Directly Observed Therapy (DOT) Can Be Implemented Successfully in Research Settings to Evaluate PrEP PK among Pregnant and Postpartum Adolescents and Young Women in Africa

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BACKGROUND

Daily oral FTC/TDF as pre-exposure prophylaxis (PrEP) can effectively reduce HIV acquisition. However, PrEP efficacy and pharmacokinetics (PK) are poorly understood among pregnant and postpartum women, complicated by the physiological changes women undergo during this period and low adherence observed in previous oral PrEP studies. Research studies designed to create conditions of near-perfect adherence are advantageous when studying PrEP PK in this population as they eliminate adherence as a confounding variable in PK analysis. We assessed the feasibility of directly observed therapy (DOT), the gold standard metric for adherence, within a clinical research context.

METHODS

The PK Component of IMPAACT 2009 evaluated the PK characteristics of daily oral PrEP (FTC 200mg/TDF 300mg) among pregnant (enrolled at 14-24 weeks gestation) and postpartum (enrolled 6-12 weeks after delivery) young women (16-24 years) in Malawi, South Africa, Uganda, and Zimbabwe. Daily FTC/TDF was administered under direct observation for 12 weeks. Acceptable methods of observation included in-person dosing by study staff, real-time video (e.g., WhatsApp), or recorded timestamped video. Qualitative themes surrounding barriers and challenges to PrEP DOT as well as facilitators of success were solicited from site staff and summarized.

Of 3360 expected PrEP doses, **3352 (>99%) were directly observed**; five doses (<1%) were missed and three (<1%) were taken but not observed.

BARRIERS AND CHALLENGES TO PrEP DOT

Barriers to PrEP Uptake

- Low perception of HIV risk by prospective participants
- Negative stigma attached to taking PrEP

Logistical Challenges with DOT Completion

- Interference with daily activities
- Unexpected out of town travel (e.g., for a funeral or to visit a sick relative)
- Intense workload for study staff
- Technological issues with video DOT (e.g., dead battery, no timestamp on recorded video)

Cross-Cutting Factors

- Pregnancy and childcare
- Concerns about PrEP safety during pregnancy and while breastfeeding
- Last minute disruptions due to typical pregnancy complications and/or childcare (e.g., participant feeling ill, scheduling around infant sleep/feeding times)
- Lack of support from partners or family members for PrEP use and/or commitment to DOT

FACILITATORS OF SUCCESSFUL PrEP DOT

Site-Level

Expect the unexpected

Daily DOT is challenging. Pre-established back-up plans are crucial. This was accomplished by:

- Ensuring transportation was readily available for unanticipated off-site dosing schedules
- Offering and training on multiple DOT options
- Collecting detailed locator information, including multiple contact methods

Assign DOT champions

Setting staff up for success matters. Ensure adequate training and support measures are in place. This was accomplished by:

- Assigning staff with prior PK experience
- Assigning DOT workers based on proximity to participants
- Allocating adequate staff, including temporarily shifting off other projects
- Ongoing training and review of best practices

Establish a participant-friendly environment at the site

Ensuring a positive clinic experience at every visit makes participants want to return. This was accomplished by:

- Prioritizing DOT visits to minimize waiting time
- Creating a youth-friendly environment (e.g., access to television, refreshments, nail polish, etc.)
- Providing and/or reimbursing costs for transportation

Participant-Level

Identify a strong social support network

Sharing experiences with others fosters long-term success. This was accomplished by:

- Disclosure of study participation to household members
- Facilitating peer support among study participants, either in-person at the clinic and through social media (e.g., WhatsApp group chat)

Maintain two-way communication

Establishing open and honest lines of communication can help to avoid surprises. This was accomplished by:

- Agreeing to a plan for daily DOT reminders
- Confirming participants' access to mobile phones
- Re-visiting individualized DOT plans as often as needed
- Timely follow-up for no-shows

Build rapport between participants and staff

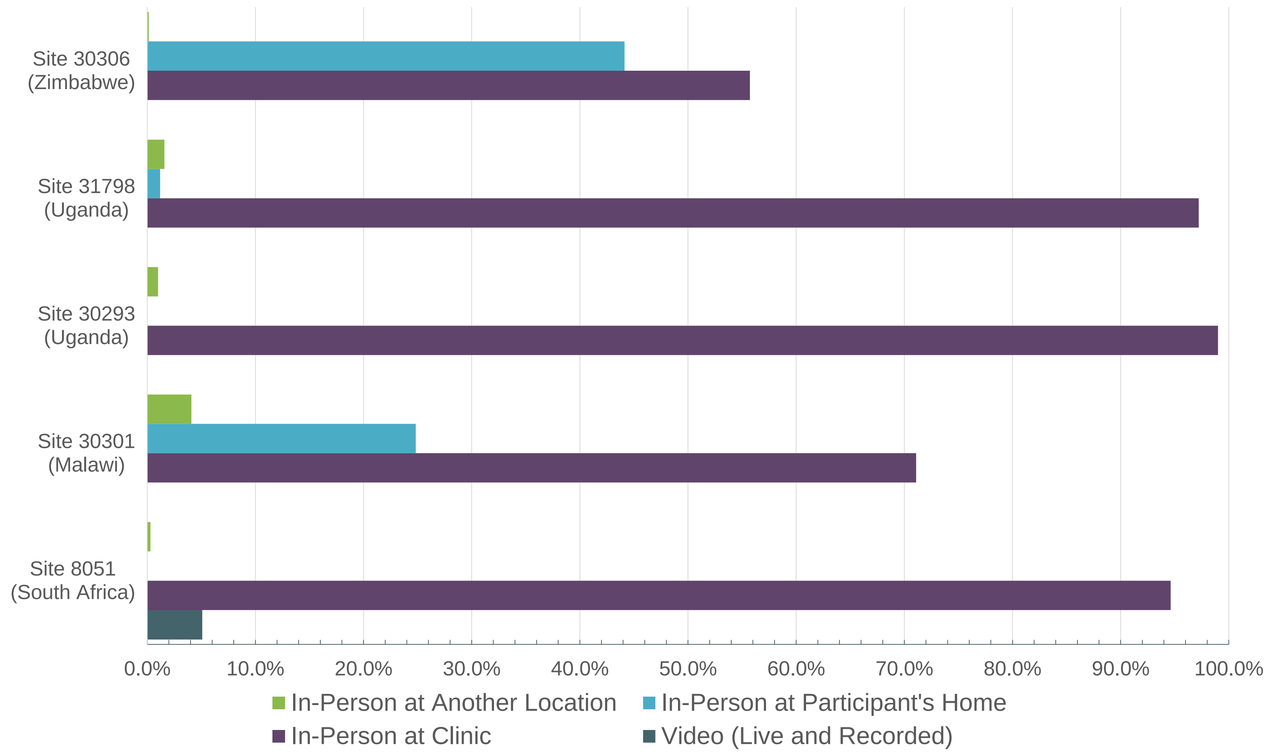
Cultivating a trusting relationship between participants and site staff is key to success. This was accomplished by:

- Listening to participants and providing ongoing support and encouragement
- Frequently checking in on participants' wellbeing
- Being patient and flexible; accommodating participants' needs

RESULTS

- Forty adolescents and young women (median age: 20 years) were enrolled from March to June 2019; 4 in South Africa, 7 in Malawi, 12 in Uganda (6 at each of two sites), and 17 in Zimbabwe. Twenty were enrolled during pregnancy (median gestational age: 18 weeks) and 20 postpartum (median time after delivery: 7 weeks).
- Of the directly observed doses, 2515 (75%) were observed in-person at the clinic, 780 (23%) were observed in-person at the participant's home, 40 (1%) were observed in-person at another location, and 17 (<1%) were observed by video (real-time and recorded timestamped).
- Of the 40 participants, 34 (85%) achieved perfect adherence (i.e., 84/84 expected doses were taken and directly observed).

FIGURE 1. Distribution of Observed Doses by Method of Observation at Each Site



CONCLUSIONS

With appropriate staff preparation and participant support strategies, PK studies with daily DOT can be implemented successfully among pregnant and postpartum adolescents and young women in southern Africa. While promising, video-based modalities were infrequently used and may need further innovation for such populations in this region. Given the complexities in establishing protective PrEP drug levels during pregnancy, this rigorous methodology should be considered in the design of future clinical trials.

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