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STUDY PROTOCOL

ADDICTION SSA

Preventing Overdose Using Information and Data from the Environment (PROVIDENT): protocol for a randomized, population-based, community intervention trial

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Abstract

Background and Aims: In light of the accelerating drug overdose epidemic in North America, new strategies are needed to identify communities most at risk to prioritize geographically the existing public health resources (e.g. street outreach, naloxone distribution efforts). We aimed to develop PROVIDENT (Preventing Overdose using Information and Data from the Environment), a machine learning-based forecasting tool to predict future overdose deaths at the census block group (i.e. neighbourhood) level.

Design: Randomized, population-based, community intervention trial.

Setting: Rhode Island, USA.

Participants: All people who reside in Rhode Island during the study period may contribute data to either the model or the trial outcomes.

Intervention: Each of the state's 39 municipalities will be randomized to the intervention (PROVIDENT) or comparator condition. An interactive, web-based tool will be developed to visualize the PROVIDENT model predictions. Municipalities assigned to the treatment arm will receive neighbourhood risk predictions from the PROVIDENT model, and state agencies and community-based organizations will direct resources to neighbourhoods identified as high risk. Municipalities assigned to the control arm will continue to receive surveillance information and overdose prevention resources, but they will not receive neighbourhood risk predictions.

Measurements: The primary outcome is the municipal-level rate of fatal and non-fatal drug overdoses. Fatal overdoses will be defined as unintentional drug-related death; non-fatal overdoses will be defined as an emergency department visit for a suspected overdose reported through the state's syndromic surveillance system. Intervention efficacy will be assessed using Poisson or negative binomial regression to estimate incidence rate ratios comparing fatal and non-fatal overdose rates in treatment vs. control municipalities.

Comments: The findings will inform the utility of predictive modelling as a tool to improve public health decision-making and inform resource allocation to communities that should be prioritized for prevention, treatment, recovery and overdose rescue services.

KEYWORDS
Machine learning, overdose, overdose mortality, overdose risk, predictive analytics, predictive modelling, protocol, RCT, United States

INTRODUCTION

North America continues to experience an unprecedented epidemic of drug overdose deaths [1]. In the United States, mortality rates from unintentional drug-related overdoses have increased nearly exponentially for more than three decades [2], with more than 70 000 deaths in 2019 alone [3]. Provisional data from 2020 indicate that the rate of overdose deaths are continuing to increase [4], due in part to the adverse effects of the COVID-19 pandemic on the illicit drug supply, access to and retention in treatment, social isolation and other socio-structural risk factors for overdose (e.g. unemployment, loss of housing) [5–7].

To maximize population-level impact, strategic responses to address the nation's overdose crisis ought to focus on the highest-risk communities. Recent studies demonstrate that the magnitude of overdose morbidity and mortality can vary substantially within states and throughout neighbourhoods within cities [8]. However, despite myriad federal and state-wide initiatives [9–14], few interventions are focused in the most heavily affected neighbourhoods [15]. For example, although pharmacy- and community-based distribution of naloxone are evidence-based strategies to reduce opioid overdose deaths [16, 17], neighbourhood-level disparities in access to community overdose education and naloxone distribution (OEND) programmes have been observed [18], and pharmacies in low-income neighbourhoods are less likely to stock naloxone [19].

A second challenge that impedes efforts to curb overdose deaths is the rapidly evolving nature of the crisis [20, 21]. Sudden, unanticipated shifts in the communities most heavily affected necessitate timely public health surveillance information and the dissemination of information on the shifting landscape of risk to inform effective public health responses [22]. However, most overdose mortality surveillance systems suffer from substantial delays due to the complex nature of overdose death investigations [23]. Drug overdose surveillance using medical examiner or coroner data are often delayed by a year or more [24]. Syndromic surveillance systems using emergency department or emergency medical services data are timelier [25], but are not widely implemented in most jurisdictions. In this context, resource allocation strategies based on predictive analyticals hold promise, but have not been widely evaluated.

Building upon our successful academic–state health department partnership [26], we will first develop a novel, neighbourhood-level fatal overdose forecasting tool. This tool, called PROVIDENT (Preventing Overdose using Information and Data from the Environment), will identify neighbourhoods at high risk of future overdoses. Next, we will conduct a randomized, population-based, community intervention trial to determine whether directing resources to highest-risk neighbourhoods (as identified by the PROVIDENT model) is more effective than current responses (based on traditional surveillance data) at reducing population overdose burden. In sum, we aim to evaluate whether directing interventions to specific high-risk neighbourhoods within a city/town is more effective at reducing overdose morbidity and mortality than the same set and overall dose of interventions, but without prioritization based on forecasting models.

The study will take place in Rhode Island, a state with the 11th highest overdose mortality rate in the nation [27]. To carry out the proposed aims, we will leverage spatiotemporal and ensemble-based machine learning methods, a state-wide overdose surveillance system and a range of other data sources. This trial will also build upon a recently completed pilot study, in which machine learning methods and publicly available data were used to predict census tract-level counts of overdose deaths as a proxy for future overdose and injection drug use-related infectious disease outbreaks [28]. Importantly, the pilot study included stakeholder oversight from community-based organizations and state agency partners, as well as broad community-based dissemination of the results. The proposed trial extends and deepens this work by incorporating a wealth of additional predictors (see Table 1) and by predicting overdose at a more finely resolved geographical level (i.e. census block groups rather than census tracts).

Trial objectives and hypotheses

The specific research objectives are as follows:

1. Develop and validate PROVIDENT, a forecasting model to predict which neighbourhoods are at high risk for future overdose death.
2. In close collaboration with the state health department, we will conduct a randomized, population-based, community-level intervention trial in which the Rhode Island Department of Health (RIDOH) and other community-based organizations will receive PROVIDENT model predictions for half the state's 39 cities/towns (those assigned to the treatment arm). We hypothesize that governmental agencies and community-based organizations will utilize the PROVIDENT forecasts and direct interventions towards neighbourhoods to be at highest risk for overdose death which

TABLE 1 Summary of overdose surveillance and neighbourhood-level data sources for the PROVIDENT model

Domain	Description	Data source (agency)
Overdose deaths	All unintentional drug-related deaths that occur in Rhode Island (model outcome)	SUDORS
EMS runs for suspected opioid overdose	EMS runs for suspected opioid overdoses (based CDC case definition using ICD-10 codes) [50]	CEMS database (RIDOH)
Prescribing	Opioid analgesic prescribing rate[a]	PDMP (RIDOH)
	Rate of patients receiving > 90 MME[a]	PDMP (RIDOH)
	Rate of multiple provider episodes for opioids (≥ 5 physicians or ≥ 5 pharmacies over 6 months)	PDMP (RIDOH)
	Number of patients prescribed an opioid and a benzodiazepine within 30-day period	PDMP (RIDOH)
Treatment	Buprenorphine prescribing rate[a]	PDMP (RIDOH)
	Buprenorphine initiating rate[a]	PDMP (RIDOH)
	Buprenorphine retention rate[a]	PDMP (RIDOH)
Rescue	Rate of naloxone distribution by pharmacies[a]	PDMP (RIDOH)
Social capital and family fragmentation	Social capital (density of civic and charitable organizations, religious organizations, foundations, census response rate)	DBR
	Rate of incarceration and release from settings of incarceration	RIDOC
	Family fragmentation (household composition, proportion of children living in single parent households)	ACS
Neighbourhood advantage/disadvantage	Unemployment rate, household income, percentage below the poverty line, Gini coefficient, proportion with public assistance	ACS
Health and social resources	Rate of licensed addiction treatment programmes[a]	BHDDH
	Health insurance coverage	ACS
Physical environment	Average age of structures, heating fuel type, monthly owner costs as a percentage of household income, gross rent	ACS
	Occupancy status of residential properties	ACS

American Community Survey (ACS); BHDDH = Department of Behavioral Health, Developmental Disabilities and Hospitals; Census Block Group = Census Block Group; CEMS = Centers for Emergency Medical Services; MME = morphine milligram equivalents; PROVIDENT = Preventing Overdose Using Information and Data from the Environment; OSME = Office of the State Medical Examiner; RIDOH = Rhode Island Department of Health; RIDOC = Rhode Island Department of Corrections; DBR = Department of Business Regulation; SUDORS = state unintentional drug overdose reporting surveillance.

[a]All rates expressed as number per 1000 residents.

will, in turn, reduce the population-level overdose burden compared to control cities, that will continue to receive the same overall dose of interventions in accordance with the state's strategic plan, but will not receive PROVIDENT model predictions.

METHODS

Trial design

This will be a two-arm, parallel-group, population-based randomized controlled trial, with community-level 1:1 randomization comparing the PROVIDENT intervention with a comparator condition (i.e. standard overdose prevention, treatment, harm reduction and rescue interventions with no targeting based on PROVIDENT model predictions).

Setting

The study will take place in Rhode Island, a state in the New England region of the United States, which historically has among the nation's highest rates of non-medical opioid use, illicit substance use and unintentional drug-related mortality [3, 29, 30].

Participants

This trial will not enrol individual participants. As described below, randomization and assessment of study outcomes will occur at the municipal level, and all study outcomes will be assessed at the same level. However, during the study period, all people who reside in Rhode Island or who experience a qualifying event—defined as a fatal or non-fatal overdose captured by the state's multi-component overdose surveillance system—may contribute data to either the PROVIDENT model or the study outcomes.

Informed consent

The study will involve a retrospective review of existing overdose-related surveillance data to build the PROVIDENT forecasting model, and a prospective review of overdose surveillance data to compare overdose morbidity and mortality rates between the municipalities assigned to the treatment and comparators arms.

As all data to be analysed as part of this study are collected through ongoing public health surveillance activities and the use of protected health information involves no more than a minimal risk to the privacy of individuals, the Institutional Review Board (IRB) of record approved a waiver of research participants' authorization for use/disclosure of information about them for research purposes, in accordance with 45 CFR § 164.512(i)(1)(iv).

Time-line and sample size

The project was launched on 10 December 2019. We anticipate that the randomized trial component of the study will begin in November 2021. Allowing for a 6-month ramp-up period to allow time for the interventions to be targeted, we anticipate 2 years of post-intervention follow-up time.

To estimate the power to detect significant differences between overdose rates in treatment and control cities/towns, we examined 2016 municipal-level overdose data [31]. We used a stratified randomization scheme to conduct power simulations. Power was calculated for relative reductions in combined fatal/non-fatal overdose rates ranging from 15 to 30%. We used data from 2016 to set the underlying state-wide overdose rate. We simulated randomization of each city to treatment versus control, estimated the expected number of events for each city based on population size and treatment assignment and then used standard calculations for two-sample comparisons of Poisson rates. Due to the finite sample of municipalities with widely varying population sizes, person-time of exposure in the control and treatment groups will vary depending on how cities are randomized. We therefore calculated power for several simulated randomizations, with 10 randomly selected instances shown (Supporting information, Figure S1). As shown, we will have at least 95% power to detect a > 25% reduction in the treatment arm compared to cities/towns assigned to the control arm. Of note, these estimates are conservative: we assumed only 1 year of post-intervention follow-up time, whereas we anticipate 2 years based on the project time-line.

Intervention

This study has two aims. First, we will develop a predictive analytics model to forecast semi-annual overdose mortality risk at the neighbourhood level. We will define neighbourhoods based on census block groups (CBGs), which are statistical divisions of census tracts, generally representing between 600 and 3000 people [32]. We chose CBG as the geographical unit of interest as they are widely considered an appropriate scale for neighbourhood-level interventions [33–35]. Moreover, they are the smallest geographical unit for which the US Census Bureau publishes sample data. Forecasts will be made at 6-month intervals at the CBG level (i.e. predicting risk of overdose death in the following 6-month period). Rhode Island consists of 809 populated CBGs spread across 39 municipalities (cities/towns); 162 CBGs (20%) will be designated as 'high risk' by the PROVIDENT model, subject to the constraint that at least one high-risk CBG is selected in each municipality.

As part of the federally funded state unintentional drug overdose reporting surveillance (SUDORS) system [36], detailed information is abstracted from medical examiner records, death certificates, law enforcement records and toxicological panels for every unintentional drug overdose death that occurs in the state. Professional abstractors also identify the location of injury, defined as the address (or nearest address) where the overdose occurred. When these data are aggregated into census block groups, significant heterogeneity is observed both within and across cities/towns (Figure 1). Overdose deaths at the census block group level (based on location of occurrence) will serve as the outcome for the PROVIDENT model.

We will use information from the state's multi-component overdose surveillance system and publicly available data sets (Table 1) as predictors for the model. Surveillance data collected from 2016 onwards will be used to estimate overdose risk for each CBG, and to select a subset of one or more CBGs within each municipality to prioritize for intervention. During the course of the project, model projections will be updated semi-annually based on the most recent available data, and will be transmitted to the RIDOH and other state agencies and community-based organizations every 6 months.

We will forecast future fatal overdose burden using a machine-learning approach to integrate the multiple data sources for improved forecasting accuracy. A rigorous model selection and parameter estimation step will be conducted based on comparing models' performance on forecasting held-out data for the following 6 months (given data up to a time-point t). Multiple models will be compared, including spatiotemporal Gaussian processes fitted to historical fatal overdose data from SUDORS, random forests incorporating subsets of predictor variables and deep learning (neural

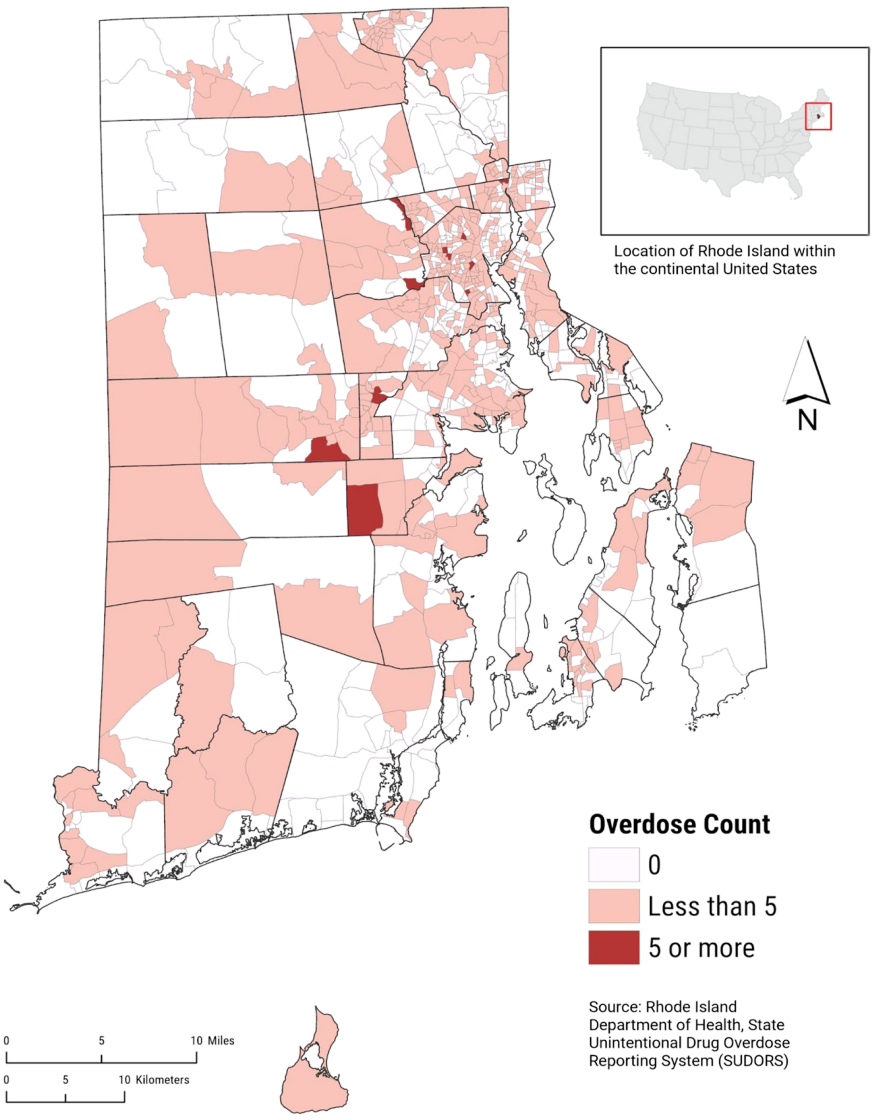

FIGURE 1 Geographical distribution of unintentional drug-related overdose deaths in Rhode Island by location of injury, aggregated to the census block group, July 2016–June 2019

network) models. We will also consider ensemble methods, which combine the predictions of multiple machine-learning algorithms [37], to determine whether the combined predictions can outperform the best individual model. Parameters of each model will be fitted via cross-validation within the training data. Each model will be evaluated based on its prediction accuracy on 2018–19 historical data, making predictions for each 6-month period using data from prior periods only. Each model will select a subset of 162 CBGs (20%) as 'high risk' areas to prioritize, subject to the constraint that at least one CBG must be selected from each municipality. Our primary comparison metric for model selection will be the proportion of all fatal overdoses captured in the predicted high-risk CBGs, with a performance goal of capturing ~40% of overdoses in the targeted 20% of CBGs. Additional criteria for comparison will include: (1) equity in balancing the targeted CBGs between urban and rural populations; (2) equity in balancing the targeted CBGs between predominately white and racialized minority communities; (3) model interpretability and transparency; and (4) logistical considerations such as computation time.

Once the PROVIDENT model has been developed and validated, we will conduct a community-randomized, population-based intervention trial to evaluate whether focusing interventions and resources on neighbourhoods with the highest estimated overdoses risks within a municipality is more effective at reducing population overdose mortality than the current strategy, in which interventions are implemented throughout municipalities universally and/or based on traditional surveillance data. The academic research team will work in close collaboration with RIDOH to conduct the trial; the health department director is a co-investigator on the study and agency staff are being supported financially to guide the work. To minimize contamination, RIDOH will only receive PROVIDENT model predictions for cities/towns randomized to the treatment arm. Within these municipalities, RIDOH will work with state

agencies and community-based stakeholders to prioritize overdose interventions to CBGs with the highest predicted overdose risk (see 'Procedures' below).

Comparator

Cities/towns in the control group (i.e. randomized to the comparator condition) will continue to receive overdose interventions in accordance with the state's strategic plan [14]. In brief, the state has deployed a number of interventions to reduce overdose mortality since a public health crisis was declared in 2015 [38]. The state's Overdose Prevention and Intervention Action Plan focuses upon four specific 'pillars' designed to reduce overdose mortality, including prevention (e.g. safer opioid prescribing), rescue (e.g. increasing access to naloxone), treatment (e.g. expanding the quality and availability of medications for the treatment of opioid use disorder) and recovery (e.g. provision of peer recovery support services throughout the health and social service system) [39]. The research team will work closely with RIDOH to ensure that municipalities assigned to the control arm will receive the same overall amount and dose of interventions that they would have received had they been randomized to the intervention arm. Finally, all cities and stakeholders will continue to receive timely surveillance information from the state health department in line with what they were receiving prior to PROVIDENT's launch, including alerts when increased overdose activity above certain thresholds are detected, regardless of treatment assignment. Specifically, stakeholders will have access to two sources for municipal-level overdose surveillance data regardless of intervention assignment, including www.preventoverdoseri.org (a publicly available overdose dashboard) and the RIDOH overdose data hub (www.health.ri.gov/od-datahub), which contains more detailed reports. These surveillance systems provide detailed information, including socio-demographic characteristics and time trends, on overdose-related emergency department visits, emergency medical service runs, overdose fatalities and opioid prescribing data at the municipal level.

Procedures

Randomization

Municipalities were randomized to the two trial arms using block randomization to ensure the balance of important city/town characteristics, given the small overall number of municipalities. To create blocks for randomization, Rhode Island's 39 municipalities were first classified as urban or non-urban. Consistent with local definitions from the Rhode Island Division of Statewide Planning [40], urban municipalities are those with population densities of at least 2500 people per square mile and that have at least 50% of their land developed. All other municipalities are considered non-urban. Within the strata defined by urbanicity, municipalities were ranked in terms of their average overdose death rates between 2016 and 2018 and grouped into quintiles to create 10 blocks. A summary of key characteristics of municipalities assigned to the treatment versus comparator arm (blinded) is shown in Supporting information, Table S1.

Logic model

A summary of project activities and logic model is shown in Figure 2. In brief, a web tool and interactive dashboard will be developed to visualize the neighbourhood-level risk predictions from the PROVIDENT model. The web tool will consist of a separate, password-protected portal available through the state's current overdose information dashboard (www.preventoverdoseri.org). These predictions will be updated semi-annually and shared with RIDOH on a regular basis. The decision to update the model every 6 months was made collaboratively with RIDOH and balances a

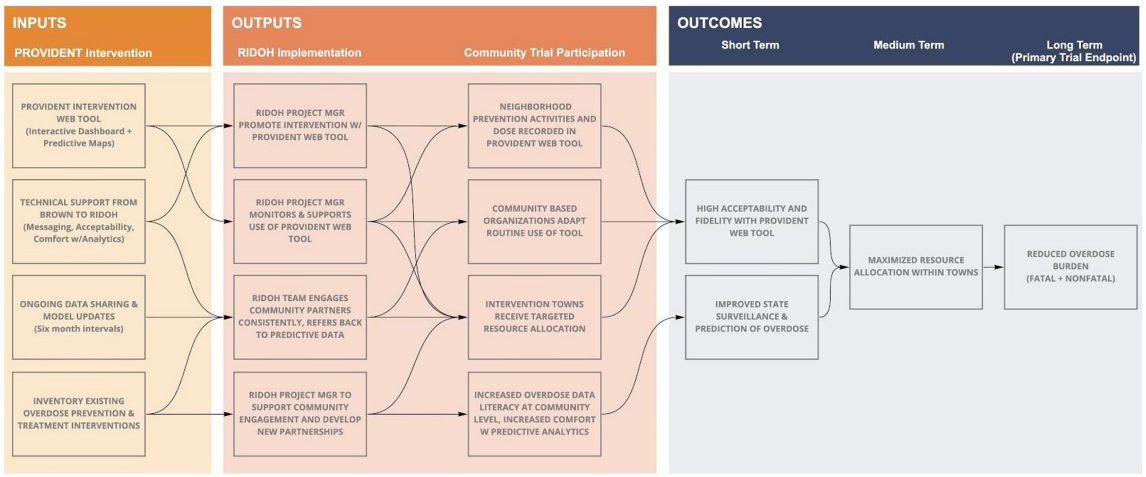

FIGURE 2 PROVIDENT community intervention trial logic model

number of factors, including timeliness of the model predictions, with sufficient time to allow community-based organizations to adapt, guide and shift their work.

The research team and staff at RIDOH will work to promote uptake of the web tool with organizations, community agencies and other stakeholders that work to provide overdose prevention services in municipalities assigned to the treatment arm. To help to ensure that the health department and community-based organizations will use the PROVIDENT forecasts we will implement a number of stakeholder engagement activities, which we piloted successfully in our earlier work [28]. First, prior to the pilot launch, we will conduct a 4-day 'data academy' with key stakeholders to increase data literacy, explain the machine-learning methodology, help organizations to develop needs assessments and plans for using the predictions, and train users on the web tool. Second, technical assistance will be available throughout the conduct of the trial, and focus groups with community stakeholders will be held to troubleshoot issues and increase buy-in. Finally, community-based organizations are being reimbursed for participating in the implementation activities and are considered research partners, rather than end-users. We hypothesize that use of the PROVIDENT predictions will lead to prevention activities which are more focused on neighbourhoods at high risk which, in turn, will maximize the efficiency of allocated resources and reduce overdose burden at the municipal level.

Interventions and intervention delivery

We will work with a diverse set of stakeholders to identify specific interventions that can be delivered to high-risk neighbourhoods based on the PROVIDENT model predictions. Throughout the trial, PROVIDENT model predictions will be disseminated to community-based organizations and other entities (e.g. state working-groups) which work in the cities/towns randomized to the treatment arm. A summary of exemplar interventions (organized by strategic plan pillar) is presented in Table 2. For example, we hypothesize that harm reduction organizations conducting street-based outreach and naloxone distribution activities will be able to use the PROVIDENT predictions to direct resources to specific neighbourhoods that the model identifies as being at highest risk. The goal is not to change the overall amount or dose of interventions a specific municipality receives, but to direct interventions to high-risk neighbourhoods relative to other neighbourhoods within cities/towns. While organizations already have access to municipal-level overdose surveillance data (see 'Comparator' section above), these information sources do not represent real-time data and are often delayed by several months. Moreover, we hypothesize that the PROVIDENT predictions will improve upon the use of existing surveillance data by providing organizations with useful predictions to inform programme planning and resource allocation prospectively over 6-month time periods, rather than prioritizing intervention delivery based on historical trends.

Measures

Primary outcome measure

The primary outcome for this trial will be the 2-year cumulative incidence of fatal and non-fatal overdose at the city/town level. Although the PROVIDENT model will only forecast future overdose deaths (because the exact locations of non-fatal overdoses are not available), we will include a composite measure of municipal-level fatal and non-

TABLE 2 Exemplar neighbourhood-focused interventions to be informed by the PROVIDENT model

Strategic plan domain	Interventions
Prevention	Academic detailing to encourage safer opioid prescribing practices for patients initiating opioid medications and those on long-term opioid therapy
	Substance use prevention programming in RIDOH Health Equity Zones, a grant programme for organizations working in underserved neighbourhoods
Treatment	Post-release engagement programmes to ensure people released from prison/jail are connected with treatment services and transition to community-based care
	Academic detailing and physician education efforts to promote screening for opioid use disorder and initiation medications for OUD treatment
	Licensed social workers embedded within the state police department offer referrals and pre-arrest diversion towards treatment resources for people with substance use disorder and/or who have recently overdosed
Rescue/harm reduction	Syringe services programmes, including mobile delivery of harm reduction supplies
	Street-based outreach and naloxone distribution programmes to high-risk people
	Naloxone distribution and training in public settings (e.g. libraries, shelters)
Recovery	Peer recovery coaches respond to hospital emergency departments and EMS calls for overdose. The coaches support patients and provide referrals to health and addiction treatment services, including medications for OUD
	Street-based peer recovery coaches conduct outreach in areas where people who use drugs are known to congregate

EMS = emergency medical services; OUD = opioid use disorder; PROVIDENT = Preventing Overdose using Information and Data from the Environment; RIDOH = Rhode Island Department of Health.

fatal overdose events as the primary end-point in the trial to ensure adequate power. We will compare fatal and non-fatal overdose rates in the treatment and control municipalities for 2 years after intervention assignment, allowing for a 6-month ramp-up period to allow time for the targeted interventions to be implemented. We will use the person-time method to aggregate 2 years of outcome data. Fatal overdoses will be defined as drug-related deaths deemed unintentional by the state medical examiner. Specifically, we will include all deaths that: (1) occur in a Rhode Island municipality; (2) the final manner of death was deemed an accident; and (3) a drug is listed on the death certificate as the primary cause of death or a significant contributing factor. The state-wide nature of Rhode Island's centralized medical examiner system means that all accidental deaths are investigated in a similar and consistent manner (including robust toxicological analyses, death scene investigation and autopsy by a medical professional); all deaths are certified by the chief medical examiner, resulting in a highly reliable reporting system [41]. Non-fatal overdose events will be defined as an emergency department visit for an overdose. These data are captured in the state's 48-hour overdose reporting system [42], which requires hospitals to report overdoses to RIDOH within 48 hours. The system has been validated against state-wide emergency medical services (EMS) data; furthermore, the RIDOH conducts regular quality assurance procedures to ensure that hospitals are reporting with fidelity and in a timely fashion [43]. In exploratory analyses, we will examine the effect of the intervention on overdose fatalities and non-fatal overdoses separately to determine whether the intervention produced similar changes in rates of each outcome, and/or produced shifts in the distribution of fatal and non-fatal events without affecting the overall incidence rate.

Process measures

Process measures will be based on the logic model (Figure 2) and grounded in the RE-AIM (Reach, Effectiveness, Adoption, Implementation and Maintenance) framework for implementation outcomes [44], including acceptability (e.g. increased data literacy and comfort with predictive analyticals), adoption and reach (e.g. use of the web tool based on site traffic and user engagement statistics), fidelity and penetration (e.g. what and how many directed overdose prevention activities are driven in part by the PROVIDENT model). Specific process metrics and evaluative activities will be developed and finalized during the stakeholder engagement process. However, all stakeholders will be asked to submit regular reports through the web tool describing if and how the PROVIDENT predictions were used to prioritize resources and focus interventions upon neighbourhoods at highest risk.

Data management and monitoring

In order to transfer, store and analyse protected health information, we will rely upon Brown University's Stronghold Research Environment for Data Compliance. Stronghold is certified to meet Health Insurance Portability and Accountability Act (HIPAA) requirements and other federal data privacy regulations.

A single data safety monitoring board (DSMB) will be appointed to oversee the clinical trial component of the project. The DSMB will have access to the unblinded data, and will have the authority to recommend termination of the trial to the principal investigators and the IRB for medical, safety, regulatory or other reasons consistent with applicable laws, regulations or good clinical practice.

Analysis

The analysis plan will be finalized and uploaded to the Open Science Framework (osf.io) before the start of the data analysis, in accordance with the pre-specified analysis plan. We will employ standard methods for community intervention trials [45, 46]. The intervention effect will be quantified as a composite fatal and non-fatal overdose incidence rate ratio. We will have at least 5 years of data (from 2016 to 2020) to serve as the pre-intervention period. We will use generalized linear mixed-effect modelling with Poisson or negative binomial link functions to estimate incidence rate ratios comparing overdose rates in treatment cities/towns to control cities/towns. Each municipality will have its own random intercept and slope to account for pre-intervention differences and time trends. Municipal population size will be incorporated as an offset, and 95% confidence intervals will be calculated using standard bootstrapping techniques to account for possible overdispersion of the data and the relatively small number of geographic units per arm. Although we will use stratified randomization to reduce pre-intervention differences in the treatment and control groups, potential biases from the imbalance can be corrected by including other covariates in the model. For example, measures of municipal-level racial/ethnic composition (e.g. percentage Hispanic/Latino) will be included as covariates, given some evidence of imbalance in these variables between the two arms (see Supporting information, Table S1). Next, we will construct time-lagged regression models to consider the delayed impact of the interventions by staggering outcomes by zero to 6 months.

Ethics statement

Ethical approval has been given from the RIDOH and Brown University Institutional Review Boards (1910002566).

DISCUSSION

This study addresses one of North America's top health priorities and aims to improve public health decision-making and community response to regional overdose crises. If successful, the trial results will inform more efficient and equitable resource allocation to communities at highest risk for future overdose morbidity and mortality.

Moreover, the rigorous study design—a randomized trial with objective end-points assessed through population-based surveillance systems—will generate valuable knowledge that can inform predictive modelling approaches in other settings. In this manner, the PROVIDENT forecasting model aims to serve as a robust, adaptable tool for other states to prioritize overdose prevention efforts. Specifically, although SUDORS began in 2016 and originally funded only 12 states, 47 jurisdictions are now participating [47]; therefore, if found to be efficacious, the PROVIDENT model could be expanded to other regions of the United States. More broadly, the research will help to determine which data domains are particularly strong predictors of community-level overdose rates, which could have important implications for surveillance efforts and programme planning in national and international settings. Finally, the proposed study leverages a unique academic partnership with a state health department and strong governmental support to conduct a randomized, state-wide, community-level intervention trial.

There are four main anticipated challenges that may impede project success. First, there is an established evidence base demonstrating that machine-learning-based predictive algorithms can reinforce and/or produce health disparities (including racial/ethnic inequities) due to incorrect or inaccurate predictions among subgroups, bias in data collection processes and/or predictions leading to withholding of resources [48]. To protect against algorithmic bias, we will adopt best practices for advancing health equity using the principle of distributive justice [49], including ongoing evaluation of the accuracy of the model predictions and intervention allocations across population subgroups (including racial/ethnic minority neighbourhoods) and undertaking a comprehensive stakeholder engagement process prior to trial launch. Secondly, the use of PROVIDENT predictions by certain entities, such as law enforcement, has the capacity to increase surveillance of, stigma towards and harm in neighbourhoods identified by the model as being at highest risk. To mitigate this, the PROVIDENT tool will not be shared with any law enforcement, criminal justice or public safety entities. Thirdly, the collection, collation and transfer of data that constitutes the predictive modelling outcome (i.e. counts of fatal overdoses at the census block group level) is a time-consuming process that can take up to 12 months. As such, the resulting predictions do not necessarily rely upon real-time information, which could adversely affect their utility. Nonetheless, we hypothesize that resource allocation decisions informed by machine-learning algorithms—which integrate information from diverse data sources—will lead to greater reductions in overdoses than approaches relying upon surveillance data alone. Finally, as part of the intervention, community-based organizations are receiving both financial support and ongoing technical assistance, which could limit sustainability. However, we believe that such support is necessary to achieve a valid process and outcome evaluation. Future research will be needed to determine pathways to sustainability if the intervention is found to be effective.

In summary, to our knowledge this study will be the first state-wide, population-based, randomized community intervention trial to reduce overdose deaths. Given the escalating nature of the crisis, there is an urgent need for a more effective approach to reduce overdose mortality, particularly in communities most affected by the epidemic. If successful, this study will demonstrate improved efficiency with which state and local resources are deployed to reduce overdose mortality and maximize public health impact.

Dissemination policy

Primary results will be disseminated in peer-reviewed journals (open access when feasible), presentations at scientific meetings, state-wide convenings (e.g. the state overdose task force), plain language posts on our team's Medium page (https://medium.com/pphc) and through other outlets as directed by RIDOH. All study materials and analysis protocols will be made available on the Open Science Framework (https://osf.io/), and the PROVIDENT source code will be released publicly on GitHub.

Disclaimer

Data from this study were obtained through an approved data request to the Rhode Island Department of Health (RIDOH). Data were obtained from July 2016 to June 2019. The agency is not responsible for any analyses, opinions or conclusions contained in this document. The views expressed in this report are those of the authors and do not represent the official positions or policy of the RIDOH.

DECLARATION OF INTERESTS

None.

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Brandon D. L. Marshall: Conceptualization; funding acquisition; investigation; methodology; resources; supervision. **Nicole Alexander-**

Scott: Conceptualization; funding acquisition; resources; supervision. **Jesse L. Yedinak:** Project administration; supervision. **Benjamin D. Hallowell:** Data curation; methodology. **William C. Goedel:** Investigation; methodology. **Bennett Allen:** Investigation; methodology. **Robert C. Schell:** Investigation; methodology. **Yu Li:** Formal analysis; methodology. **Maxwell S. Krieger:** Data curation; software; visualization. **Claire Pratty:** Data curation; software; visualization. **Jennifer Ahern:** Investigation; methodology. **Daniel B. Neill:** Investigation; methodology. **Magdalena Cerda:** Conceptualization; funding acquisition; project administration; supervision.

CLINICAL TRIAL REGISTRATION

This trial is registered at ClinicalTrials.gov (NCT05096429).

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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