanyl injections divided by rate of overdose after heroin injections; and rate of overdose following fentanyl injections divided by rate of overdose after other PO injections. We also calculated 95% confidence intervals (95% CI), z-statistics and associated P-values for these RRs using MedCalc Software 16.4.3 (Mariakerke, Belgium).

Results

A total of 189,203 injections were undertaken by 4177 individual MSIC clients during the audit period. These included 97,369 other PO injections (58%); 45,702 heroin injections (24%); and 2454 fentanyl injections (0.01%). The remaining injections were of meth/amphetamines (13%); cocaine (4%); benzodiazepines (0.3%); and other drugs (1%).

The number of fentanyl injections increased by 1000% between Year 1 and Year 3 of the audit period (Table 1). During the same

Table 1
Injections overdoses and rate per 1000 injections of heroin, fentanyl and other prescription opioids at the Sydney MSIC, September 2012–August 2015.

	Drug type			
	Fentanyl	Heroin	Other PO ^a	
Onsite injections (N)				
Year 1 ^b	180	11,810	47,385	
Year 2 ^c	495	13,170	33,147	
Year 3 ^d	1779	20,722	16,837	
Total ^e	2454	45,702	97,369	
Onsite overdoses during audit period				
Number	108	874	467	
% of injections resulting in overdose	4.4	1.9	0.48	
Rate per 1000 injections during the audit period	44/1000 injections	19/1000 injections	5/1000 injections	
Comparison	Relative risk ^f	95% CI	z-statistic	p-value
Fentanyl vs. heroin	2.21	1.8–2.6	8.459	<0.0001
Fentanyl vs. heroin + other PO combined	4.58	3.8–5.5	16.044	<0.0001
Fentanyl vs. other PO	7.95	6.7–9.5	23.187	<0.0001

Note: all injections are discrete events.

^a Other PO: all formulations of oxycodone and morphine.

^b Year 1: September 2012–August 2013.

^c Year 2: September 2013–August 2014.

^d Year 3: September 2014–August 2015.

^e Total: September 2012–August 2015.

^f Crude relative risk (cell size too small for age adjustment).

period, the number of onsite heroin injections increased by 70%; while there was a sharp decline in the number of injections of other PO from September 2012 to September 2015.

MSIC managed an average of 40 opioid overdoses per month during the audit period (Fig. 1). Fentanyl overdoses increased from mid-2013, with an average of 7 per month from late 2014 (Fig. 1).

Four percent of fentanyl injections were followed by a subsequent overdose, compared with 2% of heroin injections, and <1% of other PO injections (Table 1). Crude relative risk estimates demonstrated that fentanyl injections had approximately four and a half times the risk of resulting in overdose than injections involving either heroin or other PO (RR = 4.6; 95%CI 3.8–5.5). Specifically, fentanyl injections had two times the risk of overdose than heroin injections, and eight times the risk of overdose than other PO injections, to result in overdose (RR = 2.2; 95%CI 1.8–2.7; and RR = 7.9; 95%CI 6.7–9.5 respectively). Fig. 2 presents the percentage of overdoses, by drug type, at the Sydney MSIC, September 2012–August 2015, which shows fentanyl as the higher proportion of all overdoses since 2014.

Discussion

To our knowledge, this study is the first to estimate the absolute and relative risks of overdose following injection of fentanyl extracted from transdermal patches. Notwithstanding the relatively small number of fentanyl injections undertaken at MSIC – accounting for just 0.01% of the approximately 145,525 injections reviewed for this audit – fentanyl use increased ten-fold during the audit period, an observation consistent with recent evidence of increased diversion in Australia (Roxburgh et al., 2013), and reflective of trends in North America (Compton & Volkow, 2006). Fentanyl accounted for almost 8% of all overdoses occurring at MSIC during the audit period. Indeed, between September 2012 and August 2015, clients injecting fentanyl at a drug consumption room had two times the risk of overdosing compared to those injecting heroin, and eight times the risk of overdose of those injecting PO, findings which corroborate previous documentation of fentanyl's overdose and mortality burden (Kronstrand et al., 1997; Tharp et al., 2004). The increased use of fentanyl onsite appears to match the introduction of the reformulation of Oxycontin in April 2014 and there may be some displacement from one drug to the other among a small number of PWIDs.

Biological mechanisms can plausibly account for the markedly higher risk of overdose among people who inject fentanyl. Opioid effects depend on lipid solubility, which affects the rate at which drugs and their metabolites cross the blood-brain barrier and are transported to the site of action; highly lipid-soluble opioids have a more rapid onset of action (Biancofiore, 2006). Morphine is the standard against which the pharmacokinetic and

pharmacodynamic properties of other opioids are compared. While oxycodone has a liposolubility similar to morphine (Biancofiore, 2006), the relative lipid solubility of heroin and fentanyl are 200 and 500 times higher, respectively (Anaesthesia UK). This rapid onset, in combination with fentanyl's sheer potency (Chodoff & Domino, 1965), underlies the drug's comparative overdose risk. This is in addition to the variability of dose that PWID are able to derive from transdermal patches of varying sizes and strength.

Interpretation of this study's findings is limited by the lack of information on known overdose risk factors, such as concurrent use of other drugs and recent periods of abstinence. For example, a review of fentanyl-related mortality in Australia demonstrated that approximately 50% of deaths involved multiple drug toxicity (Roxburgh et al., 2013). However, the great majority of both fatal and non-fatal heroin overdoses also involve polydrug toxicity (Darke & Hall, 2003; Dietze, Jolley, Fry, & Bammer, 2005) and we know of no reason that the heroin overdoses reported in this paper would deviate from this pattern. Notwithstanding the potential role of other drugs in fentanyl overdose, the relative risks presented here are of clinical significance, and warrant further investigation. The study is further limited by the fact that the analysis is not of genuinely independent groups (i.e. the same person may have made multiple visits and risk may be correlated). Further analysis of this issue that tests change over time and accounts for individual risks is a worthy next step, following this initial clinical audit.

As an emerging drug of misuse among PWID, fentanyl poses significant risks. Anyone dealing with overdoses should be aware of the increased risk of fentanyl overdose relative to other opioids, including those working in harm reduction services (such as Drug Consumption Rooms and Needle and Syringe Programs); people who are injecting drugs and their friends and families; user groups; as well as emergency services, Emergency Department staff and paramedics. Prescribers of transdermal patches should be informed of the potential for diversion to non-medical use by PWID, and the ease with which fentanyl can be extracted. Appropriate methods for safe disposal of used patches to discourage diversion should be established. Further research would usefully establish risk factors for fentanyl overdose, including prediction of overdose in light of the complexities posed by the variations in the potency of fentanyl extracted from transdermal patches likely across both individuals and extraction methods. Such findings are required to inform the development and dissemination of successful harm reduction strategies for this seemingly exceptionally high-risk drug.

This study documents significant changes in opioid injection during the audit period, with decreased use of other POs offset by increases in both heroin and fentanyl injection. The dynamic

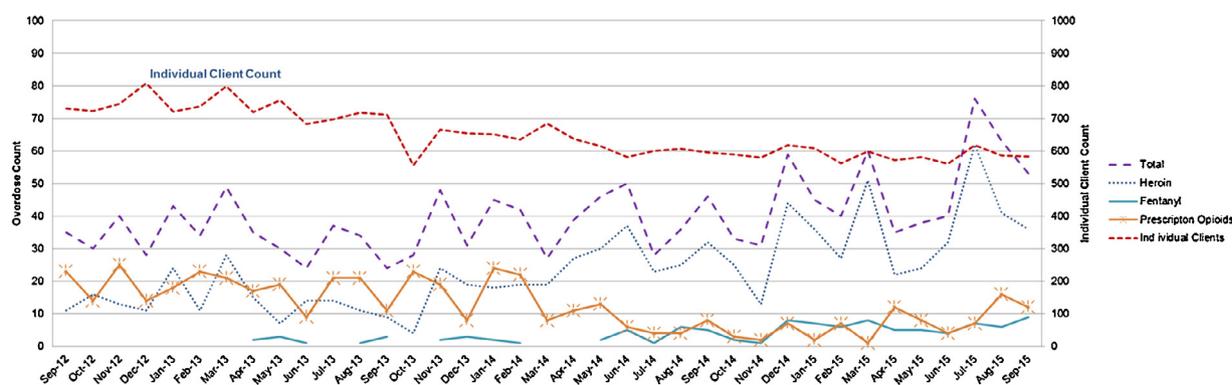


Fig. 1. Opioid overdoses per month at the Sydney MSIC, September 2012–August 2015.

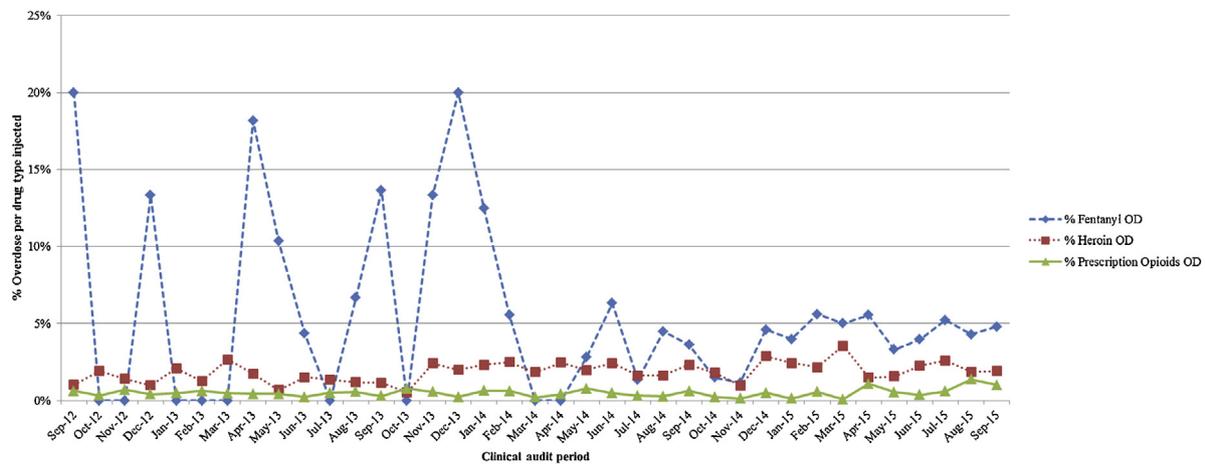


Fig. 2. Monthly overdose rate at the Sydney MSIC by drug type, September 2012–August 2015.

nature of drug markets requires that harm reduction services such as SIFs and DCRs can quickly adapt to the changing needs of their clients. SIFs such as MSIC are uniquely placed to provide not only real-time data that delineates evolving drug use trends, but also safer injecting advice to those engaging in new practices.

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Conflicts of interest

None.

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