



## SEARCH Youth *Primary Endpoint Results*

July 31, 2022  
Late breaker; Track E



 **AIDS 2022**

## Florence Mwangwa for the SEARCH Youth team

*I have no relevant financial relationships with ineligible companies to disclose*



# Background

## Adolescents and young adults with HIV (AYAH)

- Suffer a disproportionate burden and have poorer treatment outcomes in sub-Saharan Africa
- \*SEARCH study: **55%** of youth 15-24 years vs **80%** of adults >24 years achieved viral suppression after 2 years
- Have lower rates of retention in care
- Face many barriers to medication adherence and remaining in care during a time of many major life events



# Hypothesis: Dynamic HIV care model supporting patients and providers through these changes could improve clinical outcomes vs standard of care

Interviews with AYAH	Barrier	Intervention [PRECEDE Concept]	Postulated Mechanism of Action
What makes taking medication HARDER? e.g. "Eventually I got married and had to stop medication for the sake of my husband as I had not disclosed my status."	Life-stage changes (marriage, school) that affect adherence	<b>Life-stage specific counseling</b>  [Predisposing]	Recurrent re-evaluation of life-stage events builds relationship between AYAH providers, and enables them to promptly act when social structures change
What makes attending appointments HARDER? e.g. "Sometimes I don't want other people to see me when I come on my day of convenience";	Structural	<b>Choice of clinic access</b>  [Enabling]	Choice respects developing sense of autonomy among AYAH; multiple options allow clinic access be tailored to the case-specific pressures
Do you think that knowing your viral load helps you take your medications better? 88% replied yes; "It helps me because it gives me courage to take my medication"	Feedback/motivation for adherence	<b>Rapid viral load feedback &amp; counseling</b>  [Reinforcing]	Prompt identification of adherence issues. Concept of viremia adapts to abstract thinking development among AYAH.

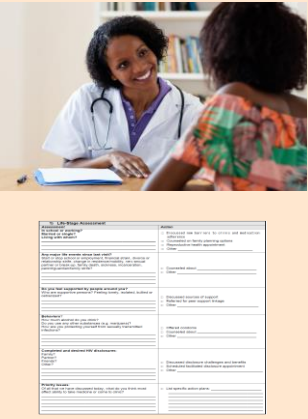
Green, L.W. (1974). Toward cost-benefit evaluations of health education: some concepts, methods, and examples. *Health Education Monographs* 2 (Suppl. 2): 34-64.

Green, L.W., Kreuter, M.W. (1992). CDC's Planned Approach to Community Health as an application of PRECEDE and an inspiration for PROCEED. *Journal of Health Education* 23(3): 140-147



# SEARCH-Youth Study Intervention

- Barrier**
- Life-stage changes that affect adherence**
- Structural barriers to care**
- Feedback/motivation for adherence**
- Isolated providers struggle to address challenging cases**



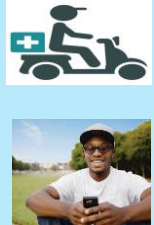
**Life-stage Assessment**

- Start of each visit
- Guides discussion between providers and AYAH to reveal life events and issues.
- Prompts action to address new issues (e.g. referral to counseling for depression, assistance with disclosure)

*Changes the AYAH clinical encounter on multiple levels:*


- *AYAH-provider interaction*
- *Clinic operations*
- *AYAH-cognition/communication*
- *Inter-provider collaboration*

**Choice of clinic Access**



- Offered to address barriers to the next visit.
- After-hour visits, phone visits, offsite drug delivery

**Rapid viral load feedback**



- Results shared with patient in < 72 hours.
- Positive feedback or prompt discussion of adherence issues

**Provider E-collaboratives**



**3- months Fup visit**

A 22 year old male barber who started ART 3 months ago came into the clinic 2 days ago for his scheduled routine visit. His baseline VL was 72500 copies/ml. Three weeks later, his VL reduced to 253 copies/ml before he travelled out of the the study area because of work related issues. NB. He moved with enough drug supply and he reports good adherence to his medication.

Fear and worry that attending the clinic would risk disclosure to his salon customers that he has HIV was the only adherence barrier identified during life stage assessment.

- Providers often isolated in rural clinics
- WhatsApp platform for discussion of especially difficult cases
- Encrypted & de-identified info only

# Methods

Design: Cluster randomized control trial

- *Randomization unit: clinics*

Population: Females and males aged 15-24 years

*Inclusion criteria: HIV-infection, care in study clinic*

Setting: Government sponsored health clinics in rural western Kenya and southwestern Uganda

Time period: Mar 2019- Mar 2022

## **Descriptive:**

- Baseline demographics and
- Non-study secular influences

**Primary endpoint:** Percent with viral suppression (HIV RNA < 400c/mL) after 2 years of individual follow up

- Excludes participants who moved out of study region or transferred care
- Compared by arm with targeted minimum loss-based estimation (TMLE)\*
- Pre-specified one-sided hypothesis testing at the 5% significance level

**Power:** With 28 clinics each with 50 AYAH , the study would have 83% power to detect a difference in virologic suppression 24% between control vs intervention clinics

## **Secondary endpoints:**

- Intervention implementation and uptake

\*Balzer, Biostatistics, 2021

# Results

Consort

Baseline characteristics

Intervention implementation

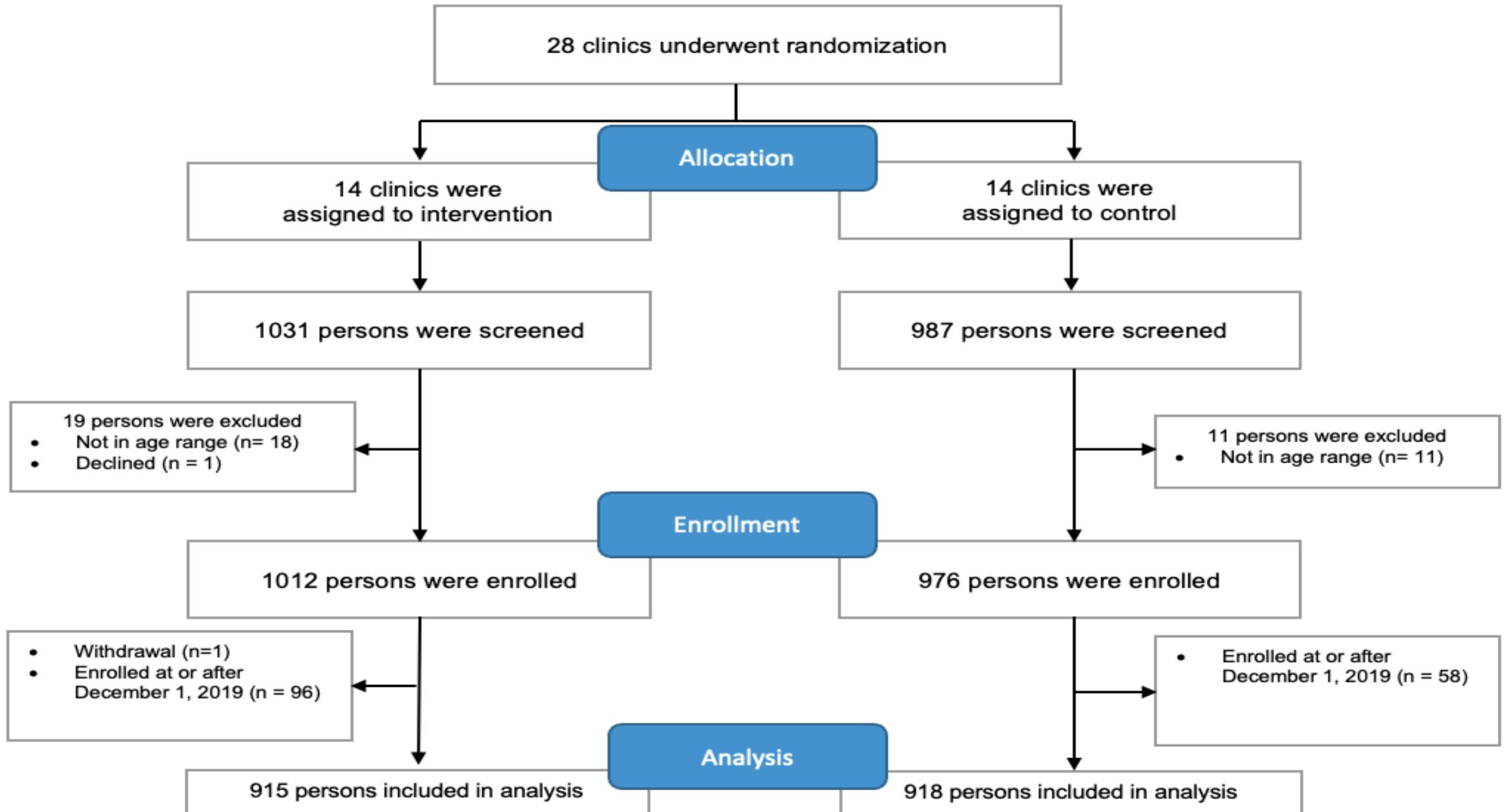
Primary endpoint: viral suppression at 2 years

- Subgroups and sensitivity analyses





# CONSORT





# Baseline characteristics

82% female

Median age: 21 years

40% single

58% had at least 1 child

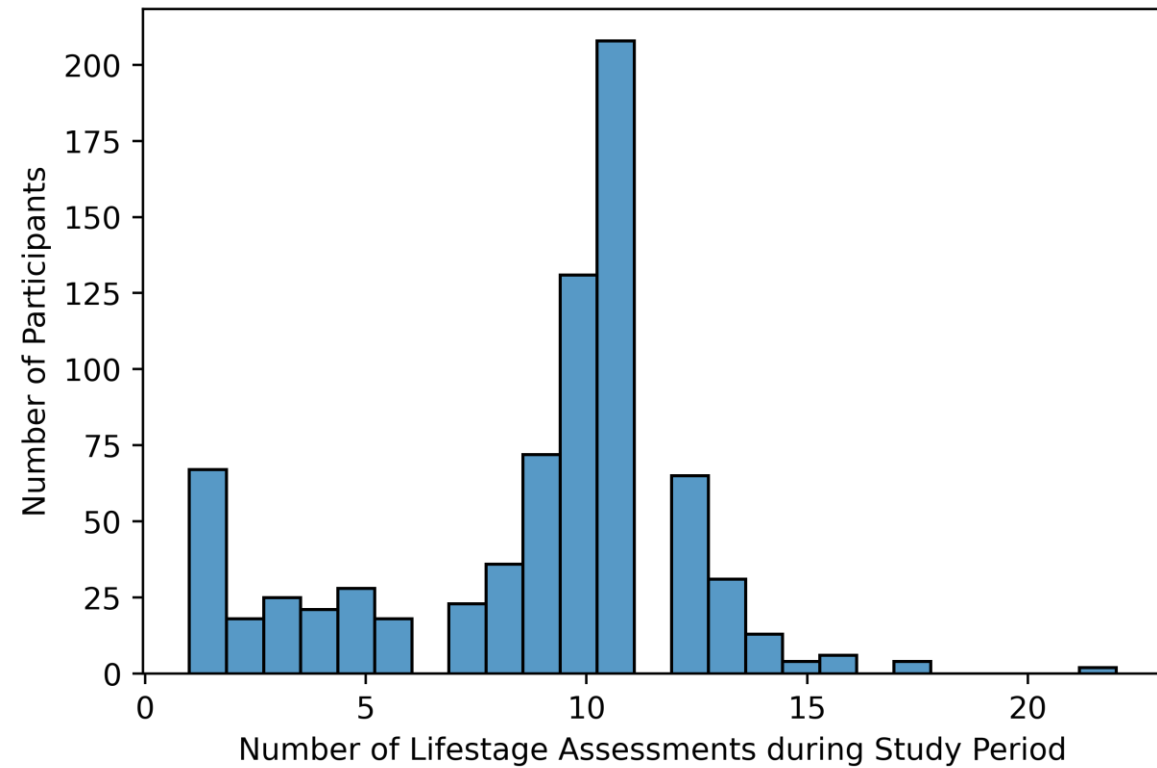
75% on EFV/3TC/(TDF or ABC) at enrollment

74% suppressing viral replication <400 c/mL

Care status

- 34% recently engaged: started ART within the prior 6 months or at enrollment
- 62% engaged: started ART more than 6 months ago, with a clinic visit in prior 6 months
- 4% re-engaging: started ART more than 6 months ago, without a clinic visit in prior 6 months

# Intervention Implementation: *Life Stage Assessments*



## Life-stage Assessment

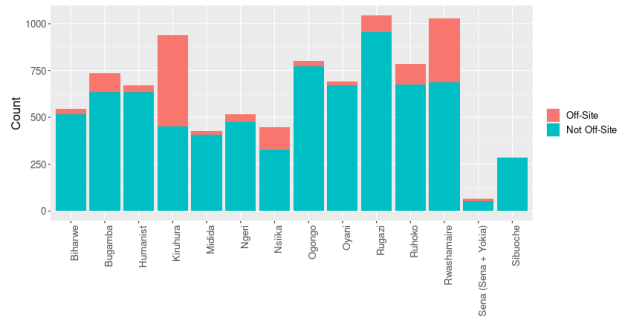
- Guides discussion between providers and AYAH to reveal life events and issues.
- **At the start of routine visits , ~ every 3 months**



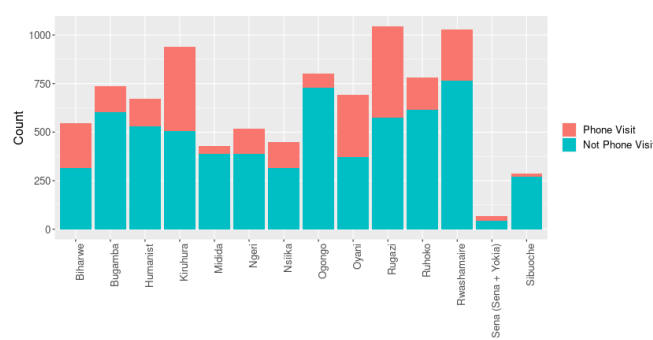
84.5% of 785 participants, remaining in the region during the two-year study period, had 4+ life-stage assessments

# Intervention Implementation: *Alternative Access Choice*

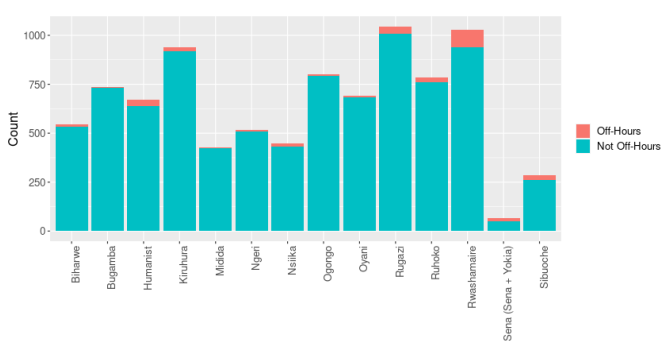
### Off-site appointment



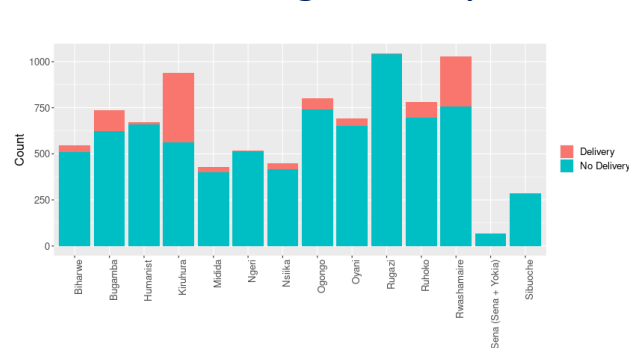
### Phone appointment



### Off-hours appointment



### Off-site drug delivery



### Alternative Access Choice

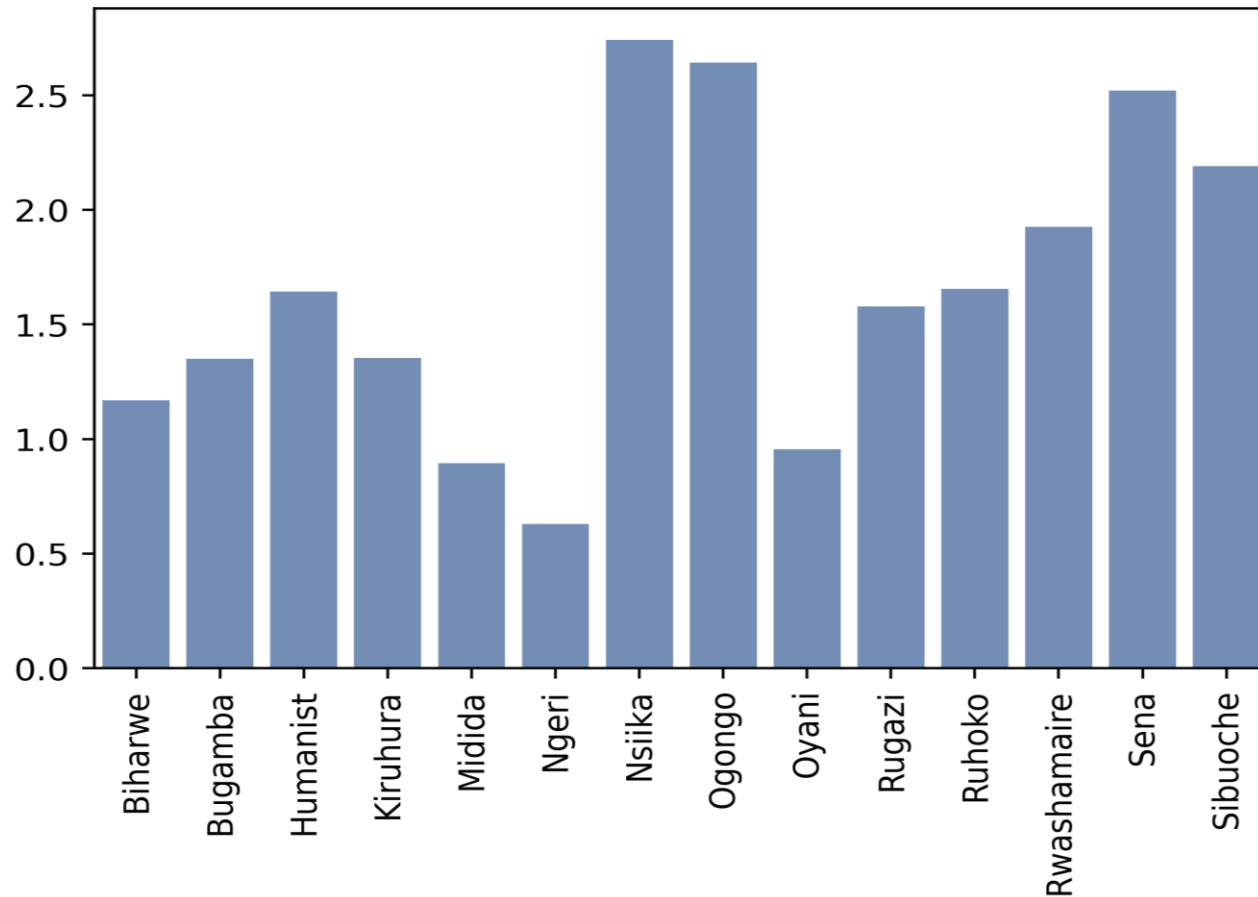


- To address barriers to the next visit.
- Offered if prompted and planned per participant choice

- Off-site, phone appointments, drug deliver were selected by many participants
- Varied by clinic
- Options useful during COVID disruptions

# Intervention Implementation: *Rapid Viral Load Feedback*

Mean VL delivery time (in days)



- Median time to results delivery was 38.4 hours
- In 13/14 clinics, over 80% of VL results delivered within 72 hours



# Intervention Implementation: *Provider E-collaboratives*

253 chats initiated for  
128 unique participants

## Provider E-collaboratives



### 3- months F/up visit

A 22 year old male barber who started ART 3 months ago came into the clinic 2 days ago for his scheduled routine visit.

His baseline VL was 72500 copies/ml. Three weeks later, his VL reduced to 253 copies/ml before he travelled out of the study area because of work related issues.

NB. He moved with enough drug supply and he reports good adherence to his medication.

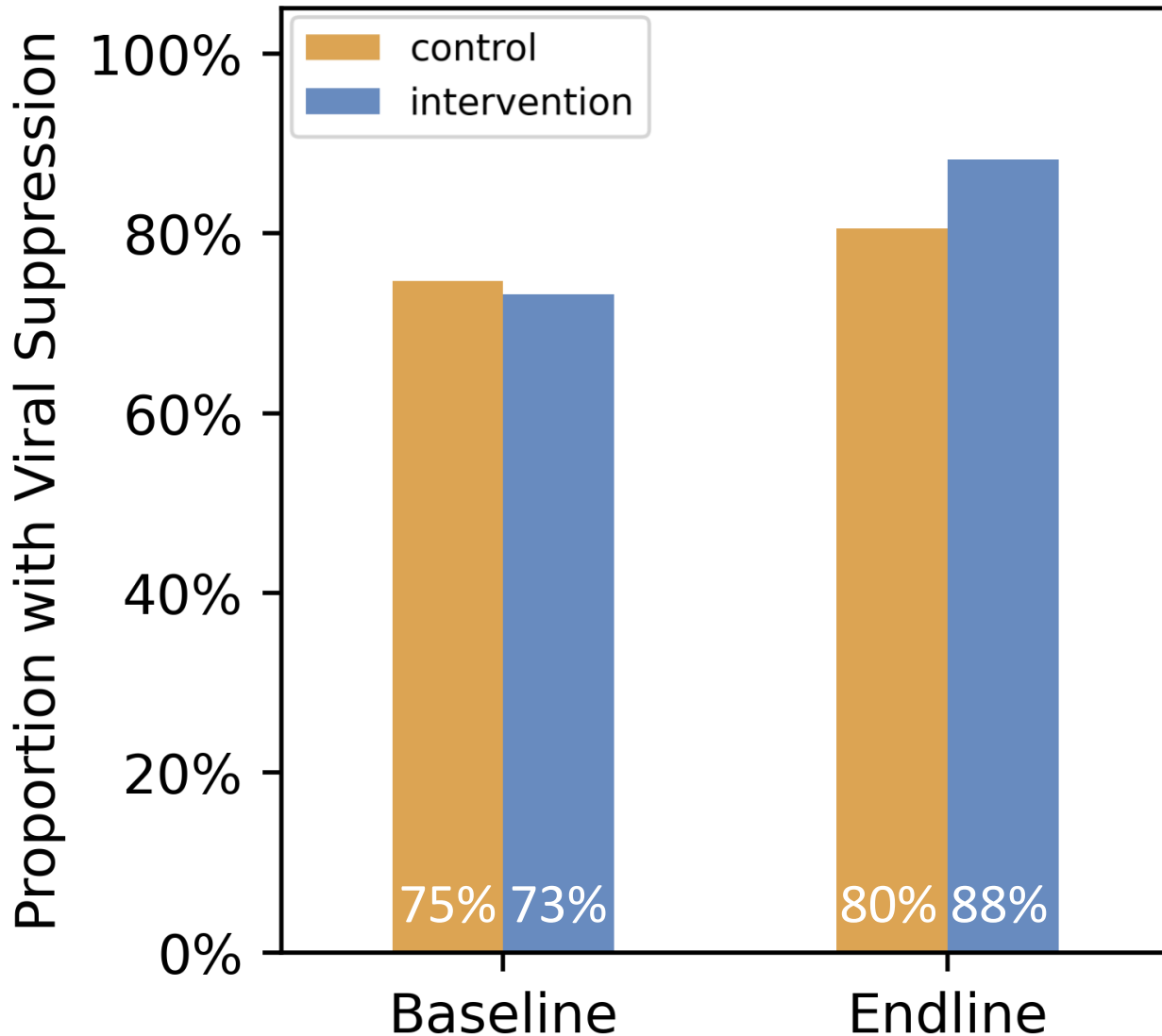
Fear and worry that attending the clinic would risk disclosure to his salon customers that he has HIV was the only adherence barrier identified during the stage assessment.

- WhatsApp platform for discussion of especially difficult cases
- Encrypted & de-identified info only

## • Examples of Content:

- *Guidance about whether to order HIV resistance testing*
- *Ideas on how to accommodate school schedule for visits*
- *Assistance with navigating disclosure to school admin*
- *Shared resources on regional COVID testing options*

# Primary Endpoint: *Viral suppression at 2 years*

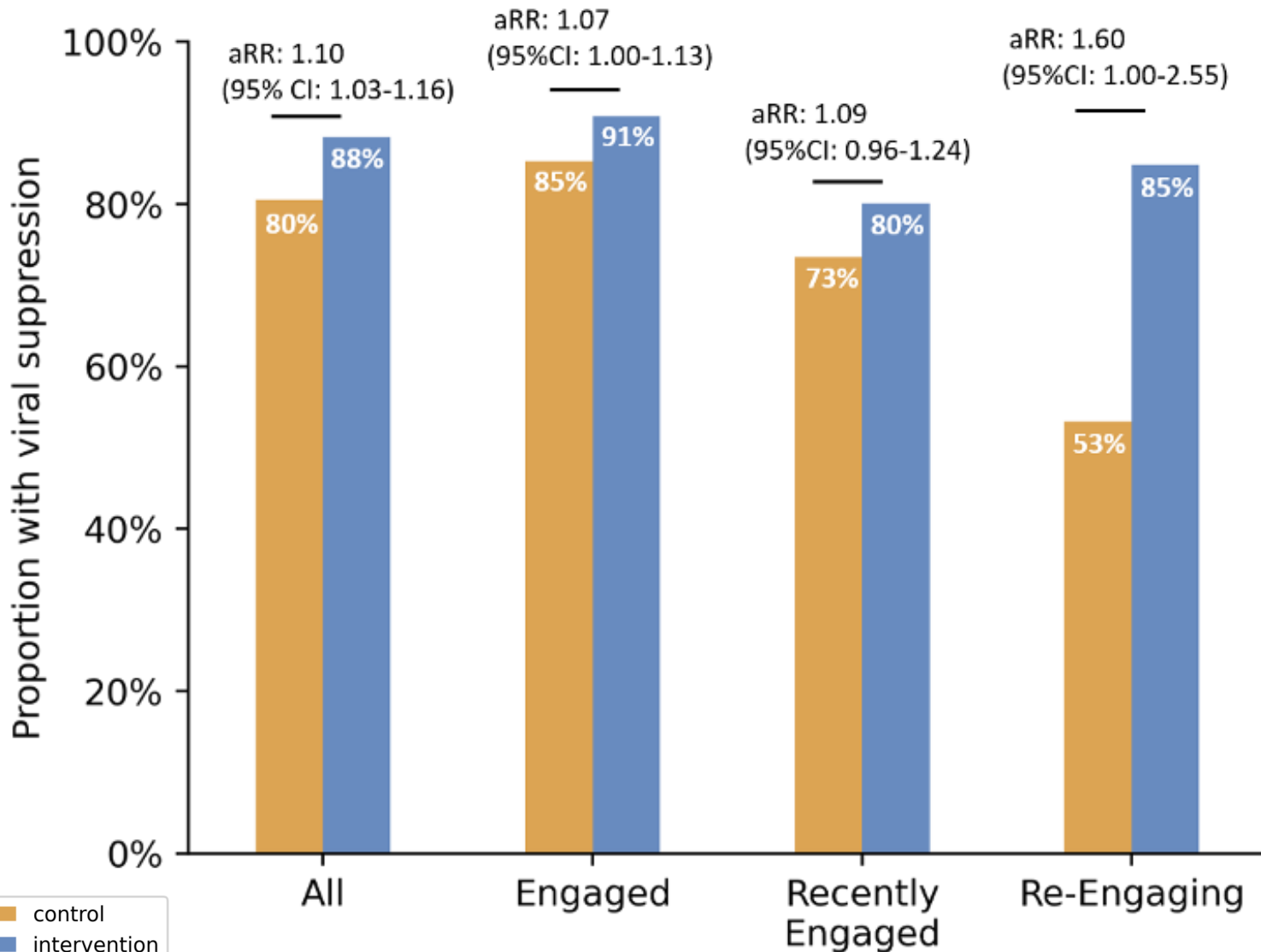


} 15% increase in intervention  
} 5% increase in control

Endline: **88% in intervention**  
vs. **80% in control**

**Relative effect: 1.10**  
(95%CI: 1.03-1.16); p=0.002

# Primary Endpoint: *Subgroups*



Improvements across subgroups defined by *baseline care status*

Especially those re-engaging

**85% in intervention**

vs. **53% in control**

**Relative effect: 1.60**

(95%CI: 1.00-2.55) p=0.03

Engaged – started ART 6+ mo ago, with a clinic visit in past 6 mo

Recently Engaged – started ART ≤6 mo or at enrollment

Re-engaging – started ART 6+ mo ago, without a clinic visit in past 6 mo



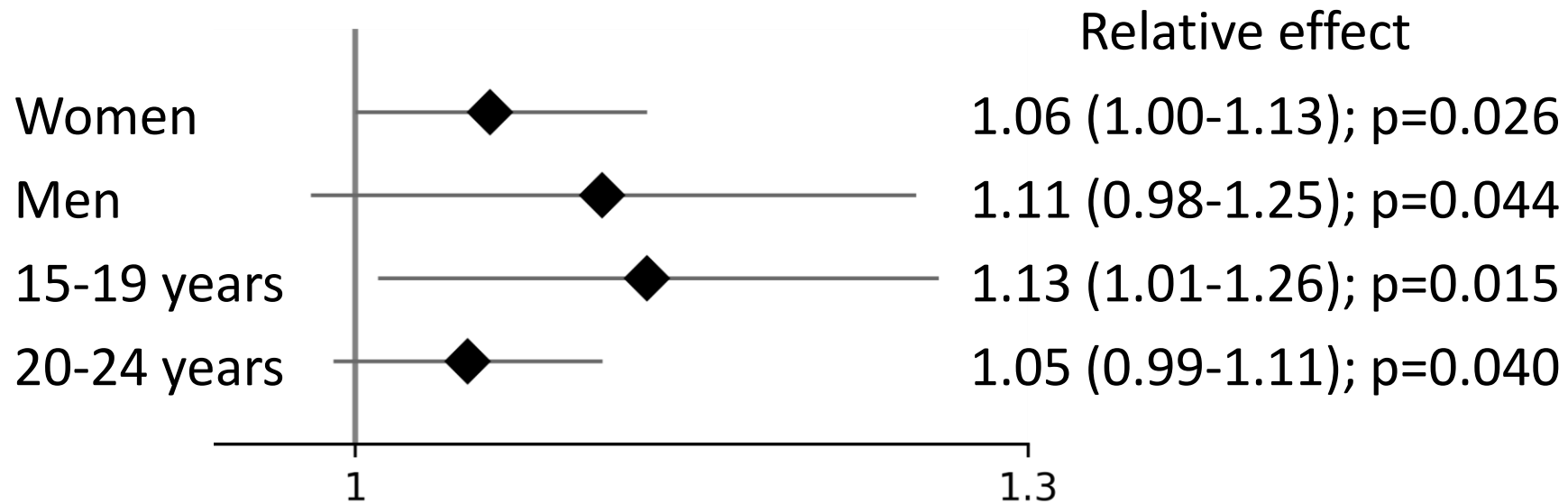
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# Primary Endpoint: *Subgroups 2*

Improvements across subgroups defined by *sex* and *age group*

Largest effect among the younger age group

- **85% in intervention** vs. **76% in control**
- **Relative effect: 1.13** (95%CI: 1.01-1.26); p=0.015

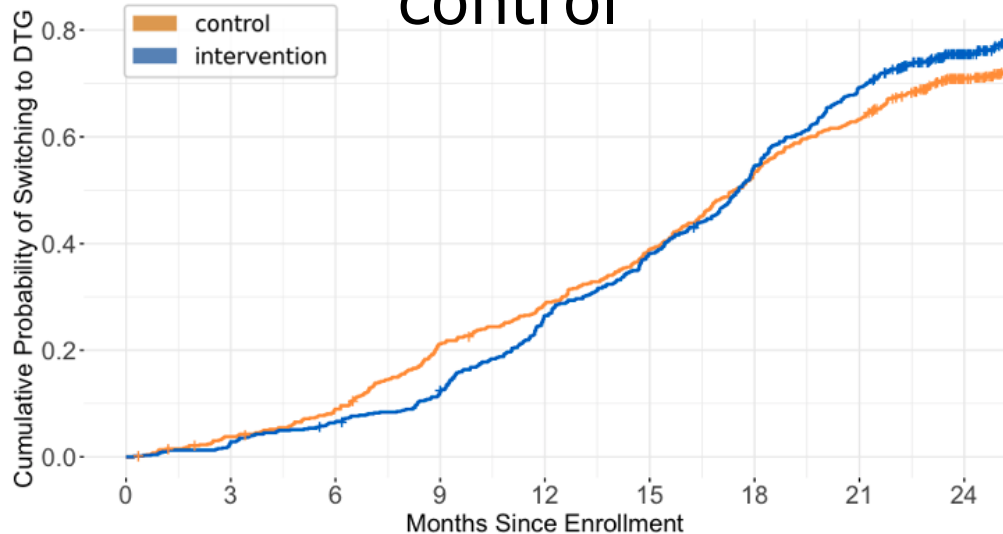




# *Did the intervention still benefit participants who had switched to dolutegravir (DTG)? YES*

**Majority of participants switched to DTG in both arms during study period**

77% in intervention vs. 71% in control



**The intervention was associated with higher probability of virologic suppression**

In persons who had switched to DTG

- 92% in intervention vs. 88% in control

In persons who had not switched to DTG

- 70% in intervention vs. 64% in control



# Summary of primary endpoint results

Multi-level SEARCH-Youth intervention increased virologic suppression compared to standard care

- Overall and for key subgroups
- During a period of transition to dolutegravir and the COVID-19 pandemic

Added to current efforts, life-stage-based assessment and support could help bring AYAH closer towards a goal of universal virologic suppression



# Acknowledgments

Community and government partners in Uganda and Kenya



*SEARCH- youth retreat  
Last meeting pre-COVID*

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