Study Protocol and Statistical Analysis Plan

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Title:	A Gender Transformative Implementation Strategy With Providers to Improve HIV Outcomes in Uganda
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Inclusion criteria

Provider cohort for training intervention, assessment, and exit focus groups (intervention trial). We will recruit providers for participation in our intervention trial for the provider training from the two selected clinics. The goal is to recruit the entire population of providers at each of the two clinics, which is approximately 20-35 providers per clinic (Luwero Hospital, Mityana Hospital, Kalagala HCIV and Namayumba HCIV) for participation. This cohort will include all HIV care providers at the 4 selected clinics, including: medical officers, clinical officers, HIV nurses, midwife, linkage facilitators, and counselors. These participants will be 18 years of age or older and fluent in English or Luganda.

Patient cohort assessment (intervention trial). In addition to the assessment of the cohort of ~80-140 HIV providers, we will obtain additional data on the impact of the provider training on patient outcomes including quality of care, patient satisfaction, clinic attendance, ART adherence, and viral load (from patient clinic records) by assessing 240 (60 per treatment facility, gender balanced) purposively sampled patients at baseline, 6-, and 12-month follow-up.

Eligibility includes:

1. HIV-infected;
2. enrolled in care at the clinic of recruitment;
3. pre-ART (newly diagnosed) or newly initiated on ART (within 1 year) **or** struggling with treatment adherence, defined in two ways:
    a. most recent viral load results unsuppressed as assessed through clinic records
    b. or self-reported non-adherence as by the Adult AIDS Clinical Trials Group (AACTG) scale 4-day adherence recall questions. This scale has demonstrated good construct validity in Uganda and strong correlations with viral load;
4. 18 years of age or an emancipated minor;
5. fluent in Luganda or English.

Recruitment & Sampling

Provider cohort for training intervention, assessment, and exit focus groups (intervention trial). Once research staff are trained and our two clinics have been randomly assigned as intervention or control arm, we will recruit providers for participation in our intervention trial for the provider training. The goal is to recruit the entire population of providers at each of the four clinics, which is approximately 20-35 providers per clinic (Luwero Hospital, Mityana Hospital, Kalagala HCIV, and Namayumba HCIV) for participation; approximately 35 at each hospital and 25 at each HCIV (total: 80-140). With support from Mildmay Uganda (see Letter of Support), we will generate support for the training first in the broader Health Districts (with medical superintendents and District Health Officers) through in-person meetings and garnering their feedback on the intervention through invitations to serve on/make recommendations for a “Training Steering Committee.” After District support is attained, we will then conduct facility mobilization with an in-person presentation of the goals research study at each of the four clinics. Eligibility for providers includes being an HIV care provider at one of the four selected clinics. After the larger facility

mobilization meeting, the research assistant will meet one-on-one with HIV providers to individually inform them of the study, allow them to ask any questions in a private space, and obtain written informed consent. Though we aim to recruit all HIV providers at each clinic for participation, any provider can decline to participate. The informed consent process will include consent for both participation in the provider training, baseline, 6- and 12-month assessments, and an exit focus group. To mask the randomization of intervention and control, we will consent participants for participation in all aspects of the training.

Patient cohort assessment (intervention trial). In addition to the assessment of the cohort of ~140 HIV providers, we will obtain additional data on the impact of the provider training on patient outcomes including quality of care, patient satisfaction, clinic attendance, ART adherence, and viral load (from patient clinic records) by assessing 240 (60 per clinic, gender balanced) purposively sampled patients at baseline, 6- and 12-month follow-up. Patients will be non-randomly approached when presenting to care by a Research Assistant based on a review of clinic records. After being referred by a clinician, our research assistant will inform individuals of the study and assess eligibility using an eligibility screening tool. No identifying information will be recorded during the eligibility screening. If eligibility is met and the patient would like to participate, the research assistant will obtain written informed consent and collect patients' contact information (for follow-up reminders) and conduct the baseline questionnaire in the clinic or another agreed upon location.

Data collection

Questionnaires

For the provider cohorts randomized to the Intervention clinics, the chronological activities include: enrollment; baseline interview immediately after enrollment; participation in ~21 hours of intervention content; follow-up assessments at 6-months and 12-months follow-up; one exit focus group post-intervention. Each data collection activity and its duration is detailed below:

- **Baseline provider assessment (for all provider participants)**. After the informed consent process a one-on-one interview (~25 minutes) using a computerized structured questionnaire in the clinic or another agreed upon location will be conducted with providers at both clinics. The questionnaire will collect demographic information and measures to assess provider outcomes. The total duration of participation for the baseline survey is approximately 25 minutes.

- **6-, and 12-, month follow-up provider assessments (all provider participants).** Research Assistants will conduct the 2 follow up interviews using an individual structured interviewer-administered computer-based interview in the clinic or another agreed upon location for patient and providers. Providers have the option to complete these assessments over the telephone only if they have transferred to working at another clinic and cannot be reached in person. The follow-up questionnaires will serve as a measure of intervention effects on provider's gender equitable attitudes and gender awareness and other related constructs (see Measures). This questionnaire is approximately 25 minutes per time point. Across the 2 assessments, the total duration for survey participation is approximately 50 minutes.

For the patient cohort (n=240) enrolled in the intervention and control clinics. To assess the effect of the provider training on patient-level outcomes, we will assess change overtime in patient outcomes in a cohort of HIV patients enrolled at the 2 clinics. These patients do not receive any intervention, but will participate in an assessment across 3 time-points (following the same schedule as the provider assessment). They will also agree to a review and data extraction of health information from of their HIV clinic records at each time point.

- **Baseline patient assessment (all patient participants).** HIV patients referred to the study and interested in participating will first answer a brief set of questions to assess enrollment. No data will be recorded at this time. If eligible and interested, we will obtain written informed consent before continuing with the baseline questionnaire. Using a computerized structured questionnaire, a research assistant will conduct the survey in the clinic or another agreed upon location at both clinics. The questionnaire will collect demographic information and measures to assess patient outcomes related to HIV care engagement (e.g., clinic attendance, medication adherence, patient satisfaction). Data will also be extracted at this time and directly entered into the computerized survey from patient clinic records (e.g., treatment regiment, CD4 count, viral load). Total duration of baseline interview is approximately 60 minutes.

- **6- and 12-month follow-up patient assessments (all patient participants).** Patients at both clinics will complete a follow-up assessments at 4 time points, specifically 6 and 12-months post-baseline. In a private space in the clinic or another agreed upon location, an interviewer will administer a structured questionnaire entered in CAPI software. Follow-up assessments may be administered via telephone for participants not returning to the clinic (incentives delivered elsewhere). At each time point, information will again be reviewed and extracted from clinic records and entered into CAPI software. Across all 2 assessments, the total duration for survey participation is approximately 90 minutes (~45 minutes per assessment). Patient participation will end after the completion of the 12-month follow-up survey.

Process Data

Exit interviews with facilitators and key-stakeholders (post-intervention). Semi-structured qualitative interviews will be held with the 2 trainers (intervention facilitators), any provider not able to attend focus groups, as well as with 2-4 Mildmay leaders in charge of the integration of courses into Mildmay's training programs to assess barriers and facilitators to the implementation and future adoption of the training and maintenance sessions. See Table 3 for more detail on the CFIR constructs explored through these interviews. An audio-recorded, one-on-one semi-structured interview will be conducted in a private setting by one of the PIs or research staff. After the completion of the key-informant interview, the key informants' involvement in the study will end (total participation approximately 15-30 minutes).

Exit focus groups with providers (post-intervention). We will conduct approximately 8 additional exit focus groups with HIV providers participating in the training (6-8 provider per group) or until saturation is reached. We will purposively sample from each of the intervention health centers and include health workers and lay workers in separate groups. The purpose of these focus groups are to assess the perceived acceptability, feasibility, barriers to

implementation/adoption and other measures of implementation (see Table 1) among providers who participated in the training. The different constructs and their definition measured through focus groups mapped onto the CFIR framework are highlighted in Table 1.

Data collection to assess intervention fidelity. To assess fidelity, each group training session will be observed by staff or Dr. Sileo with a checklist to assess 5 implementation fidelity dimensions: adherence, quality of delivery, program component differentiation, intervention exposure, participant responsiveness. We will observe ~5 randomly selected maintenance sessions (for rapid feedback). At the completion of the study, randomly selected maintenance transcripts (20%) will be qualitatively analyzed.

Table 1. CFIR domains and constructs explored as barriers and facilitators to the implementation and adoption of the intervention

CFIR Domain and constructs	Sample*
CFIR Domain: Intervention characteristics	
Intervention source: Perception of key stakeholders about whether the intervention was externally or internally developed	Trainers, Stakeholders
Complexity/barriers: Perceived difficulty of/barriers to implementation/application of content into clinical care	Trainers, Providers Stakeholders
Appropriateness: The perceived fit of the intervention for the setting and to improve care quality and patient outcomes	Trainers, Providers Stakeholders
CFIR Domain: Outer setting	
Patient needs: The extent to which patients' gendered barriers and facilitators to care are accurately known and prioritized	Trainers, Providers Stakeholders
CFIR Domain: Inner setting	
Relative Priority: Perceived importance of implementation within the clinic and broader health system	Trainers, Providers Stakeholders
Culture: Organizational norms, values, and basic assumptions specific to: a) innovations in care and b) gender equity	Trainers, Providers, Stakeholders
CFIR Domain: Individual characteristics	
Knowledge and beliefs about the intervention: Attitudes towards and value placed on the intervention, including perceptions on acceptability (satisfaction with intervention) and feasibility (can intervention be carried out within clinic/broadly)	Trainers, Providers, Stakeholders
Self-efficacy: Beliefs in own ability to execute implementation goals (trainers) and training content (providers)	Trainers, Providers
Other personal attributes: Gender, age, and other traits	Trainers, Providers

*Data collection methods = Providers: focus group discussions, Trainers: in-depth interviews; Stakeholders: key informant interviews

Data management

Qualitative data

Audio recordings of all qualitative data will be transferred to a password protected computer. All focus group discussions, observations, key informant interviews, and qualitative exit interviews will be transcribed and translated into English and entered into a software analysis system (Atlas.ti). Electronic audio recordings of intervention sessions will be transcribed within 6 months of the session and the audio recordings will be destroyed once the information from the recordings is written down and double-checked for accuracy.

Quantitative data

Data for the baseline, 6- and 12-month follow-up questionnaires will be entered in real-time while the interviewers are conducting the interviewer-administered CAPI questionnaires (using

KoboCollect software). Using the KoboCollect system also eliminates the possibility of any out of range responses and therefore, data cleaning is not necessary. Data collected using Kobo is easily exported into R, SPSS, and other statistical programs for analysis. A research assistant will extract data form medical charts and enter it into a database identified only by study ID number. Clinical record data will be double entered by the research assistant into this same data file upon receipt. The double entered data will be checked and any discrepancies will be corrected by double checking the clinic records, and by comparisons with the laboratory report.

Data safety monitoring plan

The proposed study will conform to rigorous monitoring procedures, standardized reporting of adverse events using Event Report Forms, and regular review of the study by the Principal Investigators, Drs. Wanyenze and Sileo. Dr. Sileo will have primary responsibility for the overall conduct of the study with oversight from Drs. Wanyenze and Kershaw, including the safety of human subjects. With the assistance of research staff, the PIs will ensure appropriate: (1) conduct of the informed consent process (e.g., that informed consent is obtained before proceeding with study procedures and properly stored), (2) enrollment of study subjects, (3) collection and analysis of data, (4) implementation of study procedures to ensure consistent monitoring of subjects for possible adverse events, (5) review of adverse events and reporting to the IRB, and (6) maintenance of the privacy and confidentiality of study subjects.

Drs. Wanyenze and Sileo will be responsible for meeting with the research team on a regular basis (either in person or by conference call) to review the progress of the study and address any human subject issues that occur. These discussions may involve adverse event prevention measures, recruitment of appropriate study subjects, research staff training on protection of human subjects, as well as occurrence of adverse events, unexpected incidents, or protocol problems. Dr. Sileo will meet with the research assistants regularly to go over the progress of the study and communicate any issues or adverse events to the mentorship team. The research assistants will compile reports on this information and submit them to the Principal Investigator for review. Drs. Wanyenze and Sileo will present this information to Co-Investigators as needed to troubleshoot any issues and seek guidance in decision-making.

Adverse events

The study is of minimal risk and therefore no serious anticipated events are expected. Serious unanticipated events will be reported within 48 hours to the Makerere School of Public Health and University of Texas at San Antonio IRBs, the co-investigators listed on the protocol, and NIH. We expect the risk of adverse events resulting from participation in the intervention to be low. Further, we have developed procedures to reduce any adverse events and closely monitor participants in the provider training intervention. The implementation of these procedures will ensure any unanticipated adverse events are identified and addressed immediately (see “Protection of Human Subjects” section) for more details.

The Principal Investigators will conduct a review of all adverse events (serious and non-serious) every month during a scheduled meeting and keep a log of all events. They will evaluate the frequency and severity of the adverse event(s) and, in conjunction with the Makerere School of Public Health and University of Texas at San Antonio IRBs, determine if modifications to the protocol or consent forms are required. A report to the Makerere and University of Texas at San Antonio IRBs will be made when re-approval for the protocol is sought on a yearly basis, or more frequently if deemed necessary by the Principal Investigators and Co-Investigators based on the number and severity of adverse events. The summary will include the number of participants enrolled in the study and a summary of the adverse events to date (including relation to study and severity).

The Principal Investigators, in conjunction with the Makerere School of Public Health and University of Texas at San Antonio IRBs, will be responsible for monitoring the data and conducting performance safety reviews at a minimum of every 3 months. The Principal Investigators will present this data to the full-team of Co-Investigators for guidance at bi-annual team meetings. The Principal Investigators, Makerere IRB, and the University of Texas at San Antonio IRB have the authority to stop or modify the study at any time. During the review process, the Principal Investigators will monitor and evaluate whether the study should continue unchanged, require modification, or close to enrollment. Discussions will be brought to the larger team of mentors as needed.

Training of the RAs/Facilitators

Training of research assistants

To collect baseline and follow-up interview data for the intervention trial experienced research assistants/interviewers will be hired for the purposes of the study. These individuals will be trained in the study procedures by one or more of the investigators. The two-day training will cover the detailed standard-operating-procedures (SOP) as relevant to the role of research assistants. Procedures covered will include the schedule of data collection, procedures for contacting participants, storage of hard copies, storage and exporting of electronic data, and procedures related to obtaining informed consent. Safeguards to protect human subjects and reporting of adverse events will also be covered. Finally, the training will cover the objectives and content of the study and the tools. Mock interviews will be conducted by the research team to further get acquainted with the study tools during the training. The training will help the research assistants to master the data collection tools. Clinic staff will also be oriented to the study and the study procedures by the investigators.

Training of intervention facilitators

Group facilitators experienced in the delivery of behavioral interventions and Mildmay Expert Trainers who will deliver the intervention will undergo a 5-day curriculum-based training of the intervention content using role playing and simulated group discussions led by Dr. Sileo with oversight from Dr. Wanyenze. Training will emphasize the protection of human subjects and confidentiality, the role of gender norms in patient-provider relationships, managing group dynamics, facilitating transformative dialogues without creating conflict, and identifying and minimizing adverse outcomes.

Statistical Analysis Plan

To evaluate the time by intervention effect on primary and secondary outcomes, we used Generalized Estimating Equations (GEE) in SPSS v. 28, which can account for dependency in the data related to the clinic clusters and repeated measures. First, we used GEE to examine baseline equivalence between treatment arms in both HIV care provider and client cohorts. We tested variables that differed at a level of $p < 0.10$ between treatment arms as covariates in the models testing intervention effect; only variables significant at $p < 0.05$ and/or making a difference in the intervention effect were maintained in the final models. We report the time by arm interaction. For all provider and client analyses, we tested the time by intervention by gender effect. For providers, we also tested the time by intervention by cadre effect, categorizing providers into certified health workers (licensed doctors, nurses, counselors) vs. lay health workers or non-specialized staff (e.g., peers). These interactions are only presented if they were statistically significant ($p < 0.05$). We report unstandardized betas (b) and standard errors (SE) for continuous outcomes and odds ratios (ORs) and adjusted odds ratios (AORs) and 95% confidence intervals (CIs) for binary outcomes.