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Study protocol for a multisite randomized controlled trial of a peer navigator intervention for emergency department patients with nonfatal opioid overdose

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Abstract

Background: Patients presenting to emergency departments (EDs) after a nonfatal opioid-involved overdose are at high risk for future overdose and death. Responding to this risk, the New York City (NYC) Department of Health and Mental Hygiene operates the Relay initiative, which dispatches trained peer "Wellness Advocates" to meet patients in the ED after a suspected opioid-involved overdose and follow them for up to 90 days to provide support, education, referrals to treatment, and other resources using a harm reduction framework.

Methods: In this article, we describe the protocol for a multisite randomized controlled trial of Relay. Study participants are recruited from four NYC EDs and are randomized to receive the Relay intervention or site-directed care (the control arm). Outcomes are assessed through

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.cct.2023.107111.

survey questionnaires conducted at 1-, 3-, and 6-months after the baseline visit, as well as through administrative health data. The primary outcome is the number of opioid-related adverse events, including any opioid-involved overdose or any other substance use-related ED visit, in the 12 months post-baseline. Secondary and exploratory outcomes will also be analyzed, as well as hypothesized mediators and moderators of Relay program effectiveness.

Conclusion: We present the protocol for a multisite randomized controlled trial of a peer-delivered OD prevention intervention in EDs. We describe how the study was designed to minimize disruption to routine ED operations, and how the study was implemented and adapted during the COVID-19 pandemic. This trial is registered with ClinicalTrials.gov [NCT04317053].

Keywords

Overdose; Opioid use disorder; Addiction; Emergency care; Peer intervention; Randomized controlled trial

1. Introduction

Overdose deaths are an urgent public health issue in the United States (U.S.) and worldwide. In the U.S., annual overdose deaths rose dramatically—by over 30%—from 2020 to 2021 [1]. Over 70% of overdose deaths involve an opioid, with deaths increasingly driven by synthetic opioids such as fentanyl [2]. In New York City (NYC), 2668 people died from an overdose in 2021 [3]. As is the case nationally, fentanyl is highly prevalent, and in 2021 was involved in 80% of NYC overdose deaths [3].

Emergency department (ED) visits for overdose have increased year-to-year [4]. Individuals who have experienced a prior nonfatal overdose are at much greater risk of subsequently dying from overdose [5–8]; over 5% of patients presenting to an ED after a nonfatal overdose die within the next year [9,10]. Additionally, ED patients may have few other contacts with health care providers [11]. ED visits for nonfatal overdose present an opportunity to reach a high-risk, underserved patient population [12], and experts have called on EDs to do more to address the overdose crisis [13–15]. A growing literature has described ED-based interventions for patients at risk for overdose, including naloxone distribution and education, brief counseling and referral to treatment, and ED initiation of buprenorphine through ED provider prescribing and/or connecting patients with “bridge clinics” after their ED visits, though evidence for their effectiveness remains limited [14–19]. In Rhode Island, EDs have implemented a peer recovery coach program for patients at risk for overdose [20]. Although a randomized controlled trial (RCT) did not show a significant difference in subsequent treatment engagement for patients receiving the peer coach intervention compared to patients receiving a standard behavioral intervention delivered by a social worker, the lack of a control group limits the conclusions that can be drawn from this study [21]. Studies in other fields, including cancer and HIV care, have shown positive results from peer navigator interventions [22–25]. Research suggests that a peer-led approach is particularly well-suited to patient populations that are highly stigmatized and potentially mistrustful of health care professionals [26]. Peer navigators, by drawing on their lived experiences, may aid in reducing stigma and are positioned to serve as effective positive role models [27]. In summary, theory and past research suggest the

potential promise of peer-based interventions, yet there is still very limited knowledge about the effectiveness of such approaches for ED patients at risk for overdose.

NYC's multi-pronged response to overdose includes Relay, a novel initiative operated by the NYC Department of Health and Mental Hygiene (DOHMH) that utilizes trained peer "Wellness Advocates" to connect with NYC ED patients following suspected opioid-involved overdose [28]. Wellness Advocates provide support, education, and referrals to treatment and other resources in the ED and for up to 90 days following the ED visit. Relay began in 2017 and has expanded to 14 NYC EDs. The initiative has been described in the literature [28], but its effectiveness on patient outcomes has not yet been studied. We seek to fill this research gap by conducting a multisite, RCT of the Relay peer-led opioid overdose response initiative in NYC EDs. Results will provide critical knowledge relevant to Relay and more broadly to peer-based overdose response approaches in EDs.

2. Methods

2.1. Study design

This two-arm RCT compares ED site-directed care (control) to the Relay intervention for patients presenting to the ED with a suspected opioid-involved overdose (see Section 2.3 for details). As per standard Relay processes, when patients present to the ED with a suspected opioid-involved overdose, ED staff call the Relay hotline. The hotline operator then notifies the research team, and a research assistant (RA) meets the patient in the ED to assess the patient for study eligibility. Study participants are randomly assigned to the site-directed care or Relay arm; a Relay Wellness Advocate is dispatched for participants assigned to the Relay arm. Fig. 1 shows a schematic of the study design. The study was approved by the Institutional Review Board (IRB) at NYU Grossman School of Medicine.

2.2. Setting

At the time of study initiation, Relay operated in 13 NYC EDs. The study is being conducted at four of those EDs: St. Barnabas Hospital (in the Bronx), NYU Langone Health-Tisch (on Manhattan's east side), NYU Langone Hospital-Brooklyn (in southern Brooklyn), and Mount Sinai Beth Israel (in Manhattan's East Village neighborhood). These EDs were selected with consideration for their volume of calls to the Relay program, research capacity, and geographic diversity. Each study ED had participated in Relay for at least a year prior to the start of the study. Each Relay hospital has a designated "ED Champion," an ED staff member who works with Relay staff to provide training on Relay, both at launch and on an ongoing basis by conducting pop-in visits, staff huddles, and presentations. Relay staff also distribute promotional items to ED staff, including pens, lanyards, and mousepads with the Relay phone number.

2.3. Study population and eligibility

When a study hospital ED provider calls the Relay hotline, the operator immediately contacts the appropriate study team member. Study RA shifts generally span weekdays 7:00 am to 1:00 am and weekends 7:00 am to 6:00 pm. If a Relay hotline call is received from a

study ED at a time when no RA is available, the hotline operator activates a Relay Wellness Advocate directly to see the patient (i.e., the patient is not assessed for study eligibility).

Patients for whom the study team receives an alert from the Relay hotline are assessed for eligibility. Eligibility criteria include: age 18 years or older; English-or Spanish-speaking; living in NYC; and presenting to the ED with a suspected opioid-involved overdose. An opioid-involved overdose includes any overdose severity involving at least one suspected opioid, whether or not it was the primary drug used, whether or not use of the opioid was intentional (i.e., patients who overdose after using non-opioid drugs suspected to be contaminated with an opioid are eligible), and whether or not naloxone was administered.

In their eligibility assessment, RAs ascertain patient self-report of having had an opioid-involved overdose with the following question: "*The next question is about taking too much drugs or medications/pills, and/or drinking too much alcohol. This is sometimes called 'poisoning,' 'passing out,' 'nodding out,' 'blacking out,' or an 'overdose' or 'OD.' Did you have an experience like this today that involved any opioid?"* "Opioids" are described as including opioid medications for pain or addiction treatment in addition to illicit opioids, and patients are instructed, *"please let me know if you used any opioid today, even if you don't think the opioid was the cause of the overdose."* This question was adapted from research conducted by Bohnert, et al. with ED patients [29]. If the patient answers "no," RAs ask the patient's ED care provider whether they believe based on clinical presentation (e.g., physical exam findings, response to naloxone) that the patient had an opioid-involved overdose. If *either* the patient or their ED provider reports a suspected opioid-involved overdose, the patient is potentially eligible for study participation.

Study exclusion criteria include: unable to provide informed consent; currently incarcerated or in police custody; known to be pregnant; already participating in the study; or currently engaged in Relay. Additionally, one of the study EDs, which has a relatively lower volume of Spanish-speaking patients, does not have Spanish-speaking RAs so patients who cannot speak English are excluded at that site.

2.4. Study recruitment and consent

The study team member receiving the Relay hotline referral generally arrives at the ED within one hour to assesses the patient for study eligibility. RAs follow a standardized series of eligibility screening questions and procedures and obtain written informed consent. If the patient is too sedated (e.g., due to overdose) or agitated (e.g., due to opioid withdrawal) at the time of initial RA assessment, RAs remain in the ED to reassess the patient at regular intervals. If there is any question about a patient's capacity to provide informed consent, RAs consult the ED treating team (e.g., attending physician) and/or complete a brief consent capacity quiz [30]. If the patient is ineligible or declines study participation, RAs call the Relay hotline to activate a Wellness Advocate for the patient.

2.5. Randomization

Enrolled patients are randomly assigned to the site-directed care or Relay arm. Randomization uses a 1:1 ratio and is stratified by site; permuted blocks with variable block

sizes are used to maintain balance over time and prevent prediction of assignment by RAs. Given the nature of the intervention, blinding is not possible for study participants or staff.

2.6. Control group (site-directed care)

Participants randomized to the site-directed care arm receive a standard set of education and materials provided by RAs: 1) overdose education and naloxone distribution (OEND), 2) list of local addiction treatment programs, and 3) flyer with information about Relay. OEND includes RAs providing participants with 1–2 naloxone kits and overdose education materials (including naloxone use instructions). RAs also give participants a printed list of local addiction treatment programs and a flyer with information about Relay including a telephone number participants can call to receive Relay services if desired after their ED visit. DOHMH and research staff track any Relay services provided in this participant-initiated manner. Clinical equipoise exists to justify an RCT, as there has not yet been research demonstrating a convincing benefit of peer navigator approaches for ED patients presenting after opioid overdose compared to standard ED care. After 12-month study follow-up for the primary outcome, DOHMH will attempt to contact participants who have been assigned to the site-directed care arm to offer Relay services.

As is the case across the U.S., standard care at a given ED for patients presenting after overdose is variable. Study EDs have implemented their own protocols and initiatives for patients who present with opioid use disorder or after overdose, which vary by site and are provided independent of the study. For example, one study ED provides fentanyl test strips and two study EDs have pharmacist-driven naloxone distribution for relevant patients. The study team will track the overdose prevention-related ED care that study participants receive with a baseline visit exit survey.

2.7. Intervention (Relay)

Relay is delivered by trained peer navigators (“Wellness Advocates”) who have lived experience with substance use (see Appendix for details on Wellness Advocate training). After being dispatched to an ED, a Wellness Advocate attempts to contact the patient within one hour, usually by meeting them in person in the ED, or by talking with them by phone if meeting in person is not feasible (e.g., patient expected to leave the ED before the Wellness Advocate would arrive). Usually when patients present to an ED after a nonfatal overdose there is a period of several hours when they are assessed, observed, and possibly complete additional testing (e.g., laboratory studies). Thus, Wellness Advocates have an opportunity to meet with patients while they are still in the ED, which is particularly important because many patients have unreliable telephone access or practical barriers to attending scheduled follow-up visits. The initial meeting focuses on patient engagement and providing peer support, using a person-centered harm reduction approach [31]. The Wellness Advocate describes Relay, obtains consent for participation in Relay, and collects patient contact information. They provide brief, tailored overdose risk reduction education; opioid overdose rescue training and naloxone kit distribution for the patient and any friends or family members; referrals and navigation to harm reduction, drug treatment, or other services (if this is of interest to the patient); and support in the ED (e.g., helping mediate communication between the patient and ED treatment team). The Wellness Advocate also

offers a care bag which includes a toothbrush and toothpaste, socks, a water bottle, a snack, a public transportation ticket, and educational materials.

After the initial ED encounter, a Wellness Advocate follows up with the participant within 24–48 h of discharge to discuss further how Relay can assist the participant in avoiding future overdose. The Wellness Advocate continues to follow up and provide support and connections to services for up to 90 days, with occasional extensions to 120 days permitted on a case-by-case basis. These follow-up contacts can occur by telephone (including text message) or in person. Contact frequency is dependent on participant needs and desires, with follow-up intensity decreasing over the course of three phases following a Critical Time Intervention approach [32–34] (see Appendix for details). Wellness Advocates are assigned no >20 participants at one time.

Both in the ED and at follow-up visits, Wellness Advocates serve as positive role models while providing tangible and instrumental support to foster motivation, reduce stigma, and build individuals' capacity to change risk behaviors and initiate treatment.

2.8. Study procedures

An overview is shown in Fig. 1. Procedures conducted at the baseline ED visit following eligibility assessment and informed consent are: baseline questionnaire, site-directed care or Relay intervention, collection of identifying and locator form information, exit survey, and incentive payment. Follow-up questionnaires are administered at 1-month, 3-month, and 6-months. For all questionnaires, RAs read questions and response choices aloud and record responses using REDCap [35].

2.8.1. Baseline questionnaire—RAs administer baseline questionnaires to all study participants while they are in the ED. Baseline questionnaires take approximately 45–60 min and capture self-reported prior nonfatal overdose history, overdose risk behaviors, naloxone behaviors, readiness to change across various domains, opioid overdose knowledge, perceived stigma toward people who use drugs, service use and access, substance use history, health, and sociodemographics. See Section 2.10 for details.

2.8.2. Collection of identifier and locator form information—To allow for linkage with administrative data for outcome assessment, RAs collect participant personally identifying information including full name, birthdate, social security number (if the participant has one), and medical record number.

To facilitate contact for follow-up questionnaires, RAs collect detailed locator form information, including participants' phone numbers, addresses, email addresses, secondary contacts (e.g., friends, case workers), and social media handles. Collecting such detailed locator information is necessary given that many participants are homeless or unstably housed and do not have a stable phone number. While restricting study eligibility to those who had cellular phones would enhance reliability to follow-up, we felt that this would unacceptably alter the representativeness of the study sample. Participants are also given a study "contact card" which has the study team phone number and the schedule of follow-up assessments, so that they can reach the study team if their contact information has changed.

2.8.3. Baseline visit exit survey—The baseline visit exit survey documents relevant services received by the participant in the ED and includes both an RA-completed checklist (based on RA observation and review of electronic medical records for the visit) and a patient-reported assessment. RAs complete the baseline visit exit survey after all study procedures have been completed, ideally near the conclusion of the participant's ED visit.

2.8.4. Follow-up assessments (1-month, 3-month, and 6-months post-baseline)—Follow-up assessments are conducted 1-, 3-, and 6-months after the baseline visit. At each time-point, RAs administer a questionnaire by phone or, more rarely, in person. Questionnaires are identical at each follow-up time point except questions with "look back periods" use different periods capturing the time since completion of the last study questionnaire.

To enhance follow-up assessment completion rates, RAs make multiple attempts to contact participants, using all locator form information. Particularly given anticipated challenges in reaching the study population for follow-up questionnaires, generous time windows are allowed: +14 days/−7 days for the 1-month assessment and + 30 days/−14 days for the 3- and 6-month assessments.

2.9. Fidelity assessment

The baseline visit exit survey (Section 2.8.3) assesses the interventions relevant to overdose that the participant received in the ED, from the Wellness Advocate (for participants assigned to the Relay arm) or ED providers. RAs also complete a check-list confirming they have delivered the elements of the site-directed care arm (Section 2.6). Participants are asked at follow-up assessments (Section 2.8.4) about any additional Relay contacts they have received in the interval since the last assessment. Relay Wellness Advocates also document each participant encounter in an electronic database; data collected include the type of interaction (e.g., in-person, telephone), services provided, and activities performed during the session. This data will be used for analyses at the conclusion of the study to consider intervention dose and fidelity, including fidelity to the Relay program model (see Appendix for details).

2.10. Outcomes

Study outcomes are summarized in Table 1 and detailed in the sections that follow.

2.10.1. Data sources—There are three data sources for outcome assessment: 1) self-reported follow-up assessments, 2) NYC Regional Health Information Organization (RHIO) administrative data, and 3) overdose death data provided by NYC DOHMH.

There are two RHIOs covering NYC: Healthix and Bronx RHIO. Together, these RHIOs cover visits to nearly all hospitals in NYC aside from Veterans Affairs hospitals. Data for each RHIO include dates of ED visits and diagnostic codes connected with each visit; data are generally available in near-real time. Study investigators will provide RHIO administrators with a list of participants' personally identifying information, which will be used to conduct a match with the RHIO data.

Investigators will provide a list of participants' personally identifying information to the DOHMH Office of Vital Statistics, which will be used to match study participants to data on all deaths occurring in NYC. These data include cause of death, substances involved in the death based on post-mortem toxicology reports from the NYC Office of the Chief Medical Examiner, and whether the death was opioid-related.

2.10.2. Primary outcome—The primary outcome is a composite measure of opioid-related adverse events in the 12 months following the baseline ED visit. Opioid-related adverse events include any opioid-involved overdose (fatal or nonfatal) or any other substance use-related ED visit. Including any substance use-related ED visit (rather than only overdose or opioid-specific visits) reduces concerns related to potential misclassification and lack of sensitivity in visit diagnosis coding [37].

The primary outcome will be ascertained by administrative data abstraction supplemented with self-reported data from follow-up questionnaires. Our approach is to utilize the strengths and mitigate the weaknesses of administrative and self-report data by using both together. Any fatal or non-fatal opioid-involved overdoses or substance-use related ED visits are expected to be found in administrative data for all participants for a full year of follow-up. Self-reported data will capture non-fatal opioid-involved overdoses that do not lead to an ED visit, but will not cover the second half of the follow-up year and will sometimes be missing. However, missing self-report data will be imputed multiple times under a missing at random assumption, allowing outcome estimation for a full year. This is feasible even for participants missing all three follow-up interviews, because opioid-related adverse events at baseline and administrative data will be available for all participants.

2.10.3. Secondary and exploratory outcomes—Secondary outcomes (Table 1) include: initiation of medication for opioid use disorder (MOUD); overdose risk behaviors; self-reported opioid-involved overdose; time to next opioid-involved overdose; all-cause ED visits; ED visits for opioid overdose; and ED visits for other substance use reasons. Exploratory outcomes (Table 1) include: health services contacts (medical, mental health, harm reduction program); possession of naloxone; number of times naloxone used; naloxone carrying by social network members; all-cause deaths; opioid-involved overdose deaths; and any overdose deaths. Participants assigned to the Relay arm are also asked questions about the usefulness of and their satisfaction and comfort with speaking with a Wellness Advocate (with responses on a 10-point scale) at baseline and follow-up time points.

2.10.4. Mediators and moderators—We will examine multiple potential mediators and moderators (Table 2) of the effects of Relay.

2.11. Analysis

The primary outcome analysis will use a Poisson generalized linear regression model to evaluate the intervention effect on the total number of opioid-related adverse events. We will include adjustment for study site, as well as baseline factors that may be unbalanced across arms. The primary effect measure will be the incidence rate ratio comparing Relay to site-directed care. If there is overdispersion of the count outcome due to some participants

being routinely high utilizers of the ED, we will use a negative binomial model instead of a Poisson model.

For analysis of secondary and exploratory outcomes we will compare the Relay and site-directed care arms using models as appropriate for count vs. categorical variables, and again adjusting for factors that may be unbalanced across study arms. We will perform additional exploratory analyses examining differences in outcomes by study site.

2.11.1. Dose response analysis—The primary analysis is an intent-to-treat analysis, with all participants retained in their original randomly assigned arm. We will also conduct a secondary dose response analysis to examine treatment effects based on actual level of receipt of the Relay intervention (e.g., number, type, and duration of contacts). Intervention dose is captured in the baseline visit exit survey and the follow-up assessments conducted by study research staff as well as Relay program data on Wellness Advocate contacts with participants. We will examine the impact of dose using randomly assigned study arm as an instrumental variable [49].

2.11.2. Mediation and moderation analysis—We will examine intervention effect mediation and moderation in structural equation models (SEMs). We will estimate SEMs to measure the degree to which the Relay intervention affects mediating variables and will estimate the impact of these putative mediators on the risk of opioid-related adverse events and other outcomes. Models will be fit that include paths from Relay to mediators and outcomes, and paths from mediators to outcomes. The magnitude and significance of the direct and indirect effects of Relay will be provided. Bootstrapping will be used to derive estimates of mediated (indirect) effects. To capture potential effect moderation (regarding effects of Relay on mediators and effects of mediators on outcomes), SEMs will include interaction terms [50].

2.12. Sample size

The target sample size is 350 participants. Please see the Appendix for sample size calculations.

2.13. Safety and data monitoring including study stopping rule

An external Data and Safety Monitoring Board (DSMB) meets twice yearly. The trial has a stopping rule based on fatal opioid overdose; the study will be stopped if we observe a rate ratio of overdose deaths in the site-directed care arm versus the Relay arm of ≥3.0 and a one-sided p-value of <0.01, or a one-sided p-value of <0.01 when the rate ratio is undefined due to zero deaths in the Relay arm.

2.14. Study incentives

RCT participants receive $75 after the baseline visit, $30 after each of the 1- and 3-month follow-up assessments, and $50 after the 6-month follow-up assessment. At the baseline visit participants are given a Greenphire ClinCard, which can be used either as a prepaid credit card or as a debit card to withdraw money from an ATM (which incurs a fee) or to receive money from a bank teller (which does not incur a fee but requires proof of

identification). RAs load onto the participant's ClinCard the compensation amounts for follow-up assessments upon completion of each assessment. Participants who have lost their ClinCard are mailed a new one.

2.15. Effects of the COVID-19 pandemic

The study's start was delayed due to the COVID-19 pandemic. In-person Relay responses to the ED were paused early in the pandemic through summer 2020. Study enrollment began in October 2020. Research staff wear appropriate personal protective equipment (PPE), depending on the requirements of the specific ED. The pandemic has created changes in ED volume and processes, as well as changes, at times, related to the Relay intervention itself. For example, during the pandemic, post-ED follow-up visits with Wellness Advocates have shifted to primarily be telephonic. Pandemic-related effects on the study are being monitored and will be described in future publications.

3. Discussion

In this article, we describe the protocol for an RCT of Relay, a peer-based intervention for patients presenting to an ED after suspected opioid-involved overdose. Several elements of the study protocol are unique and may be of interest to others seeking to conduct related research. First, we designed this trial to minimize disruption to routine ED operations, which became especially important during the COVID-19 pandemic when EDs faced significant new stressors. The ED provider workflow remains unchanged: when a patient presents after a suspected opioid-involved overdose they call the Relay hotline to provide the operator with information about the patient. The Relay hotline call center then routes the information to our research team, and an RA travels to the ED to assess the patient for study eligibility.

Design of the RCT benefitted from robust collaboration between the study investigators and the NYC DOHMH. Leaders from NYC DOHMH reached out to the study investigators due to their interest in evaluating the effectiveness of Relay. While the DOHMH and the NYU School of Medicine study teams meet regularly, the study investigators do not influence Relay's design or operations.

Leaders in addiction and emergency medicine have called for a more coordinated and robust response in EDs following overdose [14]. Trials examining brief interventions such as motivational interviewing have shown mixed results related to future overdose risk among ED patients [29,51]. A growing body of research has examined buprenorphine initiation by EDs [16–19,52–56]. However, less research has examined peer-based interventions for ED patients [20,21,57–59]. One observational retrospective study examined the Rhode Island Lifespan Opioid Overdose Prevention (LOOP) program—which, similar to Relay, uses peers to engage and support patients after an overdose event in the ED and for 90 days following the event—compared to naloxone distribution alone and usual care [57]. Non-significant trends were observed suggesting the recovery coach intervention was associated with a decreased number of days to opioid agonist therapy (OAT) initiation and increased number of days to death after an ED visit, though those receiving the recovery coach intervention appeared less likely to initiate OAT overall [57]. Other studies of the same intervention found that peer recovery coach consultation in EDs was feasible and sustainable [20], and

used qualitative interviews to examine program barriers and facilitators [60]. More recently, a RCT comparing the peer recovery coach intervention versus a social worker delivered intervention for ED patients presenting for overdose or having opioid use disorder found no difference between the groups in the primary outcome of connection to substance use treatment within 30 days of the ED visit, though both groups had notably high rates of connection to treatment (approximately 30%) [21]. Similar to Relay, the peer-delivered intervention included a 90 day follow-up component. Other current trials that utilize peer coaches include a NIDA Clinical Trials Network trial (CTN-0107) [61] and a multisite cluster RCT in Indiana EDs [62].

The Relay intervention, with its peer-based and individually tailored harm reduction model, may hold promise for reducing future overdose risk among ED patients. Because Relay is administered centrally by NYC's public health department, it can be scaled up rapidly in multiple EDs across the city. Similar models of centralized program control rather than requiring each individual ED to staff and implement a new program may be scalable across the country. As the overdose crisis continues to worsen, discovery and implementation of effective, scalable interventions are urgently needed, and our RCT represents an important contribution to the evidence base for one promising approach.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Data availability

No data was used for the research described in the article.

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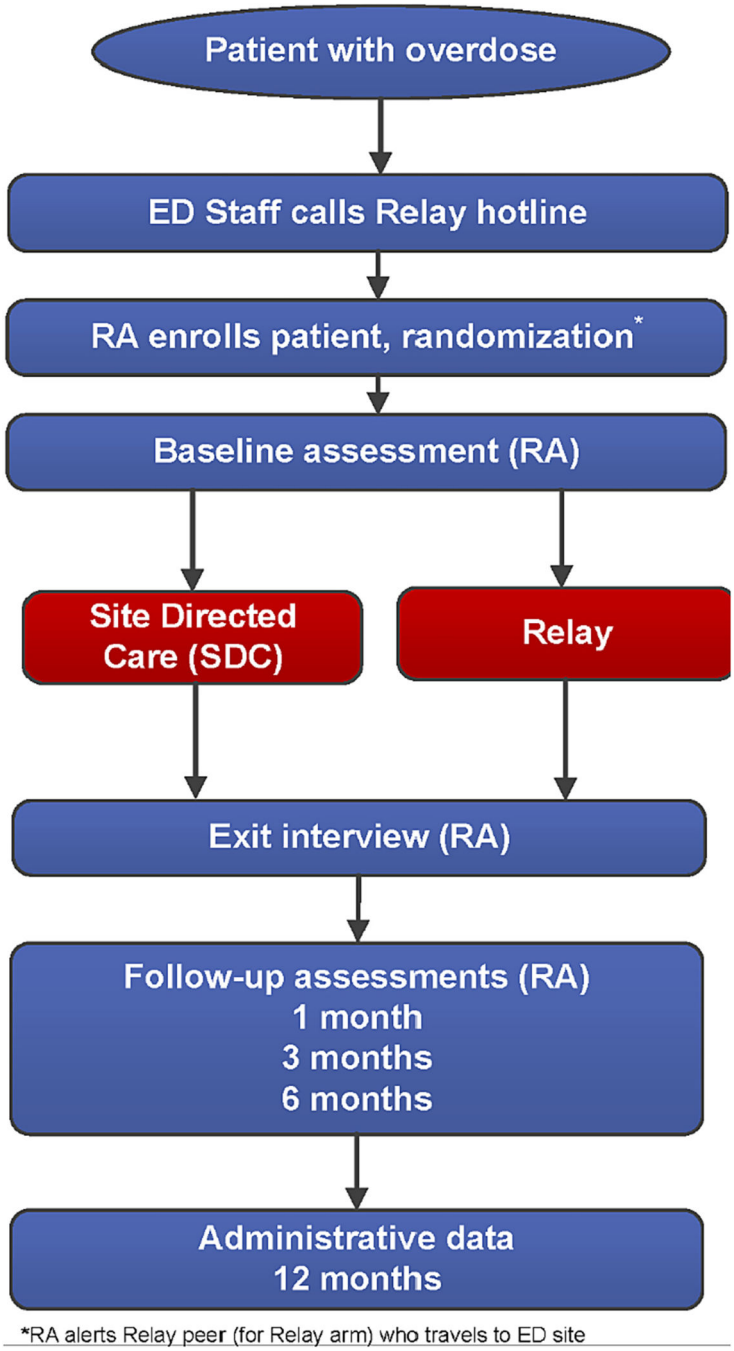

Fig. 1.
Study design.

Table 1

Study outcomes.

	Measures	Details
Primary outcome		
Opioid-related adverse events	Opioid-involved overdose (OD) (fatal or nonfatal) plus substance use related ED visits (12 mo. post-baseline)	Vital statistic and RHIO[a] data for deaths and ED visits; nonfatal opioid-involved OD by self-report[b] using question from Bohnert, et al. [29]
Secondary outcomes		
MOUD treatment initiation	Outpatient MOUD received among those not already on MOUD at baseline (90 days post-baseline)	Self-reported information about types and timing of MOUD use.
Overdose risk behaviors	Risk behavior questionnaire score based on frequency of 11 risk behaviors (1, 3, and 6 mo. post-baseline)	OD risk behavior questionnaire adapted from Bohnert, et al. [29]
Opioid-involved overdose	Number of self-reported opioid-involved ODs (6 mo. post-baseline)	Self-report using question adapted from Bohnert, et al.
Time to subsequent overdose	Time to first self-reported opioid-involved OD event post-baseline	Based on self-reported date(s) of OD(s).
ED visits	All cause, substance use related, and opioid OD specific ED visits (12 mo. postbaseline)	Administrative data (RHIOs) using ED visit date and diagnosis codes.
Exploratory outcomes		
Naloxone behaviors	Possession of naloxone, number of times naloxone used, naloxone carrying by members of social network (1, 3, and 6 mo. post-baseline)	Self-report of whether participant has own naloxone, is carrying it, how often carries, and knows where to get; how many times administered naloxone to someone else; and if have any friends or family members who carry naloxone (author-developed questions)
Health services contacts	Medical, mental health, harm reduction program (1, 3, and 6 mo. post-baseline)	Self-report of outpatient medical and mental health care receipt (adapted from Gelberg, et al. [36]) and harm reduction program use (including streetbased or outreach services)
Death	Death from any cause, opioid-involved OD deaths, any OD deaths (12 mo. post-baseline)	From NYC DOHMH Office of Vital Statistics and Office of the Chief Medical Examiner data

[a] Regional Health Information Organization (RHIO) administrative data on ED visits in the 12 months post-baseline.

[b] All self-reported outcomes are from survey questionnaires administered at the baseline ED visit and at 1-, 3-, and 6-months after baseline.

Table 2

Mediators and moderators of study outcomes.

	Measures[a]	Details
Mediators		
Opioid overdose knowledge	12-item scale with 3 subscales (opioid knowledge, opioid OD knowledge, opioid OD response knowledge)	Brief Opioid Overdose Knowledge (BOOK) questionnaire [38,39]
Motivation to change	10-point ruler for importance of making a change; readiness to make a change; and confidence one could make a change for each of 4 items: 1) carrying naloxone, 2) initiating MOUD, 3) attending an addiction treatment program, 4) reducing OD risk	Adapted from prior research [40]
Social/emotional support	4-items on emotional support	PROMIS short form for emotional support [41]
Perceived stigma	8-item scale on perceptions of the prevalence of stigmatizing beliefs toward substance use	Perceived Stigma Toward Substance Users Scale [42]
Barriers to services	1 item assessing whether needed but did not get help with drug use, 2 items assessing barriers (e.g., fear, lack of knowledge, tangible barriers)	Adapted from prior research by Gelberg, et al. [36]
Moderators		
Demographic characteristics	Age; gender; race and ethnicity reported at baseline	Self-reported
Sexual orientation	Reported at baseline	Self-reported on questions adapted from CDC National Health Interview Survey [43]
Relationship status	Reported at baseline	Self-reported
Housing status	Current homelessness (spent last night in a shelter or unsheltered); recent homelessness; current unstable housing	VA Homelessness Screening Clinical Reminder [44] and Accountable Health Communities survey [45] questions
Mental and physical health	Depression; anxiety; overall physical health (excellent, very good, good, fair, or poor); level of pain interfering with daily activities (not at all, a little bit, moderately, quite a bit, extremely)	Depression indicated by PHQ- 2 score ≥ 3. Anxiety indicated by GAD-2 score ≥ 3. Physical health questions from CDC HRQOL-4 [46] and SF-12 [47]
Substance use history	Lifetime and recent (past 3 mo.) polysubstance use and risk level; injection drug use; types of opioids used; whether this was first OD	Baseline responses from ASSIST [48]
Criminal justice involvement	Lifetime and current (past 3 mo.) history of being in jail or prison	Self-reported at baseline

[a] Collected at baseline and at 1-, 3-, and 6-months after baseline unless otherwise specified.