Strategies to Improve the HIV Care Continuum among Key Populations in India: a Cluster Randomized Trial

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2. KEY ROLES

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3. LIST OF ABBREVIATIONS

AE	Adverse event
AIDS	Acquired immunodeficiency syndrome
ART	Antiretroviral therapy
CD4	Cluster of differentiation 4
DALY	Disability-adjusted life years
eCRF	Electronic case report forms
GCLP	Good clinical laboratory practice
GCP	Good clinical practice
GDP	Gross domestic product
JHM	Johns Hopkins Medicine
JHU	Johns Hopkins University
HCV	Hepatitis c virus
HIV	Human immunodeficiency virus
ICC	Integrated care center
IDI	In-depth interview
ICER	Incremental cost-effectiveness ratio
INR	Indian National Rupee
JHU	Johns Hopkins University
LMIC	Low and middle income countries
MI	Motivational interview
MSM	Men who have sex with men
NACO	National AIDS Control Organisation (India)
NIDA	National Institute on Drug Abuse
OAT	Opioid agonist treatment
PrEP	Pre-exposure prophylaxis
PWID	People who inject drugs
RDS	Respondent driven sampling
SAE	Serious adverse effect
STI	Sexually transmitted infection
SSP	Syringe Service Program
TB	Tuberculosis
USD	United States Dollar
WHO	World Health Organization
YRGCARE	Y.R. Gaitonde Centre for AIDS Research and Education

4. PROTOCOL SUMMARY

Strategies to Improve the HIV Care Continuum among Key Populations in India: a Cluster Randomized Trial

Purpose:
People who inject drugs (PWID) and men who have sex with men (MSM) have a high HIV prevalence in India. In prior work, we found that key population-specific integrated care centers (ICCs), which provide HIV testing, risk reduction services, and assistance linking HIV-positive persons to government HIV clinics, increased HIV testing rates and were popular and acceptable to PWID and MSM. However, by itself, the ICC intervention was not associated with improvements in the HIV care continuum among HIV-positive persons. The purpose of this trial is to evaluate the effectiveness of non-cash HIV care incentives – a demand creation strategy – to improve progress on the care continuum among HIV-positive PWID and MSM in India.

Design:
Matched-pair cluster randomized trial.

Study Population:
HIV-positive ICC clients who are 18 years of age or older, antiretroviral therapy (ART)-naïve or have taken ART for less than 12 months, and do not receive HIV care in the private sector.

Study Size:
The study will be conducted at 16 sites (clusters) and we aim to enroll up to 150 participants at each site (2400 participants overall).

Treatment Regimen:
Participants at sites randomized to the intervention will (in addition to receiving usual linkage services provided by ICCs) be eligible to receive incentives (non-cash vouchers for goods) for achieving HIV care milestones, including visiting a government HIV clinic prior to ART initiation, initiating ART, attending HIV treatment motivational interview sessions, and collecting timely ART refills.

Participants at sites randomized to the control condition will receive usual linkage to care services provided by ICCs, including outreach worker assistance with linkage to HIV treatment and reminders to remain in care.

Study Duration:
The study duration will be approximately 48-54 months. Ethnography and preparatory work at the sites will take 6 months. Participants will be enrolled over 12 months and then followed for a 24-month intervention phase. Finally, an epidemiologic survey will be conducted at all sites at the conclusion of the intervention phase that will extend another 6-12 months.

Primary Objective:
To determine if HIV care incentives increase survival with viral suppression at 12 months among

HIV-positive PWID and MSM, compared with the control condition. The primary endpoint was changed from 24 months to 12 months due to the COVID-19 pandemic and the resulting suspension of research activities.

Secondary Objectives:

- To determine if HIV care incentives increase survival with viral suppression at 6, 18, and 24 months among HIV-positive PWID and MSM, compared with the control condition.

- To determine if HIV care incentives increase the proportion with at least one suppressed viral load during study follow-up among HIV-positive PWID and MSM, compared with the control condition.

- To determine if HIV care incentives increase other indices of the care continuum among HIV-positive PWID and MSM, compared with the control condition, including:
    - Time to ART initiation (among those ART-naïve at baseline)
    - Retention to HIV care during follow-up
    - ART medication possession ratio

- To determine if HIV care incentives reduce mortality among HIV-positive PWID and MSM, compared with the control condition.

Exploratory Objectives:

- To determine if offering HIV care incentives at ICCs increases:
    - HIV testing rates at ICCs
    - New HIV diagnosis rates at ICCs

- To determine whether treatment incentives are acceptable to participant and providers.

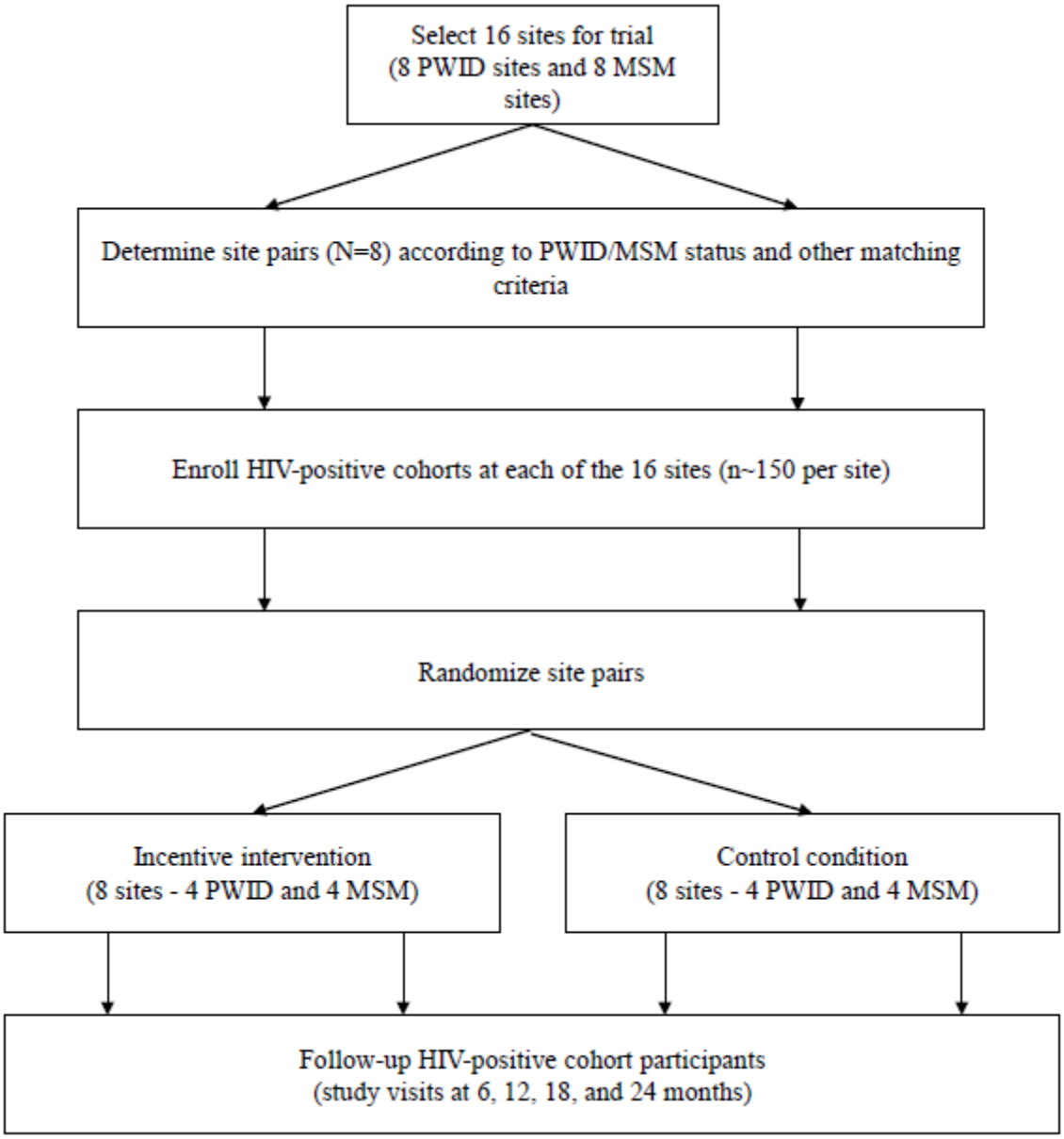
- To determine whether treatment incentives affect community-level indicators of engagement across the HIV care continuum including:
    - Recent HIV testing (among HIV-negative and unknown HIV-positives)
    - Awareness of status (among HIV-positive)
    - Recent visit with HIV medical provider (among HIV-positive)
    - Current use of ART (among HIV-positive)
    - HIV RNA suppression (among HIV-positive)
    - Prevalence of viremic individuals in the population
    - HIV incidence estimated by multi-assay algorithm

- To assess the incremental cost-effectives ratio of providing HIV care incentives for PWID and MSM, compared with the control condition.

Study Sites:

PWID ICCs based in the following Indian cities: 1) Amritsar, 2) Aizawl, 3) Bilaspur, 4) Churachandpur, 5) Delhi, 6) Dimapur, 7) Kanpur, and 8) Ludhiana. MSM ICCs based in the following Indian cities: 1) Bangalore, 2) Belgaum, 3) Bhopal, 4) Delhi, 5) Hyderabad, 6) Madurai, 7) Vijayawada, and 8) Visakhapatnam.

Figure 1. Overview of Study Design and Randomization Scheme:



5. INTRODUCTION

5.1 Background Information

Ongoing trial among PWID and MSM in India. In 2011, we initiated a cluster-randomized trial to evaluate the effectiveness of integrated care centers (ICCs) to improve HIV outcomes among marginalized people who inject drugs (PWID) and men who have sex with men (MSM) populations across India (1). ICCs provide vertically integrated risk reduction (condoms, OST, needle/syringe exchange [NSEP]), HIV counseling and testing, treatment services (CD4 testing, sexually transmitted infection [STI] treatment, referral to government centers for antiretroviral therapy [ART]), and support services (mental health and substance use counseling, ART adherence counseling, and couples counseling) in stand-alone stigma-free venues. The primary outcome of this trial was annual uptake of HIV testing in these high risk populations. Of equal importance; however, has been the enthusiasm that coalesced around the ICC model as we engaged national, local, and community stakeholders in the design and implementation processes. Results from the trial showed that ICCs increased rates of recent HIV testing in these key populations (2).

Limited impact of ICC intervention on HIV care and treatment outcomes. However, data from the ICC trial also showed that, despite increasing the uptake of HIV testing, the ICCs had no apparent impact on downstream outcomes in the HIV care continuum (e.g., initiation of ART, retention to care, viral suppression) that are critical for reducing HIV-related morbidity, mortality, and transmission (2). In contrast with HIV testing, which only requires a single visit to the ICC, achieving these downstream outcomes requires a durable commitment to HIV treatment and repeated visits to government ART centers. By addressing the supply side of evidence-based HIV prevention and treatment services in a supportive environment, the ICCs appear to have affected lower-barrier outcomes such as HIV testing. However, longer-term engagement in care, particularly among these impoverished populations, will require additional interventions/motivation.

Pilot study of voucher incentives for HIV care. We conducted a pilot trial of voucher incentives for HIV care in Chennai, India (3). We randomized 120 ART-naïve, HIV-positive PWID to an incentive intervention, which provided vouchers for completing verifiable HIV care steps, or to an active control condition, in which participants could win vouchers through prize-bowl drawings. Over 12 months of follow-up, participants in the incentive arm were more likely than those in control arm to visit a government HIV clinic at least once (49% vs. 33%, P=0.002) and to start ART (hazard ratio 2.33, 95% CI: 1.15, 4,73). However, viral suppression was not significantly different in the two arms

5.2 Rationale

Engagement in HIV care begins with risk awareness and HIV testing, but, for HIV-positive people, requires long-term commitment, sustained HIV care visits and life-long ART to achieve viral suppression, which will reduce HIV transmission within a community. Our **ICC intervention** addresses structural and health service barriers by **increasing the supply** of vital HIV-related services in a non-discriminatory atmosphere. We hypothesize that a supplemental

demand-focused intervention will be effective in overcoming individual barriers to engaging in HIV care and treatment. Behavioral economic theory suggests that people discount the future in favor of current utility. Behaviorists have conceptualized this phenomenon in terms of intertemporal discounting; empirical data suggest that people discount the value of things as a hyperbolic function of delay time. As a consequence, decision-making related to important issues with long-term implications can be disproportionally influenced by factors of much smaller importance that have immediacy (e.g., lost time, costs, perceived risks, side effects). Behavioral theory and economic principles of demand suggest that incentives may be effective in promoting behaviors that have long-term health benefits by providing an offset to the immediate 'costs' of these behaviors.

Rationale for focusing on PWID and MSM in India. India is home to the third largest number of people living with HIV globally. While India's HIV epidemic is predominantly heterosexual, there is a growing burden among PWID and MSM who have not been a major focus of the National AIDS Program until recently. India, similar to other low- to middle-income countries (LMIC), has seen nearly 50% decline in overall HIV prevalence over the past decade (0.41% to 0.27% from 2001 to 2011 among adults); however, among PWID and MSM, prevalence remains stable, with increasing trends in some regions. India is also home to the largest number of opiate users globally and an estimated 1.1 million PWID (4). India is situated between the two largest heroin producing regions globally – the 'Golden Crescent' and the 'Golden Triangle' – which has resulted in a geographically diverse epidemiology of drug use. In the Northeast, drug injection has been endemic for decades, because of proximity to the 'Golden Triangle.' However, epidemics are emerging in North/Central India because of a shared border with the 'Golden Crescent'. In fact, in our survey of PWID in 15 cities, we found the highest HIV incidence (by a factor of 2) in the central Indian city of Kanpur (12%). India is also home to an estimated 2.35 million high-risk MSM with other estimates suggesting the prevalence of same-sex behavior among adult men to be as high as 9% - 11% (translating to ~45 million MSM).

Both PWID and MSM have HIV burden that is 15-25 times higher than the general population. While HIV care and ART have been available free of charge through government programs since 2004, data suggest limited uptake of these services by these groups. PWID and MSM in India face multidimensional barriers to engaging in optimal HIV care and treatment. Stigma and discrimination are pervasive. This and cultural norms in India, which, for example, stipulate marriage to women even for MSM, leave many PWID and MSM to live on the margins of society. Moreover, in both PWID and MSM, substance use both increases risk behavior and is a barrier to successful HIV treatment. In a recent analysis by our group, the primary barrier to viral suppression among 443 PWID on ART was active injection drug use (OR: 0.04; 95% CI: 0.01, 0.11) and similarly among 347 HIV-infected MSM alcohol dependence was the primary barrier to viral suppression (OR: 0.26; 95% CI: 0.12, 0.57). Compounding these barriers is poverty; in our baseline data, the median monthly income among PWID and MSM was 3 USD/day and 5 USD/day, respectively, and the majority reported being daily wage earners – 56% of PWID and 37% of MSM. While our ICC intervention was focused on addressing issues of stigma and comorbidity, including substance use, the addition of incentives will help to overcome other barriers related to poverty and potential lost wages.

UNAIDS has proposed a "90-90-90" target by 2020, with the aims that 90% of HIV-infected

persons become aware of their status, 90% of those aware of their status receive sustained ART, and 90% of those receiving ART achieve viral suppression. In India, as in several other LMICs, the "90-90-90" target will be unattainable without making substantial inroads in HIV prevention and treatment among these hard-to-reach groups. Indeed, controlling HIV among PWID and MSM in LMICs has been identified one of the greatest barriers to controlling HIV globally. Strategies to identify HIV-infected PWID and MSM in the community, link them to care and successfully maintain them on ART are critical to achieving ambitious UNAIDS targets globally.

5.3 Study Hypotheses

We hypothesize that non-cash HIV care incentives will improve rates of survival with viral suppression in PWID and MSM in India. Providing incentives for achieving verifiable HIV care benchmarks is a demand-stimulation approach, in contrast to supply-focused approaches, such as efforts to increase accessibility or reduce barriers to services. In prior work, we found that a supply-focused intervention – ICCs - was popular and associated with increased HIV testing rates but did not have a discernible effect on the HIV care continuum.

6. OBJECTIVES

6.1 Primary Objective

To determine if HIV care incentives increase survival with viral suppression at 12 months among HIV-positive PWID and MSM, compared with the control condition.

6.2 Secondary Objectives

- To determine if HIV care incentives increase survival with viral suppression at 6, 18, and 24 months among HIV-positive PWID and MSM, compared with the control condition.

- To determine if HIV care incentives increase the proportion with at least one suppressed viral load during study follow-up among HIV-positive PWID and MSM, compared with the control condition.

- To determine if HIV care incentives increase other indices of the care continuum among HIV-positive PWID and MSM, compared with the control condition, including:
    - Time to ART initiation (among those ART-naïve at baseline)
    - Retention to HIV care during follow-up
    - ART medication possession ratio

- To determine if HIV care incentives reduce mortality among HIV-positive PWID and MSM, compared with the control condition.

6.3 Exploratory Objectives

- To determine if offering HIV care incentives at ICCs increases:
    - HIV testing rates at ICCs

  - New HIV diagnosis rates at ICCs

- To determine whether treatment incentives are acceptable to participant and providers.

- To determine whether treatment incentives affect community-level indicators of engagement across the HIV care continuum including:
  - Recent HIV testing (among HIV-negative and unknown HIV-positives)
  - Awareness of status (among HIV-positive)
  - Recent visit with HIV medical provider (among HIV-positive)
  - Current use of ART (among HIV-positive)
  - HIV RNA suppression (among HIV-positive)
  - Prevalence of viremic individuals in the population
  - HIV incidence estimated by multi-assay algorithm

- To assess the incremental cost-effectives ratio of providing HIV care incentives for PWID and MSM, compared with the control condition.

7. STUDY DESIGN

This is a phase III, two-arm, matched-pair, cluster randomized trial. The study will be conducted at 16 sites across India (8 PWID and 8 MSM). Eligible, HIV-positive PWID or MSM will be recruited at each site prior to randomization. In each site pair, one site will be assigned to the control condition and the other site to the incentive intervention.

1. Control condition – Free-of-charge HIV care and ART available at government HIV clinics. ICCs provide HIV counseling, risk reduction services, and peer outreach to support HIV treatment linkage, adherence and retention.
2. Incentive intervention – Control condition services plus ICCs offer HIV treatment incentives (non-cash vouchers for goods) for completing verifiable HIV care activities.

In addition to the quantitative endpoints from the trial, we will also collect mixed methods data to understand how treatment incentives were perceived by different stakeholders. During the latter part of the intervention phase, we will conduct an epidemiologic survey among PWID and MSM at all study sites using RDS. The survey will provide insight into the community-level impact of the intervention and to trends in HIV testing, prevention, and treatment (by comparing with results of 2 prior surveys). Finally, a cost-effectiveness evaluation with be conducted.

The study duration will be approximately 48 months. Ethnography and preparatory work at the sites will take 6 months. Participants will be enrolled over 12 months and then followed for a 24-month intervention phase. Finally, an epidemiologic survey will be conducted at all sites at the conclusion of the intervention phase that will extend another 6 months.

8. STUDY POPULATION

We will recruit cohorts of HIV-positive participants at each ICC site, with roll-out of the study arm allocation (incentive intervention or control condition) after or near the conclusion of cohort

enrollment. Cohort participants will be followed for 24 months during the intervention phase in order to accomplish primary and secondary objectives. The exploratory objectives require i) collecting of mixed methods data on HIV care incentives from key stakeholders, ii) conducting an RDS survey at each site targeting either PWID or MSM, depending on the site, and iii) conducting cost-effectiveness analyses.

8.1 Inclusion/Exclusion Criteria

8.1.1 Participant Inclusion Criteria

Inclusion criteria for cohort participants in cluster randomized trial
Men and women who meet all of the following criteria are eligible for inclusion as a cohort participant:

- 18 years of age or older
- Registered client at the local ICC
- Documented HIV seropositive
- Is either ART-naïve or has been taking ART less than 12 months
- Competent to understand the study and provide written informed consent
- If previously linked to HIV care, willing and able to provide government ART book for documentation of care received

Inclusion criteria for mixed methods evaluation of treatment incentives
Men and women who meet any of the following criteria are eligible for inclusion in the qualitative component of the study:

- 18 years of age or older

and a or b

a) ICC client at one of the 8 intervention sites who was participated in the incentive program
or
b) ICC staff member involved in incentive delivery at one of the 8 intervention sites

Inclusion criteria for the RDS survey
Men and women who meet all of the following criteria are eligible for inclusion as an RDS survey participant:

- 18 years of age or older
- Presents a valid RDS recruitment coupon (unless a "seed")
- Competent to understand study and provide oral consent
- Meets key population risk factor specific for the site [a) self-identifies as male and reports oral/anal intercourse with another man in the prior 12 months, or b) reports injection drug use in the prior 24 months]

8.1.2 Participant Exclusion Criteria

Exclusion criteria for cohort participants in cluster randomized trial
Men and women who meet any of the following criteria are ineligible for inclusion as a cohort participants:

- Does not speak Hindi, English, or the local language
- Plans to migrate in the next 12 months
- Receives HIV care in the private sector

Exclusion criteria for mixed methods evaluation of treatment incentives
Men and women who meet any of the following criteria are ineligible for inclusion as a cohort participants:

- Does not speak Hindi, English, or the local language

Exclusion criterion for the RDS survey
Men and women who meet the following criterion are ineligible for inclusion as an RDS survey participants:

- Does not speak Hindi, English, or the local language

8.2 Recruitment Process

Recruitment of study cohorts for cluster randomized trial
We will recruit HIV-positive individuals who access services at the 16 ICCs in this cluster-randomized trial. Individuals will be recruited into the cohort by referrals from ICC clinical staff. Research assistants will meet with individuals who express interest in the study in a private office space. In addition, during the enrollment period, in collaboration with local non-governmental organizations, ICC staff will conduct outreach at local hotspots to identify persons from the target population to come to the ICC for HIV testing and potential assessment for cohort eligibility.

Recruitment for mixed methods evaluation of treatment incentives
A quantitative survey will be administered to all participants participating in the cohort study. For the qualitative component, the study team will identify persons with specific characteristics related to HIV care and provide a list to the ICC Site Coordinator who will then work with other study staff to contact these participants and invite them for this additional evaluation. The ICC staff will introduce them to a Research Assistant who will provide them with further information on the qualitative assessment. The Research Assistant will directly approach ICC staff for the staff qualitative assessment.

Recruitment for RDS survey
We will recruit members of the target populations (PWID or MSM depending on site) via RDS at the conclusion of the intervention period (year 4 of the study). RDS is a structured version of snowball sampling, where recruitment begins at each site with 2 to 5 “seeds” (representative individuals identified through ethnography). Participants who meet eligibility requirements and complete the study visit will be given 2 coupons to recruit other members of their network. Individuals who come to the study site will meet with a research assistant in a private office setting. The research assistant will briefly describe the study and the eligibility assessment.

8.3 Participant Retention

Once a participant enrolls in the cohort study, the study site will make every effort to retain

him/her for the full study period (24 months), to minimize possible bias associated with loss-to-follow-up. Retention rates of 80% at 24 months are targeted among non-deceased participants. Study site staff are responsible for developing and implementing local standard operating procedures to target this goal. Components of such procedures include:

- Thorough explanation of the study visit schedule and procedural requirements during the informed consent process and re-emphasis at each study visit.
- Collection of detailed locator information at the baseline visit, and active review and updating of this information at each subsequent visit.
- Use of mapping techniques to establish the location of participant residences and other locator venues.
- Use of appropriate and timely visit reminder mechanisms to retain participants.
- Immediate and multifaceted follow-up on missed visits.
- Mobilization of trained outreach workers or "tracers" to complete in-person contact with participants at their homes and/or other community locations.
- Regular communication with the study community at large to increase awareness about HIV/AIDS and explain the purpose of HIV treatment research and the importance of completing research study visits.

9. INTERVENTIONS

Study sites (clusters) will be randomly allocated to either the incentive intervention or to the control condition (**Table 1**). All sites will receive a core packet of services provided by population-targeted ICCs (either PWID or MSM).

Table 1. Summary of services in control and intervention conditions

Service/Intervention	Control Condition sites (n=8)	Incentive Intervention sites (n=8)
HIV counseling and testing	X	X
Harm reduction services		
Condoms	X	X
Risk reduction counseling	X	X
Syringe service program (SSP)	PWID sites	PWID sites
Opioid agonist treatment (OAT)	PWID sites	PWID sites
STI screening and syndromic treatment	X	X
TB symptom screening and referral	X	X
Hepatitis C virus (HCV) antibody testing and counseling	PWID sites	PWID sites
Services for HIV-positive clients		
Referral for ART and peer outreach	X	X
Motivational interviewing	X	X
Incentives for achieving HIV treatment milestones		X

9.1 Control Condition

This trial incorporates an active control condition. In a prior trial, we evaluated the acceptability, feasibility, and effectiveness of PWID- or MSM-focused ICCs (2). The goal of ICCs was to provide a menu of population-specific services in non-discriminatory settings. We found that ICCs served large numbers of clients (median of 1,500 per ICC over 2 years), were favorably reviewed in anonymous client surveys, and increased community level HIV testing rates (2). Although the integrated population-focused venue is distinct, the services provided by ICCs are consistent with the standard of care in India. At the present time, pre-exposure prophylaxis (PrEP) is not endorsed by the National AIDS Control Organisation (NACO) in India and is not available in ICCs. In the control condition, the following care package will be routinely available

- HIV counseling and testing
- Harm reduction services
    - Condoms
    - Risk reduction counseling
    - SSP (PWID sites only)
    - OAT (PWID sites only)
- STI screening/syndromic treatment
- Tuberculosis (TB) symptom screen and referral
- HCV antibody testing (PWID sites only)
- Services for HIV-positive clients
- Referral for ART and peer outreach/support
- Motivational interviewing for HIV treatment adherence

9.2 Incentive Intervention

The incentive intervention will include all services available at control condition sites plus HIV care incentives. Cohort participants at intervention sites will be eligible to receive treatment incentives (**Table 2**). Additionally, ICCs assigned to the intervention will offer treatment incentives to additional HIV-positive clients (up to a maximum of 300 persons per site).

Table 2. HIV treatment incentive schema

Target	Eligibility	Incentive criteria	Value	Frequency available	Maximum possible over 24 months
Pre-ART retention	ART-naïve	Attend visit at govt. HIV clinic	INR 250 (USD 3.60)	Once every 6 months	INR 1000 (USD 14.30)
ART initiation	ART naive	Initiate ART at govt. HIV clinic	INR 500 (USD 7.10)	Once (non-repeatable)	INR 500 (USD 7.10)
ART persistence	Initiated ART	Timely monthly refills	INR 150 (USD 2.10)	Once every month	INR 3600 (USD 51.40)
Internal motivation	All	MI counseling at ICC	INR 100 (USD 0.70)	Once every 3 months	INR 800 (USD 11.40)

Similar to our approach in a pilot trial in Chennai (3), vouchers will be redeemable for food, clothing, household goods, and specialty items at the ICC or from collaborating stores. Non-cash incentives support a drug- and alcohol-free lifestyle and were acceptable and effective in the pilot trial. Some items that will be stocked at ICCs for voucher redemption are toothpaste, soap,

shampoo, biscuits, tea, coffee, rice (1kg, 5kg), lentils, wheat flour (1kg packs), shirts, sweaters, and backpacks. Each site will decide on the options for incentives based on local experience/needs. Participants may choose to save incentives in an account to redeem for larger gifts (e.g., mobile phone).

Incentives will be given for verified activities, not self-report alone. Governmental HIV clinics record visits, laboratory results, and dispensations of antiretroviral drugs in notebook that patients keep (government ART book). Entries in the government ART book (and if needed verification by records at the clinic) will be used to verify incentivized activities. Incentives for ART refills will be given if the refill is no more than 3-days late, following a typical 30-day prescription.

10. STUDY PROCEDURES/EVALUATIONS

10.1 Clinical Evaluations and Procedures

Clinical evaluations and procedures for study cohorts in cluster randomized trial
Eligible participants who meet inclusion criteria and provide written informed consent will be enrolled in the local cohort. Cohort participants will complete a baseline study visit, most often on the day of screening, and will be asked to complete follow-up visits at 6 months, 12 months, 18 months, and 24 months, for a total of 5 study visits. However, due to delays from the COVID-19 pandemic, not all participants were able to complete the 18- and 24-month visits. Detailed information on the evaluation and procedures of study visits are shown in **Appendix I**. Study visits will include the following evaluations:

- Biometric capture (fingerprint) to confirm identity
- Blood draw, laboratory assessments described below
- Collection of contact and locator information
- Interviewer-administered survey covering the following domains
    - Demographics
    - Quality of life
    - Engagement/experience with HIV care
    - ART adherence
    - Beliefs about ART
    - Alcohol and drug use
    - Injection- and sex-related risk behaviors
    - Depression symptoms
    - Health care utilization
    - Fentanyl and overdose (from 18 months onward)
- Abstraction of information from government ART book

Clinical evaluations and procedures for mixed methods evaluation of treatment incentives
We will query cohort participants at incentive sites about their experiences with and perceptions of treatment incentives in the 24-month visit interview. Additionally, individuals eligible for the qualitative component will be invited to participate in in-depth interviews (IDI). IDIs will use a semi-structured format to address the following domains:

IDIs with ICC clients at intervention sites

- Perceived purpose of the incentive program
- Process of learning about the incentive program
- Experiences with receiving incentives
- Opinions about the value of incentives and how frequently incentives could be earned
- Impact of incentive program on client opinions and beliefs about HIV care

IDIs with ICC staff

- Familiarity with the incentive program
- Perceived purpose of the incentive program
- Challenges with implementing the incentive program
- Good and bad things about the incentive program
- Opinions about how the program affected HIV-positive clients' behaviors

Clinical evaluations and procedures for RDS survey

The RDS survey will be a cross-sectional assessment of PWID or MSM populations in each study city. Beginning with 2-5 "seed participants," eligible participants who complete a one-time study visit are eligible to recruit up to 2 network members to the study with coupons (described above). Participants will be reimbursed both for completing the study visit and for each eligible participant that they refer to the study (up to 2). RDS participants who present with a valid recruitment coupon will be asked to undergo the following procedures:

- Biometric scan (fingerprints) to assure individual has not already participated in the study
- Rapid HIV counseling and testing, described below
- Interviewer-administered survey covering the following domains
    - Demographics
    - Peer network information
    - Substance use (including alcohol)
    - Drug-related and sexual risk behavior
    - HIV treatment literacy
    - HIV care continuum outcomes (e.g., experience with HIV testing, HIV care and HIV treatment)
    - General utilization of health care including hospitalizations, physician and non-physician outpatient visits, medications, productivity (full-time, part-time work), out of pocket medical costs, and time and wages lost due to medical appointments including travel as well as utilization of harm reduction services (OAT, syringe service program [SSP])
    - Depression
    - Quality of Life
    - Social Support
    - Stigma

10.2 Laboratory Evaluations

Laboratory evaluations for the study cohort in the cluster randomized trial

- HIV RNA will be measured from plasma at all cohort study visits by the central laboratory (YR Gaitonde Centre for AIDS Research and Education [YRGCARE]) in

Chennai, India using RealTime HIV-1 (Abbott Laboratories, Abbott Park, IL, USA). The HIV RNA result at the 24-month visit will be shared with participants
- CD4 cell counts will be measured at baseline by flow cytometry in a local or regional laboratory. The CD4 test result will be shared with participants.
- At the 6-month, 12-month, and 18-month cohort visits we will measure serum glucose, serum creatinine, and a liver function panel, respectively. These assays will be conducted at local or regional laboratories. Results from these tests will be shared with participants as a value-added benefit of participating in the trial.

Laboratory evaluations for mixed methods evaluation of incentives
None

Laboratory evaluations for RDS survey
- Rapid HIV testing - This point-of-care testing will be used to test all RDS participants. The rapid testing protocol includes the use of 3 rapid test kits in an algorithm: Alere Determine HIV-1/2 (Alere Medical, Chiba, Japan), First Response HIV Card test 1-2.0 (Premier Medical Corporation, Daman, India), and Signal Flow Through HIV 1+2/Immunodot Test Kit (Span Diagnostics, Surat, India).
- HIV-1 RNA - HIV RNA will be measured from plasma in HIV-positive survey participants by the central laboratory (YRGCARE) in Chennai, India, using RealTime HIV-1 (Abbott Laboratories, Abbott Park, IL, USA).
- CD4 cell count - CD4 cell counts will be measured in all HIV-positive participants by the central laboratory (YRGCARE) in Chennai, India using Flow Cytometry (EPICs XL-MCL, Beckman Coulter, Inc., USA.
- Recent HIV infection - Recent HIV infection will be assessed using a validated multi-assay algorithm in all HIV-positive survey participants. The algorithm testing includes Limited Antigen (LAg) Avidity EIA (Maxim Biomedical Inc, Rockville, MD, USA) and the JHU-modified Bio-Rad Avidity assay (Bio Rad Laboratories, Hercules, CA, USA). Individuals are characterized as having recent infection if CD4 count >50 cells/mm^3, HIV RNA >400 copies/mL, LAg avidity <2.9 OD-n, and JHU-modified Bio-Rad avidity index<85% (5).

11. ASSESSMENT OF SAFETY

11.1 Safety Assessment Overview

This section provides information on the definition of adverse events (AE), serious adverse events (SAE) and the procedures for reporting. Procedures for prompt reporting of AE and SAE will be standardized across the field sites.

11.2 Definitions

11.2.1 Definition of Adverse Events (AE)

An AE is any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or diagnosis that occurs in a study participant during the conduct of the study

regardless of the attribution (i.e., relationship of event to medical treatment/study product/device or procedure/intervention). This includes any occurrence that is new in onset or aggravated in severity or frequency from the baseline condition.

11.2.2 Definition of Serious Adverse Events (SAE)

An SAE is defined as any untoward medical occurrence that:

- Results in death
- Is life-threatening
- Requires inpatient hospitalization or prolongation of existing hospitalization
- Results in persistent or significant disability/incapacity
- Is a congenital anomaly/birth defect
- Is an important medical event that may not be immediately life-threatening or result in death or hospitalization but may jeopardize the patient or may require intervention to prevent one of the other outcomes listed in the definition above).

11.3 Reporting Requirements for this Study

The research procedures in our study include 1) qualitative work (interviews with key informants), 2) study visits with cohort participants, and 3) a RDS surveys. These research procedures are minimal risk (involve only a blood draw), and do not include a drug or medical device. Furthermore, study sites (or clusters) are the unit of randomization, not individual participants. Participants at intervention sites have access to the intervention (non-cash HIV treatment incentives), but are not required to seek or accept the intervention. Finally, the study population, HIV-positive PWID and MSM have substantially higher risks of morbidity and mortality than person in the general population. Given these considerations, our reporting obligations for the trial focus only on events that are more likely than not to be associated with i) study procedures, or ii) participation in the intervention. Two types of events will be reportable:

1. Unanticipated problems involving risks to participants or others will be reported to the YRGCARE and JHM IRBs within 10 working days (unless the event is death, in which case # 2 applies). Such events are defined as:
    a. The information is unexpected in terms of nature, severity, or frequency, given:
        i. The research procedures described in the protocol and informed consent document; and
        ii. The characteristics of the subject population being studied
    b. The information indicates that the participants or others are at greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.
2. Deaths of study participants in close association with study procedures will be reported to the IRB within 3 working days.

12. CLINICAL MANAGEMENT

12.1 Clinical Management of Adverse Events

Research staff will interact with participants at study visits and during the intervention (dispensing non-cash incentives). Research staff will refer participants to a clinic or hospital for medical conditions that arise.

12.2 Criteria for Discontinuation

12.2.1 Criteria for Permanent Intervention Discontinuation for an Individual Participant

Potential reasons for permanent or premature discontinuation of intervention are:

- Request by the participant to stop.
- Request of site coordinator if s/he thinks the intervention is no longer in the best interest of the participant.
- At the discretion of the IRB/Ethics Committee, Office for Human Research Protections (OHRP), other government agencies as part of their duties, or investigator

12.2.2 Criteria for Premature Study Discontinuation for an Individual Participant

Potential reasons for permanent or premature discontinuation of study are:

- Request by the participant to withdraw.
- Request of site coordinator if s/he thinks study participation is no longer in the best interest of the participant.
- At the discretion of the IRB/Ethics Committee, Office for Human Research Protections (OHRP), other government agencies as part of their duties, or investigator

13. STATISTICAL CONSIDERATIONS

13.1 Overview and General Design Issues

The primary objective of this study is to determine whether offering non-cash HIV care incentives increases survival with viral suppression among HIV-positive PWID and MSM. Key secondary endpoints include engagement in HIV treatment and retention to care as mediators of survival with viral suppression, qualitative evaluation of treatment incentives, and costs and cost effectiveness. We will address these objectives with a phase III, two-arm, matched-pair, 16-site cluster randomized trial. We selected a cluster randomized as opposed to an individually randomized trial for two reasons. First, the cluster randomized design minimizes the likelihood of contamination effects that might occur if incentives were being offered to some but not to other participants at the same site. Second, we hypothesize that offering incentives will have favorable off-target effects at the ICCs, such as encouraging more key population members to visit for HIV-testing. This can be meaningfully assessed in a cluster randomized design, but not in an individually randomized design. Participants who are HIV-positive and have limited or no prior ART exposure will be enrolled and followed for 24 months at the 16 study sites. The control condition includes linkage and support services provided by ICCs and standard HIV

treatment provided free-of-charge by government HIV clinics.

To provide context for the results from the cluster randomized trial, we will conduct a mixed methods evaluation of treatment incentives and cost-effectiveness analyses. In addition, near the conclusion of the trial intervention phase, we will conduct a concurrent epidemiologic survey of PWID or MSM at all study sites using RDS. The survey will provide insight into the community-level impact of the intervention and to trends in HIV testing, prevention, and treatment (by comparing with results of 2 prior surveys conducted in the same cities).

Protocol revisions due to COVID-19: Cohort study participant enrollment was completed in October, 2018. Study activities (follow-up visits and incentive intervention) were suspended indefinitely in March 2020. At the time research activities were suspended, all participant visit windows had closed for the 6- and 12-month follow-up visits. However, 65 and 959 participants had not completed the 18- and 24-month visits, respectively, but had not reached or were within the visit window. Because of this, in Protocol Version 2.0 we revised the primary endpoint from 24 months to 12 months. Data that was collected at 18 and 24 months will be considered in secondary and sensitivity analyses.

13.2 Study Endpoints

Primary and secondary study endpoints will be assessed at follow-up cohort visits on the basis of laboratory testing, structured interviews, and external sources of data, including government HIV clinic treatment records and death reports from family and friends. Exploratory endpoints will be assessed on the basis of i) costing data collected during the study, ii) qualitative IDIs, and iii) RDS surveys conducted in the key populations near the conclusion of the intervention phase.

13.2.1 Primary Endpoint

Survival with suppressed viral load, defined as HIV RNA <150 copies/mL in plasma or serum, at 12 months.

13.2.2 Secondary Endpoints

- Survival with suppressed viral load at 6, 18, and 24 months.
- Proportion with at least one suppressed viral load during study follow-up (6, 12, 18, or 24 months).
- Time to ART initiation, recorded from government HIV treatment records, among cohort participants that were ART-naïve at baseline.
- Retention to HIV care during follow-up, defined as having 1 or more visits to a government ART clinic in each 6-month period of study follow-up.
- ART possession ratio (a measure of medication adherence), defined as the time in possession of ART divided by the follow-up time. Follow-up time will commence at enrollment for ART-experienced participants and at ART initiation for ART-naïve participants. Follow-up time will be censored at the end of trial follow-up, death, or loss-to-follow-up. The amount of time in possession of ART will be determined from ART dispensation logs maintained by government HIV clinics.
- Mortality, defined as a report of a participant's death from a family member or a close

friend. Death records are not maintained by local, state, or national governments in India.

13.2.3 Exploratory Endpoints

- Rate of HIV testing in ICCs, defined as number of HIV tests performed in an ICC per unit time. This is an ICC-level endpoint. The number of HIV tests and the testing results are recorded in a computerized ICC database. For each matched site pair, follow-up will commence on the date that the intervention is rolled-out at the intervention site in the pair. Follow-up will end at the conclusion of the active intervention period.
- New HIV diagnosis rate in ICCs, defined as the number of persons testing newly HIV-positive in the ICC per unit time. This is an ICC-level endpoint. For each matched site pair, follow-up will commence on the date that the intervention is rolled-out at the intervention site in the pair. Follow-up will end at the conclusion of the active intervention period.
- Mixed methods evaluation of treatment incentives obtained by i) survey questions of cohort participants at the final (24-month) study visit (quantitative component), and ii) IDIs with ICC clients and ICC staff (qualitative component).
- Community-level effects will be assessed by an end-of-study RDS survey among PWID or MSM (according to site). RDS is a network-based sampling method, in which participants recruit people from their social networks with a coupon tracking system. Sampling weights are generated that provide unbiased estimates of characteristics of interest in the underlying population. Our team has experience using RDS to assess the community-level impact of a structural intervention (1). In this trial, we will use RDS estimates to 1) assess for community-level impact of the incentive intervention compared with the control condition, and 2) to assess epidemiologic trends in HIV prevention, care continuum, HIV prevalence, and HIV incidence by comparison with prior surveys conducted in these cities. Endpoints to be assessed in the RDS survey include:
    - Recent HIV testing, defined as the proportion that self-report HIV testing in the prior 12 months among all survey participants, except those who are aware of their HIV-positive status and report diagnosis more than 12 month previously.
    - Awareness of HIV-positive status, defined as the proportion that self-report HIV-positive status in interview among participants subsequently determined to be HIV seropositive.
    - Recent HIV care visit, defined as the proportion of HIV-positive participants who report a visit with an HIV care provider in the prior 6 months.
    - Current ART use, defined as the proportion of HIV-positive participants who report ART use in the prior 30 days.
    - HIV RNA suppression, defined as the proportion of HIV-positive participants with measured HIV RNA <150 copies/mL
    - Prevalence of viremic individuals in the population, defined as the proportion of all participants (HIV-negative and HIV-positive) with a measured HIV RNA ≥150 copies/mL
    - HIV incidence, estimated with a validated multi-assay algorithm (5) measured in HIV-seropositive participants.
- Cost-effectiveness of the incentive intervention versus control condition using the primary and secondary outcome measures, for example, the cost per additional cohort

participant with viral suppression.

13.3 Study Objectives and Hypotheses

We hypothesize that non-cash HIV care incentives will improve rates of survival with viral suppression in PWID and MSM in India. Providing incentives for achieving verifiable HIV care benchmarks is a demand-stimulation approach, in contrast to supply-focused approaches, such as efforts to increase accessibility or reduce barriers to services. In prior work, we found that a supply-focused intervention – ICCs - was popular and associated with increased HIV testing rates, but did not have a discernible effect on the HIV care continuum. In a pilot trial, we found that treatment incentives were associated with increased access of HIV care and initiation of ART (3). Our objectives for the current trial are as follows:

Primary Objective
To determine if HIV care incentives increase survival with viral suppression at 12 months among HIV-positive PWID and MSM, compared with the control condition.

Secondary Objectives

- To determine if HIV care incentives increase survival with viral suppression at 6, 18, and 24 months among HIV-positive PWID and MSM, compared with the control condition.

- To determine if HIV care incentives increase the proportion with at least one suppressed viral load during study follow-up among HIV-positive PWID and MSM, compared with the control condition.

- To determine if HIV care incentives increase other indices of the care continuum among HIV-positive PWID and MSM, compared with the control condition, including:
    - Time to ART initiation (among those ART-naïve at baseline)
    - Retention to HIV care during follow-up
    - ART medication possession ratio

- To determine if HIV care incentives reduce mortality among HIV-positive PWID and MSM, compared with the control condition.

Exploratory Objectives

- To determine if offering HIV care incentives at ICCs increases:
    - HIV testing rates at ICCs
    - Rates of identifying out-of-care HIV-positive persons at ICCs

- To determine whether treatment incentives are acceptable to participant and providers.

- To determine whether treatment incentives affect community-level indicators of engagement across the HIV care continuum including:
    - Recent HIV testing (among HIV-negative and unknown HIV-positives)
    - Awareness of status (among HIV-positive)
    - Recent visit with HIV medical provider (among HIV-positive)

- Current use of ART (among HIV-positive)
- HIV RNA suppression (among HIV-positive)
- Prevalence of viremic individuals in the population
- HIV incidence estimated by multi-assay algorithm

- To assess the incremental cost-effectives ratio of providing HIV care incentives for PWID and MSM, compared with the control condition.

13.4 Sample Size Considerations

We calculated power for comparing the primary endpoint within matched cluster pairs, *survival with suppressed viral load, defined as HIV RNA <150 copies/mL in plasma or serum, at 24 months*, among the cohorts of HIV-positive study participants. Cluster-randomized designs require consideration of the between-cluster coefficient of variation (k), a measure of variation between clusters. In general, the more variability in outcome between clusters, the larger the sample size required to detect a given difference. The coefficient of variation in a matched study needs to take into account the matching correlation (k_m), in other words how much of a reduction in pair variability is accomplished by matching. More successful matching is associated with lower k_m values. We calculated the k_m using baseline RDS data from a prior trial for a hypothetical set of matched pairs based on the proposed matching criteria for this trial as described above. The values of k_m ranged from 0.08 to 0.15 when considering RDS-II weighted and unweighted estimates of the outcome of interest. In addition to consideration of k_m, we also considered other factors specified by the sample size formula from Hayes at al. (6):

$$c = 2 + (Z_{\alpha/2} + Z_{\beta})^2[\pi_0(1-\pi_0)/n + \pi_1(1-\pi_1)/n + {k_m}^2(\pi_0{}^2 + \pi_1{}^2)](\pi_0 - \pi_1)^2$$

where π_0 and π_1 are the true population proportions in the absence and presence of the intervention, respectively, n is the number of individuals within each cluster, $z_{\alpha/2}$ and z_{β} are the standard normal distribution values corresponding to the upper tail probabilities of $\alpha/2$ and β, respectively and k_m is the coefficient of variation within matched pairs.

Within our calculations, we varied the k_m from 0.10-0.20 based on our preliminary data, the sample size per cluster from 50-150 to account for varying levels of loss to follow-up, and the outcome prevalence in control condition clusters from 25-45%. The number of cluster pairs needed was relatively insensitive to the prevalence of outcome in the control group and the cluster size as long as the sample size was >70 per cluster. **Figure 2** shows the number of cluster pairs needed (y-axis) to provide 80% power to detect differences of 0.05 to 0.30 (x-axis) across a range of k_m values (different colored lines) assuming a sample size of 150 per cluster, two-sided alpha=0.05, and 25% outcome prevalence in the control clusters. With 8 cluster pairs, we will have 80% power to detect differences of 8 percentage points (risk ratio = 1.32) if the k_m is 0.10, and 10 percentage points (risk ratio = 1.4) if the k_m is 0.15. If the prevalence in control clusters is 40% then the detectable difference is 10 percentage points (risk ratio = 1.4) if the k_m is 0.10.

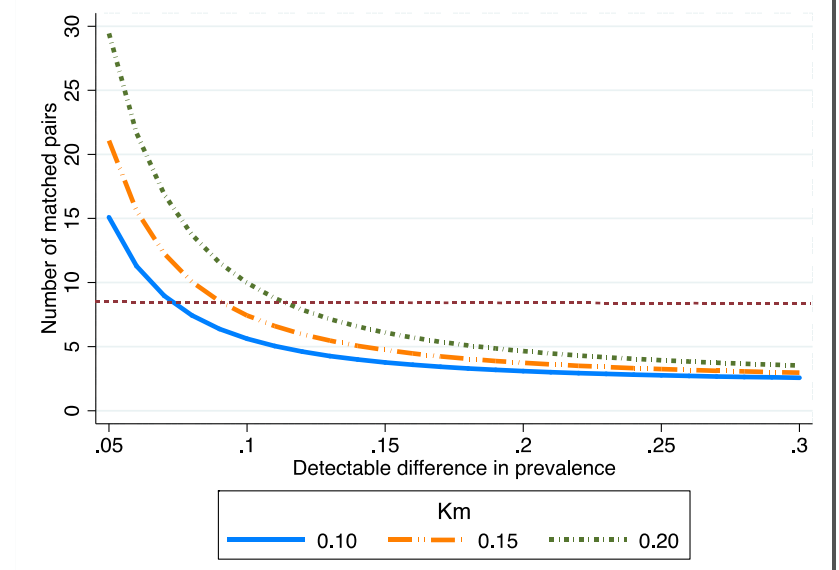


Figure 2. Number of matched pairs needed to detect differences. Red dotted line indicates 8 pairs of clusters

13.5 Study Site Selection and Pair Matching

Study sites (cities) are the units of randomization in the current trial. In a prior cluster randomized trial that concluded in June 2017, we evaluated the effectiveness of ICCs for increasing rates of HIV testing among PWID and MSM in 22 sites across India (ClinicalTrials.gov identifier: NA00047702) (1, 2). From the sites in the prior trial, we selected 16 well-characterized sites for the current trial. The site selection criteria included 1) large estimated number of HIV-positive key population members (PWID or MSM depending on the site), 2) poor HIV care continuum indicators (low awareness of HIV status, low linkage to care and ART, and low prevalence of viral suppression), and 3) ability to match the site with another site (see below).

Close matching of characteristics of interest in matched pairs can increase the efficiency of cluster randomized trials (6). To match sites, we considered data from RDS surveys of PWID or MSM conducted in 2012/2013 and again in 2016/2017 (n~1000 participants per site), but also drew from our research team's prolonged experience at the sites. Absolute matching criteria included the key population (PWID sites could only be paired with PWID sites and MSM sites could only be paired with MSM sites) and whether or not the site was an intervention site (ICC) or usual care site in the prior trial - former intervention sites already had ICCs up and running, but new ICCs needed to be launched in former usual care sites (former intervention sites were

paired only with other former intervention sites and former usual care sites were paired only with former usual care sites). These strata resulted in the categorization shown in Figure 3.

Figure 3. Stratification of sites for pair matching

		Treatment condition in trial ending 2017	
		Former ICC site	**Former usual care site**
Key population	**PWID**	• Aizawl • Bilaspur • Dimapur • Ludhiana	• Amritsar • Churachandpur • Delhi • Kanpur
	MSM	• Bangalore • Belgaum • Hyderabad • Visakhapatnam	• Bhopal • Delhi • Madurai • Vijayawada

Within the above stratification, we considered PWID/MSM population size, geography, and HIV-related community characteristics - HIV prevalence, viral suppression, and prevalence of viremia - when evaluating potential pair matches. Final criteria that were considered in the matching process in order of prioritization were: 1) proportion of HIV-positive persons with viral suppression; 2) HIV prevalence; and 3) prevalence of viremic persons, 4) estimated size of the target population. Final pair matching is listed in Figure 4:

Figure 4. Site pairs, by key population	
PWID	**MSM**
Pair 1: Aizawl and Bilaspur	*Pair 1:* Bangalore and Visakhapatnam
Pair 2: Churachandpur and Amritsar	*Pair 2:* Belgaum and Hyderabad
Pair 3: New Delhi and Kanpur	*Pair 3:* Bhopal and Vijayawada
Pair 4: Dimapur and Ludhiana	*Pair 4:* Madurai and New Delhi

13.6 Randomization and Masking Procedures

In cluster-randomized trials with a relatively low number of sites (clusters), substantial imbalances between study arms can emerge easily by chance. To reduce the likelihood of large study arm imbalances for key variables, we restricted the pool of potential allocation combinations by removing combinations with large baseline imbalances. With no restrictions, there were a total of 16 potential allocations (i.e., 4^2) within each stratum (PWID/MSM), or 256 overall allocations. First, to reduce large imbalances within the strata, randomization allocations were dropped (n=8, 4 in each stratum) due to imbalances in prevalence of viremic persons or viral suppression (i.e., all sites with higher/lower prevalence were allocated to one arm). This resulted in 12 allocations for each stratum. These allocations crossed (PWID x MSM), resulted in 144 potential allocations (i.e., 12^2). Then, an additional overall restriction was placed in which allocations were dropped (n=36) due to imbalances in prevalence of viremic persons or viral suppression (i.e., higher/lower prevalence 6:2 pair ratio in different arms). This resulted in a total of 108 potential allocations. We checked across all these potential allocations for sites that either always or never appeared in the same study arm. No sites always or never appeared in the same

arm - with the exception matched sites, which, by definition, never appeared in the same arm.

Of the 108 allocation combinations that remained after site pairing and restriction, one allocation was selected in a ball drawing ceremony on January 3, 2018 that was refereed by two statisticians who were independent of the study. The ceremony was video recorded and is available at https://youtu.be/UmXBG2CluNA. Because of the cluster randomized design, masking participants or research staff was not feasible. However, the randomization team withheld the randomization results for each site pair until cohort recruitment was complete or nearly complete at both sites in the pair. The implementation teams in India recruited cohorts at each site without knowing whether the site would be intervention or control.

13.7 Participant Enrollment and Follow-up

Cohort participants will be assessed for eligibility and enrolled at ICCs as described above. These participants will complete a baseline study visit as soon as possible after screening and will be asked to complete follow-up research visits at 6, 12, 18, and 24 months. Participants in the qualitative evaluations will be enrolled at ICCs and be asked to complete an in-depth interview. There will be no follow-up visits in the qualitative evaluation. Participants in the RDS survey will be enrolled after being recruited by network members using a coupon system as described above. RDS survey participants will be asked to compete a single study visit with no follow-up.

13.8 Data and Safety Monitoring

Procedures to ensure the validity and integrity of the data

All field staff, interviewers, phlebotomists and clinicians who will come into contact with study participants will be required to complete research ethics and good clinical practice (GCP) training. All staff will undergo a three-day training program on the study protocol and the standard operating procedures, followed by a one-day one-on-one training session for staff who will be administering and/or recording information on tablet PCs/netbooks (RDS) or study case-report forms (ICCs). Mock interviews will also be included. If new staff members are hired during the course of the trial, they will undergo similar training prior to coming into contact with study participants.

Lab technicians/phlebotomists at YRGCARE have undergone training on research ethics and good clinical laboratory practices (GCLP). The YRGCARE ID Lab is certified by the College of American Pathologists, United Kingdom National External Quality Assurance Scheme, and the Virologic Quality Assessment Program, US and by the AIDS Clinical Trial Group and Abbott Laboratories Inc, US. GCLP are monitored by Johns Hopkins, Family Health International, and PPD.

Procedures to guarantee the accuracy and completeness of the data

Our primary mode of data collection will be through the cohort and RDS surveys. In addition, some process measure data will be collected in the ICCs. We have chosen to use a laptop data entry system rather than paper case report forms. Given the large number of surveys/study visits that will be conducted (16,000 in RDS and ~8,000 in cohort), the electronic data collection method has advantages over the paper method, including 1) immediate data upload to the central

server, 2) increased portability for multiple sites, 3) reduced need to transport paper forms, and 4) logic checks and field restrictions can be built into the program to minimize data capture errors. Finally, the ability to upload data from the field to a central server in real time will help us identify potential overlap between sites (i.e., participants who are recruited at more than one site). The central database will include the unique alphanumeric codes that will be obtained from fingerprint images. Therefore, once a survey is completed the code will be centrally available, enabling us to quickly identify individuals recruited at multiple sites.

13.9 Analysis Plan

The analysis plan has five components. First, we will compare primary and secondary endpoints in cohort participants at sites randomized to the intervention or the control condition. Second, we will assess whether the intervention, in comparison with the control condition, was associated with "off-target" effects at ICCs (number of unique persons tested for HIV and number of HIV-positive persons diagnosed). Third, we will conduct a mixed methods evaluation of the HIV care incentives. Fourth, we will evaluate the impact of the HIV care incentives on PWID and MSM community-level outcomes with a dedicated RDS survey. Fifth, we will evaluate the cost-effectiveness of the HIV treatment incentive intervention.

13.9.1 Analysis plan for primary outcome

In the primary analysis, we will use an intent-to-treat, missing equals failure approach. The primary outcome will be the proportion of participants who have survived with a suppressed viral load (HIV RNA <150 c/mL) at the 12-month cohort follow-up visit. Participants that die prior to the 12-month visit or miss the 12-month visit will be considered failures in the analysis. The primary analysis will be at the site-level and will use a two-stage procedure beginning with fitting an individual-level logistic regression model with terms for each matched pair and individual-level viral suppression at the baseline visit (HIV RNA <150 copies/mL), but ignoring the intervention effect. The model computes the expected number of events in each cluster. The observed and expected number of events in the two clusters in each matched pair are compared and if there is no intervention effect these values will be the same. An adjusted prevalence ratio and 95% confidence interval will be calculated by estimating the mean within-pair difference of the natural log transformed adjusted prevalences by arm. The exponentiated difference is the ratio and a paired t-test will be used for significance testing. An adjusted prevalence difference and 95% confidence interval will be calculated in a similar manner, estimating the mean within pair difference of the non-transformed prevalences by arm. Analysis of the primary outcome will also be stratified by viral suppression status at baseline (HIV RNA <150 copies/mL). In this site-level one-stage approach, we will calculate the difference in the proportion with suppressed viral load within each matched pair among strata defined by baseline viral suppression. We will calculate the unweighted mean of the pair-wise difference with a 95% confidence interval and use a paired t-test to test the hypothesis that within each stratum the observed difference is statistically different from zero. We will further explore whether there is statistically significant interaction by baseline viral suppression status and intervention effect.

Primary outcome sensitivity analyses
We will conduct several supplemental analyses to assess whether inferences are sensitive to different analytic specifications. First, we will conduct an analysis in which participants who

miss the 12-month visit (but are not known to be deceased) will be excluded (missing ignored), and death or non-suppression of the HIV RNA at month 12 will be considered failure. Second, we will conduct an analysis that includes only individuals that complete the 12-month visit (deaths and missing ignored) and non-suppression of the HIV RNA at month 12 will be considered failure. In a third sensitivity analysis, we will consider adjusting for additional potential confounders using the same two-stage procedure described above (6). We will only consider factors measured at the baseline visit (no post-randomization measures) that have a large (odds ratio >2 or <0.5) and statistically significant ($p<0.05$) association with the intervention status and the outcome. Fourth, we will conduct pre-specified analyses that are stratified by key population (PWID and MSM).

13.9.2 Secondary outcomes

Secondary binary outcomes including i) survival with suppressed viral load at other time points (6, 18, and 24 months), ii) proportion with at least one suppressed viral load during follow-up, iii) proportion retained to HIV care (defined as the proportion with at least one visit to the ART center per 6-month follow-up interval), and iv) mortality will be analyzed similarly resulting in pair-wise differences in proportions with a two-stage procedure for confounder adjustment, if appropriate (criteria for confounders outlined in prior section).

For two other secondary outcomes, we will use similar pair-matched cluster approaches with a two-stage procedure for confounder adjustment. First, we will compare risk of initiating ART at intervention vs. control sites (among the subset that is ART-naïve at baseline) using a Cox proportional hazards model. Second, we will compare ART possession ratio (defined as number of days covered by ART dispensations divided by the number of days under observation) by calculating a mean difference between intervention and control conditions.

13.9.3 Exploratory outcomes

Intervention effects on HIV testing and diagnosis at ICCs
We will assess whether the intervention, when compared with the control condition, is associated with off-target effects at ICCs. We hypothesize that treatment incentives for HIV-positive clients may also attract more people to the ICC for HIV testing, and subsequently, lead to more newly diagnosed HIV-positive persons. We will use a similar two-stage procedure as described above to calculate the mean pair-wise differences in rates.

Analysis plan for mixed methods evaluation of HIV care incentives
The mixed methods evaluation will include a quantitative and qualitative component. The quantitative component comprises close-ended questions about perceptions of and experiences with incentives that will be included in the questionnaire for the final (24-month) study visit at the 8 incentive sites. These data will be summarized to quantify overall and site-level variability in perceptions about treatment incentives.

Qualitative data will be obtained by in-depth interviews as described. Transcribed interviews will be translated from the local language and entered into Atlas.ti, a free-text organizing program and analyzed using content analysis. We will identify core consistencies and meanings in the data through careful repeated reading of interview texts. Coding involves labeling sections of

text based on themes and particular domains of interest related to the study aims. We will use an "open coding" procedure whereby the beginning phases of data analysis will involve an inductive approach to elucidate patterns and themes in the data to generate codes for analysis. New themes can be generated from the analysis in addition to those established a priori. Early coding will be followed by a more deductive process whereby relevant text from the remaining interviews is coded using Atlas.ti within the framework established early on. The outputs of the coded text will then be reviewed for similarities and differences and synthesized using matrices structured by the main themes of the analysis. Quotes representing each theme will be reviewed again within the context of the full text of the interview to contextualize and confirm interpretation. Results will be summarized/presented by main themes. We will focus on codes/themes related to barriers to using the ICCs, perceived quality, and perceptions about incentives.

Analysis plan for community-level effects assessed by RDS surveys
Inferences about the effect of HIV care incentives on community-level outcomes will be based on study arm differences in outcomes measured at the evaluation RDS survey, adjusted for values of outcomes at the baseline survey (which was done in 2016/2017). Because RDS participants are recruited without respect to whether they have accessed services at ICCs, they can provide an unbiased estimate of community-level impact.

The primary community-level outcome will be viral suppression among HIV-positive individuals in the RDS sample. Using the same approach as the primary outcome analysis, we will calculate the difference in the RDS II weighted proportions within each matched pair and then calculate the unweighted mean of the pair-wise differences with a 95% confidence interval. Comparisons will use RDS-weighted proportions, which will be calculated using the RDS-II estimator (7), which accounts for the self-reported network size of each individual in the analysis. With these weights, RDS can provide inferences about the prevalence of viral suppression (and other outcomes) in the underlying population. RDS weighting is subject to assumptions, some of which cannot be validated, therefore we will also compare the unweighted prevalence estimates. A paired t-test will test the hypothesis that the observed pair-wise difference is statistically different from zero. Adjustment for baseline viral suppression at the baseline survey as a cluster-level factor will be conducted using the two-stage approach as described in the primary analysis. Similar analytic methods will be applied to secondary outcomes that are proportions including recent HIV testing, awareness of HIV status, HIV care, current ART use, and prevalence of viremic individuals in the community, as well as the HIV incidence rate (unweighted only).

As a sensitivity analysis, we will adjust for demographic factors as confounders (age, sex, marital status, educational attainment) using the two-stage procedure if the factor has a large (odds ratio >2 or <0.5) and statistically significant ($p<0.05$) association with the intervention status and the outcome. Additional sensitivity analyses will consider other approaches including an analysis of the within-cluster difference in outcome prevalence between serial cross-sectional studies (baseline RDS and evaluation RDS after 24 months of intervention) and individual-level models. These models include fixed effects (e.g., matched pair effect), random effects (e.g., clusters), scaled RDS weights as sampling weights, and allow adjustment for baseline covariates at the individual and cluster level. Additionally, we will conduct pre-specified analyses that are stratified by key population (PWID and MSM).

Analysis plan for cost-effectiveness

We will conduct 2 cost-effectiveness analyses from 3 perspectives (patient out-of-pocket costs, health care payer (governmental), and societal, combining patient and payer costs). The first analysis will compare the cost-effectiveness of HIV care incentives versus the control condition using the primary and secondary outcome measures to yield, for example, the cost per additional individual surviving with viral suppression at 24 months. Using the same approach, we will also explore cost-effectiveness with respect to secondary outcomes including newly identified HIV-infected persons and HIV incidence.

1. Costing: We will apply standard micro-costing methods from the US Task Force on Cost effectiveness Analysis to assess care and intervention costs. The intervention costs will be based on fair market value of the non-cash incentives. For individuals, we will focus on the following major and readily captured medical and productivity measures: hospitalizations, physician and non-physician outpatient visits, medications, productivity (full-time, part-time work), out of pocket medical costs, and time and wages lost due to medical appointments including travel. We will adhere to recommendations for trial-based economic data collection (e.g., identifying resource measures, data collection, baseline cost, pilot testing, validation, patient-level costing, national costing and standard reporting). We will consult policymakers for the most relevant outcomes of interest to them and for their preferred sources of national resource unit costs, e.g., based on India's National Pharmaceuticals Pricing Policy and National Health Accounts of India.

2. Effectiveness: The initial cost-effectiveness analysis will combine the costing analysis from 3 perspectives (patient, payer and societal) for the 24-month intervention period with the primary and secondary outcomes of the cluster-randomized trial using statistical analyses delineated above. A second cost-effectiveness analysis will extend the end of trial results to a lifetime time horizon. Because induced benefits or costs may extend beyond the time horizon of the study (e.g., mortality benefit from viral suppression), we will project the future implications on health and on costs using computer simulation models. Markov or Monte Carlo simulation models track hypothetical cohort members as some individuals develop HIV or as those with HIV infection have stable, improved, or worsened health status or die. The computer simulations track the proportion of the cohort that is alive each year until all cohort members have died or the desired analytic time horizon has been reached. Consistent with WHO recommendations, we will obtain quality of life estimates as disability-adjusted life years (DALYs).

   Economic model development will include the following steps: (1) systematic literature search to identify existing data to estimate model parameters and previously published economic models, (2) data synthesis to estimate means and ranges of uncertainty, (3) Markov and Monte Carlo simulation model development based on the primary study and literature data. Search strategies will include those recommended by Health Technology Assessment, supplemented by hand-searching of bibliographies and consultation with experts. Data synthesis will apply standard quantitative pooling methods typically used in meta-analysis (such as a random effects model) when sample sizes are available. When sample size is not available, means or medians of published data will be applied with ranges specified in the

literature. The Markov model construction will use standard decision analysis software (Decision Maker, DATA by Treeage or equivalent). Because costs are discounted to reflect time preferences (money spent now is more valuable than money spent one year from now), life expectancy will also be discounted in accordance with cost-effectiveness recommendations. Model validation or calibration to external data (comparison and adjustment, if necessary, of predicted to observed outcomes) will be performed.

3. Cost-effectiveness analyses: By extending the time horizon for the analysis and by translating trial outcomes into DALYs, the cost-effectiveness analysis becomes a cost-utility analysis where the outcome is expressed as the incremental cost-effectiveness ratio (ICER) per disability-adjusted life-year gained. We will compare of the ICER for the incentive intervention with the ICERs of other well-accepted medical interventions. Based on WHO criteria, the intervention will be considered "highly cost-effective" if the ICER falls below the per capita GDP of the country (~$1500 for India) and "cost-effective" if the ICER falls below 3 times the per capita GDP.

   Extensive sensitivity analyses will be performed, varying each variable or groups of variables over their plausible ranges to determine their impact on the cost-effectiveness of HIV care incentives versus the control condition. The translation of the Markov model into a Monte Carlo simulation will involve assigning distribution functions for each parameter and determining the range of plausible values to capture their uncertainty, and re-evaluating the computer simulations with boot strap samples. This will be used to determine cost-effectiveness acceptability curves, which incorporate all of the uncertainty to estimate the likelihood that the intervention will have an ICER that makes it cost-effective or cost-saving.

14. DATA HANDLING AND RECORDKEEPING

14.1 Data Management Responsibilities

This study will be conducted a 16 field sites throughout India, but will be coordinated by a single site, the YR Gaitonde Centre for AIDS Research and Education (YRGCARE) in Chennai, Tamil Nadu, India with oversight from investigators at the Johns Hopkins Bloomberg School of Public Health and the Johns Hopkins School of Medicine. Investigators from Johns Hopkins and YRGCARE will oversee all aspects of the trial including participant recruitment, data collection, laboratory testing, biological sample storage, and data management. Additional details can be found in the Data and Safety Monitoring Plan.

14.2 Essential/Source Documents and Access to Source Data/Documents

Source documents for this study are i) electronic case report forms (eCRFs), into which data from interviews will be directly entered, and ii) government ART treatment books, which will be photocopied and stored electronically at each study visit. Additional details can be found in the Data Safety and Monitoring Plan.

14.3 Quality Control and Quality Assurance

14.3.1 Procedures to ensure the validity and integrity of the data

All field staff, interviewers, phlebotomists and clinicians who will come into contact with study participants will be required to complete research ethics and good clinical practice (GCP) training.

Lab technicians/phlebotomists at YRGCARE have undergone training on research ethics and good clinical laboratory practices (GCLP). The YRGCARE ID Lab is certified by the College of American Pathologists, United Kingdom National External Quality Assurance Scheme, and the Virologic Quality Assessment Program, US and by the AIDS Clinical Trials Group and Abbott Laboratories Inc, US to perform HIV-1 genotypic resistance testing. GCLP are monitored by Johns Hopkins, Family Health International, and PPD.

14.3.2 Procedures to guarantee the accuracy and completeness of the data

Our primary mode of data collection will be through the EHR at the ICCs and study specific eCRFs. Additional details can be found in the Data Safety and Monitoring Plan.

15. CLINICAL SITE MONITORING

ICCs are key population-focused sites that provide HIV and HCV testing, STI screening and treatment, and (in PWID sites) OST and SSP. They are staffed by a site coordinator, one or two nurses, a counselor, a phlebotomist, and a part-time physician. This ICC staff provided clinical overview for the site. The current study evaluates a behavioral economic intervention, which is minimal risk. No additional clinical monitoring is needed for the current protocol.

16. HUMAN SUBJECTS PROTECTIONS

16.1 Institutional Review Boards

The protocol and informed consent documents are approved by the Institutional Review Boards of the Johns Hopkins School of Medicine in the US and YRGCARE in Chennai, India. In addition, the study is approved by the Indian Council of Medical Research and the Health Ministry Screening Committee. Any subsequent modifications will be reviewed and approved by both the Johns Hopkins and the YRGCARE IRBs. IRB continuing review and approval will be obtained from both the Johns Hopkins and YRGCARE IRBs once a year. If IRB approval expires or lapses, all ongoing research activities will stop unless the PIs determine that it is the best interests of already enrolled participants to continue their study-related activities. New participants will not be enrolled in the study until the IRB approval to continue the research is obtained.

16.2 Vulnerable Participants

16.2.1 Pregnant Women and Fetuses

Pregnant women who meet eligibility criteria for inclusion in the PWID stratum of the study may be included in any aspect of the study (cohort, mixed methods evaluation, or RDS survey). The study does not provide medications or interventions that pose a risk to pregnant women or their fetuses. We will not test women for pregnancy as part of this study.

16.2.2 Prisoners

It is possible that persons who are enrolled may become prisoners during the course of the study. We do not have formal agreements in place to provide the incentive intervention or conduct study visits while participants are in prison. We will not conduct any research activities while participants are in prison. We will continue to track participants and re-engage them in the study when they are released from incarceration if still in the follow-up window.

16.2.3 Children

Children younger than 18 years will not be included in any aspect of the study.

16.2.4 Illiterate participants

Some of our research participants will be illiterate. As required by the JHM and YRGCARE IRB, all informed consent documents will be read verbatim.

16.3 Informed Consent

16.3.1 Informed Consent Process

Study cohorts: Written informed consent will be used for HIV-positive participants enrolled in the cohorts at each ICC. Consent will be obtained by a trained, supervised research assistants in a private office setting. Approximately 20 minutes will be allotted for consent. Participants will not generally have access to the consent form in advance, but they may take a consent form with them if they wish to take more time in making a decision to join the study. The research assistants will present the consent form to participants in detail and encourage them to ask questions. The research assistants will assess participation understanding of the consent form by querying whether 1) identifying information will be collected in the study (yes), and 2) whether the study will have any follow-up after the initial visit (yes, we will use locator information to locate participants at the end of the study and ask them questions about their HIV care and get a sample of blood). Because this study will be conducted in numerous cities across India, multiple translations are needed to accommodate local languages.

In-depth interviews: A research assistant will meet with individuals in a private office to describe the study and obtain oral consent. The research assistant will read the OCS verbatim to potential participants in the relevant language for the study site.

RDS survey: We will use an oral consent script for RDS participants. With the exception of the

RDS "seeds" (2 or 3 participants to begin the recruitment chain), individuals must present a valid to the study site with a valid referral coupon. A research assistant will meet with such individuals in a private office to describe the study and obtain oral consent. The research assistant will read the oral consent script verbatim to potential participants in the relevant language for the study site.

16.3.2 Assent Process

Not applicable

16.3.3 Documentation of Informed Consent

Participants who provide written consent will be given a copy of the consent. In addition, a signed copy of the consent will be maintained in locked cabinets at each of the study field sites.

16.4 Risks

a. Medical risks, listing all procedures, their major and minor risks and expected frequency.

Study procedure	Medical Risks	Frequency	Severity
HIV-positive ICC cohort participant	Pain from phlebotomy	Most	Minor
	Phlebitis or skin infection from phlebotomy	< 1%	Minor to moderate
In-depth interviews	None		
Baseline/Evaluation RDS	Pain from phlebotomy	Most	Minor
	Phlebitis or skin infection from phlebotomy	< 1%	Minor to moderate
	Psychological discomfort from questions about personal behaviors	< 20%	Minor
	Anxiety about HIV testing	Most	Minor

b. Steps taken to minimize the risks.
The proposed study poses only minimal medical risks. We will minimize the risk of phlebotomy-associated adverse events by using trained and experienced phlebotomists and by adhering to sterile practice. We will minimize the risk of participant discomfort with personal questions by a) training interviewers to query and respond in non-judgmental manner and b) to inform participants that they may skip questions they are not comfortable answering. Finally, we will minimize anxiety about HIV testing by using trained HIV testing counselors.

c. Plan for reporting unanticipated problems or study deviations.
The Indian co-investigator (Aylur Srikrishnan) will report unanticipated problems and study deviations to the local IRB (YRGCARE IRB). Such events will also be communicated with the US investigators and Dr. Lucas (JHU PI) will report to the JHM IRB. Dr. Lucas will report unanticipated problems or study deviations that involve risks to participants or others

promptly to the JHM IRB in accordance with Organization Policy. Minor problems and protocol deviations (which pose no risk to subjects or others) will be reported in annual protocol continuing review.

d. Legal risks such as the risks that would be associated with breach of confidentiality.
We will collect self-reported information on illicit drug use and sexual practices that may pose legal risks to participants if confidentiality is breached. Regarding the HIV-positive ICC cohort participants, we will collect identifying information in these subjects, including name, address, and contacts. These data will be maintained at the sites on password-protected laptops that will be brought home by study staff each night. As with the RDS, data will be uploaded each night to an encrypted, internet-based clinical trial database, based at YRGACRE in Chennai. Source documents on-site will be maintained in a double-locked file cabinet.

Regarding the RDS surveys, we have a multilevel plan to minimize this risk. First, we will not collect RDS participants' names or other identifying information, and we will use oral consent to avoid the use of names and signatures on informed consent forms. Second, RDS interview data will be uploaded immediately to an encrypted, internet-based clinical trial database. RDS interviewers in the field will not have access to participant data in the database other than the participant they are currently interviewing. Third, interview and laboratory data will be stored and managed at the YRGCARE coordinating center in Chennai, India. These data will be password-protected and available only to a defined group of data managers and analysts who are working on the trial.

e. Financial risks to the participants.
This study entails no financial risks to participants.

16.5 Social Impact Events

Individuals enrolled in this study may experience personal problems resulting from the study participation. Such problems are termed social impact events. Although study sites will make every effort to protect participant privacy and confidentiality, it is possible that participants' involvement in the study could become known to others, and that participants may experience stigmatization or discrimination as a result of being perceived as being HIV-infected. For example, participants could be treated unfairly, or could have problems being accepted by their families and/or communities. Problems may also occur in circumstances in which study participation is not disclosed, such as impact on employment related to time taken for study visits.

In the event that a participant reports a social impact event, every effort will be made by study staff to provide appropriate assistance, and/or referrals to appropriate resources. Social impact events are documented and reviewed on a scheduled basis by the protocol team leadership with the goal of reducing their incidence and enhancing the ability of study staff to mitigate them when possible. Social impact events that are judged by the designee to be serious, unexpected, or more severe or frequent than anticipated, will be reported to the overseeing IRBs in accordance with the IRB's reporting policy.

16.6 Benefits

Participants in the HIV-positive ICC cohorts, have the potential to benefit if the intervention leads to improved HIV treatment outcomes and retention to care. Persons who participate in the RDS may benefit from HIV counseling and testing and learning their HIV status. No benefits are anticipated for those who participate in in-depth interviews. The study has the potential to benefit society if the tested intervention is found effective and are adopted in routine service delivery.

16.7 Compensation

HIV-positive cohort participants will receive 250 Indian Rupees (4.17 USD) for successfully completing each study visit (maximum of 5 visits). For the last 2 visits (18-month and 24-month visits) we will offer a bonus of 200 Indian Rupees (3.33 USD), in addition to the base reimbursement, for participants who complete the visits in a +/- 14 day window around the scheduled visit date. The maximum possible reimbursement for ICC cohort participants is 1650 Indian Rupees (27.50 USD) for those who complete all 5 study visits and complete the last 2 visits within the specified window.

Compensation for time and travel will be provided to in-depth interview participants – 150 Indian Rupees (2.50 USD).

Compensation will be provided to RDS participants. They will receive 250 Indian Rupees (4.17 USD) for completing the survey and phlebotomy. They will also be eligible to receive an additional payment for each coupon returned by an eligible participant up to 2 coupons maximum (50 Indian Rupees or 0.83 USD per coupon). Thus, the maximum possible compensation for RDS participants will be 350 Indian rupees (6.83 USD).

16.8 Participant Privacy and Confidentiality

All participant-related information including eCRFs, laboratory specimens, evaluation forms, reports, etc., will be kept strictly confidential. All paper records will be kept in a secure, double-locked location and only research staff will have access to the records. For electronic records, an encrypted network-based data collection storage system will be used. Trained interviewers will conduct face-to-face interviews with participants and enter responses directly onto a laptop computer or tablet. Information will be routed directly to a central server via a local network. Encrypted data will then be transferred over the internet (a minimum of once daily) to the central data storage at YRGCARE where it is stored and backed-up every 24 hours. Data will be cleaned at YRGCARE and de-identified before being encrypted and transferred via a secure internet portal to the analytical team at Johns Hopkins. Human specimens (blood) will be labeled using study specific ID numbers only, with no personal identifying information on the tube or paperwork. Samples will be shipped under specified conditions and time frames to YRGCARE for laboratory testing. The biometric system that will be used generates a unique and reproducible hexadecimal code when a fingerprint is scanned or rescanned. The software does not store fingerprint images and hexadecimal codes cannot be back-converted to a fingerprint image.

Only the field teams delivering care to participants will have access to identifying information of

study participants. Any data that is sent to US investigators for analysis will be deidentified. Upon request, participant records will be made available to the study sponsor, the sponsor's monitoring representative and applicable regulatory entities.

16.9 Certificates of Confidentiality

This study is protected by a Certificate of Confidentiality for data stored in the U.S. Certificates of confidentiality are not recognized by the Indian Government.

16.10 Study Discontinuation

The study may be discontinued at any time by the IRB or NIDA as part of their duties to ensure that research participants are protected.

16.11 Post-Trial Access

Not relevant

16.12 Community Advisory Board and Other Relevant Stakeholders

Community advisory boards are already present in each of the study field sites as part of ongoing research activities and they will continue to be engaged throughout this protocol. Community meetings will occur quarterly.

17. ADMINISTRATIVE PROCEDURES

17.1 Protocol Registration

Not applicable

17.2 Regulatory Oversight

Not applicable

17.3 Study Implementation

Additional details can be found in the Study standard operating procedures (SOP)

17.4 ClinicalTrials.gov

This trial is registered with ClinicalTrials.gov – NCT02969915

18. REFERENCES

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19. APPENDICES

Appendix I. Schedule of procedures and evaluations for cohort participants followed in cluster randomized trial

Procedures/Evaluations	Screening	Baseline visit	Follow-up evaluations and intervention				
			6 mo.	12 mo	18 mo	24 mo	Interim visits
Screening questionnaire	X						
Enrollment informed consent	X						
Register biometric code (fingerprint based) in database		X					
Abstract HIV treatment data from govt. ART books	X		X	X	X	X	X
Locator information		X	X	X	X	X	X
Study interview							
Demographics		X					
Quality of life		X	X	X	X	X	
HIV care continuum		X	X	X	X	X	
ART use & adherence		X	X	X	X	X	
Beliefs about ART		X	X	X	X	X	
Drug & alcohol use		X	X	X	X	X	
Drug related risk behaviors		X	X	X	X	X	
Sexual risk behaviors		X	X	X	X	X	
Depressive symptoms		X	X	X	X	X	
Healthcare utilization		X	X	X	X	X	
Laboratory tests							
Rapid HIV test	X						
CD4 cell count		X					
HIV RNA		X	X	X	X	X	
Blood glucose			X				
Creatinine				X			
Hepatic panel					X		
Study visit compensation		X	X	X	X	X	
HIV care incentives provided (intervention sites only)			X	X	X	X	X