

From Data to Action: Advances and Evolving Strategies in HIV and STI Prevention



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Financial Relationships With Ineligible Companies (Formerly Described as Commercial Interests by the ACCME) Within the Last 2 Years

Dr Hazra reported receiving research grant funding from Gilead Sciences, Inc, and serving as a consultant to Abbott Laboratories, Gilead Sciences, Inc, and ViiV Healthcare. (Updated September 14, 2026)

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Learning Objectives

After attending this presentation, learners will be able to:

- Analyze the current HIV preexposure prophylaxis (PrEP) landscape and differentiate available prevention options
- Evaluate real-world outcomes and implementation considerations for long-acting PrEP in key populations
- Describe evidence and public health implications of doxycycline postexposure prophylaxis
- Assess emerging biomedical sexually transmitted infection prevention strategies in development

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The PrEP Landscape in 2025

	Daily FTC/TDF
Men who have sex with men	FDA approved, guideline recommended ^{1,4}
Transgender women	
Heterosexual men	
Heterosexual women	
Transgender men	
Persons Who Inject Drugs	

¹FTC/TDF PI, ²Gilead. JAMA. 2024. ³WHO implementation tool for pre-exposure prophylaxis (PrEP) of HIV infection. 2024. ⁴CDC PrEP guidelines. 2021. ⁵FTC/TAF PI, ⁶Abbott extended-release injectable suspension PI, ⁷LEN PI, ⁸Lenovo. JAMA. 2025. ⁹CDC LEN PrEP guidelines. MMWR. 2025. 2025.1

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Daily vs On-Demand (2-1-1) TDF/FTC

- Low HIV incidence across cohort (0.99/1000 PY, 13 cases) over mean follow-up 49.1 months
 - Daily PrEP 0.6/1000 PY (95%CI 0.1-1.8)
 - On-Demand PrEP 1.5/1000 PY (95%CI 0.6-3.0)
 - Switch 0.9/1000 PY (95%CI 0.2-2.6) (lowest rate of study discontinuation)
- Significant population level reductions in new HIV diagnoses in Paris, but progress is uneven
 - 33% reduction in HIV diagnoses among MSM born in France
 - 73% increase in HIV diagnoses MSM who migrated or immigrated to France
 - 95% increase in HIV diagnoses in transgender women regardless of country of birth

Daily and on-demand TDF/FTC both highly effective in preventing HIV

Molina JM. CROI 2024. Abstract 127. Slide 5

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PURPOSE 1 & 2 OLE Wk 52

- 95% of eligible participants opted to continue/ switch to LEN in the OLE
- High adherence through OLE
 - PURPOSE 1: ~96–97% on-time injections at OLE doses #2–#3
 - PURPOSE 2: ~90–96% on-time injections at OLE doses #2–#3
- ISRs remain common (65-90%) but Grade 3 ≤1%
 - Most frequent: nodules, pain, swelling, induration

Kiserukwa. IAS 2026. Abstract CAC2002. Lenovo IAS 2026. Abstract CAC2002.6. Slide 6

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HIV Acquisition on LEN PrEP (PURPOSE 1 & 2 OLE Wk 52)

§ seroconversions across PURPOSE 1 & 2 studies through OLE Wk 52

PURPOSE 1

- 2 new seroconversions post-primary analysis
 - Case 1: Occurred after LEN discontinuation with sub-therapeutic drug levels; no capsid inhibitor mutations
 - Case 2: Low-level viremia, target LEN levels, genotype unsuccessful

PURPOSE 2

- 2 seroconversions on study
 - On-time injections, target concentrations
 - N74D capsid mutations detected in both
- 1 seroconversion post-primary analysis
 - On-time injections, target concentrations
 - Q67H / K70R capsid mutations detected
- 1 seroconversion OLE through Wk 52
 - On-time injections, target concentrations
 - Q67H capsid mutations detected

Klemke, IAS 2024, Abstr CAC2805
Lewin, IAS 2024, Abstr CAC2805.6
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LEN ISRs in PURPOSE and Real-World

- ISRs were less frequent with LEN administered in non-abdomen sites in PURPOSE 1 and 2
- Early real-world data demonstrates abdominal site associated with:
 - ISRs needing clinical contact
 - Early LEN discontinuation

Characteristic	OR (95% CI)	P-value
Site of LEN injection		
High	Reference	
Abdomen	10.10 (1.14-218.12)	.001
Needles/needle reaction requiring discontinuation		
No	Reference	
Yes	10.08 (3.35-49.93)	<.001

Birkus, AIDS 2024, Abstr TUPECT184
Pattar, A et al, C20 2024
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OPERA Cohort: CAB-LA PrEP Use Among Women

- Among 5330 women who initiated PrEP between 2021 and 2024, 6% (n = 315) received CAB-LA
- Median follow-up for women initiating CAB-LA PrEP: 13 mo (IQR: 8, 19)
- Among 1193 maintenance injections, 88% were on time
- Incident HIV infections among women receiving LA CAB PrEP: 0

Amman-Rohrborn et al, AIDS 2024, Abstr CAC2805
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CAB-LA in Pregnancy Updates

- Pregnancy Infant and Maternal health Outcome (PrIMO)
- Prospective cohort designed to study CAB-LA during pregnancy and breastfeeding in Malawi
- Interim analysis based on first 545 births
- CAB-LA injections had similar pregnancy outcomes to women who used daily oral PrEP

Adverse Pregnancy Outcome	n	%	p-value
Stillborn	2	0.4	0.99
Neonatal death	2	0.4	0.99
Fetal death	2	0.4	0.99
Neonatal death	2	0.4	0.99
Fetal death	2	0.4	0.99
Neonatal death	2	0.4	0.99

Stillborn (0.4%), Neonatal death (0.4%), Fetal death (0.4%), Neonatal death (0.4%), Fetal death (0.4%), Neonatal death (0.4%).

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Alimatravir (MK-8527)

- Nucleoside reverse transcriptase translocation inhibitor with once monthly PK properties when taken orally
- 11mg q month selected for phase 3
- Efficacy predicted to 38 days to allow +/- 7 day window
- Efficacy predicted by PK model in adolescents and pregnancy

Time (months)

MK-8527 TP Concentration (ng/mL)

Time (months)

MK-8527 TP Concentration (ng/mL)

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Preferences for Monthly Oral PrEP Over Other PrEP Modalities

National survey of 723 GBMSM on PrEP preferences

- Monthly oral PrEP most preferred (28.6%); >50% preferred an oral option
- Preferences varied by race, stigma, healthcare trust, PrEP/HIV knowledge, and psychosocial resources
- Four distinct psychosocial profiles emerged; monthly oral PrEP led in 3 of 4 groups, while long-acting options remained important across groups
- Predominantly Black, less-resourced group strongly preferred daily oral PrEP
- Cost, side effects, visit burden, route & dosing frequency shaped preferences

Monthly oral PrEP vs other modalities

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Completed Doxycycline Prophylaxis Studies				
Study	Sample Size and Population	STI Rate or Outcome		Reduction in Relative Risk
		Doxycycline PPK	No Doxycycline PPK	
DoxyPEP Pilot (Los Angeles, USA, 2011-2012)	Men with HIV (n=30)	12.3 per 100 PY	33.2 per 100 PY	73% (p=0.02)
ANRS PERCOAT (Paris, France, 2015-2016)	Men on HIV PEP (n=232)	37.7 per 100 PY	69.7 per 100 PY	47% (p<0.0001)
DoxyPEP (Seattle and San Francisco, USA, 2020-2022)	Men with HIV (n=174)	11.6% per quarter	30.5% per quarter	62% (p<0.001); NNT: 5.3;
	Men on HIV PEP (n=327)	10.7% per quarter	31.9% per quarter	66% (p<0.001); NNT: 4.7
DOXYMAC (Paris, France, 2021-2022)	Men on HIV PEP (n=502)	8.8 per 100 PY**	53.2 per 100 PY*	83% (p<0.0001)
DuHS (Vancouver, Canada, 2019-2020)	Men on HIV PEP (n=62)	0 per 100 PY**	81.6 per 100 PY**	82% (p<0.01)
DuHS (Toronto and Vancouver, Canada, 2020-2022)	Men with HIV (n=52)	23.7 per 100 PY	119.4 per 100 PY	80% (p<0.001)
sPEP (Kisumu, Kenya, 2020-2022)	Women on HIV PEP (n=449)	25.1 per 100 PY	29.0 per 100 PY	12% (p=0.51)
DoxyPEP Pilot (Tokyo, Japan, 2022-2023)	Women sex workers (n=40)	79.2 per 100 PY	232.3 per 100 PY	67% (p<0.02)
doxyDOT (Kisumu, Kenya 2020)	Women on HIV PEP (n=60)	11.2 per 100 PY	29.6 per 100 PY	61% (p<0.039)

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Weekly Doxy Prophylaxis Among Cisgender Women (DoxycDOT Study)

- Open-label, single-arm pilot study
- Doxycycline 200 mg once weekly**
- 60** nonpregnant cisgender women in Kenya (ages 18–30)

Key Findings

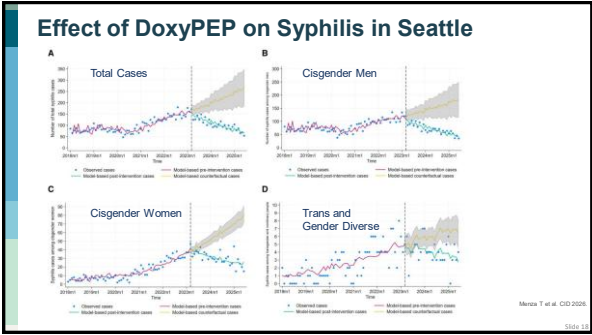
- 91%** adherence to weekly dosing
- 61%** reduction in chlamydia incidence

Adolescent Trial Network launched a trial of doxyPEP vs weekly doxy vs SOC among adolescent girls and young women in US (ATN-173/HPTN-115)

Stewart J et al. ISSTOR 2025

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Effect of DoxyPEP on Syphilis and CT in Australia

ACCESS
Antenatal and Community Cohort Study
Sydney, Australia

Syphilis diagnoses

Estimated 2019 cases: 20% reduction

Chlamydia diagnoses

Estimated 2019 cases: 20% reduction

Time-series interruptions

Gonorrhoea diagnoses

Estimated 2019 cases: no significant change

Tranjan Aids 2026; 2026: 00003

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DoxyPEP and GC Resistance

- Retrospective cohort (Italy, 2022–2025)
- 376 gonorrhoea episodes (n=318); 20.5% with DoxyPEP exposure
- High baseline resistance:
 - CIP 73%, TET 96% (17% high-level), AZM 10%, penG 12%
 - ORO decreased susceptibility (DS): 2.1%
- DoxyPEP associations:
 - 1 Tetracycline high-level resistance (OR 1.87, p=0.045)
 - 1 Ceftriaxone decreased susceptibility (OR 8.35, p=0.01)
- No association: ciprofloxacin, azithromycin, penicillin resistance
- MICs similar regardless of DoxyPEP exposure

Association between DoxyPEP use and resistance (aOR)

Antibiotic	Resistance Type	OR (95% CI)	p-value
Azithromycin	Resistance	1.78 (0.82–3.84)	0.144
Ciprofloxacin	Resistance	0.97 (0.33–1.86)	0.930
DoxyPEP	Resistance	0.73 (0.28–2.05)	0.587
Acetylsalicylic acid	High-level resistance	1.93 (0.21–1.87)	0.045
Ceftriaxone	Reduced susceptibility	8.35 (1.42–49.71)	0.020
Other infections	Positive	1.80 (0.59–5.46)	0.023

Raccagnoli AP, et al. CRO 2026, Abstract 1038, Slide 20

DoxyPEP and GC Resistance

Real-world Kaiser Permanente Southern California cohort, 2021–2025

- 26,582 MSM and transgender women with HIV or receiving HIV PrEP/PEP underwent STI testing
- 2,262 (8.5%) received DoxyPEP
- Retrospective **test-negative design** assessing doxyPEP fills ≤ 90 days before STI testing

Overall doxyPEP effectiveness

- Chlamydia: 66.5% (95% CI 53.6–79.5)
- Syphilis: 60.7% (28.3–78.5)
- Gonorrhea: -1.8% (-18.5–12.5)

Gonorrhea effectiveness declined over time

- 42.3% before statewide doxyPEP implementation
- 15.0% by Jan–Jun 2025

Decline coincided with rapid expansion of *tetM*, which confers high-level tetracycline resistance

Effectiveness fell from 47.2% when *tetM* prevalence was 20–29.9% → -6.5% when *tetM* was $\geq 50\%$

Figure 1 consists of three panels. Panel A is a line graph showing gonorrhea effectiveness over time from 2021 to 2025. The effectiveness starts at 42.3% before statewide doxyPEP implementation and declines to -15.0% by Jan–Jun 2025. Panel B is a line graph showing gonorrhea effectiveness by tetracycline resistance prevalence. Effectiveness is 47.2% when *tetM* prevalence is 20–29.9% and drops to -6.5% when *tetM* prevalence is $\geq 50\%$. Panel C shows box plots of gonorrhea effectiveness for different tetracycline resistance prevalence ranges: <20%, 20–29.9%, 30–49.9%, and $\geq 50\%$. The effectiveness decreases as resistance prevalence increases.

Yehoshelli M et al. *Lancet* 01 2026.

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Syphilis Diagnostics in the DoxyPEP Era

- Delayed seroconversion — may extend >2 weeks after ulcer onset
- Potential impact of DoxyPEP on syphilis diagnostic algorithms warrants monitoring

Seattle Sexual Health Clinic, 2023–2024 (n = 1,777 PrEP patients)

- Median RPR titer: 1:8 in DoxyPEP users vs. 1:32 in non-users
- Early syphilis: 12% among users vs. 88% among non-users
- Possible explanations:
 - Attenuated or delayed antibody response from recent doxycycline use
 - Higher prevalence of past treated infections among DoxyPEP users

Rucinski AR et al. 2024
Cannon C et al. ISSTD 2025

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4CMenB Vaccine Does Not Prevent Gonorrhea

Randomized, double-blind, placebo-controlled trial in Australia

- 587 MSM, age 18–50, at high vulnerability for gonorrhea
- Randomized to 2 doses of 4CMenB (Bexsero) vs placebo, 3 months apart
- Primary outcome: first *N. gonorrhoeae* infection ≥4 weeks after dose 2

No reduction in gonorrhea

- 4CMenB: 48.1 infections/100 person-years
- Placebo: 47.8 infections/100 person-years
- Vaccine efficacy: **−0.5%**
- IRR 1.01 (95% CI 0.80–1.26; **P=0.97**)

Despite encouraging observational data, 4CMenB did not reduce gonorrhea incidence in a randomized trial. The study was not powered to assess efficacy by symptoms, anatomic site, or subgroup.

Sub XL, CHOR 2025. Abstract 197
Zubin N, et al. NEJM 2024

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Prior Immunity Still Protects Against Severe Mpox

Multicenter U.S. cohort (7 sites, 186 mpox cases in 2025)

- 68 (36.6%) had prior immunity from vaccination and/or prior infection
- 118 (63.4%) had no prior evidence of immunity

Prior immunity associated with substantially less severe disease

- Median MPOX-SSS: 5 vs 7 (p<0.001)
- Severe disease: 24% vs 52% (p<0.001)
- Hospitalization: 2.9% vs 17.8% (p=0.006)
- 70% lower adjusted odds of severe disease aOR 0.30 (95% CI 0.14–0.60)

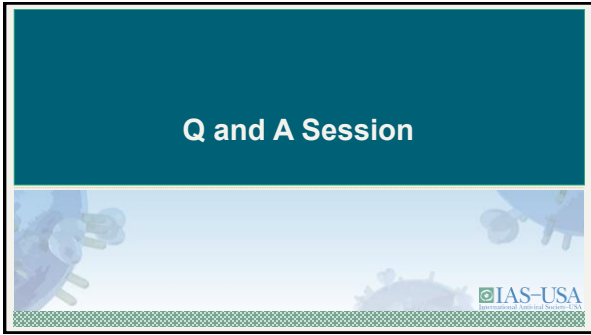
Protection appears durable

- Among 66 post-vaccination cases, median time since vaccination was 36 months
- No increase in disease severity with increasing time since vaccination

Zucker J. CHOR 2025. Abstract 305

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