

BHIVA 'Best of CROI' feedback webinars 2024 Prevention Strategies

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Thanks to Dr Conor Moran for support with slides

This educational event is supported by



With thanks to those presenting research for permission to use slides for 'Best of CROI'



Conflict of Interest

Attended advisory boards for Gilead sciences, MSD, ViiV Healthcare. Paid for talks by MSD.

Organisation receives funding to run clinical trials by Gilead Sciences, Viiv Healthcare, GSK & MSD.



Plan

- HIV PrEP
 - Persistence/ key populations
 - CAB LA
 - New agents
- Doxycycline PEP
 - Doxyvac Final results
 - DoxyPEP open label extension
 - Resistance
- Miscellaneous

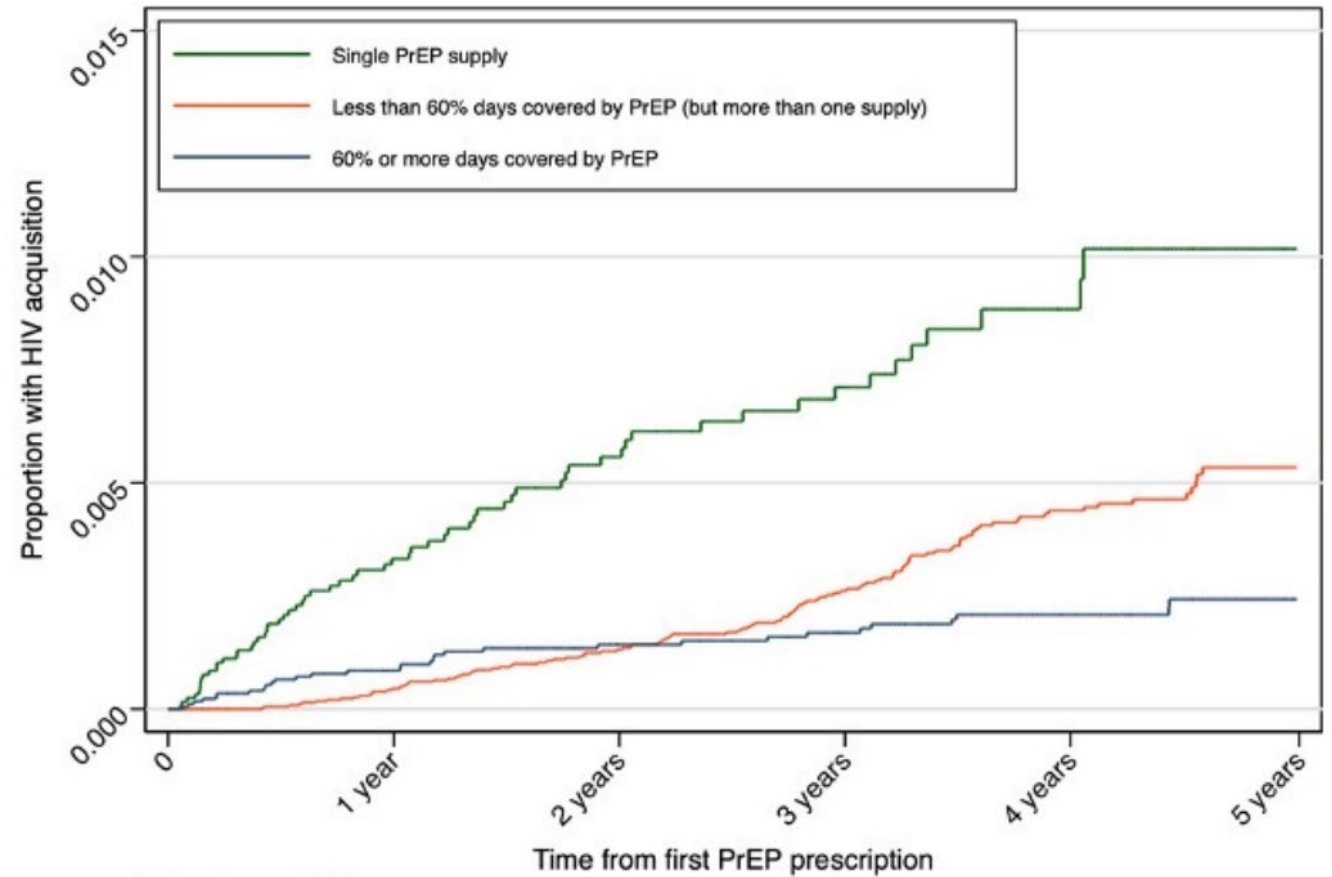
HIV Incidence of HIV PrEP in Australia (Medland #166)

First 5 years of Govnt subsidised PrEP programme
n=66,200; 2% women, age 33 (27-43)

207 new HIV diagnoses (1.07/1000 person years):
15% in those good coverage (IR 0.56)
30% in those received PrEP only once (IR 2.61)
55% in those with low coverage (IR 0.99)

Adjusted incidence rate ratios:

- One PrEP supply only**
- <60% days covered by PrEP**
- Younger age <30**
- Active HCV Rx**
- Year of initiation (start)**



	Number dispensed PrEP					
	0	1 year	2 years	3 years	4 years	5 years
Single supply	12582	7900	5342	3694	1560	0
<60%	35434	32239	27263	21858	13675	0
>=60%	18190	14546	12516	10692	8119	0

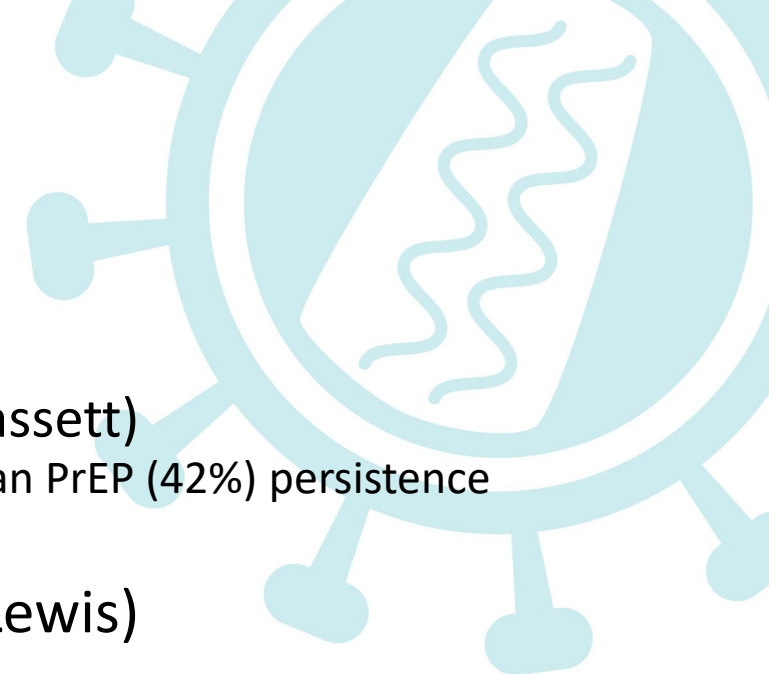
PrEP Persistence



- PrEP non persistence & HIV incidence (#1124 Tao)
 - n=123,901 USA PrEP Naïve, age 31yrs, used IQVIA RX & diagnosis database
 - Periods on-PrEP HIV diagnosis 2.15/ 100py
 - Periods off-PrEP (30d gaps in Rx) 4.22/ 100py
- = 2 fold higher HIV incidence during 'off-PrEP' periods**
across subgroups incl TGW, age & geographic areas

PrEP Persistence/ Key populations

- **PrEP persistence & contraception in Hair salons, S Africa.** (#1253 Bassett)
 - Novel venue, less stigma, acceptable to clients, better contraception (69%) than PrEP (42%) persistence
- **Mobile vs fixed location PrEP clinics Miami** (#1254 Doblecki-Lewis)
 - 87% male, 75% Hispanic/Latino
 - Increased PrEP persistence mobile location aHR 1.68
- **Mobility of Healthworkers with motorcycles to improve PrEP uptake amongst key populations.** Tanzania (#1140 Mohamedi)
 - Bolster efforts of community-based health workers in key populations
 - 40 motorbikes/ HWs; data Jan-sept 2022
 - Targeted areas including bars, brothels, truck parks, fishing/ construction sites
 - New clients increased 100% (n=2412), 97% FSW.
 - 88% refilled Rx through hot spots, 12% through health facilities



PrEP Persistence/ Key populations



- **Enhancing PrEP coverage through primary care:** Nationwide French study (#1141 Bamouni)
 - Since 2021 any practitioner allowed to prescribe PrEP, data 2021-2022
 - Profile of PrEP users was similar to before implementation; extending to women & SE disadvantaged people needs raising awareness amongst targets and HCPs
- **PrEP uptake in prisons** (# 1127 Classen). Zambia. HIV neg incarcerated persons offered PrEP; 78% uptake, persistence good (so far)
- **Post Abortion PrEP** (#169 Heffron) Kenya - initiation & phone call intervention for adherence support post PrEP initiation , RR2.5 of PrEP refill with calls cf without; RR 2 for urine TFV levels (but overall uptake/adherence poor for all)
- **Transgender Adults** – DCE re LA-PrEP Programs (#1244 Wilson-Barthes). USA. Cash incentive, F2F adherence counselling, Rx for injectable cf oral GAH , blood PrEP levels.
- **Choice** eg LA-CAB (#172 Kamya), increased uptake PrEP

INSIGHT cohort – Tenofovir Point of care tests and PrEP Persistence (#167 Mirembe)

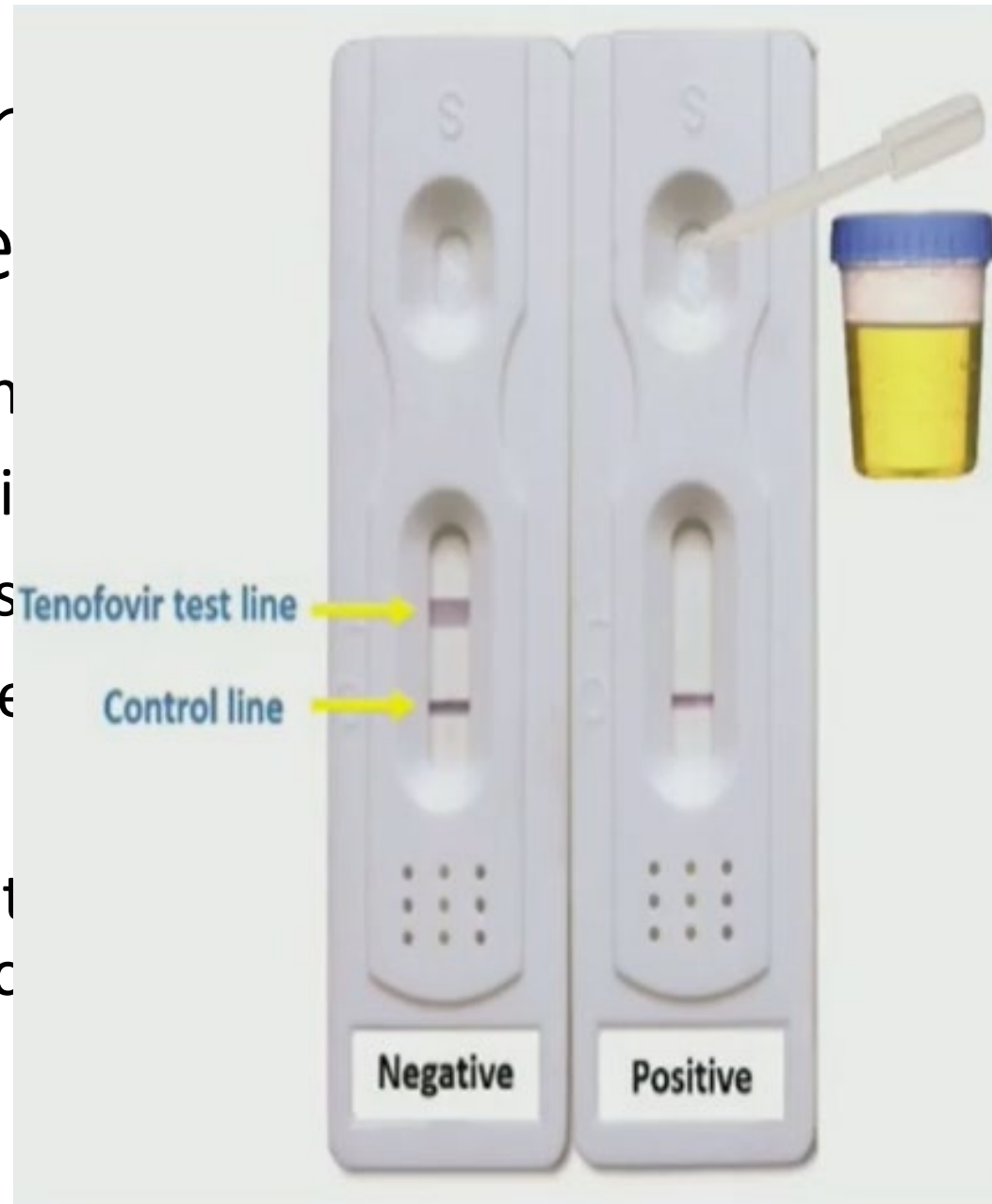
- Uptake/persistence/adherence TFV POC/experience POC
- 6 African Countries, Aug 2022-23
- Women 16-30yrs, sexually active last 3/12, interested in PrEP
- Offered PrEP, questionnaires, counselling – risk reduction/adherence

- POC TFV
 - Detects TFV intake last 4 days
 - Strongly predictive protection from HIV acquisition in Partners PrEP & IPrEX OLE



INSIGHT cohort and PrEP Pe

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INSIGHT cohort – Tenofovir Point of care tests and PrEP Persistence #167 Mirembe

3087 enrolled, uptake > 90% , 90% persistence m6 , high adherence

Results: Impact of POC Urine TFV Test on subsequent PrEP adherence

Prior urine test	Positive urine test at month 3 or 6	Adj. Risk Ratio	p-value
No prior test	233/560 (42%)	reference	
Any prior test (M1 or M3)	592/839 (71%)	1.45 (1.29, 1.62)	<0.001

Among sites where at least 5 women with and without prior urine TFV tests at prior visit. Women included in analysis if eligible for urine testing at a prior visit.



INSIGHT cohort – Tenofovir Point of care
and PrEP Persistence

**UK data – PrEP users- all men- self reported
adherence high and consistent with TFV drug levels -
acceptable and feasible but not necessary (#1111 Pool)**

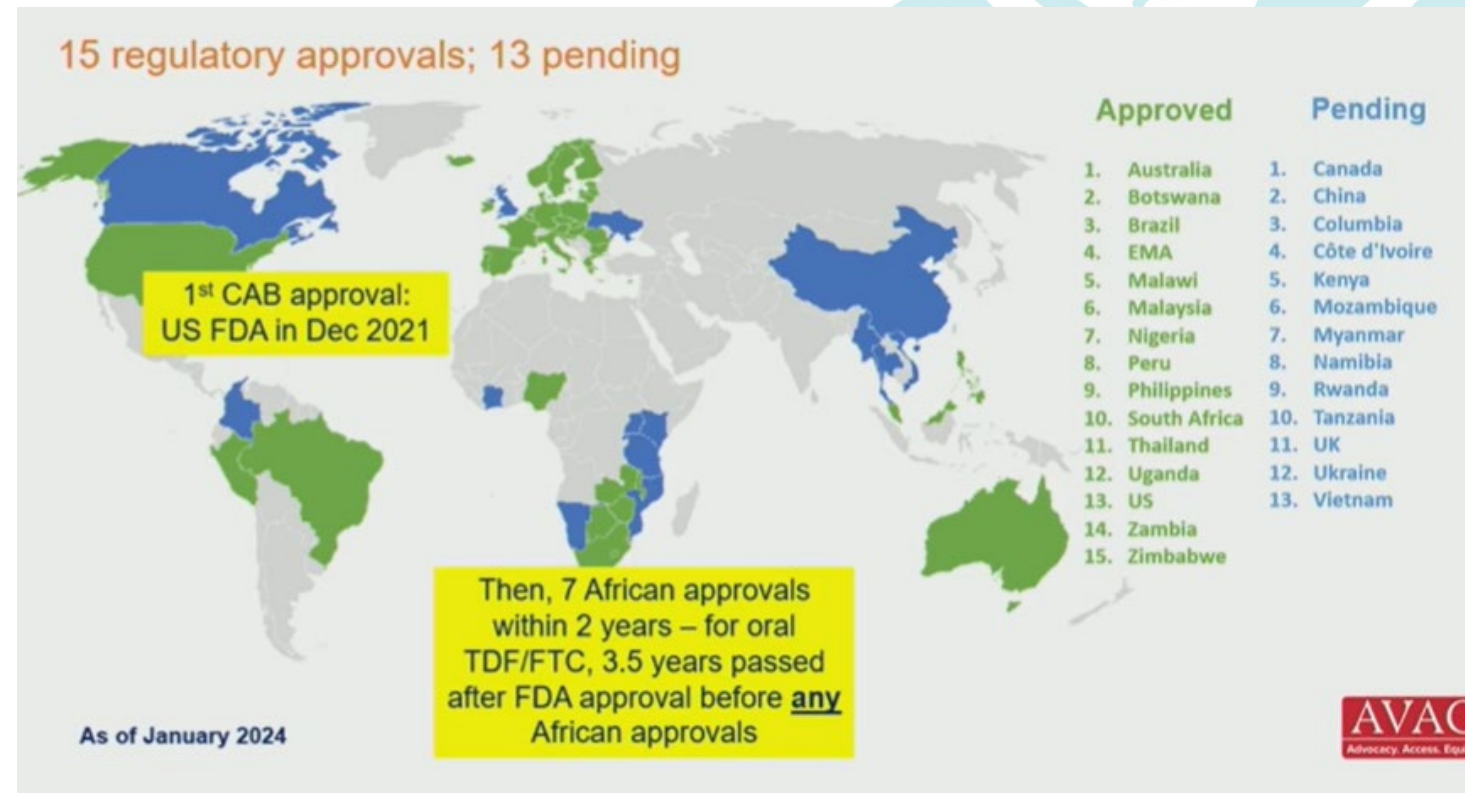
**Latin America – PrEP users – self report/ medication
possession ration (MPR) DBS levels all correlated – incl
young & TGW (#1115 Torres)**

... tests at prior visit.
... testing at a prior visit.



HIV PrEP – Cabotegravir long acting (CAB LA)

- HPTN 083 (Cis men & TGW) & 084 (cis women) shown CAB LA *superior* to oral TDF/FTC
- LA CAB approved US FDA as PrEP Dec 2021
- UK – currently with NICE
- Generic due 2027.....



(#48 Patel, CROI 2024)

HIV PrEP – Cabotegravir long acting (CAB LA)

• **Opera Cohort (USA) Uptake in routine care (#1109, Mills)**

- 498 completed initiation
- 13% women, 32% black
- 42% had STI within 12m
- 11% missed injection (bridging?)
- 7% Discontinued
- 1 seroconversion (@3rd injection)

• **Implementation in large urban HIV clinic, San Diego (#1108, Turner)**

- Clinic providing PrEP 400 pts, offered CAB LA
- 165 started (78% previous oral)
- 91% cis male, 48% white, 3% black
- 26 (16%) discontinued (11 ISR) - younger age, missing dose assoc with discontinuation

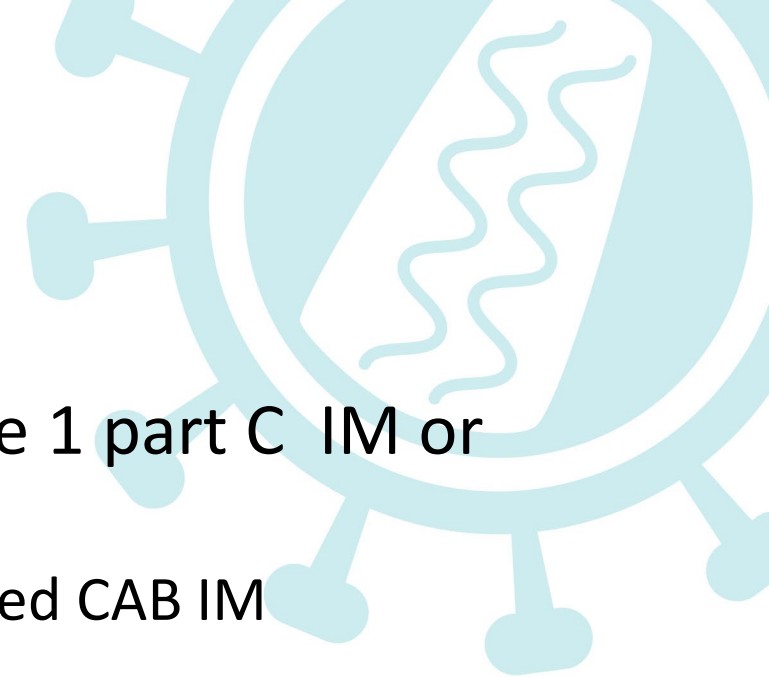
1 HIV seroconversion with CAB emergent resistance (#1107 Koss)

Robust uptake – importance of choice

New PrEP Agents



- Tenofovir alafenamide (TAF) implant phase 1, S Africa, women, first in human, n=36 (#123 Gengiah)
 - 110mg TAF, same size as contraceptive implant, 0.25mg release/day
 - Bicep, 1 or 2 implants/placebo, up to 48 weeks
 - AEs: 11 (31%) needed early removal (only one placebo) due to AE
 - PK – lower planned release/day, better with 2 implants
 - Challenge is to increase drug release while decreasing ISRs
- MK-8527 Novel NRTTI (phase 1 results, n= 66, adults without HIV, varying oral doses vs placebo) (# 129 Gillepsie)
 - Well tolerated, mild AEs & no SAEs
 - Terminal half life 216-291- potential for weekly and longer dosing
 - Proceeded to phase 2 studies in USA – monthly, varying doses



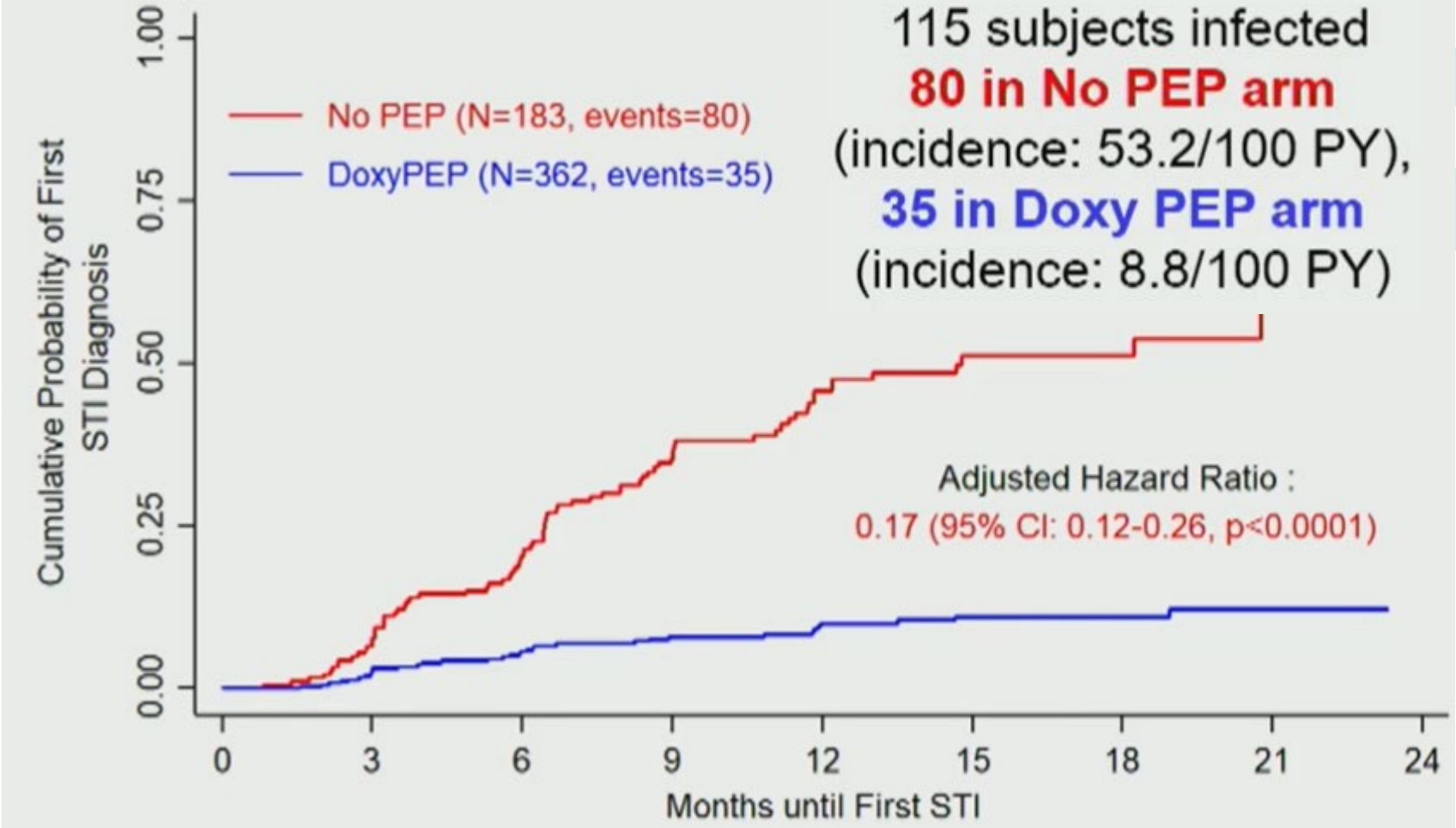
New PrEP Agents

- CAB-U LA (ultra long acting), new formulation, phase 1 part C IM or SC 800-1600mg 2 or 3mls) (#130 Han)
 - ISR: IM better tolerated than SCs, comparable to approved CAB IM
 - $T_{1/2}$ IM x2 and SC X6 predicted that of CAB
 - Dose intervals > 4 months supported – HIV-1 PREP & ART studies
- Ultra Long acting Dolutegravir in situ forming implant (#1137 Benhabbour)
 - Biodegradable and removable. Further studies

DOXYVAC – Final results (#124 Molina)

Molina, et al. (CROI 2023) DOXYVAC	
Study design	Factorial: 2:1 dPEP vs none + Men B vax vs none
Inclusion criteria	Adult MSM with ≥1 recent STI, at least 6 mo on oral HIV PrEP
Primary outcome	Time to first syphilis or CT

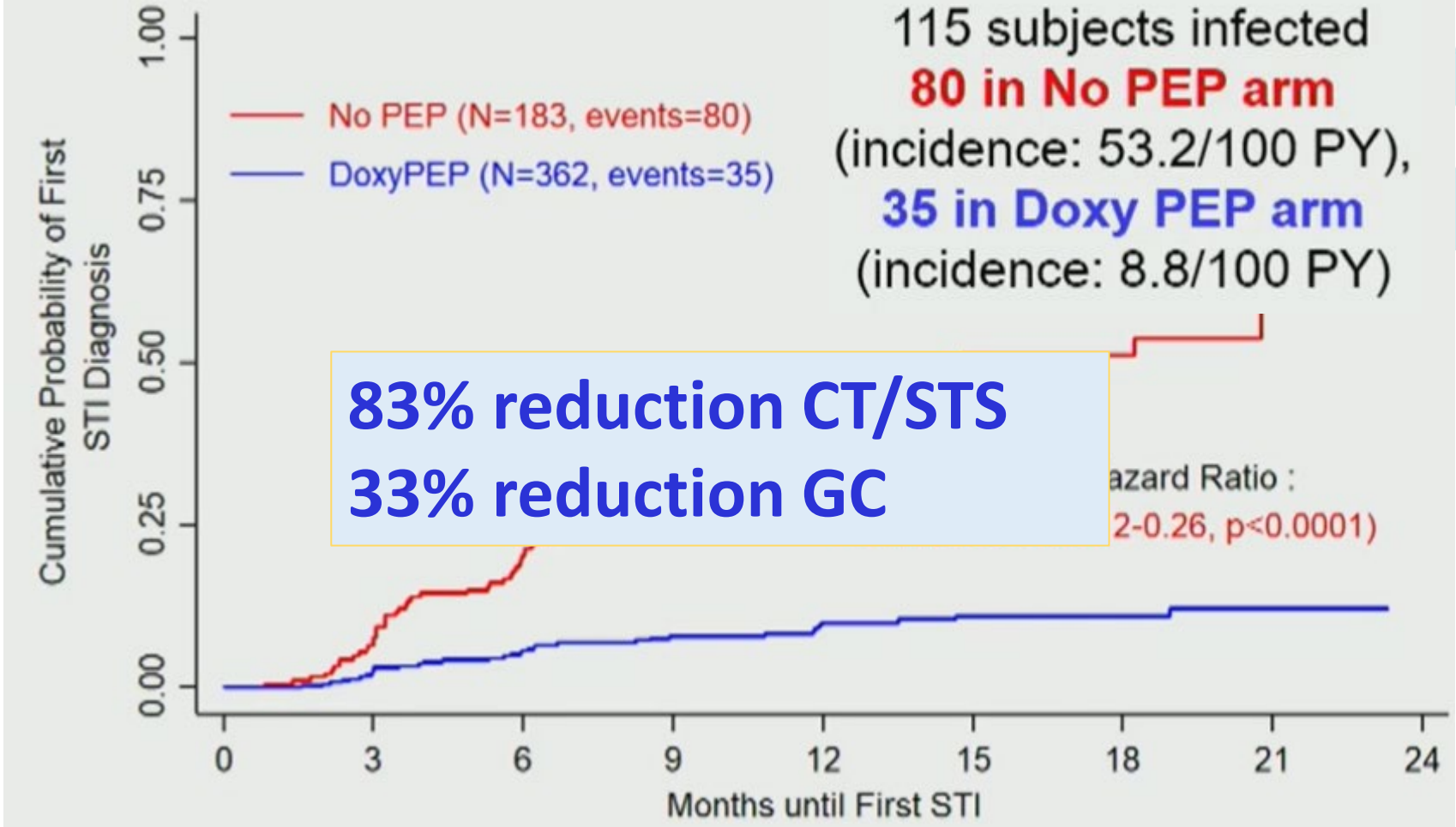
N=545 analysed
 Median age 40yrs
 Condomless sex (4 weeks) = 4 (2-10)
 Partners (3/12) = 10 (5-20)



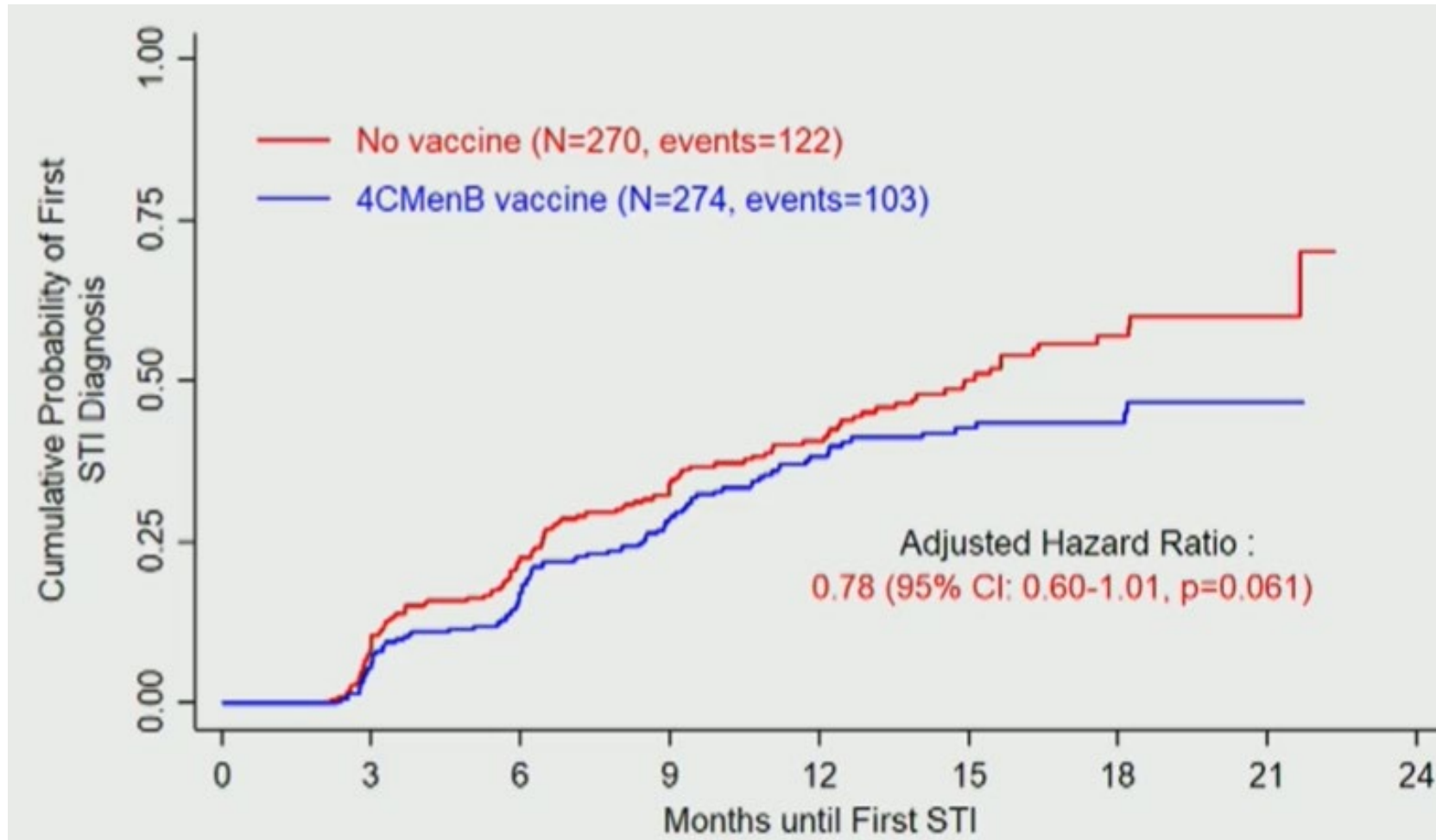
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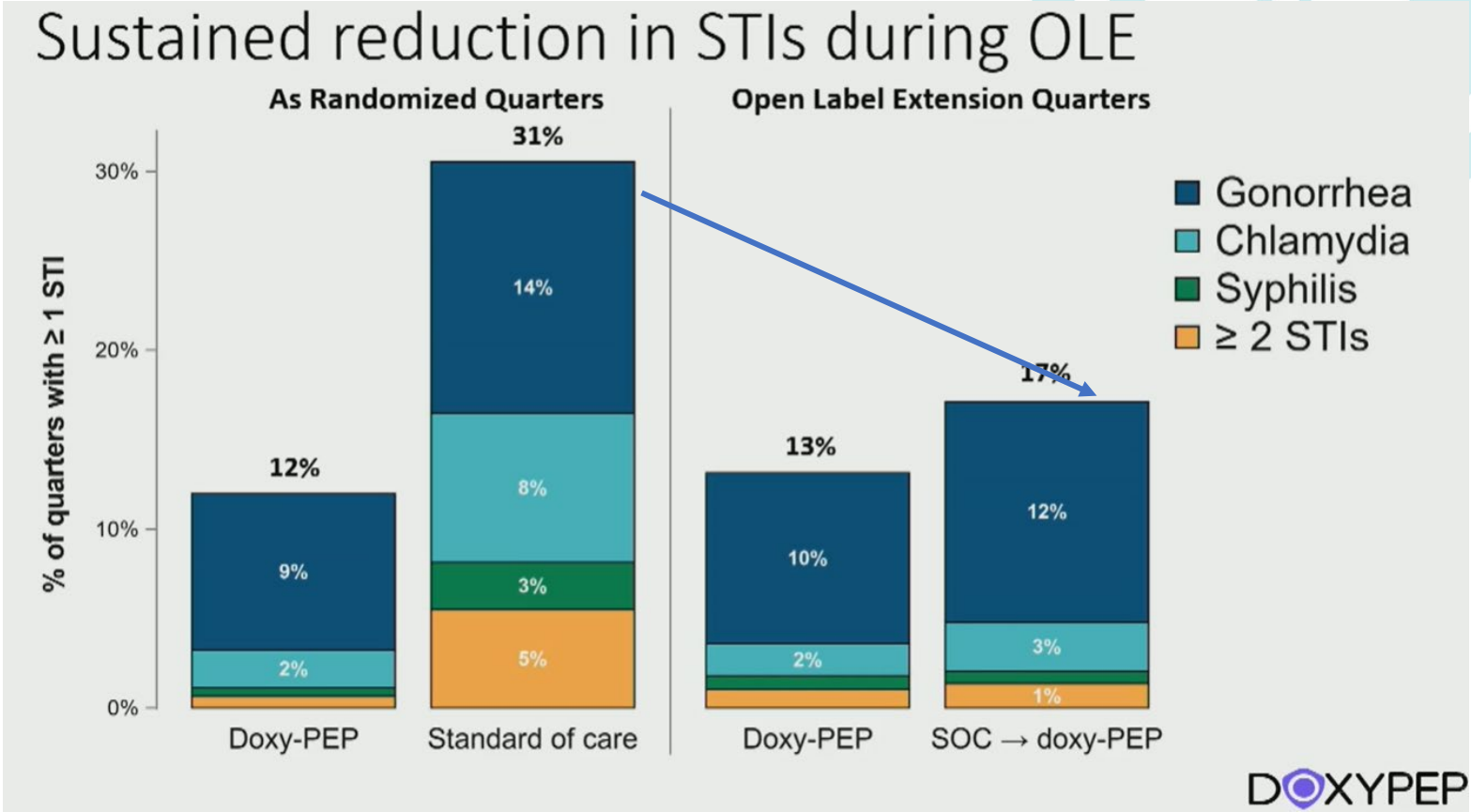
DOXYVAC – 4CMenB Vaccine – no signif efficacy



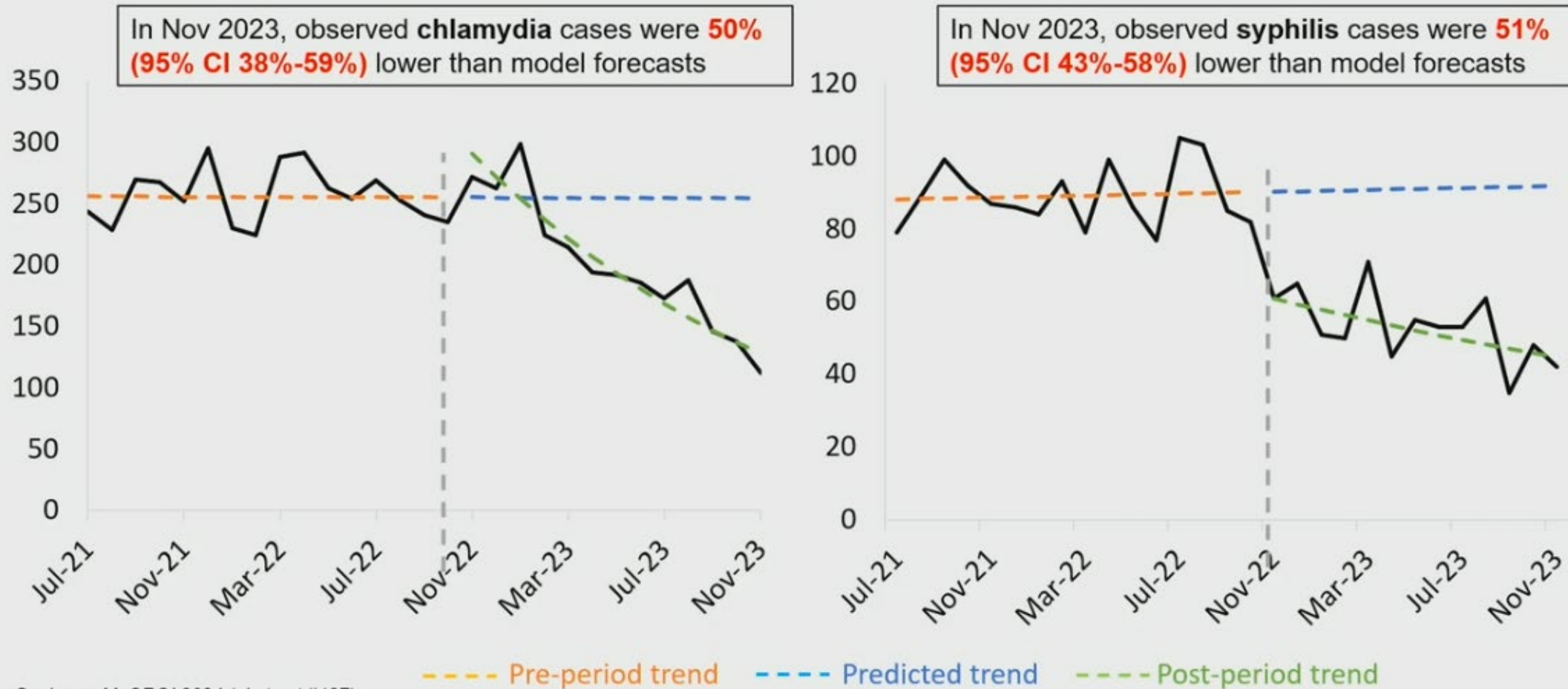
DOXYPEP – open label extension results # 125 Luetkemeyer

Luetkemeyer, et al. (2023) DoxyPEP	
Study design	Open-label, randomized 2:1 dPEP vs SOC
Inclusion criteria	Adult MSM/TGWSM HIV+ or PrEP; ≥1 recent STI
Participants	501; early stop for effectiveness

Overall 65% ↓ reduction in bacterial STIs each quarter
 ≈ 80% ↓ chlamydia & syphilis
 ≈ 50% ↓ gonorrhea
 Effectiveness independent of HIV serostatus



Decline in **citywide** chlamydia and early syphilis cases in MSM in SF after release of doxy-PEP guidelines



Qualitative benefits of doxy-PEP



Emotionally...that confidence [due to doxy-PEP] counts for a lot in terms of my mood, and my positivity, and my... sex positivity...before, there would be this kind of cloud of shame come over [a sex act]. (Age 44, HIV-, Seattle)

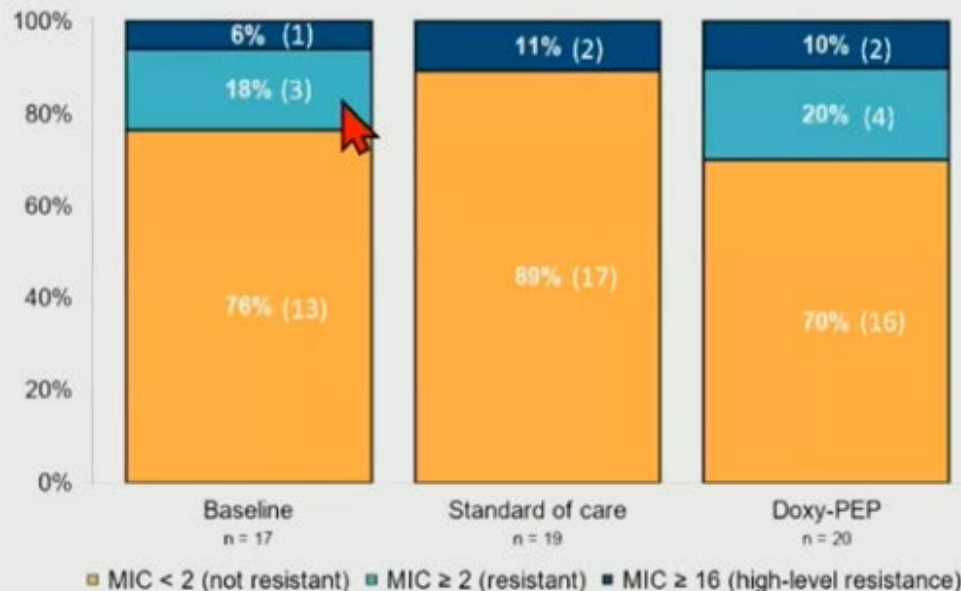
Sex-positive and person-first intervention

- Improved peace of mind & sexual pleasure
- Decreased stigma around STI diagnosis and disclosure
- Increased self-awareness about sexual behavior
- Facilitates communication with partners

GC: Impact in Doxyvac/DoxyPEP trials (2020-22)

DOXYPEP

- GC: 56 cultures



Doxyvac

- GC: 78 cultures

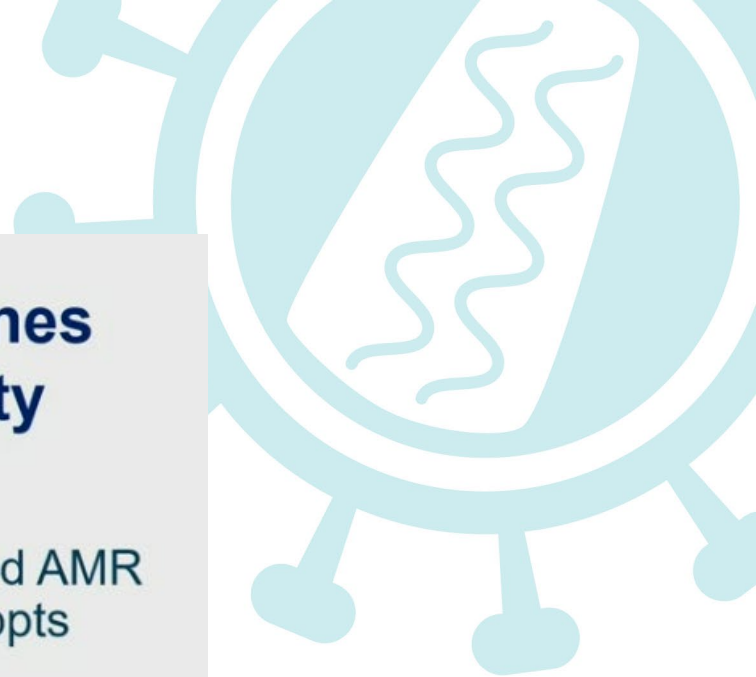


Resistance defined by MIC ≥ 2 mg/L

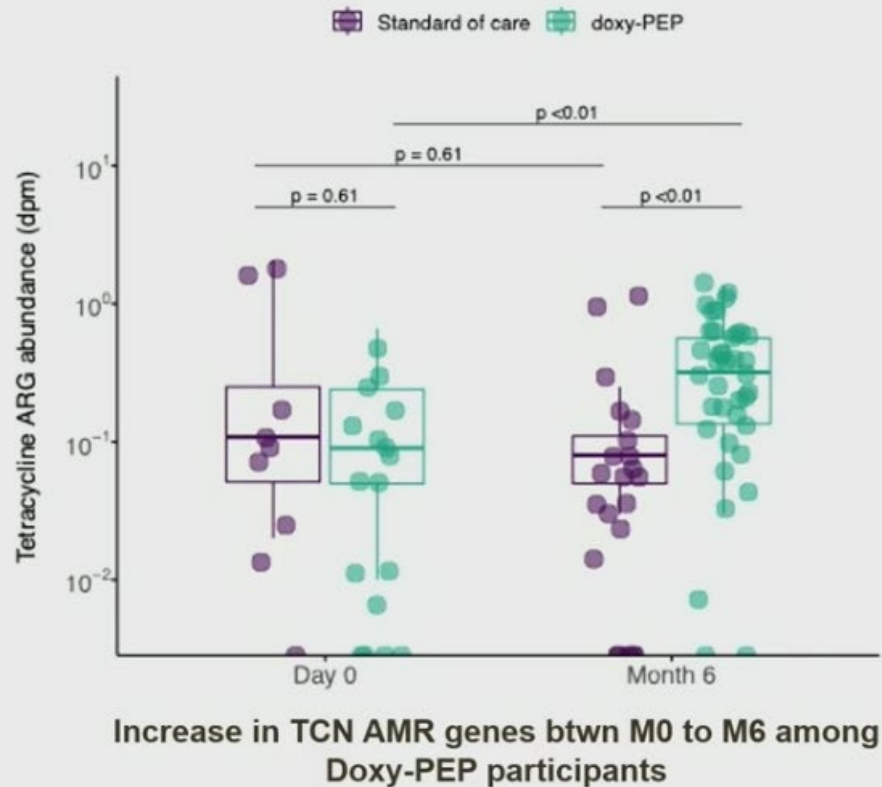
Increased TCN-R in doxy-PEP vs. standard of care suggests doxy-PEP may be less protective against GC strains with existing TCN-R.

More high-level tetracycline-resistant isolates in the PEP group ($p=0.04$)

Impact on resistance



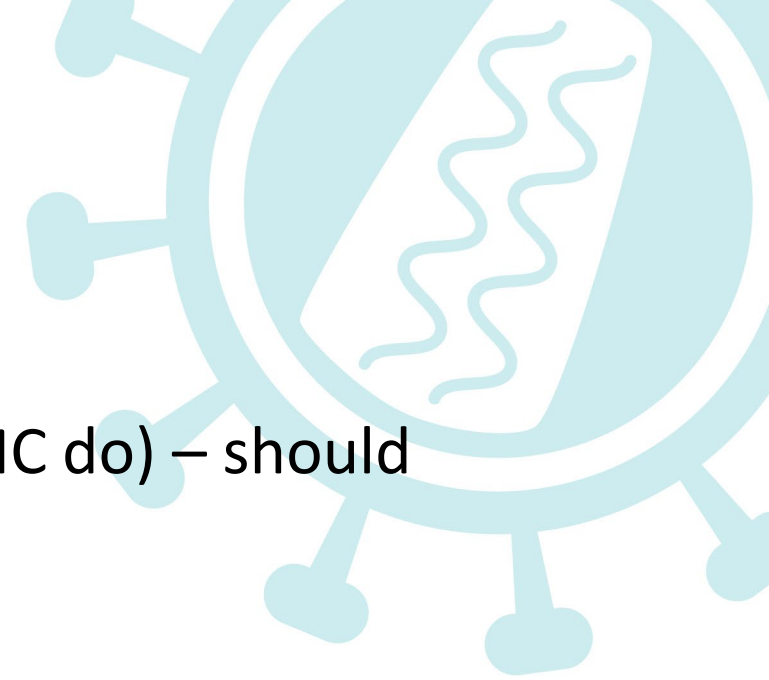
Doxy-PEP associated with higher number of AMR genes without significant alteration of microbiome diversity



- Comparison of actively expressed AMR genes in 46 dPEP and 24 SOC pts
- No difference in gut bacterial microbiome α - or β -diversity or total abundance between arms at M0 or M6, or over time by arm
- Actively expressed TCN-R genes increased by median of 2 in dPEP group ($P < 0.01$) without change to non-TCN classes

Chu, et al. CROI 2024 (Abstract 3404)
dPEP = doxycycline post-exposure prophylaxis
SOC = standard care group

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Prevention miscellaneous

HIV PrEP challenging EBD dogma talk (#50 Stewart)

- TDF mucosal levels don't correlate with protection (PBMC do) – should reconsider EBD vaginal/frontal sex.
- Await results of study of TAF vs TDF as EBD (ANRS)

BIC/F/TAF as PEP – (n= 119) well tolerated, no seroconversions (# 1134 Tan)

PLWH HBV vaccine non responders (#209 Marks, Clinical Late breakers)

- 2/3 doses of HepB-CpG Vaccine superior to 3 doses conventional vaccine.
- 93/99% seroprotection response cf 80%

Human papilloma vaccination/cervical cancer

Plenary #17 Nelly Mugo

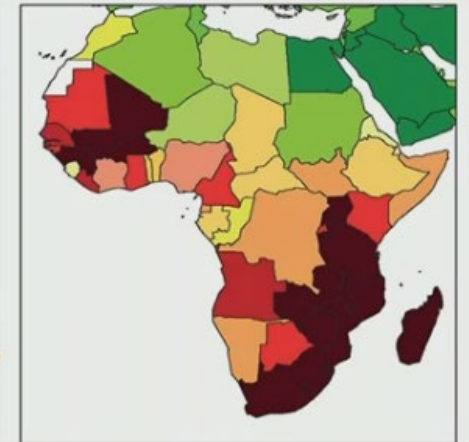
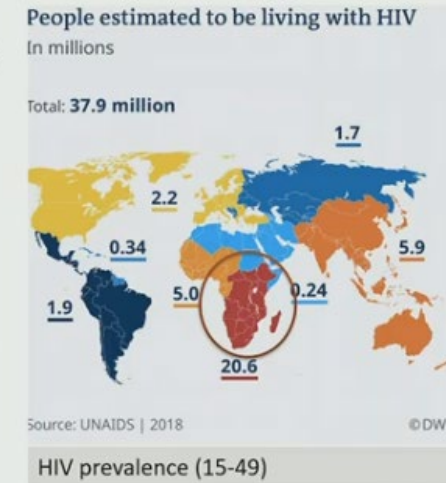
- Globally cervical cancer is the 4th most common cause of cancer among women
- Leading cause of cancer death among women in low- and lower-middle-income countries (LMIC)
 - > 604,000 cases and 341,000 deaths occur annually,
 - >90% of deaths occurring in LMIC
 - East Asia has the largest number of women with ICC
- Strong economic gradient: Incidence is 3 times higher in LIC compared to HIC
 - Mortality rates range from 1.0 in Switzerland to 55.7/100,000 woman years in Eswatini

*LIC; HIC: low income country, high income country

Geographic Overlap: HIV and cervical cancer

Women living with HIV have:

- Higher prevalence of hr-HPV coinfection, persistence, & faster progression to ICC
- Women with HIV have 6-fold increased risk of ICC
- 20% of cervical cancer is attributable to HIV infection



Bruni et al. Human Papillomavirus and Related Diseases in South Africa. Summary Report 17 June 2019

Lancet HIV, Local Burden of Disease collaborators; Stelzle 2021

Hr: high risk

CROI
2024

Human papilloma vaccination/cervical cancer

Plenary #17 Nelly Mugo

- Globally common cause of cancer
- Leading cause of cancer death in low- and middle-income countries (LMIC)
 - > 604,000 deaths annually
 - >90% of deaths in LMIC
 - East Asia and Southeast Asia
- Strong economic burden, especially in LMIC
 - Mortality rate of 100,000 per 100,000 women

WHO 90-70-90 cervical cancer elimination strategy

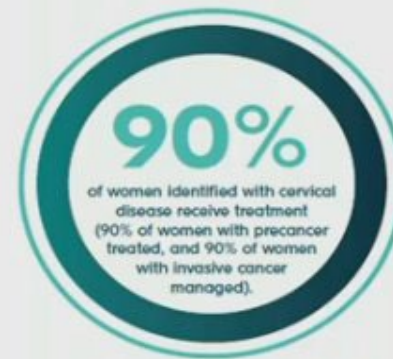
In 2018 the World Health Director General Tedros Ghebreyesus **made a call for 'elimination of cervical cancer'**.
The elimination strategies with the following 2030 targets



VACCINATION



SCREEN AND TREAT



CANCER TREATMENT

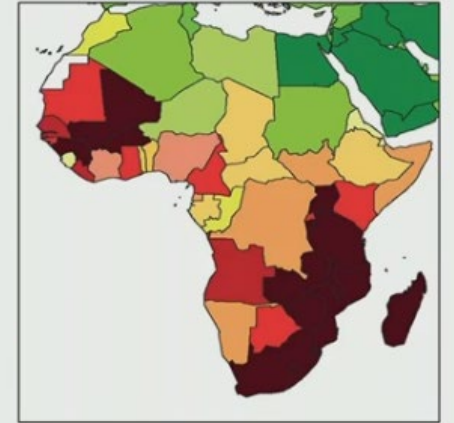
Implementing this strategy could prevent >62 million deaths from cervical cancer in the next 100 years

<https://www.who.int/publications/i/item/9789240014107>

<https://gco.iarc.fr/today/data/factsheets/cancers/23-Cervix-uteri-fact-sheet.pdf>

CROI 2024

Cervical cancer



Cervical cancer incidence >43 per 100K

Africa. Summary Report 17 June 2019

CROI 2024

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