

INNOVAZIONE E RICERCA
PER LA PRATICA CLINICA

XIV Workshop Nazionale

**TERAPIA
E PREVENZIONE
DELL'INFEZIONE
DA HIV
E MICRORGANISMI
EMERGENTI**

III SESSIONE PREVENZIONE HIV & HCV

Croi 2022 Highlights
C. Torti (Catanzaro)



HIV and HCV trends: methodological hints and disparities

EFFECT OF DIRECT-ACTING ANTIVIRALS ON HCV INCIDENCE AMONG PEOPLE LIVING WITH HIV

Daniela Katinka Van Santen

Burnet Institute

Background

- Progress on WHO HCV elimination
 - By 2020, 30% reduction in new cases of HCV
- New absolute targets: $\leq 5/100,000$ py & $\leq 2/100$ py PWID
- Evidence of decreased incidence after DAAs were introduced in individual cohorts*
- Large international datasets allow assessing variability in trends in different settings

*Smit, Lancet HIV, 2021; Doyle, CID, 2020; Harney, CID, 2021

InCHEHC

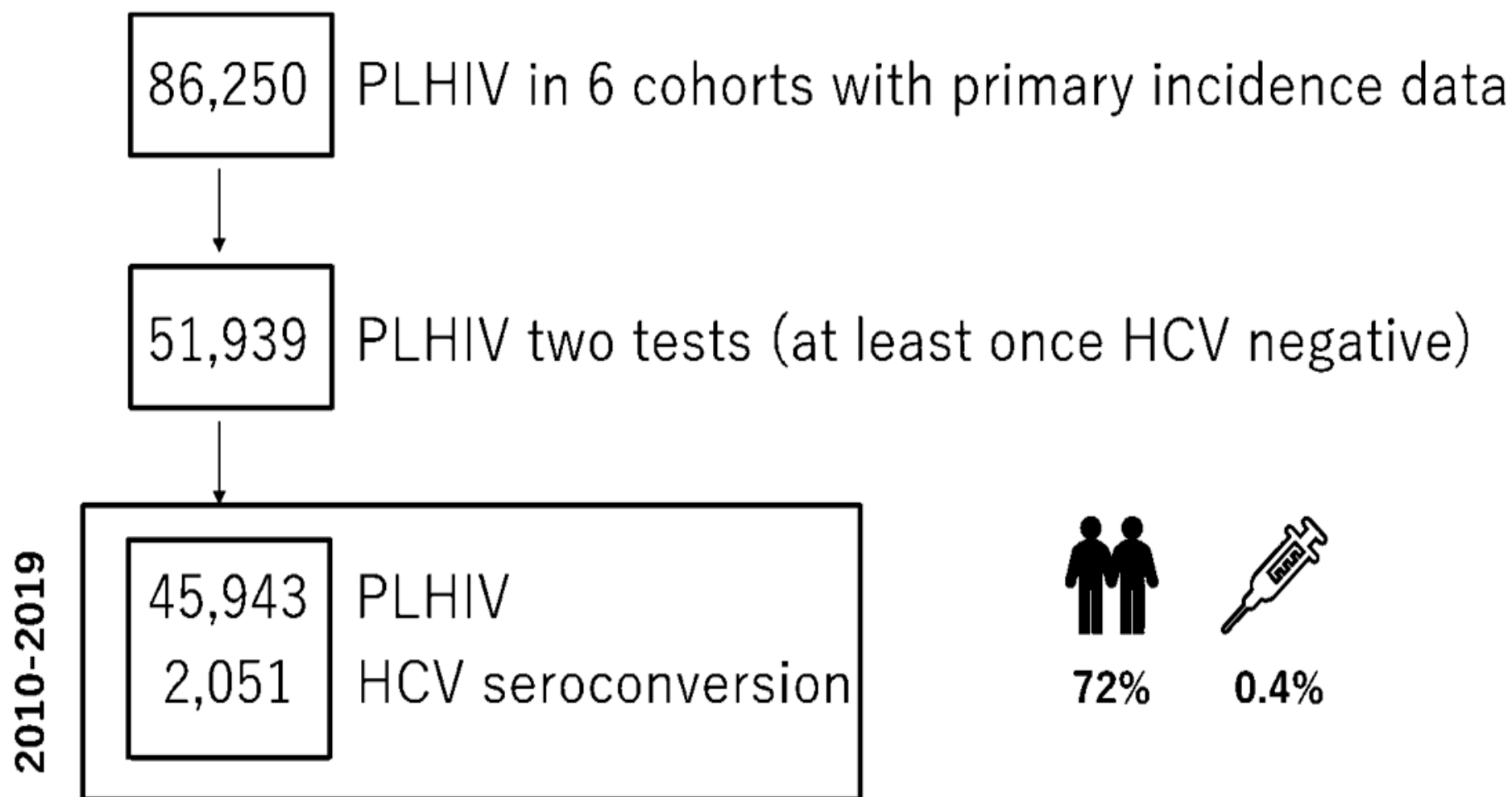
The International Collaboration
on Hepatitis C Elimination in
HIV Cohorts

Combined, the study
includes **N=105,402**
participants from 10
cohorts.

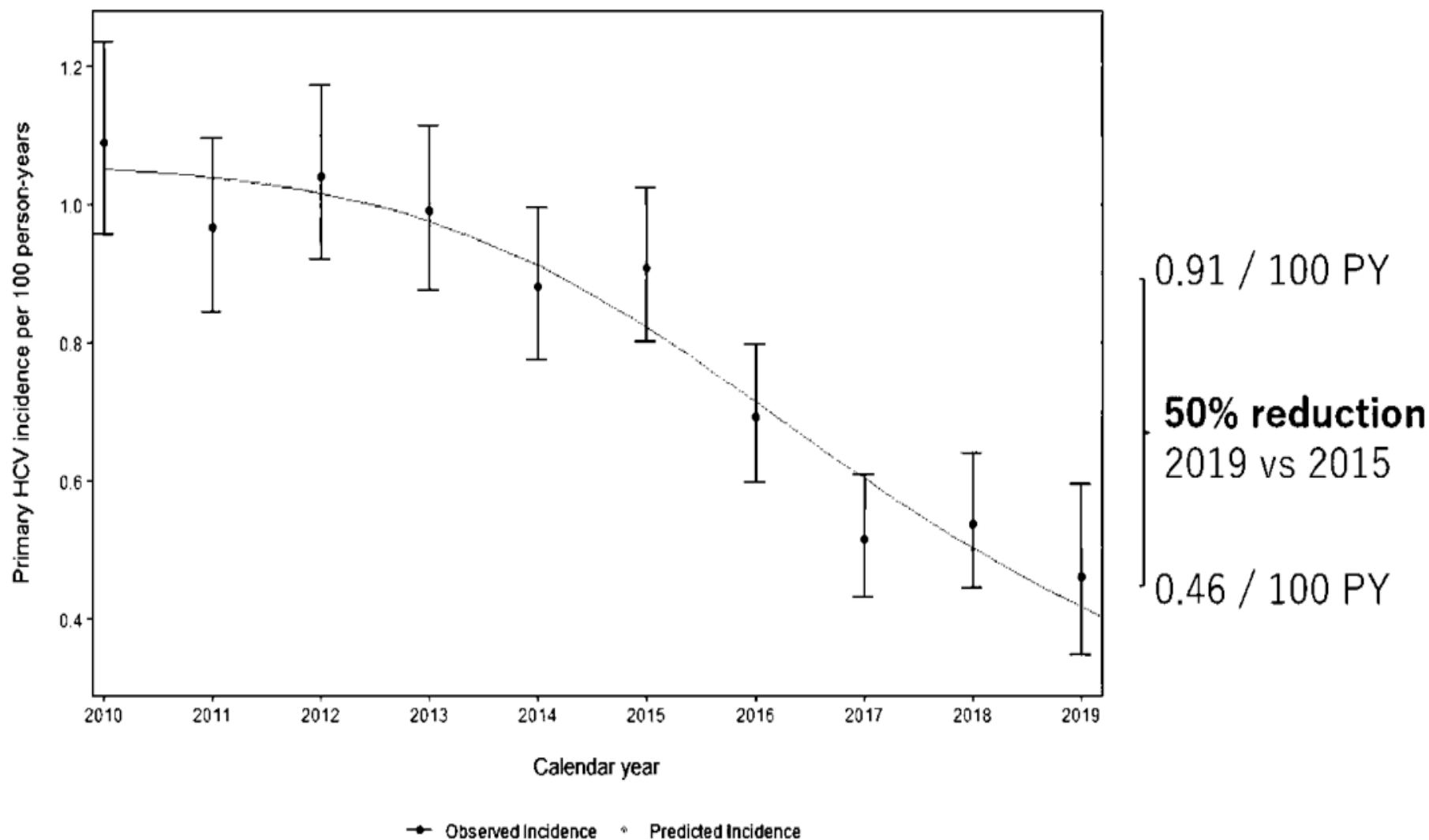


6 of 10 cohorts from Australia
& Europe have data on primary
HCV infection

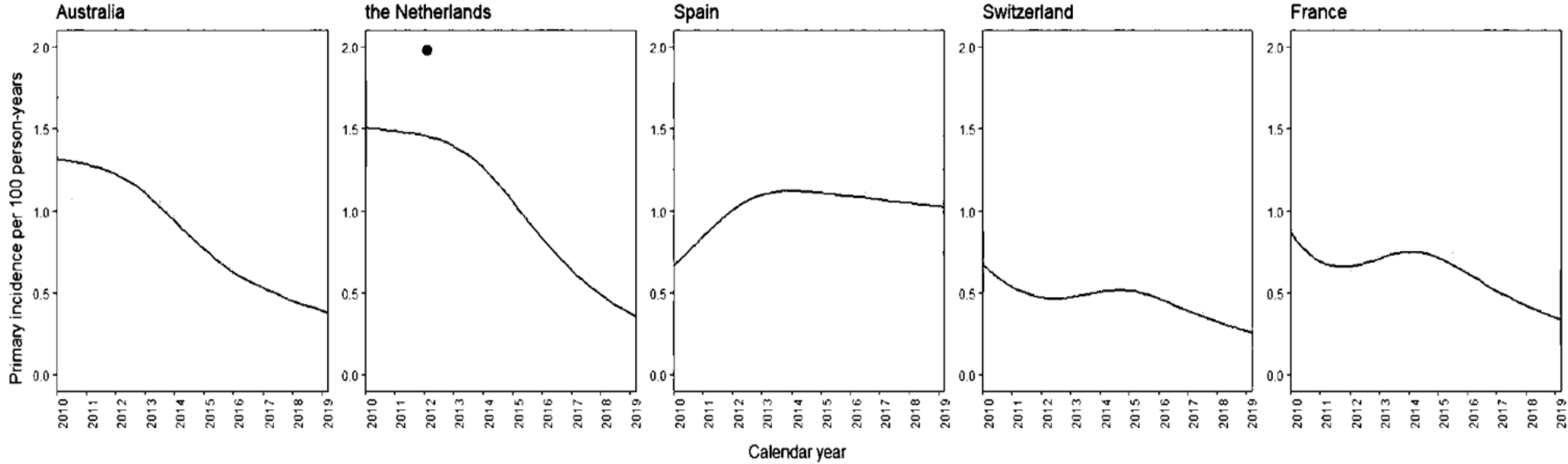
Flow chart: participant selection



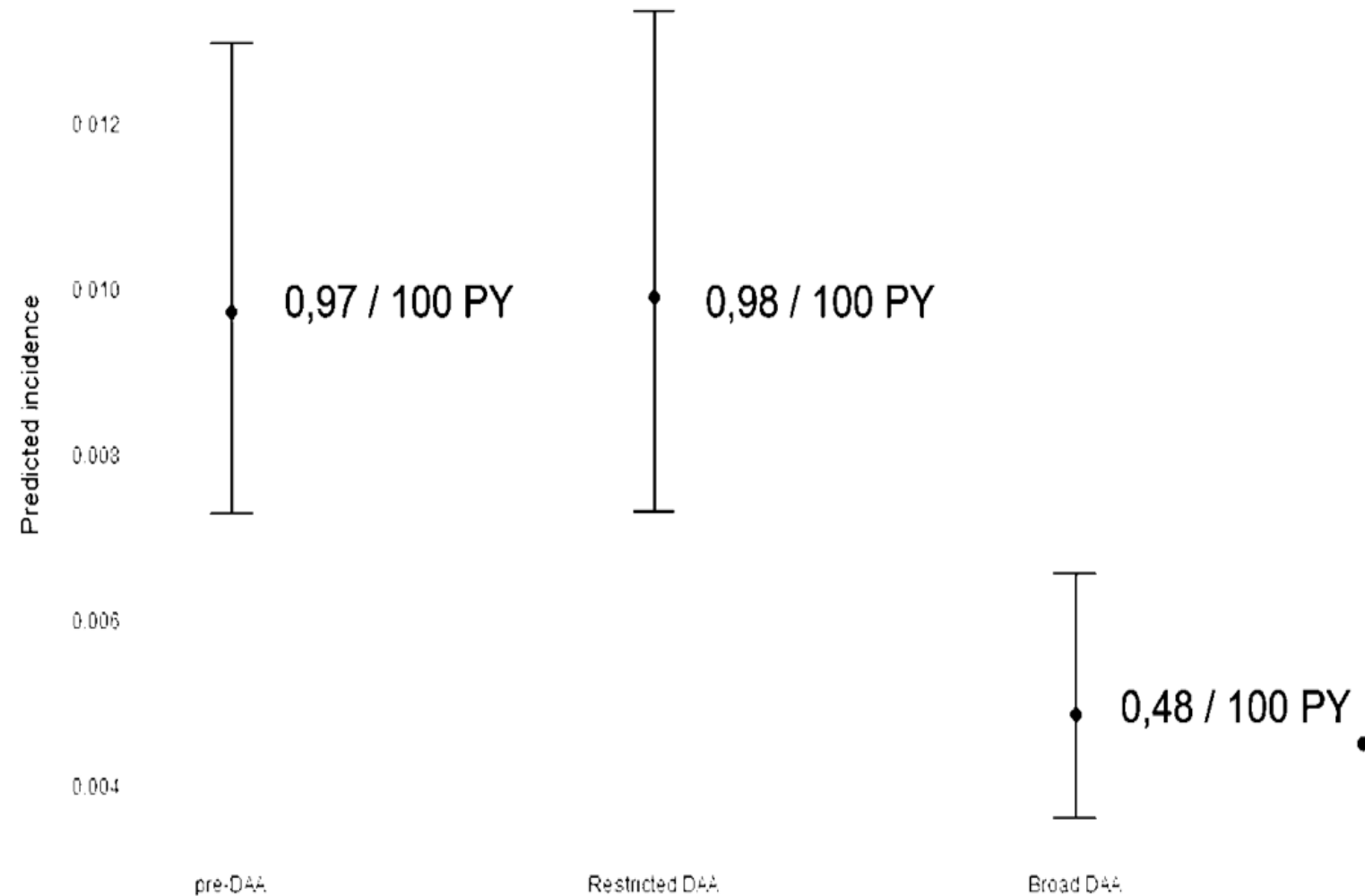
Trends in primary HCV incidence: pooled



Trends in primary HCV incidence: by country



Predicted HCV incidence per DAA period



ESTIMATING THE LIFETIME RISK OF A DIAGNOSIS OF HIV INFECTION IN THE UNITED STATES

Sonia Singh

Centers for Disease Control and
Prevention

Lifetime Risk

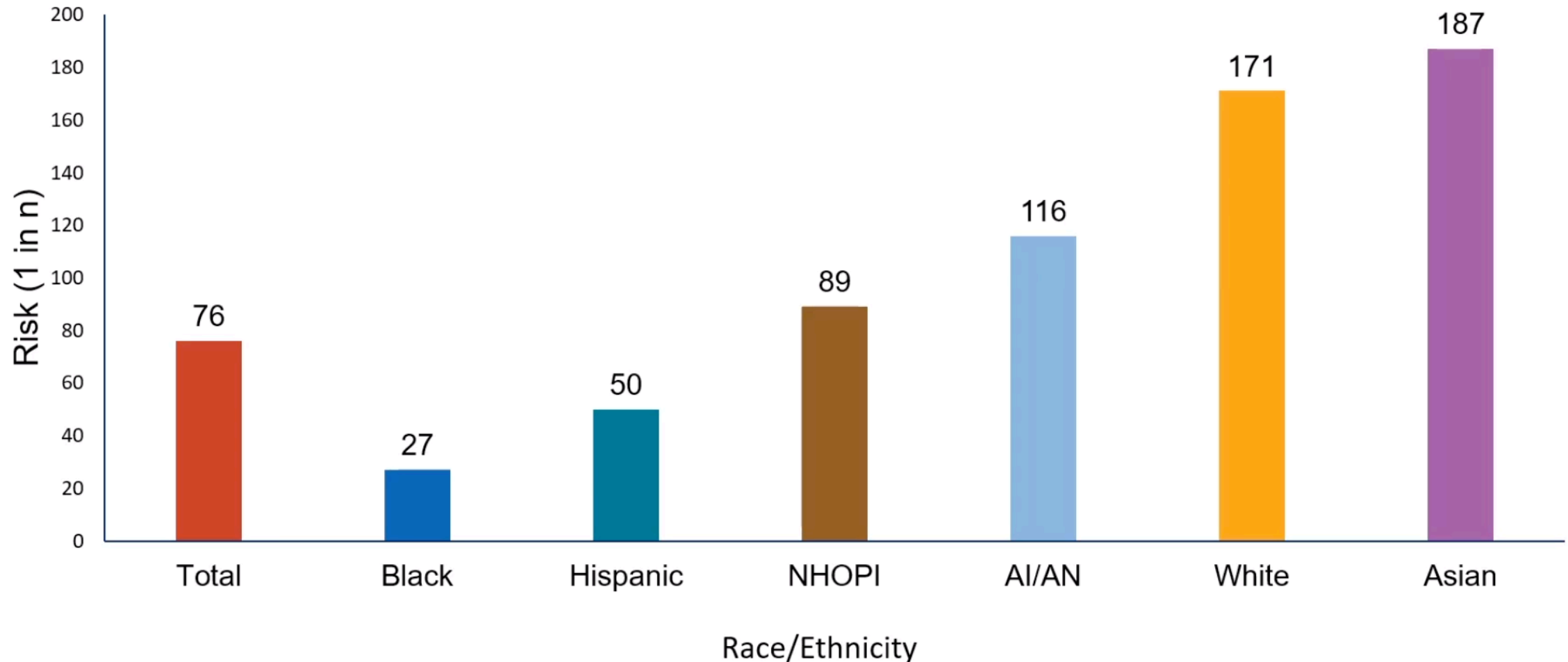
- Used to compare the burden of disease across populations
- Frequently used to describe cancer risk, but infrequently used for HIV infection
- More easily understood by general population
- Could be a useful tool for clinicians, outreach workers and policy makers

Methods

- Number of HIV diagnoses and non-HIV deaths were used to calculate probability of a diagnosis of HIV at a given age assuming 2017-2019 diagnosis rates continue
- Probabilities applied to a hypothetical cohort to obtain risk estimates
- Lifetime risk = Cumulative probability of an HIV diagnosis from birth (results presented as “1 in n”)
 - e.g., 20% = 1 in 5
- 10-year age-conditional risk = probability of an individual of a specific age receiving an HIV diagnosis within ten years
- DevCan 6.7.3, <http://surveillance.cancer.gov/devcan>
- Future analysis will estimate lifetime risk for transmission category

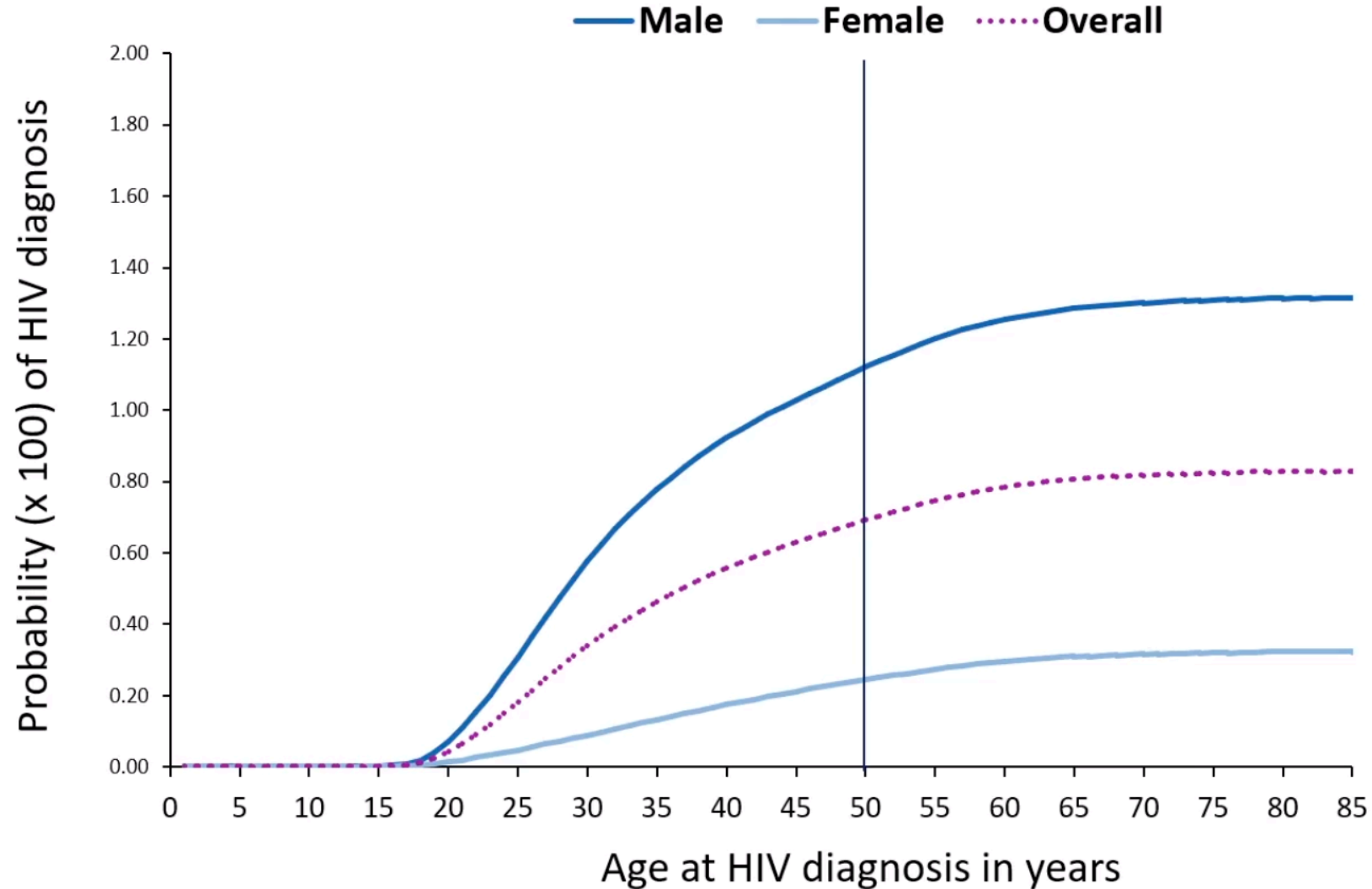
Lifetime Risk of an HIV Diagnosis Among Males

Assuming 2017-2019 Diagnosis Rates Continue

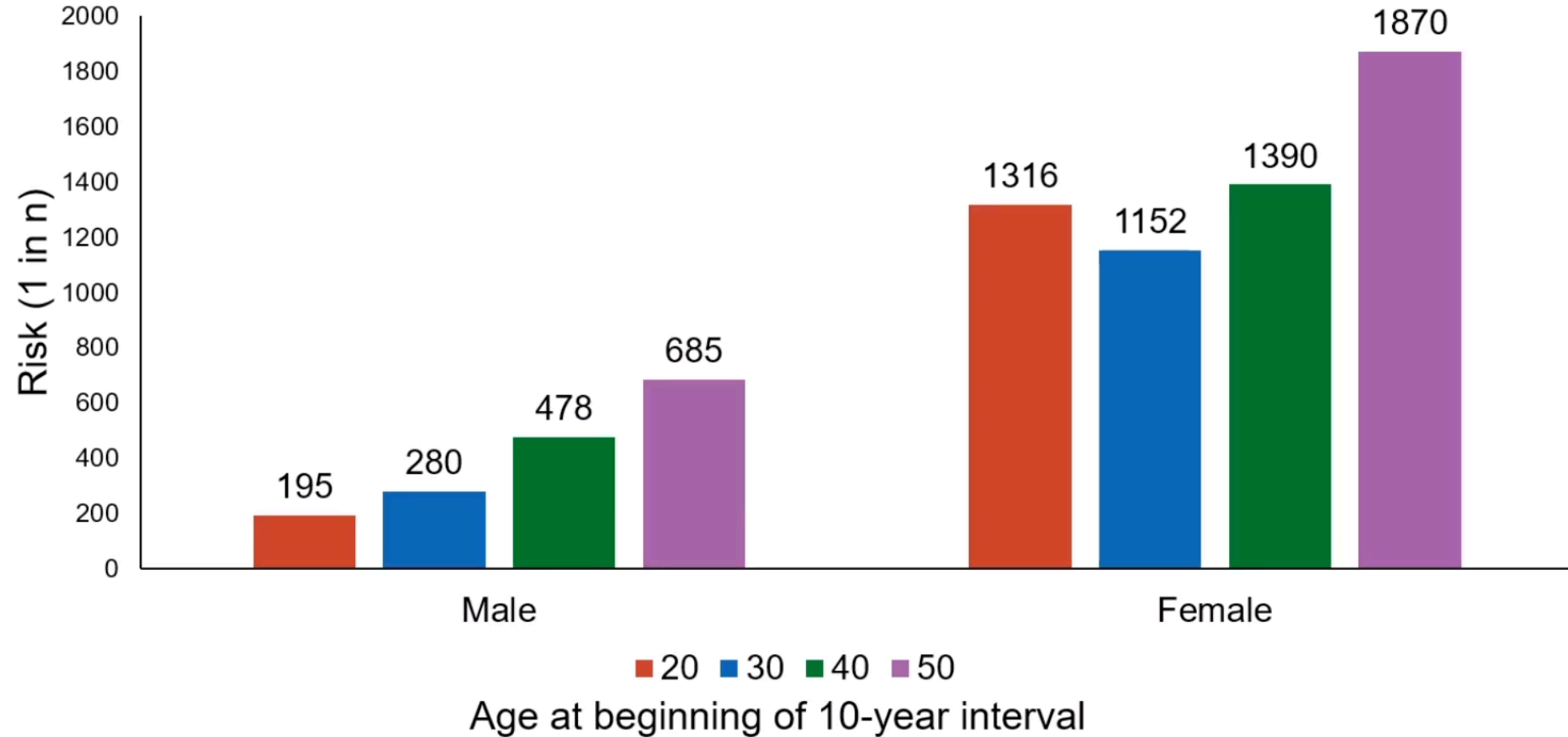


AI/AN = American Indian/Alaskan Native; NHOPI = Native Hawaiian/Other Pacific Islander

Lifetime Risk of an HIV Diagnosis by Age and Sex



10-Year Age-Conditional Risk of an HIV Diagnosis by Sex



Summary of Results

- **Compared to an earlier 2010-2014 analysis, lifetime risk has decreased**
- **Disparities persist by sex and race/ethnicity**
 - Risk among males:
 - Black/African American 6.9 times Asian males
 - Hispanic/Latino 3.7 times Asian males
 - Native Hawaiian/other Pacific Islander 2.1 times Asian males
 - American Indian/Alaska Native 1.6 times Asian males
 - White 1.1 times Asian males
 - Risk among females:
 - Black/African American 17.3 times Asian females
 - Hispanic/Latina 4.5 times Asian females
 - American Indian/Alaska Native 3.0 times Asian females
 - Native Hawaiian/other Pacific Islander 2.1 times Asian females
 - White 1.5 times Asian females

Summary of Results

- **Black/African American males 1 in 27, Hispanic/Latino males 1 in 50, Black/African American females 1 in 75**
- **Males and females experienced their highest risk of a HIV diagnosis at a young age**
- **9/10 areas of residence with the highest possibility of a lifetime HIV diagnosis were located in the South**

Conclusions

- **Lifetime risk may be a useful tool to more effectively communicate the burden of HIV overall and in specific communities**
- **Identify areas where prevention efforts can be accelerated**
- **Can help to highlight disparities**
 - e.g., the Ending the HIV Epidemic in the U.S. initiative is designed to scale up key HIV prevention and treatment strategies and is also working to address disparities
- **Groups with the highest 10-year age-conditional risk may suggest a need for more testing**

HIV perinatal transmission

Sibiude et al. Perinatal HIV-1 transmission in France: U=U for mothers on ART from conception. Conference on Retroviruses and Opportunistic Infections, abstract 684, 2022.

- Between 2000 and 2017, there were 15,959 live births to mothers living with HIV-1. Excluded from the analysis were 37 infants who were breastfed and 1292 infants who were lost to follow-up. Data were collected up to two years of age.
- The proportion of women receiving HIV treatment increased from 68% in 2000-2005 to 99.2% in 2011-2017, as did the proportion taking it at the time of conception (from 28% to 66%) and the proportion who had an undetectable viral load at delivery (from 70% to 93%).
- Perinatal transmission rates decreased steadily, from 1.1% in 2000-2005 and 0.7% in 2006-2010, to 0.2% in 2011-2017.
- Transmission was frequent when the mother did not receive treatment (8.3%).
- The earlier treatment was started, the rarer transmission was (0.1% before conception, 0.5% in the first trimester, 0.8% in the second trimester and 1.7% in the third trimester).
- While there were zero transmissions with a viral load below 50, the rate was 0.2% with a viral load between 50 and 400, and 2.4% above 400.
- Premature delivery also increased the risk, with a rate of 1.3% for babies delivered between 32 and 36 weeks and 2.1% for those delivered before 32 weeks.

Among 5482 HIV-infected women treated at conception, virally suppressed at delivery, and not breastfeeding, **no case of perinatal transmission was observed:**

(0/5482, 95% CI [0-0.07])

virtually eliminating in this group and this context the risk of perinatal transmission.

Immunoglobulin-free strategy to prevent HBV mother-to-child transmission in Cambodia: the ANRS 12345 TA-PROHM study

Olivier SEGERAL

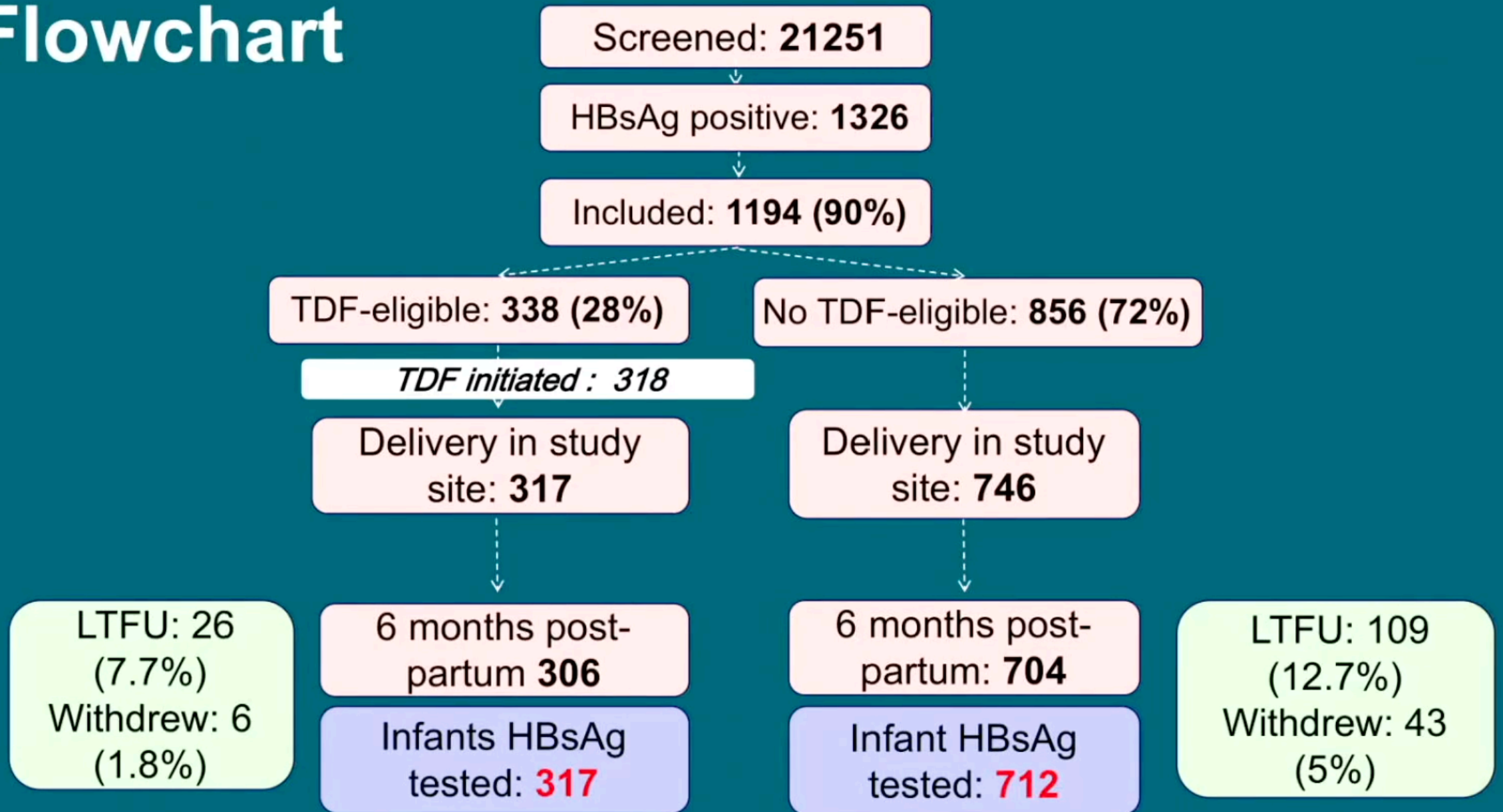
ANRS, University of Health Sciences

Phnom Penh, Cambodia

Disclosure: None



Flowchart



- **The rate of mother-to-child HBV transmission was 1.26% (95% CI, 0.34-3.2) among the cohort of infants who received immunoglobulin and 1.48% (95% CI, 0.4-3.74) among those who did not receive immunoglobulin.**
- **In addition, the transmission rate was 0% (95% CI, 0-1.41) among women who received TDF more than 4 weeks before delivery vs. 8.33% (95% CI, 1.75-22.5) among women who received TDF fewer than 4 weeks before delivery.**
- **For the women who were not eligible to receive TDF, the mother-to-child transmission rate was 0.98% (95% CI, 0.4-2.02), and 1.06% (95% CI, 0.39-2.3) in the absence of hepatitis B immunoglobulin.**

Results: Primary outcomes

Outcome	TDF-eligible			No TDF-eligible		
	N	Ev	% [95% CI]	N	E v	% [95% CI]
Positive HBsAg, all infants						
• Overall	317	4	1.26 [0.34-3.20]	712	7	0.98 [0.40; 2.02]
• According to TDF duration						
• > 4 weeks	254	0	0.00 [0.00-1.44]			
• ≤ 4 weeks	46	3	6.52 [1.37-17.90]			
• No TDF	10	1	10.00 [0.25-44.50]			
Positive HBsAg, infants without HB Ig						
• Overall	271	4	1.48 [0.40-3.74]	567	6	1.06 [0.39-2.30]
• According to TDF duration						
• > 4 weeks	227	0	0.00 [0.00-1.61]			
• ≤ 4 weeks	36	3	8.33 [1.75-22.5]			
• No TDF	8	1	12.50 [0.32-52.65]			

Conclusion

An HBIg-free strategy with maternal use of TDF & early vaccination at birth could be effective to prevent HBV MTCT if TDF is initiated more than 4 weeks before delivery

By using a therapeutic algorithm (HBeAg RDT/ALT) accessible in district hospitals, this strategy could be used in rural settings where most pregnant women are followed in Cambodia

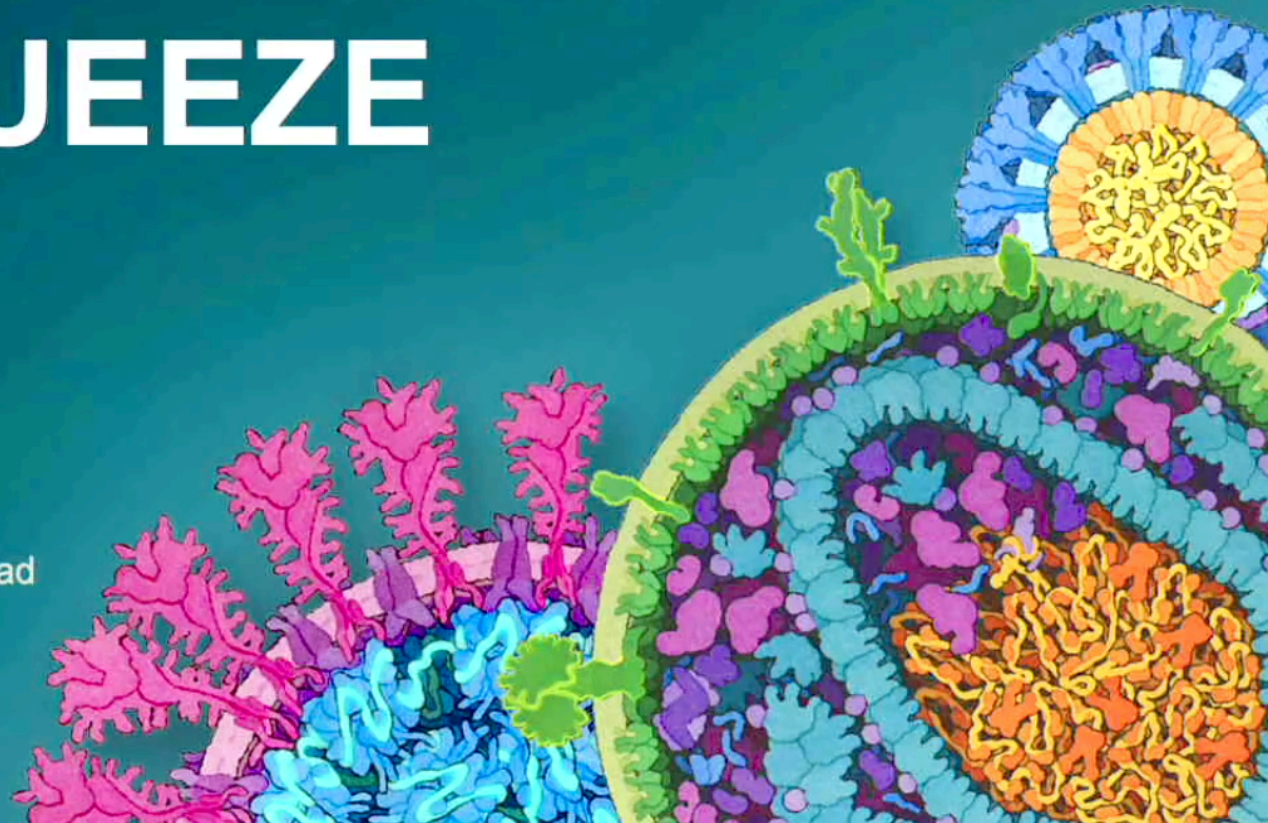
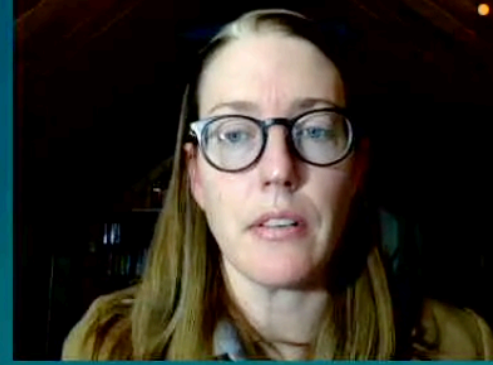
New strategy to achieve the WHO target of $< 0.1\%$ HBsAg prevalence in infants in 2030

UNIVERSAL HEPATITIS C VIRUS SCREENING IN PREGNANCY: THE JUICE IS WORTH THE SQUEEZE

Catherine A. Chappell

*University of Pittsburgh
Pittsburgh, PA, USA*

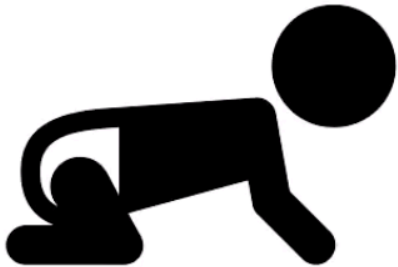
Disclosure: Catherine Chappell receives research funding from Gilead Sciences and Merck/Organon through University of Pittsburgh and Catherine Chappell has served as a consultant for Gilead Sciences.



HCV Screening in Pregnancy: Two for the price of one

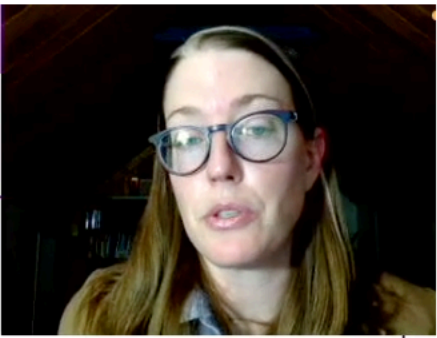


1. High engagement in healthcare
2. Unique motivation
3. Linkage to HCV care/treatment
4. Prevention of cirrhosis



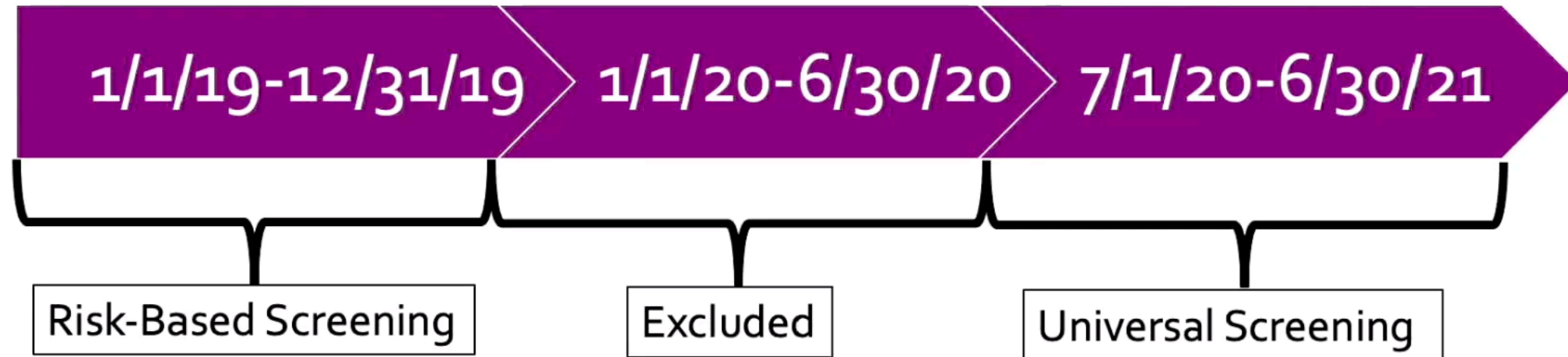
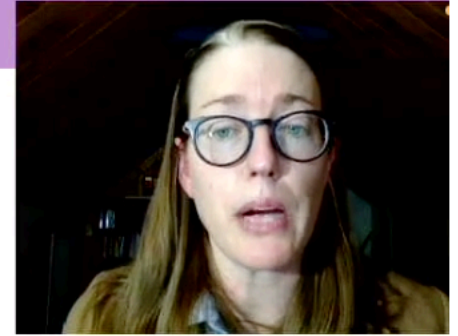
1. Identification of all infants exposed
2. Early detection of perinatal HCV
3. Linkage to HCV care/treatment
4. Prevention of cirrhosis

Universal HCV Screening Now Recommended



Methods

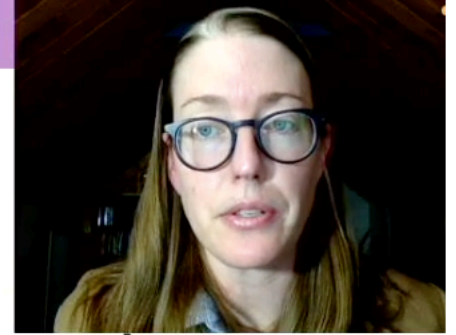
- Population: Pregnant people presenting for first prenatal visit within our health system in Western PA



- Universal Screening was initiated in June 2020 using a Best Practice Alert
- Medical records were review for HCV testing 9 months before and after initiation of prenatal care and compared using Fisher's exact test

	Risk-Based Screening	Universal Screening
Pregnant People	N=12142	N=12588
HCV IgG Tested*	2749 (23%)	10167 (81%)
HCV IgG Positive*	148 (1.2%)	237 (1.9%)
HCV RNA Tested*	33 (22% of HCV IgG+)	225 (95% of HCV IgG+)
HCV RNA Positive*	11 (0.091%)	85 (0.68%)

An Estimate of Perinatal Transmission



Risk-based screening
of 12,142 pregnancies



11 Active HCV



1 infant with HCV

Universal screening
of 12,588 pregnancies



85 Active HCV



5 infants with HCV

5.8%
perinatal
transmission

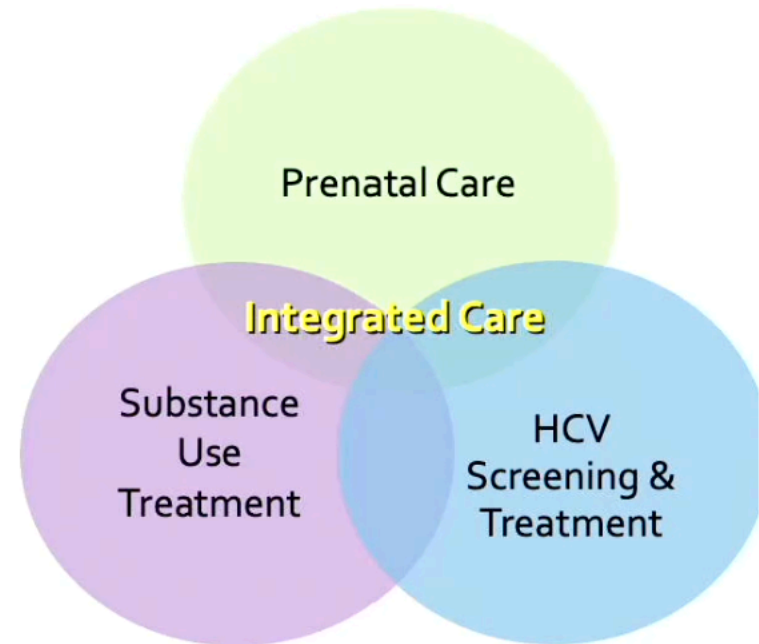
Universal Screening identified an additional 4 infants with perinatal HCV infection

Conclusions



- Risk based screening is insensitive
 - Universal HCV screening resulted in 7.5-fold increased detection rate of active HCV detection in pregnant people
- Pregnancy is a time of high healthcare engagement and pregnant people must be included in the HCV elimination strategy
- Universal HCV screening is a first step

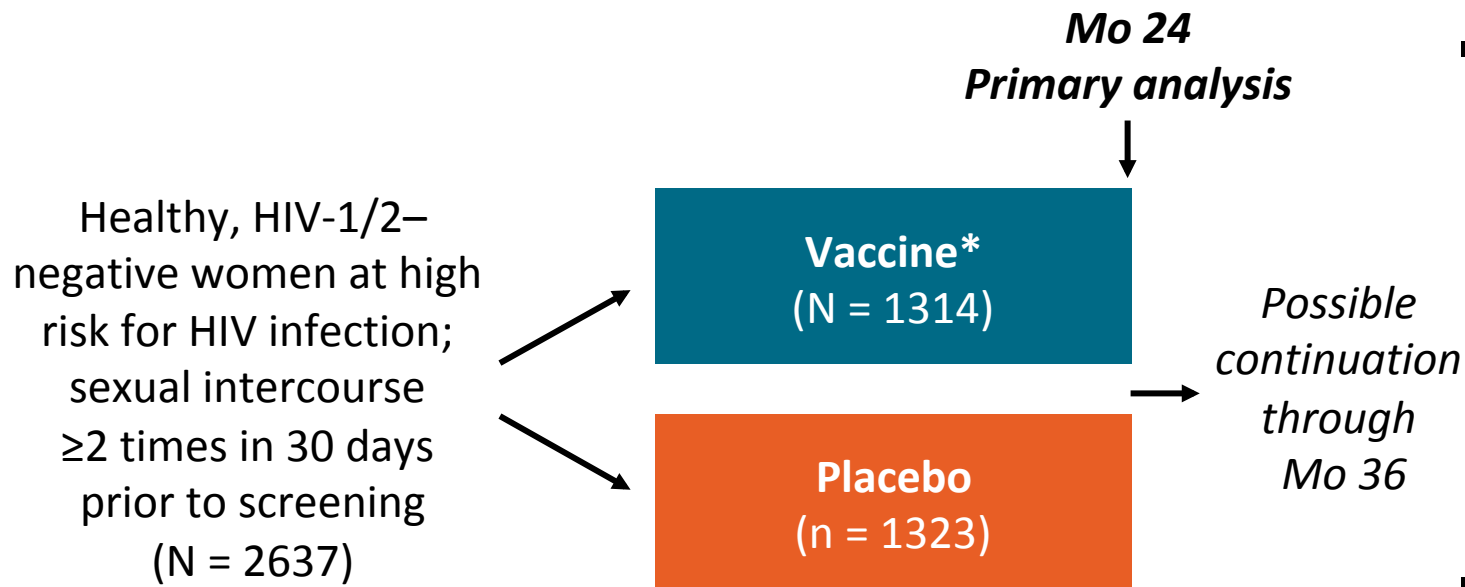
Test and Treat During
Prenatal care



HIV vaccine

Gray et al. Imbokodo: Phase IIb Trial of Heterologous HIV-1 Vaccine Regimen Among Women in Sub-Saharan Africa at High Risk for HIV Infection. Conference on Retroviruses and Opportunistic Infections, abstract 121, 2022.

- Multicenter, randomized, double-blind, placebo-controlled phase IIb trial



*Vaccine regimen consisted of 2 doses of Ad26.Mos4.HIV (1 dose at Mo 0 and 3) followed by 2 doses of Ad26.Mos4.HIV + adjuvanted clade C gp140 (1 dose at Mo 6 and 12).

- Primary endpoints
 - Vaccine efficacy from Mo 7-24 in preventing HIV-1 infection (PP population)
 - Trial continued through 36 mo only if lower bound of 95% CI for VE(7-24) >0%
 - Safety and tolerability (FAS population)
 - Secondary endpoints
 - Vaccine efficacy from Mo 7-24, 0-24, 13-24 in mITT population
 - Vaccine efficacy from months 13-24 in FIS population
- Included data are from database lock on May 28, 2021

Imbokodo: HIV-1 Vaccine Efficacy

- Vaccine did **not** provide statistically significant protection against HIV-1, failing to meet prespecified criteria for continuation through Mo 36

Vaccine Efficacy	% (95% CI)	P Value
Primary endpoint		
■ Efficacy from Mo 7-24 in PP population*	25.2 (-10.5 to 49.4)	.14
Secondary endpoints		
■ Efficacy from Mo 7-24 in mITT population [†]	18.3 (-18.5 to 43.6)	.29
■ Efficacy from Mo 0-24 in mITT population [†]	16.5 (-11.9 to 37.6)	.23
■ Efficacy from Mo 13-24 in mITT population [†]	16.4 (-40.3 to 50.2)	.5
■ Efficacy from Mo13-24 in FIS population [‡]	26.9 (-26.5 to 57.7)	.26

*All participants who were HIV-1 uninfected 4 wk after third vaccination, received all planned vaccinations at first 3 vaccination visits, and had no other major protocol deviations that might affect vaccine efficacy. [†]All participants who received ≥1 vaccine dose and were HIV-1 uninfected on date of first vaccination. [‡]All participants who were HIV-1 uninfected 4 wk after fourth vaccination visit and received all planned vaccinations.

Imbokodo: HIV-1 Incidence by Baseline Characteristics

Baseline Characteristic	Number of Events		Incidence Rate per 100 PY Through 24.13 Mo (95% CI)	
	Vaccine	Placebo	Vaccine	Placebo
Country				
▪ Malawi	3	3	3.20 (0.66-9.36)	3.15 (0.65-9.21)
▪ Mozambique	1	1	3.68 (0.09-20.5)	4.34 (0.11-24.2)
▪ South Africa	38	46	4.03 (2.85-5.53)	4.70 (3.44-6.27)
▪ Zambia	5	8	3.06 (0.99-7.14)	4.54 (1.96-8.95)
▪ Zimbabwe	4	5	2.21 (0.60-5.65)	2.73 (0.89-6.37)
Non–South Africa region	13	17	2.78 (1.48-4.76)	3.55 (2.07-5.68)
Age group				
▪ 18-20 yr	12	15	3.18 (1.64-5.55)	4.08 (2.28-6.72)
▪ 21-30 yr	36	40	3.85 (2.70-5.33)	4.02 (2.87-5.47)
▪ 31-35 yr	3	8	3.07 (0.63-8.99)	8.51 (3.67-16.8)



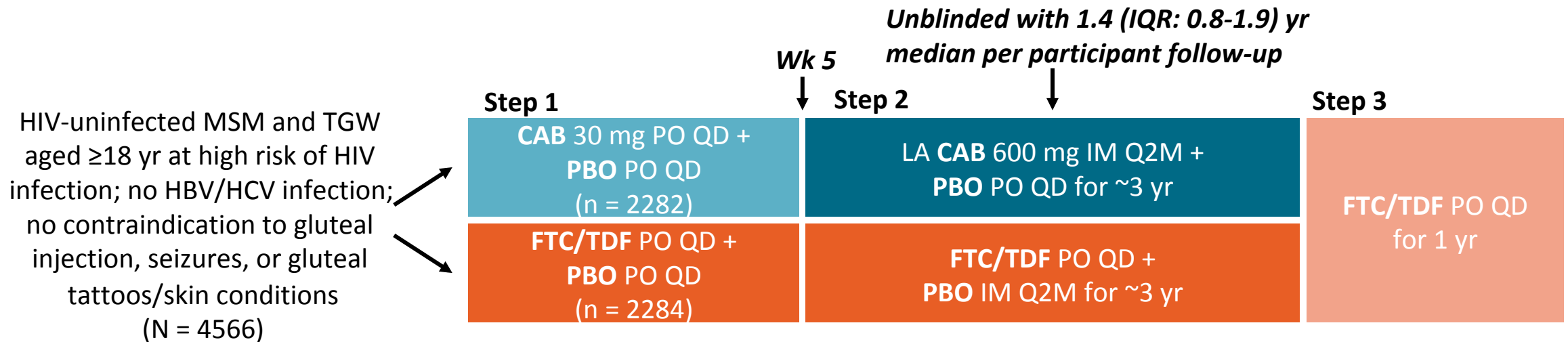
“We haven’t turned the needle on HIV in Africa in two decades,” Gray said. She noted that HIV risk is higher for African women than for gay and bisexual men in high-income countries, who have widely adopted other prevention methods. A combination of vaccines, PrEP, long-acting antiretrovirals to lower viral load in people living with HIV and other tools might be needed to overcome the HIV epidemic in Africa.

“We need a vaccine that will overcome high rates of infection,” she said. “To lower community transmission, we need a combination approach.”

PrEP studies

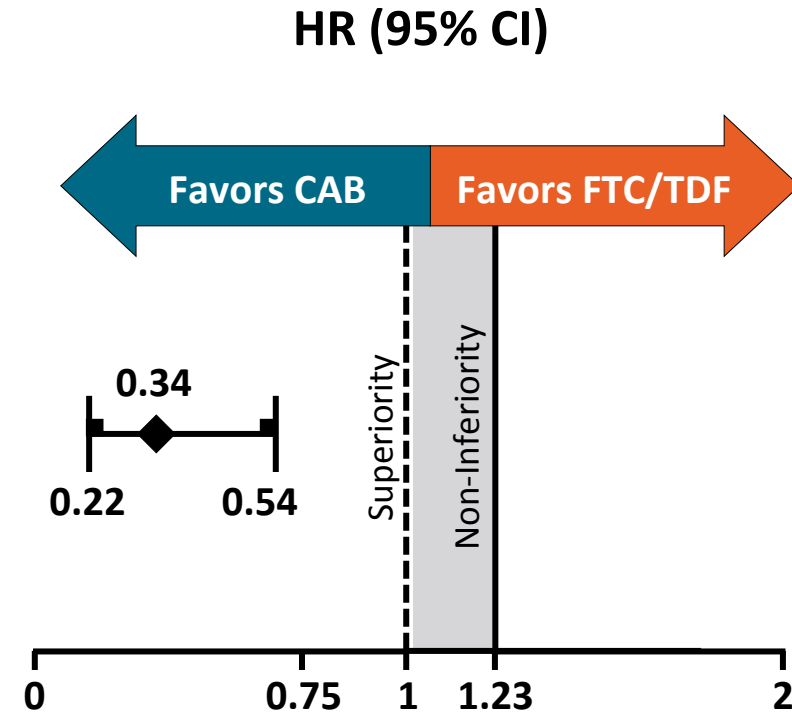
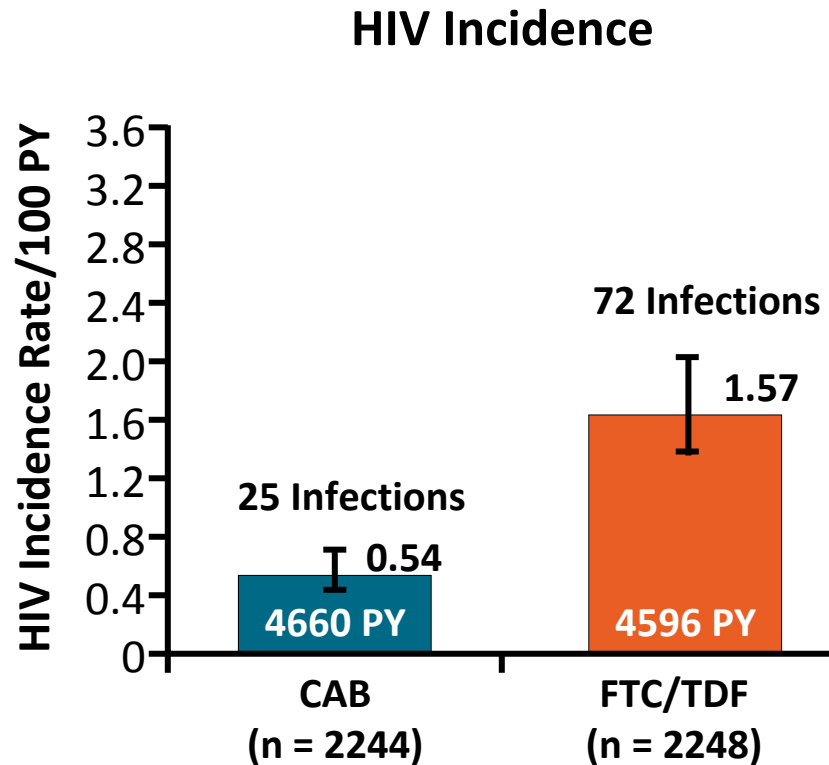
Landovitz et al. HPTN 083: Updated Safety and Efficacy of Long-Acting Injectable CAB vs Daily Oral FTC/TDF as HIV PrEP in MSM and TGW. Conference on Retroviruses and Opportunistic Infections, abstract 96, 2022.

- International, randomized, double-blind phase IIb/III study^{1,2}



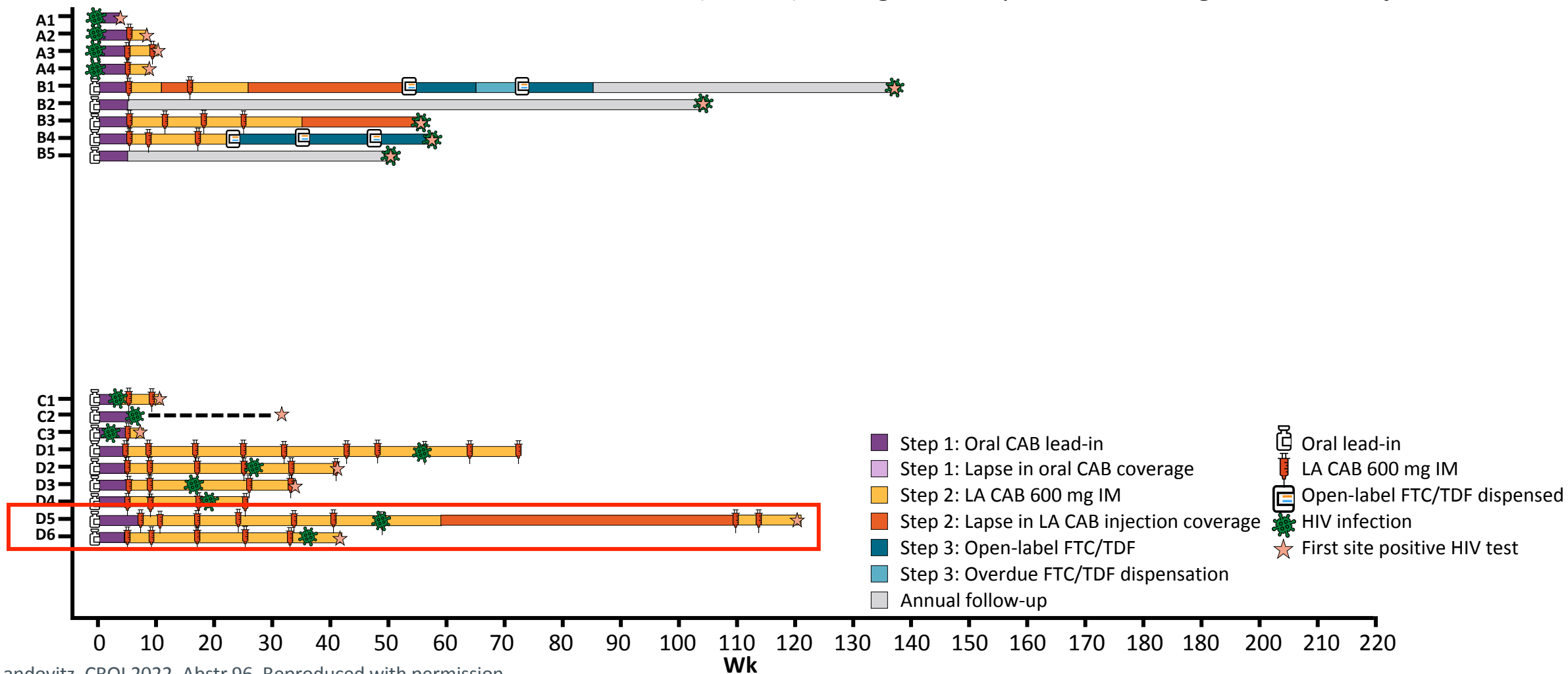
- Previously reported **13 incident infections** with CAB vs 39 with FTC/TDF; 1 incident CAB infection was later readjudicated to a BL infection (updated HR: 0.32; 95% CI: 0.16-0.58)²
- Current analysis of additional infections after 1 yr of follow-up after unblinding³

HPTN 083: HIV Incidence in Combined Efficacy Analysis



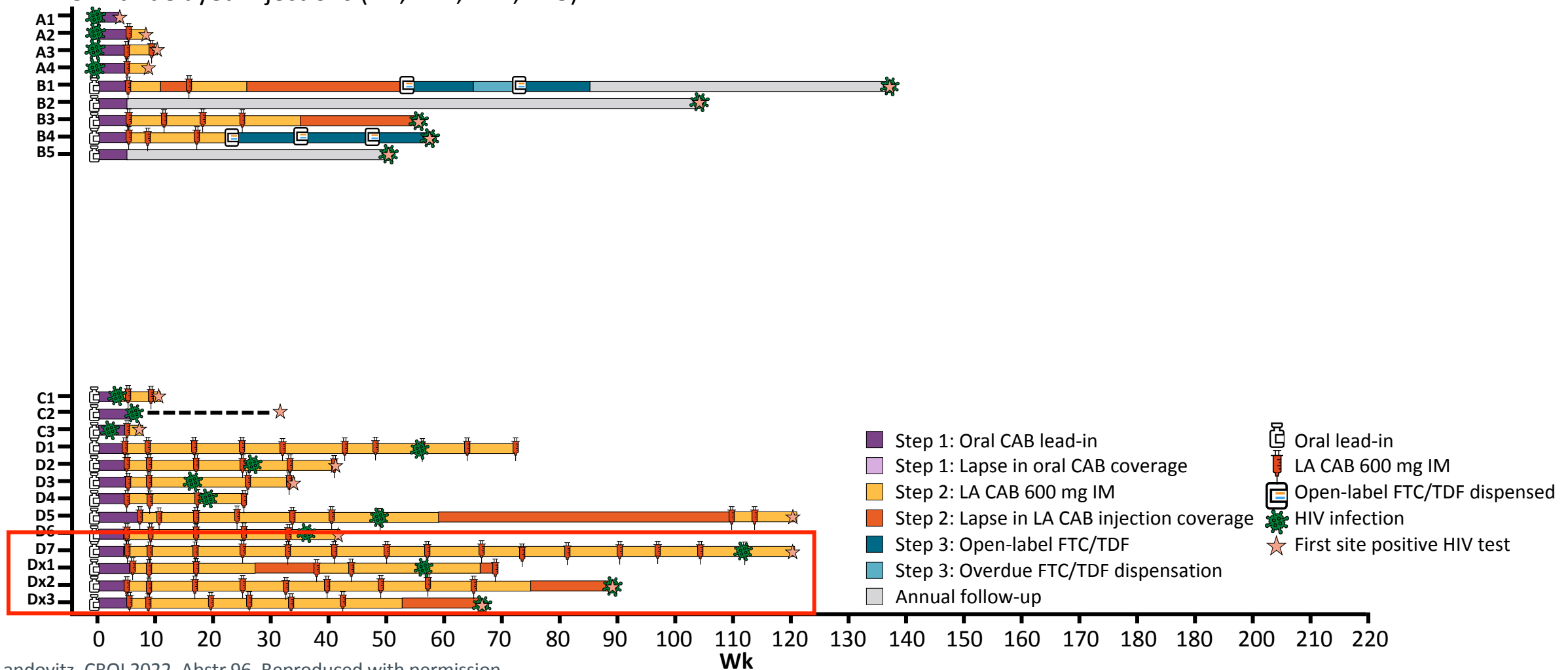
HPTN 083: Additional HIV Infections in CAB Arm During Blinded Period

- 2 additional HIV infections identified in CAB arm (D5, D6) during blinded period in setting of on-time injections



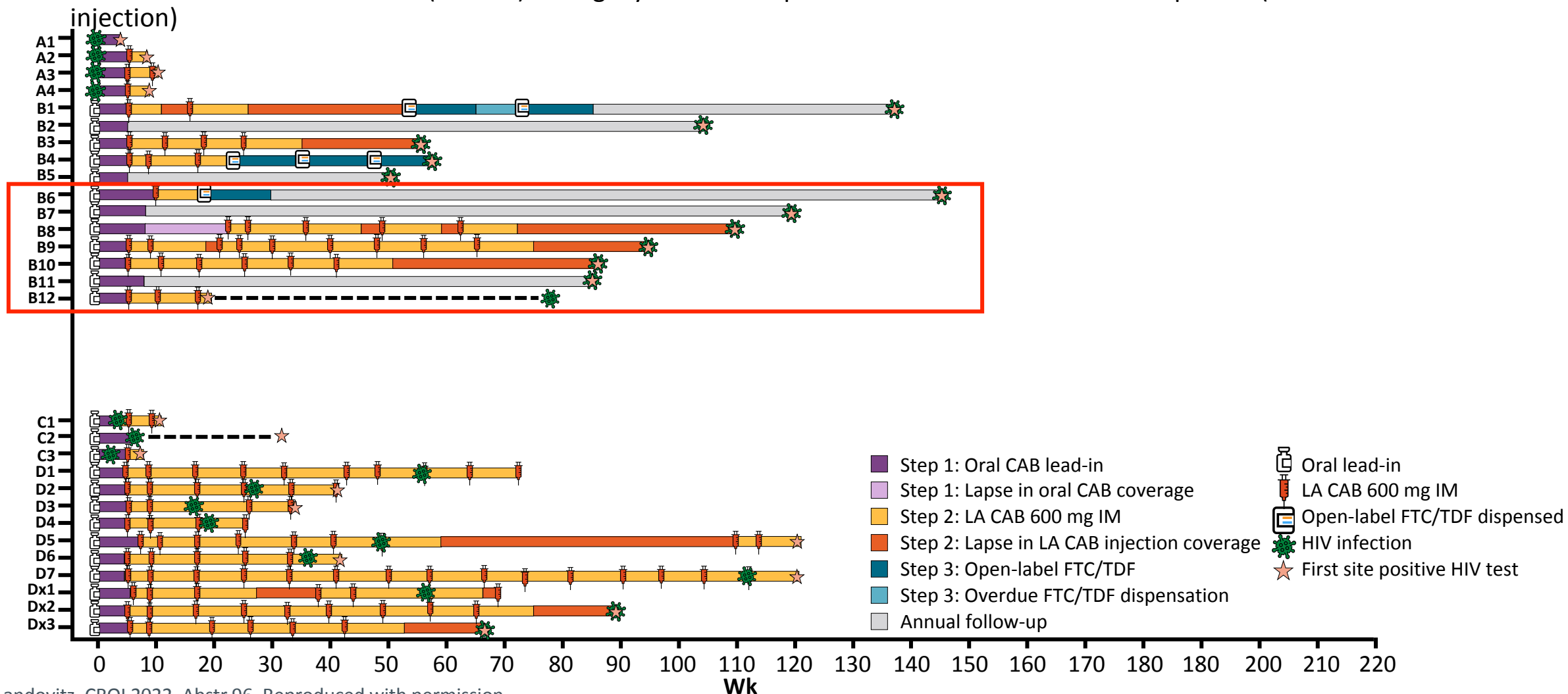
HPTN 083: HIV Infections in CAB Arm During 1 Yr Unblinded Period <6 Mo After Last Injection

- 4 new HIV infections identified during 1 yr unblinded period <6 mo after last injection: 1 with on-time injection, 3 with delayed injections (D7, Dx1, Dx2, Dx3)



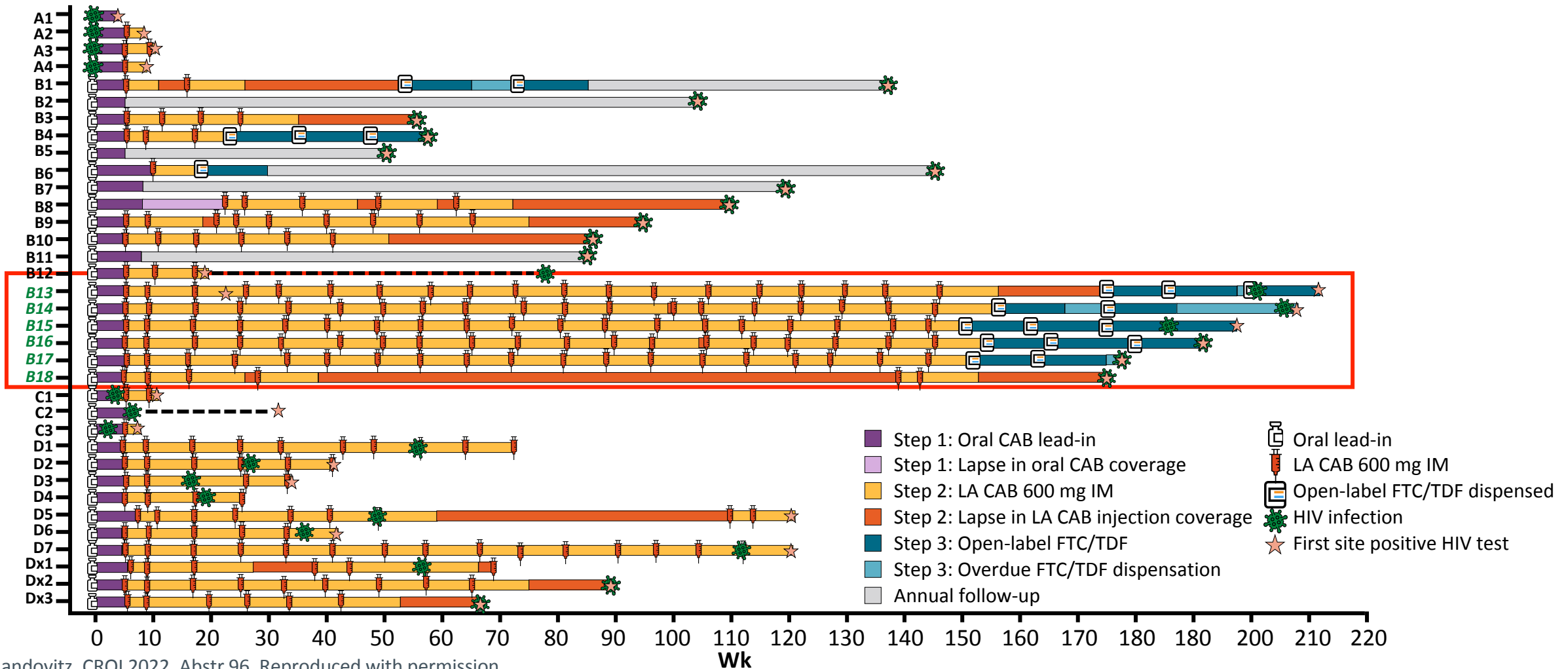
HPTN 083: HIV Infections in CAB Arm During 1 Yr Unblinded Period ≥ 6 Mo After Last Injection

- 7 new HIV infections identified (B6-B12) during 1 yr unblinded period ≥ 6 mo after the last CAB exposure (2 never received a CAB injection)



HPTN 083: HIV Infections in CAB Arm After ≥3 Yr on Study

- 6 additional HIV infections identified (B13-B18) ≥3 years on study (all ≥6 months after last CAB exposure)

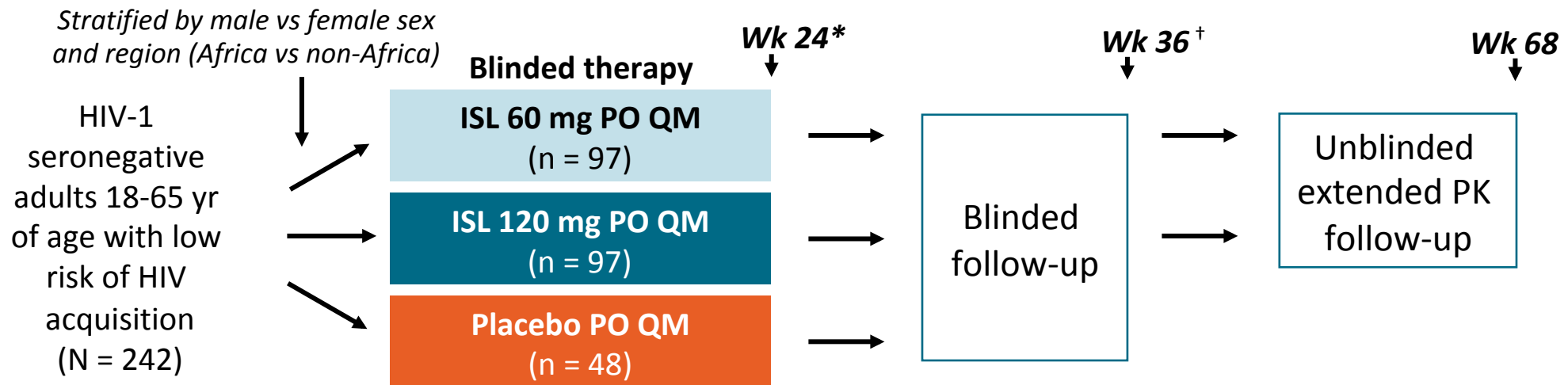


HPTN 083: Conclusions

- Additional infections were identified in the 1-yr follow-up since unblinding, but LA CAB remained superior to FTC/TDF at preventing HIV infection
 - Increase in HIV incidence during unblinded phase may have been due to decreased adherence and contribution of person-yr from high incidence regions
 - No additional safety concerns identified
- Breakthrough infections on LA CAB very rare, unexplained
 - 7 breakthrough infections reported despite on-time injections

Macdonald et al. Protocol 016: Wk 24 Metabolic and Renal Outcomes Similar for Monthly Oral Islatravir vs Placebo as HIV PrEP in Phase IIa Study. Conference on Retroviruses and Opportunistic Infections, abstract 85, 2022.

- Multicenter, randomized, double-blind, placebo-controlled phase IIa trial



*Sponsor unblinded at Wk 24 to allow for interim evaluation of safety. Participants and investigators remain blinded to Wk 36.

[†]After Wk 36, participants in PBMC/PK Bridging Subset randomized to receive ISL have an additional 32-wk unblinded PK follow-up.

- Metabolic outcomes: weight; BMI; peripheral, trunk fat distribution and hip, spine BMD (all using DXA scans)
- Renal outcomes: serum creatinine (measured at each visit); eGFR calculated by MDRD study equation; and RBP/creatinine ratio

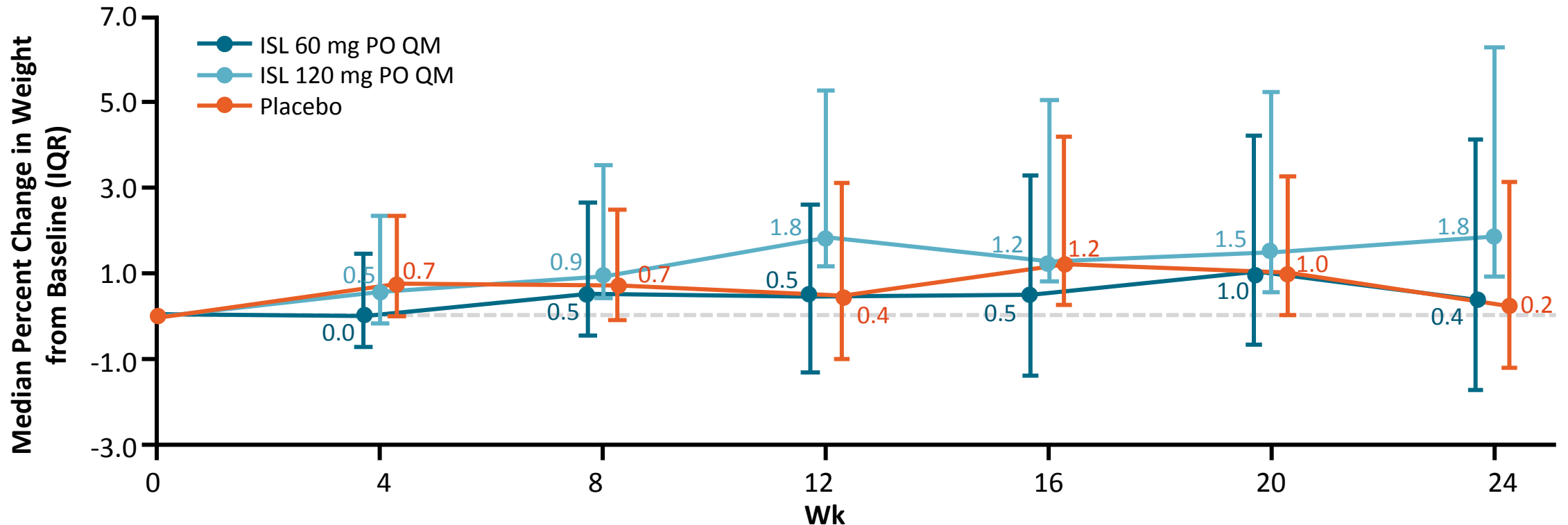
Protocol 016 Metabolic and Renal Outcomes:

Baseline Characteristics

Characteristic	ISL 60 mg PO QM (n = 97)	ISL 120 mg PO QM (n = 97)	Placebo PO QM (n = 48)
Sex at birth, n (%)			
▪ Male	31 (32)	33 (34)	15 (31.3)
▪ Female	66 (68)	64 (66)	33 (68.8)
Median age, years (min, max)	32 (20,58)	31 (18,58)	30 (19,45)
Race/ethnicity, n (%)			
▪ Black	37 (38.1)	48 (49.5)	16 (33.3)
▪ White	55 (56.7)	44 (45.4)	29 (60.4)
▪ Hispanic/Latinx	19 (19.6)	9 (9.3)	8 (16.7)
▪ Other	5 (5.2)	5 (5.2)	3 (6.3)
Country, n (%)			
▪ Israel	15 (15.5)	17 (17.5)	13 (27.1)
▪ South Africa	34 (5.1)	36 (37.1)	16 (33.3)
▪ United States	48 (49.5)	44 (45.4)	19 (39.6)
Metabolic and renal parameters			
▪ Median weight, kg	73.1	72.5	75.1
▪ Median eGFR, mL/min/1.73 m ²	114.4	119.9	118.7

Protocol 016 Metabolic and Renal Outcomes: Weight Change Through Wk 24

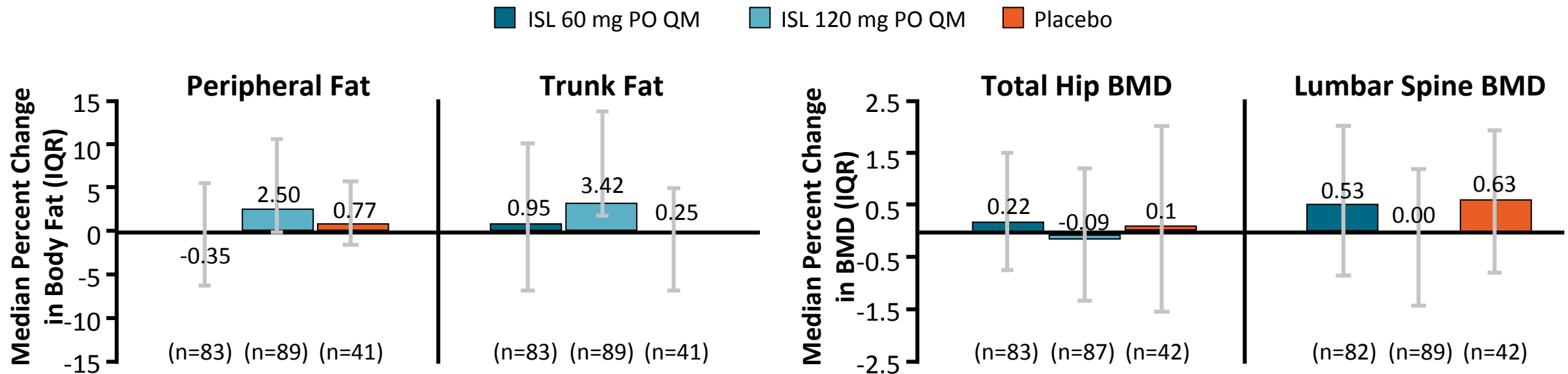
- Weight changes for ISL 60 mg PO QM and placebo groups small and comparable; weight slightly increased for ISL 120 mg PO QM group



Protocol 016 Metabolic and Renal Outcomes:

Fat Distribution and BMD Changes Through Wk 24

- Changes in peripheral and trunk fat for ISL 60 mg PO QM and placebo groups small and comparable; both slightly increased for ISL 120 mg PO QM group
- Changes in total hip and lumbar spine BMD small and comparable for all groups



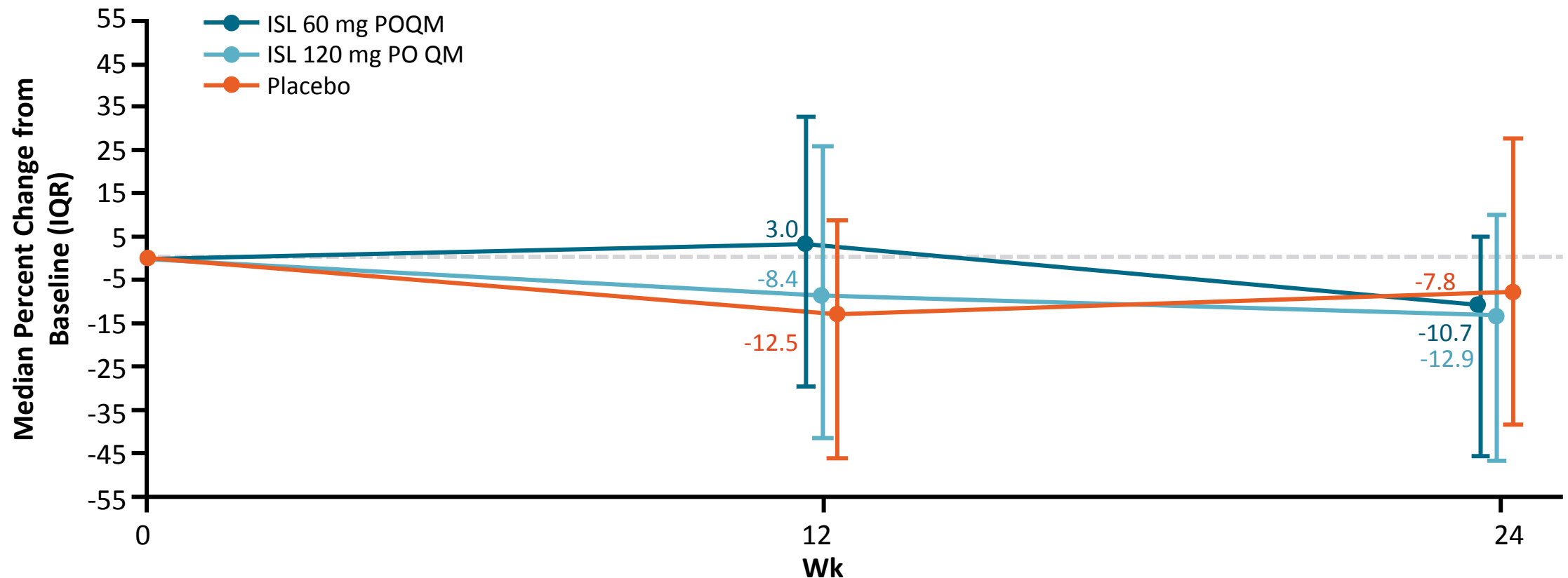
Protocol 016 Metabolic and Renal Outcomes: Serum Creatinine and eGFR Changes Through Wk 24

- No changes from baseline to Wk 24 in renal outcomes in any treatment groups

Characteristic, Median % Change (IQR)	ISL 60 mg PO QM (n = 84)	ISL 120 mg PO QM (n = 92)	Placebo PO QM (n = 44)
Serum creatinine, mg/dL	0 (-11.8 to 12.8)	0 (-5.8 to 11.1)	0 (0.0 to 14.3)
eGFR, mL/min/1.73 m ²	0 (-12.9 to 15.6)	0 (-11.5 to 7.2)	0 (-14.3 to 0.0)

Protocol 016 Metabolic and Renal Outcomes: RBP/ Creatinine Ratio Changes Through Wk 24

- Decreases in RBP/creatinine ratios small and similar across groups



Protocol 016 Metabolic and Renal Outcomes: Conclusions and Trial Information

- Observed differences through Wk 24 in metabolic and renal parameters between placebo and ISL 60 mg PO once monthly or ISL 120 mg PO once monthly not clinically relevant
- *Based on lymphocyte changes observed in ISL clinical trials, the ISL PrEP program has been placed on hold by the FDA*

**Young et al. Feasibility of Long-Acting Combination
HIV and Pregnancy Prevention Implant Demonstrated in Mouse Model.
Conference on Retroviruses and Opportunistic Infections, abstract 80,
2022.**

- 90-day in vivo study in BALB/c female mice
- 4 injectable ISFIs: DTG (278 mg/kg) + MPA (70 mg/kg), DTG (278 mg/kg) + ENG (70 mg/kg), CAB (1215 mg/kg) + MPA (76 mg/kg), CAB (1215 mg/kg) + ENG (151 mg/kg), and control (no implant)
- 12 mice/group for PK studies + 12 mice/group for safety analyses

[illegible]

Long-Acting Combination HIV And Pregnancy Prevention Implant: 90-Day Residual Drug, Inflammation

Implant, %	Approximate Residual Drug	Approximate Implant Degradation
DTG ENG	21 6	52.3
DTG MPA	23 14	65.1
CAB ENG	80 4	40.9
CAB MPA	94 70	51.2

- Microscopic analysis of excised implant and histologic analysis of surrounding tissue demonstrated predominantly absent to moderate inflammation
 - Severe inflammation observed in 2 samples at 7 days and 1 sample at 90 days
- Measurement of TNF- α and IL-6 demonstrated low levels of systemic inflammation

Long-Acting Combination HIV And Pregnancy Prevention Implant: Conclusions

- SC, biodegradable, and removable long-acting ARV + contraceptive implant is feasible in humanized mouse model
- Implant sustained release of ARV above concentration needed to inhibit viral replication for 90-day trial period
- No difference in ARV release when coformulated with either contraceptive drug
- Implant generally well tolerated
- Future studies needed to investigate additional PK parameters and expand study population to other animal models

PEP/PrEP in women

What will it take to increase PEP and PrEP use for adolescent girls and young women at risk?

Tuesdays 15th February, 12:00 PM - 1:00 PM MST

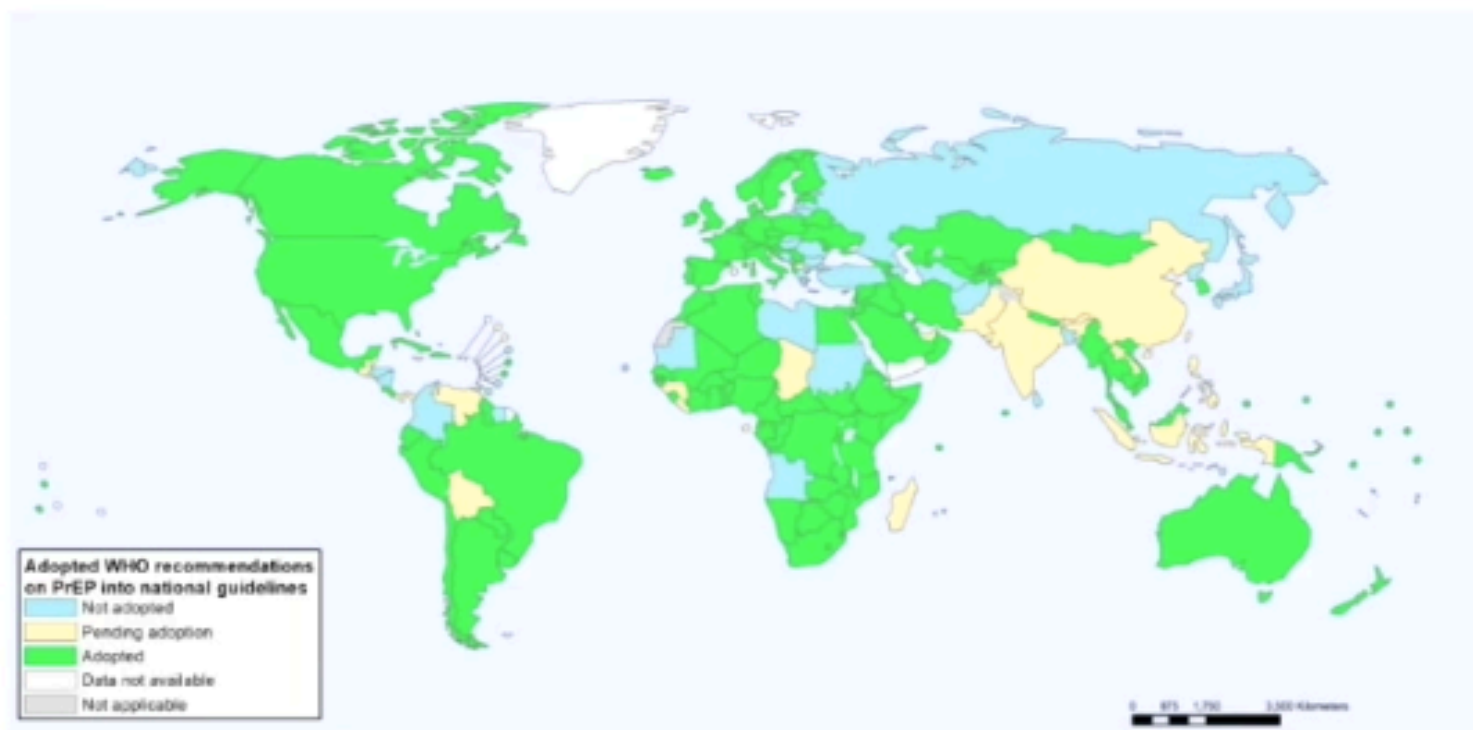
Global PrEP and PEP uptake in adolescent girls and young women

Rachel Baggaley, Global HIV, Hepatitis and STI programmes, WHO, Geneva



Adoption of WHO recommendations on oral PrEP into national guidelines

By WHO member state globally, 2020



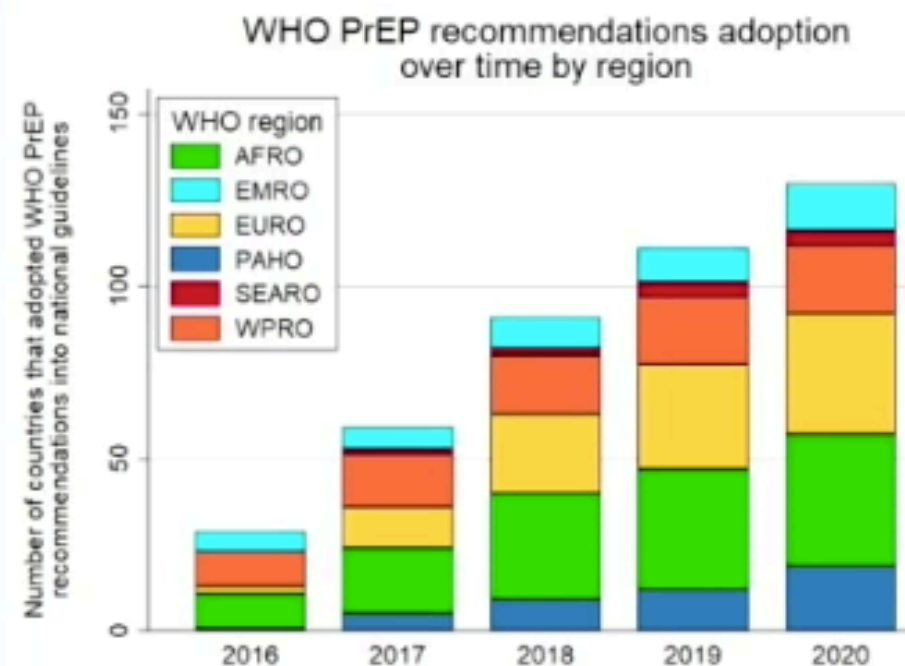
The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: WHO, GAM
Map Production: HQ UCN/HIS/TPP
World Health Organization



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By WHO region, 2016-2020



Global oral PrEP use among young people

Global AIDS Monitoring data for 2020:

Aged 15-19

12,621 PrEP users across 14 countries

Most in 3 countries: Uganda (7k), Mozambique (2.6k), Lesotho (2k)

Aged 20-24

33,658 PrEP users across 22 countries

Significant lack of reporting of PrEP user age & gender in the global data



What will it take to increase PrEP use for AGYW?

Positive messaging and better awareness

- Messages designed by women in their communities

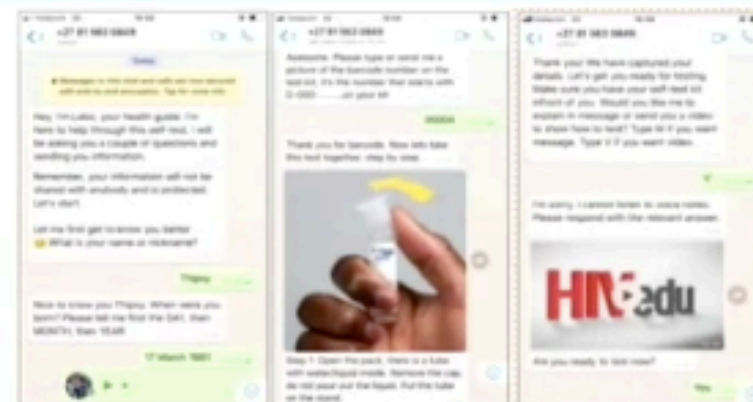


Acceptable, accessible PrEP services- differentiated and simplified PrEP services

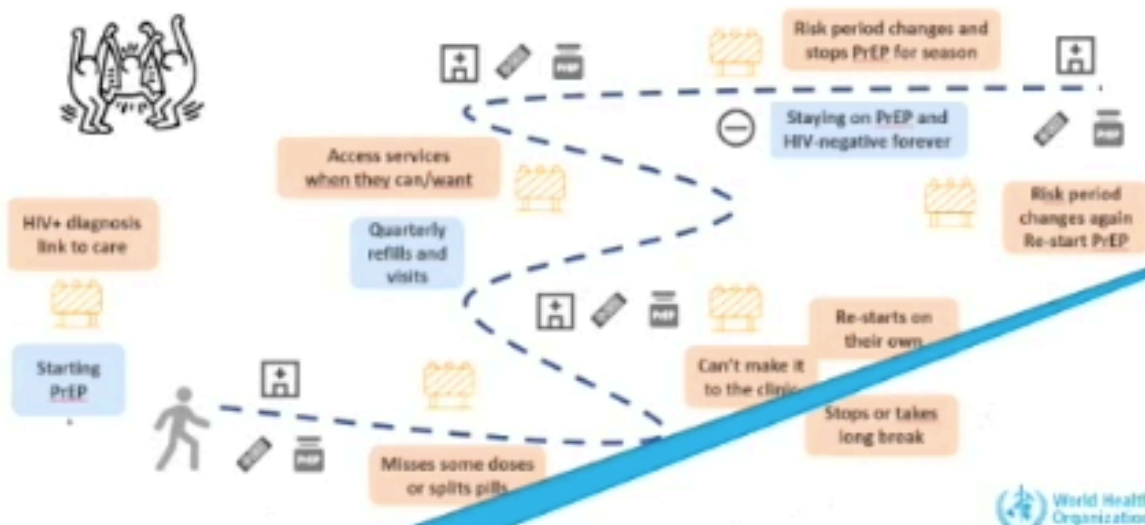
- Immediate offer
- Reduce burden of monitoring (e.g. kidney function)
- Community delivery and pickup
- HIV self-testing
- Virtual support
- Think about ANC, PNC & FP
- Think about other services



Photo: Karen Hatzold, PSI



Understanding and adapting to AGYW's PrEP Journey



WHO guidance
on DSD PrEP
April 2022

Enhancing oral PrEP uptake among adolescent girls and young women in Africa

C. Heck, Q Abdool Karim JAIS, Jan 2022

"Motivation to use HIV prevention highest at first contact, yet CrCI, before starting PrEP, creates a delay that may decrease interest, affecting PrEP uptake"

PrEP Implementation in Adolescent Girls and Young Women (AGYW): Lessons learnt from DREAMS

Nicolette Naidoo

*Programme Head: Implementation Science and Chief of Party
USAID School Based HIV and Violence Prevention*

*Wits Reproductive Health and HIV Institute (Wits RHI)
Johannesburg, South Africa*

Disclosure: None



Multiple strategies to drive demand and uptake of PrEP among AGYW

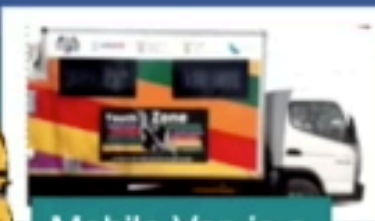


HIV Prevention Ambassadors (Community Based) and Learner Support Agents (School Based)



Gimme PrEP!

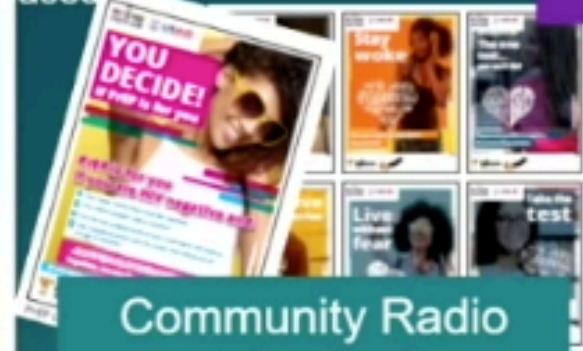
Mobile Van is a Demand Creation tool itself!



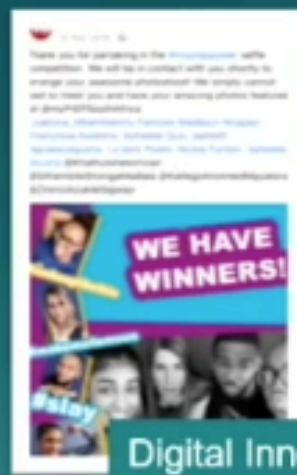
Strengthening layering pathways and co-location with DREAMS partners



Making Demand Creation FUN AND LOUD! loud-halers and PrEP roadmap game



Community Radio and Campaigns



Digital Innovations – Social Media, MyPrEP journey App, Facebook



Collaboration with CBOs for Social Mobilisation and Community Entry

Collateral Benefits for Young People - Integration of PrEP with SRH

- Multiple burden of disease among young people – STIs, violence, unplanned pregnancy, poor mental health
- PrEP delivered as part of Integrated School Health Program – delivery of SRH and Social Services for Learners in Secondary Schools to ensure holistic service delivery approach
- School based model has enabled:
 - Increased community awareness and support
 - Increased access to HIV prevention AND SRH services
 - 18% (4687/26352) of learners provided with contraception and PrEP
 - Almost universal coverage (99%) of PrEP beneficiaries screened for STIs
 - Better PrEP continuation - >60% of beneficiaries continue on PrEP at M1
- PEP provision is dependant on supply chain, particularly for community based models of service delivery – work closely with anchor facilities

What will it take to increase PEP and PrEP use for adolescent girls and young women at risk?

PrEP IMPLEMENTATION AMONG YOUNG WOMEN WHO SELL SEX IN ZIMBABWE

Primrose Matambanadzo, Key Populations Programme Director

Centre for Sexual Health and HIV/AIDS Research Zimbabwe

Tuesday 15 February 2022



Get PrEPared

Follow these steps to get PrEP medication to prevent HIV

Is PrEP right for me?

PrEP is a pill and reduces your risk of getting infected with HIV by more than 90% if taken correctly.

1

GET READY

Visit your nearest Sisters Clinic and talk to your health care provider. Benefits and side effects of PrEP will be explained.

2

GET SET

Get tested to make sure you are HIV negative.



3



GET PrEP

Get your medicine at your local SISTERS clinic. Take the medication as prescribed and see your provider 1 month after starting PrEP.

Staying on PrEP

Take the medication as prescribed and see your provider every 1 month to monitor your HIV status for continuous support. PrEP is effective when taken consistently.

Young Women who Sell Sex and HIV Prevention in Zimbabwe

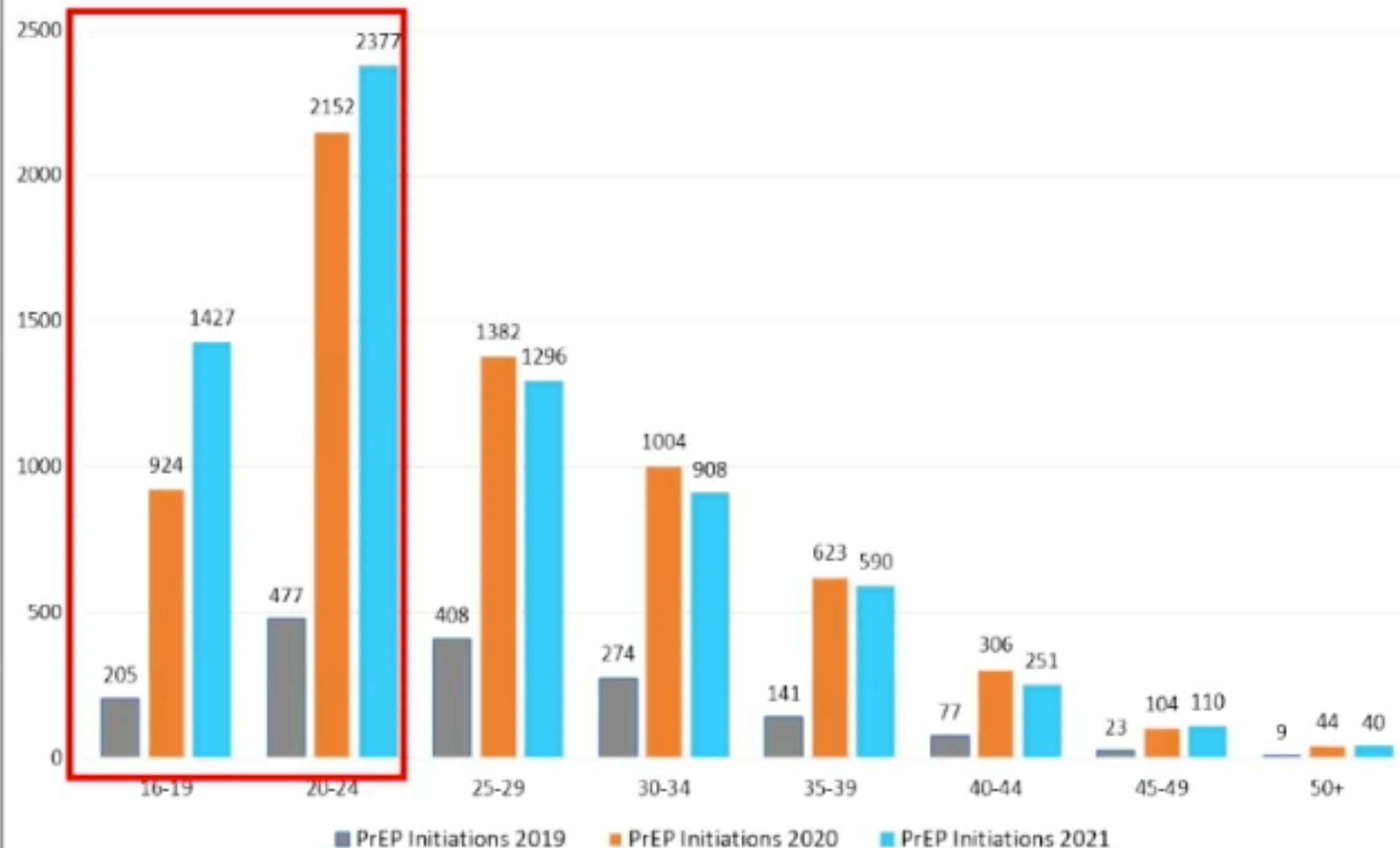
- 1 in 2 FSW in Zimbabwe are living with HIV
- HIV prevalence among **Young women who sell sex workers (YWSS) rises rapidly with age** ->
 - **2% at age 16**
 - **27% by age 19**
 - **52% by age 24**

Common barriers to PrEP uptake and continuation among YWSS

- Burden & cost of **frequent clinic visits** – can't make it to facility
- Daily **pill burden**
- **Stigma** – health worker attitudes and messaging for PrEP as only for 'certain high risk groups' perpetuated stigma
- **Confusion between PrEP & ART** (associated HIV stigma)
- **Shifts in risk** perception
- Programming and messaging **not accommodating transitions in and out of PrEP**
- **Lack of support within community** for PrEP adherence and continuation during periods of risk

PrEP uptake among YWSS in Zimbabwe 2019 - 2021

CeSHHAR FSW PrEP Initiations 2019-2021



- Roll out started April 2019
- Focus for scale up in YSW 16 – 24 years 2020 - 2021
- 4 fold surge in initiations 16 – 24 year age band in 2020
- DSD for PrEP was **scaled up** during COVID-19 with high uptake of PrEP, but sub-optimal continuation

Scaling up PrEP for YWSS: increase motivation, access & effective use

What has worked

- **Let sex workers lead!** Sex workers lead in education of KPs on PrEP – prepare communities on advantages, disadvantages, side effects, provide support
- **Increased number of PrEP access points:** facility, drop-in centre, community-based & home-based PrEP services
- Each site engages **PrEP champions/ambassadors** (3 – 5 depending on size) for demand creation/mobilisation, adherence support
- **PrEP Refill Groups/support groups** for PrEP refills
- **Linking mobile SW** to PrEP internally and outside Zimbabwe
- **Scaled up of telehealth and virtual peer support** via phone and WhatsApp
- **Multi-month dispensing (MMD) of PrEP:** 3 months, exploring beyond 3 months
- **Integrate PrEP** with family planning and STI services in a comprehensive SRH model

What is planned going forward

- **Pharmacy-based PrEP distribution**
- Exploring **HIV ST** for initiation and refill
- Intensified **SGBV prevention and support**
- Mental health services and alcohol and drug use disorders support
- Collectivise self-help groups to **address stigma**
- Explore **microplanners dispensing**

GiRLS Club Manual



New PrEP products- increased choice



9 December 2021 | Statement

WHO continues to support its conditional recommendation for the dapivirine vaginal ring as an additional prevention option for women at substantial risk of HIV



Trial results reveal that long-acting injectable cabotegravir as PrEP is highly effective in preventing HIV acquisition in women

Will new LA products increase acceptability & demand or just replace current users

DVR

- Sub-analysis women <21 years: No efficacy, low adherence (studies ongoing)
- Adherence support requirements
- Messaging around efficacy
- Investment case
- Limited data on use during pregnancy & BF (studies ongoing)
- Limited data on acceptability and use in key populations
- **Safe product – opportunity for community-based delivery, including pharmacies**

CAB-LA

- No data on adolescents <18, although significant #participants 18-24yrs
- Risk of drug resistance
- Optimal HIV testing procedures unclear
- Limited data on use during pregnant & BF (analysis & further studies ongoing)
- Limited data on some key populations, including sex workers and people who use drugs
- How to integrate into community-based delivery?
- Likely higher cost: Who/how to target?
- **Opportunity for younger PrEP users who may have challenges with adherence to oral PrEP**

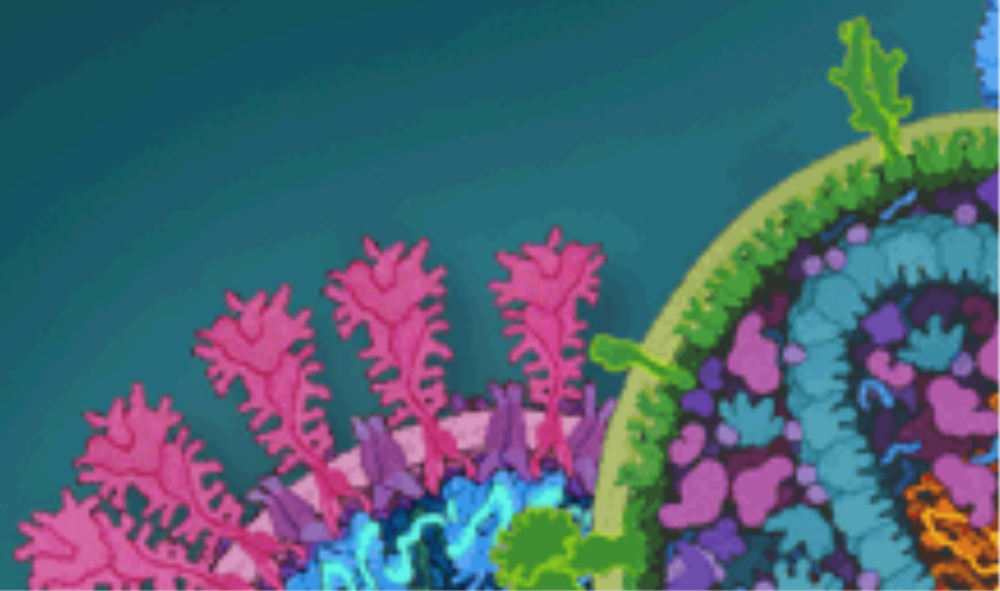
Choice and Adherence to Dapivirine Ring or Oral PrEP by Young African Women in REACH

Presenter: Kenneth Ngure PhD

*Jomo Kenyatta University (JKUAT), Nairobi, Kenya
University of Washington, Seattle, USA*

Disclosure:

- Grant from MSD
- Speaker fee from Gilead

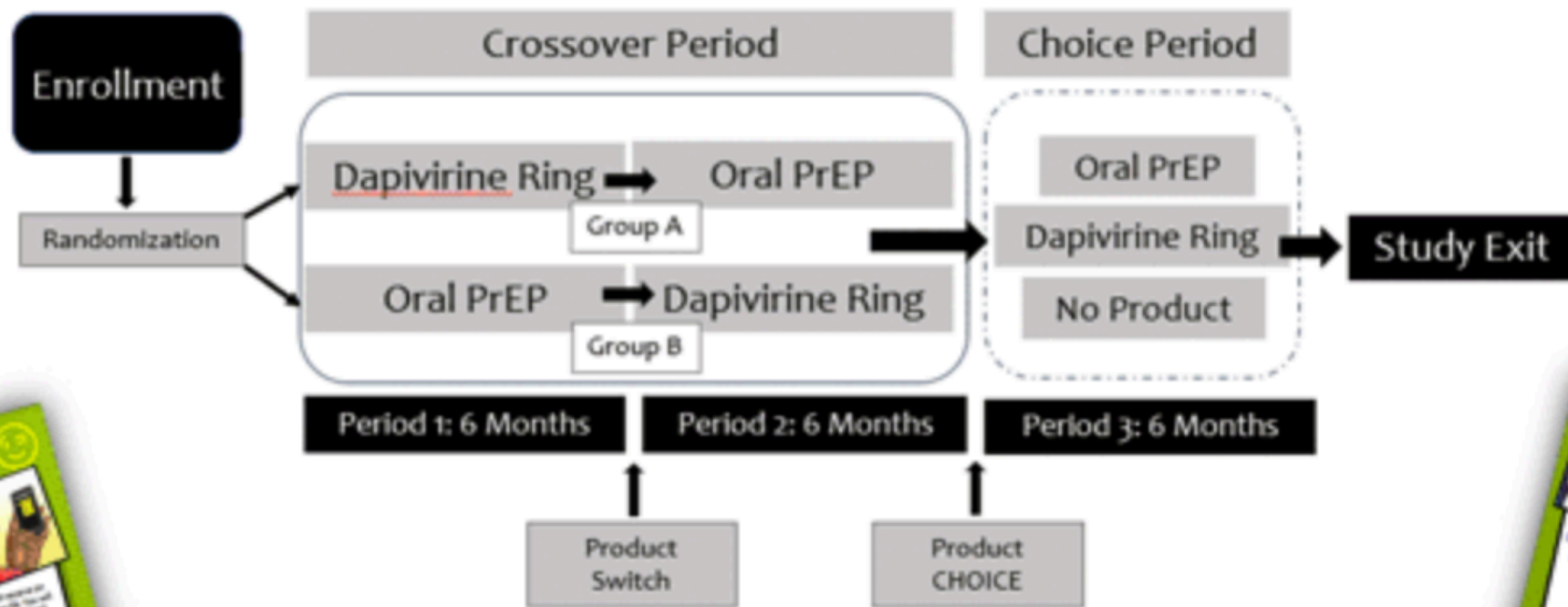


Introduction

- Adolescent girls and young women (AGYW) account for most new HIV acquisitions in Africa
- WHO recommends daily oral PrEP and the monthly dapivirine vaginal ring (ring) for women at risk of HIV acquisition
- Given low adherence among AGYW in efficacy trials, we assessed choice of and adherence to the ring and oral PrEP among African AGYW in the MTN-034/REACH trial



REACH Study Design



A randomized crossover study offering a diverse menu of adherence support options to all participants in South Africa, Uganda, and Zimbabwe.



Evaluating Adherence

Ring adherence

Based on estimated dapivirine release calculated using residual drug (RD) levels in returned rings



Non-use

- RD levels showing release of $<0.9\text{mg}$

Some use

- RD levels showing release of 0.9 to $<4.0\text{mg}$

Consistent with 28 days of use

- RD levels showing release of $\geq 4.0\text{mg}$

Oral PrEP adherence

Measured via tenofovir diphosphate (TFV-DP) levels in dried blood spots (DBS)



Non-use

- TFV-DP levels of $<16\text{fmol/DBS punch}$

Some use

- TFV-DP levels of 16-700fmol/DBS punch

High adherence

- TFV-DP levels of $\geq 700\text{fmol/DBS punch}$

We compared the proportion of visits with high adherence between the crossover and choice periods for each product

Participant Baseline Characteristics

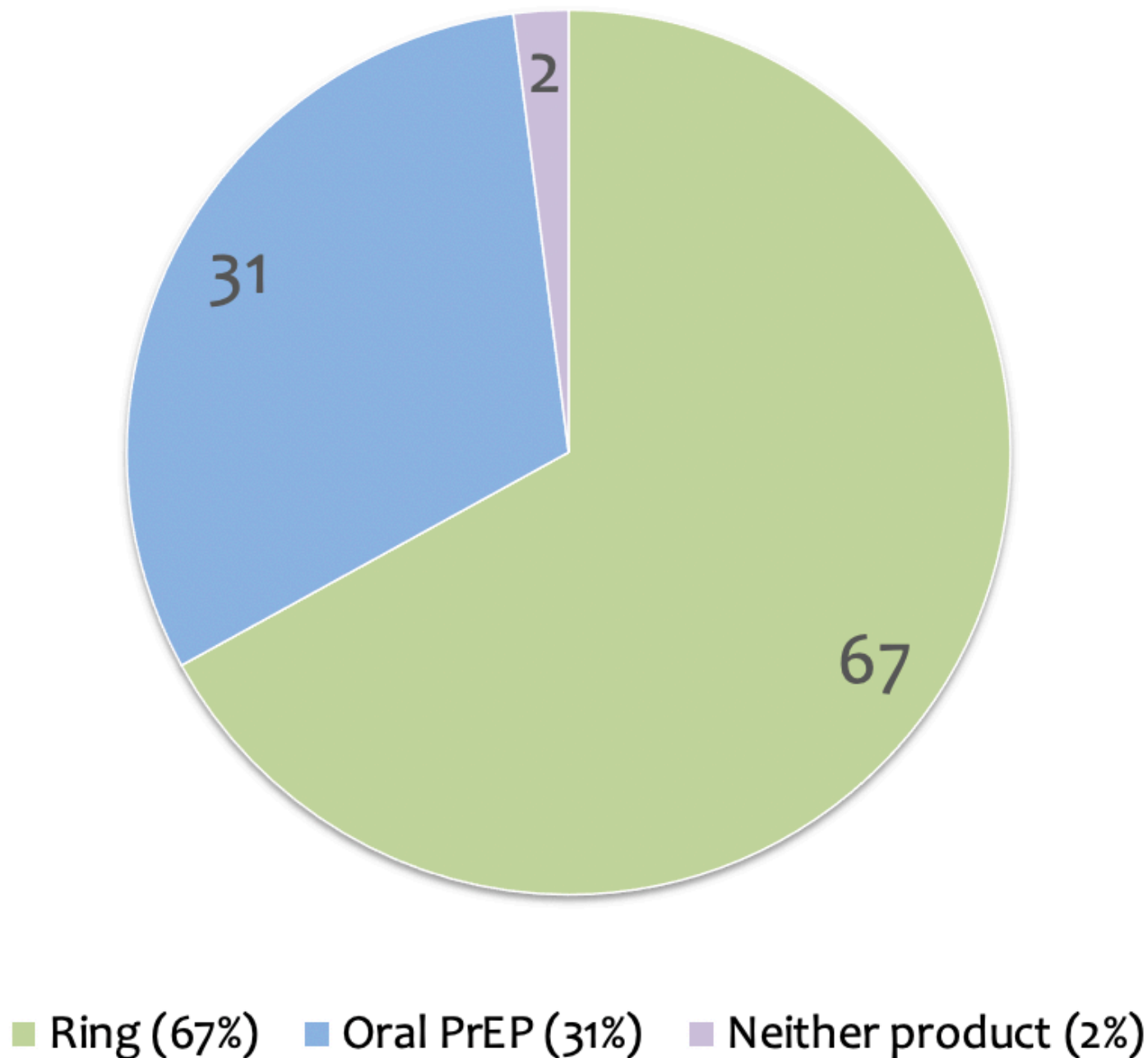
	Cape Town, South Africa N=60	Harare, Zimbabwe N=60	Johannesburg, South Africa N=67	Kampala, Uganda N=60	Total N=247
Age	18.3	17.9	18.3	18.2	18.2
Not married	60 (100%)	36 (60%)	65 (97%)	53 (88%)	214 (87%)
Ever been pregnant	5 (8%)	41 (68%)	21 (31%)	32 (53%)	99 (40%)
Contraceptive commenced in last 70 days	17 (29%)	28 (47%)	22 (33%)	26 (46%)	93 (38%)
Secondary school	55 (92%)	55 (93%)	57 (85%)	22 (37%)	189 (77%)
In school	33 (55%)	14 (23%)	36 (54%)	9 (15%)	92 (37%)
Earns own income	2 (3%)	14 (23%)	6 (9%)	31 (52%)	53 (21%)

At screening, participants were assumed to have been assigned female sex at birth and were not asked to report their gender identity. However, required safety pelvic exams that occurred during the screening process would later confirm sex at birth.

Product Choice in Period 3

Randomization sequence in the crossover period was not associated with product choice

Of 227 (92%) participants who reached the choice period, more than 2/3 (152) chose the ring



Adherence during the crossover period and subsequent product choice

Oral <u>PrEP</u> adherence	Chose oral <u>PrEP</u>	Chose ring/neither	p-value
Red/yellow at least once	32 (20%)	129 (80%)	<0.001
Always green	39 (58%)	28 (42%)	

Non-use (red): TFV-DP levels of <16fmol/DBS punch

Some use (yellow): TFV-DP levels of 16-700fmol/DBS punch

High adherence (green): TFV-DP levels of ≥ 700 fmol/DBS punch

Ring adherence	Chose ring	Chose oral <u>PrEP</u> /neither	p-value
Red/yellow at least once	134 (67%)	65 (33%)	0.85
Always green	19 (66%)	10 (35%)	

Non-use (red): RD levels showing release of <0.9mg

Some use (yellow): RD levels showing release of 0.9 to <4.0mg

Consistent with 28 days of use (green): RD levels showing release of ≥ 4.0 mg

High adherence to oral PrEP in the crossover period was strongly associated with choice of oral PrEP ($p < 0.001$)

No such association was observed for ring choice ($p = 0.85$)

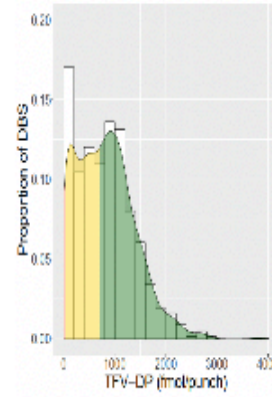
Comparing dapivirine ring use and oral PrEP adherence during the crossover and choice periods

Overall, participants used both the ring and oral PrEP consistently in the crossover and choice periods, with “some” to “high” adherence.

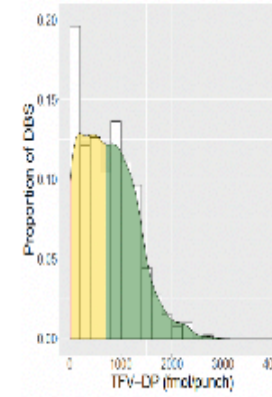
Fewer than 5% of visits were categorized as no or low adherence to study product

Oral
PrEP

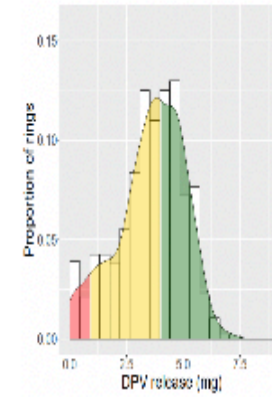
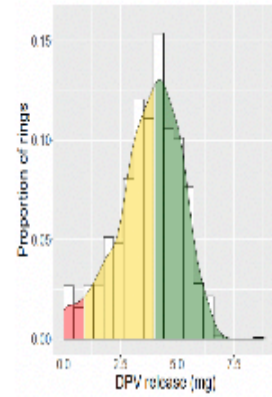
Crossover Period



Choice Period



Ring



Conclusions

- Among African AGYW who had experience with both ring and oral PrEP use, about 2/3 opted to use the ring when given a choice of products
- Participants with high adherence to oral PrEP in the crossover period were more likely to choose oral PrEP when given a choice
- Drug levels throughout the crossover and choice periods indicate partial to high adherence for both products – higher than in previous studies
- AGYW can make informed choices about HIV prevention products and can use products effectively with proper support



HIV testing in PEPFAR countries

TRENDS IN HIV TESTING AND LINKAGE TO HIV TREATMENT IN 41 COUNTRIES: 2016- 2021

Bakary Drammeh

Centers for Disease Control and
Prevention

Background



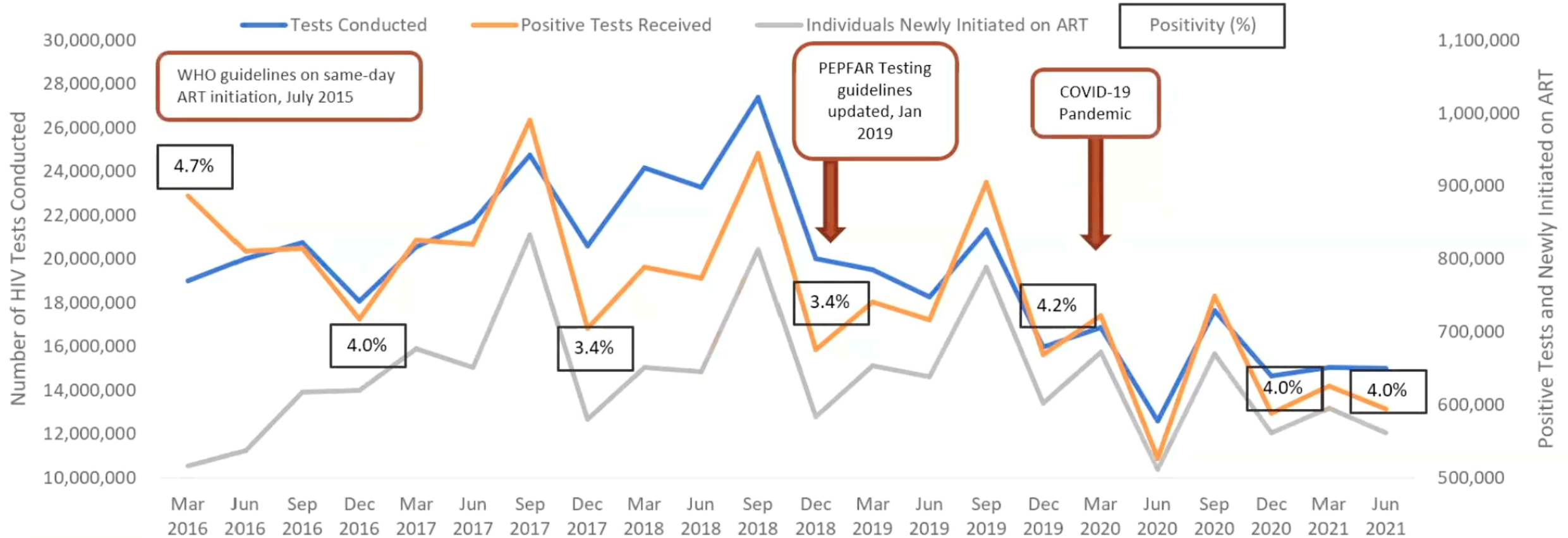
- The U.S. President's Emergency Plan for AIDS Relief (PEPFAR) seeks to accelerate progress towards epidemic control in 50+ countries and reach UNAIDS 95-95-95 goals.
- In 2019, PEPFAR updated HIV Testing Services technical guidance to:
 - Increase testing efficiencies and improve HIV case finding.
 - Shift from universal testing to targeted testing (i.e., index testing and case finding, risk screening tools).
- In 2015, PEPFAR supported same-day ART initiation as outlined in WHO's Consolidated HIV Treatment Guidelines.



Results



Number of HIV Tests Conducted, HIV-Positive Tests Results, and HIV-Positive Individuals Newly Initiated on Anti-Retroviral Treatment (ART) from 41 PEPFAR-Supported Countries, Mar 2016 to Jun 2021



2016-2021 quarterly results (final month of the quarter shown)



Conclusions



Testing

- Since 2018, HIV tests conducted decreased from approximately 20 million to 15 million with a stable percent positivity.
 - Opportunity for countries to critically review efficacy of testing approaches to identify country-specific strategic mix of strategies to increase identification of undiagnosed people living with HIV.

Proxy Linkage to Treatment

- Since 2016, the percent of newly diagnosed persons who initiated ART increased from 60% to 90% highlighting significant achievements to improve linkage to treatment by countries.
 - Building on established successes, strategies to achieve 95% linkage in a programmatically sustainable and cost-effective manner should be routinized.



The COVID-19 impact on prevention (much more ...)

Healthcare Access Among South African Youth Living With and Without HIV

Danielle Giovenco^{1,3}, Audrey Pettifor², Stephanie Chung², Gina Itzikowitz³, Yamkela Qayiya³, Linda-Gail Bekker³

¹Brown University, Providence, RI, USA, ²University of North Carolina at Chapel Hill, Chapel Hill, NC, USA,

³Desmond Tutu HIV Centre, Cape Town, South Africa

OBJECTIVE

- We examined healthcare access among South African young people living with and without HIV during the COVID-19 pandemic to identify potential disruptions in services.

METHODS

- We examined cross-sectional data from the baseline procedures of the BUDDY study conducted among young people (13-24 years) living with and without HIV in Cape Town, South Africa from February – September 2021.
- Young people living with HIV were recruited from an HIV clinic and HIV-uninfected young people were recruited through community outreach in a peri-urban township.
- Prevalence ratios were computed to estimate associations between HIV cohort and COVID-19 sexual and reproductive health (SRH) service access since March 2020.

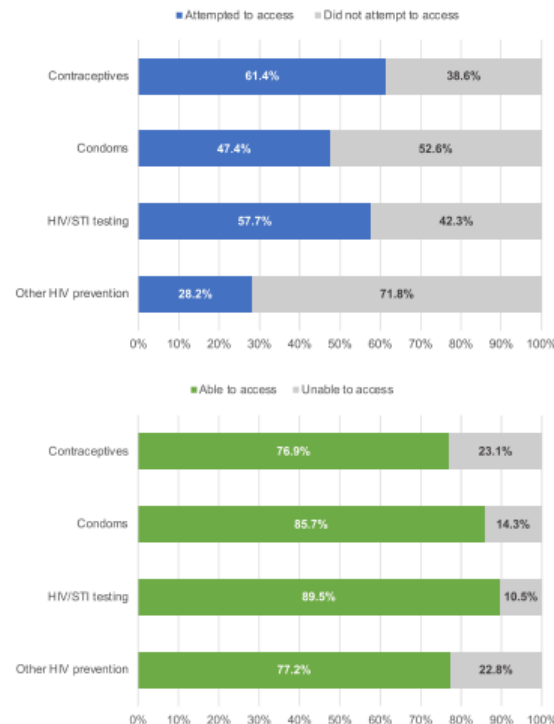


Figure 1. SRH-seeking behavior among young people since March 2020

South African young people living with HIV reported greater inability to access sexual and reproductive health services than young people living without HIV during the COVID-19 pandemic.

Table 1. Associations between HIV cohort and SRH-seeking behavior since March 2020

	Attempted to access		Able to access	
	%	PR (95% CI)	%	PR (95% CI)
Contraceptives				
YPLWH (girls only)	63.4	1.05 (0.89, 1.25)	65.4	0.78 (0.65, 0.93)
YPLWoH (girls only)	60.2	1.00 (ref)	83.9	1.00 (ref)
Condoms				
YPLWH	64.0	1.76 (1.47, 2.11)	82.0	0.91 (0.82, 1.01)
YPLWoH	36.3	1.00 (ref)	89.9	1.00 (ref)
HIV/STI testing				
YPLWH	74.8	1.63 (1.41, 1.88)	87.5	0.95 (0.88, 1.03)
YPLWoH	46.0	1.00 (ref)	91.7	1.00 (ref)
Other HIV services				
YPLWH	41.6	2.18 (1.65, 2.87)	70.8	0.82 (0.69, 0.96)
YPLWoH	19.1	1.00 (ref)	86.7	1.00 (ref)

PR=prevalence ratio, aPR=adjusted PR, p-values correspond to aPR estimates, YPLWH=young people living with HIV, YPLWoH=young people living without HIV

RESULTS

- 216 young people living with HIV and 320 young people living without HIV completed the BUDDY enrollment visit.
- Participants were a median of 19 years, 70% female, 99.6% Black African, and 98% isiXhosa speaking.
- Young people living with HIV were significantly more likely to report attempting to access condoms, HIV/STI testing, and other HIV prevention services and were significantly less likely to report being able to access contraceptives (for girls only) and other HIV prevention services since March 2020 when compared to young people living without HIV.
- Among young people living with HIV only, 37% reported missing an HIV care appointment, 15% reported they ran out of their HIV medication, and 31% reported they were worried about running out of their HIV medication since March 2020.

CONCLUSIONS

- Young people living HIV reported greater difficulty accessing SRH services than young people living without HIV, and a significant portion reported missing an HIV care appointment and running out of their HIV medication since March 2020.
- Services should devise strategies to prevent interruptions in healthcare access among South African young people.

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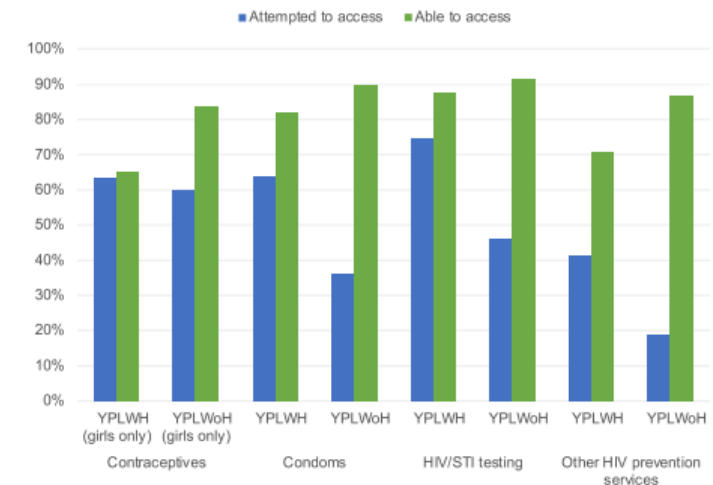


Figure 2. SRH-seeking behavior among YPLWH and YPLWoH since March 2020