

**Evaluation of Multiple Interventions to Improve HIV Treatment Outcomes Among
People Who Inject Drugs in India: a Randomized Factorial Trial With a
Randomized Adaptive Component for Those Experiencing Early Treatment
Failure**

PWID Opportunities to Improve TrEat and Retain (POINTER)

Statistical Analysis Plan

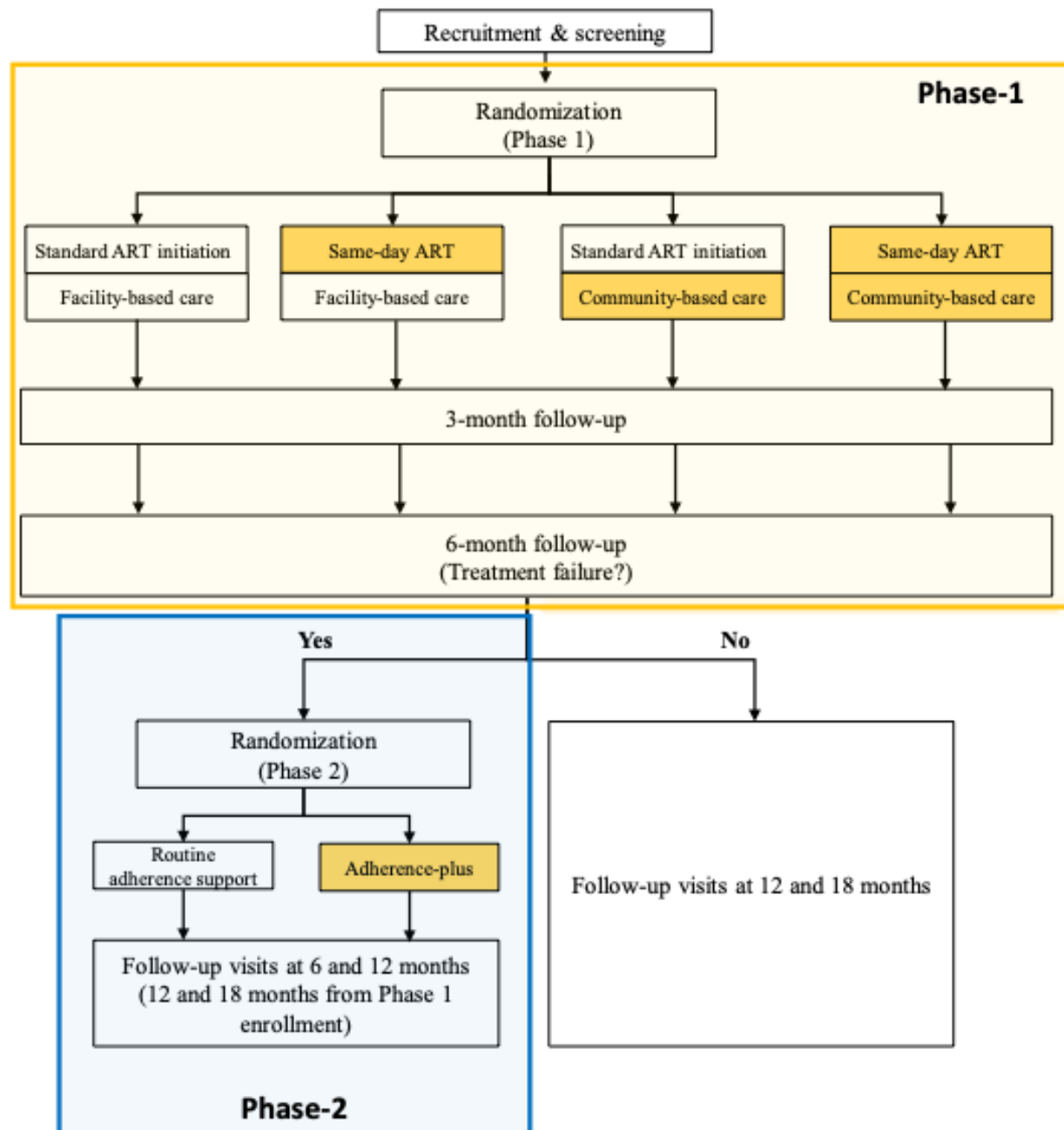
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Figure 1. Study design



1. Phase 1 design and cross-cutting analysis approaches

Phase 1: Factorial randomization.

The Phase 1 design is a 2x2 factorial trial with two interventions: 1) same-day ART vs. standard ART initiation; and 2) community-based care vs. facility-based care.

Assessment for interaction.

Same-day ART and community-based care may have complementary and non-overlapping mechanisms and assessing synergistic effects of these interventions is of interest. Thus, an interaction of these interventions with the primary outcome (i.e., viral suppression at 6 months) will be assessed using a regression model with a 2-way multiplicative interaction term (i.e., same-day ART*community-based care). If there is statistical evidence of interaction (i.e., interaction p-value<0.05) in the intention to treat (ITT) analysis of the primary outcome, intervention effects for all primary, secondary, and exploratory outcomes (unless otherwise noted) will be presented as stratified estimates from models with the interaction term. If there is no evidence of interaction in the ITT analysis of the primary outcome, regression models for all primary, secondary, and exploratory outcomes (unless otherwise noted) will include an indicator for each intervention so that the effect estimate for one intervention adjusts for the other intervention.

Adjustment for study site.

Regression models for all primary, secondary, and exploratory outcomes will adjust for study site.

1.1 Phase 1 primary outcome – Viral suppression

1.1.1 Primary ITT analysis.

Viral suppression will be defined as HIV RNA <1000 copies/mL at 6 months following randomization. The primary analysis will be ITT and include all participants randomized. Deaths prior to the 6-month study visit and those missing viral load measurements will be considered failures (i.e., not virally suppressed).

A Poisson regression model of viral suppression with robust variance will be used to estimate prevalence ratios (PRs) and 95% confidence intervals (CIs) of the factorial arms. These same models will be used to derive prevalence differences (PDs) and 95% CIs.

1.1.1a Per-protocol (PP) analyses. Three PP analyses using the same approach as the ITT analysis will be conducted:

- Analysis will be restricted to randomized participants with a viral load measurement at the 6-month study visit. Those who died prior to the study visit or are alive but did not complete the 6-month visit will be excluded.
- Deaths prior to the study visit will be considered as failures (i.e., not virally suppressed) but participants who did not complete the 6-month study visit will be excluded.
- To account for missing viral load assessments, we will conduct an additional PP analysis that excludes those participants who have died prior to the 6-month study visit or are alive but lost to follow-up but account for the informative loss to follow-up using inverse probability censoring weights.

1.1.1b Modified intention-to treat analyses. A modified ITT analysis will model each intervention separately – one regression model for same-day ART vs. standard ART initiation

and then a separate model for community-based care vs. facility-based care. For the same-day ART modified ITT analysis, we will exclude participants from the analysis who were randomized to same-day ART but did not receive same-day ART (i.e., were not eligible for same-day ART or did not complete the eligibility processes). For the community-based care modified ITT analysis, we will exclude participants who did not link to ART by 6 months following randomization (see section 1.2.4 for linkage definition).

1.1.1c Sensitivity analysis. The primary ITT analyses will be repeated defining viral suppression as HIV RNA ≤ 40 copies/mL – the lower limit of quantification for the Cepheid Xpert.

1.1.1d Subgroup analyses. Stratified ITT analyses will also be conducted to determine if effects differ by covariates at randomization including study site, age, housing status, prior history of ART use, recent frequency of drug injection, drug use and HIV-related stigma (anticipated, enacted, internalized), social support, resilient coping, and use of medication for opioid use disorder. Separately for each covariate, a Poisson regression model of viral suppression with an interaction term for the covariate and intervention (e.g., site*same-day ART and site*community-based care) and robust variance will be used to estimate subgroup-specific PRs and PDs of viral suppression for each intervention and 95% CIs.

1.2 Phase 1 secondary outcomes

1.2.1 Viral suppression at non-primary time points.

A secondary outcome is viral suppression, defined as HIV RNA < 1000 copies/mL, at non-primary time points. These will be measured at 3, 12, and 18 months following randomization. Analyses will be intention to treat (ITT) including all randomized participants. Deaths and those missing viral load measurements at the study visit will be considered failures (i.e., not virally suppressed).

Separately for each time point, we will run a Poisson regression model of viral suppression with robust variance estimating PRs and PDs and 95% CIs. For viral suppression at 12 and 18 months, we will additionally adjust for the Phase 2 adherence support arm.

1.2.1a Per protocol analyses. PP analyses will use the same analytic approach as the ITT analysis of viral suppression at non-primary time points.

- A PP analysis at non-primary time points will be conducted by restricting to only those randomized participants with a viral load measurement at the study visit for which the outcome is ascertained. Thus, participants who have died prior to the study visit or are alive but lost to follow-up (i.e., do not complete the study visit) will be excluded. Then, separate Poisson models for each time point, as described for the ITT analysis, will be conducted.
- To account for missing viral load assessments, we will conduct an additional PP analysis which excludes those participants who have died prior to the study visit or are alive but lost to follow-up but account for the informative loss to follow-up using inverse probability censoring weights.

1.2.1b Sensitivity analysis. For 12 and 18 month viral suppression, we will restrict to those with suppressed viral load at 6 months.

1.2.1c Exploratory analyses. We will consider virologic suppression as a repeated outcome, using all viral load assessments during the study period (i.e., 3, 6, 12, and 18 months). A

Poisson regression model with robust variance, adjustment for adherence support arm (when applicable), and generalized estimating equations (GEE) will be used to account for the correlation between repeated measurements from the same participant.

1.2.2 All-cause mortality.

Among all randomized participants, confirmed deaths due to any cause up to 21 months (to account for study visit window) after Phase 1 randomization will be analyzed using apportioned person-time. Person-time will begin at randomization and will be censored at either: 1) the death date, or 2) the date of the completed 18-month study visit, or 3) for those that did not complete the 18-month study visit, the mid-point date between the last study visit completed and the subsequent expected visit date.

We will use a Poisson model, adjusting for the Phase 2 adherence support arm as a time-varying covariate, to estimate incidence rate ratios (IRRs) of mortality.

1.2.2a Sensitivity analysis. The analysis will be repeated, incorporating tracking and vital status information collected by study staff which confirmed participants were alive after missed study visits; apportioned person-time will then be adjusted for this analysis.

1.2.3 Linkage to ART.

Linkage to ART will be defined as receiving ART within 3 months following randomization, documented by either verified medical record abstraction (at least one record of an ART refill within 91 days of randomization) or self-report of ART in the prior 3 months at the 3-month study visit. Receiving same-day ART alone will not qualify as linkage to ART. The primary analysis will be ITT and include all participants randomized. Participants who have no abstractions and did not complete the 3-month study visit will be considered failures (i.e., not linked to ART).

We will run a Poisson regression model of ART linkage with robust variance to estimate PRs and PDs and 95% CIs.

1.2.3a PP analysis. The primary ITT analyses will be repeated but we will exclude participants with no data to assess linkage, specifically, those participants with no abstractions and who did not complete the 3-month study visit.

1.2.3b Sensitivity analysis. The primary ITT analysis and PP analysis will be repeated only considering linkage to ART verified by medical record abstraction (at least one record of an ART refill within 91 days of randomization).

1.2.4 Linkage to ART by 6 months.

Linkage to ART by 6 months will be defined as receiving ART within 6 months following randomization, documented by either verified medical record abstraction (at least one record of an ART refill within 182 days of randomization) or self-report of ART in the prior 6 months at the 6-month study visit. Receiving same-day ART alone will not qualify as linkage to ART. The primary analysis will be ITT and include all participants randomized. Participants who have no abstractions and did not complete the 6-month study visit will be considered failures (i.e., not linked to ART).

We will run a Poisson regression model of ART linkage by 6 months with robust variance to

estimate PRs and PDs and 95% CIs.

1.2.4a PP analysis. The primary ITT analyses will be repeated but we will exclude participants with no data to assess linkage, specifically, those participants with no abstractions and who did not complete the 6-month study visit.

1.2.4b Sensitivity analysis. The primary ITT analysis and PP analysis will be repeated only considering linkage to ART verified by medical record abstraction (at least one record of an ART refill within 182 days of randomization).

1.2.5 ART medication adherence.

ART medication adherence at 6 months will be defined using two different definitions: 1) self-report and 2) medical record abstractions.

For, self-reported adherence from the 6-month study visit, participants will be classified as adherent to ART if they report using ART in the prior 30 days and report taking at least 80% of the ART they were supposed to take. Participants who did not complete the 6-month study visit will be considered failures (i.e., not adherent).

The second definition of ART adherence will be defined using verified medical record abstractions. Participants will be classified as adherent to ART if they have at least one ART refill within 91 days following randomization and a medication possession ratio (MPR) of at least 80% in the period between the first ART refill and 182 days following randomization. The MPR is calculated as the number of available ART daily doses in the time period divided by the number of days in the time period. Participants without abstractions will be considered failures (i.e., not adherent).

Separately for each adherence outcome, we will run Poisson regression models with robust variance to estimate PRs and PDs and 95% CIs.

1.2.5a PP analyses. For the PP analysis of self-reported adherence, participants who did not complete the 6-month study visit will be excluded. For the PP analysis of adherence using medical record abstractions, participants without abstractions will be excluded. The PP analyses will use the same analytic approach as the ITT analysis of ART adherence.

1.3 Phase 1 exploratory outcomes

1.3.1 Quality of life.

Quality of life will be measured using a modified EQ-5D-3L questionnaire¹ assessed at 3, 6, 12, and 18 month study visits. Two separate values for each participant will be derived: 1) an index value using value sets which summarizes the 5 question responses with a range from 0 (worst health state) to 1 (full health); and 2) the self-reported health status from the EQ visual analog scale (VAS) which ranges from 0 (worst health imaginable) to 100 (best health imaginable). Participants with missing quality of life assessments (i.e., missed study visits), will be excluded from analyses.

Both the index value and VAS will be analyzed as continuous outcomes using linear regression models to estimate the difference in quality of life associated with the interventions. Models will be run separately for each outcome (i.e., index and VAS) and time point. For quality of life at 12

and 18 month study visits, we will adjust for Phase 2 adherence support arm.

1.3.1a Sensitivity analyses. We will consider the index and VAS as repeated outcomes, using all assessments during the study period (i.e., 3, 6, 12, and 18 months).

1.3.2 Use of medication for opioid use disorder.

Medication for opioid use disorder (MOUD) will be self-reported at 3, 6, 12, and 18 month study visits. Two outcomes will reflect MOUD use: 1) any use in the prior time period and 2) frequency of use in period (i.e., 6-7 days/week, 3-5/week, ≤ 2 days/week). Participants with missing MOUD survey responses (i.e., missed study visits), will be excluded from analyses.

Any MOUD use will be analyzed using Poisson regression models with robust variance to estimate PRs and PDs and 95% CIs. Frequency of MOUD use will be analyzed as a categorical variable using multinomial logistic regression, estimating odds ratios (ORs) and 95% CIs, relative to the base outcome. Models will be run separately for each outcome (i.e., any use and frequency) and time point. For MOUD at 12 and 18 month study visits, we will adjust for Phase 2 adherence support arm.

1.3.2a Sensitivity analysis. We will consider MOUD use as repeated outcomes, using all assessments during the study period (i.e., 3, 6, 12, and 18 months).

1.3.3 HIV- and drug use-related stigma.

HIV^{2,3}- and drug use-related⁴ stigma will be assessed at 3, 6, 12, and 18 month study visits. Each stigma type (i.e., HIV and drug-use related) has three sub-scales: 1) anticipated healthcare, 2) enacted healthcare, and 3) internalized stigma. Participants with missing stigma assessments (i.e., missed study visits), will be excluded from analyses. Each type and subscale will be analyzed separately. For internalized stigma, the subscale mean score will be analyzed. For anticipated and enacted stigma, any reported stigma (i.e., endorsement of ever for any item) will be analyzed as dichotomous outcomes.

For the continuous internalized stigma score, linear regression models will be conducted to estimate the difference in stigma associated with the interventions. Then for any anticipated and enacted stigma, we will run Poisson regression models with robust variance to estimate PRs and PDs and 95% CIs. Models will be run separately for each time point. For stigma at 12 and 18 month study visits, we will adjust for Phase 2 adherence support arm.

1.3.3a Sensitivity analysis. We will consider each stigma as repeated outcomes, using all assessments during the study period (i.e., 3, 6, 12, and 18 months).

1.3.4 Depression.

Depression will be measured using the PHQ-9 questionnaire⁵⁻⁷ and assessed at 3, 6, 12, and 18 month study visits. A PHQ-9 score of ≥ 10 will be defined as moderate-severe depression. Participants with missing PHQ-9 assessments (i.e., missed study visits), will be excluded from analyses.

Separately for each time point, we will run a Poisson regression model of depression with robust variance to estimate PRs and PDs and 95% CIs. For depression at 12 and 18 month study visits, we will adjust for Phase 2 adherence support arm.

1.3.4a Sensitivity analysis. We will consider depression as a repeated outcome, using all assessments during the study period (i.e., 3, 6, 12, and 18 months).

1.3.5 HIV treatment self-efficacy.

HIV treatment self-efficacy will be measured using a modified HIV Treatment Adherence Self-Efficacy Scale (HIV-ASES)⁸ and assessed at 3, 6, 12, and 18 month study visits. Scale items will be averaged to calculate a self-efficacy score, ranging from 0 to 100 with higher scores indicating higher self-efficacy. Participants with missing self-efficacy assessments (i.e., missed study visits), will be excluded from analyses.

Separately for each time point, we will run a linear regression model of self-efficacy to estimate the difference in self-efficacy associated with the interventions. For self-efficacy at 12 and 18 month study visits, we will adjust for Phase 2 adherence support arm.

1.3.5a Sensitivity analysis. We will consider self-efficacy as a repeated outcome, using all assessments during the study period (i.e., 3, 6, 12, and 18 months).

1.3.6 Drug resistance.

To assess development of antiretroviral drug resistance, we will conduct HIV genotyping among participants who are virologically failing at the 12 month study visit (i.e., HIV RNA ≥ 1000 c/mL). We will simultaneously test corresponding stored samples from baseline. We will test the reverse transcriptase, protease, and integrase genes for established drug-resistance mutations according to Stanford University HIV Drug Resistance Database (<https://hivdb.stanford.edu>). We will categorize persons as acquiring new drug resistance if their 12-month sample has new NRTI or INSTI mutations.

We will run a Poisson regression model of drug resistance with robust variance, adjusting for the Phase 2 adherence support arm, to estimate PRs and PDs and 95% CIs.

2. Phase 2 design and cross-cutting analysis approaches

Phase 2: Adaptive randomization.

Phase 2 is adaptive and includes only those participants experiencing treatment failure, defined as an HIV RNA ≥ 1000 c/mL, at 6 months in Phase 1, who will be randomized a second time to adherence-plus vs. routine adherence support.

Adjustment for Phase 1 within Phase 2 analyses.

Regression models for all primary, secondary, and exploratory outcomes will adjust for the 4 factorial arm assignment in Phase 1.

Adjustment for study site.

Regression models for all primary, secondary, and exploratory outcomes will adjust for study site

2.1 Phase 2 primary outcome – Viral suppression

2.1.1 Primary ITT analysis.

Viral suppression will be defined as HIV RNA < 1000 copies/mL at 6 months following the Phase 2 randomization (i.e., the 12-month study visit). The primary analysis will be ITT and include all those randomized a second time. Deaths prior to the 12-month study visit and missing viral load measurements at the 12-month visit will be considered failures (i.e., not virally suppressed).

We will use a Poisson regression model of viral suppression with robust variance to estimate the PR and PD and 95% CIs of adherence-plus.

2.1.1a PP analyses. Three PP analyses using the same analytic approach as the ITT analysis will be conducted:

- Analysis will be restricted to randomized participants with a viral load measurement at the 12-month study visit. Those who died prior to the study visit or are alive but did not complete the 12-month visit will be excluded.
- Deaths prior to the study visit will be considered as failures (i.e., not virally suppressed) but participants who did not complete the 12-month study visit will be excluded.
- To account for missing viral load assessments, we will conduct an additional PP analysis that excludes those participants who have died prior to the 12-month study visit or are alive but lost to follow-up but account for the informative loss to follow-up using inverse probability censoring weights.

2.1.1b Modified intention-to treat analysis. A modified ITT analysis will use the same analytic approach as the ITT analysis but exclude those who did not receive the minimum exposure to adherence-plus counseling sessions. The minimum is defined as 2 visits in the first 8 weeks following randomization and then serial sessions with a gap of no more than 35 days in between for the remainder of the intervention period (i.e., 6 months).

2.1.1c Sensitivity analysis. The primary ITT analyses will be repeated defining viral suppression as HIV RNA ≤ 40 copies/mL – the lower limit of quantification for the Cepheid Xpert.

2.1.1d Subgroup analyses. Stratified ITT analyses will also be conducted to determine if effects differ by covariates at Phase 2 randomization including study site, age, housing status, prior history of ART use, recent frequency of drug injection, drug use and HIV-related stigma (anticipated, enacted, internalized), social support, resilient coping, use of medication for opioid

use disorder, and Phase 1 factorial arms. Separately for each covariate, a Poisson regression model of viral suppression with an interaction term for the covariate and intervention (e.g., site*adherence-plus and site*routine adherence support) and robust variance be used to estimate subgroup-specific PRs and PDs of viral suppression for adherence-plus and 95% CIs.

2.2 Phase 2 secondary outcomes

2.2.1 Viral suppression at non-primary time point.

A secondary outcome is viral suppression, defined as HIV RNA <1000 copies/mL, at the non-primary time point of 12 months following the Phase 2 randomization (i.e., the 18-month study visit / 18 months since Phase 1 randomization). The analysis will be intention to treat (ITT) including all randomized participants randomized in Phase 2. Deaths and those missing viral load measurements at the study visit will be considered failures (i.e., not virally suppressed).

We will use a Poisson regression model of viral suppression with robust variance to estimate the PR and PD and 95% CIs.

2.2.1a Per protocol analyses. PP analyses will use the same analytic approach as the ITT analysis of viral suppression at non-primary time points.

- A PP analysis at the non-primary time point will be conducted restricting to only those randomized participants with a viral load measurement at the 18-month study visit. Thus, participants who have died prior to the 18-month study visit or are alive but lost to follow-up (i.e., do not complete the study visit) will be excluded.
- To account for missing viral load assessments, we will conduct an additional PP analysis which excludes those participants who have died prior to the 18-month study visit or are alive but lost to follow-up but account for the informative loss to follow-up using inverse probability censoring weights.

2.2.2. All-cause mortality.

Among all Phase 2 randomized participants, confirmed deaths due to any cause up to 21 months (allowing for 3 month window beyond 18 month visit) after Phase 1 randomization will be analyzed using apportioned person-time. Person-time will begin at Phase 2 randomization and will be censored at either: 1) death date, or 2) the date of the completed 18-month study visit, or 3) for those that did not complete the 18-month study visit, the mid-point date between the last visit completed and the subsequent expected visit date.

We will use a Poisson model to estimate IRR of mortality.

2.2.2a Sensitivity analysis. The analysis will be repeated, incorporating tracking and vital status information collected by study staff which confirmed participants are alive after missed study visits; apportioned person-time will then be adjusted for this analysis.

2.2.3 Linkage to ART by 6 months.

Linkage to ART by 6 months will be defined as receiving ART within 6 months following the Phase 2 randomization, documented by either verified medical record abstraction (at least one record of an ART refill within 182 days of Phase 2 randomization) or self-report of ART in the prior 6 months at the 12-month study visit. Receiving same-day ART alone will not qualify as linkage to ART. The primary analysis will be ITT and include all participants randomized in

Phase 2 who were not linked to ART by 6 months following the Phase 1 randomization. Participants who have no abstractions and did not complete the 12-month study visit will be considered failures (i.e., not linked to ART).

We will run a Poisson regression model of ART linkage by 6 months with robust variance to estimate the PR and PD and 95% CIs.

2.2.3a PP analysis. The primary ITT analyses will be repeated but we will exclude participants with no data to assess linkage, specifically, those participants with no abstractions and who did not complete the 12-month study visit.

2.2.3b Sensitivity analysis. The primary ITT analysis and PP analysis will be repeated only considering linkage to ART verified by medical record abstraction (at least one record of an ART refill within 182 days of Phase 2 randomization).

2.2.4 ART medication adherence.

ART medication adherence at 6 months following Phase 2 randomization will be defined using two different definitions: 1) self-report and 2) medical record abstractions.

For, self-reported adherence from the 12-month study visit, participants will be classified as adherent to ART if they report using ART in the prior 30 days and report taking at least 80% of the ART they were supposed to take. Participants who did not complete the 12-month study visit will be considered failures (i.e., not adherent).

The second definition of ART adherence will be defined using verified medical record abstractions. Participants will be classified as adherent to ART if they have at least one ART refill within 91 days following the Phase 2 randomization and a medication possession ratio (MPR) of at least 80% in the period between the first ART refill and 182 days following randomization. The MPR is calculated as the number of available ART daily doses in the time period divided by the number of days in the time period. Participants without abstractions will be considered failures (i.e., not adherent).

Separately for each adherence outcome, we will run Poisson regression models with robust variance to estimate the PR and PD and 95% CIs.

2.2.4a PP analyses. For the PP analysis of self-reported adherence, participants who did not complete the 12-month study visit will be excluded. For the PP analysis of adherence using medical record abstractions, participants without abstractions will be excluded. The PP analyses will use the same analytic approach as the ITT analysis of ART adherence.

2.3 Phase 2 exploratory outcomes

2.3.1 Quality of life.

Quality of life will be assessed at the 12 and 18 month study visits and measured in the same manner as described for Phase 1 (i.e., index and VAS). Participants with missing quality of life assessments (i.e., missed study visits), will be excluded from analyses.

The index value and VAS will be analyzed as continuous outcomes using linear regression models to estimate the difference in quality of life associated with adherence-plus. Models will

be run separately for each outcome (i.e., index and VAS) and time point.

2.3.1a Sensitivity analyses. We will consider the index and VAS as repeated outcomes, using both assessments (i.e., 12 and 18 months).

2.3.2. Use of medication for opioid use disorder.

Medication for opioid use disorder (MOUD) will be self-reported at 12 and 18 month study visits and measured in the same manner as described in Phase 1 (i.e., any MOUD use and frequency of MOUD use). Participants with missing MOUD survey responses (i.e., missed study visits), will be excluded from analyses.

Any MOUD use will be analyzed using Poisson regression models with robust variance to estimate PRs and PDs and 95% CIs. Frequency of MOUD use will be analyzed as a multi-level categorical variable using multinomial logistic regression, estimating odds ratios (ORs) and 95% CIs, relative to the base outcome. Models will be run separately for each outcome (i.e., any use and frequency) and time point.

2.3.2a Sensitivity analysis. We will consider MOUD use as repeated outcomes, using both assessments (i.e., 12 and 18 months).

2.3.3. HIV- and drug use-related stigma.

HIV- and drug use-related stigma will be assessed at 12 and 18 month study visits and measured in the same manner as described in Phase 1 (i.e., three sub-scales (anticipated, enacted healthcare, and internalized) for each stigma type (HIV and drug-use related). Participants with missing stigma assessments (i.e., missed study visits), will be excluded from analyses. Each type and subscale will be analyzed separately. For internalized stigma, the subscale mean score will be analyzed. For anticipated and enacted stigma, any reported stigma (i.e., endorsement of ever for any item) will be analyzed as dichotomous outcomes.

For the continuous internalized stigma score, linear regression models will be conducted to estimate the difference in stigma associated with adherence-plus. Then for any anticipated and enacted stigma, we will run Poisson regression models with robust variance to estimate PRs and PDs and 95% CIs. Models will be run separately for each time point.

2.3.3a Sensitivity analysis. We will consider each stigma as repeated outcomes, using both assessments (i.e., 12 and 18 months).

2.3.4 Depression.

Depression will be assessed at the 12 and 18 month study visits and measured in the same manner as described in Phase 1 (i.e., PHQ-9). Participants with missing PHQ-9 assessments (i.e., missed study visits), will be excluded from analyses.

Separately for each time point, we will run a Poisson regression model of depression with robust variance to estimate PRs and PDs and 95% CIs.

2.3.4a Sensitivity analysis. We will consider depression as a repeated outcome, using both assessments (i.e., 12 and 18 months).

2.3.5 HIV treatment self-efficacy.

HIV treatment self-efficacy will be assessed at the 12 and 18 month study visits and measured in the same manner as described in Phase 1 (i.e., HIV-ASES). Participants with missing self-efficacy assessments (i.e., missed study visits), will be excluded from analyses.

Separately for each time point, we will run a linear regression model of self-efficacy to estimate the difference in self-efficacy associated with adherence-plus.

2.3.5a Sensitivity analysis. We will consider self-efficacy as a repeated outcome, using both assessments (i.e., 12 and 18 months).

3. Interim analyses and early stopping rules

There were no early stopping rules associated with interim analyses.

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