

# Depressive Symptoms of Adolescents Enrolling in a Clinical Trial of a Long-Acting Injectable for HIV Prevention (HPTN 084-01)

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APHA 2022

Monday, 7 November 2022



- I have no financial support or conflicts of interest to disclose.
- Product for this study (CAB LA) was provided by ViiV Healthcare.

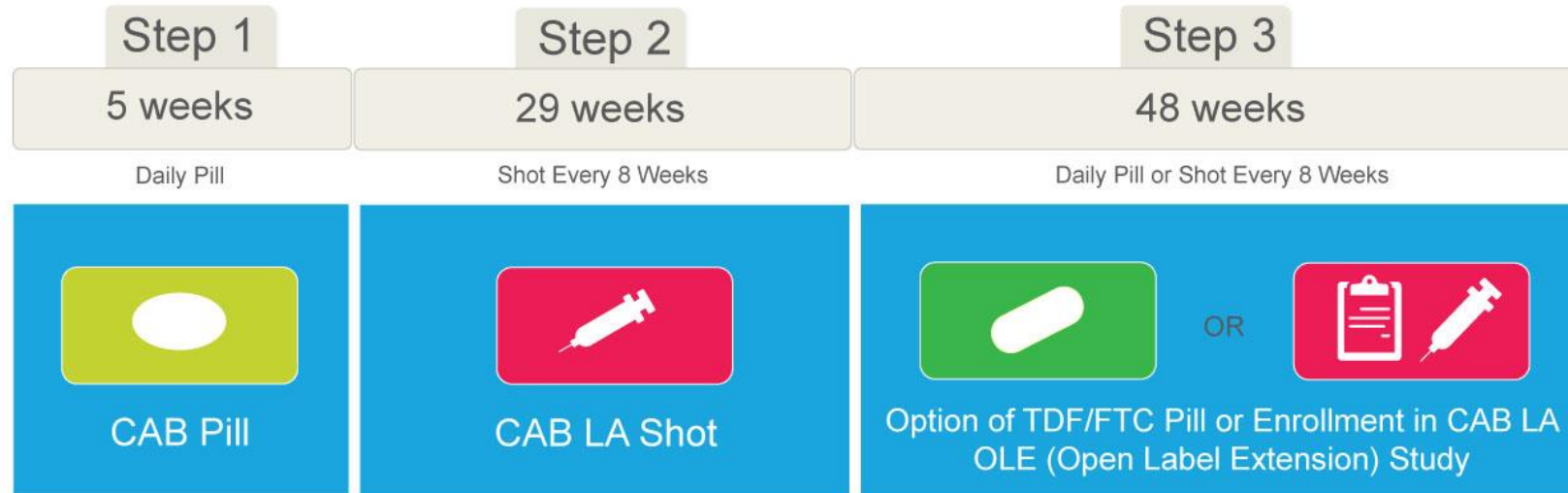


## *HPTN 084-01: Safety, Tolerability and Acceptability of Long-Acting Cabotegravir (CAB LA) for the Prevention of HIV among Adolescent Females – A Sub-study of HPTN 084*

- Long-acting Injectable for Teens (LIFT)
- Safety, tolerability, and acceptability bridging study
- N = 55 cisgender female adolescents <18 years of age
- ~19 months on trial
- 3 high burden countries in Africa (South Africa, Uganda, Zimbabwe)

# Study Schema

## HPTN 084-01 Study Participant Plan



\*In step 2, the first two shots are four weeks apart and 8 weeks apart after that

# HPTN 084-01 Clinical Research Sites N = 55

**MU-JHU CRS**  
Kampala, Uganda  
n = 17

**Spilhaus CRS**  
Harare, Zimbabwe  
n = 20

**Ward 21 CRS**  
Johannesburg, South Africa  
n = 18



- Good mental health can be considered a global public good and can contribute to the achievement of the Sustainable Development Goals (SDGs) set forth by the United Nations.<sup>1</sup>
- Mental distress and mental ill-health are very common experiences globally and, thus, represent an ongoing public and global health crisis.
- Circumstances that place an adolescent at increased risk for acquiring HIV often mirror those that threaten mental well-being.
  - Context can contribute to and/or mitigate risk.
  - Within a socioecological framework, risk for both mental ill-health and HIV acquisition include factors at the society, policy, community, organization, relationship (family), and individual levels.
  - Common mental disorders (e.g. anxiety, depression) may influence PrEP uptake and persistence.<sup>2,3</sup>
- High rates of depressive symptoms have also been documented in those presenting for HIV prevention and treatment trials (those “at risk” of acquiring HIV).
- In the context of clinical trials, it is important to have a baseline measure to accurately determine relatedness (to study drug) of subsequent depressive symptoms.

1. *United Nations Sustainable Development Goals, 2015*

2. *Collins et al., JIAS, 2021*

3. *Celum et al., PLoS Med, 2021*



# Depressive Symptoms in Adolescents

- Adolescence and young adulthood are critical periods of an individual's development.
  - Mental health is often poor, yet life-long health behaviors are established.
  - It is crucial to intervene appropriately and timely.
- Globally, suicide was the second most common cause of death in young people ages 15-29 in 2016.
  - Ninety percent of adolescents who died by suicide lived in LMICs.<sup>4</sup>
  - Recent research has called for suicide prevention interventions for adolescents living with HIV at risk for suicide, particularly in LMICs, and for mental health treatment as a fundamental component of their HIV care.<sup>5,6</sup>



4. *Suicide in the world: Global Health Estimates*. Geneva: World Health Organization; 2019

5. Kreniske P, et al., *Journal Adolesc Health*, 2019

6. Bhana A, et al., *JIAS*, 2021

# PHQ-9

## Patient Health Questionnaire 9<sup>7</sup>

Administered at Enrollment / Week 0





- Administered at Enrollment only (Dec 2020-Aug 2021)
- Asks questions about the previous 2 weeks (“How often have you been bothered by each of the following symptoms during the past two weeks?”)
  - Items are scored using a Likert scale 0-3 (not at all, several days, >half the days, nearly every day)
  - Mirror criteria for DSM diagnosis of major depressive disorder
- PHQ-9 was clinician administered in-person at all sites
  - Nurse administered in-person at Zimbabwe site
  - Doctor administered in-person at Uganda and South Africa sites
  - All site staff administering the PHQ-9 had received relevant training, whether specifically for this study or previously via their line of work

- All sites submitted their PHQ-9 data directly into Medidata Rave Electronic Data Capture (EDC) in real time
- Parents were not in the room at any site, but could have been on site at the CRS in Uganda
- Validated in PLHIV in Zimbabwe, translated and back-translated in Luganda in Uganda, all ppts completed in English in South Africa

## Scoring of depressive symptoms:

0-4 = none/minimal

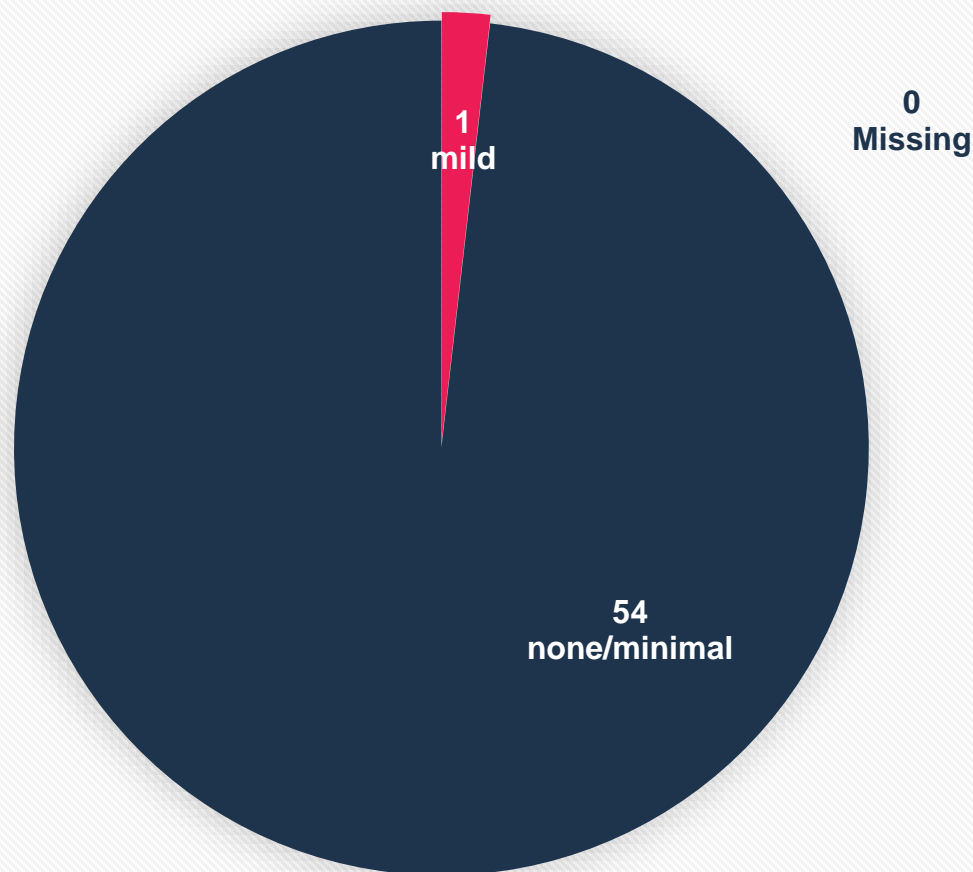
5-9 = mild

$\geq 10$  = moderate, moderately severe, or severe depression

(10-14 = moderate, 15-19 = moderately severe, 20-27 = severe)

# PHQ-9 Scores at Enrollment

PHQ-9 scores – all sites (N=55)



**1 (2%) overall = score 5-9 (mild)**

PHQ-9 Scores by Site

Site	N (missing)	Scores 5-9 (mild)
Uganda	17 (0)	0 (0%)
Zimbabwe	20 (0)	1 (5%)
S. Africa	18 (0)	0 (0%)

# CES-D-10

Centre for Epidemiological Studies  
Depression Scale 10<sup>8,9</sup>

Administered at Weeks 4 & 17  
(during Steps 1 and 2)



# CES-D (during Steps 1 and 2)

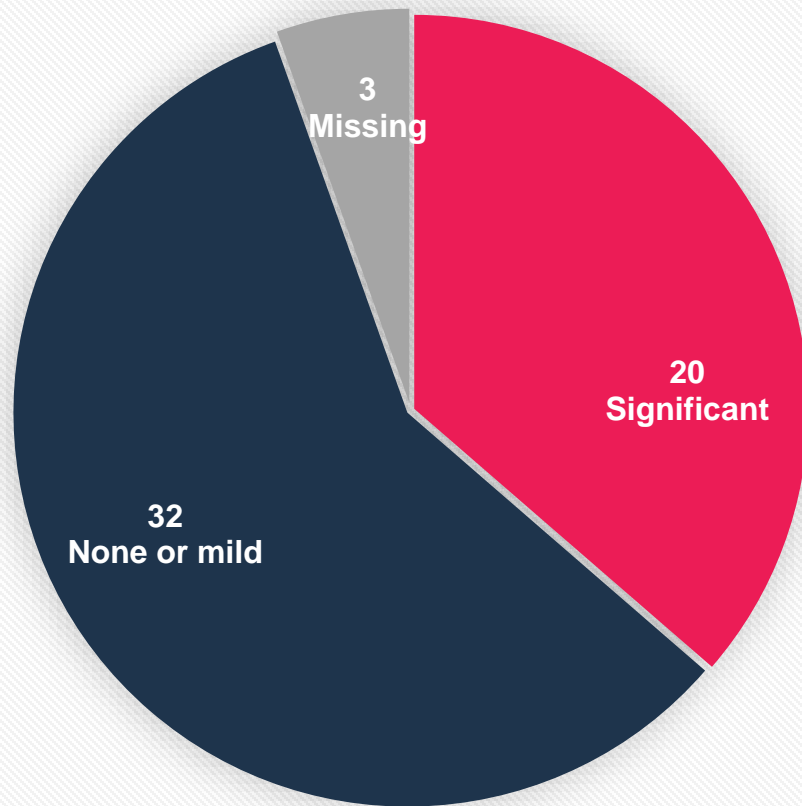


- Enrollment, Week 4, and Week 17
- CASI (Computer-Assisted Self-Interview)
- Validated:
  - In youth populations
  - In pregnant women in Zimbabwe
- Translation and back-translation:
  - Luganda in Uganda
  - All South African ppts completed CASI in English
- Score calculation:
  - Clinical cutoff score of 10 for significant depressive symptoms
  - If > 1 response was missing/prefer not to answer, then CES-D-10 score counted as “missing”



# Significant Depressive Symptoms at Enrollment

Significant Depressive symptoms –  
all sites (N=55)



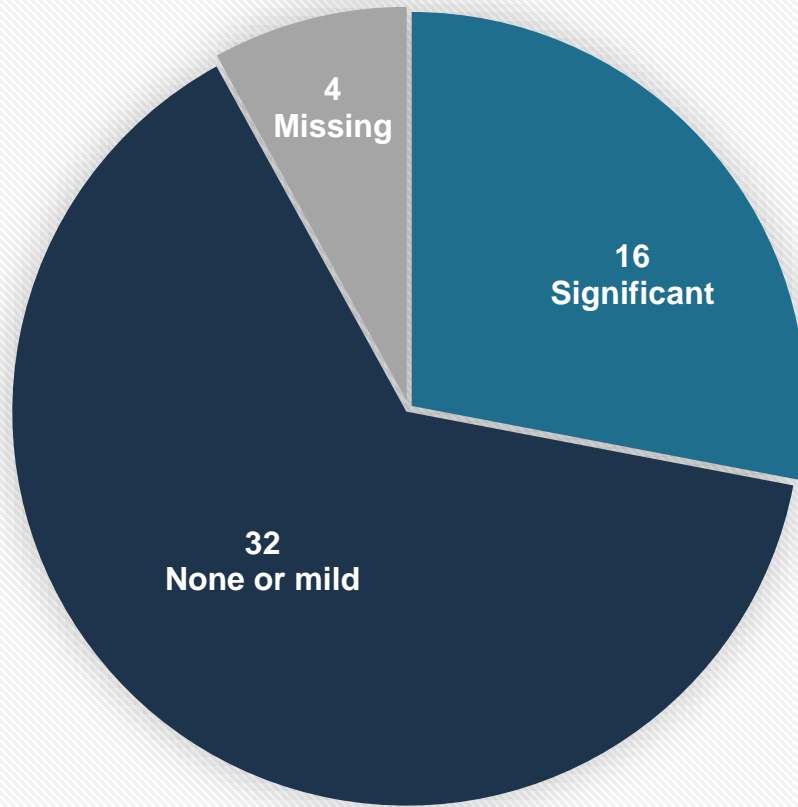
20 (36%)  $\geq 10$

Significant Depressive Symptoms by Site

Site	N (missing)	Scores $\geq 10$
Uganda	16 (1)	6 (35%)
Zimbabwe	18 (2)	7 (35%)
S. Africa	18 (0)	7 (39%)

# Significant Depressive Symptoms at Week 4

**Significant Depressive symptoms –  
all sites (N=52)**



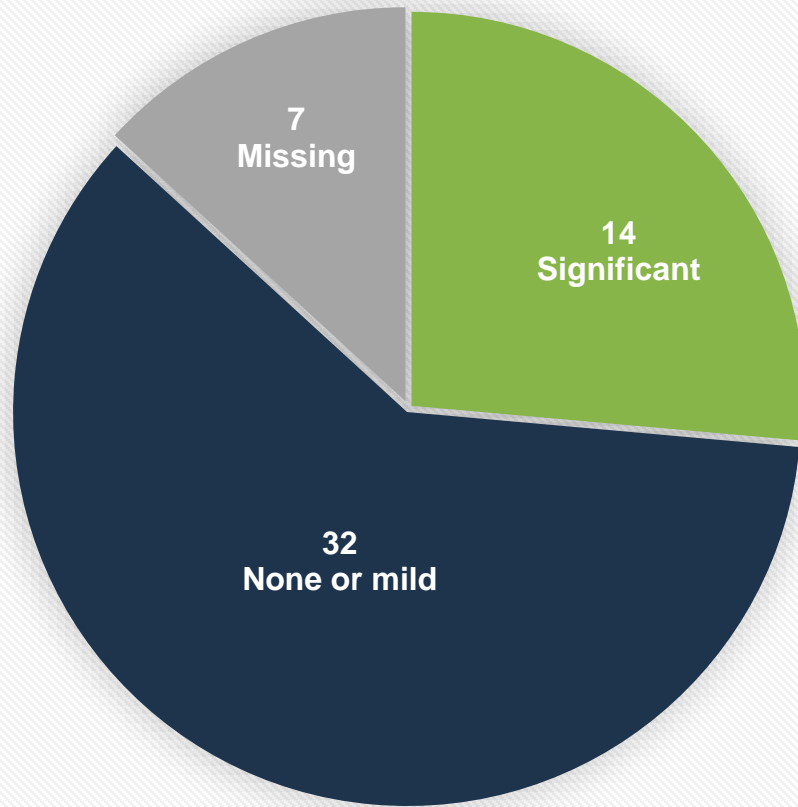
**16 (30.77%)  $\geq 10$**

**Significant Depressive Symptoms by Site**

Site	N (missing)	Scores $\geq 10$
Uganda	14 (1)	5 (33%)
Zimbabwe	17 (3)	7 (35%)
S. Africa	17 (0)	4 (23.53%)

# Significant Depressive Symptoms at Week 17

Significant Depressive symptoms –  
all sites (N=53)



14 (26.42%)  $\geq 10$

Significant Depressive Symptoms by Site

Site	N (missing)	Scores $\geq 10$
Uganda	17 (0)	5 (29.41%)
Zimbabwe	13 (7)	4 (20.00%)
S. Africa	16 (0)	5 (31.25%)

# Conclusions



- Baseline depressive symptoms (on the PHQ-9) lower than other adolescent HIV prevention trials<sup>10</sup>
- PHQ-9 administered by either nurse or doctor at all sites, potentially leading to social desirability bias, but may be overcome by Computer Assisted Self-Interview (CASI)
- CES-D results during follow-up indicate higher levels of depressive symptoms than what was captured at Enrollment with the PHQ-9 – decreasing over time
- Assessment and treatment for common mental disorders should be fully integrated with adolescent sexual health and STI/HIV services

**Acknowledging mental health experiences is crucial for person-centered and effective response to ending the HIV pandemic**

# Acknowledgments



**A BIG THANK YOU to all of the HPTN 084-01 participants, their families, and the communities that support them for their commitment to the study and to the site staff for their dedication to study implementation!**

- Overall support for the HIV Prevention Trials Network (HPTN) is provided by the National Institute of Allergy and Infectious Diseases (NIAID), Office of the Director (OD), National Institutes of Health (NIH), National Institute on Drug Abuse (NIDA), and the National Institute of Mental Health (NIMH) and the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) under Award Numbers UM1AI068619-15 (HPTN Leadership and Operations Center), UM1AI068617-15 (HPTN Statistical and Data Management Center), and UM1AI068613-15 (HPTN Laboratory Center).
- HPTN 084-01 is also co-funded by the Bill and Melinda Gates Foundation (BMGF) and support is provided by ViiV Healthcare.
- The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.



# Thank you

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