International Journal of Drug Policy 46 (2017) 172–179

Contents lists available at ScienceDirect

International Journal of Drug Policy

journal homepage: www.elsevier.com/locate/drugpo

Commentary

Naloxone for heroin, prescription opioid, and illicitly made fentanyl overdoses: Challenges and innovations responding to a dynamic epidemic

Nadia Fairbairn[a,b,*], Phillip O. Coffin[c,d], Alexander Y. Walley[e]

[a] British Columbia Centre on Substance Use, British Columbia Centre for Excellence in HIV/AIDS, Vancouver, Canada
[b] Department of Medicine, University of British Columbia, Canada
[c] San Francisco Department of Public Health, United States
[d] University of California, San Francisco, United States
[e] Clinical Addiction Research and Education Unit, Boston University School of Medicine, Boston Medical Center, United States

ARTICLE INFO

Article history:
Received 21 March 2017
Received in revised form 28 May 2017
Accepted 12 June 2017

Keywords:
Naloxone
Overdose
Fentanyl
Synthetic opioids

ABSTRACT

Community-based overdose prevention programs first emerged in the 1990's and are now the leading public health intervention for overdose. Key elements of these programs are overdose education and naloxone distribution to people who use opioids and their social networks. We review the evolution of naloxone programming through the heroin overdose era of the 1990's, the prescription opioid era of the 2000's, and the current overdose crisis stemming from the synthetic opioid era of illicitly manufactured fentanyl and its analogues in the 2010's. We present current challenges arising in this new era of synthetic opioids, including variable potency of illicit drugs due to erratic adulteration of the drug supply with synthetic opioids, potentially changing efficacy of standard naloxone formulations for overdose rescue, potentially shorter overdose response time, and reports of fentanyl exposure among people who use drugs but are opioid naïve. Future directions for adapting naloxone programming to the dynamic opioid epidemic are proposed, including scale-up to new venues and social networks, new standards for post-overdose care, expansion of supervised drug consumption services, and integration of novel technologies to detect overdose and deliver naloxone.

Introduction

The groundwork for the public health concept that opioid overdose death is preventable in the setting of illicit opioid use was first laid with research articles published in the 1970s describing the risk factors for opioid overdose (Brecher, 1972; Monforte, 1977). The first community-based overdose prevention programs for people who use opioids emerged in the 1990s (Darke, 2016). The key elements of these programs were the education of people who use opioids about how to reduce their overdose risk and equipping them with naloxone, the antidote to an opioid overdose, so that they could rescue each other. Since then, these programs have expanded substantially in the United States and Canada to become a leading public health intervention for the prevention of overdose mortality (Oluwajenyo Banjo et al., 2014; Wheeler et al., 2015).

These programs have emerged on a backdrop of a dynamic epidemic of opioid use and opioid overdose in the United States and Canada. In the 1990s and 2000s, expansion of the treatment of acute and chronic pain with prescription opioids was associated with concomitant rise in diversion of prescription opioids to the illicit market, opioid use disorders, and opioid overdose deaths (Centers for Disease & Prevention, 2011; Modarai et al., 2013; Piercefield, Archer, Kemp, & Mallonee, 2010; Shah, Lathrop, Reichard, & Landen, 2008). As the connection between increased opioid prescribing and rising overdose deaths were recognized and efforts were made to limit opioid prescriptions, heroin use increased, likely to meet the rising demand for illicit opioids (Rudd, Aleshire, Zibbell, & Gladden, 2016). Along with increased heroin use, the introduction of illicitly manufactured fentanyl and other synthetic opioids into many illicit opioid markets has resulted in an acute surge in overdose deaths in many communities (Peterson et al., 2016; Rudd, Aleshire et al., 2016). These changes

* Corresponding author at: B.C. Centre on Substance Use, B.C. Centre for Excellence in HIV/AIDS, University of British Columbia, St. Paul's Hospital, 608-1081 Burrard Street, Vancouver, B.C., V6Z 1Y6, Canada. Fax: +1 604 806 9467.
E-mail address: nfairbairn@cfenet.ubc.ca (N. Fairbairn).

http://dx.doi.org/10.1016/j.drugpo.2017.06.005
0955-3959/

have brought challenges and raised new questions about what was previously known regarding overdose and our response to it.

The heroin era

In the late 1990s and early 2000s, when community overdose education and naloxone rescue kits initially emerged among programs serving people who inject drugs (PWID), heroin was the primary opioid involved in overdose events. In the United States and Canada, most naloxone programs were based in syringe needle access programs (SNAPs) that served people who injected heroin. In the 1990s, SNAPs were recognized as an important evidence-based public health strategy to reduce HIV transmission and the medical complications from injection drug use, yet U.S. federal funding ban was not lifted, in part, until January of 2016. While some local and state health departments supported these programs to reduce HIV and hepatitis rates among PWID, many programs relied on volunteers, foundation and individual funding and operate without any support from health departments.

Programs distributing naloxone to PWID through SNAPs first emerged in the U.S. in Chicago in 1996, the Jersey Channel Islands in Europe in 1998, Berlin, Germany, in 1999, and New Mexico, in 2001 (Dettmer, Saunders, & Strang, 2001; Maxwell, Bigg, Stanczykiewicz, & Carlberg-Racich, 2006). Multiple ecological and other observational studies of community naloxone distribution programs demonstrated that PWID can learn overdose prevention and administer naloxone successfully (Doe-Simkins, Walley, Epstein, & Moyer, 2009; Green, Heimer, & Grau, 2008; Seal et al., 2003; Seal et al., 2005; Tobin, Sherman, Beilenson, Welsh, & Latkin, 2009), and suggested potential ancillary benefits such as decreased substance use, social connection, and empowerment (Wagner et al., 2014; Wagner et al., 2010). San Francisco documented a dramatic reduction in heroin overdose mortality in the early 2000s, from approximately 180 heroin overdose deaths per year in the late 1990s to 10–11 per year from 2010 to 2012, although some of that decrease was a result of transitions to prescription opioids (Visconti, Santos, Lemos, Burke, & Coffin, 2015). Scotland's National Naloxone Programme, which started in 2011, was associated with a 36% reduction in the proportion of opioid-related deaths that occurred in the 4 weeks following release from prison (Bird, McAuley, Perry, & Hunter, 2016). Massachusetts demonstrated reduced opioid overdose mortality rates in communities where overdose education and naloxone distribution programs were implemented compared to communities where they were not implemented (Walley, Xuan, et al., 2013). Community overdose education and naloxone rescue programs have expanded substantially since the 1990s and are now present in 30 U.S. states (Wheeler et al., 2015).

Overdose education and naloxone rescue was not the only public health intervention associated with reductions in heroin overdoses. Baltimore documented a reduction in heroin overdose death that was attributed to expansion of methadone and buprenorphine treatment for opioid use disorder (Schwartz et al., 2013). Vancouver, Canada, responding to a dual epidemic of overdose and HIV infection that developed in the 1990s, opened North America's first supervised injection facility, Insite, in 2003. Research has demonstrated multiple benefits of Insite, including a substantial local reduction in opioid overdose mortality (Marshall, Milloy, Wood, Montaner, & Kerr, 2011). Since opening in 2003, no deaths have ever occurred at Insite.

The opioid analgesic era

Increases in opioid prescribing drove rising opioid overdose death rates at the beginning of the 21st Century across the United States, resulting in the recognition of an opioid epidemic. Between 1999 and 2008, prescription opioid-related overdose deaths, sales of prescription opioids, and treatment admissions for prescription opioid use disorders, each increased by four-fold or more (Centers for Disease & Prevention, 2011). The rise in prescription opioid-related overdose deaths slowed in 2010, a year when the formulation of long-acting oxycodone was changed to make it harder to insufflate or inject (Cicero, Ellis, & Surratt, 2012), propoxyphene was taken off the market, and Florida restricted high volume opioid prescribing through pill mills (Dart et al., 2015; Kennedy-Hendricks et al., 2016; Larochelle, Zhang, Ross-Degnan, & Wharam, 2015; Rutkow et al., 2015). Prescription drug monitoring programs proliferated during this period as an effort to make opioid prescribing safer (Delcher, Wagenaar, Goldberger, Cook, & Maldonado-Molina, 2015; Green, Zaller, Rich, Bowman, & Friedmann, 2011; Paulozzi, Kilbourne, & Desai, 2011). In conjunction with these opioid stewardship initiatives, overdose education and naloxone rescue for people using prescription opioids was increasingly considered a necessary component of the response to the opioid epidemic. As a result, all but three U.S. states in 2016 have laws supporting naloxone provision to lay persons (Brodrick, Brodrick, & Adinoff, 2016). In recognizing opioid-related overdose as a major public health concern, the US Department of Health and Human Services highlighted naloxone rescue kit access and emergency overdose response as one of three priority areas to address this crisis in 2015 ("HHS takes strong steps to address opioid-drug related overdose, death and dependence," March 26, 2015). Though nation-wide systematic monitoring remains a challenge in Canada, similar increases in opioid prescribing and related harms were observed during the same time period (Fischer & Argento, 2012; Hospitalizations and Emergency Department Visits Due to Opioid Poisoning in Canada, 2016), with subsequent reductions in opioid prescribing following implementation of interventions, such as the adoption of prescription monitoring programs in the provinces of Ontario and British Columbia and delisting of long-activing formulations of oxycodone from public drug formularies in several provinces in 2012 (Murphy, Goldner, & Fischer, 2015).

Naloxone programming has demonstrated benefits in some localities in the context of escalating prescription opioid analgesic use and overdose. In San Francisco, for example, there was no increase in opioid overdose mortality during the period of expanding opioid access, notwithstanding data suggesting a large increase in the population of opioid injectors (San Francisco Sentinel Community Site (SCS) Drug Use Patterns and Trends, 2016). Nonetheless, a persistent number of opioid analgesic deaths – approximately 110 per year – led the local health department to offer naloxone prescriptions to patients on long-term opioids in selected primary care clinics. Some of the earliest efforts in naloxone co-prescription were made by Project Lazarus in Wilkes County, North Carolina, which saw a 70% decrease in prescription opioid-related overdose death rates during the implementation phase of the project from 2009 to 2010 (Albert et al., 2011). Naloxone co-prescribing was found to be acceptable to clinicians and it was associated with reductions in emergency department visits for opioid-related adverse events (Behar et al., 2016; Coffin et al., 2016).

These findings contributed to initiation of a national overdose education and naloxone distribution program through the Department of Veterans Affairs (Oliva et al., 2016) and informed the CDC chronic pain guidelines that encourage naloxone co-prescribing to patients on prescription opioids long-term for non-cancer pain (Dowell, Haegerich, & Chou, 2016).

The synthetic opioid era

As opioid prescribing rates declined and novel opioid formulations that deter injection were developed, the United States