EXPANDING HIV PREVENTION OPTIONS FOR ADOLESCENT GIRLS AND YOUNG WOMEN (PROJECT ENGAGE)

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1. Program Overview

Project Engage contributes to the advancement of new HIV prevention methods, especially for adolescent girls and young women (AGYW), and is funded by a Global Development Alliance between USAID and Gilead Sciences. Research activities are focused on evaluating the acceptability of and adherence to the new Descovy® (F/TAF)-based oral PrEP regimen compared to Truvada® (F/TDF) in AGYW at risk of HIV acquisition in Africa, as well as advancing innovative adherence support and monitoring tools essential to facilitating effective implementation of oral PrEP in this population. Data on barriers and facilitators to oral PrEP uptake and adherence in AGYW will be gathered to inform future decision-making and programming. Project Engage will also generate effectiveness and implementation data on an AGYW-tailored adherence support intervention via a newly-designed smartphone app, *Vuka+*. Furthermore, we will develop and validate a new point-of-care (PoC) adherence monitoring assay and conduct pilot implementation studies of two PoC adherence assays in African settings. Altogether, Project Engage will provide evidence supporting the implementation of HIV oral PrEP regimens for AGYW in Africa.

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2. Activities - Progress To-date and Future Plans

Acceptability Study of Oral F/TAF vs F/TDF for the Prevention of HIV Acquisition in AGYW

In partnership with MatCH Research Unit and CAPRISA in South Africa, and Harare Health and Research Consortium in Zimbabwe, we are conducting a study to assess AGYW acceptability and adherence to daily regimens of F/TAF and F/TDF. The study will recruit 330 participants (aged 15-24) who will be randomized to receive F/TAF or F/TDF orally once daily for 24 weeks. The main endpoint of the study is acceptability measured by discontinuation rate, attendance at follow-up visits, responses to quantitative assessments, and qualitative data collected through in-depth interviews and focus group discussions. Secondary and exploratory endpoints include adherence, measured through dried blood spot (DBS) analysis and behavioral assessments, and validity of psychometric adherence scales.

Status**:** Study preparatory activities including protocol and study document development have been initiated with input from local partners, community/regional AGYW advisors, civil society, USAID and Gilead. Regulatory, Institutional Review Board and Ethics Committee submissions in South Africa and Zimbabwe are ongoing.

Future plans**:** A capacity building virtual workshop on psychometric scales will be held late 2021. Pending regulatory approvals, sites will initiate in late 2021/early 2022. The study is expected to complete in 2023.

Refinement & Testing of a Novel Smartphone-Based Adherence Support Intervention

The objective of this activity is to assess the effectiveness and implementation of a new mobile health (mHealth) PrEP adherence support intervention designed specifically for AGYW in Africa. In collaboration with Desmond Tutu Health Foundation (DTHF) in South Africa and University of North Carolina, CONRAD is conducting a two-phase testing of the new adherence support smartphone app, *Vuka+*. The first phase is a 4-week pilot study recruiting 30 AGYW to assess the usability and acceptability of the intervention app. After refinement of the app based on the pilot data, phase 2 will consist of a Type I Hybrid effectiveness-implementation study in service delivery sites in South Africa, recruiting 330 participants (aged 15-24). Participants will take daily oral F/TDF and be randomized to standard of care (SOC) counseling vs SOC plus app intervention. The primary endpoints are adherence measured by DBS, acceptability and usability of the app, and feasibility of app implementation in a service delivery setting.

Status: App development and initial beta testing was completed under previous USAID funding (MAPS1 AID-OAA-A-14-00011). App refinement is ongoing in preparation for the pilot study to be initiated October 2021, pending Institutional and Ethical Review Board approvals.

Future plans: Data from the pilot study will be used to further refine the app in preparation for the Effectiveness and Implementation study, to be initiated mid-2022. Related capacity building activities focused on the mHealth app will also be conducted.

Clinical Validation & Implementation of Point-of-Care Adherence Diagnostics

To address a gap in implementation and increase adherence to oral PrEP, Project Engage will clinically test and validate two complementary point-of-care (PoC) adherence diagnostics: UrSure's tenofovir (TFV) urine test kit and a novel assay being developed by CONRAD called SAM (Spectral Adherence Monitoring), which has potential to measure TFV, emtricitabine (FTC) and possibly their active metabolites from a single blood sample. Pilot implementation studies for both assays in service and research settings will also be conducted.

Status: SAM optimization is ongoing with focus on increasing method sensitivity for detection of TFV in plasma and blood. CONRAD is also preparing for the initiation of the UrSure Pilot Implementation study in late 2021, in collaboration with MatCH Research Unit in South Africa.

Future plans: Pending successful completion of SAM optimization, CONRAD will conduct a Clinical Validation Study of Objective Markers of Adherence Measured in Blood and Urine by SAM and UrSure PoC Tests. The study will enroll 60 women randomized to a regimen of oral F/TDF or F/TAF reflecting different adherence levels (2, 4, or 7 pills/week). Adherence assay trainings will be held in South Africa.

Capacity Building, Research Utilization & Community Engagement

Working closely with local partners and their respective research community needs, Project Engage will strengthen research capacity focusing on innovative aspects of the program's activities, including mHealth and PoC adherence monitoring. CONRAD has also partnered with AVAC to strengthen awareness, local community engagement, and dissemination of Project Engage activities to broad stakeholders, and have established a Project Advisory Group of 14 AGYW and young men from South Africa and Zimbabwe to serve as an ongoing, independent mechanism for bidirectional stakeholder engagement and program input.

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