Early ART Uptake and Adherence: The *Tambua Mapema Plus* Study

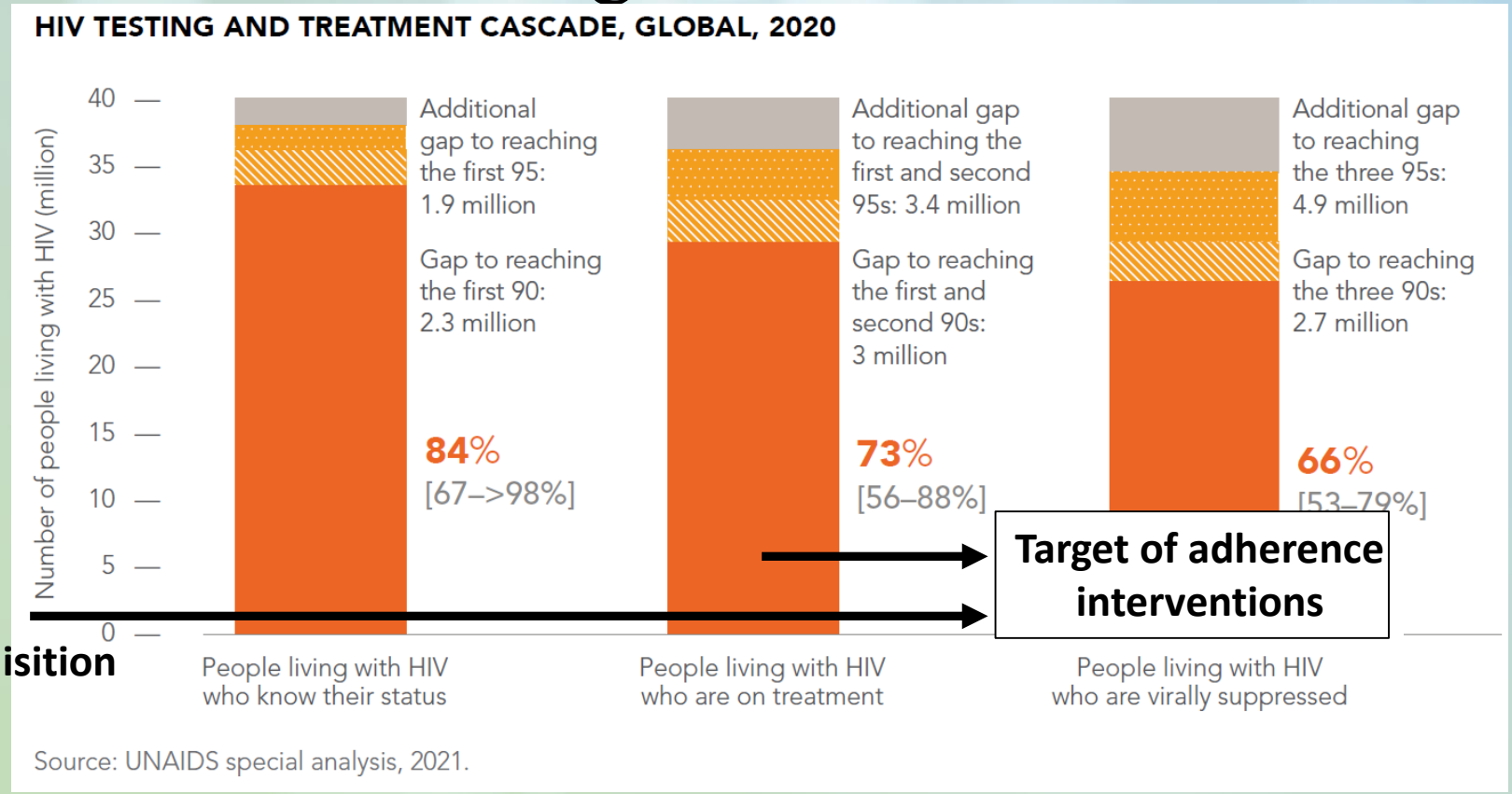
Susan M. Graham, MD MPH PhD
University of Washington

Adherence 2022 • November 7-9 • Washington, DC

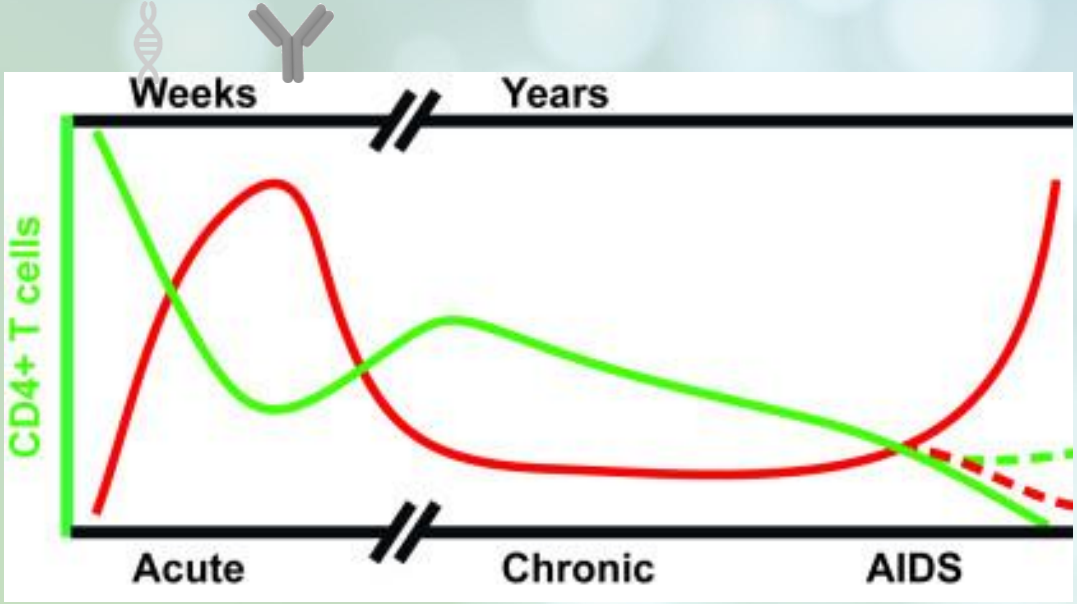
Disclosures

- I have received research support from Gilead and Cepheid

Global HIV Testing and Treatment Cascade



Acute HIV Infection (AHI)



10%-50% of onward transmission

Cohen NEJM 2011

- Acute HIV-1 infection, despite its short duration, can account for 10%–50% of all new HIV-1 transmissions, especially in persons who have multiple concurrent sex partners or high rates of partner change

- *"AHI is routinely missed in healthcare encounters, despite the presence of clinical, behavioral, and serological clues."*

– Kim Powers and Mike Cohen AIDS 2014

HIV Testing Intervention

- Point-of-care HIV-1 Qual Test (Cepeid Xpert®) used for all samples
- Detects HIV-1 nucleic acid at levels >1,000 copies/mL
- Samples positive by HIV-1 Qual can be tested with standard HIV rapid tests to distinguish acute from chronic HIV infection

Systematic Review, Agutu PLoS One 2019

Tambua Mapema Plus Trial

- To conduct a proof-of-concept study to determine outcomes of a **multi-component health facility-based intervention including**
- **HIV-1 RNA testing** to identify undiagnosed acute (RNA+, rapid test-) and prevalent (RNA+, rapid test+) HIV infection in adults aged 18-39 years seeking care for symptoms, compared to standard care
- Newly diagnosed patients linked to HIV care and **immediate treatment**
- **Partners notified and tested** with the same "enhanced" HIV testing intervention, with linkage to ART or PrEP as indicated

R01 AI124968 (MPI Graham, Sanders)

Tambua Mapema Plus Eligibility

- Aged 18-39
- HIV negative or unknown HIV status
- Scoring ≥ 2 on AHI risk score
  - 1 point each for:
    - ✓ age 18-29 years
    - ✓ reported fever
    - ✓ fatigue
    - ✓ body pains
    - ✓ diarrhea
    - ✓ sore throat
  - 3 points for:
    - ✓ genital ulcer disease

Sanders AIDS 2019

Stepped Wedge Design

Objectives:

- Use GeneXpert machines efficiently
- Capture baseline data at each site (3-6 months)
- Capture 6 months of intervention data at each site

Stepped Wedge Design at Six Sites

Clinic	0-3	4-6	7-9	10-12	13-15	16-18	19-21	22-24
Site 1	O	I	I					
Site 2	O	O	I	I				
Site 3		O	O	I	I			
Site 4			O	O	I	I		
Site 5				O	O	I	I	
Site 6					O	O	I	I
N enrolled	250	375	500	500	500	375	250	125

I = intervention period, N = number, O = observation period

Graham JMIR Res Protocols 2020

Results – HIV Diagnoses

Outcome	Observation Period	Intervention Period
Enrolled	1374	1500
Tested	352 (25.6%)*	1500 (100%)†
Chronic infections	13	35
Acute infections	—	2
Total infections	13	37
Yield among enrolled	0.9%	2.5%

* 92% of participants would have accepted an HIV test if offered
† 5% of eligible individuals refused due to HIV testing requirement

- Odds of a new diagnosis: 2.2 (95% confidence interval: 1.4–3.5)
- 1 chronic HIV infection for every 40 patients tested and 1 AHI patient for every 750 patients tested

Agutu PLoS One 2021
Sanders HIV Medicine 2022

Treatment and PNS Outcomes, 6 weeks

Outcome	Observation N=13	Intervention N=37
Linked to ART	9 (69%)	33 (89%)
Enrolled in research cohort	—	30 (81%)
Accepted enhanced aPNS	—	16 (53%)
Partners named	10 (7 regular, 3 casual)	65 (39 regular, 26 casual)
Partners tested	3 (1 regular, 2 casual)	10 (8 regular, 2 casual)
Partners with chronic HIV	2	2 regular
Partners with acute HIV	—	0
Partners starting PrEP	—	4 regular

- More index cases were successfully linked to ART in the intervention period (p=0.05)
- Ratio of named partners to index 1.76, tested partners to index 0.27
- Disclosure and partner testing rates improved over follow-up

Sanders HIV Medicine 2022

Patient Experiences

- "*When I was tested, my viral load was high. Both of us [my wife and I] decided that I should take the drugs [ART] and use protection [condoms] to prevent transmission and a pregnancy. . . Starting medication immediately at least gives you time to change. . . to make up, what do we call this. . .? It helps with the acceptance [of HIV status].*" — 36-year-old male, 1st clinic visit after ART initiation

- *"I thought I was suffering from malaria and pneumonia. . . I was feeling tired, my stomach was aching, and I was just feeling pain all over. When I went to the chief's clinic, . . . I was told that I was going to be (HIV) tested. I got to know my HIV status and I got HIV treatment."*– 24-year-old female, 1st clinic visit after ART initiation

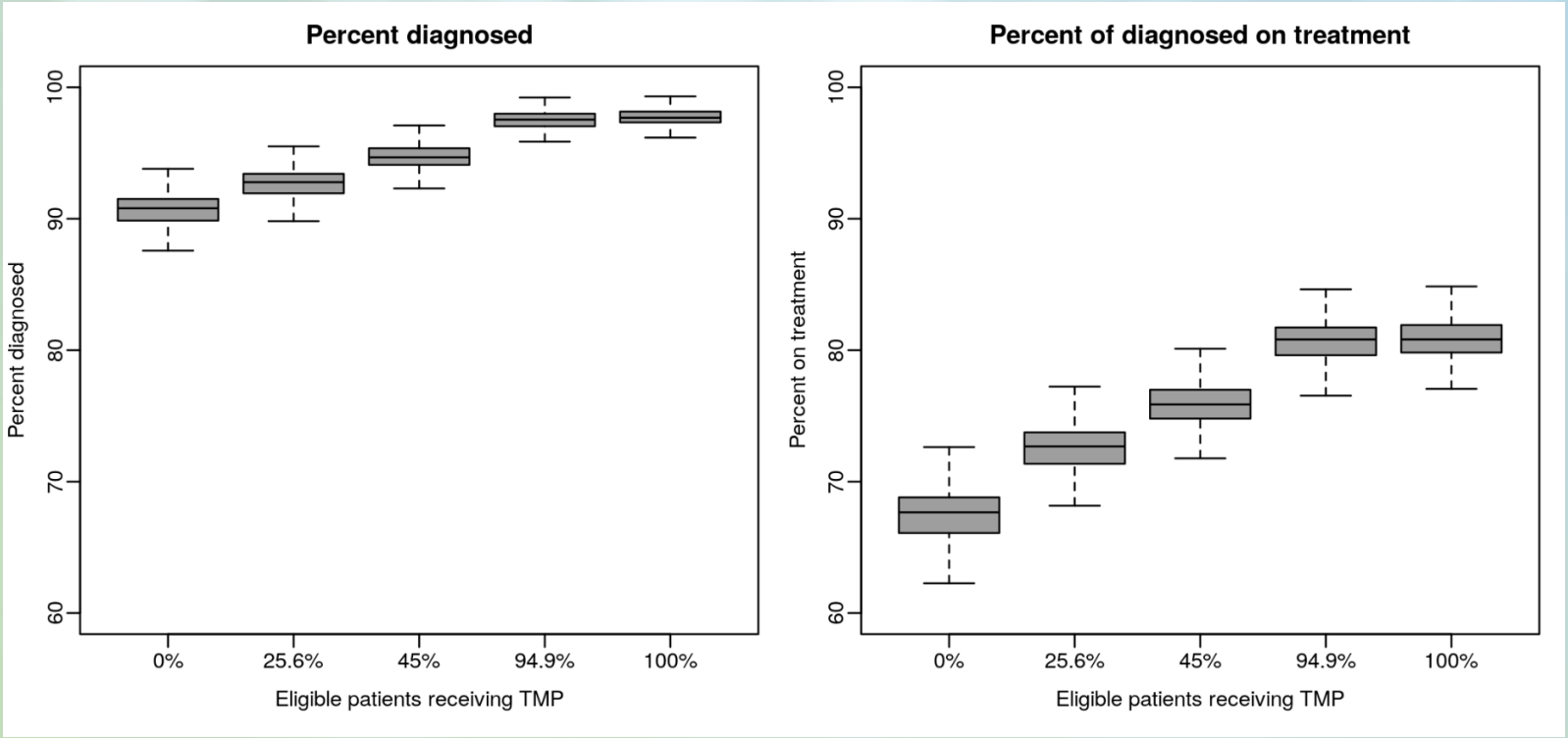
Van der Elst PLoS One 2022

TMP Impact and Cost-Effectiveness

- Developed an agent-based network model of HIV-1 transmission using TMP data and Kenyan statistics
- Estimated potential population-level impact of a scaled-up TMP intervention over 10 years
- Three scenarios modeled:
  - Standard care (PITC at current rates)
  - Scaled-up opt-out rapid testing with similar uptake as the TMP intervention
  - The TMP testing intervention as applied in the trial
- Evaluated cost-effectiveness of each scenario from Kenyan government perspective over a 10-year time horizon

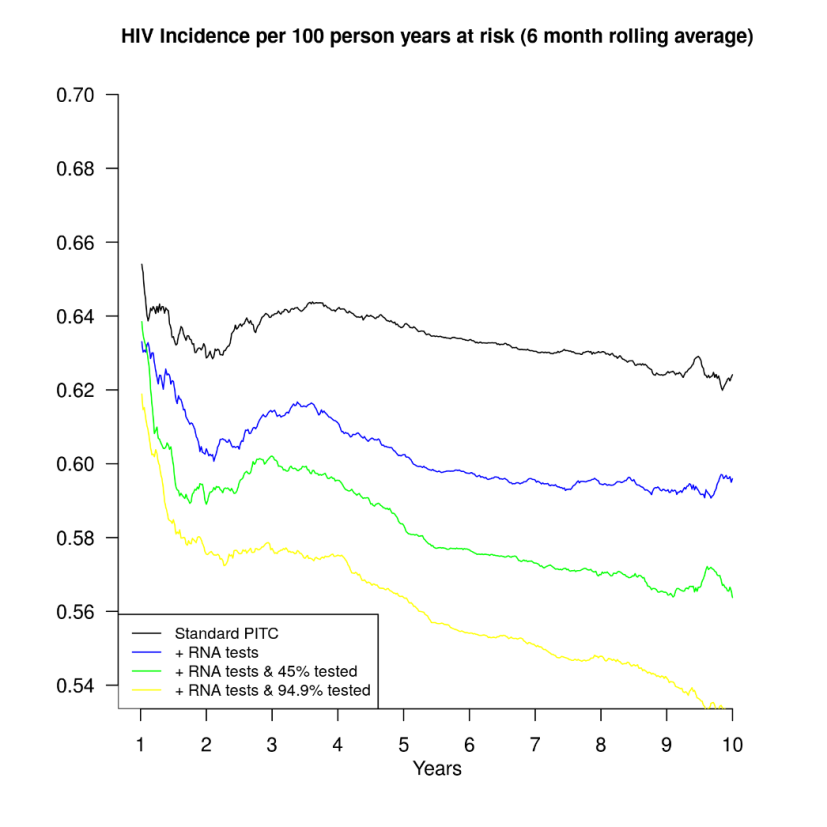
Hamilton JAIDS 2022, Babigumira BMJ Open 2022

Percentage of HIV-1-infected individuals aware of their status and percent diagnosed on treatment in Kenya over 10 years with current rates of PITC compared to four levels of TMP intervention uptake



Hamilton JAIDS 2022

HIV-1 incidence in Kenya over 10 years with current rates of PITC compared to three levels of TMP intervention uptake



- Percentage of infections averted was 1.0% for scaled-up PITC versus 9.4% for TMP
- Identifying acute HIV AHI among symptomatic outpatients is superior to scaled-up PITC, resulting in >95% knowledge of HIV status, and would reduce new HIV infections in Kenya

Hamilton JAIDS 2022

Cost-Effectiveness Results

- Average per patient cost of POC NAAT was $214 compared with $173.6 for scaled-up PITC and $47.3 for standard PITC
- Mean DALYs accumulated per patient for POC NAAT were 0.160 compared with 0.176 for scaled-up PITC and 0.214 for standard PITC
- Incremental cost-effectiveness ratio (ICER) comparing POC NAAT to standard PITC was $3,098 per DALY averted
- Scaled-up PITC had no advantage (lower cost but less effective)
- Results were sensitive to disability weights for HIV/AIDs and costs of antiretroviral therapy
- **TMP intervention offered to adults in Kenya was cost-effective and should be considered for inclusion as the standard of HIV testing**

Babigumira BMJ Open 2022

What if we offered PrEP to those testing negative in *TMP* (97.5 of participants%)?

- Four scenarios modeled:
  - PrEP for uninfected participants in disclosed serodiscordant couples
  - PrEP for individuals with concurrent partnerships (≥2 partners at interview)
  - PrEP for all uninfected individuals
  - PrEP integrated into the enhanced PNS component of TMP
- Providing PrEP to uninfected individuals in serodiscordant, disclosed partnerships had no impact on the overall number of infections in this model, but disclosure was only 3% in main partnerships
- Providing PrEP for all uninfected individuals identified through TMP averted as much as 12.7% of new infections but was not efficient based (NNT 200)
- Providing PrEP to individuals with concurrent partnerships (2.8% of infections averted, NNT 22.5) and to uninfected partners identified through enhanced PNS (4.6% of infections averted, NNT 27.6) was most efficient based on numbers needed to treat

Hamilton, in submission

Limitations

- *TMP* was conducted in Kenya and modeling reflects the Kenyan epidemic – local situations may differ
- Recently available antigen-antibody tests less expensive (Determine Early Detect), may work as well and is cheaper
- Different targeting strategies to enhance HIV test positivity could improve results
- Partner services results were disappointing – this is a challenging area for future research!

Key Take-Home Messages

- The need for prevention-effective ART adherence starts at HIV acquisition
- Motivation to adhere to HIV treatment is increased during health-setting for symptoms and when viral load is high
- Missed opportunities for timely HIV diagnosis and linkage to ART are undermining progress towards the 95/95/95 goals
- Testing for AHI in healthcare settings is cost-effective and should be scaled up
- PrEP should be offered to patients testing negative in health facilities, and is most efficient when offered to those with HIV+ partners and those who report concurrent relationships

Acknowledgments

- KEMRI
  - Eduard Sanders (co-PI)
  - Clara Agutu
  - Salome Chira
  - Fred Ogada
  - Elise van der Elst
  - Bernadette Kombo
  - Peter Mugo
  - Amin Hassan
- University of Washington
  - Steven Goodreau
  - Deven Hamilton
  - Joseph Babigumira
  - Carey Farquahar
- NIH
  - Usha Sharma
  - Wairimu Chege
  - R01AI124968