The Association Between Use of Adherence Support Interventions and Adherence to HIV Pre-Exposure Prophylaxis Among Young African Women

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Background

- Adolescent girls and young women (AGYW) aged 15-24 years continue to be at high risk of contracting HIV in Sub-Saharan Africa (SSA).
- In SSA, AGYW accounted for more than 77% of new infections among young people aged 15-24 years in 2022.
- Adherence to PrEP is a known challenge among AGYW in SSA.
- Group-based trajectory modeling (GBTM) is a novel methodological approach used to analyze the trajectories of an outcome of interest over time.

Rationale

- No previous study has used GBTM to characterize trajectories of
  - An objective PrEP adherence marker [tenofovir-diphosphate (TFV-DP) levels in dried blood spot (DBS)] *and*
  - Adherence support strategies (2-way SMS messages and adherence support clubs) and identify the association between them.
- Characterizing trajectories may be beneficial to:
  - Customize targeted interventions to increase adherence
  - Estimate exposure to adherence support interventions

HPTN 082

HPTN 082: Evaluation of daily oral PrEP as a primary prevention strategy for young African women

Study Population

Uninfected women
Ages 16-25 yrs

Johannesburg & Cape Town, South Africa
Harare, Zimbabwe

Eligibility criteria: Sexually active in past month; VOICE risk score ≥5; interest in PrEP; access to mobile phone; hepatitis B seronegative
Conducted October 2016-October 2018

Target Enrollment

- 400 women who accept PrEP at enrollment
- ≤200 women who decline PrEP at enrollment

Standard adherence support

Standard adherence support *plus* drug level feedback

Standard Adherence Support in HPTN 082

- Weekly two-way SMS in first 3 months
- Monthly optional adherence clubs
  - Peer support
  - Address concerns & share experiences about PrEP
  - Problem-solve adherence challenges
- Brief counseling at visits: Months 1, 2, 3, 6, 9 and 12
- Discrete pill containers

Project Aims

Aim 1: To determine the association between trajectories of response to weekly 2-way SMS and high TFV-DP levels at week 13 of follow-up as an indicator of early adherence to PrEP.

Aim 2: To assess the association between trajectories of TFV-DP levels and trajectories of participation in peer support adherence clubs during the follow-up period.

Methods/Analysis Plan

- GBTM was used to identify latent trajectories of
  - Participation in (1) monthly peer support adherence clubs and (2) intracellular TFV-DP levels using censored normal finite mixture models
  - Two-way SMS using a logit model.
- Used Chi-square test to
  - Compare baseline variables between the identified TFV-DP levels trajectories.
  - Determine the association between high PrEP adherence and responses to SMS trajectories and the association between TFV-DP levels and trajectories of participation in peer support adherence clubs.
- *P* value <0.05 was considered statistically significant.
- Statistical analyses were performed using Stata software (version 17).
- Stata Plugin was used to estimate GBTM parameters

Results

Background data at study enrollment

- 398 AGYW initiating PrEP included in analysis.
- Almost two-thirds aged ≥ 20 years
- 85% attained a secondary level of education.
- A large majority (86.4%) had a primary sex partner during the previous 3 months.
- Almost half reported not using a condom during vaginal sex in the previous month.
- The median VOICE risk score was 7 (Interquartile range (IQR) 6,8)
- Two-thirds perceived themselves to not be at risk of HIV infection in the next year.

Results

- High adherence: TFV-DP≥ 700 fmol/punch
  - 91 (24.5%) at month 3
  - 76 (20.9%) at month 6
  - 31 (8.9%) at month 12
- GBTM identified two latent trajectories of TFV-DP levels:
  - **consistently low** trajectory (N=274, 68.8% with constant TFV-DP level of 100 fmol/punch)
  - **high decreasing** (N=124, 31.2% with TFV-DP level started at 900 that dropped to 500 fmol/punch)

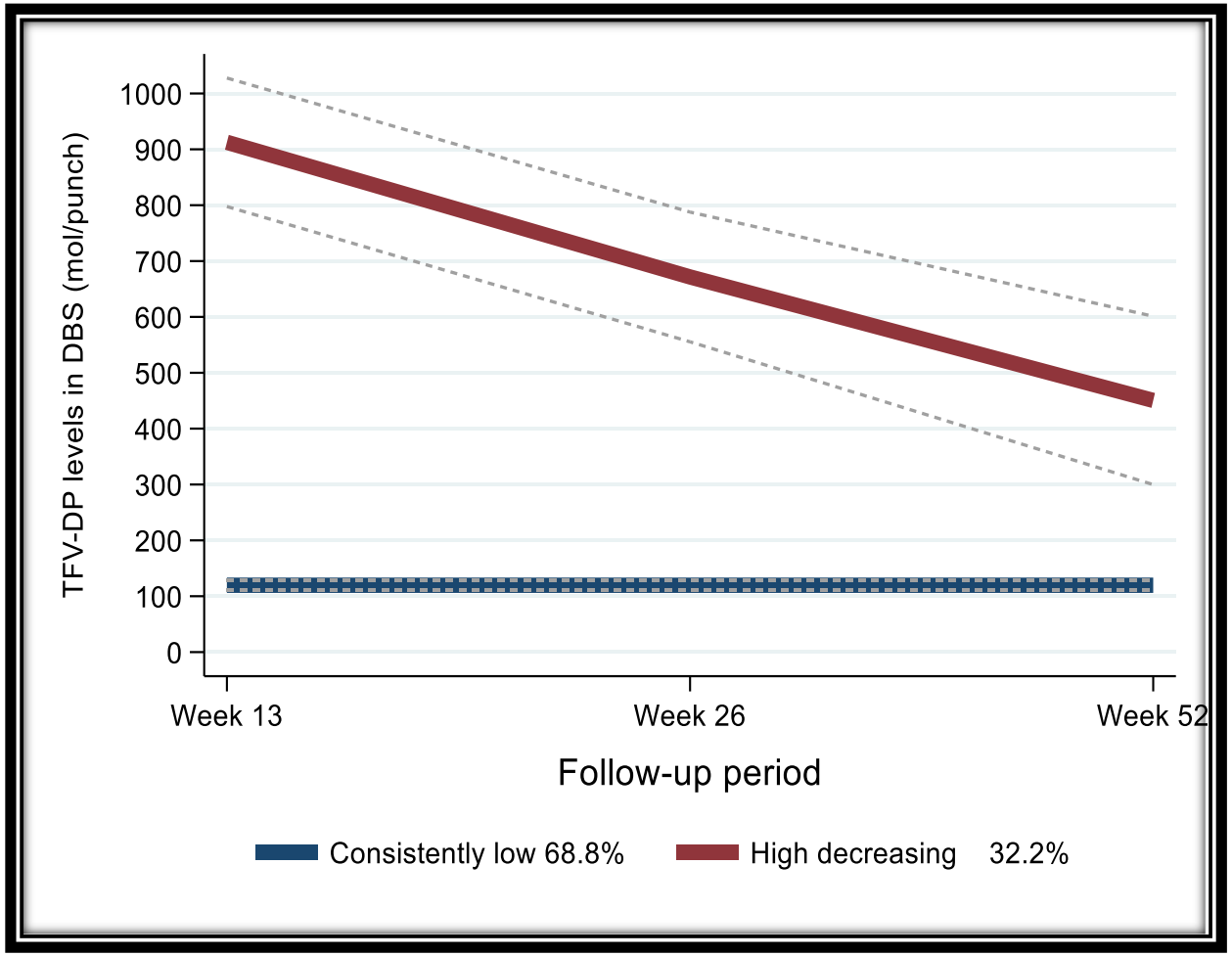

Figure 2. Trajectories of TFV-DP levels in DBS

Intracellular TFV-DP levels were measured in DBS at the University of Cape Town, which validated the DBS testing in partnership with the University of Colorado Pharmacology lab

Results

Table 1. Baseline participant characteristics by TFV-DP levels trajectory groups

Background characteristics	Trajectory groups of TFV-DP levels in DBS			P value
	Consistently low (n= 274)	High decreasing (n = 124)	Total (n=398)	
Treatment arm				
Standard adherence	133 (48.5)	61 (49.2)	194	0.90
Enhanced adherence	141 (51.5)	63 (50.8)	204	
Age groups				
< 20 years	101 (36.9)	29 (23.4)	130	**0.008**
> =20 years	173 (63.1)	95 (76.6)	268	
Education				
College or university	34 (12.4)	9 (7.3)	43	**0.01**
Secondary school	238 (86.9)	109 (87.9)	347	
Primary school	2 (0.7)	6 (4.8)	8	
Perceived risk of getting HIV in the next year (n=373)				
No risk at all	142 (56.1)	46 (38.3)	188	
Small chance	71 (28.1)	50 (41.7)	121	**0.01**
Moderate chance	19 (7.5)	12 (10.0)	31	
Great chance	21 (8.3)	12 (10.0)	33	
Condom use with vaginal sex, past month (n= 300)				
No	106 (53.0)	62 (62.0)	168	
Part of the last time	7 (3.5)	6 (6.0)	13	0.12
Yes	87 (43.5)	32 (32.0)	119	
VOICE risk score, median (IQR)	7 (6-8)	7 (6-8)		0.14

Results

Trajectories of participation in monthly adherence clubs

GBTM identified two trajectories of voluntary participation in optional peer adherence clubs:

- **consistently moderate** with an approximately 0.7 clubs per month rate of participation (N=267, 67.1%)
- **low slightly increasing** (N= 131, 32.9%)

- Rate of participation in adherence clubs was calculated by dividing the frequency of participation in clubs reported in each visit by the number of months between visits.

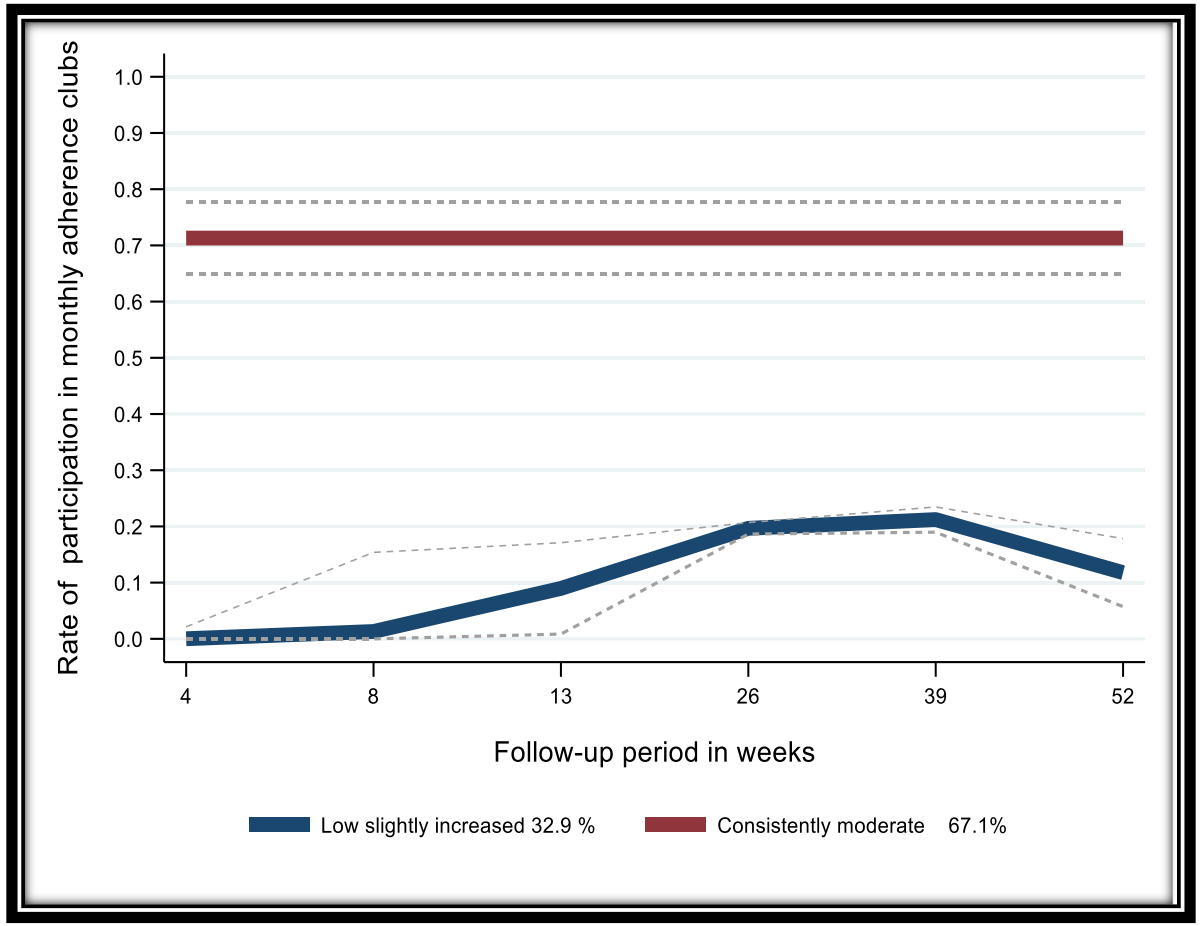

Figure 1. Trajectories of voluntary participation in monthly adherence clubs

Results
Trajectories of responses to 2 way SMS

- GBTM identified three latent trajectories of responses to weekly SMS
- 218 (62.1%) had **consistently high** (categorized as responding to approximately 90% of the weekly SMS messages)
- 108 (30.8%) **moderate decreasing** responses
- 25 (7.1%) having **consistently low** responses.

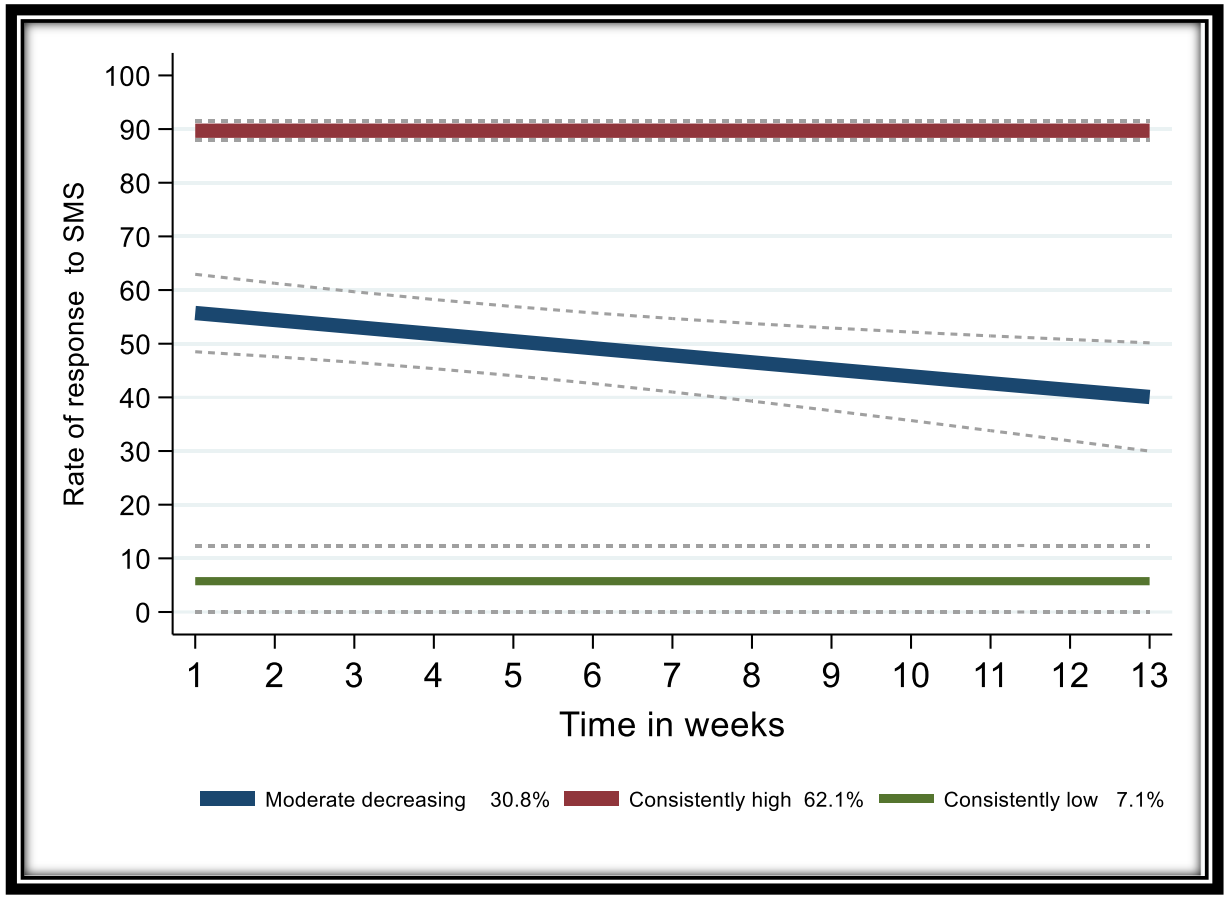

Figure 3. Trajectories of responses to 2-way SMS

2-way SMS asked participants about their general health, with an option to type OK or not OK.

Results

Table 2. Association between TFV-DP levels in DBS trajectories and participation adherence support clubs trajectories

Trajectories of participation in adherence clubs	**Trajectory groups of TFV-DP levels in DBS**			**P value**
	Consistently low (n= 274)	High decreasing (n = 124)	Total (n=398)	
Low slightly increasing	103 (37.6)	28 (22.6)	131	**0.003**
Consistently moderate	**171 (62.4)**	**96 (77.4)**	267	

Results

Table 3. Association between responses to SMS trajectories and TFV-DP levels in DBS at months 3

Trajectory of responses to SMS	TFV-DP levels in DBS (fmol/punch)		Total (n=351)	P value
	< 700 (n= 262)	≥700* (n=89)		**< 0.001**
Consistently high	**146 (55.7)**	**72 (80.9)**	221	
Moderate decreasing	92 (35.1)	16 (18.0)	111	
Consistently low	24 (9.2)	1 (1.1)	19	

TFV-DP level in DBS ≥ 700 (fmol/punch) was considered as high adherence to PrEP corresponding to taking four or more doses/week

Summary

- Adherence to PrEP was a challenge among South African and Zimbabwean AGYW in this early PrEP demonstration study conducted in 2016-2018.
- Based on TFV-DP levels one-third had high initial adherence which decreased over 12 months and approximately two-thirds of participants had consistently low adherence over time.
- AGYW who are adherent to attending support clubs and responding to SMS are also adherent to PrEP.

Discussion

- The dose-response relationship with response to the weekly 2-way SMS warrants further investigation to determine long-term effect on high adherence.
- Peer support groups might be used to support adherence initially and may provide support to AGYW who start with high adherence and motivation.
- Adherence support strategies should be utilized to provide education to AGYW on how to align PrEP use with periods of HIV risk *(prevention-effective adherence)*.

Study Strengths/Limitations

- Strengths
  - The use of an objective measure of intracellular TFV-DP levels which indicates average cumulative PrEP adherence in the prior 6-8 weeks.
  - Using GBTM to delineate trajectories of TFV-DP levels and adherence support strategies to understand the association between trajectories of drug levels and adherence support strategies
- Limitations
  - PrEP adherence declined substantially during the follow-up period, which limits the ability to identify associations between SMS responses and monthly adherence support clubs with longer-term high PrEP adherence.
  - Drug levels were measured at three data points, which limited the potential number of identified trajectories to two.

Conclusions

- PrEP adherence support strategies in the form of 2-way SMS responses and participation in peer-led adherence support clubs were used by a majority of HPTN 082 participants and were associated with higher TFV-DP levels
- Oral PrEP remains the major PrEP option available to African AGYW and additional research is needed on adherence support strategies to improve oral PrEP adherence
- In parallel need to increase access to longer-acting PrEP formulations

Presentation Highlights

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Question

Is there an association between use of adherence support interventions and adherence to HIV pre-exposure prophylaxis among adolescent girls and young African women?

Key finding

High participation in adherence support clubs and 2-way SMS were associated with high levels of adherence to PrEP.

Implication on advancing HIV prevention efforts

Provision of acceptable PrEP adherence support strategies in the form of 2-way SMS and peer-led adherence support clubs could improve PrEP adherence and prevention effectiveness.

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