Owete Statistical Analysis Plan

Contents

Section 1: Administrative Information

1) Title and trial registration

a. Title: *"Self-Test Strategies and Linkage Incentives to Improve ART and PrEP Uptake in Men" or "Owete"*

b. Trial registration number: NCT04772469

2) SAP version number with dates

a. V1 – Sept. 2021

3) Protocol version

This SAP references Owete Protocol Version 4.0, last updated May 5, 2020.

4) SAP revisions

a. SAP revision history.

b. Justification for each SAP revision.

c. Timing of SAP revisions in relation to interim analyses, etc.

5) Roles and responsibilities – names, affiliations, and roles of SAP contributors

a. Carol Camlin, PhD—Principal Investigator (MPI). University of California, San Francisco.

b. Harsha Thirumurthy, PhD—Principal Investigator (MPI). University of Pennsylvania.

c. Jim Moody, PhD—Social Network Analysis lead, Co-Investigator, Duke University

d. Edwin Charlebois, PhD—Senior statistician. University of California, San Francisco.

e. Monica Getahun, MPH—Owete Study Director. University of California, San Francisco.

f. Hellen Awuoche, BSc --Data manager. Impact Research and Development Organization.

g. Lila Sheira, MPH—Data manager and analyst for Owete study. University of California, San Francisco.

6) Signatures

a. Person(s) writing the SAP

b. Senior statistician responsible

c. Multiple-PIs

Section 2: Introduction

7) Background and rationale:

Ending the AIDS epidemic in sub-Saharan will require further engagement of men in HIV testing, prevention, and treatment, a challenging task given that nearly 50% of HIV-positive men in many countries are unaware of their HIV status and men have lower uptake of HIV antiretroviral therapy (ART) and pre-exposure prophylaxis (PrEP). This study focuses on a highly mobile population of men – fishermen – in Kenya's Lake Victoria shoreline communities, where HIV incidence rates are extremely high. Two recent innovations – HIV self testing (HIVST) and social network-based interventions – hold promise for overcoming barriers to HIV testing and linkage to services for both HIV-positive and HIV-negative men. This study seeks to determine if an HIV status-neutral, social network-based approach, along with low-cost incentives, can promote HIV testing, linkage to care and prevention, and better health outcomes in men.

8) Objectives:

This study aims to identify strategies needed to close gaps in the HIV care and prevention cascades in high priority populations and settings in sub-Saharan Africa. These gaps are most pronounced in men, who are less likely than women to test for HIV and seek HIV treatment or prevention services, and in high HIV incidence settings such as western Kenya. We will harness the power of peer influence within men's close social networks and leverage new technologies such as HIV self-tests and point-of-care PrEP adherence assays to increase

men's HIV testing rates and strengthen men's ongoing engagement in HIV care and prevention. We will pursue three aims:

a. **Aim 1**: Determine whether providing HIV self-tests to network-central men for distribution to other men in their close social networks increases men's HIV testing uptake. We will conduct social network mapping in study communities in Siaya Country, Kenya to identify distinct close social networks of men. We will then randomize these social networks to intervention and control groups. Network-central, highly- connected men in each network will be recruited as "promoters", and receive HIVST training. Promoters in networks assigned to the intervention will then receive self-tests for distribution to men in their networks. Promoters in networks assigned to the control will instead distribute vouchers for free self-tests at nearby health clinics.

b. **Aim 2**: Determine whether network-central promoters and small incentives can improve ART and PrEP uptake among men. We will test whether network-central promoters can enhance linkage to ART and PrEP after self-testing, thereby addressing a key limitation of HIVST. Promoters in the Aim 1 intervention group will be asked to distribute information and transport vouchers for ART or PrEP to men in their networks. Our primary hypothesis is that the intervention will result in higher rates of linkage to ART or PrEP (confirmatory testing and ART referral for positives, and PrEP screening for negatives).

c. **Aim 3**: Test the impact of interventions on ART or PrEP retention and adherence. We will measure 6- and 12-month VL and tenofovir urine levels and provide results to participants. Tenofovir levels will be measured with a recently-developed low-cost PrEP adherence urine immunoassay28 that detects tenofovir levels in urine at the point-of-care. We will test whether the Aim 1 & 2 interventions have lasting effects on retention and adherence.

Section 3: Study Methods

9) Trial design:

In Aim 1, following the study pilot, community selection, and preparation (see 'recruitment and retention plan') the study team will conduct a census/BMU registry verification in study communities to identify the population of men eligible for the study. We will screen, recruit and enroll eligible men who give their informed consent to participate, then measure their close social networks and baseline characteristics. We will identify network-central, highly-connected men ("promoters") and randomize their close social networks 1:1 to intervention and control groups. Promoters in the intervention group will receive HIVST training, multiple HIVST for distribution to other men, and a small amount of remuneration. Promoters in the control group will receive basic HIV education and training about the study, and will be given vouchers that can be exchanged for HIV tests (standard or free HIVST kits) at nearby health facilities. Using follow-up survey data, we will test the hypothesis that a higher rate of HIV testing will be observed after 3 months among men in networks that receive the intervention compared to control.

In Aim 2, we will test whether network-central promoters can enhance linkage to ART and PrEP (including screening and uptake) after HIV testing among men in their close social networks. Promoters in the Aim 1 intervention group will be asked to distribute information and transport vouchers for ART or PrEP when distributing HIV self-tests to men in their close social networks. We will use clinic data (abstracted from MOH records by the study staff) to test the primary hypothesis that the intervention will result in higher rates of linkage to ART or PrEP (confirmatory testing and ART referral for positives, and PrEP screening for negatives). We also will test the hypothesis that higher ART and PrEP uptake will be observed within 3 months (+ or – about one month) in the intervention group.

In Aim 3, we will measure 6- (+/– about 1 month) and 12-month (+/– about 1 month) VL tenofovir levels using routine viral load testing and a novel point of care PrEP adherence assay (an antibody-based assay permitting measurement of tenofovir levels in urine) among men living with HIV and initiating ART and those HIV-seronegative men initiating PrEP in study sites, respectively, and test the hypothesis that higher rates of virologic

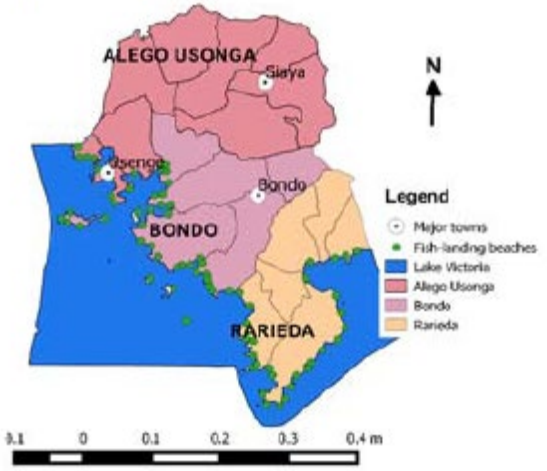
suppression will be observed in HIV-infected men, and PrEP adherence in un-infected men, in the intervention group. The timeline will begin when men are enrolled into the study and complete their baseline interview.

Across all aims, we will assess the pathways of intervention action using qualitative and mixed methods. We will identify the mechanisms of action, and barriers and facilitators of the social network and incentives intervention implementation, using qualitative and mixed methods assessments embedded in Aims 1, 2 and 3. The data collection approach will include in-depth interviews with participants in both groups, key informant interviews with network-central promoters, and focus group discussions with study participants stratified by HIV status and study group. Data will be collected at baseline and three follow-up periods corresponding to the timing of quantitative outcome measurements in Aims 1 through 3.

10) Randomization

The study will take place in Siaya county, which borders Lake Victoria and has a population of ~1 million.[1,2] Its sub-counties, Rarieda, Bondo, and Alego Usonga, have an estimated 79 beaches and nearly 38,000 fisherfolk. Its population relies heavily on fishing and subsistence farming, and has high rates of poverty. Siaya County is also burdened by high rates of HIV, tuberculosis and malaria.[3,4] HIV prevalence is 19.5%, 28.9% in those aged 25-49 years,[5,6] and highest among fisherfolk at 32.1%. High-risk behaviors, including concurrent partnerships, the "jaboya" sex-for-fish economy, and low condom use, enhance HIV risks.[7,8]

Figure 1: Map of beach landing sites, Siaya County



To implement this study, trained RAs will conduct a census of selected beach communities in Siaya. In addition to the census, we will rely on the BMU registries to account for the possibility that the census omits some fishermen. Using the social network data obtained from the census along with a name matching algorithm, we will identify close male social networks that exist in study communities. " close "networks will typically include 4-10 men. Their defining characteristic will be that individual members of any given network will be connected to each other on multiple domains that indicate strong ties between them. Following the identification of distinct close social networks in communities, we will analyze the network data to determine a *network-central man* having a high degree of connectedness across domains within each network. This man will be considered as the network-central 'promoter' of HIV testing and will be the main individual study staff will contact to implement intervention and control group activities and approached for consent. If a central man is not interested in participation, we will approach the next most central man. Local close networks with consenting promoters will be eligible for randomization.

Close social networks will be randomized 1:1 to intervention and control arms using a computer algorithm that performs randomization stratified by beach and network size in 8 blocks of 2 networks. All network members will receive the study arm condition to which their network is assigned. Participation of all network members is not a requirement for network randomization.

In networks randomized to the intervention, promoters will then be given multiple self-tests labeled with a unique network specific number, and they will be encouraged to offer self-tests to men in their close social networks and to motivate them to use the self-tests privately or with their support. During training, each promoter will be asked to demonstrate self-test use in order to confirm correct understanding of this process before they are asked to offer the self-tests to their peers. Training will also cover best practices on self-test distribution and role-playing of multiple potential distribution and promotion scenarios (we will build upon materials we developed in other HIVST studies). By the end of the training, promoters will be capable of explaining self-test usage to others and have

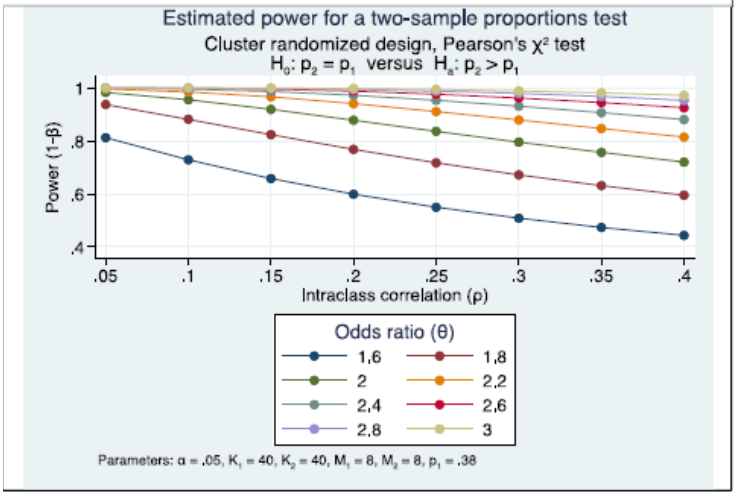
guidance on which individuals they offer self-tests to. Promoters will be encouraged to offer self-tests to their close social network members only, and not others in their community.

SMS messages (not individualized) with status neutral messaging will be sent out to participants in the intervention arm to promote ART/PrEP retention.

11) Statistical Power:

Aim 1: We calculate that the study will have an 80% or greater power to detect a significant difference in the proportion of HIV self-testing associated with the intervention arm, assuming a proportion self-testing in the control arm of 38% (*observed data from SEARCH study in fishermen*) if the proportion testing in the intervention arm is 52% or greater (odds ratio of 1.8), calculated using an Intraclass Correlation Coefficient (ICC) of 0.15 (*conservative based on SEARCH data*), 40 clusters each in the intervention and control arms, average cluster size of 8 in both arms, and a type-1 error rate of 5%.[9,10] Figure 2 shows statistical power and the range of detectable odds ratios over extremes of clustering effects.

Figure 2: Aim 1 power calculations



Aim 2: For the Aim 2 combined primary outcome of successful linkage to ART or PrEP within 3 months of intervention start, defined as when the promotor receives the kits at the end of the promotor training which will be upon completion of the baseline survey for that beach. This study will have a 80% or greater power to detect a significant increase in successful linkage, assuming a proportion successfully linked at 3 months in the control arm of 24% (*based on observed SEARCH trial linkage rates weighted for the number of eligible PrEP HIV-negative men and HIV positive men not currently in HIV care*) if the observed proportion in the intervention arm is 39% or greater (odds ratio of 2.0), using an ICC of 0.15, 40 clusters each in intervention and control arms, a cluster size of 8 in both arms, and a type-1 error rate of 5%. Statistical power for combined ART or PrEP start is similar, with a reduction in anticipated eligible numbers per cluster reduced to 6 resulting in a small increase in the detectable odds ratio to 2.2 or greater. Power for a separate analysis of ART initiation alone is likely to be low given the small numbers of new HIV infections in the study sample with odds ratios in excess of 3 or 4 required.

Aim 3: For the primary outcome, we will have ≥80% power to detect a significant increase in viral suppression and adherence in those on ART and PrEP, respectively, assuming a proportion of successes in the control arm of 70% or greater power (*based on SEARCH trial data on viral suppression rates among fishermen and projected urine TFV detection rates of 70%, weighted for the likely number of men on PrEP (n=168) and men on ART (n=72)*). We assume the observed proportion of successes in the intervention arm will be 89% or greater using an ICC of 0.10, a design effect from clustering of 1.7, and a type-1 error rate of 5%. For the combined primary outcome of retention on ART or PrEP at 12 months, this study will have 81% or greater power to detect a significant increase in linkage assuming a proportion retained in care in control arm of 81% (*based on SEARCH data on retention rates weighted for the likely number of men on PrEP (n=168) and ART (n=72)*) if the observed proportion in intervention arm is 96% or greater using the above assumptions.

12) Framework

We will use the superiority hypothesis testing framework, testing whether exposure to the intervention results in better outcomes than exposure to the control standard of care. Comparisons will be presented as differences between arms in changes in outcomes during the study follow up period.

13) Statistical interim analyses and stopping guidance

a. Information in interim analyses specifying what interim analyses will be carried out and listing time points
    i. No interim analyses will be conducted.
b. Any planned adjustment of the significance level due to interim analysis
    i. Not applicable
c. Details of guidelines for stopping the trial early
    i. None

14) Timing of final analyses:

Analysis of baseline data will occur as beach communities are enrolled and will continue for one calendar year. Final analyses will begin immediately upon completion of all field data collection which is estimated to be completed within twelve months of freezing of the study database *c*.

15) Timing of outcome assessments:

Research staff will collect data from all study participants in both arms at approximately 0 months/baseline, 3 months, 6 months, and 12 months. All assessments will have a window of +/- 1 month. Outcome assessments collected via clinical chart abstraction (HIV confirmatory testing and results, PreP screening and uptake, and ART screening and regimen, clinic attendance), survey (self-reported testing), and via specimen collection and analysis (HIV viral load testing and PreP adherence) will be assessed within one month of each participant's 6 or 12 month outcome window, through a study-scheduled visit.

Section 4: Statistical Principles

16) Level of statistical significance:

Standard levels of significance testing will be used (p=0.05) for two sided-tests. We will report 95% confidence intervals and exact p-values (or p<0.001).

17) Description and rationale for any adjustment for multiplicity: (if so, detailing how the type I error is to be controlled.) Our primary outcomes were established in our protocol, and thus no adjustments will be made for multiplicity.

18) Confidence intervals:

95% confidence intervals will be reported alongside exact p-values.

19) Adherence and protocol deviations:

a. Definition of exposure to the intervention and how this is assessed including extent of exposure:
    ii. Exposure to the intervention will be measured in two independent parts:
        1. Being randomized to the intervention or control group. An individual's cluster will be randomized to either intervention or control group if they are part of a social network or designated as the promotor, or
        2. Receipt of the intervention (self-testing kit) from the social network promotor.
b. Description of how adherence to the intervention will be presented - consort diagram and brief description in the narrative

iii. Adherence to the intervention will be measured in the following ways:

Table 1: Owete Study Fidelity Measures

Intervention Component	Corresponding Study Aim	Fidelity Measure	Components	Time
Promotors training	Aim 1	Pre- and post-evaluation	Covers self-evaluation of knowledge of HIVST, confidentiality, and the roles of promotors	At beginning and end of promotor training
Promotors training	Aim 1	Pre- and post-evaluation	Promotor training attendance—sign in sheet	At training
Distribution of HIVST	Aim 2	Record of distribution by FRAs	Documentation of kits distributed by RAs to promotors which includes serial #s, expiry date, & distribution date.	At kit distribution date which should be last day of training.
Distribution of HIVST	Aim 2	Record of distribution by promotors	Self-reported list of fishermen the promotors gave kits to.	Collected by FRAs after all kits have been distributed during promotor follow up visit?
Receipt of HIVST	Aim 2	Record of receipt of HIVST from promotor	In 3 month survey. Need to add to survey to ask for name of promotor	During 3 month follow up
Usage of HIVST	Aim 2	Record of use of HIVST	In 3 month survey, will ask about use since baseline	During 3 month follow up
Engagement in Care	Aim 3	Linkage register – blue/green card extraction	Record (to validate self-reported clinic attendance)	During follow up visits
Receipt of HIVST, Engagement in Care	Aim 2-3	Receipt of transport voucher with unique ID	Transport voucher with unique network ID to give to clinic staff.	Attending confirmatory test visit

c. Definition of protocol deviations for the trial

Protocol deviations are defined as any failure to achieve full exposure to the defined procedures or treatment plans outlined in the study protocol version previously approved by the IRB except if intended to eliminate a hazard to the study participant or protect the wellbeing or life of the study participant in an emergency. The noncompliance may be either on the part of the investigator or the study site staff and may result in significant added risk to the study subject. As a result of deviations, corrective and preventive actions are developed by the site and implemented promptly.

d. Definition of which protocol deviations will be summarized:
    i. Enrolling someone who doesn't meet the eligibility
    ii. Study visits that fall outside the scheduled evaluation window (Anything outside of +/- 1 window would be a SERU issue)

20) Analysis populations:

Definition of analysis populations, e.g. intention to treat, per protocol, complete case, safety, and other.

a. Intent to treat: Those who were randomized to intervention and control groups (regardless of whether or not they received the kit from their "promotor")
b. Per protocol: Those who were members of a cluster that was randomized to the intervention and meet specific criteria per aim will be part of the per-protocol analysis. For Aim 1, it will be those individuals in the intervention arm who received an HIV self-testing kit. For Aims 2 and 3, it will be those individuals in the intervention arm who received a kit and attended a clinic visit.
c. Complete case— We will not conduct complete case analyses as we will attempt to use all available data from all participants (see section 29: Missing Data).

Section 5: Trial Population

21) Screening Data: We will report the screening data to describe representativeness of trial sample by age, cluster size, education, and other demographic characteristics by trial arm and beach community.

22) Eligibility: Eligibility criteria is outlined below.

In order to participate in the study individuals must meet all of the following criteria:

1. Adult (18 years or older)
2. Male
3. Working as a fisherman or fishing support occupation (e.g. net repairers, boat builders etc.)
4. Willing and able to provide informed consent for participation
5. Not participating in another research study related to HIV testing, treatment and/or prevention

Criteria for exclusion of subjects:

1. Younger than 18 years of age
2. Female
3. Included in another study on HIV/AIDS
4. Inadequate cognitive and/or hearing capacity to complete planned study procedures, at the discretion of the study team

23) Recruitment – information to be included in the CONSORT flow diagram.

24) Withdrawal/follow-up

d. Level of withdrawal, e.g. from intervention and/or from follow-up
    i. Reasons for withdrawal might be that an individual moves out of the area, begins work at a different beach or in a different industry, decides they no longer wish to participate, or are simply lost to follow up. We will attempt to document all reasons for withdrawal.
e. Timing of withdrawal/LTFU data
    i. Withdrawal can happen at any time however will be documented best at each study assessment/visit.
f. Reasons and details of how withdrawal/LTFU data will be presented

i. These will be noted in the CONSORT diagram and tables by study arm and beach community.

25) Baseline patient characteristics

We will evaluate several socio-demographic and clinical characteristics at baseline by which we will describe our study sample. These are outlined in Table 1 below. We will stratify these characteristics by intervention and control arms and report median and the inter-quartile range for continuous variables and the N and percent for categorical and dichotomous variables. No significance testing or p-values will be conducted or reported per CONSORT guidelines.

Table 1: Baseline characteristics of Owete participants, by study arm	
Socio-demographic	Age, sex, household size, marital status, polygamous marriage or not, educational attainment, livelihood strategies/ main income sources, household assets, health behaviors and characteristics (general health status, alcohol use, sexual behavior, mental health status).
Clinical outcomes	HIV status, ART Status, PrEP Status.
Network structure	(Add in section for **characterization of network structures and membership** – details to be obtained from Dr. Moody).

Section 6: Analysis

26) Outcome definitions

a. Primary Outcomes:

i. Proportion of HIV testing: The first primary outcome will be the proportion of study participants who self-report HIV testing in the last three months (at the 3 month follow up visit) compared to those who self-report not using testing during the last three months.

ii. Proportion of HIV self-testing: The second outcome will be the proportion of study participants who self-report using the self-testing kit in the last three months (at the 3 month follow up visit) compared to those who self-report not using a self-testing kit during the last three months.

iii. Proportion with successful linkage to ART or PrEP within 3 months of intervention start (ie: when promoters receive self-test kits to distribute). The second primary outcome will be defined as the proportion of individuals who link to ART (if confirmatory HIV testing is positive) or PrEP evaluation (if confirmatory HIV testing is negative), meaning they present at a study facility/clinic (depending on results of HIV testing) within three months of the intervention start (defined as from when study promotors receive the kits for distribution).

iv. HIV treatment and prevention success: The third primary outcome is a composite measure meant to capture "success" in HIV prevention and/or treatment behaviors (ie: Viral suppression among HIV+ and adequate TFV among those prescribed PrEP). The measure will be defined as either adequate levels of tenofovir, indicating PrEP adherence (defined as TFV levels of <1500 ng/mL in urine indicating inadequate adherence vs. ≥ 1500 ng/ml) among HIV seronegative individuals who screened eligible for PrEP *or* the proportion of HIV-positive participants with viral suppression (defined as HIV RNA <400 c/mL using the Abbott realTime HIV-1 platform and assay, with a detectable threshold of 40 cells per microlitre) at 6 and 12 months. Secondary thresholds of <1000 copies/mL will also be examined. PrEP adherence will be measured at 6 and 12 months after initiation using our novel technology of *point-of-care rapid testing to assess TFV adherence in urine* (developed by Co-I Gandhi in collaboration with Alere Rapid Diagnostics™). For both components of the measure, we will define missing values as failure (i.e. inadequate adherence or unsuppressed).

b. Secondary Outcomes:

v. Retention on ART or PrEP at 6 and 12 months: Using clinic records, we will assess whether men who initiated PrEP and ART attended scheduled appointments, and will compare them to those who were either prescribed PrEP or tested positive for HIV.

27) Analysis methods: Analysis methods to be used and how the treatment effects will be presented:

a. Aim 1: For the test of the intervention effect on the primary outcome of self-reported HIV testing in past 3 months, we will utilize a cluster adjusted Pearson's Chi-square test comparing the proportion of subjects self-testing in the intervention versus the control arm. In secondary analysis we will utilize multilevel mixed-effects logistic regression with cluster adjusted standard errors and a binary outcome of reported HIV self-testing or not (including cluster as one of the levels with random effects allowed). We will investigate factors that influence the probability of success of HIV self-testing, including characteristics of clusters (the close social networks' size and composition, metrics of connectedness, mean cluster self-testing rate), characteristics of the cluster's promoter (age, marital status, HIV status, ART/ PrEP status, measures of the promoter's ties to close-social-network cluster members), and individual level characteristics (demographics, SES, prior HIV testing, self-reported HIV risk, and other health behaviors and characteristics).

b. Aim 2: For the test of the social network-central promoters and small incentive intervention effect on the primary outcome of linkage to care or prevention within 3 months of intervention start we will utilize a cluster adjusted Pearson's Chi-square test comparing the proportion of subjects with documented linkage to care or prevention in the intervention versus the control arm. In secondary analysis we will utilize multilevel mixed-effects logistic regression as described in Aim 1 to investigate factors that influence the probability of success of linkage to care and prevention. We will also evaluate the secondary outcomes of ART initiation among HIV-positive persons not currently on treatment, and initiation of PrEP among HIV-negative persons who screen as eligible. We will compare the initiation proportions between study arms using cluster adjusted Chi-square tests and additional multilevel mixed-effects logistic regression to identify influencing factors.

c. Aim 3: We will utilize a cluster adjusted Pearson's Chi-square test comparing the proportion of successes (HIV viral suppression and adequate TFV levels) among men (on ART and PrEP, respectively) in the intervention and control networks. For the outcome of retention on ART or PrEP at 12 months, we will utilize a cluster adjusted Pearson's Chi-square test comparing the proportion of subjects on ART or PrEP at 3 months post-trial start who are retained in care at 12 months in intervention versus control group. In secondary analysis we will utilize Cox proportional hazards regression to investigate factors that influence time to discontinuation of ART or PrEP based on clinic visits and chart abstraction . We will also use multilevel mixed-effects logistic regression to investigate factors that influence the probability of viral suppression and TFV detection in urine.

d. Any adjustment for covariates: Randomization should yield equivalence between arms on covariates, but if non-equivalence is found on baseline measures or from differential attrition, we will control for it by including the covariate in the model.

e. Methods used for assumptions to be checked for statistical methods:
Distributional assumptions for outcome variables will be checked using descriptive statistics. For mediation models, the assumption of no interaction between exposure (i.e., intervention vs. control) and mediators will be checked using product terms. Transformations will be used for continuous outcome variables that are skew to obtain more symmetric distributions.

f. Any planned sensitivity analyses for each outcome, where applicable:

Not applicable.

g. Any planned subgroup analyses for each outcome including how subgroups are defined: NA

28) Missing data:

The study team will employ several strategies to account for and address missing data during the *Owete* trial period. Missing data will be categorized into: 1) missed individual questions, 2) missed visits, and 3) missing clinical data.

a. Missed individual questions: For instances when participants missed questions as part of a validated scale, we will first assess the amount of missingness by making a variable for the number of questions missed per participant. We will check the assumption of missing at random[11] by tabulating basic socio-demographic characteristics on questions and participants for missing values. For missing questions truly missed at random and comprising less than 20% of the total sub-scale length, however, we will use single imputation. For questions related to alcohol consumption where non-standardized liquid portions and/or alcohol contents were reported, we will use mean imputation to report drinks per day for these participants. In situations where questions that were not part of a sub-set or scale of questions were missing, these variables were left as missing. Information on percent of questions missing and imputed will be reported for each variable as appropriate in study manuscripts.

b. Missed visits: When a participant misses a visit this will be noted in the study register. No data will be imputed for this participant for the missed visit.

Analytic approach: For the primary intent to treat analysis, we will treat missing outcome variables as failure, i.e. utilizing a failure approach for primary outcomes where the values are treated as zero, not missing. For the per-protocol sample, we will either exclude cases with incomplete data or apply multiple imputation techniques.

29) Additional analyses – None required

30) Harms

a. Data safety**:**

The study team is employing a number of proactive strategies to insure the highest levels of data safety. First, data will be collected on password protected tablets. Data are being collected using Research Data Capture (REDCap). Further, data from the REDCap server will be downloaded on a weekly basis to a secure UCSF-based file system. The data will be stored in a separate folder than other study materials, and only members of the data team (Ms. Lila Sheira and Hellen Awuoche) as well as the study director (Ms. Monica Getahun) have access to this data. Lastly and in line with the data-sharing agreement, any individual who requests study data will be required to sign a data agreement which included not sharing the data as well as recommendations for data safety. No identifiers have or will be shared with external investigators.

b. Details on how adverse events are coded or categorized:

Deaths will be reported to IRDO and SERU (KEMRI IRB) by email within 48 hours after the study team and PIs learn of the occurrence and hard copies forwarded to SERU within five working days utilizing standard templates.

Individuals will be provided with information on how to contact the study staff to report adverse events associated with study participation.

Examples of adverse events include:

- Occurrence of social harm related to HIVST use or testing results
- Threats of self-harm or self-injury

31) Statistical software

The following software systems may be used in the analysis of *Owete* data: 1) SAS 9.4; 2) Stata SE version 16 [College Station, TX: StataCorp LP]; Stat Transfer 14; and potentially 4) MPlus for causal mediation models since Stata can handle only one mediator at a time if causal mediation methods are needed.

32) References

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