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Kentucky Outreach Service Kiosk (KyOSK): A community-level, controlled quasi-experimental, Type 1 hybrid effectiveness study to assess implementation, effectiveness, and cost-effectiveness of a community-tailored harm reduction kiosk on HIV, HCV, and overdose risk in rural Appalachia

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Abstract

Introduction: Many rural communities bear a disproportionate share of drug-related harms. Innovative harm reduction service models, such as vending machines or kiosks, can expand access to services that reduce drug-related harms. However, few kiosks operate in the U.S. and their implementation, impact, and cost-effectiveness have not been adequately evaluated in rural settings. This paper describes the Kentucky Outreach Service Kiosk (KyOSK) study protocol to test the effectiveness, implementation outcomes, and cost effectiveness of a community-tailored, harm reduction kiosk in reducing HIV, hepatitis C, and overdose risk in rural Appalachia.

Methods and analysis: KyOSK is a community-level, controlled quasi-experimental, non-randomized trial. KyOSK involves two cohorts of people who use drugs, one in an intervention county (n=425) and one in a control county (n=325). People who are 18 years or older, are community-dwelling residents in the target counties, and have used drugs to get high in the past six months are eligible. The trial compares the effectiveness of a fixed-site, staffed syringe service program (standard of care) to the standard of care supplemented with a kiosk. The kiosk will contain various harm reduction supplies accessible to participants upon valid code entry, allowing dispensing data to be linked to participant survey data. The kiosk will include a call-back feature that allows participants to select needed services and receive linkage-to-care services from a peer recovery coach. The cohorts complete follow-up surveys every 6 months for 36 months (three preceding kiosk implementation and four post-implementation). The study will test the effectiveness of the kiosk on reducing risk behaviors associated with overdose, HIV, and hepatitis C, as well as implementation outcomes and cost effectiveness.

Ethics and dissemination. The University of Kentucky IRB approved the protocol. Results will be disseminated in academic conferences and peer-reviewed journals, online and print media, and community meetings.

Trial Registration Number. NCT05657106

Strengths and limitations of this study

- The intervention was designed through extensive engagement with community stakeholders, including people who use drugs.
- The hybrid effectiveness trial design will yield insights on effectiveness, economic impact, and implementation outcomes, increasing its applicability to guiding future intervention.
- A limitation of the protocol is the inability to blind participants and staff to arm assignment due to the county-level nature of the intervention.

Introduction

Policies and risk environments surrounding drug use place people who use drugs (PWUD) at increased vulnerability to numerous harms,[1-4] including the transmission of blood-borne viruses,[5-9] overdose,[9-11] and injection-related bacterial infections.[12-20] Harm reduction programs reduce PWUD's risk of these adverse health outcomes[21-30] but access to these services in the U.S. and globally remain insufficient.[31] In the U.S., inadequate harm reduction infrastructure is especially problematic in the medically underserved epicenters of the nation's intertwined overdose and hepatitis C (HCV) crises.

Central Appalachia, a predominantly rural, mountainous area encompassing Eastern Kentucky and parts of West Virginia, Virginia, and Tennessee, has long experienced a disproportionate burden of HCV,[32 33] overdose,[34] and elevated risk for an HIV/HCV outbreak among people who inject drugs (PWID).[35] Due to elevated rates of new HIV diagnoses among rural residents, Kentucky was one of few states designated as a priority region for Ending the HIV Epidemic, an initiative by U.S. federal agencies to reduce new infections in the U.S. by 90% by 2030.[36]

In an effort to reduce its vulnerability to an HIV outbreak, Kentucky has expanded its harm reduction infrastructure,[37] launching 84 syringe service programs (SSPs)[37] in less than eight years. SSP implementation in Kentucky has been associated with decreases in injection-related infections,[38] but there remain substantial gaps in SSPs' reach.[39-41] In studies of rural Appalachian PWID, only half have used an SSP citing anticipated stigma, lack of privacy, fear of law enforcement, and limited transportation and hours of operation as barriers.[40-46] Nearly all of Appalachian Kentucky's SSPs are traditional, fixed-site, staffed programs operated within health departments. Supplementing these traditional programs with alternative harm reduction service models might reduce barriers and expand access.

Harm reduction vending machines, or kiosks, have been dispensing safe injection supplies in Europe, Australia, and elsewhere for up to 30 years,[47 48] but few have been implemented in the U.S.. The first kiosks that dispense injection supplies were installed in the U.S. in 2009[49] and are largely still limited to Puerto Rico and Nevada. In the U.S. and elsewhere, kiosk characteristics vary, but typically include supplies for safe injection and overdose prevention, are installed near existing SSPs, and accessed through code, card, token, or payment. Previous studies have demonstrated acceptability and uptake among PWID,[50-53] but findings on effectiveness have been mixed, with some studies, finding an association with reduced syringe sharing[50 54 55] and reuse,[50] and others not.[48 53 56-59]

Mixed findings from prior research, study design limitations (i.e., ecologic, absence of a control group, limited data on individuals not accessing services), and gaps in the studies' geographic coverage underscore the need for more research on harm reduction kiosks. The Kentucky Outreach Service Kiosk (KyOSK) study tests the effectiveness, implementation outcomes, and cost effectiveness of a community-tailored, harm reduction kiosk in reducing HIV, HCV, and overdose risk behavior in rural Appalachia. KyOSK is significant in that it will be, to our knowledge, the first controlled trial testing the effectiveness of a harm reduction kiosk in the U.S., and the first globally to examine cost-effectiveness. We hypothesize that participants who reside in the intervention county, in which the kiosk is installed, will have reduced overdose, HIV, and HCV risk behaviors compared to participants who reside in a comparison county without a kiosk.

Methods

Study Setting

KyOSK involves two rural Appalachian Kentucky counties that are similar in their demographic and epidemiological profile (Table 1). These counties have been designated as "Distressed" or "At-Risk" based on several economic indicators.[60] Standard, fixed-site SSPs have been operating in the counties since 2017.

Table 1. Description of Counties

	Intervention County	Comparison County
Population per square mile[61]	84	88
Total population age 18 or older[61]	22,252	19,815
Percent living in poverty[61]	30%	21%
Rural-Urban Continuum Code (Range: 1-9)[62]	7	7
Percentage of population that is rural[61]	72%	65%
White, non-Hispanic (%)[61]	94%	92%
Percent of population that speaks English in home[63]	97%	96%
Number of HIV cases (total)[64]	34	29
Number of opioid overdose deaths (2020-2022)[65]	53	48
Number of opioid overdose emergency department admissions (2021)[66]	27	35
Number of buprenorphine providers[67]	15	10
Average number of SSP clients per month[68]	90	94

Eligibility Criteria

People who are 18 years or older, are community-dwelling residents in the target counties and used drugs (excluding marijuana, tobacco, or alcohol) to get high in the past six months are eligible. Exclusion criteria include not being able to speak or understand English, conviction in the past 10 years of a violent crime (i.e., murder, manslaughter, rape, robbery, and /or aggravated assault) or stalking, current charges of violent crime or stalking, having plans to move out of the study counties in the next 6 months, or residing in an inpatient facility.

Investigators may remove a participant from the study if worsening health precludes participation; they pose a safety risk to staff; participation is determined to be due to external pressure; or the study is terminated by the Institutional Review Board (IRB), Data Safety Monitoring Board (DSMB), or funder. Participants are not prohibited from concurrent research or care.

Randomization

KyOSK is a community-level, controlled quasi-experimental trial involving two cohorts of PWUD, one in an intervention and one in a control county. County intervention arm assignment was not random. A waitlist control design was originally envisioned, but one county's political leaders expressed hesitancy about kiosk installation, desiring instead to serve as the control county and await trial results for guidance on future kiosk installation.

Trial Arms

Our trial will compare changes in a cohort accessing a standard, fixed site SSP staffed by health department personnel in a control county to changes in a cohort accessing this standard model enhanced with a kiosk in an intervention county. We will enroll 750 PWUD, including 425 in the intervention county and 325 in the control county. The intervention county sample is larger because it will require more within-county stratified analyses for SSP and kiosk usage alone and in combination. Participants will complete 8 waves of bi-annual surveys until the participants reach 48 months of follow-up, with the kiosk being implemented at approximately 18-month follow-up. The study timeline is described in Table 2.

Comparison Condition

The SSP staffed by the local health department will serve as the standard-of-care comparison. The SSP provides syringes, cookers, cottons, naloxone, wound care kits, condoms/lubricant, snacks, drinks, and sharps containers. At their first visit, clients receive a unique ID and complete a brief survey, with these data stored in a statewide, REDcap database. SSP clients will have similar access to harm reduction supplies as those accessing the kiosk and will receive a trifold resource guide with information on services and contact information for recovery coaches (described below). The staffed SSP currently operates three hours per week but scale up to 40 hours per week will be pursued to align with the timing of the kiosk's implementation.

Intervention Condition

The intervention involves enhancing an existing SSP with a kiosk. Approximately 18 months after initiation of cohort recruitment, a kiosk will be installed and will remain in place for approximately three years. While the kiosk is operating, the intervention county will continue its staffed SSP.

Cohort participants in the intervention county will receive a swipe card and alphanumeric code to access the machine. To ensure integration with the state's REDCap data system, the card and code will use the standard SSP client ID code format. Staff will deactivate cards when a replacement is issued, a participant withdraws, or if the card is lost or stolen.

The kiosk will be located adjacent to the local health department which operates the staffed SSP. The local health department was the most preferred location for a kiosk based on previous research.[40] The kiosk will resemble a traditional vending machine with a small touchscreen interface for making selections and receiving education on overdose prevention. The kiosk will be stocked with harm reduction supplies (see Table 3 for potential supplies). To ensure compliance with the counties' existing 1:1 exchange requirement, the kiosk will have a sharps receptacle equipped with technology to approximate the number of returned syringes and communicate to the kiosk the number allowed to be dispensed.

Table 2. Participant timeline

	STUDY PERIOD							
	Enrollment	**Allocation**	**Post-allocation**					**Closeout**
Time point	**-18 to 0 months**	**0 months**	**6 months**	**12 months**	**18 months**	**24 months**	**25-30 months**	**30-36 months**
Enrollment								
Eligibility Screen	X							
Informed Consent (baseline)	X							
Informed Consent (preceding kiosk implementation)		X						
Interventions								
Staffed SSP (Control)		X	X	X	X	X	X	
Staffed SSP + kiosk (Intervention)		X	X	X	X	X	X	
Assessments								
Baseline Survey	X							
Follow-up survey		X	X	X	X	X	X	
Analysis							X	X

Table 3. Potential kiosk supplies and service menu for facilitated referral

Supplies	**Services to be listed on menu to which there can be facilitated referral**
Naloxone	Housing
Fentanyl test strips	Food assistance
Needles/syringes	Transportation
Condoms	HIV/HCV testing and treatment
Food	Mental health care
Water	Support groups
Hygiene kits	Domestic violence
Wound care kits	Substance use disorder treatment
Naloxone voucher for redemption at pharmacy	Help obtaining an identification card
Alcohol pads	HIV pre-exposure prophylaxis
Xylazine test strips	Health insurance registration
Hats and gloves	Wound care
Female hygiene supplies	Legal aid
Housing vouchers	STI treatment and testing
Transportation vouchers	Pregnancy testing
At-home HIV tests	Maternal care
Resource guides	Education assistance

A common concern about kiosks is the potential missed opportunities for linkage to care.[54 69] To address this concern, the kiosk will feature a care navigation call-back menu. Care navigation can increase PWUD use of community-based services, including increased engagement in substance use disorder treatment.[70-72] Participants will select services displayed on the kiosk's interface (see Table 3 for potential menu) and provide access to their phone number(s) for call-back.

People with lived experience with substance use who are certified and trained Recovery Coaches (RCs) will monitor the kiosk data dashboard and field call-back requests within three business days. RCs will briefly assess service needs and potential barriers and make facilitated referrals to health and support services. RCs will also share that they are a person in recovery and relate where possible to the participant's situation and provide hope and encouragement. With permission, RCs will follow up in seven days to offer further assistance. Clients can continue to contact RCs with follow-up questions.

Outcomes

Study outcomes are described in Table 4 and in detail on the study overview in ClinicalTrial.gov.[73] All measures are continuous. Self-reported measures will be assessed using time-line follow-back methods.[74] Survey logic is used to identify reporting discrepancies in real time and prompt the interviewer to resolve the discrepancy with the participant (i.e., reporting more injections involving a clean needle in the past 30 days than total number of injections).

Table 4. Outcomes

Outcomes	**Recall period**
Primary outcomes	
Number of injections where a clean syringe was used divided by total number of injections among participants who inject drugs	30 days
Number of injections where a clean syringe from the [kiosk/SSP] was used divided by the total number of injections among participants who inject drugs	30 days
Number of syringes obtained at the SSP and/or kiosk (obtained from kiosk data)	30 days
Secondary outcomes	
Change in frequency of receptive syringe sharing among participants who inject drugs	30 days
Change in frequency of distributive syringe sharing among participants who inject drugs	30 days
Change in number of people with whom person shared syringes and injection equipment	30 days
Change in frequency of syringe reuse among participants who inject drugs	30 days
Change in frequency of safe syringe disposal among participants who inject drugs	30 days
Change in frequency of condomless anal and/or vaginal sex	30 days
Change in number of days carrying naloxone	30 days
Change in number of days on medications for opioid use disorder (MOUD) among participants who use opioids to get high	30 days
Change in frequency of use of harm reduction services among participants who inject drugs	30 days
Change in frequency of use of fentanyl test strips among participants who use drugs	30 days
Change in frequency of engagement in overdose protective behaviors among participants who use drugs	30 days
Change in frequency of overdose among participants who use drugs	6 months
Change in use of naloxone during overdose events by participants who witnessed an overdose	6 months
Change in number of times contacting or visiting a pharmacy to obtain naloxone	6 months

Following the Implementation Outcomes Framework[75], we will assess acceptability, appropriateness, fidelity, cost, penetration/reach, and sustainability. Acceptability and appropriateness will be assessed in the cohort surveys using the Acceptability of Implementation Measure (AIM) and Intervention Appropriateness Measure (IAM), respectively.[76] Fidelity is described in the *Blinding, Contamination, and Fidelity* section. Using established methods,[77-81] costs will be estimated from the provider's perspective and employ a micro-costing approach that measures and values in monetary terms all resources invested and links costs to the primary and secondary outcomes to evaluate economic impact. *Penetration* (i.e. reach) will be determined by examining the number who engage with the kiosk and/or staffed SSP divided by the number enrolled at the time of intervention/comparison condition implementation (i.e. percent who use the kiosk or SSP) and per supply (i.e. percent who accessed each supply) at monthly intervals. Finally, prospects for sustainment will be explored in final year using qualitative, semi-structured interviews with SSP and other health department staff and local and state leadership.

Building on existing models,[82-85] we will develop and calibrate[86] a dynamic, deterministic model of HCV transmission and overdose among PWUD in the intervention county to estimate the kiosk's impact and cost-effectiveness. The kiosk's effects will be parameterized using trial

data. Impact will be measured as reductions in HCV incidence/prevalence, HCV infections and overdoses averted and quality-adjusted life-years (QALYs) saved over the study and longer timeframes (10/20/50 years). Using cost data, we will estimate cost-effectiveness by comparing discounted (3% annually[87]) costs and QALYs over 50-years between model scenarios with and without kiosk introduction. The mean incremental cost-effectiveness ratio will be estimated and compared to US relevant willingness-to-pay per QALY thresholds.[88]

Data collection

Participants are recruited from (1) existing cohort studies of PWUD, (2) the two SSP programs, and (3) peer-referral. Recruitment from these sources occurs simultaneously; staff l extend invitations and advertise in the SSP, and those who enroll are invited to refer peers (paid for up to five each, $10/peer). KyOSK recruitment commenced in March 2023. The target sample size is 750, including 425 from the intervention county and 325 from the control county.

Community-based field staff administer surveys programmed in Questionnaire Development System (QDS)'s computer-assisted self-interviewing program, with staff asking participants questions aloud and entering participants' responses. Participants can skip any question. The survey collects demographic characteristics, sexual and drug-related risk behavior, houselessness, criminal justice involvement, SUD treatment, medical care access, harm reduction service access, and social, drug, and sexual network characteristics. Staff administer follow-up surveys every 6 months. Participants receive $35 at baseline and $25 for each follow-up survey.

At baseline, staff administer a 14-panel saliva drug test and fingerstick HIV and HCV antibody tests. Trained staff use the rapid-rapid protocol for HIV testing,[70,71] involving INSTI HIV 1/HIV 2 Rapid Antibody Test (BioLytical® Laboratories Inc., Richmond, B.C., Canada) followed by Sure Check® HIV-1/2 Antibody Test (Chembio Diagnostic Systems, Inc., Medford, NY). Staff use OraQuick® *HCV* Rapid Antibody Test (OraSure, Bethlehem, PA) for HCV testing.[72] Staff provide post-test counseling and facilitated referrals for those testing positive.

The kiosk's software will capture detailed, de-identified data linked only to user ID code. Data will be stored in a secure password-protected database. Data include client- and visit-level usage including day/time, frequency of use, supply selection and quantity, number of syringes returned, and call-back requests. The same data will be collected on clients visiting the SSP.

Retention

Following standard procedures used in longitudinal research,[89] participants provide detailed locator information to assist with retention and/or contact for future research including names, pseudonyms, phone numbers, addresses, email addresses, social media contact information, and contact information for up to three people who should know how to reach the participant if contact information changes. Participants are contacted at the mid-point of each follow-up interval to update locator information and remind them about their follow-up appointment. Participants receive $10 for updating or verifying locator information between the baseline and 6-month follow-up appointment (the period at which most attrition occurs). In addition, local jail systems are searched to identify if a person is incarcerated. Participants who are incarcerated and have consented to be contacted while incarcerated may complete follow-up surveys from jail (with permission from jail administrative staff).

Blinding, Fidelity, and Contamination.

Analysts remain blinded through recruitment and follow-up until completion of primary and secondary analyses, using uninformative participant labels. Due to the nature of the interventions, participants and site staff administering the intervention are not blinded. These staff are instructed to use uninformative labels when discussing participants with blinded investigators.

Fidelity of kiosk and staffed SSP implementation will be assessed early and mid-trial on three domains: (1) supply availability, (2) operation, and (3) recovery coaching. *Supply availability* will be assessed using the kiosk's internal data in which item selections unfilled due to insufficient stock are recorded. *Operation* will be assessed by examining the number of kiosk malfunctions and number of times in which the staffed SSP operated < 40 hours per week excluding holidays. The latter will be assessed five unannounced visits per month by research staff at opening, lunch, and near closing. *Recovery coaching* fidelity to best practices will be assessed by monthly review of 10% of randomly selected, audio recorded sessions and completion of a fidelity checklist, which includes tailoring the conversation to stage of change, using motivational interviewing, engaging in resource brokering, and so on.

Potential for contamination is low, as the travel distance between sites is two hours. Participants enrolled in the control county will not be provided with a swipe card to access the kiosk in the intervention county. Nevertheless, to assess potential contamination, data will be collected at each follow-up survey about county of residence, SSP and kiosk use, and in which county they accessed services.

Data management

Data are imported to a single warehouse file on our secure network drive. Using the QDS Warehouse Manager program, the data manager assesses transferred data for completeness and consistency and tracks data modifications. Stored data are exported as SAS and SPSS datasets for analysis. The list linking participants to their unique identifier is maintained on a secure REDCap database. To protect confidentiality, only de-identified data are shared for analysis.

Statistical methods

The Intention-to-Treat (ITT) population will contain all enrolled participants according to their assigned study arm. The Per-Protocol population will include participants who complete the trial as originally allocated. We hypothesize that values on our primary outcome measures of syringe coverage (see *Outcomes* for operationalization) in the intervention county will be greater than the control county in the ITT and Per-Protocol populations. We anticipate that the secondary outcomes of risk behaviors (see *Outcomes* for operationalization) in the intervention county will be less than that reported by those in the control county. We hypothesize that participants in the intervention county will be more likely to engage the secondary outcomes related to naloxone carriage and MOUD and HCV treatment than those in the comparison county.

All models will be analysed using generalized estimating equations (GEE) assuming an AR(1) residual structure to account for within person autocorrelation due to repeated measures, and will include fixed effects for county intervention condition, intervention period, and condition*period interaction. This interaction estimates the relative change in the intervention county compared to the control county due to kiosk's introduction. Although the counties are remarkably similar, we will model county specific linear time effects to allow for different

secular trends that may confound estimation of the intervention effect. Multiple baseline measures allow better capture of any potential differential trends. Models will include an indicator variable reflecting whether participants also received services at the staffed SSP and institutionalization (hospitalized or incarcerated) at the time of the survey. Other theoretically justified time varying covariates and recruitment method (i.e., enrolled from cohort, SSP, or peer-referral) will be examined. We will examine homophily in peer referral chains and incorporate autocorrelation within chains if significant homophily on outcomes is present. Of note, GEE models are robust to minor misspecifications of the correlation structure that may arise due to the sampling scheme.

Our prior research has shown that the rates of our primary outcomes are high enough to be well approximated as normal. If this does not hold true, we will use Poisson models with appropriate offsets to account for the distribution of the primary ratio outcomes. Type 1 error (α) will be set to 0.05 in primary and secondary outcome analyses, and two-tailed tests will be used. For outcomes that apply only to a subset of participants (e.g., syringe sharing analyses are restricted to PWID), data from time points at which participants do not report the relevant behavior (e.g., injection drug use) will be omitted from these models. Resulting estimates will be unbiased under the assumption that the kiosk did not cause a change in the overall behavior defining the subset (e.g., in injection drug use). Sensitivity analyses including all data will be performed using multinomial logistic regression where the outcomes are specified as, for example, no injection drug use, injection drug use with a clean syringe, and injection drug use without a clean syringe.

We will use multiple imputation by chained equations (MICE)[90] to account for attrition in all analyses. Our imputation model will include interactions between intervention county and baseline risk measures to allow for differential selection effects between the intervention and comparison groups should differential attrition arise.[91]

To analyze reach, we will perform segmented regression analyses using existing data from the statewide SSP database beginning in January 2020 allowing for 3 years of pre-intervention data. We will assess change in total reach by comparing the difference in the changes in both intercept and slope between counties. All models will account for first-order autocorrelation and use appropriate link functions based on outcome distributions. We will also explore changes in reach by gender, age, IDU, or other characteristics, by generating separate series by participant characteristic and then analyzing these series in a pooled interaction model.

Power Calculation

Based on prior published simulations,[92] our segmented regression analyses (n=72 months, 3 years pre- and 3 years post-intervention implementation) are well powered to achieve study aims for small effects across a wide variety of link functions and autocorrelation values. We estimated power for our primary intervention models using 5000 Monte Carlo simulations for each set of parameters, with a type-1 error rate of 0.05 and an unbalanced design (sample unevenly distributed across counties). We simulated autocorrelated outcomes for three pre-intervention and five post-intervention survey waves with an expected 750 enrollees. We conservatively used 70% retention for the power analysis. Not all outcomes will be applicable to the full cohort; for example, approximately 25% are estimated[93] to have not recently injected and therefore will not contribute to analyses of outcome variables related to injection. Therefore, we estimated power for various effect sizes for a cohort of "completers" of N=300, 400, and 500. Based on these simulations, all sample sizes are powered to detect a standardized mean difference

of at least 0.2, a small effect. As enrollment nears the target sample size, the accuracy of projected estimates of retention and injection drug use will be evaluated and the sample size may be increased if needed.

Data monitoring

A DSMB with a physician, statistician, infectious disease epidemiologist, and behavioral scientist with expertise in research among PWUD oversees the study. The DSMB is independent of the sponsor and competing interests. The DSMB meets at least annually to review emerging data, and make recommendations about the trial's conduct, including stopping the trial. No formal interim analyses are planned.

Social Harms

Social harms related to participation will be actively assessed and documented. Social harms include any intended or unintended cause of physical; emotional; or psychosocial injury or hurt from one participant to another, a participant to themselves, or an institution to a participant, occurring as a result of study participation.[94] Participants will complete a social harms questionnaire at each study visit. Study staff are trained to provide appropriate care, counseling, and referral as needed. Any identified social harms are reported to study investigators who determine severity and provide details to the IRB as required.

Auditing

The Data Scientist regularly assesses data for missingness and data quality and provides feedback to the PI and field staff regarding any issues that need to be addressed. The PI and Project Director review study consent materials to assure appropriate documentation of consent at least semi-annually.

Patient and Public Involvement

Participants were not directly involved in the development of the research question, outcome measures, or conduct of the trial; however, officials from public health, behavioral health, drug policy agencies, and a community advisory board of PWUD were involved in intervention design. Upon funding, six focus groups with PWUD and local health department personnel were conducted to gain feedback on kiosk features. Then, a KyOSK Design Team of two SSP staff, a health department director and nurse administrator, six representatives of four key state agencies, and eight PWUD was convened to meet monthly or bimonthly to guide kiosk design. A separate community advisory board of PWUD provided feedback on recruitment methods and participated in survey question review and piloting. Upon completion of the study, results will be distributed via study social media pages, websites, local community advisory board, the KyOSK Design Team, and to community partners.

Ethics and Dissemination

The KyOSK study is reviewed and approved by the University of Kentucky IRB. Study staff complete human subjects training and are approved as personnel by the IRB. Protocol modifications, revisions to consent forms, and changes to other participant-facing documents are submitted to the University of Kentucky IRB for approval prior to implementation. Protocol modifications are submitted to the IRB prior to implementation and reflected in clinicaltrials.gov.

Approval from the funding agency will be sought for major protocol modifications, such as changes in inclusion criteria or aims, prior to submitting those changes to the IRB.

All participants complete an informed consent process at baseline and at the follow-up appointment preceding kiosk implementation, with the latter going into more detail about the kiosk design and supplies. The consent form describes the protocol, risks, and benefits. Consent procedures are completed in person in a private area with only the participant and study staff present.

Findings will be disseminated to the public and healthcare professionals in peer-reviewed journals, professional conferences, and community forums. Authorship eligibility guidelines follow ICMJE criteria. We will submit manuscripts to NIHMS to be made publicly available no later than 12 months after the official date of publication in compliance with the funder's open access policy. De-identified data will be made available to interested parties upon submission and approval of a written request describing data security protocols and intended use.

Authors' contributions
The following individuals contributed to the design of the protocol described in this manuscript: AMY, MDL, HKK, JRH, AFB, PRF, JS, PV, HLFC, CC, and KEM. All members of the KyOSK Design Team contributed to the design of the intervention. The following made substantial contributions to the implementation of the protocol: AMY, MDL, HKK, JRH, EF, AFB, PRF, JS, PV, HLFC, CW, KEM, KyOSK Design Team, and KyOSK Project Staff. The following individuals made substantial contributions to the drafted work and/or substantively revised it: AMY, MDL, HKK, JRH, AFB, PRF, JS, PV, HLFC, KEM, EF, and TJ. All authors read and approved the final manuscript and agree to be accountable for all aspects of the work.

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Competing interest statement
Amanda Fallin-Bennett is a co-founder of Voices of Hope, the contracted recovery community organization providing the recovery coaching services. The device to facilitate syringe disposal and dispensing that will be installed in conjunction with the kiosk is intellectual property of the University of Kentucky, with April Young designated as the inventor. Chelsi Cheatom is a paid consultant on the implementation of harm reduction vending machines, including on the described project.

Data Sharing Statement
De-identified data will be made available upon written request to Principal Investigator, April Young.

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The Kentucky Outreach Service Kiosk (KyOSK) Study Protocol: A community-level, controlled quasi-experimental, Type 1 hybrid effectiveness study to assess implementation, effectiveness, and cost-effectiveness of a community-tailored harm reduction kiosk on HIV, HCV, and overdose risk in rural Appalachia

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Abstract

Introduction: Many rural communities bear a disproportionate share of drug-related harms. Innovative harm reduction service models, such as vending machines or kiosks, can expand access to services that reduce drug-related harms. However, few kiosks operate in the U.S. and their implementation, impact, and cost-effectiveness have not been adequately evaluated in rural settings. This paper describes the Kentucky Outreach Service Kiosk (KyOSK) study protocol to test the effectiveness, implementation outcomes, and cost effectiveness of a community-tailored, harm reduction kiosk in reducing HIV, hepatitis C, and overdose risk in rural Appalachia.

Methods and analysis: KyOSK is a community-level, controlled quasi-experimental, non-randomized trial. KyOSK involves two cohorts of people who use drugs, one in an intervention county (n=425) and one in a control county (n=325). People who are 18 years or older, are community-dwelling residents in the target counties, and have used drugs to get high in the past six months are eligible. The trial compares the effectiveness of a fixed-site, staffed syringe service program (standard of care) to the standard of care supplemented with a kiosk. The kiosk will contain various harm reduction supplies accessible to participants upon valid code entry, allowing dispensing data to be linked to participant survey data. The kiosk will include a call-back feature that allows participants to select needed services and receive linkage-to-care services from a peer recovery coach. The cohorts complete follow-up surveys every 6 months for 36 months (three preceding kiosk implementation and four post-implementation). The study will test the effectiveness of the kiosk on reducing risk behaviors associated with overdose, HIV, and hepatitis C, as well as implementation outcomes and cost effectiveness.

Ethics and dissemination. The University of Kentucky IRB approved the protocol. Results will be disseminated in academic conferences and peer-reviewed journals, online and print media, and community meetings.

Trial Registration Number. NCT05657106

Strengths and limitations of this study

- The intervention was designed through extensive engagement with community stakeholders, including people who use drugs.
- The hybrid effectiveness trial design will yield insights on effectiveness, economic impact, and implementation outcomes, increasing its applicability to guiding future intervention.
- A limitation of the protocol is the inability to blind participants and staff to arm assignment due to the county-level nature of the intervention.

Introduction

Policies and risk environments surrounding drug use place people who use drugs (PWUD) at increased vulnerability to numerous harms,[1-4] including the transmission of blood-borne viruses,[5-9] overdose,[9-11] and injection-related bacterial infections.[12-20] Harm reduction programs reduce PWUD's risk of these adverse health outcomes[21-30] but access to these services in the U.S. and globally remain insufficient.[31] In the U.S., inadequate harm reduction infrastructure is especially problematic in the medically underserved epicenters of the nation's intertwined overdose and hepatitis C (HCV) crises.

Central Appalachia, a predominantly rural, mountainous area encompassing Eastern Kentucky and parts of West Virginia, Virginia, and Tennessee, has long experienced a disproportionate burden of HCV,[32 33] overdose,[34] and elevated risk for an HIV/HCV outbreak among people who inject drugs (PWID).[35] Due to elevated rates of new HIV diagnoses among rural residents, Kentucky was one of few states designated as a priority region for Ending the HIV Epidemic, an initiative by U.S. federal agencies to reduce new infections in the U.S. by 90% by 2030.[36]

In an effort to reduce its vulnerability to an HIV outbreak, Kentucky has expanded its harm reduction infrastructure,[37] launching 84 syringe service programs (SSPs)[37] in less than eight years. SSP implementation in Kentucky has been associated with decreases in injection-related infections,[38] but there remain substantial gaps in SSPs' reach.[39-41] In studies of rural Appalachian PWID, only half have used an SSP citing anticipated stigma, lack of privacy, fear of law enforcement, and limited transportation and hours of operation as barriers.[40-46] Nearly all of Appalachian Kentucky's SSPs are traditional, fixed-site, staffed programs operated within health departments. Supplementing these traditional programs with alternative harm reduction service models might reduce barriers and expand access.

Harm reduction vending machines, or kiosks, have been dispensing safe injection supplies in Europe, Australia, and elsewhere for up to 30 years,[47 48] but few have been implemented in the U.S.. The first kiosks that dispense injection supplies were installed in the U.S. in 2009[49] and are largely still limited to Puerto Rico and Nevada. In the U.S. and elsewhere, kiosk characteristics vary, but typically include supplies for safe injection and overdose prevention, are installed near existing SSPs, and accessed through code, card, token, or payment. Previous studies have demonstrated acceptability and uptake among PWID,[50-53] but findings on effectiveness have been mixed, with some studies, finding an association with reduced syringe sharing[50 54 55] and reuse,[50] and others not.[48 53 56-59]

Mixed findings from prior research, study design limitations (i.e., ecologic, absence of a control group, limited data on individuals not accessing services), and gaps in the studies' geographic coverage underscore the need for more research on harm reduction kiosks. The Kentucky Outreach Service Kiosk (KyOSK) study tests the effectiveness, implementation outcomes, and cost effectiveness of a community-tailored, harm reduction kiosk in reducing HIV, HCV, and overdose risk behavior in rural Appalachia. KyOSK is significant in that it will be, to our knowledge, the first controlled trial testing the effectiveness of a harm reduction kiosk in the U.S., and the first globally to examine cost-effectiveness. We hypothesize that participants who reside in the intervention county, in which the kiosk is installed, will have reduced overdose, HIV, and HCV risk behaviors compared to participants who reside in a comparison county without a kiosk.

Methods

Study Setting

KyOSK involves two rural Appalachian Kentucky counties that are similar in their demographic and epidemiological profile (Table 1). These counties have been designated as "Distressed" or "At-Risk" based on several economic indicators.[60] Standard, fixed-site SSPs have been operating in the counties since 2017.

Table 1. Description of Counties

	Intervention County	Comparison County
Population per square mile[61]	84	88
Total population age 18 or older[61]	22,252	19,815
Percent living in poverty[61]	30%	21%
Rural-Urban Continuum Code (Range: 1-9)[62]	7	7
Percentage of population that is rural[61]	72%	65%
White, non-Hispanic (%)[61]	94%	92%
Percent of population that speaks English in home[63]	97%	96%
Number of HIV cases (total)[64]	34	29
Number of opioid overdose deaths (2020-2022)[65]	53	48
Number of opioid overdose emergency department admissions (2021)[66]	27	35
Number of buprenorphine providers[67]	15	10
Average number of SSP clients per month[68]	90	94

Eligibility Criteria

People who are 18 years or older, are community-dwelling residents in the target counties and used drugs (excluding marijuana, tobacco, or alcohol) to get high in the past six months are eligible. Exclusion criteria include being under the age of 18, not living in the intervention or comparison county, having not engaged in drug use as defined above, not being able to speak or understand English, conviction in the past 10 years of a violent crime (i.e., murder, manslaughter, rape, robbery, and /or aggravated assault) or stalking, current charges of violent crime or stalking, having plans to move out of the study counties in the next 6 months, or residing in an inpatient facility.

Investigators may remove a participant from the study if worsening health precludes participation; they pose a safety risk to staff; participation is determined to be due to external pressure; or the study is terminated by the Institutional Review Board (IRB), Data Safety Monitoring Board (DSMB), or funder. Participants are not prohibited from concurrent research or care.

Randomization

KyOSK is a community-level, controlled quasi-experimental trial involving two cohorts of PWUD, one in an intervention and one in a control county. County intervention arm assignment was not random. A waitlist control design was originally envisioned, but one county's political leaders expressed hesitancy about kiosk installation, desiring instead to serve as the control county and await trial results for guidance on future kiosk installation.

Trial Arms

Our trial will compare changes in a cohort accessing a standard, fixed site SSP staffed by health department personnel in a control county to changes in a cohort accessing this standard model enhanced with a kiosk in an intervention county. We will enroll 750 PWUD, including 425 in the intervention county and 325 in the control county. The intervention county sample is larger because it will require more within-county stratified analyses for SSP and kiosk usage alone and in combination. Participants will complete 8 waves of bi-annual surveys until the participants reach 48 months of follow-up, with the kiosk being implemented at approximately 18-month follow-up. The study timeline is described in Table 2. Data collection for the trial began on March 6, 2023 and is anticipated to end in July 2026.

Comparison Condition

The SSP staffed by the local health department will serve as the standard-of-care comparison. The SSP provides syringes, cookers, cottons, naloxone, wound care kits, condoms/lubricant, snacks, drinks, and sharps containers. At their first visit, clients receive a unique ID and complete a brief survey, with these data stored in a statewide, REDcap database. SSP clients will have similar access to harm reduction supplies as those accessing the kiosk and will receive a trifold resource guide with information on services and contact information for recovery coaches (described below). The staffed SSP currently operates three hours per week but scale up to 40 hours per week will be pursued to align with the timing of the kiosk's implementation.

Intervention Condition

The intervention involves enhancing an existing SSP with a kiosk. Approximately 18 months after initiation of cohort recruitment, a kiosk will be installed and will remain in place for approximately three years. While the kiosk is operating, the intervention county will continue its staffed SSP.

Cohort participants in the intervention county will receive a swipe card and alphanumeric code to access the machine. To ensure integration with the state's REDCap data system, the card and code will use the standard SSP client ID code format. Staff will deactivate cards when a replacement is issued, a participant withdraws, or if the card is lost or stolen.

The kiosk will be located adjacent to the local health department which operates the staffed SSP. The local health department was the most preferred location for a kiosk based on previous research.[40] The kiosk will resemble a traditional vending machine with a small touchscreen interface for making selections and receiving education on overdose prevention. The kiosk will be stocked with harm reduction supplies (see Table 3 for potential supplies). To ensure compliance with the counties' existing 1:1 exchange requirement, the kiosk will have a sharps receptacle equipped with technology to approximate the number of returned syringes and communicate to the kiosk the number allowed to be dispensed.

Table 2. Participant timeline

	STUDY PERIOD							
	Enrollment	**Allocation**	**Post-allocation**					**Closeout**
Time point	**-18 to 0 months**	**0 months**	**6 months**	**12 months**	**18 months**	**24 months**	**25-30 months**	**30-36 months**
Enrollment								
Eligibility Screen	X							
Informed Consent (baseline)	X							
Informed Consent (preceding kiosk implementation)		X						
Interventions								
Staffed SSP (Control)		X	X	X	X	X	X	
Staffed SSP + kiosk (Intervention)		X	X	X	X	X	X	
Assessments								
Baseline Survey	X							
Follow-up survey		X	X	X	X	X	X	
Analysis							X	X

Table 3. Potential kiosk supplies and service menu for facilitated referral

Supplies	**Services to be listed on menu to which there can be facilitated referral**
Naloxone	Housing
Fentanyl test strips	Food assistance
Needles/syringes	Transportation
Sharps container	HIV/HCV testing and treatment
Condoms	Mental health care
Food	Support groups
Water	Domestic violence
Hygiene kits	Substance use disorder treatment
Wound care kits	Help obtaining an identification card
Naloxone voucher for redemption at pharmacy	HIV pre-exposure prophylaxis
Alcohol pads	Health insurance registration
Xylazine test strips	Wound care
Hats and gloves	Legal aid
Female hygiene supplies	STI treatment and testing
Housing vouchers	Pregnancy testing
Transportation vouchers	Maternal care
At-home HIV tests	Education assistance
Resource guides	

A common concern about kiosks is the potential missed opportunities for linkage to care.[54 69] To address this concern, the kiosk will feature a care navigation call-back menu. Care navigation can increase PWUD use of community-based services, including increased engagement in substance use disorder treatment.[70-72] Participants will select services displayed on the kiosk's interface (see Table 3 for potential menu) and provide access to their phone number(s) for call-back.

People with lived experience with substance use who are certified and trained Recovery Coaches (RCs) will monitor the kiosk data dashboard and field call-back requests within three business days. RCs will briefly assess service needs and potential barriers and make facilitated referrals to health and support services. RCs will also share that they are a person in recovery and relate where possible to the participant's situation and provide hope and encouragement. With permission, RCs will follow up in seven days to offer further assistance. Clients can continue to contact RCs with follow-up questions.

Outcomes

Study outcomes are described in Table 4 and in detail on the study overview in ClinicalTrial.gov.[73] All measures are continuous. Self-reported measures will be assessed using time-line follow-back methods.[74] Survey logic is used to identify reporting discrepancies in real time and prompt the interviewer to resolve the discrepancy with the participant (i.e., reporting more injections involving a clean needle in the past 30 days than total number of injections).

Table 4. Outcomes

Outcomes	**Recall period**
Primary outcomes	
Change in syringe coverage for injections (number of injections where a clean syringe was used divided by total number of injections among participants who inject drugs)	30 days
Change in harm reduction program supplied syringe coverage for injections (number of injections where a clean syringe from the [kiosk/SSP] was used divided by the total number of injections among participants who inject drugs)	30 days
Change in SSP/KyOSK-provided syringe coverage for injections (number of syringes obtained at the SSP and/or kiosk)	30 days
Secondary outcomes	
Change in frequency of receptive syringe sharing among participants who inject drugs	30 days
Change in frequency of distributive syringe sharing among participants who inject drugs	30 days
Change in number of people with whom person shared syringes and injection equipment	30 days
Change in frequency of syringe reuse among participants who inject drugs	30 days
Change in frequency of safe syringe disposal among participants who inject drugs	30 days
Change in frequency of condomless anal and/or vaginal sex	30 days
Change in frequency of overdose	6 months
Change in use of naloxone during overdose events by participants who witnessed an overdose	6 months
Change in number of days carrying naloxone	30 days
Change in number of times contacting or visiting a pharmacy to obtain naloxone	6 months
Change in number of days on medications for opioid use disorder (MOUD) among participants who use opioids to get high	30 days
Change in frequency of use of harm reduction services among participants who inject drugs	30 days
Change in frequency of use of fentanyl test strips among participants who use drugs	30 days
Change in frequency of engagement in overdose protective behaviors among participants who use drugs	30 days

Following the Implementation Outcomes Framework[75], we will assess acceptability, appropriateness, fidelity, cost, penetration/reach, and sustainability. Acceptability and appropriateness will be assessed in the cohort surveys using the Acceptability of Implementation Measure (AIM) and Intervention Appropriateness Measure (IAM), respectively.[76] Fidelity is described in the *Blinding, Contamination, and Fidelity* section. Using established methods,[77-81] costs will be estimated from the provider's perspective and employ a micro-costing approach that measures and values in monetary terms all resources invested and links costs to the primary and secondary outcomes to evaluate economic impact. *Penetration* (i.e. reach) will be determined by examining the number who engage with the kiosk and/or staffed SSP divided by the number enrolled at the time of intervention/comparison condition implementation (i.e. percent who use the kiosk or SSP) and per supply (i.e. percent who accessed each supply) at monthly intervals. Finally, prospects for sustainment will be explored in final year using qualitative, semi-structured interviews with SSP and other health department staff and local and state leadership.

Building on existing models,[82-85] we will develop and calibrate[86] a dynamic, deterministic model of HCV transmission and overdose among PWUD in the intervention county to estimate the kiosk's impact and cost-effectiveness. The kiosk's effects will be parameterized using trial data. Impact will be measured as reductions in HCV incidence/prevalence, HCV infections and overdoses averted and quality-adjusted life-years (QALYs) saved over the study and longer timeframes (10/20/50 years). Using cost data, we will estimate cost-effectiveness by comparing discounted (3% annually[87]) costs and QALYs over 50-years between model scenarios with and without kiosk introduction. The mean incremental cost-effectiveness ratio will be estimated and compared to US relevant willingness-to-pay per QALY thresholds.[88]

Data collection

Participants are recruited from (1) existing cohort studies of PWUD, (2) the two SSP programs, and (3) peer-referral. Recruitment from these sources occurs simultaneously; staff l extend invitations and advertise in the SSP, and those who enroll are invited to refer peers (paid for up to five each, $10/peer). KyOSK recruitment commenced in March 2023. The target sample size is 750, including 425 from the intervention county and 325 from the control county.

Community-based field staff administer surveys programmed in Questionnaire Development System (QDS)'s computer-assisted self-interviewing program, with staff asking participants questions aloud and entering participants' responses. Participants can skip any question. The survey collects demographic characteristics, sexual and drug-related risk behavior, houselessness, criminal legal system involvement, SUD treatment, medical care access, harm reduction service access, and social, drug, and sexual network characteristics. Staff administer follow-up surveys every 6 months. Participants receive $35 at baseline and $25 for each follow-up survey.

At baseline, staff administer a 14-panel saliva drug test and fingerstick HIV and HCV antibody tests. Trained staff use the rapid-rapid protocol for HIV testing,[70,71] involving INSTI HIV 1/HIV 2 Rapid Antibody Test (BioLytical® Laboratories Inc., Richmond, B.C., Canada) followed by Sure Check® HIV-1/2 Antibody Test (Chembio Diagnostic Systems, Inc., Medford, NY). Staff use OraQuick® *HCV* Rapid Antibody Test (OraSure, Bethlehem, PA) for HCV testing.[72] Staff provide post-test counseling and facilitated referrals for those testing positive.

The kiosk's software will capture detailed, de-identified data linked only to user ID code. Data will be stored in a secure password-protected database. Data include client- and visit-level usage including day/time, frequency of use, supply selection and quantity, number of syringes returned, and call-back requests. The same data will be collected on clients visiting the SSP.

Retention

Following standard procedures used in longitudinal research,[89] participants provide detailed locator information to assist with retention and/or contact for future research including names, pseudonyms, phone numbers, addresses, email addresses, social media contact information, and contact information for up to three people who should know how to reach the participant if contact information changes. Participants are contacted at the mid-point of each follow-up interval to update locator information and remind them about their follow-up appointment. Participants receive $10 for updating or verifying locator information between the baseline and 6-month follow-up appointment (the period at which most attrition occurs). In

addition, local jail systems are searched to identify if a person is incarcerated. Participants who are incarcerated and have consented to be contacted while incarcerated may complete follow-up surveys from jail (with permission from jail administrative staff).

Blinding, Fidelity, and Contamination.

Analysts remain blinded through recruitment and follow-up until completion of primary and secondary analyses, using uninformative participant labels. Due to the nature of the interventions, participants and site staff administering the intervention are not blinded. These staff are instructed to use uninformative labels when discussing participants with blinded investigators.

Fidelity of kiosk and staffed SSP implementation will be assessed early and mid-trial on three domains: (1) supply availability, (2) operation, and (3) recovery coaching. *Supply availability* will be assessed using the kiosk's internal data in which item selections unfilled due to insufficient stock are recorded. *Operation* will be assessed by examining the number of kiosk malfunctions and number of times in which the staffed SSP operated < 40 hours per week excluding holidays. The latter will be assessed five unannounced visits per month by research staff at opening, lunch, and near closing. *Recovery coaching* fidelity to best practices will be assessed by monthly review of 10% of randomly selected, audio recorded sessions and completion of a fidelity checklist, which includes tailoring the conversation to stage of change, using motivational interviewing, engaging in resource brokering, and so on.

Potential for contamination is low, as the travel distance between sites is two hours. Participants enrolled in the control county will not be provided with a swipe card to access the kiosk in the intervention county. Nevertheless, to assess potential contamination, data will be collected at each follow-up survey about county of residence, SSP and kiosk use, and in which county they accessed services.

Data management

Data are imported to a single warehouse file on our secure network drive. Using the QDS Warehouse Manager program, the data manager assesses transferred data for completeness and consistency and tracks data modifications. Stored data are exported as SAS and SPSS datasets for analysis. The list linking participants to their unique identifier is maintained on a secure REDCap database. To protect confidentiality, only de-identified data are shared for analysis.

Statistical methods

The Intention-to-Treat (ITT) population will contain all enrolled participants according to their assigned study arm. The Per-Protocol population will include participants who complete the trial as originally allocated. We hypothesize that values on our primary outcome measures of syringe coverage (see *Outcomes* for operationalization) in the intervention county will be greater than the control county in the ITT and Per-Protocol populations. We anticipate that the secondary outcomes of risk behaviors (see *Outcomes* for operationalization) in the intervention county will be less than that reported by those in the control county. We hypothesize that participants in the intervention county will be more likely to engage the secondary outcomes related to naloxone carriage and MOUD and HCV treatment than those in the comparison county.

All models will be analysed using generalized estimating equations (GEE) assuming an AR(1) residual structure to account for within person autocorrelation due to repeated measures,

and will include fixed effects for county intervention condition, intervention period, and condition*period interaction. This interaction estimates the relative change in the intervention county compared to the control county due to kiosk's introduction. Although the counties are remarkably similar, our planned analyses do not rely on baseline equivalence to identify intervention effects. Instead, intervention effects are identified under the assumption that the trend in outcomes over time in the control condition are parallel with those that would be observed in the intervention county in the kiosk's absence. To further relax this assumption, we will model county specific linear time effects to allow for different secular trends that may confound estimation of the intervention effect. Multiple baseline measures allow better capture of any potential differential trends. Models will include an indicator variable reflecting whether participants also received services at the staffed SSP and institutionalization (hospitalized or incarcerated) at the time of the survey. Other theoretically justified time varying covariates and recruitment method (i.e., enrolled from cohort, SSP, or peer-referral) will be examined. We will examine homophily in peer referral chains and incorporate autocorrelation within chains if significant homophily on outcomes is present. Of note, GEE models are robust to minor misspecifications of the correlation structure that may arise due to the sampling scheme.

Our prior research has shown that the rates of our primary outcomes are high enough to be well approximated as normal. If this does not hold true, we will use Poisson models with appropriate offsets to account for the distribution of the primary ratio outcomes. Type 1 error (α) will be set to 0.05 in primary and secondary outcome analyses, and two-tailed tests will be used. For outcomes that apply only to a subset of participants (e.g., syringe sharing analyses are restricted to PWID), data from time points at which participants do not report the relevant behavior (e.g., injection drug use) will be omitted from these models. Resulting estimates will be unbiased under the assumption that the kiosk did not cause a change in the overall behavior defining the subset (e.g., in injection drug use). Sensitivity analyses including all data will be performed using multinomial logistic regression where the outcomes are specified as, for example, no injection drug use, injection drug use with a clean syringe, and injection drug use without a clean syringe.

We will use multiple imputation by chained equations (MICE)[90] to account for attrition in all analyses. Our imputation model will include interactions between intervention county and baseline risk measures to allow for differential selection effects between the intervention and comparison groups should differential attrition arise.[91]

To analyze reach, we will perform segmented regression analyses using existing data from the statewide SSP database beginning in January 2020 allowing for 3 years of pre-intervention data. We will assess change in total reach by comparing the difference in the changes in both intercept and slope between counties. All models will account for first-order autocorrelation and use appropriate link functions based on outcome distributions. We will also explore changes in reach by gender, age, IDU, or other characteristics, by generating separate series by participant characteristic and then analyzing these series in a pooled interaction model.

Power Calculation

Based on prior published simulations,[92] our segmented regression analyses (n=72 months, 3 years pre- and 3 years post-intervention implementation) are well powered to achieve study aims for small effects across a wide variety of link functions and autocorrelation values. We estimated power for our primary intervention models using 5000 Monte Carlo simulations for each set of parameters, with a type-1 error rate of 0.05 and an unbalanced design (sample

unevenly distributed across counties). We simulated autocorrelated outcomes for three pre-intervention and five post-intervention survey waves with an expected 750 enrollees. We conservatively used 70% retention for the power analysis. Not all outcomes will be applicable to the full cohort; for example, approximately 25% are estimated[93] to have not recently injected and therefore will not contribute to analyses of outcome variables related to injection. Therefore, we estimated power for various effect sizes for a cohort of "completers" of N=300, 400, and 500. Based on these simulations, all sample sizes are powered to detect a standardized mean difference of at least 0.2, a small effect. As enrollment nears the target sample size, the accuracy of projected estimates of retention and injection drug use will be evaluated and the sample size may be increased if needed.

Data monitoring

A DSMB with a physician, statistician, infectious disease epidemiologist, and behavioral scientist with expertise in research among PWUD oversees the study. The DSMB is independent of the sponsor and competing interests. The DSMB meets at least annually to review emerging data, and make recommendations about the trial's conduct, including stopping the trial. No formal interim analyses are planned.

Social Harms

Social harms related to participation will be actively assessed and documented. Social harms include any intended or unintended cause of physical; emotional; or psychosocial injury or hurt from one participant to another, a participant to themselves, or an institution to a participant, occurring as a result of study participation.[94] Participants will complete a social harms questionnaire at each study visit. Study staff are trained to provide appropriate care, counseling, and referral as needed. Any identified social harms are reported to study investigators who determine severity and provide details to the IRB as required.

Auditing

The Data Scientist regularly assesses data for missingness and data quality and provides feedback to the PI and field staff regarding any issues that need to be addressed. The PI and Project Director review study consent materials to assure appropriate documentation of consent at least semi-annually.

Patient and Public Involvement

Participants were not directly involved in the development of the research question, outcome measures, or conduct of the trial; however, officials from state and local agencies, and community advisory boards were involved in intervention design. Upon funding, six focus groups with potential clients and local health department personnel were conducted to gain feedback on kiosk features. Then, a KyOSK Design Team including people with lived experience with substance use, local health department partners, state government officials, and service leaders was convened to guide kiosk design. A separate community advisory board of people with lived experience with substance use provided feedback on recruitment methods and participated in survey question review and piloting. Upon completion of the study, results will be distributed via study social media pages, websites, local community advisory board, the KyOSK Design Team, and to community partners.

Ethics and Dissemination

The KyOSK study is reviewed and approved by the University of Kentucky IRB (Protocol #78081). Study staff complete human subjects training and are approved as personnel by the IRB. Protocol modifications, revisions to consent forms, and changes to other participant-facing documents are submitted to the University of Kentucky IRB for approval prior to implementation. Protocol modifications are submitted to the IRB prior to implementation and reflected in clinicaltrials.gov. Approval from the funding agency will be sought for major protocol modifications, such as changes in inclusion criteria or aims, prior to submitting those changes to the IRB.

All participants complete an informed consent process at baseline and at the follow-up appointment preceding kiosk implementation, with the latter going into more detail about the kiosk design and supplies. The consent form describes the protocol, risks, and benefits. Consent procedures are completed in person in a private area with only the participant and study staff present.

Findings will be disseminated to the public and healthcare professionals in peer-reviewed journals, professional conferences, and community forums. Authorship eligibility guidelines follow ICMJE criteria. We will submit manuscripts to NIHMS to be made publicly available no later than 12 months after the official date of publication in compliance with the funder's open access policy. De-identified data will be made available to interested parties upon submission and approval of a written request describing data security protocols and intended use.

Authors' contributions
The following individuals contributed to the design of the protocol described in this manuscript: AMY, MDL, HKK, JRH, AFB, LF, PRF, JS, PV, HLFC, CC, and KEM. The following made substantial contributions to the implementation of the protocol: AMY, MDL, HKK, JRH, EF, AFB, LF, PRF, JS, PV, HLFC, CW, EL, and KEM. The following individuals made substantial contributions to the drafted work and/or substantively revised it: AMY, MDL, HKK, JRH, AFB, LF, PRF, JS, PV, HLFC, KEM, EF, CW, and TJ. The KyOSK Community Staff authors provided valuable input on the project design, are key to the project's implementation, and represent the project in the community. The KyOSK Design Team has guided the design of the intervention, made valuable contributions to the plan for its implementation, and will provide guidance throughout its implementation. All authors read and approved the final manuscript and agree to be accountable for all aspects of the work.

Collaborators
The KyOSK Community Staff authors include Kenneth Lane, Nathan Bartrum, Rhonda Gilliam, Sarah Hurlburt, Kristen Johnson, Lisa Maybrier, Cindy Oliver, Lana Rose, Renée Tabor, and Jennifer Watson. The KyOSK Design Team authors include Chase Barnes, Shirley Candybar Combs, William H. Feltner, Kerri Dawn Knight, Anthony S. Lockard, Magic Man, Paula Stidham, Patty Stidham, Elizabeth De'Hart Sword, Larry M. Sword, and Pamela Wright.

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Competing interest statement
Amanda Fallin-Bennett is a co-founder of Voices of Hope, the contracted recovery community organization providing the recovery coaching services. The device to facilitate syringe disposal and dispensing that will be installed in conjunction with the kiosk is intellectual property of the University of Kentucky, with April Young designated as the inventor. Chelsi Cheatom is a paid consultant on the implementation of harm reduction vending machines, including on the described project.

Data Sharing Statement
De-identified data will be made available upon written request to Principal Investigator, April Young.

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SPIRIT
STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	Page 3, Line 3-7
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	Page 3, Line 36
	2b	All items from the World Health Organization Trial Registration Data Set	Not applicable
Protocol version	3	Date and version identifier	Not applicable
Funding	4	Sources and types of financial, material, and other support	Page 17, Line 25
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	Page 17, Lines 3-22
	5b	Name and contact information for the trial sponsor	Page 17, Line 25
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	Page 17, Lines 27-30

	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	Not applicable
Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	Page 6, Lines 4-53
	6b	Explanation for choice of comparators	Not applicable
Objectives	7	Specific objectives or hypotheses	Page 6, Line 50-53
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	Page 31, Line 49-50
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	Page 31, Line 6-30
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	Page 31, Lines 32-46
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	Page 32, Line 16 to Page 34, Line 44
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	Page 15, Line 16-32

	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	Page 13, Lines 15-25
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	Not applicable
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	Page 10, Line 45 – Page 12, Line 13
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	Page 9, Line 3-40
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	Page 14, Line 50 -Page 15, Line 14
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	Page 12, Line 16-21

Methods: Assignment of interventions (for controlled trials)

Allocation:

Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	Not applicable
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	Not applicable
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	Not applicable

Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	_Not applicable_
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	_Not applicable_
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	_Page 12, Line 15-44
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	_Page 12 Line 47 – Lage 13, Line 6
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	__Page 13, Line 34-39
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	_Page 13, line 42-Page 14, line 47
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	_Page 14, Line 16-20
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	Page 13, Line 42-49
Methods: Monitoring			

Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	Page 15, Line 16-22
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	Not applicable
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	Page 15, Line 24-32
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	Page 15, Line 34-39
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	Page 16, Line 4
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	Page 16, Line 6-12
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	Page 16, Line 12-17
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	Not applicable
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	Page 13, Line 38-39
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	Page 17, Line 33-40

Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	_Page 16, Line 23-24_
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	_Not applicable_
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	_Page 16, Line 18-23_
	31b	Authorship eligibility guidelines and any intended use of professional writers	_Not applicable_
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	_Not applicable
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	_Included as supplemental file_
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	_Not applicable_

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.