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Research Paper

Reducing opioid overdose in Kazakhstan: A randomized controlled trial of a couple-based integrated HIV/HCV and overdose prevention intervention "Renaissance"

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ABSTRACT

Objectives: To evaluate the efficacy of a couple-based integrated HIV/HCV and overdose prevention intervention on non-fatal and fatal overdose and overdose prevention behaviors among people who use heroin or other opioids in Almaty, Kazakhstan.
Methods: We selected 479 participants who reported lifetime heroin or opioid use from a sample of 600 participants (300 couples) enrolled in a randomized controlled trial (RCT) conducted between May 2009 and February 2013. Participants were randomized to either (1) a 5-session couple-based HIV/HCV and overdose prevention intervention condition or (2) a 5-session Wellness Promotion and overdose prevention comparison condition. We used multilevel mixed-effects model with modified Poisson regression to estimate effects of the intervention as risk ratios (RR) and the corresponding 95% CIs.
Results: About one-fifth (21.9%) of the sample reported that they had experienced an opioid overdose in the past 6 months at baseline. At the 12-month follow-up, both the intervention and comparison conditions reported significant reductions in non-fatal overdose and injection heroin/opioid use and significant increases in drug treatment attendance and naloxone use to prevent death from overdose. However, we found no differences between the study arms on any of these outcomes. There were three intervention condition participants (1.3%), compared to seven comparison condition participants (2.9%) who died from opioid overdose during the 12-month follow up period although this difference was not significant.
Discussion: There were no significant conditions on any outcomes: both conditions showed promising effects of reducing non-fatal overdose and overdose risks. Integrating overdose prevention into a couple-based HIV/HCV intervention may be an efficient strategy to target the syndemic of opioid overdose, HIV and HCV in Kazakhstan.

Introduction

Burgeoning heroin use in Central Asia is fueling the intertwined epidemics of opioid overdose, HIV and HCV, which represent the leading causes of mortality among people who people who inject or use heroin or other opioids in the region and worldwide (Mathers et al., 2013). A meta-analysis found that people who inject drugs (PWID) who are HIV positive are twice as likely to experience opioid overdose as those who are HIV negative (Green, McGowan, Yokell, Pouget, & Rich, 2012). Recent research has also found a strong association between HCV and overdose (Arasteh, Des Jarlais, & Perlis, 2008; Mateu-Gelabert et al., 2017). The overlapping structural, behavioral and biological factors driving overdose, HIV and HCV have prompted researchers to call for integrated overdose and HIV/HCV prevention interventions (Arasteh et al., 2008; Coffin, Rowe, & Santos, 2015; Mathers et al., 2013; Mueller, Walley, Clacaterra, Glanz, & Binswanger, 2015).

The syndemic of opioid overdose, HIV and HCV is particularly acute in Kazakhstan and other countries in Central Asia. Some of the highest rates of injection heroin use in the world are found in towns along major drug trafficking routes in Central Asia (Aceijas

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et al., 2006). Although there remains a dearth of surveillance data on overdose, data suggests between 21 and 24% of people who use heroin or other opioids in Central Asia experienced a non-fatal overdose in the past year (Kazakhstan RAC, 2016; Tajikistan RAC, 2011). Central Asia also has some of the fastest growing HIV and HCV epidemics in the world (Mohd Hanafiah, Groeger, Flaxman, & Wiersma, 2013; UNAIDS, 2017). There is an urgent need for integrated overdose and HIV/HCV interventions that can stem the tide of deaths and morbidity from overdose, HIV and HCV among PWID in this region.

Over the past two decades, emerging evidence has documented the safety and effectiveness of brief overdose prevention interventions that include lay administration of naloxone, an opioid antagonist to reverse potentially fatal respiratory suppression of heroin and other opioids (Beletsky et al., 2006; Bird, Parmar, Perry, & Hunter, 2016; Clark, Wilder, & Winstanley, 2014; Giglio, Li, & DiMaggio, 2015; Mann, 2003). A meta-analysis of pooled data found that naloxone (Narcan) administration by bystanders was associated with significantly increased odds of recovery compared to no naloxone administration (Giglio et al., 2015). This meta-analysis and other systematic reviews, however, noted several methodological limitations of these overdose prevention studies and highlighted several gaps in existing evidence-based overdose prevention strategies (Clark et al., 2014; Giglio et al., 2015; Mueller et al., 2015). To date, only two recent overdose prevention interventions have been evaluated using more rigorous randomized controlled trial (RCT) designs (Dunn et al., 2017; Parmar, Strang, Choo, Meade, & Bird, 2016) and very few have been evaluated outside of North America or Europe, or in low or middle income countries. To our knowledge, none of the existing evidence-based overdose prevention and naloxone administration interventions have combined HIV or HCV intervention strategies although non-fatal overdose has been associated with HIV, HCV and drug-related and sexual risk behaviors (Gilbert et al., 2013; Green et al., 2012). By addressing the primary life-threatening concern of overdose, HIV services are more likely to build trust with people who use heroin or other opioids and link and retain them in a continuum of HIV and HCV services, including HIV and HCV testing, treatment and care services as well as drug treatment and harm reduction services (Curtis & Dasgupta, 2010; El-Bassel et al., 2011; Gilbert et al., 2013).

Couple-based interventions have been shown to be efficacious in reducing HIV risk behaviors, completing HIV testing, increasing ART adherence as well as reducing drug and alcohol misuse (El-Bassel et al., 2010, 2011, 2014; Winters, Fals-Stewart, O'Farrell, Birchler, & Kelley, 2002). Recent research indicates that romantic injection partnerships may be at increased risk of both overdose and HIV/HCV infection as a result of frequent injecting and syringe sharing within the relationship, which suggests that a couple-based modality may be optimal in addressing overdose and HIV/HCV infection (Rowe, Santos, Raymond, & Coffin, 2017). A couple-based modality may also be particularly effective in preventing overdose as both partners can work together to reinforce overdose prevention behaviors and administer naloxone to each other in the event of an overdose. To date, however, no known couple-based naloxone overdose prevention interventions have been evaluated using randomized or non-randomized designs.

This study aimed to address several gaps in overdose prevention research by evaluating the efficacy of a 5-session couple-based integrated HIV/HCV and overdose prevention education, which included lay naloxone administration (HIV/HCV + OD), compared to an attentional comparison condition (WP + OD) in reducing overdose risk behaviors among people who inject or use heroin, opium, or prescription opioids over the 12-month follow-up period. The attentional comparison condition delivered the same overdose prevention and naloxone administration intervention in a single gender group session to opioid users and their heterosexual partners in a 5-session wellness promotion intervention (El-Bassel et al., 2014). The primary outcome paper from this RCT found that this couple-based integrated intervention, entitled "Renaissance", was efficacious in reducing the number and proportion of unprotected sex acts and significantly lowering the HCV incidence by 69%, compared to the wellness promotion comparison condition (El-Bassel et al., 2014). The overdose prevention outcomes for this study include: reducing non-fatal and fatal opioid overdose, injection heroin use and any opioid use and increasing access to naloxone, naloxone use and linkage to drug treatment.

Methods

This RCT was conducted in Almaty, Kazakhstan between May 2009–February 2013 among 300 couples (N = 600 participants) where one or both partners reported injecting heroin. This paper includes a subset of this sample, 479 participants who reported any lifetime use of heroin, opium or any opioid prescription drug at baseline, and therefore may be at risk of opioid overdose. The large majority of these participants (91%, N = 436) reported injecting heroin in the past 90 days at baseline. We have described detailed methods, sample characteristics, and sample power calculations elsewhere (El-Bassel et al., 2014) and included a CONSORT diagram in Fig. 1.

Recruitment and eligibility

Research assistants conducted recruitment primarily using word-of-mouth from participants to their injecting network members as well as from street-based venues where PWID congregate and needle syringe programs (NSPs). Eligibility criteria included: (1) age 18 or older; (2) having had an intimate relationship with a partner of the opposite sex that lasted for at least six months, who would be willing to participate in the study for the following 12 months; (3) at least one partner reporting injecting drugs in the past year and (4) having had unprotected sex with study partner in the past 90 days. Couples were excluded if either partner: (1) showed evidence of significant impairment as determined during informed consent; (2) reported severe violence perpetrated by the study partner in the past year; or (3) was not fluent in Russian.

After providing informed written consent, participants completed a pre-intervention baseline assessment with repeated follow-up assessments at 3, 6, and 12 months post-intervention using an Audio Computer-Assisted Self-Interview (ACASI), which was administered in a private room, as well as biological testing for HIV and HCV. The Institutional Review Boards at Columbia University and the Kazakhstan School of Public Health approved all study protocols. Participants received $10 USD (1500 tenge) for completing the ACASI interview and biological testing for each assessment visit to cover their time, as well as $5 USD (750 tenge) for travel at each intervention session.

Randomization and masking

We used a computer-generated randomization algorithm to randomly assigned couples in a one-to-one ratio to receive the five-session HIV/HCV + OD intervention or a five-session WP + OD intervention, which served as a comparison condition. The algorithm was designed to balance the number of couples per study arm via an adaptive, biased-coin procedure (Wei, Smythe, & Smith, 1986). The investigator who designed the randomization program was not involved in the conduct of the trial, but consulted on the statistical analysis. Investigators were masked to treatment