Analysis Plan

Project Name: Increasing ART Adherence and Retention in Care for HIV+ Women in Ethiopia

Project Code: 1722

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This document serves as a basis for distinguishing between planned (confirmatory) analysis and any exploratory analysis that might be conducted on project data. It is what has been variously called an "analysis plan," a "pre-analysis plan," or a "pre-specification plan." In order that it fulfill this purpose, it is essential that it be finalized and date-stamped before we begin looking at the data (ideally, before data are even received from our agency partners or collaborators). Once finalized, a date should be entered above, and a copy of the document should be archived on the OES team drive as a record that we have committed to this analysis plan before looking at the data.

Outcome Variables to Be Analyzed:

The main outcome variables of interest in our study are:

- ART initiation (yes=1, no=0)
- ART retention in care at 1 month (yes=1, no=0)
- ART retention in care at 3 months (yes=1, no=0)
- ART retention in care at 6 months (yes=1, no=0)

In addition, secondary outcome variables of interest in our study are:

- ART adherence at 1 month (yes=1/no=0)
- ART adherence at 3 months (yes=1/no=0)
- ART adherence at 6 months (yes=1/no=0)

ART initiation is defined as "yes" for a study participant if she attends her initial ART appointment (or attends a rescheduled appointment within 1 week) and as "no" if she does not attend that appointment (or, if she reschedules for an appointment within 1 week, she does not attend the rescheduled appointment).

ART retention in care at 1 month is defined as "yes" for a study participant if she attends her 1 month follow-up ART refill appointment (or attends a rescheduled appointment within 1 week of the 1 month follow-up) and as "no" if she does not attend that refill appointment (or, if she reschedules for an appointment within 1 week, she does not attend the rescheduled appointment). We classify participants lost to follow-up (LTFU) as not retained in care. A participant is LTFU if they miss a scheduled appointment and do not attend a rescheduled appointment within three months of the missed appointment.

ART retention at 3 months and at 6 months are defined similarly to ART retention in care at 1 month, but using 3 and 6 month intervals, respectively.

ART adherence at 1 month is defined as "yes" for a study participant is the study nurse records the participant's adherence as "good" and as "no" if the nurse records the adherence as "fair"/"poor". We classify participants lost to follow-up as not adhering to ART.

In addition, we will examine a second measure of ART adherence defined as "yes" for a study participant is the study nurse records the participant's adherence as "good" or "fair" and as "no" if the nurse records the adherence as "poor".

Study nurses will follow pre-existing thresholds defined by the Ethiopian Ministry of Health (MOH) for classifying adherence as "good"/"fair"/"poor". The MOH definitions are: (i) "good" if 95% or more of doses are taken from the prescription bottle, (ii) "fair" if 85-94% of doses are taken, and (iii) "poor" if fewer than 85% of doses are taken.

ART adherence at 3 months and at 6 months are measured similarly to ART adherence at 1 month, but using 3 and 6 month intervals, respectively.

The main intervention variable of interest is assignment to the praise message phone call treatment arm or to the standard of care control arm. Assignment to the praise message phone call treatment arm is defined as "yes" if the study participant is recorded as being randomized into the praise message phone call treatment arm and as "no" if the study participant is recorded as being randomized into the standard of care control arm.

Statistical Models:

Balancing Checks

We will check balance between treatment and control groups by comparing observable characteristics recorded at baseline in the existing MIS across these two groups. The observable characteristics will be age, educational attainment, marital status, pregnancy status, and referral point (i.e. Drop-in-Clinic or community outreach)

We will implement this check by regressing an indicator variable (i.e. 0/1) for assignment to the treatment group (i.e. praise message phone call group) on the aforementioned set of observable characteristics at baseline using linear ordinary least squares (OLS) regression. We will conduct a joint F-test that all of the regression coefficients on the observable characteristics equal zero.

Treatment Effects - Intent to Treat

We will estimate the causal effect of the intent to treat using linear OLS regression. In our basic OLS specification, we will regress the outcome of interest (e.g., the indicator variable for ART initiation) on an indicator variable for assignment to treatment (i.e. to the praise message phone

call group) and the set of indicator variables for each DIC (excluding one study DIC indicator variable to avoid the problem of multicollinearity). In additional specifications, we will add control variables such as study participant age, educational attainment, marital status, region, referral point (i.e. Drop-in-Clinic or community outreach), and pregnancy status.

Thus, our main regression specification is:

$$outcome_i = \propto + \beta\, praise_i + X_i'\theta + \mu_j + \varepsilon_i \qquad (1)$$

where $outcome_i$ is an indicator variable for the outcome of interest for individual *i*, $praise_i$, is an indicator variable equal to one if the respondent was randomized for assignment to treatment (i.e. to the praise message phone call group), X_i' is a vector of sociodemographic controls (included in our additional specifications), μ_j are DIC fixed effects, and ε_i is an idiosyncratic error term. The coefficient on the treatment indicator variable is the estimate of the causal effect of the intent to treat.

Treatment Effects - Treatment on the Treated

We will estimate treatment on the treated using two-stage least squares (2SLS), where we will instrument for an indicator variable for having received the treatment (i.e. the praise message phone call) using an indicator variable for assignment to treatment (i.e. to the praise message phone call group). In other regards (e.g., baseline controls, additional specifications), our treatment on the treated analysis will follow the analysis described in "Intent to Treat" (see above).

The coefficient on the instrumented (having received) treatment indicator variable is the estimate of the causal effect of the treatment on the treated.

Standard Error Adjustments

In our primary analysis, we will estimate heteroskedasticity robust standard errors and cluster standard errors at the Drop-in-Clinic (DIC) level. To complement our primary analysis, we will calculate HC2 standard errors and exact standard errors.

Follow-Up Analyses:

Heterogeneous Effects

Power calculations for our main analysis suggest that our study is not powered to identify heterogeneous effects. Nonetheless, we will test for several sets of heterogeneous effects in case the study has a larger than expected study size. First, we will test for heterogeneous effects across FSW diagnosed with HIV in the community and those diagnosed at the DICs. Second, we will test for heterogeneous effects across FSW at or above the median age in our sample and below the median age in our sample.

Heterogeneous Effects - Intent to Treat

First, we will interact our intent to treat indicator variable as defined previously with an indicator variable for being diagnosed with HIV in the community. We will follow the same regression specification as in the main "Treatment Effects" section (see Statistical Methods), except now we will include the interaction term we just defined and the indicator variable for being diagnosed with HIV in the community as additional regressors. We will limit our heterogeneous effects estimation to ordinary least squares (OLS) regression.

The coefficient on the treatment indicator variable is the estimate of the causal effect of the intent to treat for participants diagnosed with HIV at DICs. The coefficient on the newly defined interaction variable is the estimate of the causal effect of the intent to treat that is specific to participants diagnosed with HIV in the community. To test whether the total effect for participants diagnosed with HIV in the community is statistically significant, we will test for the joint significance of the coefficient estimates on the newly defined interaction term and the treatment indicator variable using a F-test.

Second, we will repeat these steps using an indicator variable for age equal to or above the median age in our sample instead of the indicator variable for being diagnosed with HIV in the community.

Heterogeneous Effects - Treatment on the Treated

Our analysis of heterogeneous effects for treatment on the treated will follow the same steps as described in "Intent to Treat", except we will replace our intent to treat indicator variable with the (having received) treatment indicator variable described in the main "Treatment Effects" section (see Statistical Methods).

Inference Criteria:

We will use standard inference criteria. We will use two-tailed tests and three threshold p-values: 1%, 5%, and 10%. Given the very small cost of the intervention and the large health benefits of adhering to antiretroviral therapy, any effect we can detect statistically is certainly policy relevant.

Data Exclusion:

We will exclude duplicate observations.

Limitations:

There are at least three main limitations of this study. First, a secular increase in retention/adherence may mechanically limit the scope for the intervention to have an effect. For example, suppose adherence is 99.5%. Then the largest (positive) effect size we can estimate is 0.5 percentage points.

Second, the minimum detectable effects (MDEs) are relatively large, particularly for 6 month outcomes. Thus, failure to find an effect in the study would not be evidence that the intervention was not effective at policy-relevant levels.

Third, we do not have viral load data and will not be able to directly assess the effects of the intervention on a key clinical outcome.