



Research Paper

Effects of naloxone distribution to likely bystanders: Results of an agent-based model



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ARTICLE INFO

Keywords:

Opioid overdose
Naloxone distribution
Harm reduction
Agent-based modeling

ABSTRACT

Background: Opioid overdose deaths in the US rose dramatically in the past 16 years, creating an urgent national health crisis with no signs of immediate relief. In 2017, the President of the US officially declared the opioid epidemic to be a national emergency and called for additional resources to respond to the crisis. Distributing naloxone to community laypersons and people at high risk for opioid overdose can prevent overdose death, but optimal distribution methods have not yet been pinpointed.

Methods: We conducted a sequential exploratory mixed methods design using qualitative data to inform an agent-based model to improve understanding of effective community-based naloxone distribution to laypersons to reverse opioid overdose. The individuals in the model were endowed with cognitive and behavioral variables and accessed naloxone via community sites such as pharmacies, hospitals, and urgent-care centers. We compared overdose deaths over a simulated 6-month period while varying the number of distribution sites (0, 1, and 10) and number of kits given to individuals per visit (1 versus 10). Specifically, we ran thirty simulations for each of thirteen distribution models and report average overdose deaths for each. The baseline comparator was no naloxone distribution. Our simulations explored the effects of distribution through syringe exchange sites with and without secondary distribution, which refers to distribution of naloxone kits by laypersons within their social networks and enables ten additional laypersons to administer naloxone to reverse opioid overdose.

Results: Our baseline model with no naloxone distribution predicted there would be 167.9 deaths in a six month period. A single distribution site, even with 10 kits picked up per visit, decreased overdose deaths by only 8.3% relative to baseline. However, adding secondary distribution through social networks to a single site resulted in 42.5% fewer overdose deaths relative to baseline. That is slightly higher than the 39.9% decrease associated with a tenfold increase in the number of sites, all distributing ten kits but with no secondary distribution. This suggests that, as long as multiple kits are picked up per visit, adding secondary distribution is at least as effective as increasing sites from one to ten. Combining the addition of secondary distribution with an increase in sites from one to ten resulted in a 61.1% drop in deaths relative to the baseline. Adding distribution through a syringe exchange site resulted in a drop of approximately 65% of deaths relative to baseline. In fact, when enabling distribution through a clean-syringe site, the secondary distribution through networks contributed no additional drops in deaths.

Conclusion: Community-based naloxone distribution to reverse opioid overdose may significantly reduce deaths. Optimal distribution methods may include secondary distribution so that the person who picks up naloxone kits can enable others in the community to administer naloxone, as well as targeting naloxone distribution to sites where individuals at high-risk for opioid overdose death are likely to visit, such as syringe-exchange programs. This study design, which paired exploratory qualitative data with agent-based modeling, can be used in other settings seeking to implement and improve naloxone distribution programs.

Introduction

In the United States, overdose deaths from opioid pain relievers and heroin rose dramatically in the past 16 years. The Centers for Disease

Control and Prevention reports a sharp increase in opioid deaths from 5,990 in 1999 to more than 33,000 in 2015 (“Drug Overdose Death Data,” 2016). Most of these deaths were preventable (“Facing addiction in America: The Surgeon General’s report on alcohol, drugs, and

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health.” 2016). One way to prevent these overdose deaths is by administering naloxone, an opioid overdose reversal drug. Naloxone is a full antagonist and binds to the same receptors in the central nervous system that receive opioids, thus displacing opioids for 30–90 min and reversing the respiratory depression caused by overdose that would otherwise lead to death. In overdose situations where fentanyl is present, repeated doses of naloxone may need to be administered before successful reversal (Armenian, Vo, Barr-Walker, & Lynch, 2017). Paramedics, emergency room physicians, and other health professionals in many countries have long used naloxone as an antidote to opiate overdose (Chamberlain & Klein, 1994; Clarke, Dargan, & Jones, 2005).

In recent years, numerous programs have been developed in communities to train and provide likely bystanders with naloxone for peer administration (Best et al., 2002; Galea et al., 2006; Maxwell, Bigg, Stanczykiewicz, & Carlberg-Racich, 2006). Bystanders are people who may have the opportunity to administer naloxone due to their proximity to someone experiencing an overdose. Bystanders are laypersons, not health professionals, and may include friends and family members as well as people who use opioids themselves and are likely to be nearby when an individual experiences overdose. Some states in the US have passed “standing order” policies to expand access to naloxone without a patient-specific prescription (Davis & Carr, 2017). The strategy is to distribute naloxone, along with a basic knowledge of how and when to use it, to laypersons who are likely to be nearby when someone experiences an overdose. Though overdose may occur within a 1–3 h window after using opioids, once overdose has begun and breathing is impaired, rescue breathing and naloxone should be administered immediately (“Facing addiction in America: The Surgeon General’s report on alcohol, drugs, and health,” 2016).

Some guidelines recommend that a bystander first call for Emergency Medical Services before administering naloxone and many states have ‘Good Samaritan Laws’ protecting the bystander and the user from arrest if the bystander reports an overdose, even if one or both were using drugs (Wickramatilake et al., 2017). However, many bystanders fear calling 911 due to potential arrest despite Good Samaritan Laws, and even when a fearful person does call for emergency aid they may devote valuable time removing drug paraphernalia from the site rather than tending to the person who has overdosed (Seal et al., 2003; Tobin, Davey, & Latkin, 2005). Thus, while bystanders might hesitate to call emergency services, they might administer naloxone themselves.

A growing body of research examines the impact of naloxone distribution programs targeted to laypersons. A recent review of 41 studies of overdose education and naloxone distribution efforts determined that layperson distribution programs are feasible, that laypersons are willing to administer naloxone to reverse opioid overdose, and that these programs can reduce overdose mortality (Mueller, Walley, Calcaterra, Glanz, & Binswanger, 2015). A meta-analysis using pooled data from four studies assessing the effectiveness of layperson distribution programs reported significantly increased odds of recovery after overdose when comparing these programs to no naloxone administration (OR = 8.58, 95% CI = 3.90 to 13.25) (Giglio, Li, & DiMaggio, 2015). The effectiveness of layperson-administered naloxone has resulted in overdose survival rates reaching as high as 96% (Bennett, Bell, Tomedi, Hulseley, & Kral, 2011; Clark, Wilder, & Winstanley, 2014; Doe-Simkins et al., 2014; Doe-Simkins, Walley, Epstein, & Moyer, 2009; Enteen et al., 2010; Lewis, Vo, & Fishman, 2017; Loimer, Hofmann, & Chaudhry, 1992; McDonald & Strang, 2016; Tobin, Sherman, Beilenson, Welsh, & Latkin, 2009).

The implicit mental model underlying our study is that distributing naloxone to likely bystanders will increase overdose reversals over and above reversals that result from bystanders calling emergency response teams. This conceptual framework has fueled policies supporting layperson reversal including the standing order approach as mentioned above, which is now active in many states in the US (Wickramatilake et al., 2017). It would be useful to examine how various dynamics

related to naloxone distribution might interact and then simulate their effects on overdose deaths, which could be used to refine and broaden existing interventions. To do this we conducted a sequential exploratory mixed methods design using qualitative data to inform an agent-based model (Creswell & Clark, 2011). In phase one of the design we conducted qualitative interviews with providers of substance use treatment programs as well as with consumers who were at risk for opioid overdose, had personal experience with naloxone, or had received services from substance use intervention programs. In phase two of the design we built an agent-based model to simulate the effects of various models of naloxone distribution as informed by our qualitative results and by the extant literature.

Our study builds on previous research that has demonstrated value of this design, particularly in studies addressing illicit substance use. Improving health outcomes for people who use opioids and other illicit drugs requires an understanding of the social context of those most affected, yet a long history of criminalizing and marginalizing this population demands the use of research methods that do not place these individuals at additional risk of exposure or exploitation. Building the agent-based model on the lived experiences of the community provides an important opportunity to magnify the use of ethnographic data, which can in turn inform policy and intervention development (Hoffer, Bobashev, & Morris, 2009).

Qualitative methods

Purpose of qualitative study

The purpose of the qualitative study was to explore feasibility and acceptability of various models of community-based naloxone distribution for layperson reversal. Interviews were chosen as the most appropriate method to elicit rich qualitative data given the sensitive nature of questions related to substance use. A harm reduction framework guided our selection of general issues to explore (Hawk et al., 2017), and topics related to layperson naloxone administration were derived from the literature (Bennett et al., 2011; Clark et al., 2014; Doe-Simkins et al., 2014, 2009; Lewis et al., 2017; Loimer et al., 1992; McDonald & Strang, 2016; Tobin et al., 2009). Domains that were explored with both providers and consumers focused on knowledge and experience with naloxone, access and barriers to naloxone distribution, thoughts about ideal naloxone distribution methods and messaging that would be appropriate for such methods, and finally subjective responses to naloxone administration.

Sample

From July through September 2016 we conducted qualitative interviews with 7 substance use treatment providers covering a large portion of the service area and with 22 people at high risk for opioid overdose (current or recent injection drug users). All interviews took place in urban or suburban settings in Southwestern Pennsylvania and took approximately 45–60 min to complete. We conducted online research to identify local substance use treatment agencies then called or emailed directors of the programs to explain the study purpose and invited them to participate in interviews. We included providers of abstinence-based services as well as those that provide harm reduction-informed services. Consumers who were interviewed were those at high risk for overdose, i.e., those actively using opioids, as well as individuals who had previously experienced overdose reversals personally or who had administered naloxone to reverse someone else’s opioid overdose. We also included consumers from Medication Assisted Treatment (MAT) programs, such as Suboxone clinics. Consumers were recruited through treatment providers, primarily by placing flyers in waiting rooms of provider settings or at the local syringe exchange van. Several other participants learned of our study via word-of-mouth referrals from their social networks. We purposively sampled consumers

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