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Protocol: A usability assessment of intramuscular, atomized intranasal, and nasal spray administration of naloxone by untrained community members

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Background: Opioid abuse and addiction is a growing epidemic both in the United States and globally. It impacts the health, social welfare, and economic stability of those directly affected and society as a whole. According to the National Institute on Drug Abuse there are approximately 2.1 million people in the United States with substance use disorders related to prescription opioid medications and another 467,000 addicted to heroin. Data from the Center for Disease Control National Vital Statistics System demonstrated that the number of drug poisonings involving opioid analgesics tripled from 2000 to 2014, and in 2010 opioid pain relievers were responsible for 82.8% of all unintentional deaths in the United States.[1] In an attempt to combat this epidemic many states have implemented community-based opioid overdose prevention programs aimed at increasing resources to combat addiction and distributing naloxone to community members. These programs increase knowledge of overdose prevention and the factors that increase a person's risk for overdose. Evaluations of these programs have also demonstrated that nonmedical bystanders are able to administer naloxone effectively after completing training.[2] Naloxone can be administered intravenously, intramuscularly, or via inhalation. Opioid overdose prevention programs are typically initiated by local and state governments, which allows for interprogram variability regarding the route of naloxone administration used by community members. Pre-hospital data has demonstrated that intranasal naloxone is a safe and effective alternative to intravenous naloxone.[3] A usability assessment comparing a naloxone auto-injector (Evzio®) to the use of a nasal atomizer suggested that the route of administration did impact the rate of successful naloxone administration by nonmedical community members.[4] Opioid overdose prevention programs typically utilize intranasal atomizers, nasal inhalers, or intramuscular administration routes. In 2016 we conducted a usability assessment of naloxone administered by community members who received training on how to use the naloxone device they were assigned. Our data supported that intranasal administration with an atomizer or spray resulted in a higher administration success rate when compared to intramuscular injection. Recently, New York, along with many other states, passed legislation allowing individuals to purchase naloxone over-the-counter without a prescription. This legislation has drastically expanded access to naloxone, but has reduced the opportunity to train community members purchasing the medication. We plan to conduct a usability assessment of simulated naloxone in community members in the absence of training to assess the rate of successful administration and time to successful administration.

Objectives:

Primary: The successful administration of simulated naloxone without training. A successful administration will be defined as administration of the simulated naloxone to the mannequin head or simulated flesh pad within 7 minutes and without any critical errors (defined below).

Secondary:

-Total time required to successfully administer the simulated naloxone without training.

-Comparison of successful administration with standard and simplified instrubtions

-Comparison of total time required for successful administration with standard and simplified instructions

-Likert-item assessment of the usability of the simulated naloxone product

-Likert-item assessment of usability of the naloxone administration instructions

Design: Single site, open-label, randomized usability assessment of intramuscular, intranasal, and nasal spray administration of simulated naloxone using standard (package-insert) or simplified (developed by study team) instructions. A convenience sample of participants will consent to volunteer in the study at a public venue. Participants will provide verbal consent and will be randomly assigned a simulated naloxone kit containing either intramuscular standard, intramuscular simplified, intranasal standard, intranasal simplified, nasal spray standard, or nasal spray simplified administration materials. The participant will enter a use scenario station where they will be asked to assemble and administer the simulated naloxone kit to a mannequin (intranasal and nasal spray) or simulated flesh pad (intramuscular). The participant will be instructed to start and will be timed until the simulated naloxone has been successfully administered or 7 minutes has elapsed. The participant will be observed by one trained investigator who will assess for successful administration of the simulated naloxone and critical errors. The environment will contain distracters to mimic a community based setting. Once the participant has successfully administered the simulated naloxone or 7 minutes has elapsed the timer will be stopped. Successful administration of simulated naloxone will be defined as administration of the agent without any critical errors occurring (defined below). Data collected will include demographics (defined below), successful administration of simulated naloxone, product assessment information, instruction assessment information, and time to successful administration of simulated naloxone.

Eligibility: healthy adults (18 years of age and older) at a public venue will be asked to participate in the study. Participants will be excluded if they are severely visually or hearing impaired (defined as: legally deaf, legally blind, unable to read print size provided on instructional handout, or unable to hear instructions from a research staff member), have previous naloxone administration training, are not English proficient, state that they may be pregnant, or they have previously participated in the trial.

Statistical Methods: All data will be analyzed using IBM SPSS Statistics software. Demographics data will be analyzed using descriptive statistics for continuous measures and percentages for categorical measures. The successful administration of naloxone will be compared between groups using the Chi-square test and a significant difference will be defined as a p-value of less than 0.05 for the result. The time to administration between groups will be assessed using a one-way ANOVA and a significant difference will be defined as a p-value of less than 0.05 for the result. The Likert-item data will be reported as percentage of response level and analyzed using a one-way ANOVA with a significant difference defined as a p-value of less than 0.05 for comparison between administration methods and instruction methods.

Data Analysis/Interpretation: As stated above data will be collected to assess both the successful administration of and time to administration of naloxone. The rate of successful administration will be

reported as a percentage for each of the three groups and analyzed using the Chi-square test. Successful administration is defined as administration of the simulated naloxone within 7 minutes without committing any critical errors. Critical errors are as follows:

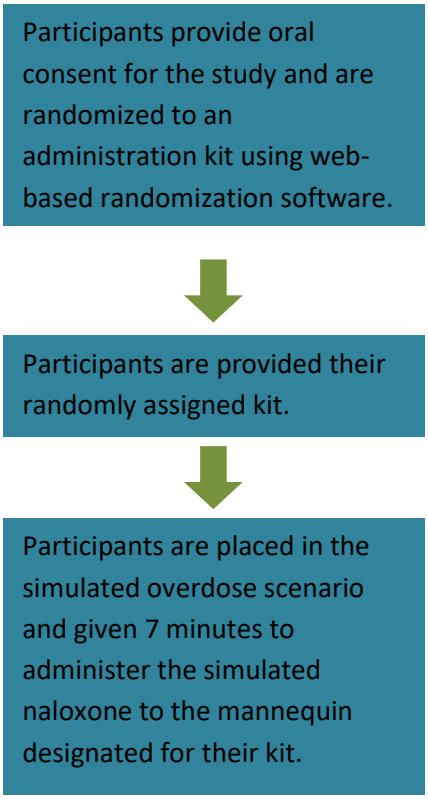
- Intranasal (atomizer): failure to remove both yellow caps from bristoject, failure to remove cap from simulated naloxone, failure to attach atomizer, failure to attach simulated naloxone, drug leak prior to administration, administration in only one nostril, and failure to administer within 7 minutes.
- Intramuscular: failure to attach the needle to the syringe, failure to remove cap from simulated naloxone, failure to draw up >90% (0.9 mL) of the simulated naloxone, failure to puncture simulated flesh pad with needle, failure to push entire volume of fluid in the syringe into the simulated flesh pad, and failure to administer within 7 minutes.
- Intranasal (spray): failure to place the tip of the device into one nostril, failure to depress the device and release the simulated naloxone, failure to administer within 7 minutes.

Time to successful administration will be reported using descriptive statistics (mean time to administration) and analyzed using a one-way ANOVA. Times for participants who commit a critical error or who do no administer the simulated naloxone within 7 minutes will not be included in the analysis. The Likert-item data will be reported as a median with an inter-quartile range and analyzed using a one-way ANOVA.

A route of administration will be considered to be more user-friendly if it demonstrates a statistically significantly higher rate of successful administration compared to another route of administration. Additionally, a route or instruction type will be considered user preferred if the Likert-item data demonstrates a significantly better score on usability.

Study Procedures: No study procedures will be performed on study participants.

Diagram of Study Design:



Investigators observe the administration and record if the administration is successful, the time to administration, and the critical error that occurred if applicable. Survey data is

Works Cited

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