CLINICAL STUDY PROTOCOL

Leveraging Social Networks to Increase COVID-19 Testing Uptake

A Comparison of Credible Messenger and Chain Referral Recruitment Approaches

National Clinical Trial (NCT) Identified Number: NCT04873401

Sponsor

National Institute on Drug Abuse

National Institute of Health

Grant Title: Leveraging Social Networks to Increase COVID-19 Testing Uptake: A Comparison of Credible Messenger and Chain Referral Recruitment Approaches

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Conducted by the New York State Psychiatric Institute with Alliance for Positive Change, Argus Community Inc., Columbia University

Protocol Version 2.0

[01/17/2023]

Section 1: Basic Information

1.1. Study Title

Leveraging Social Networks to Increase COVID-19 Testing Uptake: A Comparison of Credible Messenger and Chain Referral Recruitment Approaches

1.2. Is this study exempt from federal regulations?

No

1.3. Exemption Number

NA

1.4. Clinical Trial Questionnaire

1.4.a. Does the study involve human participants?

Yes

1.4.b. Are the participants prospectively assigned to an intervention?

Yes

1.4.c. Is the study designed to evaluate the effect of the intervention on the participants?

Yes

1.4.d. Is the effect that will be evaluated a health-related biomedical or behavioral outcome?

Yes

1.5. Provide the ClinicalTrials.gov Identifier for this trial, if applicable

NCT04873401

Statement of Compliance

New York State Psychiatric Institute (NYSPI) Institutional Review Board (IRB) is duly constituted, has written procedures for initial and continuing review of clinical trials; prepares written minutes of convened meetings, and retains records pertaining to the review and approval process; all in compliance with requirements of FDA regulations 21 CFR Parts 50 and 56, HHS regulations 45 CFR 46, and International Conference on Harmonization (ICH) E6, Good Clinical Practice (GCP), as applicable.

Investigator's Signature

X_____

20 January 2023

Section 2. Study Population Characteristics

Introduction:

Study Rationale

COVID-19 has severely impacted underserved populations and their communities. Higher incidence of COVID-19, hospitalization and mortality, have been found in neighborhoods in NYC with high poverty rates, where HIV, HCV, opioid use and justice involvement/arrests are endemic. In Harlem, Washington Heights, and the South Bronx, where the proposed supplement will take place, rates of infection and mortality were some of the highest in NYC. Historically, those who use opioids and other substances inconsistently accessed services due to a confluence of structural (e.g., housing instability, stigma, discrimination, and lack of insurance) and individual-level factors (e.g., mental illness; medical mistrust). Identification of positive cases requires widespread testing of this vulnerable yet "hidden" population.

Guided by social cognitive theory (SCT), Andersen's model of health care access and the EPIS framework, Specific Aims are: 1) Adapt two implementation strategies to support COVID-19 testing uptake and sustainability, adapting elements of existing efficacious social network-based interventions via a CBPR approach. 2) Examine and compare the efficacy of two sets of implementation strategies on (i) reach, (ii) testing uptake, (iii) service delivery (i.e. quarantine, medical care, contact tracing) and (iv) sustainability for individuals who use opioids and other drugs. Use of data drawn from Healthix, a public health information exchange, will supplement this comparison by generating a baseline of participant prior testing and health behavior to determine access to underserved populations as well as long-term influence on future testing behavior. 3) Elucidate and compare the system/organizational-, staff-, and individual-level factors that influence implementation (i.e. fidelity, acceptability, feasibility, sustainability) of the strategies to develop a plan for dissemination and scale-up in other CBOs who serve opioid and other substance using individuals in NYC.

Background

The present project aims to adapt and conduct a trial examining the ability of two recruitment strategies, chain-referral and credible messenger, proven efficacious in reaching hidden populations to improve HIV testing uptake, to reach those who use opioids and other substances in order to increase their uptake of onsite point of care COVID-19 testing that will be delivered in two community-based organizations (CBOs). The CBOs -- Alliance for Positive Change and Argus Health Inc -- have a well-established partnership with members of the parent grant team (Cohall, Wilson, Cohall, Gordon) following collaborations on numerous initiatives targeting HIV, HCV and STIs prevention, testing and treatment for over 15 years. These agencies have again agreed to work with the team on the proposed supplement and adapt the existing infrastructure in their agencies to now tackle COVID-19, which devastated the communities they serve in the initial wave of the COVID-19 epidemic in New York City. Argus and Alliance combined have had a presence in the communities of Washington Heights, Harlem and the South Bronx for over 50 years, and have subsequently developed considerable trust, support and "credibility" within these communities. It is this community presence that we will tap into as we adapt the two recruitment strategies. The staff and clients from these agencies have extensive experience developing and adapting programming and, guided by a community participatory based research approach, will partner with the research team in these adaptation efforts.

The aims of the proposed supplement are independent of the parent grant, yet draw on the team, existing partnerships and our implementation expertise in the development of this new proposal. This investigation will provide much needed information to improve health outcomes and to identify effective system-level responses to prevent or arrest the spread of COVID-19 among the social networks of those who use opioids and other substances, a highly vulnerable and often overlooked population.

2.1.1. Conditions or Focus of Study

Condition 1: COVID-19
Condition 2: Substance use

Condition 3: Opioid Use

2.1.2. Study Aims
Following a CBPR approach that builds on the expertise and community outreach infrastructure of Argus and Alliance, we propose to adapt two implementation strategies that have been proven to increase the reach, access, and uptake of HIV testing and related services in order to support the uptake and sustainability of point-of-service (POS), onsite COVID-19 testing in CBOs that target underserved people who use opioids and other substances. Guided by social cognitive theory (SCT), Andersen's model of health care access and the EPIS framework, the specific aims are to:

Aim 1. Adapt two implementation strategies to support COVID-19 testing uptake and sustainability, adapting elements of existing efficacious social network-based interventions via a CBPR approach.

Aim 2. Examine and compare the efficacy of two sets of implementation strategies on (i) reach, (ii) testing uptake, (iii) service delivery (i.e. quarantine, medical care, contact tracing) and (iv) sustainability for individuals who use opioids and other drugs. Use of data drawn from Healthix, a public health information exchange, will supplement this comparison
by generating a baseline of participant prior testing and health behavior to determine access to underserved populations as well as long-term influence on future testing behavior.

Aim 3. Elucidate and compare the system/organizational-, staff-, and individual-level factors that influence implementation (i.e. fidelity, acceptability, feasibility, sustainability) of the strategies to develop a plan for dissemination and scale-up in other CBOs who serve opioid and other substance using individuals in NYC. This investigation will provide much needed information to improve health outcomes and to identify effective system-level responses to prevent or arrest the spread of COVID-19 among the social networks of those who use opioids and other substances, a highly vulnerable and often overlooked population.

2.2. Eligibility Criteria
Sample 1: Testing Participants. Must endorse opioid or other substance abuse in the past 6 months and must speak English or Spanish; >18years.

Sample 2: Staff Participants. Currently employed at either Argus or Alliance, including POLs participating in Peer programs. PI/PD will present the study to staff and interested staff will be asked to contact the research team.

2.3. Age Limits
Samples 1-2
Minimum: 18 years
Maximum: NA

2.4. Inclusion of Women, Minorities and Children
Inclusion of Women. There is no inclusion or exclusion of participants based on gender. Based on demographic and community/area data of Argus and Alliance clients, staff, and credible messengers we anticipate females will comprise approximately 40% of the sample.
Inclusion of Minorities. We will not exclude participants based on ethnicity. Based on the demographic data of Argus and Alliance clients, staff, and credible messengers we anticipate 51% African American and 39% will be Hispanic.
Inclusion Across the Lifespan. Children will not be enrolled. The proposed study involves those who are using opioids and other drugs and who are largely underserved and at risk for COVID- 19 infection. In NYS, the current

opioid epidemic does not center on those younger than 18 and currently, those at greatest risk for negative sequalae from complications due to COVID-19 are older than 18.

2.5. Recruitment and Retention

Recruitment of agency staff and credible messengers for staff surveys and focus groups. All agency staff will be invited to participate in the staff surveys; those staff and credible messengers directly involved in the recruitment strategies and on-site COVID-19 test delivery, either via educating testing participants and supervising credible messengers (staff) or recruiting peers in the community (credible messengers) will be invited to participate in the staff surveys and focus groups in the same way. The PI/PD will present the study to agency staff both in-person at a staff meeting and via email and interested staff will be asked to contact the research team. An email from the PI (with an attached information sheet) explaining the project and staff participation in the survey and focus group will be sent to agency leadership who will then distribute it to staff and Credible Messengers. These methods have been used successfully in our prior work with probation offices and treatment staff. The email will instruct interested staff to contact research staff directly to ask questions. For those interested in participating in focus groups, efforts will be made to schedule interviews at times that do not interfere with staff roles (e.g. lunch breaks; staff meetings). Considerable effort will be taken to ensure that staff do not feel coerced to participate. It will be emphasized to staff that participation (Y/N) is voluntary and will in no way affect their employment status. These procedures have been successfully used in PIs prior work recruiting justice and treatment staff. Retention and engagement activities will include small thank you gifts for participation in surveys, one at baseline and the other after study activities have been completed. We are unable to address staff-turnover which may impact on study retention.

Recruitment of testing participants. Testing participants will be recruited in one of two ways: chain referral and credible messenger. In the chain referral strategy, an initial set of n=8 "seed" participants are recruitment by staff of eligible clients receiving services at Argus and Alliance (n=16 total seeds). For clinic-based recruitment of "seeds", participants will be recruited from among those individuals who use opioids and other drugs who are receiving services through Argus or Alliance; services do not need to be substance use related. (Following a brief training, these "seed" participants then recruit additional participants ("peer recruits") from among their own peer networks of those known to use opioid or other drugs in community settings (peer- recruitment). "Seed" participants are given three unique, numbered coupons, which they can give to people they know (peers) who are also use opioids and other drugs. The coupons will have information, by which peers who are interested in participating in the study can contact the research team to be screened for eligibility. Participants will receive renumeration for each peer recruit who enrolls in the study by redeeming a coupon given to them by that participant. Peer-recruits then repeat the same process with members of their peer network.

The credible messenger strategy involves leveraging the existing infrastructure at both Argus and Alliance, which includes credible messenger programs that are well-established, with considerable influence and impact within the respective communities served by these two agencies. The credible messengers within these programs have been trained to conduct community outreach to target individuals at increased risk for HIV, STIs, HCV and SUD and encourage testing and/or linkage to services. Interested credible messengers (n=4 from each site) will serve as messengers in the current study and will be trained to also include education about COVID-19, ways to reduce risk as well as ways to increase motivation to test for COVID-19 at the respective clinics. Credible messengers will conduct community outreach, targeting those locations and venues where potentially credible participants are located, and will provide education and encourage these individuals to seek testing. The potential participants will be given a coupon which will be redeemed at the clinic when the participant is enrolled in the study after being determined as eligible.

As testing participants are assessed once and then offered a test immediately thereafter, study retention is not a considerable focus of procedures. Participants recruited by chain-referral will be given a brief survey following their recruitment efforts to document number of attempts, time etc. This brief survey will occur at the visit when the participant comes to the clinic to receive payment for redeemed coupons that s/he distributed to peers; it is anticipated the payment will serve to adequately retain participants for the purpose of completing the brief survey.

2.6. Recruitment Status
Not recruiting

2.7. Study Timeline
Study timelines have been attached to the end of this protocol; the first timeline documents study activities by wave (Figure 1, pg. 36).

2.8. Enrollment of First Subject
03/18/2020

Table 1. Inclusion Enrollment Table for RADx Participants

	Hispanic Ethnicity											
	Hispanic or Latino (n = 334)				**Not Hispanic or Latino (n = 140)**			**Prefer not to answer / Unknown (n = 12)**				
	Gender Identity Categories				***Gender Identity Categories***			***Gender Identity Categories***				
	Man	**Woman**	**Non-binary/ Other**	**Prefer not to answer**	**Man**	**Woman**	**Non-binary/ Other**	**Man**	**Woman**	**Non-binary/ Other**	**Unknown**	**Total**
Racial Categories												
American Indian/Alaska Native	9	1	1	0	1	1	0	2	0	0	0	15
Asian	2	0	0	0	1	1	0	0	0	0	0	4
Native Hawaiian or Other Pacific Islander	4	0	0	0	0	0	0	0	0	0	0	4
Black or African American	23	6	0	0	44	22	3	2	1	0	0	101
White	19	13	1	0	30	25	1	2	0	0	0	91
Some other race	138	29	3	0	3	2	0	3	0	0	0	178
More than one race	11	6	1	0	2	2	0	1	0	0	0	23
Prefer not to answer	44	5	0	1	1	0	0	0	0	0	0	51
Unknown	14	3	0	0	1	0	0	0	0	0	1	19
Total	264	63	6	1	83	53	4	10	1	0	1	486

Table 2. Inclusion Enrollment Table for Staff Participants

Racial Categories	Ethnic Categories				Total
	Not Hispanic or Latino		Hispanic or Latino		
	Female	**Male**	**Female**	**Male**	
American Indian/Alaska Native	0	0	0	0	0
Asian	0	0	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0	0	0
Black or African American	2	1	1	2	6
White	0	0	0	0	0
More than One Race	0	0	1	1	2
Total	2	1	2	3	8

Section 3. Protection and Monitoring Plans

3.1.1(a) Human Subjects Involvement, Characteristics, and Design

Scientific Rationale for Study Design

The primary goals of this proposal are to 1) adapt and compare the efficacy of two evidence-based outreach and recruitment strategies that target and identify (reach) individuals who use opioids and other drugs to increase uptake of COVID-19 testing and related services (quarantine, treatment); and 2) document the organizational, staff and individual-level factors t*hat influence implementation (i.e. fidelity, acceptability, feasibility, sustainability*) *of the strategies* to develop a plan for dissemination and scale-up in CBOs and other settings who serve opioid and other substance using individuals in New York City. The subjects will be recruited from two areas in New York City (NYC), northern Manhattan (Washington Heights and Harlem) and the South Bronx, areas served by two community based organizations (CBOs) that specialize in SUD treatment and provide a wealth of supportive services for individuals who abuse substances: Argus and Alliance (see **Facilities and Other Resources**)..

There are **three phases** to the proposed study:

- **Phase 1: Strategy Adaption,** will comprise a series of meetings (n=8) attended by a Working Group (WG) that will include n=7 members of the research team, n=10 members of the project Community Advisory Board (CAB), which will be assembled from interested members of the CABs of Argus and Alliance, and interested staff from both agencies. Using community-based participatory research (CBPR) approaches, the WG will develop protocols and materials (e.g. messaging, target locations, training protocols, visual materials) for two recruitment strategies that aim to encourage individuals who use opioids and other drugs to seek COVID-19 testing. As we will not be collecting data from WG members, nor will consent/assent be obtained for their participation, they are not considered human subjects.
- **Phase 2: Efficacy Test and Implementation Evaluation**, a trial will be performed in which the two strategies will be compared with respect to reach, testing uptake and related services; we will aim to recruit 500 participants who use opioids or other substances over an 8 month period of time (n=250 in each strategy). Participants will be assessed upon enrollment into the study. In addition, n=8 credible messengers (n=4 at each site), and n=20 staff members at each site employed at our community partners agencies Alliance and Argus, will complete baseline and 12-month follow-up surveys, fidelity/feasibility checklists, PDSA cycle and will participate in a workgroup at the completion of Phase 2.
- **Phase 3: Sustainment**, CBOs will implement the strategy proven efficacious based on outcomes, and we will examine their sustainment of the program.

- The **two recruitment strategies** used in Phase 2 are **chain referral** and **credible messenger**:
  1) In the **chain referral strategy**, an initial set of n=8 "seed" participants are recruitment by staff of eligible clients receiving services at Argus and Alliance (n=16 total seeds). For clinic-based recruitment of "seeds", participants will be recruited from among those individuals who use opioids and other drugs who are receiving services through Argus or Alliance; services do not need to be substance use related. (Following a brief training, these "seed" participants then recruit additional participants ("peer recruits") from among their own peer networks of those known to use opioid or other drugs in community settings (peer-recruitment). "Seed" participants are given three unique, numbered coupons, which they can give to people they know (peers) who are also use opioids and other drugs. The coupons will have information, by which peers who are interested in participating in the study can contact the research team to be screened for eligibility. Participants will receive renumerationfor each peer recruit who enrolls in the study by redeeming a coupon given to them by that participant. Peer-recruits then repeat the same process with members of their peer network.
  2) The **credible messenger strategy** involves leveraging the existing infrastructure at both Argus and Alliance, which includes credible messenger programs that are well-established, with considerable influence and impact within the respective communities served by these two agencies. The credible messengers within these programs have been trained to conduct community outreach to target individuals at increased risk for HIV, STIs, HCV and SUD and encourage testing and/or linkage to services. Interested credible messengers (n=4 from each site) will serve as messengers in the current study and will be trained to also include education about COVID-19, ways to reduce risk as well as ways to increase motivation to test for COVID-19 at the respective clinics. Credible messengers will conduct community outreach, targeting those locations and venues where potentially credible participants are located, and will provide education and encourage these individuals to seek testing. The potential participants will be given a coupon which will be redeemed at the clinic when the participant is enrolled in the study after being determined as eligible.

Justification for Intervention

Social network strategies effective at identifying hidden populations and improving access to HIV related services may improve uptake of COVID-19 testing. Social network interventions utilize existing patterns of relationships to accelerate behavior change have been successful in increasing the uptake of HIV testing among marginalized populations, including people who use drugs. Moreover, social network approaches successfully counter stigma, medical mistrust, and misinformation around HIV, making them uniquely suited for addressing similar issues in the context of COVID-19. Two distinct social network recruitment strategies, chain-referral and Popular Opinion Leader (POL or "credible messenger") models may be promising for increasing rapid COVID-19 testing. In chain-referral a discrete number of "seeds" are identified and incentivized to refer members of their social networks, who in-turn repeat the process. In POL models, popular and socially influential individuals with lived experience are trained to engage within formal and informal social networks to promote behavior change. Based on the efficacy of chain-referral and POL recruitment in the context of the HIV/AIDS epidemic, the success of these strategies to promote COVID-19 testing in underserved populations of substance users is highly plausible. Given the distinct differences of these strategies, it is important to contrast them to determine the comparative benefits of one approach over the other.

Ongoing quality improvement (QI) to promote an adaptive response to an evolving epidemic and promote sustainability. Plan-do-study-act (PDSA) is an evidence-based, rapid-cycle change model for testing enhancements on a small scale before incorporating them on a larger scale. Training staff, and POLs to use data (e.g. testing uptake, client feedback) to monitor and improve program performance may be a useful tool to develop sustainable strategies that address a rapidly changing pandemic as well as incorporate new testing, treatment and prevention (i.e., vaccine) technology.

The theoretical approach will integrate Andersen's Model, Social Cognitive Theory (SCT), and the Exploration Preparation Implementation Sustainability (EPIS) framework to understand contextual/system- and individual-level factors that influence implementation of a community outreach and testing uptake approach. Andersen's Model provides a framework to identify key domains to target when developing interventions to improve service utilization.

We propose research to establish efficacy and sustainability of a community-social network outreach model that partners infectious disease health providers with community based organizations to successfully implement (reach, uptake, delivery and sustainment) COVID-19 rapid POS testing among a highly vulnerable and often underserved population, those who use opioids and other substances. Two distinct social network recruitment strategies, found efficacious for identifying HIV+/high risk populations and increasing uptake of HIV testing (cites) will be adapted and compared. Guided by the EPIS framework, SCT, and Andersen's model, this 2-year study will comprise three phases. In Phase 1: Adaptation of outreach recruitment strategies, we will work with our project CAB, via a CBPR approach, to adapt chain-referral and credible messenger strategies for uptake of COVID-19 testing, to finalize recruitment and on-site testing protocols, and to train the CAB in the new protocols and in continuous quality improvement strategies (Aim 1). In Phase 2: Strategy Efficacy Trial and Implementation Evaluation, we will compare the two strategies in a cross-over design at two CBOs, with initial strategy assignment randomly determined and rolled out for 4 months before the cross-over occurs. The comparison of chain-referral and credible messenger strategies is not to identify the statistical superiority of one sampling strategy in providing population estimates over the other, but instead to identify the ability of each recruitment strategy to reach the target population and increase uptake of COVID-19 tests. We will examine the impact of each strategy on (i) reach (recruitment of target population), (ii) COVID-19 testing/repeat testing, and (iii) service delivery (i.e. quarantine, medical care and contact tracing) among those who test positive for COVID-19 (exploratory) (Aim 2). In Phase 3: Sustainment, CBOs will implement the strategy proven efficacious based on outcomes, and we will examine their sustainment of the program (Aim 2). Implementation evaluation will identify participant-, staff-, and organizational-level factors that influence the feasibility, acceptability, and sustainability of each strategy in these CBOs. Participants will be assessed just prior to receipt of testing. Argus and Alliance staff will be assessed before and after the roll-out of strategies (Aim 3).

We will examine the impact of the intervention on (i) reach, (ii) testing uptake and (iii) service delivery (i.e. quarantine, medical care and contact tracing among COVID-19 positive cases); and (iv) sustainability for individuals who use opioids and other drugs as well as potential mediating/moderating variables from the Andersen, SCT and EPIS models. Data drawn from Healthix on prior and future COVID-19 testing will augment study data to determine access to underserved populations and influence on future testing behavior. RAs will conduct interviews in private rooms at Argus and Alliance. Participants will be assured that responses are confidential (see Human Subjects). Interviewers will be trained with established protocols, covering informed consent, confidentiality, reporting requirements, interview content, and cultural sensitivity.

End-of-Study Definition

This study will be stopped prior to its completion if: (1) the intervention is associated with adverse effects that call into question the safety of the intervention such as increased rates of COVID-19 infection; (2) difficulty in study recruitment or retention, or enrollment of participants will significantly impact the ability to evaluate the study endpoints; (3) any new information becomes available during the trial that necessitates stopping the trial; or (4) other situations occur that might warrant stopping the trial.

Human Subjects Characteristics

Setting. Participants will be recruited from Washington Heights, Harlem two neighborhoods in northern Manhattan, the Lower East Side, a neighborhood in southern Manhattan, and the South Bronx, the locations and geographic catchment areas of Argus and Alliance. In addition to current demographics of their current

substance using clientele, we anticipate participants will comprise 64% male, 51% African American, 39% Hispanic.

Randomization. Just prior to the onset of Phase 2, the chain referral strategy will be randomly assigned (50:50) to a clinic in order to begin the first roll out. After the initial roll out and plan-do-study-act cycle (PDSA), the assignment will be switched such that the chain referral is then implemented at the other site.

Testing Participants. We anticipate enrolling n=500 participants across both strategies in an 8 month period of time. Based on demographic characteristics of the neighborhoods where recruitment will occur in addition to current demographics of the substance using clientele of Argus and Alliance, we anticipate participants will comprise 64% male, 51% African American, 28% Hispanic. Inclusion/exclusion criteria. All participants, regardless of recruitment strategy, must 1) be >18 years of age; 2) endorse opioid or other substance abuse in the past 6 months, and 3) speak English or Spanish. Those who deny history of substance use (but will be offered COVID-19 testing), or present with intoxication that prevents meaningful study participation at the time of enrollment will be excluded. Individuals too intoxicated to participate, but otherwise willing and eligible will be rescheduled up to two times. Finally, those recruited by peer chain referral (see 3.7.2) who test positive for COVID-19 will be excluded from participating in the recruitment of other individuals until such time as they receive a negative nucleic acid COVID-19 test. This more stringent assessment of non-infectiousness is being used given the likely inclusion of immunocompromised individuals in the study groups.

Agency staff and credible messengers. We will enroll n=2 staff and n=8 credible messengers across both sites. Based on current staffing demographics we anticipate staff will be 50% female, 50% Hispanic; 50% white, and credible messengers will be 63% male; 70% Hispanic; 60% White. Inclusion/exclusion criteria: staff must be 1) >18 years old; 2) employed by either Argus or Alliance

3.1.1(b) Study Procedures, Materials, and Potential Risks

Research data will be drawn from 1) self-completed questionnaires, 2) staff focus groups, 3) participant

responses to process measures, 4) Healthix health data management information system, 5) analysis of saliva

Phase 2.

Staff surveys. At the beginning of Phase 2, staff and credible messengers will complete brief surveys. Guided by EPIS, Andersen and SCT, surveys will collect data on theoretically-defined inner-, outer-, and individual-level factors that may influence the implementation of the recruitment strategies and testing. Surveys will capture demographics and professional history, and attitudes and knowledge regarding COVID-19, risk reduction behaviors and testing. Surveys will be available in paper/pencil format as well online via Redcap link; surveys will be administered again at the end of Phase 2 with similar content as well as items on palatability and felt-utility of the different strategies.

Test participant surveys. Following consent and study enrollment, all participants will complete a brief assessment consisting of structured survey examining predisposing and enabling factors (e.g. mental health, substance use, social support/capital), social-cognitive factors (COVID-19 attitudes, knowledge perceived risk, stigma) and structural variables (e.g. housing security; food insecurity) and a social network inventory. A social network inventory will be adapted from previous inventories.[1,2] The inventory will consist of a set of standard "alter generators," which are questions asking participants to list names, pseudonyms or initials of individuals within their social networks ("alters") who fit certain descriptions (e.g. friends, loved ones, drug sharing partners, people who provide material support, etc.). Once alters have been generated and listed in an anonymized fashion, additional questions are asked about each alter to assess their age, frequency of interaction and duration of the relationship. Participants will also be asked about alters' drug use, as well as previous disclosures of COVID-19 exposure or seropositivity between the participant and his/her alters. RAs will conduct interviews in private rooms at either Argus or Alliance locations. At the end of this survey the participant will receive COVID-19 testing; brief follow-up interviews will occur for those participants included in the chain-referral recruitment strategy when they return to receive compensation for redeemed coupons.

Staff, credible messenger and CAB member focus group. At the end of Phase 2, interested agency staff, credible messengers and CAB members will be invited to participate in two focus groups to understand staff attitudes and perspectives on integration of each recruitment strategy and COVID-19 testing and related services into ongoing agency workflow; changes in job role, performance, or load. Staff focus groups will be run separately from CM/CAB member group and will be conducted in a private room at the home agency. The focus groups will each take approximately 1 hour to complete. Focus groups will be digitally recorded and transcribed, with the participants' consent, to facilitate the coding and analysis of these data.

Process measures: During Phase 2, participants recruited via chain-referral or credible messengers will complete a process measure, created for the study, consisting of a brief set of questions to monitor for potential ethical concerns arising among participants during the recruitment process. These questions will be defined during the intervention development process in Phase 1 and will address issues related to any unwanted disclosure of sensitive information, perceived or actual coercion or other potential psychological harms. Staff and CMs will complete a series of checklists capturing fidelity and feasibility of either recruitment method and delivery of the on-site testing.

Biological samples: During Phase 2 participants recruited via chain-referral or credible messenger will be asked to provide biological samples for COVID-19 testing, namely anterior nasal swabs for the BD Veritor™ SARS CoV 2 and Cepheid Xpert SARS CoV 2 testing platforms. Further details of the testing process can be found in Section 3.3 Testing Capacity.

Healthix (MIS) data**:** In Phase 2, participants will be asked to provide informed consent for disclosure of their HIPAA-protected health information (PHI) that is stored in Healthix, the large public NYC based health information exchange (HIE). Participant data drawn from Healthix will include prior and future (12m after end of Phase 2) COVID-19 test dates, location of testing, and results. This will improve our understanding of the potential unique reach of our underserved population recruitment strategy, the frequency and temporality of repeat testing, and the future impact of any project derived mitigation strategies to reduce barriers to appropriate testing in SUD populations. The inclusion of serologic test results also holds the potential of facilitating future COVID-19 vaccine initiatives, including the identification of high-risk members of the cohort without evidence of serologic immunity - if such immunity is found to be a reliable predictor of future risk.

Potential risks and risk related to the generalized global pandemic of COVID-19:

The physical risks of study participation are minimal as the biologic material that will be collected is limited to a one-time self collection of anterior nasal samples by us of nasal swabs. There is an additional minimal risk of exposure to SARS-CoV-2 associated with study participants proximity to another individual during recruitment activities and during testing, though this minimal risk will be mitigated by the use of appropriate PPE. To the extent possible, this research will be conducted in-person in coordination with in-person visits to Alliance and Argus for clinical and other related services (eg housing, vocational support) that are otherwise necessary. It will therefore involve a minimal additional risk of exposure to SARS-CoV-2 that is equivalent to the risk associated with any additional social contact between any two individuals.

There may also be several privacy-related and psychological risks associated with this study: (1) the risk a participant may reveal sensitive information about themselves; (2) the risk a participant may feel coerced into participating or may attempt to coerce others into participating during peer-recruitment; (3) the risk of contact between participants in treatment/recovery for substance use disorders and their peers who are actively using substances; (4) the risk a participant may reveal sensitive information about individuals who have not consented to be in the study; (5) the risk of an unintended breach of confidentiality; and (6) the risk of discomfort in participating in study procedures. Each of these risks is discussed below:

1) Participants may reveal sensitive information in this study regarding their substance use, mental health, motivation to receive treatment for substance use disorders, and relationships to members of their social networks, perceived risk of infection of COVID-19, risk reduction behaviors and social and socioeconomic impact of COVID-19. Interviews will take place in private offices at clinical sites. For all interviews, it is possible that subjects may experience feelings of distress when answering questions concerning these topics. Furthermore, some participants will be asked to recruit their peers for participation in the study. In

doing so, it is possible that sensitive information about the participant may come up as a topic of conversation with those they are attempting to recruit. This may cause feelings of distress if unexpected or unwanted.

2) Participants may also feel coerced into participating, believing that their decision to participate (yes/no) may affect, either positively or negatively, their ability to receive COVID-19 testing or other services. Conversely, it is also possible that during the recruitment process, participants or credible messengers might attempt to coerce others to enroll in the study.
3) Some participants may be engaged in treatment for substance use disorders or otherwise attempting to abstain from substance use (i.e. in recovery) at the time they engage in peer-recruitment. During the study, participants will be asked to focus recruitment on individuals they believe to be actively using substances. Therefore, it is possible that participants in recovery will have contact with peers who are actively using substances, which they would not otherwise have. Such contact may cause participants to experience cravings to return to active use.
4) Participants may reveal sensitive information about individuals who have not consented to participate in the study in one of two ways: a) while completing social network inventories, participants will be asked sensitive questions about their social network contacts who, in most cases, will not themselves be enrolled in the study; and b) during peer-recruitment, participants may ask social contacts about their substance use behavior, treatment access and COVID-19 risk and testing behaviors.
5) Staff and credible messenger participants will be asked to complete questionnaires about their organization's mission, structure, culture/climate, resources. Participants will not be asked questions that would put them at risk of criminal or civil liability or damage to financial standing, employability or reputation. Some organizational culture and climate questions, although not structured or intended to do so, could invite negative opinions critical of leaders, supervisors and/or coworkers and the risk of accidental disclosure of their responses may create discomfort for respondents or may increase the risk of repercussions to participants from supervisory staff who may be present in the focus group. In addition to being asked to complete surveys and/or to be interviewed, the work- related interactions of staff participants may be observed and other data related to quality assurance (e.g. activities that occur within Interagency work group meetings) will be collected.
6) Unintended breach of confidentiality may occur during the collection, storage or analysis of study data. When collecting data via the Internet for staff interviews as opposed to face-to-face, there is a risk for potential linking of work emails to study IDs, and thereby to other responses, when participants sign up for and complete the online staff survey. To an extent, these risks are mitigated by advantages with respect to data quality when collecting data via the Internet as opposed to face-to-face. Web-based surveys offer substantial advantages regarding cost and speed96.
7) Finally, although unlikely, it is possible that some participants may experience emotional discomfort by the questions they are asked in the interview sessions.

3.1.2 ADEQUACY OF PROTECTION AGAINST RISKS

3.1.2(a) Recruitment and Informed Consent

Staff, Credible Messenger and CAB recruitment

Staff will be eligible if they are currently employed at either Argus or Alliance, including Credible Messengers and CAB members. PI/PD will present the study to agency staff both in-person at a staff meeting and via email and interested staff will be asked to contact the research team. An email from the PI (with an attached information sheet) explaining the project and staff participation in the survey and focus group will be sent to agency leadership who will then distribute it to staff, Credible Messengers and CAB members. These methods have been used successfully in our prior work with probation offices and treatment staff. The email will instruct interested staff to contact research staff directly to ask questions. For those interested in participating in focus groups, efforts will be made to schedule interviews at times that do not interfere with staff roles (e.g. lunch breaks; staff meetings). Considerable effort will be taken to ensure that staff do not feel coerced to participate. It will be emphasized to staff that participation (Y/N) is voluntary and will in no way affect their employment status. These procedures have been successfully used in PIs prior work recruiting justice and treatment staff.

Staff, CAB and Credible Messenger consent

For all activities, the consent process will involve an information sheet included with the staff survey or distributed before the beginning of the focus group. In the recruitment email and on the information sheet, participants will be informed that their participation in staff surveys and/or focus groups is voluntary and that they may discontinue their participation in the research at any time. The consent forms will describe all aspects of the study, including that each the survey will last about 30 minutes, focus group about 1 hour, and explain that confidentiality will be maintained unless concerns about the participant warrants reporting, such as suicidality, homicidality or child abuse/neglect. Participants will also be told that any disclosed, observed, or inferred child abuse/neglect must be reported to the New York State Registry. Participants will also be notified that we have obtained a Federal Certificate of Confidentiality. This Certificate protects the investigators from having to release the names or other identifying characteristics of research participants. To respect agencies who request staff not be paid for research work conducted during clinic time, they will receive a small thank you gift only for participation in surveys and focus groups.

Testing Participant Recruitment is described in Section 3.1.1(a)

Testing participant consent:

Written informed consent will be obtained from all testing participants at the time of enrollment. The consent process will take place in a private office at either alliance or Argus without any agency staff present. Potential participants will be assured that their decisions about participation (yes or no) will in no way affect current or future services received at these agencies. Consent will be obtained either by RAs. Potential participants will be observed for signs of active intoxication that might interfere with their capacity to meaningfully consent to participation (e.g. excessive drowsiness, slurred speech, etc.). For those who are excluded due to excessive intoxication, clinical staff will be notified immediately, and the individual will be assessed by a medical provider for risk of impending overdose (intranasal naloxone and other supplies for emergency response are readily available at both clinical sites). Appropriate medical care or observation will be provided by clinical staff as indicated based on that assessment. If the individual is not determined to be at immediate risk of overdose, he or she will be asked to reschedule enrollment for a later date. Up to three attempts will be made to obtain informed consent from participants who are excessively intoxicated. If informed consent cannot be obtained by the third attempt due to excessive intoxication, the individual will be excluded from participation.

The consent forms will describe all aspects of the study and explain that confidentiality will be maintained unless concerns about the participant warrants referral to a mental health provider, such as active suicidal or homicidal ideations. Participants will also be notified that we have obtained a Federal Certificate of Confidentiality. This Certificate protects the investigators from having to release the names or other identifying characteristics of research participants. Sufficient time will be allowed for questions about the consent forms or about the study in general. The consent forms will also specify the expected range of financial incentives for study participation. At the time of enrollment, participants will also be asked to provide consent for disclosure of HIPAA-protected health information (PHI) located in Healthix. All consent forms for all phases of study participation will be developed in accordance with the Internal Review Board (IRB) at New York State Psychiatric Institute.

3.1.2(b) Protection Against Risk

Measures will be taken to address the specific risks associated with study participation mentioned above as well as general measures to ensure that the research is conducted at the highest standards of research ethics and responsibility.

Measures to address specific risks:

1) <u>The risk a participant may reveal sensitive information about themselves:</u> The study will involve a careful protocol outlining the responsibilities of the interviewers, which will be reviewed with all research staff to ensure coordination of management strategies that best meet the participant's needs and well-being. This protocol will mitigate the risk that disclosure of sensitive information results in psychological distress by: a) including an informed consent process that provides advanced warning about the sensitive nature of the topics to be discussed and ensures participants are aware they can decline to answer any

questions that cause discomfort, b) maintaining privacy and confidentiality, and c) attending to emotional responses and providing breaks or emotionally supportive statements as needed. Research staff will be trained in Mental Health First Aid (for which training and certification are offered free of charge by the New York City Department of Health and Mental Hygiene), and emergency protocols will be in place for responding to severe emotional responses involving threatened or actual aggressive or self-harming behavior.

Additionally, specific measures will be taken to mitigate the risk of unwanted disclosures during the peer-recruitment process. First, chain-referral participants will be instructed to focus peer-recruitment efforts on peers with whom they have already had mutual disclosures of substance use at the time of enrollment. Second, all participants participating in peer-recruitment or Credible Messenger recruitment will be asked about any new disclosures of their substance use or other sensitive information. Participants will complete a brief process measure related to ethical concerns related to their recruitment and will include questions about unwanted, unintended and/or distressing disclosures of sensitive information. Finally, content will be created during strategy adaptation to guide participants in making informed decisions about health-related disclosures and anticipating and managing their consequences.

2) The risk a participant may feel coerced into participating or may attempt to coerce others into participating during peer-recruitment: The utmost care will be taken to ensure that participants do not feel coerced in anyway and that they understand taking part in the proposed studies are voluntary. Specifically, during informed consent of potential participants the research staff will emphasize that their choice whether or not to be in this study will not impact either their own ability the ability of those who recruited them to receive services at either Argus or Alliance. Though enrollment will occur in private offices located at Argus and Alliance, agency staff will not be present for the informed consent process. Furthermore, research staff will make explicitly clear that the research study is not a part of usual care at those clinical sites.

   The prospect of coercion by study participants during peer-recruitment has long been a consideration for studies using respondent-driven sampling (RDS), which serves as the basis for the peer-recruitment protocols planned for the proposed study. However, in a comprehensive review of ethical and regulatory concerns related to the use of RDS in scientific research, the authors found that the empirical literature, concerns related to coercion by study participants are offset by appropriate safeguards, including: a) limiting amount of reimbursement per peer-recruitment coupon; b) limiting the maximum number of coupons per participant; c) asking individuals redeeming coupons about perceived coercion; and d) having research staff obtain informed consent for new peer-recruits.[10]

3) The risk of contact between participants in treatment/recovery for substance use disorders and their peers who are actively using substances: As with the risk of disclosures above, the risk of cravings to return to active substance use among participants in recovery will monitored through process measures in Phase 2. Similarly, content for the recruitment strategies will also be created in Phase 1 that helps to help participant recruits anticipate, mitigate and manage potential cue-associated cravings resulting from peer-recruitment efforts.
4) The risk a participant may reveal sensitive information about individuals who have not consented to be in the study: During the social network inventory, alters identified by participants will be anonymized in a manner mutually agreed upon and understandable by the research staff and the participant. For example, alters will be listed by first name and last initial, first and last initial only, a nickname used by the alter or a pseudonym invented by the participant. While the age of each alter will also be elicited, no other personal identifiers (e.g. date of birth, address, etc.) will be elicited about alters. Therefore, while sensitive information will be disclosed about individuals who have not consented to participate in the study, the risk of breach of confidentiality to those individuals will be minimized. It is worth noting that our proposed approach is comparable to “ring vaccination,” which was instrumental in smallpox eradication, as well as contact tracing and partner notification which have been used successfully to interrupt the transmission of HIV and other sexually transmitted diseases The ethical application of these techniques by public health programs is predicated on the balance between beneficence and privacy concerns.[13] While this

balance differs for the purposes of this research study, there are two relevant considerations: a) the ultimate objective of this research project is to develop a technique that can and will be applied by public health programs; and b) we are minimizing privacy risks by only collecting data about non-participants in a de-identified form (full surnames will not be collected for alters).

In order to minimize the risk that participants will ask social contacts about sensitive information during peer-recruitment, participants will be instructed to focus peer-recruitment efforts on peers who are known by the participant to be someone who uses opioids and other drugs and with whom they have already had mutual disclosures of a substance use at the time of enrollment.

5) The risk of an unintended breach of confidentiality: To address concerns of breach of confidentiality, all study documents and data will be maintained in password-protected computer files or stored in an electronically secured database. Any paper copies of documents will be maintained in locked file cabinets and transferred in locked document carrier bags. Participant consent forms and ID logs will be kept in a separate location in a locked cabinet. Transcriptions and audio digital files will be identified by ID numbers only and not connected with the participants' names or IDs. Digital recordings will be erased, and source documents will be shredded.
6) The risk of discomfort in participating in study procedures: The structured assessments and qualitative interview techniques to be employed in this study are used widely in behavioral research.[77-79,105-107] In addition, research staff who are administering the structured assessments, interviews and behavioral sessions will be trained to inquire about and address any feelings of discomfort among participants, and all participants will have access to the PI in case of any concerns.

   The risk of discomfort associated with COVID-19 testing is minimal when using nasal swabs, as detailed in Section 3.3, compared to COVID-19 testing that utilizes nasopharyngeal or mid-turbinate swabs or phlebotomy for COVID-19 serologic assessment. Any discomfort would be mild and transient and most study subjects are expected to not experience any overt discomfort at all. In order to minimize any risk study subjects will be instructed by project staff in the appropriate technique of sample self-collection. Staff will be available to assist in the collection of the sample if the study subject exhibits any concerns about their ability to self-collect the sample.

In addition to the above specific measures, this study protocol will follow the recommendations of the President's National Bioethics Advisory Commission. Procedures will accommodate fiduciary responsibility to protect our subjects' autonomy and welfare, respect their expectations for confidentiality and yet produce reliable information.

Six steps will be taken to minimize risk:

1) A Certificate of Confidentiality issued by the federal government will be obtained for this study. The Certificate protects the data from subpoena and thus prevents the data from being used against the participant.
2) All data will be coded with identification numbers. There will be no names on any questionnaires, audio files or research forms. A master list connecting identification numbers and subjects' names will be kept in a separate computer file with access limited to the PI. These data will be stored on a computer separate from that used for any other project endeavors. Tracking information will also be kept on a different computer than issued for data analyses. The master list is only used to coordinate data collection. In addition, all staff will receive training on confidentiality issues and be certified in the handling of human subjects in research, including HIPAA regulations. The PI will review all interview materials to ensure that all personal identifiers have been removed prior to submission to the data management team.
3) Participants may experience feelings of discomfort during study procedures (e.g. assessments, interviews, intervention sessions) when answering questions about substance use, HCV serostatus, HIV/HCV risk behaviors, motivation to receive treatment for substance use disorders, criminal justice involvement and relationships to members of their social networks. Interviewers will be trained to help participants who may experience feelings of distress when answering sensitive questions, including

training and certification in Mental Health First Aid (see above). Referral to mental health resources can be made on either a routine or urgent basis as needed through clinical staff at both Argus and Alliance. In addition, Drs. Elkington and Ms R. Cohall are licensed clinical psychologist and social worker, respectively, and will be available via cell phone to provide clinical backup in emergencies.

4) All participants will be informed that they do not need to answer questions or participate in intervention activities if they feel uncomfortable doing so. If they chose to answer study questions, all participants will be informed that their responses will not be shared with Argus or Alliance staff, except under specific circumstances (see below in Step 5). This will help safeguard against feelings of coercion.
5) The limits of confidentiality will be clearly explained to all participants of the current study. Confidentiality will be maintained unless it is revealed that a participant is suffering from a severe and active mental disorder, where he or she is in danger of hurting him/herself or others. Participants will be told that in such cases, a Argus or Alliance staff member will be informed. These limits of confidentiality will be expressed to the participants repeatedly during the course of this study: before and during the consent procedure, before participation in the proposed intervention, and again before any of the assessments begin.
6) In non-emergent situations, a "Service Information Sheet" will be distributed listing addresses and phone numbers where mental health and substance abuse services can be obtained. During the receipt of CVOID-19 testing, following the assessment, participants may express an interest in referral to substance use treatment services, or mental health services. In such cases, the participant will be asked for their permission to share this information with Alliance/Argus clinical staff. If permission is not granted, individuals will be encouraged to self-refer. Encouraging self-referrals is appropriate in situations where the risk to the individual is not life-threatening or potentially dangerous to others and may encourage participants to obtain help for problems that would otherwise be ignored.

The risk of SARS-CoV-2/COVID-19 exposure: This research will be conducted in accordance with all infection control policies of state and local health authorities as well as guidelines for social distancing released by the Centers for Disease Prevention and Control. In order to comply with these mandates, we will take a set of measures throughout the conduct of this research, regardless of the phase of reopening present in New York State at the time data collection begins. Additionally, anticipating that there may be further waves of workplace restrictions (i.e. "shut-downs" or "New York on Pause" executive order), other measures will be put in place depending on the reopening phase present in New York State at the time of data collection. We will outline these measures separately as follows:

<u>Measures to be in place regardless of the phase of reopening:</u>

1. Research staff will wear surgical or cloth masks covering their nose and mouth at all times during any contact with research participants
2. Research staff will wash their hands with soap and water for ≥ 20 seconds upon arrival at Argus and Alliance. Research staff will again wash their hands and/or use hand sanitizer immediately prior to beginning contact with a potential research participant. Research staff will again wash their hands with soap and water for ≥ 20 seconds after completing contact with any research participant.
3. At the beginning of each meeting with research participants (or potential research participants), research staff members will offer the participant a disposable surgical mask and hand sanitizer for their personal use and reinforce the use of masks throughout the research visit. Nitrile gloves will also be available upon request by a participant.
4. The private space where research assessments are conducted will be set up to allow 6 feet of physical space between research participants and research staff.
5. Research staff members will recommend that participants adhere to social distancing guidelines during all peer-recruitment attempts, favoring contact by phone or video conference over in person communication.

6. If at all possible, research visits will be coordinated with pre-scheduled in-person visits to consolidate risk

Measures contingent on reopening phase:

In the event of a repeat "shut-down" or return to the previous "New York on Pause" executive order, all in-person research visits will stop. Furthermore, all participants who have received chain-referral coupons will be contacted and instructed to stop all in-person attempts at peer-recruitment. In accordance with recent experience we expect a phased reopening would allow the safe resumption of research activities after the initial (Phase 1) reopening phase is successfully completed, i.e. during Phases 2-4 of NYS' reopening protocol.

Phase 1 reopening:

If New York State remains in Phase 1 of reopening at the time of data collection or in the event of a repeat "New York on Pause" order with subsequent Phase 1 of reopening, in-person research visits will only occur if they can be timed to coincide with in-person medical follow up that is deemed essential by the medical providers of Argus. Research visits that cannot be coordinated to coincide with necessary in-person medical follow up will be delayed.

Phase 2-4 reopening:

All measures outlined above to adhere to social distancing guidelines will be maintained. No additional measures will be taken for Phases 2-4, at which point research participation will pose considerably less risk than other business activities allowed under health department guidelines (e.g. hair salons, non-essential retail, etc.)

3.1.2(c) Vulnerable populations:

This study will not involve recruitment of fetuses, neonates, pregnant women, children, or other institutionalized individuals as research subjects. However, individuals who use opioids and other substances themselves may be considered a vulnerable population. We include members of this vulnerable population as research participants, because our study aims contribute directly to addressing a critical health need in this population. We would not be able to answer our specific research questions without the direct involvement of individuals who use opioids and other substances.

3.1.3 POTENTIAL BENEFITS OF THE PROPOSED RESEARCH TO THE SUBJECT AND OTHERS.

The benefits of this study include the potential for improved identification of vulnerable and underserved populations enrolled in this study and increasing their linkage to and uptake of COVID-19 testing and related services as necessary. Moreover, via a social network approach, the propose research may be able to interrupt the spread of COVID-19 throughout a social network by testing asymptomatic persons who would ordinarily not seek testing, treatment or services

3.1.4 IMPORTANCE OF THE KNOWLEDGE TO BE GAINED

People who use opioids and other drugs have a very high burden of COVID-19, yet these individuals are often overlooked and not adequately provided care and services. In this evolving global pandemic, as testing and treatments advance and novel approaches come online, strategies that successfully enable community outreach to these most vulnerable populations and yet can pivot to incorporate novel and cutting-edge technologies are necessary. Social network-based peer-recruitment has been successfully used for HIV prevention programs in various high risk populations. The proposed study will explore the potential for two peer-recruitment strategies, one which harnesses endogenous peer support (chain referral) and one which leverages exogenous peer support (credible messenger) to identify which can achieve greater reach and resulting uptake of COVID-19 tests.

3.2 Single IRB plan

The protocol will not require a Single IRB (sIRB) as this not a multi-site study that will use the same protocol to conduct non-exempt human subjects research at more than one domestic site. The NYSPI IRB will serve as the IRB of record for the proposed study.

RESOURCE SHARING PLAN (DATA SHARING PLAN)

The proposed research will include data from n=500 testing participants and n=20 community-based organizations (CBOs) agency staff and credible messengers who will be recruited from two CBOs. Alliance for Positive Change (Alliance) and Argus Community Inc (Argus). In addition, data will include medical records of testing participants drawn from Healthix. The final dataset will include self-reported demographic, behavioral, health, treatment service use, organizational-level and implementation data from surveys and focus-groups completed by CBO staff, credible messengers and testing participants.

Even though the final dataset will be stripped of identifiers prior to release for sharing, disclosure of opioid or other substance use and a positive COVID status is potentially highly stigmatizing. Thus, we will make the data and associated documentation available to users under a data-sharing agreement among the user and the study PI (Elkington) that provides for (1) a commitment to using the data only for research purposes; (2) a commitment to securing the data using appropriate computer technology; and (3) a commitment to destroying or returning the data after analyses are completed. We will also draw on the expertise of the consortium, particularly the CDCC as well as the study's Performance and Safety Monitoring Board (See Section 3.3) to guide us in evaluating users' proposals for working with these data. Data will be made available under these conditions only after the main study outcome papers have been accepted for publication.

We will provide CDCC with access to all de-identified data, under provisions that safeguard privacy and confidentiality, generated under this award, subject to the rules specified under a standard Certificate of Confidentiality which will cover the work of our research team. Data will also be made available for external monitoring if required by NIDA/NIH's agreement with other Federal agencies. In accordance with the plan outlined in the RADX-UP RFA, our plans include submission of annual progress reports to the designated NIDA Program Official, for results to be reported at least semi-annually to the CDCC and to NIDA. We also commit to providing the CDCC with timely, accurate data to facilitate the ability of the CDCC to provide NIDA with accurate data-driven updates of consortium progress and facilitate creation of a cohesive data set with shared data definitions, formats, etc. detailed in data dictionaries as required, along with data on effective testing uptake strategies.

3.3. Data and Safety Monitoring Plan

3.3.1 Safety Monitoring Framework

Data and safety will be monitored on several levels. At the first level, the Principal Investigator, Dr. Elkington, will have ultimate responsibility for reviewing conduct of the study and data produced from it, including the reporting of any adverse events to the IRB of the New York State Psychiatric Institute (single IRB of record). At the second level, the project will use a Performance and Safety Monitoring Board (PSMB), as described below. Adverse events and results of PSMB reviews also will be reported to the NIDAs program officer, as described below. All research protocols will be approved by New York State Psychiatric Institute IRB and NIDA.
Data to be collected and monitored includes demographics, a variety of attitudinal/beliefs toward COVID-19 risk and infection transmission, and organizational functioning via surveys, focus groups and medical *records* on COVID-19 test dates, location of testing, and results drawn from Healthix, the large public NYC based health information exchange (HIE).

3.3.2 Data Monitoring

Interim Analysis Plans: The DSMB will review safety reports quarterly (see below). More frequent meetings will be scheduled if indicated by interim findings. A written summary will be submitted to the IRB following each meeting.

The data analyst will conduct interim analyses quarterly to verify that recruitment is consistent with projections. To support ongoing quality assurance and uniformity in data collection, interim analyses will also be conducted to examine patterns of missing data from surveys. Analyses to assess the psychometric properties of the measures will be conducted following the first implementation cycle. These data will be made available to the DSMB. In addition, data from the Site Recruitment Monitoring Form will be made available to the DSMB for monitoring of recruitment and participation rates for all assessments, as well as refusal and attrition rates and study progress.

Stopping Rules: This study will be stopped prior to its completion if: (1) the intervention is associated with adverse effects that call into question the safety of the intervention such as increased rates of COVID-19 infection; (2) difficulty in study recruitment or retention, or enrollment of participants will significantly impact the ability to evaluate the study endpoints; (3) any new information becomes available during the trial that necessitates stopping the trial; or (4) other situations occur that might warrant stopping the trial.

3.3.3 Management and Reporting of Adverse Events (AEs), Serious Adverse Events (SEAs) and Unanticipated Problems (UP).

This study will use the NIH Reportable Events Policy definition of Adverse Events (AEs), Serious Adverse Events (SAEs) and Unanticipated Problems Involving Risk to Subjects (UP).

We will define and measure risk as indicated in the table below.

Table 3.3a. Method of Ascertainment of Serious and Adverse Events, and Unanticipated Problems for STAFF (Sample 2)
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Reportable Event	What they are in the study	Method of Ascertainment	Reporting Requirements		
			IRBs	PSMB	NIDA PO
Death	- Employee/staff death during study operations	We will ask peer supervisors, site coordinators and agency leadership to report any deaths as soon as they learn of them.	ASAP, but no later than 3 working days	Immediately	ASAP, but no later than 3 working days
SAEs	- Employee injury requiring hospitalization during study events	We will monitor these directly at study events that research staff are present at, and ask employee leadership/staff/peers to report them if we are not in attendance.	ASAP, but no later than 3 working days, regardless of whether SAE is study-related	ASAP, but no later than 3 working days	ASAP, but no later than 3 working days
Other AEs	- Employment discipline for improper handling of participant	We will document these events, when we learn of them, per peer supervisors/CBO	Annually. Note that documentation of these events	Tri-Annually	Tri-Annually

	- Employee distress related to managing a participant positive for COVID-19 - Staff breach of confidentiality	leadership and peer to self-report.	must also indicate whether they are thought to be study related and why or why not.		
Unexpected AEs	An AE whose nature, severity, or frequency has not previously been identified. Also includes any adverse event that results in a participant's withdrawal from the study; or is due to a deviation in the research protocol	We will ask all study staff to raise concerns that they have directly via email.	ASAP, but no later than 5 working days.	Immediately if related to study. Tri-Annually if not related to study.	Immediately if related to study. Tri-Annually if not related to study.
Unanticipated Problems that are Not AEs	Incidents or outcomes that occur during human subjects research that are not AEs, but that involve social or economic harm (instead of physical or psychological harm), or are problems that place subjects or others at increased risk of harm, but where no harm occurs.	We will ask all study staff to raise concerns that they have directly in-person or via email.	ASAP, but no later than 5 working days. If MPIs deem the event likely to affect participants, it must be reported to the IRB immediately.	Immediately if related to study. Tri-Annually if not related to study.	ASAP, but no later than 3 working DAYS
Protocol Violations	Deviations from the IRB-approved study procedures, as outlined in the Protocol Summary Form that has received review and approval by	We will meet internally once a week to review study activities and, if we determine we have violated our protocol, we will record the incident	Within 2 weeks of staff becoming aware of the violation; no later	Annually	Annually- Should be included in the full data report

	the IRB. A significant protocol deviation would be a deviation that increases the risk to participants or others, or decreases the potential benefits of the study, undermines the scientific integrity of the study, or occurs more than once	and remediate immediately.	than 5 days if the violation results in an unanticipated problem.		
IRB-or-PSMB determined suspension	Any suspension or termination of approval must be reported including a statement of the reason(s) for the action.	We will comply with IRB, DSMB, and NIMH procedures and guidance.	3 business days	3 business days	3 business days

Table 3.3b Method of Ascertainment of Serious and Adverse Events, and Unanticipated Problems for TESTING PARTICIPANTS (Sample 1)

Reportable Event	What they are in the study	Method of Ascertainment	Reporting Requirements		
			IRBs	PSMB	NIDA PO
Death	- Suicide event - Non-suicide death during study operations – Death by overdose	Via peer supervisors, site coordinators and agency leadership self- report any deaths as soon as they learn of them. Note: follow-up appointment status update	ASAP, but no later than 3 working days	Immediately	ASAP, but no later than 3 working days
SAEs	- Suicide attempt following disclosure of suicidal ideation during assessment - Participant transport to	Participants who endorse suicidal ideation and present as high-risk after emergency protocol is enacted may be referred to emergency services	ASAP, but no later than 5 working days, regardless of whether SAE is study-related.	ASAP, but no later than 3 working days	ASAP, but no later than 3 working days

	emergency services Non-lethal Overdose	by study staff if applicable. We will follow-up with participants who initially endorse suicidal ideation and are determined to be low-risk 3-7 days from their initial visit to assess suicidal risk. If participant self-reports suicide attempt we will document the SAE and report it as required, and link participant to mental health services.			
Other AEs	- Distress related to a COVID-19 positive test - Remission (substance use) following recruitment - Coercion into participating by peer recruit - Breach of confidentiality	We will ask all study staff to raise concerns that they have directly in-person or via email and we will also ask about any potential problems during our check-in calls with CBO leadership and peer supervisors.	Annually. Note that documentation of these events must also indicate whether they are thought to be study related and why or why not.	Tri-Annually	Tri-Annually
Unexpected AEs	An AE whose nature, severity, or frequency has not previously been identified. Also includes any adverse event that results in a participant's withdrawal from the study; or is due to a deviation in the research protocol	We will ask all study staff to raise concerns that they have directly in-person or via email and we will also ask about any potential problems during our check-in calls with CBO leadership and peer supervisors.	ASAP, but no later than 5 working days.	Immediately if related to study. Tri-Annually if not related to study.	Immediately if related to study. Tri-Annually if not related to study.

Unanticipated Problems that are Not AEs	Incidents or outcomes that occur during human subjects research that are not AEs, but that involve social or economic harm (instead of physical or psychological harm), or are problems that place subjects or others at increased risk of harm, but where no harm occurs.	We will ask all study staff to raise concerns that they have directly in-person or via email and we will also ask about any potential problems during our check-in calls with CBO leadership and peer supervisors.	ASAP, but no later than 5 working days. If MPIs deem the event likely to affect participants, it must be reported to the IRB immediately.	Immediately if related to study. Tri-Annually if not related to study.	ASAP, but no later than 3 working days
Protocol Violations	Deviations from the IRB-approved study procedures, as outlined in the Protocol Summary Form that has received review and approval by the IRB. A significant protocol deviation would be a deviation that increases the risk to participants or others, or decreases the potential benefits of the study, undermines the scientific integrity of the study, or occurs more than once	We will meet internally weekly to review study activities and, if we determine we have violated our protocol, we will record the incident and remediate immediately.	Within 2 weeks of staff becoming aware of the violation; no later than 5 days if the violation results in an unanticipated problem.	Annually	Annually-Should be included in the full data report.
IRB-or-DSMB determined suspension	Any suspension or termination of approval must be reported including a statement of the reason(s) for the action.	We will comply with IRB, DSMB, and NIMH procedures and guidance	3 business days	3 business days	3 business days

3.3.3.1.Protocols for preventing/mitigating specific risks. Participant distress will be managed by supervising clinical staff at either Argus or Alliance. Should additional assistance be required, supervising clinical personal within either agencies will contact the PI Elkington, a licensed clinical psychologist, who will provide further assistance. Risks associated with breaches of confidentiality and resulting retribution due to staff responses are a concern. Breaches of confidentiality are unlikely, given the PI's commitment to and experience in maintaining participant confidentiality. Breaches are not anticipated at NYSPI/CUMC offices, because as a research facility, standards for maintaining participant confidentiality have been rigorously maintained since we began research. Breaches might nonetheless occur. During the informed consent process, participants will be told of the confidentiality procedures that are in place, but will be informed that a breach is still possible, however rare, despite these procedures. Should a breach occur, four steps will be taken. First, the participant will be informed as to the nature of the breach, and its possible ramifications. Second, the PI will immediately notify the NIDA Project Officer and the IRB. Third, the PI will review existing confidentiality safeguards to determine why and how the breach occurred (outlined below). Fourth, the PI will halt data collection until such time that the IRB can review existing procedures as to their quality and completeness. The following steps are in place to guard against breaches of confidentiality and to protect confidentiality of research data:

1) Provisions in all protocols will be made to ensure that a) all participants review IRB approved consent (information) forms, b) all surveys are conducted on-line via secure login and data held on a secure server or conducted via pen/paper at the participants choice of location and pace , c) no personal identifying information is collected on data forms, d) all administrative data collected are stripped of identifying information, e) no public data files contain any HIPPA identifiers, f) participants understand the voluntary nature of study participation, g) all data collected are kept in a secured, locked area with access by only certified research staff, and h) all approvals and documentation from the IRB and other approval entities are easily accessible by the PIs and research coordinators.
2) All staff in focus groups, or any study related meetings, will be asked will be asked to respect the confidentiality and privacy of the other participants
3) The research data will be collected electronically (Healthix, participant survey data, recording of coupons). Only trained researchers will be involved in data extraction efforts and delivery of survey forms to study sites. All project staff are required to obtain the NIH web-based certification for protection of human subjects and to sign statements of confidentiality. All staff will be aware of the NYSPI/CUMC confidentiality agreements, the NIH Confidentiality Certificate, and their responsibilities regarding the Certificate's special protections. Staff members that leave the project will be reminded of their continuing obligations to maintain confidentiality. The team has internal procedures to ensure that all staff are aware of federal and state statutes and regulations regarding confidentiality of data.
4) Completed surveys will be downloaded from the web to a secure drive or hand delivered or mailed securely to NYSPI/CUMC offices. Research questionnaires will be coded with a unique number only. The unique ID number will appear on all records in lieu of personal names or other identifying information. Separate follow-up locator forms with identifying information will be digitally stored on password protected servers at NYSPI/CUMC offices. Unique file numbers linking questionnaires with locator forms and identifiers will be stored on the PIs computer in a password protected file NYSPI/CUMC servers. Data from agency records (Healthix) will be provided to the NYSP team via secure data transfer. Any identifiable data will be removed from these data before transferring them to project files; the unique ID number associated with the individual will also be used exclusively with these data. The research team will not release any individually-identifiable data back to the agencies involved in the research.
5) Any data entry and verification/clean will occur on secure NYSPI/CUMC servers under the supervision of the data manager. Computerized copies of research data will be kept on a password protected hard drive maintained by the Data Manager; back-up copies will be kept in locked files at the NYSPI/CUMC offices. The project statistician, Dr. Shea, will ensure that it will not be possible to reconstruct participant identities from the data collected. Security of the data is maintained through the use of secure servers and regular backups, including off-site storage. On a quarterly basis, the PI will meet with the project

staff to review and monitor data safety and monitoring procedures. The PI provide the logistical and operational support for DSMB meetings.

3.3.3.2 Protocol for identifying and tracking individual staff SAEs, AEs and UPs. Adverse events may be ascertained (1) by direct report of a participant during a planned research visit or activity, (2) interaction with research staff, or (3) as reported by agency leadership to research staff. All events, regardless of how ascertained, will be recorded by the research Project Director in an AE/SAE log as they occur. The master copy of the log will be updated and stored on RFMH/CUMC secure servers. Upon learning of an SAE, AE or UP, research staff will be instructed to inform the PI as soon as possible (but within 48 hours of discovery) and get the necessary information for completing the Negative Event Incident Report. The PI reviews the Negative Event Incident Report and adds additional information as necessary, and submit it to the DSMB (See below), the NIDA Program Official, and to the IRBs as required. The PI will ensure that SAEs AEs and UPs are followed until a final disposition of the event is made and a final report on the SAE, AE or UP is filed with the DSMB. If a study participant withdraws from the study or the PI/co-Is decide to discontinue a participant due to an SAE, the PI will monitor the participant until (1) a resolution is reached; (2) the SAE is determined to be clearly unrelated to the study intervention; or (3) the SAE results in death. Using the rating system for SAEs , the PI will evaluate each SAE or unanticipated AE to determine whether it is related to the study, whether it affects the risk/benefit ratio of the study, and whether modification to the protocol or the consent form is required.

3.3.3.3 Protocol for reporting of adverse events. Events that are serious or unexpected must be recorded using the ethics committees' SAE/Unexpected Event forms and submitted to the New York State Psychiatric Institute (NYSPI) IRB within 5 working days from the time that research staff becomes aware of the SAE or AE (See Table). The PI must review the SAE form and sign and date the form; the PI will be responsible for informing the NYS Psychiatric Institute (Columbia University) IRB and the NIDA Program Officer.
Regular monitoring of the study will be undertaken by the PI and other research designated staff (e.g. PD) every three months to ensure that all study procedures are being adhered to, that record-keeping is accurate, and that adverse events are being identified and followed up. Below we summarize types of events and reporting requirements.

3.3.4 DSMB Project Review. While the PI (Elkington) will have ultimate responsibility for reviewing conduct for the study and data emanating from it, including the reporting of any adverse events to the Institutional Review Boards of Columbia University/the New York State Psychiatric Institute (NYSPI), the Data Safety Monitoring Board as assembled by the CDCC through the RADx-UP consortium will meet to review this project at least once each year in addition to reviewing quarterly data safety reports prepared by the research. After the meeting, the DSMB members present written feedback to the research. This feedback will be shared with NIDA program officers, and with the respective IRBs.

3.4 Overall Structure of the Study Team

The multi-disciplinary team of senior researchers and clinicians has expertise with hard-to-reach, urban, populations (**Elkington, A.Cohall, Wilson, Gordon**); HIV/HCV prevention, testing, including community outreach (**Elkington, A.Cohall, R. Cohall, Wilson, Gordon**); chain-referral and peer recruitment procedures (**Wilson**); implementation evaluation and rapid QI to inform procedures and implementation of evidence-based approaches (**Elkington, Wilson, Cohall**) and CBPR (**A.Cohall, Wilson, Elkington**). The research team at embraces engagement of community partners in all service and research programs and team members have extensive experience with community collaboration.

Community Partners and Academic-Community Partnership Structure.
Community partners (see Facilities and Resources). For the RADX initiative, we will build upon this sturdy framework and collaborate with both governmental and community-based agencies. We will engage representatives from the **NY State Department of Health (NYDOH)** and **NY State Office of Addiction Services and Supports (OASAS)**. On a local level, we will work with two community-based organizations which are part

of the OASAS network: **Argus Community Inc. (Argus)** and the **Alliance for Positive Change (Alliance)**. Argus has been in operation since 1967. Annually, they serve over 15,000 clients. Their services include: HIV and HCV prevention and linkage to care, rapid testing, substance abuse treatment, syringe access, behavioral health services, nutrition and housing support, legal services, and **peer street outreach**. **Alliance** has been in operation since 1990. Annually, they serve over 7,000 clients at six sites. Specific services include: comprehensive HIV care coordination, syringe exchanges, outpatient substance use treatment, reentry support services for the formerly incarcerated, HIV and HCV screening, and mental health services. Further, they operate a **Peer Training Institute** which annually trains 350 people living with HIV, HCV and substance use to become prevention/harm reduction peer interns.

Roles of Partners (see Letters of Support)

NYSDOH: will be involved in our scientific advisory board (SAB) and will ensure that study related COVID-19 testing, contact tracing, and referrals meet local, state, and federal regulations and evolving best practices.

OASAS: will be involved in our SAB and in working with our team to consider how to replicate the program into other OASAS sites, if additional funding is obtained.

Alliance and Argus: These community partners have well-established programs serving vulnerable populations. Their successful models for reaching community members with multiple co-morbidities through utilization of innovative street outreach and peer navigators will be adapted for the proposed study.

CUIMC: CUIMC partners have considerable experience in utilizing multiple media platforms to educate, engage vulnerable populations to engage in care, and substantial expertise providing clinical services at a leading medical institutions in the US. A notable strength of this application is a 15-year history of collaboration with proposed community partners. CUIMC partners will assist in developing educational and training content, recommending COVID screening tools, and reviewing emerging testing technologies for possible utilization.

Decision-making structure. Using lessons learned from prior academic-community partnerships, leadership from community partner organizations (Lowy-Argus; and Duke-Alliance) and CUIMC (Elkington, Gordon, Cohall, Wilson) were involved in the initial development of the proposed project and will continue to collaborate for the duration of the project. This team will meet monthly via Zoom to review program implementation and make necessary adjustments. Broad project outcomes, timelines and implementation plans will be set by community partner leaders in collaboration with CUIMC investigators. On a day-to-day basis, site coordinators will coordinate activities and supervise social network recruitment within each agency and will collaborate with the project director at CUIMC. Periodically, program partners will meet with both the Community Advisory Board (CAB) and SAB to obtain feedback and advice.

Community (CAB) and Scientific Advisory Boards (SAB). CAB. Alliance and Argus have CABs who provided input on the proposed project. If funded, representatives from both boards will form a project-specific CAB who will meet **bi-monthly** with partner leaders and CUIMC researchers throughout the study. Initially, they will be involved in developing the structure and implementation of the project. They will then assist in reviewing project outcomes and advising on modifications, as necessary. The SAB will comprise C. Gonzalez, MD, Associate Medical Director for Science and Policy, NYS DOH, M. Manseau, MD, Chief of Medical Services, OASAS, M. Sobieszczyk, MD, Chief, Division of Infectious Disease, CUIMC and S. Whittier, MD, Director of Clinical Microbiology, CUIMC. The SAB will meet **quarterly** with leadership from both community organizations and CUIMC researchers. They will review project outcomes and suggest modifications, as necessary. Further, they will assist project leadership in sustainability and dissemination efforts.

Section 4. Protocol Synopsis

4.1. Brief Summary

We propose research to establish efficacy and sustainability of a community-social network outreach model that partners infectious disease health providers with community based organizations to successfully implement (reach, uptake, delivery and sustainment) COVID-19 point of service, rapid-testing among a highly vulnerable

and often underserved population, those who use opioids and other substances. Two distinct social network recruitment strategies with demonstrated efficacy identifying hidden populations and increasing uptake of HIV testing will be adapted and compared. Guided by the EPIS framework, social cognitive theory, and Andersen's model, this study comprises three phases. Phase 1: Adaptation of outreach recruitment strategies, we will work with our project community advisory board (CAB) to adapt chain-referral and credible messenger strategies for uptake of COVID-19 testing, to finalize recruitment and on-site testing protocols, and to train the CAB in the new protocols and in continuous quality improvement strategies (Aim 1). Phase 2: Strategy Efficacy Trial and Implementation Evaluation, we will compare the two strategies in a cross-over design at two community based organizations (CBOs) with long standing history of serving hard-to-reach populations in their communities. We will examine the impact of each strategy on (i) reach (recruitment of target population), (ii) COVID-19 testing/repeat testing, and (iii) service delivery (i.e. quarantine, medical care and contact tracing) among those who test positive for COVID-19 (exploratory) (Aim 2). Phase 3: Sustainment, CBOs will implement the strategy proven efficacious based on outcomes, and we will examine their sustainment of the program (Aim 2). Implementation evaluation will identify participant-, staff-, and organizational-level factors that influence the feasibility, acceptability, and sustainability of each strategy in these CBOs. (Aim 3). This investigation will provide much needed information to improve health outcomes and to identify effective system-level responses to prevent or arrest the spread of COVID-19 among the social networks of those who use opioids and other substances, a highly vulnerable and often overlooked population. Until the advent of treatment or a vaccine, our ability to contain COVID-19 must rely on widespread identification of (asymptomatic) positive cases, their subsequent quarantine, and contact tracing of those potentially exposed. Therefore testing efforts must be targeted to those highly vulnerable yet unserved populations, including individuals who use opioids and other substances. These individuals may have poor respiratory or pulmonary health due to substance use (e.g. opioids, methamphetamine), which may make them more susceptible to the virus. Also, these individuals are more likely to have been incarcerated, or reside on the street, in shelters, or in crowded accommodation, further placing them at risk for transmission.

4.2. Sample Size Determination

Power calculations assume that we will be able to recruit 500 participants in total (250 recruited in each strategy) for this supplement study over Phases 2a and 2b. We also assume alpha (type I error rate) of 0.05. Our primary outcome of interest is testing occurrence. Based on zip-code level testing data, the average baseline testing in the communities of interest (i.e., northern Manhattan, the Bronx) is 7842.2/100,000. If we assume t that one of the methods of recruitment will have a testing rate similar to this baseline average, we will have > 80% power to detect an approximately 8 percentage point difference in testing among the recruitment strategies (7.8% vs. 16.1%) corresponding to an odds ratio of 2.27, a moderate effect size.

4.3. Outcome Measures

Table 5. Outcome Measures

Name	Type	Time Frame	Description
Reach	Primary	Baseline	# of coupons redeemed; (secondary # redeemed/# distributed)
Testing Uptake	Primary	Baseline	Y/N; (secondary # redeemed/# distributed)
Service Delivery (exploratory): Quarantine Medical care Contact tracing	Primary	Baseline	For positive test results only: Y/N self-quarantine Y/N (date 1st apt) Y/N (Agreed to provide names/addreses of network)

Acceptability; Sustainability	Primary	Baseline	Continued recruitment; testing beyond Implementation phase
Feasibility	Primary	Baseline	Recruitment and testing delivery facilitators and barriers;
Fidelity	Primary	Baseline	Recruitment and testing protocol TBD during Phase 1
Organizational Climate, support and functioning, leadership	Secondary	Baseline and post implementation	Innovation/Flexibility; Organization support; Communication, Job satisfaction
Staff Demographics	Secondary	Baseline and post implementation	Gender, age, race/ethnicity, position, job tenure, education
COVID-19 knowledge /attitudes	Secondary	Baseline and post implementation	a) knowledge of symptoms b) subjective effectiveness of safety practices c) subjective safety/unsafety of activities d) vaccination acceptability e) COVID-19 stigma
Perceived potential sustainability of testing program	Secondary	Baseline and post implementation	Program Sustainability Assessment Tool: Political support, Partnerships, Capacity, Evaluation, Communications, (20 items; (.79-.92)

4.4 Statistical Design and Power

Participants

Testing Participants: participants will endorse opioid or other substance abuse in the past 6 months, and must speak English or Spanish; they will be clients at either Argus or Alliance or recruited via chain-referral or credible messenger strategies.

Staff/Credible Messenger Participants will be currently employed at either Argus or Alliance, including Credible Messengers. N=500 testing participants and n=20 staff will be recruited. Main study outcome data are to be drawn from study developed testing database and form participant and staff surveys.

4.4.1 Primary data analysis overview

Primary data analysis overview.

1. Examine and compare the efficacy of two sets of implementation strategies on (i) reach, (ii) testing uptake, (iii) service delivery (i.e. quarantine, medical care, contact tracing) and (iv) sustainability for individuals who use opioids and other drugs. Use of data drawn from Healthix, a public health information exchange, will supplement this comparison by generating a baseline of participant prior testing and health behavior to determine access to underserved populations as well as longterm influence on future testing behavior
    a) We **hypothesize** that chain-referral will demonstrate better (i) reach, (ii) testing uptake, (iii) service delivery and (iv) sustainability compared to credible messenger.
    b) **Analytic approach**: For our primary (dichotomous) outcome the form of the logistic model will be used to examine the differences in testing uptake (reach, service delivery and sustainability) between credible messenger an chain-referral.
2. 2) Elucidate and compare the *system/organizational-, staff-, and individual-level factors that influence implementation (i.e. fidelity, acceptability, feasibility, sustainability*) *of the strategies* to develop a plan for

dissemination and scale-up in other CBOs who serve opioid and other substance using individuals in NYC.

a) **Example hypothesis**: As an illustrative example, we hypothesize that housing instability will be negatively associated with testing uptake.
b) **Analytic approach**. Implementation features related to acceptability, sustainability, feasibility, and fidelity will be assessed at both the staff- and individual-level. The logistic model will take the form logit(pi) = β0 + βRecStr(Recruitment Strategy)i + βSite(Site)i + βTimeCon(Time Constraint)i where pi is the probability of being tested post-recruitment for the ith individual. This model assesses the effect of a time barrier on the likelihood of getting testing while controlling for the differing recruitment strategies and sites.

Consortium Data Reporting**.** We will use our existing protocols for data checking, cleaning, and data editing and/or will rely on those proposed by the Coordination and Data Collection Center (CDCC) as relevant to ensure that collected data are clean and in compliance with confidentiality protections (e.g., de-identified) before they are forwarded to the CDCC for pooled analysis. We commit to providing the CDCC with timely, accurate data on number of tests conducted, their results, and subsequent actions taken. We will also provide data on effective implementation recruitment strategies to facilitate dissemination across the broader consortia.

4.5 Statistical Analyses

4.5.1 Analysis overview and main outcomes. The primary outcome of interest comparing the strategies will be testing occurrence (yes vs. no) as an indicator of testing uptake. An important secondary outcome will be reach measured through the number of coupons redeemed. Prior to the main analysis, all variables will be examined for distribution and outliers. Continuous outcomes will be described through means and standard deviations, while dichotomous and categorical outcomes will be described through proportions.

4.5.2 Statistical analysis for Aim 2. Models that compare the effect of recruitment strategy on outcomes related to reach, testing uptake, and service delivery will adjust for measures assessed at baseline (e.g., baseline substance use, testing history). For our primary (dichotomous) outcome (testing uptake) logistic regression will be used: logit (pi= $\beta\beta$0 + $\beta\beta$RecStr(Recruitment Strategy)ii + $\beta\beta$Site(Site)ii + $\beta\beta$SubUse(Substance Use)ii + $\beta\beta$ TestHis (Testing History), thus be $\beta\beta$RecStr which will estimate the differential effect of chain-referral vs. POL recruitment on testing uptake. The model will be adapted for secondary outcomes. Sensitivity analyses will stratify the analyses by time to determine if recruitment strategy effects differed before and after the cross-over. Demographic characteristics and other variables related to the Andersen, SCT, and EPIS models will be examined as potential mediators/moderators.

4.5.3 Statistical analysis for Aim 3. Implementation features related to acceptability, sustainability, feasibility, and fidelity will be assessed at both the staff- and individual-level. As an illustrative example, we will consider whether participants endorse time constraints and the association with testing uptake. The logistic model will take the form logit(pi) = $\beta\beta$0 + $\beta\beta$RecStr(Recruitment Strategy)ii + $\beta\beta$Site(Site)ii + $\beta\beta$TimeCon(Time Constraint)ii where pi is the probability of being tested post-recruitment for the i^{th} individual. This model assesses the effect of a time barrier on the likelihood of getting testing while controlling for the differing recruitment strategies and sites.

4.6. Subject participation duration:

N/A

4.7. FDA regulated intervention:

No

4.8. Dissemination Plan

Tangible products from the proposed research study will include protocols that detail chain referral and credible messenger strategies and training protocols on said strategies as well as quality improvement process training manuals, specifically plan-do-study-act. All protocols/manuals will contain relevant materials developed (and tested) during the study that will support the scale up of the social network recruitment strategies of hard to reach/hidden populations in CBOs.

We plan to use our research findings and deliverables to develop a plan such that the efficacious strategy can be brought to scale across similar CBOs in New York City with the CAB and Credible Messengers (if applicable) serving as the external facilitating/training body. At the end of Year 2, we will convene a Dissemination Work Group comprising key community stakeholders, from a broad range of service systems (e.g. faither -based leaders, treatment centers, vocational programs) from across NYC to (1) review effectiveness and implementation findings; (2) understand what resources are required, and that already exist, to support the delivery of the recruitment and testing model. In addition, findings will be published in academic research journals. The study will be registered in ClinicalTrials.gov rapidly after the receipt of the Notice of Award and results will be submitted to ClinicalTrials,gov according to the policy. We will include a specific statement on all study consent forms that informs participants that clinical trial information (data from the proposed study) will be posted (in aggregate and de-identified fashion) at ClinicalTrials.gov. NYSPI has an internal policy in place, in which personnel within each Division monitor reporting of studies on ClinicalTrials.gov for their Division and approach any PIs if results are tardy, incomplete etc. This ensures that clinical trials registration and results reporting occur in compliance with policy requirements.

4.9 Conflict of Interest Policy

All participating scientific staff will be required to comply with the NYSPI's conflict of interest policy that requires the identification of any "potential" conflicts to the study team and DSMB here and in any presentation or article. The main things to declare so far include:

- *The proposed work will be completed with financial support from NIDA grant no. UG1DA050071-S1*

Abbreviations and Special Terms

The list below includes abbreviations utilized in this template. However, this list should be customized for each protocol (i.e., abbreviations not used should be removed and new abbreviations used should be added to this list). Special terms are those terms used in a specific way in the protocol. For instance, if the protocol has therapist-participants and patient-participants, those terms could be included here for purposes of consistency and specificity.

AE	Adverse Event
ANCOVA	Analysis of Covariance
BH	Behavioral Health
CRC	Clinical/Behavioral Health Research Core
CFR	Code of Federal Regulations
COC	Certificate of Confidentiality
CONSORT	Consolidated Standards of Reporting Trials
CRF	Case Report Form
DCC	Data Coordinating Core
DHHS	Department of Health and Human Services
DSMB	Data Safety Monitoring Board
EBI	Evidence-Based Interventions
eCRF	Electronic Case Report Forms
EPIS	Exploration, Preparation, Implementation, Sustainment
FDA	Food and Drug Administration
FFR	Federal Financial Report
GAIN	Global Appraisal of Individual Needs
GCP	Good Clinical Practice
HIPAA	Health Insurance Portability and Accountability Act
IB	Investigator's Brochure
ICH	International Council on Harmonization
IRB	Institutional Review Board
ITT	Intention-To-Treat
JDAI	Justice Diversion Alternatives Initiative
JJ	Juvenile Justice
JRC	Justice Research Core
LSMEANS	Least-squares Means
MedDRA	Medical Dictionary for Regulatory Activities
MIS	Management Information Systems
MMC	Milestone Monitoring, Coordination and Finance Core
MOP	Manual of Procedures
NCT	National Clinical Trial
NIH	National Institutes of Health
NIH IC	NIH Institute or Center
NSSI	Non-Suicidal Self Injury
OHRP	Office for Human Research Protections
PI	Principal Investigator
PO	Probation Officer
QA	Quality Assurance
QC	Quality Control
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan

SB	Suicidal Behavior
SMC	Safety Monitoring Committee
SOA	Schedule of Activities
SOC	System Organ Class
SOP	Standard Operating Procedure
UP	Unanticipated Problem
US	United States

Protocol Amendment History

The table below is intended to capture changes of IRB-approved versions of the protocol, including a description of the change and rationale. A ***Summary of Changes*** *table for the current amendment is located in the* ***Protocol Title Page****.*

Ver	Date	Source	Description of Change	Brief Rationale

Figure 1. Study Timeline