#Adherence2014

9th International Conference on HIV TREATMENT AND PREVENTION ADHERENCE

jointly sponsored by

IAPAC
INTERNATIONAL ASSOCIATION OF PROVIDERS OF AIDS CARE

PIM
Postgraduate Institute for Medicine

9th International Conference on HIV TREATMENT AND PREVENTION ADHERENCE

Participant Explanations for Study Product Adherence in FEM-PrEP

Amy Corneli, PhD, MPH

presenting on behalf of Brian Perry, Kawango Agot, Khatija Ahmed, Fulufhelo Malamatsho, Joseph Skhosana, Jacob Odhiambo, Lut Van Damme

Disclosures

- None to declare

Overview of FEM-PrEP

- Assessed the safety and efficacy of once-daily, oral emtricitabine/tenofovir disoproxil fumarate (FTC/TDF) as pre-exposure prophylaxis (PrEP) for the prevention of HIV in women in Bondo, Kenya; Bloemfontein and Pretoria, South Africa; and Arusha, Tanzania
- Did not demonstrate a reduction in HIV acquisition because of low adherence to the study pill (Van Damme, NEJM, 2012)
- Closure timeline:
  - August 2011: regular follow-up visits completed
  - July 2012: follow-up visits for seroconverters completed

Previous Adherence Analyses

- In collaboration with Angela Kashuba's lab (UNC), we examined concentrations of plasma tenofovir (TFV) and intracellular tenofovir diphosphate (TFV-DP) from specimens collected at each 4-week study visit among a randomized, prospective sub-cohort of participants (n=150) (Corneli, JAIDS, in press)
- A semi-ordinal, composite adherence score was developed

Previous Adherence Analyses (2)

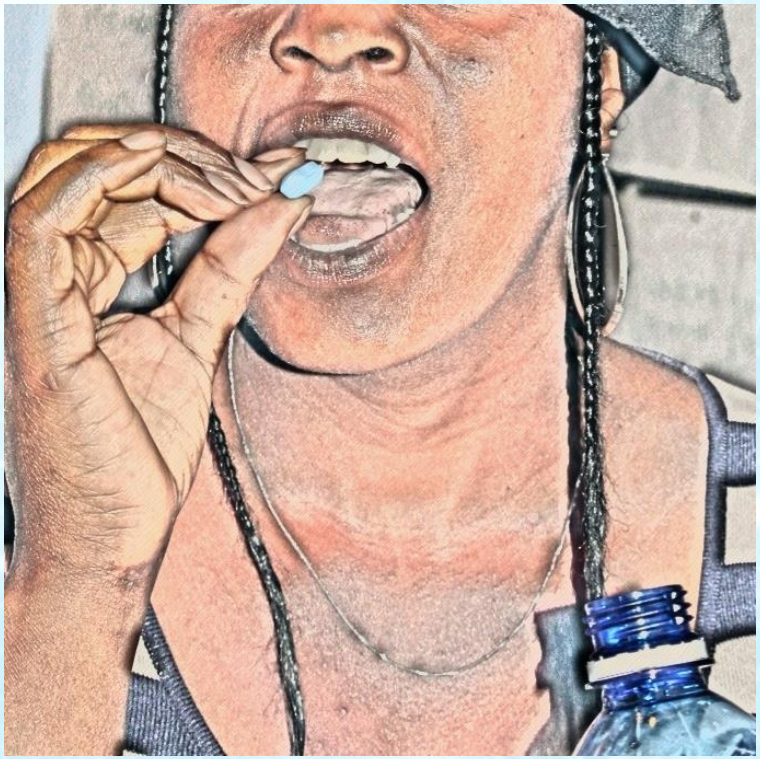
Adherence Composite Score	TFV in Plasma and TFV-DP in Upper Layer Packed Cells	Estimated Doses per Interval
0	No detectable TFV and <10,000 femtomoles/mL TFV-DP	A low number of doses or no doses at all in the interval
1	Detectable TFV but < 10,000 femtomoles/mL TFV-DP	A few doses in the entire interval
2	10,000-100,000 femtomoles/mL TFV-DP, regardless of TFV	1-2 doses per week
3	Less than 10 ng/ml TFV and >100,000 femtomoles/mL TFV-DP	Several doses early in the interval, followed by a stop in the week or two leading up to the sampling visit
4	More than 10 ng/ml TFV and 100,000-1,000,000 femtomoles/mL TFV-DP	4-5 doses per week
5	More than 10 ng/ml TFV and >1,000,000 femtomoles/mL TFV-DP	Approximately daily dosing

Previous Adherence Analyses (3)

- 23% of the sub-cohort consistently had no or low drug concentrations
- Yet, some participants had evidence of recent pill use:
  - 55% had at least one study visit interval consistent with good adherence (i.e., TFV in plasma exceeding 10 ng/mL and intracellular TFV-DP in upper layer packed cells exceeding 100,000 fmol/mL)
  - 12% reached good adherence at each visit interval for the length of their trial participation
  - 60% had fluctuating drug concentrations over time

Follow-up Study

- We explored reasons for adherence and non-adherence among former FEM-PrEP participants in Bondo, Kenya, and Pretoria, South Africa
- Here we describe the participants' reasons for taking the study pill some or most of the time
- Data were collected from March to June 2013



9th International Conference on HIV TREATMENT AND PREVENTION ADHERENCE

USAID FROM THE AMERICAN PEOPLE

fhi360 THE SCIENCE OF IMPROVING LIVES

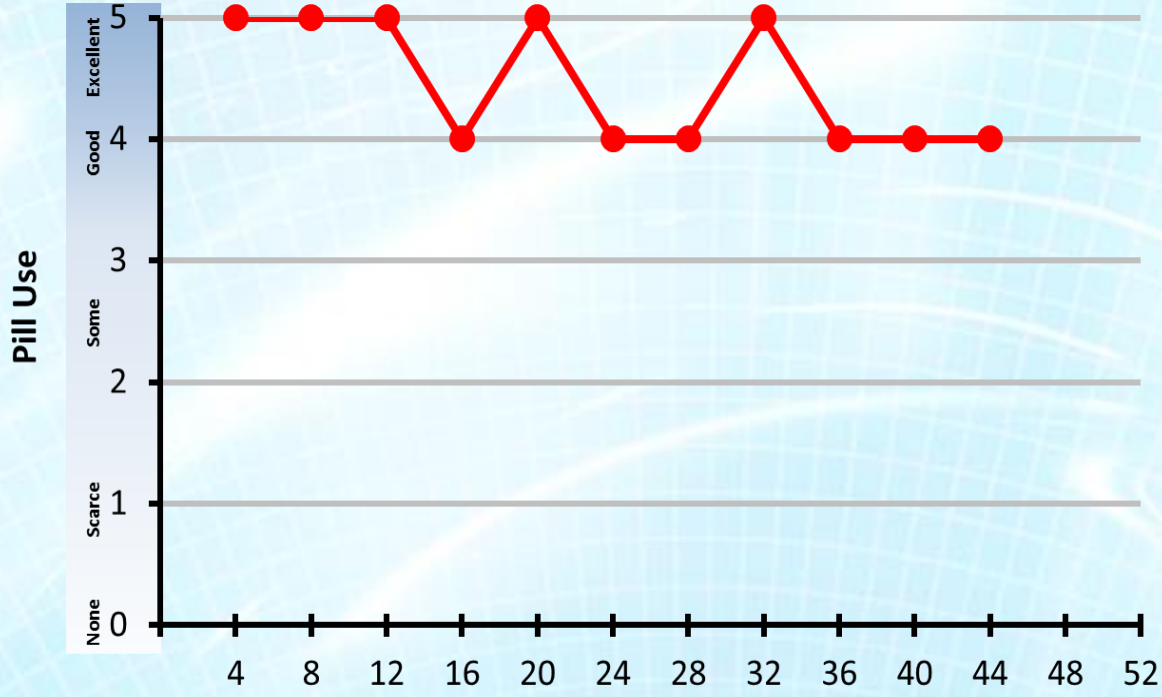
PTA PREVENTIVE TECHNOLOGIES AGREEMENT

Qualitative, Semi-Structured Interviews (SSIs)

- Purposefully selected 56 former FEM-PrEP participants (Bondo, n=26; Pretoria, n=30) based on their drug concentrations
- Participants were placed into two interview groups:
  - "Good" adherence (n=25; Bondo, n=12; Pretoria, n=13)
    - Having multiple adherence composite scores of 4 and 5 over time
  - "Moderate" adherence (n=31; Bondo, n=14; Pretoria, n=17)
    - Having scores that fluctuated between scores 0 and 5 among the available samples, or whose scores remained relatively steady between scores 2 and 4

Qualitative SSIs (2)

- As a discussion aid, participants viewed a graph displaying their adherence composite scores over the 13 study visit intervals



Qualitative SSIs (3)

- Topics covered in the interviews:
  - Good group: factors that made it easy to take the study pills
  - Moderate group: adherence patterns, reasons for adhering some of the time, and times during the trial when they took the study pill more often
- Applied thematic qualitative analysis was used to analyze the data

Overall Themes

- Most participants identified multiple factors that either motivated or assisted them to take the study pill
- Five overall themes were identified:
  - Partner awareness and support
  - Support for the research
  - Perceived HIV risk
  - Established routine/use of tools
  - Motivation after enrollment or adherence counseling

9th International Conference on HIV TREATMENT AND PREVENTION ADHERENCE

USAID FROM THE AMERICAN PEOPLE

fhi360 THE SCIENCE OF IMPROVING LIVES

PTA PREVENTIVE TECHNOLOGIES AGREEMENT

Partner Awareness and Support

- A range of partner awareness or engagement was described, from no partner knowledge or involvement to active adherence support
  - Several participants (n=8) described receiving encouraging and helpful support, such as a partner regularly reminding a participant to take her study pill:

My boyfriend use to support me. When it's time I use to drink the prevention pill at 8:00, he would ask me, "did you drink that one?"

– Pretoria participant, moderate group

Partner Awareness and Support (2)

- More participants (n=14) described only partner knowledge of trial participation:
  - Partners' knowledge aided adherence because they did not discourage or interfere with taking the study pill; partners gave participants "no problems"
  - Partners were not relied on for adherence support:

Support? There was no support he was giving me at all. But the thing is he never stopped me. But, to remind me that today, "what about your pills?" That one was not in his mind at all.

–Bondo participant, good group

Support for the Research

- Several participants in the good group (n=14) and a few in the moderate group (n=4) said they were motivated to take the pill because they supported the research
  - Half (n=9) had a strong interest in learning whether FTC/TDF was effective in preventing the acquisition of HIV:

    I wanted to know the truth about those drugs and that is the reason why I took them daily, if they could work. Even though I did not know the drug I was using, I just wanted to know if it worked or not.

    –Bondo participant, good group

Support for the Research (2)

– Several narratives (n=9) were illustrative of classic altruism, to help children or future generations:

I was taking it because I wanted [to know] if it could be found to prevent -- if it prevents us for the generation that is behind.

–Bondo participant, good group

Perceived HIV Risk

- Twelve participants in the good adherence group and 18 in the moderate group believed they were at risk of HIV
- Many (n=18) described that they were at risk because of their sexual partners, and communicated a lack of trust toward their partners' ability to remain HIV-negative:

It is because I wanted to protect myself. I can't trust my boyfriend because he stays there and I am staying here. I can't see everything that he does. Even if he can use a condom, it is possible that it can break. It is also possible that he can forget to use a condom with another girl, like when he drinks alcohol. So, I can't say I trust him.

–Pretoria participant, good group

Established Routine/Use of Tools

- Twelve participants in the good group and 13 in the moderate group established a routine or used adherence tools
- Establishing a routine – such as a daily time or activity -- to take the study pill was mentioned most often (n=17); setting a reminder alarm also frequently mentioned (n=9)
- Several participants (n=6) spoke about keeping the pills with them or visible:

I kept those pills where I could see them. Now anytime I was ready to go to sleep, I could see them and then I remembered. Then I did what? I took them. – Bondo Participant, good group

Established Routine/Use of Tools (2)

- Only four participants mentioned that using the study-provided pill box (n=3) or calendar (n=1) helped them to adhere

Motivation after Enrollment or Adherence Counseling

- Eighteen participants in the moderate group were initially motivated to take the study pill after they enrolled; data are presented elsewhere on reasons adherence decreased (Corneli, CROI, 2014)
- Twelve participants in the moderate group, and five in the good group, spoke about their motivation to adhere after adherence counseling:

Mostly if we go there the [counselor] talks to you. I feel that I regain my heart [Interviewer note: getting motivated] because how they put it to test to know if that thing works. – Bondo participant, moderate group

Discussion

- Numerous factors were reported to have supported participants' adherence to a daily, investigational drug
- Participants reported that they took the study pill primarily because of:
  - Personal motivation -- perceived HIV risk, support toward the research
  - External cues and reminders -- partner support, established routines and tools

Discussion (2)

- Adherence counseling appeared to be beneficial for some, yet other facilitators are also needed to support adherence
  - For the moderate group, facilitators were only marginally effective, as the participants in this group did not reach good adherence
- Perceiving oneself to be at risk of HIV was common; we previously reported a significant association between risk perception and good adherence within FEM-PrEP (Corneli, IAS, 2013)
- A spectrum of partner support was reported
  - Active support may not be needed; awareness may be an important factor for adherence

Discussion (3)

- Our sample was not randomly selected from all FEM-PrEP participants
  - Our findings, therefore, may not be representative of FEM-PrEP participants not included in our study
- The study was not designed to compare adherence facilitators between the two adherence groups but rather to explore factors that might be relevant to a specific adherence group
- Nonetheless, in moving forward, these findings may help inform both future biomedical HIV prevention trials and PrEP demonstration projects

Discussion (4)

- Future trials could:
  - Continue to describe, during community engagement, the importance of clinical research
  - Consider the role of risk perception when identifying potential trial participants
- Counseling should:
  - Explore the extent to which participants wish to involve partners
  - Explore and support personal motivations for adherence while being mindful of perceived risk and use of an investigational product
  - Continue to identify ways for participants to use tools and integrate pill taking into their daily lives

Acknowledgements

Study Participants

Funders: U.S. Agency for International Development (USAID) and the Bill & Melinda Gates Foundation (preparatory work)

Pretoria — Setshaba Research Centre: Khatija Ahmed, Mookho Malahleha, Malebo Ratlhagana, Shumani Makatu, Joseph Short Skhosana, Modie Constance Monedi, Elizabeth (Thupi) Rammutla

Bondo — Impact Research & Development Organization: Kawango Agot, Fred Owino, Jacob Odhiambo, Paul Mak'Oketch, Walter Agingu, Jesse Asewe, Paul Omullo

Bloemfontein — JOSHA Research: Johan Lombaard, Ilse Reblin, Makanda Mankalimeng, Gustav Venter, Phumzile Siguntu

Arusha — Kilimanjaro Christian Medical Center: Saidi Kapiga, Rachel Manongi, Temu Lucky, John Gardner Gaddiel, Martha Masaki

Prince Leopold Institute of Tropical Medicine (ITM) – Central Lab: Katrien Fransen, Tania Crucitti, Irith De Baetselier, Said Abdellati

Gladstone Institute of Virology and Immunology, University of California, San Francisco: Robert Grant, Patricia Dechefereux, Teri Liegler

UNC Chapel Hill, School of Medicine: Angela Kashuba

SCT Consulting: Savi Chetty-Tulsee, Tharnija Lalbahadur

Gilead Sciences, Inc. (study product): James F. Rooney

BMGF: Lut Van Damme

FHI 360: Amy Corneli, Lisa Saylor, Haddie Kiernan, Stella Kirkendale, Janet Kariuki, Kavita Nanda, Justin Mandala, Jen Deese, Timothy Mastro, Douglas Taylor, Ward Cates, Laneta Dorflinger, Lalitha Venkatasubramanian, Meng Wag Yun-Rong Ma, Jennifer Headley, Ansley Lemons, Michele Lanham, Kevin McKenna, Monique Mueller, Sarah Mullins, Zablon Omungo, Caleb Parker, Brian Perry, Amanda Troxler, Valentine Veena, Jamilah Taylor, Jenae Tharaldson, Christina Wong

9th International Conference on HIV TREATMENT AND PREVENTION ADHERENCE

USAID FROM THE AMERICAN PEOPLE

fhi360 THE SCIENCE OF IMPROVING LIVES

PTA PREVENTIVE TECHNOLOGIES AGREEMENT

Thank you!

9th International Conference on HIV TREATMENT AND PREVENTION ADHERENCE

USAID FROM THE AMERICAN PEOPLE

fhi360 THE SCIENCE OF IMPROVING LIVES

PTA PREVENTIVE TECHNOLOGIES AGREEMENT