Invited Review

CROI 2025: Global Epidemiology and Prevention of HIV and Other Sexually Transmitted Diseases

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Abstract: *At the 2025 Conference on Retroviruses and Opportunistic Infections (CROI), investigators presented updates on the global HIV epidemic. Although new HIV infections have been declining globally, new infections are expanding in Eastern Europe and central Asia, the Middle East and North Africa, and Latin America. HIV incidence remains high among key populations and their partners. Initiation of oral preexposure prophylaxis (PrEP) is increasing globally, with 91% of PrEP starts funded by the US President's Emergency Plan for AIDS Relief, and large rises in new HIV infections are predicted to occur due to international funding cuts. Several presentations focused on strategies to increase HIV testing, including home HIV self-testing, couples HIV testing, and use of digital strategies. Substance use continues to be a driver of new HIV infections. Implementation of harm reduction and opiate agonist therapy significantly reduced new infections among people who inject drugs in Malaysia, and other person-centered approaches tailored for people who use drugs are being investigated. The uptake of PrEP has been increasing in a number of priority populations; however, persistence on oral PrEP remains suboptimal. Although the use of long-acting injectable cabotegravir (CAB-LA) remains low in the US, several programs have demonstrated high persistence. When provided choice, many individuals choose CAB-LA over other available options, and adherence to follow-up injections has been high. Several interventions to increase PrEP uptake and adherence show promise, including pharmacy-based refills and incentives, point-of-care urine tenofovir testing with counseling, and use of mobile health tools. PrEP with emtricitabine/tenofovir alafenamide was shown to reduce HIV infections in cisgender women adherent to PrEP. A single once-yearly injection with lenacapavir showed promising pharmacokinetic results and a phase III trial is planned. Interest in doxycycline postexposure prophylaxis is high, and real-world implementation has been associated with significant declines in bacterial sexually transmitted infections.*

Keywords: CAB, cabotegravir, CROI, doxy-PEP, HIV, lenacapavir, long-acting CAB, preexposure prophylaxis, PrEP, prevention, STI

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Global Trends and Risk Factors for HIV Acquisition and Transmission

In a plenary presentation, Beyrer (Abstract 17) reported on the state of the global HIV/AIDS pandemic. He pointed to several Joint United Nations Programme on HIV/AIDS (UNAIDS) 2025 targets that were not met, even prior to the disruptions of the US Agency for International Development (USAID) and the US President's Emergency Plan for AIDS Relief (PEPFAR), with nearly one-quarter (23%) of people with HIV not on treatment. Additionally, although new HIV infections have been declining over the last 2 decades, there were still 1.3 million new HIV infections in 2023, far short of the 2025 target of fewer than 370,000 new infections, and HIV prevalence is expected to continue to rise until 2050. He highlighted 3 areas in which new infections are expanding, including Eastern Europe and central Asia, the Middle East and North Africa, and Latin America. Beyrer shared data on measured HIV incidence from recent HIV prevention trials. In the ECHO (Evidence for Contraceptive Options and HIV Outcomes) contraceptive trial in Africa, HIV incidence was 4.51 per 100 women-years, conferring a lifetime risk of HIV acquisition of 1 in 5 women; HIV incidence was similarly high (4.3/100 person-years [py]) among female participants in the placebo arm of the HIV Vaccine Trials Network 702 study. He pointed

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to data on placebo arm participants in studies over the last 15 years, showing no reductions in HIV incidence estimates during this period among female participants as well as men who have sex with men (MSM) and transgender persons. In terms of primary prevention strategies, initiations of oral PrEP have been increasing globally and were the highest in 2023 to 2024, with 91% of PrEP starts funded by PEPFAR. In Eastern and Southern Africa, there have been 6.4 million people started on PrEP since 2012, with only about 1.5 new HIV infections for every person started on PrEP on a population level, a testament to the success of PEPFAR. In contrast, PrEP uptake has been very low in Eastern Europe and Central Asia, with an estimated 42 new infections for every person on PrEP. He pointed to another challenge that the number needed to treat (NNT) with PrEP increases as the HIV incidence in a region decreases. A study by Rosenberg and colleagues highlighted policy tradeoffs between PrEP reach and efficiency in sub-Saharan Africa, and the high number of individuals that need to be on PrEP to achieve epidemic control. In African women, the NNT is 39 when PrEP is focused on 1% of the population at highest risk and can avert 5% of new infections, but to avert 95% of HIV cases, PrEP coverage needs to expand to two-thirds of the population (79 million people) where the NNT increases to 213.

Globally, there was a 39% reduction in new infections from 2010 to 2023 and a 51% reduction in AIDS-related deaths, although these reductions are not fast enough to reach UNAIDS targets

Similarly, among African men, the NNT increases from 14 to 219 when coverage increases from higher to lower risk populations, with 50 million men on PrEP needed to avert 90% of HIV cases. Given the challenges with implementing PrEP at this scale, he highlighted the need for an effective HIV vaccine. In the US, HIV incidence remains high among Black MSM and is decreasing significantly among White MSM. Due to the pause on US foreign assistance, PrEP is now only available for pregnant and breastfeeding women in PEPFAR-supported programs. Modeling studies predict large rises in HIV infections as a result of removing PEPFAR-funded PrEP for key populations in sub-Saharan Africa. In countries with higher coverages of PrEP funded by PEPFAR, PrEP interruptions could cause an increase of more than 30% of new infections among female sex workers, 20% increase among MSM and transgender women, and 15% among people who inject drugs. Beyrer called for a restoration of PEPFAR and its prevention program, supporting clinics for key populations and community partners, restoring National Institutes of Health (NIH), Centers for Disease Control and Prevention (CDC), and US Food and Drug Administration functions, and upholding human rights.

Imai-Eaton (Abstract 24) reported on immediate challenges and long-term goals of the HIV response. Globally, there was a 39% reduction in new infections from 2010 to 2023 and a 51% reduction in AIDS-related deaths during this period, although as mentioned in Beyrer's presentation, these reductions are not fast enough to reach UNAIDS targets. He pointed to diverging progress across global regions, with a 53% reduction in West, Central, East, and Southern Africa region from 2010 to 2023, but no change in estimated total infections outside sub-Saharan Africa. There has been substantial progress in preventing mother-to-child HIV transmission; however, reductions have stalled, with 120,000 new HIV infections among children in 2023, accounting for 9% of total new HIV infections, and 76,000 new AIDS-related deaths among children that year. Sources of new child infections include mothers who never initiated antiretroviral therapy (ART) or initiated late in pregnancy (57%), mothers interrupting ART during pregnancy or breastfeeding (19%), and mothers acquiring HIV during pregnancy or breastfeeding (24%). Possible interventions include access to antenatal care with universal HIV testing and ART initiation, male partner testing and increasing viral load suppression among men, long-acting injectable PrEP and ART, and

Disruptions to testing and treatment coverage and prevention could result in new HIV infections and AIDS-related deaths returning to 2005 epidemic peak levels by 2030 to 2035

retention and adherence support. Since 2015, there has been minimal progress with achieving earlier detection and treatment of HIV, with a persistent 25% to 40% with advanced HIV disease (CD4+ count <200 cells/μL) at the time of diagnosis/ART initiation. He pointed to how we can efficiently identify and reach people with effective prevention options. Outside of the African region, 80% of infections are occurring among key populations (MSM, transgender women, people who inject drugs, sex workers) and their partners, and in most of these groups, annual new HIV infections has been increasing. In sub-Saharan Africa, 25% of new infections are occurring among key populations who remain disproportionately impacted by HIV. He showed modeling data that scale-up of both treatment and prevention to their targets will be needed to achieve the greatest reductions in new infections in Eastern and Southern Africa. To help with targeting interventions, he highlighted that 73% of new HIV infections in Africa occurred in districts with incidence greater than 1 per 1000 per year. He ended with discussing the potential impact of international funding cuts, and emphasized that disruptions to testing and treatment coverage and prevention could result in new HIV infections and AIDS-related deaths returning to 2005 epidemic peak levels by 2030 to 2035.

Stevens and colleagues (Abstract 126) compared empirical HIV incidence with UNAIDS estimated incidence declines in sub-Saharan Africa. Incidence data were included from 174 studies mostly in Eastern and Southern Africa, comprising more than 23,000 infections and 3 million py. Empirical data from studies representative of the total adult population (including population cohort studies and nationally representative household surveys) were consistent with modeled estimates, and data from non-representative studies (including intervention trials and studies of pregnant/post-partum women) showed significantly higher HIV incidence (2.5- to 3-times higher) than modeled estimates. HIV incidence was significantly higher in key populations than among matched total population, with an incident rate ratio (IRR) of 6.55 for female sex workers and IRR of 46.11 for MSM. Across various population cohort studies, HIV incidence declined 75% to 90% since 2010, with incidence falling faster among adults aged 15 to 24 years than those aged 25 to 49 years. Women aged 25 to 49 experienced a growth in proportion of new HIV infections in Uganda, accounting for 17% of new infections in 1990 vs 46% in 2023, highlighting the need to ensure access to HIV prevention services among women over age 25 years.

Abrams (Abstract 1121) presented on estimated HIV incidence in 15- to 24-year-old individuals across 2 rounds of Population HIV Impact Assessments (PHIAs) in Africa. These nationally representative surveys were conducted in Eswatini, Lesotho, Malawi, and Zimbabwe from 2015 to 2017 (round 1) and 2020 to 2021 (round 2). Estimated annual HIV incidence did not significantly decline in any country for 15- to 24-year-old individuals, although declines were observed among 15- to 24-year-old females in Lesotho from round 1 to round 2 (1.49 to 0.34 per 100 individuals at risk; *P*=.02). In the most recent survey, there were approximately 25,600 adolescents and young adults (AYA) acquiring HIV annually across the 4 countries, with AYA accounting for approximately half of all people newly acquiring HIV in Eswatini (54%), Malawi (47%), and Zimbabwe (42%). These findings highlight the need for more effective and larger scale prevention efforts among youth.

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Also using PHIA data, Heck and colleagues (Abstract 1142) evaluated HIV prevalence in intersecting subgroups of Southern African women. Among 33,882 women surveyed after 2019 in Eswatini, Lesotho, Malawi, Mozambique, and Zimbabwe, HIV prevalence was 22% and varied by country. Overall, 48%, 33%, and 19% of women belonged to 0, 1, and multiple subgroups, respectively, including adolescent girls and young women (AGYW), currently pregnant and breastfeeding (PBFW), recent migrant (RM), 1 or more same-sex partners in the past 12 months (LGB), or purchased/sold sex in the past 12 months (SW). HIV was prevalent in all subgroups, with higher prevalence often observed among women in multiple subgroups. AGYW were often in multiple groupings, and HIV prevalence was greater in AGYW and PBFW characterized by multiple subgroups rather than 1. The authors highlight that maximizing epidemic responses requires reaching and engaging multiply marginalized women in southern Africa.

Risher and colleagues (Abstract 1141) evaluated couples-based homophily in HIV testing and treatment engagement across various countries in Africa. They

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characterized the couples-level HIV care continuum using data from 21 PHIAs between 2015 and 2023. Among 71,633 couples, 84% were seroconcordant negative, 8.8% seroconcordant positive, and 7.8% serodiscordant (4.3% female partner with HIV, 3.5% male partner with HIV). Among seroconcordant couples with HIV, more couples than expected were both positive but unaware of their status (4.4-times greater than under random mixing), and among seroconcordant HIV-negative couples, individuals who never tested were more likely to be coupled together (2.9-times greater). Similarly, for serodiscordant couples, more couples with individuals with HIV but unaware of their status and individuals without HIV and never tested were observed than expected (1.7-times greater when female partner with HIV and 2.4-times greater when male partner with HIV). These findings suggest that HIV testing and treatment interventions that target couples as a unit may be efficient in increasing reach.

HIV incidence was 4.4-times higher in men with partners who were female bar and sex workers in Uganda, yet only 6% of HIV-seronegative men reported using PrEP

Feng and colleagues (Abstract 1122) reported on HIV prevalence, incidence, and viral suppression among men who have sex with female bar and sex workers (FBSWs) in southern Uganda. Among 17,438 male participants evaluated in the Rakai Community Cohort Study between 2013 and 2020, 14% reported engaging in sex with FBSWs. Men with FBSW partners were older, had less education and lower incomes, and were never married, compared with men without FBSW partners. Baseline HIV seroprevalence was 3.16-times higher in men with FBSW partners (33% vs 10%; 95% CI, 2.93-3.40), which increased with the number and duration of FBSW partnerships. HIV incidence was 4.37-times higher in men with FBSW partners than in those without (1.93 vs 0.44/100 py; 95% CI, 3.04-6.16). Despite this higher risk for HIV acquisition, only 6% of HIV-seronegative men reported current PrEP use. The authors recommend including men with FBSW partners as a key population in prioritized HIV prevention programs in this region.

In the same study, Ssekubugu and colleagues (Abstract 1124) reported on contact tracing investigation of individuals with incident HIV. From 2021 to 2024, a matched case-control study was nested within the Rakai Community Cohort Study in which HIV incident cases were matched 1:1 to HIV-negative controls. Overall, 40% of men with an incident HIV infection reported 1 or more female sex worker partner, and male cases had 16-times higher odds than controls of reporting a female sex worker partner. Additionally, PrEP use (7% for FSW and female partners, 2% for male partners) and contact through assisted partner notification (16% for FSW and 19% for female partners; 5% for male partners) was low among partners of incident cases. As many men had no partner contact details beyond venue information, incorporating venue-based partner elicitation into partner notification could increase the reach of services.

Nakawooya and colleagues (Abstract 1143) reported on the use of assisted partner notification services in the Rakai Community Cohort Study in Uganda. Among 16,591 interviewed participants, 495 (3%) reported to have ever been contacted by partner notification services, of whom 383 (77%) reported having been tested for HIV because of partner notification. Overall, 217 (44%) had HIV, of whom 199 (92%) were virally suppressed. Among the 278 (56%) who tested negative for HIV, only 17% reported ever using PrEP, and of those with a history of PrEP use, only half were currently taking PrEP. The authors recommend targeted PrEP services to HIV-negative partners contacted by assisted partner notification.

Owuoth and colleagues (Abstract 1123) estimated HIV incidence among adults with multiple sex partners in Kisumu County in Western Kenya, where HIV prevalence is more than 4-times the national average. Among 619 participants without HIV (45% female; 47% age 25 years and older) enrolled in a longitudinal cohort study between January 2017 and August 2021, 11 incident HIV cases occurred over 1118 py, for an incidence rate of 9.84 per 1000 py. The HIV incidence rate decreased during the later follow-up period (13.84/1000 py in year 1 vs 5.59/1000 py in year 2), suggesting a beneficial cohort effect from routine engagement and education. In unadjusted analyses, having 4 or more sexual partners (hazard ratio [HR], 4.39), female sex (HR, 3.44), and forced participation in sexual activity (HR, 9.15) were associated with incident HIV infection; however, these were not statistically significant in multivariate analyses. The authors noted that the unexpectedly low HIV incidence among sexually active adults in this cohort could have been a result of effective HIV prevention

programs or possibly the impact of COVID-19-related behavioral changes.

Tasaneeyapan and colleagues (Abstract 1125) evaluated risk for recent HIV infections in 9 provinces in Thailand. Between 2023 and 2024, they introduced a new surveillance model that combines a rapid test for recent infection (RTRI) with HIV case surveillance data (CD4+ count greater than 200 cells/μL) to identify recent infections. Among 152,673 individuals tested for HIV, 2050 (1.3%) were diagnosed with HIV. Among the newly diagnosed, 1022 (50%) received an RTRI, and 60 (5.9%) were classified as a recent infection. RTRI coverage among the newly diagnosed was highest among MSM (87%), followed by people who inject drugs (PWID) (80%) and those aged 15 to 24 years (68%). The risk of recent infection was highest among MSM (36.8/10,000), female sex workers (20.7/10,000), and those aged 15 to 24 years (14.1/10,000), and lowest among women (2.7/10,000) and those aged 50 years and older (2.8/10,000). Using the same approach, Tanpradech and colleagues (Abstract 1126) evaluated risk factors for recent HIV infection among youth in Thailand. Among 709 newly diagnosed youth in the 9 provinces, 64 (9%) were identified as recent infections. In multivariable analyses, being single (adjusted odds ratio [aOR], 2.51; 95% CI, 1.03-7.19) compared with being married and living in the Northern region (aOR, 5.80; 95% CI, 1.66-23.7) compared with living in the central region of Thailand were risk factors for recent infection. These findings highlight the importance of implementing targeted prevention strategies to this particular youth group.

HIV prevalence was 33% among transgender women in midwest Brazil, and 50% evaluated with an avidity assay had recently acquired HIV

Teixeira and colleagues (Abstract 1108) reported on HIV prevalence and factors associated with recent HIV acquisition among transgender women from Midwest Brazil. HIV prevalence was 35% among transgender women in Brazil, and HIV incidence ranged from 5.8% to 9.2% in recent studies. Among 440 transgender women enrolled in 3 cities in Goiás, Brazil, the median age was 25 years, 71% self-identified as Black, and none were on PrEP. HIV prevalence was 33.2% overall, and 50.6% of participants (44/87) evaluated using the Limiting Antigen Avidity assay had recently acquired HIV. Transgender women with recent HIV acquisition were older (mean age, 28.3 years in those with recent HIV vs 24.7 years in those with longstanding HIV; $P = .041$), and those with longstanding HIV were more likely to have a sexually transmitted infection (STI) (58% with longstanding HIV vs 32% with recent HIV; $P = .024$). In a logistic regression analysis, there was a borderline association between older age and higher odds of recent HIV infection (OR, 1.03; 95% CI, 0.99-10.7, per 1-year increase). In the same study, Diniz e Silva and colleagues (Abstract 1109) reported on the high burden of HIV among transgender women in the state capital and rural towns in Central Brazil. HIV prevalence was similar in the state capital (32%) vs in small cities (33%). A self-reported history of an STI was associated with HIV infection in both groups (adjusted prevalence ratio [aPR], 1.5 for the capital and 2.2 for small cities), whereas group sex was only associated with HIV infection in the small cities (aPR, 2.5). Results from both presentations highlight the need for targeted prevention interventions, including increasing PrEP access, for transgender women in this region.

Erly and colleagues (Abstract 1101) assessed the impact of imprisonment on the risk of HIV, syphilis, and fatal overdose in Washington state. Baseline incidence rates for these conditions were 2.6- to 10.5-times higher among jailed individuals than among the general population in Washington. Incidence rates were higher post-incarceration, and by comparing incidence rates of each condition before and after incarceration, they estimated that 4% of fatal overdose, 2% of syphilis transmissions, and 1% of HIV transmission were attributable to the disruption caused by arrest and incarceration. Across all conditions, 55% had evidence of substance use, 46% were people of color, and 40% resided in census tracts in the lowest income quartile. The researchers call for targeted interventions in and after jail for individuals who use substances.

People recently released from prison had HIV acquisition rates that were 6.3-times higher than the general population

Also in Washington state, Troupe and colleagues (Abstract 1102) reported on HIV acquisition following

prison release. Among 58,026 individuals released from the Department of Corrections between 2010 and 2021, 120 were diagnosed with HIV. This cohort experienced HIV acquisition rates that were 6.3-times higher than the general population. Among men released from prison (HIV incidence 31.3/100,000 py), having an opioid or amphetamine disorder, a drug-related offense, and less than a high school education was the categoric cluster that most predicted HIV acquisition (HIV incidence 198.8/100,000 py). These findings highlight that people released from prison are at elevated risk of HIV acquisition, and routinely collected data can help identify high-risk subgroups to prioritize for HIV prevention programs in prison and upon release.

Bunting and colleagues (Abstract 1105) quantified new HIV diagnoses following discharge from psychiatric hospitalization. Using data from a commercial claims database for privately insured Americans from 2004 to 2022, they identified 492,363 individuals with a psychiatric hospitalization. The mean age was 33.3 years, the most common reason for hospitalization was depression (38.8%), and the average length of hospitalization was 6.35 days. During the follow-up period, 277 new HIV diagnoses were identified, with new diagnoses more common among men (67%), those who were not married (85%), and those in the Western US (40%). The median time from discharge to new HIV diagnosis was 154 days (interquartile range [IQR], 61-243), which was longest for people hospitalized for depression (171 days; IQR, 77-266) and shortest for people hospitalized for stimulant use disorder (40 days; IQR, 32-70). The authors suggest that psychiatric hospitals may serve as a point of contact for HIV screening, preventive counseling, and coordination of PrEP care.

Wensing and colleagues (Abstract 1127) evaluated generational dynamics in HIV infections among MSM in the national observational ATHENA (AIDS Therapy Evaluation in the Netherlands) cohort. Between 1998 and 2023, a total of 13,307 MSM were diagnosed with HIV in the Netherlands, with the overall number of diagnoses decreasing since 2008. Although decreases were seen in "Boomers" (those born before 1965) and "Gen-X" (those born between 1965 and 1980), HIV infections increased in "Millennials" (those born between 1981 and 1996) until 2013. From 2015, HIV was observed among "Gen-Z" (those born in 1997 or later) and accounted for 18% of cases in 2023. "Gen-Z" MSM were more likely to be diagnosed with recent infection than "Millennials" (46% vs 27%, respectively). Transmission clusters were identified using HIV-Transmission Cluster Engine (HIV-TRACE), which was available from 6744 MSM. Among the 92 "Gen-Z" MSM with polymerase sequence data, 48 (52%) had no phylogenetic link to anyone in the cohort, whereas 44 (48%) were linked to 32 transmission clusters (11 clusters present before 2015, 21 first observed after 2015), suggesting that "Gen-Z" MSM are part of both existing and new transmission clusters.

Bell and colleagues (Abstract 1139) reported on the geospatial heterogeneity in potential HIV transmission locations among MSM in Bhopal, India. Between December 2023 and April 2024, they enrolled 752 MSM through respondent-driven sampling. Almost all participants completed secondary school (99.5%) and were employed (98%). The overall prevalence of HIV and HIV viremia was 11.6% and 4.4%, respectively. MSM who met sexual partners at transportation-related venues had the highest prevalence of HIV (14.9%) and HIV viremia (6.5%), and those meeting at commercial locations had the lowest HIV prevalence (6.8%) and viremia (3.3%). They identified a 3.88 km² area south of the 1984 Bhopal Gas Tragedy site where 46% of all MSM with detectable viremia met partners. MSM who met within 1 km of the gas leak site had a 14% higher HIV prevalence, 4.3% higher HIV viremia prevalence, twice as many sexual partners (median, 15 vs 7), and 5.3% higher inconsistent condom use with causal partners. These findings suggest that spatially tailored interventions may be efficient in preventing HIV transmission among MSM in this urban Indian setting.

Cross and colleagues (Abstract 1170) compared the rate of HIV epidemic growth for countries inside and outside of existing Gilead voluntary licenses. An existing voluntary license for tenofovir alafenamide (TAF) includes 117 countries and covers an estimated 29.6 million people with HIV in countries that constitute 808,900 new HIV infections in 2023. Excluded middle-income countries (MICs) constitute 4.4 million people with HIV and 288,189 new infections. From 2010 to 2023, the increase in new infections was 55% in excluded MICs vs a decrease of 17% for countries included in the license. As new forms of injectable PrEP, including lenacapavir (LEN), have proven superior to oral PrEP and could have a substantial impact on the global HIV epidemic if accessible and affordable, the authors emphasize the importance of considering the change in rate of infection in determining country inclusion for voluntary licensing of LEN.

Imaz and colleagues (Abstract 1128) reported on the development of an HIV risk prediction model using electronic health record (EHR) data in Spain. An estimated 7.5% of people with HIV in Spain are unaware of their diagnosis, and 49% of new diagnoses are classified as late.

Using EHR data from Teletron, a European Medicines Agency registered database with 2.2 million individuals from the Spanish national health system, they developed a predictive model to help identify people to test and uncover undiagnosed HIV and reduce late diagnoses. The model identified 10 clinical conditions with the highest predictive value, 6 different age groups, and sex, and was able to identify more than 70% of HIV cases through screening less than 4% of a health department-sized population, and achieved a prevalence rate of 2.6% or higher, with a number needed to test to identify 1 positive case ranging between 12 and 48 people. When integrated into EHR systems, this tool could be used to generate automated alerts and promote proactive testing to reduce missed opportunities for HIV diagnoses.

Zalla and colleagues (Abstract 1116) reported on the effect of the Ending the HIV Epidemic (EHE) initiative on racial/ethnic disparities in HIV incidence in the US. Using the Johns Hopkins Epidemiological and Economic Model, a dynamic compartmental model of HIV transmission in the US, they modeled the impact of increasing the HIV testing rate, proportion virally suppressed, and proportion prescribed PrEP such that EHE targets were achieved by 2030. Under current epidemic trends without additional intervention, they projected that HIV incidence in Atlanta, Baltimore, Houston, and New York would decrease from 21 to 19 infections per 100,000 population by 2035. Under a race-neutral scale-up of testing, viral suppression, and PrEP, HIV incidence was projected to decrease by an additional 26%, however racial disparities would persist, with HIV incidence remaining 11.6-times higher among Black and 5.6-times higher among Hispanic individuals than among other racialized groups. These findings suggest that interventions that allocate prevention and treatment resources equitably (rather than equally) are needed to eliminate racial/ethnic disparities in HIV incidence.

Shook-Sa and colleagues (Abstract 1130) examined the impact of the HPTN (HIV Prevention Trials Network) 071 (PopART) intervention on HIV in the general populations of Zambia and South Africa. This trial was a cluster randomized trial that compared 2 interventions: (A) combination prevention with universal ART and (B) combination prevention with ART based on local guidelines compared with (C) standard of care. Although the trial did not demonstrate a difference between arms A and C when evaluated in a sampled population cohort, they noted that the HPTN 071 sample under-represented men, older adults, alcohol users, and employed individuals compared with the general population. Leveraging data from 2 probability-based surveys representing 4.5 million adults in Zambia and South Africa, they weighted the HPTN 071 sample to match the population of interest by demographics and HIV risk factors. With weighting, the risk of HIV over the study period was lower in arms A and B relative to arm C, resulting in strengthened effect estimates: risk difference of 0.10% (unweighted) vs -0.34% (weighted) for arm A vs arm C and -0.66 (unweighted) vs -1.18 (weighted) for arm B vs arm C. These findings suggest that the PopART intervention was more protective in the population of interest than in the trial and highlight the importance of accounting for selection bias when analyzing trial results.

Moyo and colleagues assessed the impact of different sources of infection in the BCPP/Ya Tsiu universal test-and-treat trial in Botswana (Abstract 1207). Using deep-sequenced phylogenetic data from 5114 trial participants, they inferred directed opposite-sex transmission pairs between trial communities. They found that most transmissions to trial communities occurred from non-trial communities ("spillover effects"), which substantially reduced the impact of the intervention. They demonstrated that a national application of the intervention would have reduced transmissions to trial communities by 59%, compared with the observed 30% reduction. They suggest that the provision of treatment as prevention to all communities nationwide would avert considerably more transmissions.

The Together Takemehome HIV self-test distribution program helped several US states meet 20% of their annual HIV testing needs. Among more than 16,000 patients treated for syphilis in Japan, only 6.2% received HIV screening

HIV Testing

In the US, 13% of the 1.2 million people with HIV are unaware of their HIV status. HIV self-testing is a promising strategy to increase access to HIV testing, reduce stigma, and is recommended by the World Health

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Organization. In a themed discussion, Sullivan and colleagues (Abstract 1178) reported on outcomes from a national HIV self-test distribution program in the US. In March 2023, the CDC-funded Together Takemehome program launched and allowed individuals 17 years or older to order 1 or 2 HIV self-tests online at no cost. From March 2023 to September 2024, a total of 297,047 people placed first orders for 1 (16%) or 2 (84%) test kits. Among 13,722 who completed a follow-up survey, 2.4% had prior evidence of HIV infection on the post-order survey, of whom 175 (63%) later used an HIV self-test. Among the 12,200 without HIV, 88% used an HIV self-test, and 228 (2.1%) had a positive result, of whom 182 previously reported no evidence of infection. Of these, 107 were tested by a clinician, 67 were diagnosed with HIV, and 50 initiated ART. Sullivan called for strengthening messaging on the need for laboratory testing following a positive HIV self-test.

Hecht and colleagues (Abstract 1179) estimated the need for annual HIV testing met by the Together Takemehome program. From March 2023 to July 2024, a total of 315,710 users placed orders with 586,099 test kits distributed, and the proportion for any HIV testing need met and past-year HIV testing need met was calculated. For both outcomes, the jurisdiction with the highest met need was Washington, DC (upper bound, 39%), followed by Puerto Rico, Georgia, Maryland, Florida, and Mississippi (upper bound, >20%). Additionally, 5 other states in the South, as well as New York, New Jersey, and Nevada, had more than 14% of their estimated HIV testing need met by this program.

Kantarida and colleagues (Abstract 1199) reported on characteristics of first-time HIV self-tests using an online HIV service in Thailand. They launched the "Stand by You" initiative that included free HIV self-test kits distributed by mail, online text-based counseling, education on HIV prevention including postexposure prophylaxis (PEP) and PrEP, and linkage to care, and disseminated the program via TikTok ads focused on at-risk adolescents and young adults. From August 2022 to December 2024, a total of 8234 participants tested used the program, of whom 57% were first-time testers (mean age, 25.4 years). Compared with repeat testers, first-time testers were younger (54% younger than age 25 years vs 39% older than age 25 years; $P < .001$), less likely to self-identify as lesbian, gay, bisexual, transgender, queer, intersex, and asexual (LGBTQIA+) (52% vs 74%; $P < .001$), less likely to use PrEP (0.6% vs 12.2%; $P < .001$) or PEP (1% vs 14%; $P < .001$), reported lower rates of condom use, and had a higher HIV positivity rate (4% vs 2.5%; $P < .001$). In multivariable analysis, having a positive HIV self-test result among first-time testers was associated with identifying as LGBTQIA+ (aOR, 7.41; 95% CI, 4.82-11.39), having a history of STIs (aOR, 1.86; 95% CI, 1.37-2.53), and being older (aOR, 1.03 per year increase; 95% CI, 1.01-1.05). These findings highlight the crucial role of digital platforms in reaching those with no prior testing history and promoting earlier HIV detection and treatment.

Darbes and colleagues (Abstract 118) described results on the efficacy of home visits for pregnant couples to promote couples HIV testing and family health in Kenya. The Jamii Bora (JB) intervention trained lay health workers to conduct home visits to support couples HIV testing and provide counseling focused on family health and relationships. Overall, 800 couples enrolled in the study and were randomly assigned to receive home visits, self-test kits, or standard of care. Couples HIV testing improved for both the home visit (aRR, 4.22; 95% CI, 2.88-6.18) and the self-test arms (aRR, 3.69; 95% CI, 2.50-5.45). At follow-up, relationship satisfaction, dyadic trust, couple communication, and commitment were higher in the home visit arm (all $P < .05$). Additionally, maternal viral suppression was higher in the home visit arm than in the standard-of-care arm (aRR, 1.07; 95% CI, 1.03-1.12). In the same study, Kweena and colleagues (Abstract 1181) reported on moderators of the JB intervention on couples HIV testing and counseling uptake in Kenya. They found that the probability of couples HIV testing was higher among HIV-negative women than among women with HIV, with marginal effects of 27% in the home visit arm, 11% in the self-test kit arm, and 12% in the standard-of-care arm. Parity was also a moderator of the intervention effect, in which women with fewer live births were more likely to test as a couple than those with numerous live births. These results suggest that other intervention modalities may be needed to support women with HIV and those with higher parity with couples HIV testing and facilitated disclosure.

Ruiz and colleagues (Abstract 1182) evaluated the effectiveness and population impact of status-neutral HIV screening focused on the Hispanic community in Arizona. They integrated opt-out HIV screening with a status-neutral health screening service that includes screening for levels of blood pressure, glucose, lipids, hemoglobin A1c, and body mass index measurements offered by 3 mobile health units in Arizona. From October 2022 to December 2024, a total of 3008 HIV tests were administered, with 83% of participants overall and 92% of Hispanic participants being first-time testers. HIV testing rates increased from 17% to 73% in Tucson

and 16% to 77% in Phoenix. Knowledge of PrEP was very low among testers (about 1%). Several benefits of this delivery model include reduced stigma, incentivized health, and raised awareness of HIV in the context of general health.

Wood and colleagues (Abstract 1183) evaluated the effectiveness of a clinical decision support tool for improving HIV screening across 31 clinics in a pediatric primary care network. The system included: (1) order sets with HIV test orders and universal HIV screening recommendations for patients aged 13 years and older; (2) an Adolescent Health Questionnaire assessing sexual activity completed by patients on arrival; and (3) an EHR best practice alert in the visit note for sexually active youth reminding practitioners to screen for HIV. In interrupted time series analysis comparing screening rates before and after intervention implementation, there were no differences in HIV screening rates for sexually active youth (OR, 1.11; 95% CI, 0.79-1.03). The authors suggest that clinical decision support interventions may need to be paired with educational interventions, endorsement by leadership, or financial incentives.

King'ori and colleagues (Abstract 1185) reported on the validation of a national HIV testing eligibility screening tool in Tanzania. In 2020, Tanzania introduced a 16-item screening tool to assess eligibility for HIV testing services. From March to June 2024, 23,444 adolescents and adults across 32 health facilities enrolled in a validation study comparing characteristics of the current tool with an optimized tool developed using logistic regression to identify the most predictive screening questions and optimal weighting, and HIV self-testing as a screening tool. Overall, 356 (1.5%) participants were diagnosed with HIV, with higher prevalence among women (1.7%) and those aged 35 years or older (2.0%). Using the national tool, 22,228 (95%) screened eligible for HIV testing services, with 98% sensitivity but only 5.2% specificity. Slightly fewer individuals (22,097; 94%) screened eligible using the optimized tool, with similar performance (98% sensitivity; 5.9% specificity). Using HIV self-testing for screening resulted in 402 (1.7%) participants eligible for HIV testing services, including all in whom HIV was diagnosed (100% sensitivity; 99.8% specificity). These findings suggest that screening with HIV self-testing may be more efficient than the 2 screening tools, resulting in fewer individuals screening eligible for HIV testing services but identifying all people in whom HIV was diagnosed.

Taniguchi and colleagues (Abstract 1189) reported on missed opportunities in HIV screening among patients tested for syphilis in Japan. Data from the National Database of Health Insurance Claims (2011-2020) and AIDS Surveillance Committee data providing HIV diagnosis and AIDS case information (2012-2020) were used for syphilis and testing analysis. Of 295,853 patients tested for syphilis, only 13,353 (4.5%) completed HIV screening. HIV screening rates varied by age and were lowest among the group older than 70 years (4.68%), despite having the highest number of syphilis tests (102,580) in this age group. Among the 16,270 patients who received antibiotic treatment for syphilis, only 6.2% received HIV screening. The rate of advanced HIV disease was higher in the older age groups, rising from 10% in the group younger than 20 years to 57% in the group older than 70 years. These results highlight the need to substantially increase HIV testing rates for all patients undergoing syphilis testing and treatment, regardless of age.

Wandina and colleagues (Abstract 1190) discussed the use of machine-aided HIV risk classification to improve HIV testing services across 95 health facilities in Kenya. Between April 2023 and June 2024, a total of 57,450 individuals tested for HIV were screened using machine learning, with 4% classified as very high risk, 19% as high risk, 46% as medium risk, and 31% as low risk. HIV test positivity was 9% for the very high-risk group, 3% for the high-risk group, and 1% for the medium-risk and low-risk group. In contrast, by following a counselor manual guided screening tool, 14% of clients screened eligible with 530,431 clients tested, and only 1.1% tested positive. These findings suggest that machine-guided HIV risk classification can help improve HIV identification and efficiency of screening.

Bessler and colleagues (Abstract 1192) evaluated the performance of the laboratory-based HIV antigen/antibody (Ag/Ab) testing in the US. Using HIV testing data among individuals tested by a major commercial laboratory (Quest Diagnostics) between 2019 and 2023, a total of 23,944,766 HIV Ag/Ab tests were identified, with 36.5% performed on men and 63.5% in women. Overall, the positive predictive value (PPV) was higher in men (88%) than in women (58%). The PPV was lowest among those aged 13 to 14 years (28%) and peaked at 89% for individuals aged 25 to 34 years, then declined to 71% for men 75 years and older. The PPV was 50% for women of reproductive age (15-44 years), likely due to near-universal screening among pregnant women, who overall have low HIV prevalence, and increased to 74% for women aged 55 to 64 years. These results highlight the need to conduct the entire recommended HIV diagnostic algorithm in those with a positive Ag/Ab test (HIV

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Ab differentiation and in the event of conflicting results, HIV RNA level) to confirm an HIV diagnosis.

White and colleagues (Abstract 1186) evaluated the transfusion risk of HIV, hepatitis B virus (HBV) infection, and hepatitis C virus (HCV) infection in low- and middle-income countries without nucleic acid testing. From October 2019 to June 2022, data from 4123 units of blood collected by the Uganda Blood Transfusion Services were tested in real time for HIV, HBV, and HCV serology on the Abbott ARCHITECT platform, and were retested using a combination of individual unit nucleic acid testing and serology. Among units screened seronegative with the ARCHITECT device, 8 were potentially infectious for HIV, 27 for HBV, and 2 for HCV. The prevalence of potentially infectious units was estimated to be 195.5 per 100,000 units for HIV, 666 per 100,000 units for HBV, and 49 per 100,000 units for HCV, which is many-fold higher than that seen in high-income countries. The authors call for policies that ensure equitable access and distribution of donor screening tools to promote safe blood transfusions globally.

Avelino-Silva and colleagues (Abstract 1191) evaluated HIV serologic reactivity in persons with HIV who started ART during acute or early stages of infection. In the RV254 cohort in Bangkok, data on 345 individuals with recent HIV acquisition had samples collected between 96 and 480 weeks after ART initiation. At ART onset, 48 individuals were Fiebig stage 1, 92 were Fiebig 2, 148 were Fiebig 3, and 57 were Fiebig 4. Overall, 24 (7%) participants had nonreactive Ag/Ab tests, with 38% nonreactive for Fiebig 1 vs 1% to 4% for Fiebig stages 2 to 4, with progressively lower signal-to-cutoff readouts for participants starting ART at earlier Fiebig stages. These findings confirm earlier studies that ART initiation at acute/early stages of infection can suppress Ab reactivity for years following infection and can result in false-negative serologic diagnostic testing in clinical settings, including blood donation screening.

Flynn and colleagues (Abstract 1188) assessed the additional time spent on facility-based and laboratory-based HIV recent infection surveillance testing per new patient with HIV in Rwanda and Eswatini. HIV-1 recent infection surveillance using the Asanté HIV-1 Rapid Recency Assay (Sedia Biosciences) launched in 2018 in Rwanda and in 2019 in Eswatini. Using time-motion methodology to observe health care worker workflows over a 3-month period, data were collected from 84 patients newly testing positive for HIV in Rwanda (10 recent, 70 long-term, and 4 control cases) and 76 patients in Eswatini (5 recent, 68 long-term, and 3 control cases), respectively. Overall, HIV-1 recent infection surveillance added an average of 17 minutes to health care worker duties per patient newly diagnosed with HIV. Returning recency test results to clients in Rwanda added up to 16 minutes, and administering a recency-specific questionnaire in Eswatini added 10 minutes. The researchers suggest that fully integrating recent infection surveillance into HIV case surveillance and removing recency questionnaires may further streamline testing visits.

Violette and colleagues (Abtract 1195) evaluated preferences for HIV testing technologies in Seattle, Washington. Between June 2023 and May 2024, they conducted a mixed-methods study consisting of a discrete choice experiment among 142 individuals (median age, 32 years; 68% cisgender male; 17% Hispanic/Latinx; 15% Asian; and 30% currently on PrEP) seeking HIV testing and prevention services at a community testing site or HIV clinic, followed by in-depth interviews with 20 participants. Accuracy was the most important test characteristic, and there was a strong preference for HIV tests with shorter window periods (eg, 2 weeks), although there was a general lack of awareness of the window period in the interviews. Faster tests were most preferred, with similar preference weights for a 20- or 60-minute test time. Fingerstick specimens were the most preferred, and oral fluid was the least preferred specimen type. In interviews, participants expressed confusion about how HIV could be detected but not transmitted via oral fluid. The authors recommend that HIV testing device developers should focus on specificity and window period sensitivity while keeping time to results under an hour.

Le Tourneau and colleagues (Abstract 1118) assessed HIV testing barriers in structurally vulnerable communities in St Louis, Missouri. Among 129 participants (median age, 29 years; 48% Black/African American) who completed a Best-Worst Scaling survey, 70% felt they did not need an HIV test and 24% reported that they had never tested. The top 4 most relevant barriers to HIV testing were not thinking they were at risk for HIV (mean preference weight [MPW], 13.86), someone with a medical background not recommending testing (MPW, 9.97), worry about being stigmatized or shamed if HIV positive (MPW, 9.65), and fear of testing positive for HIV (MPW, 9.2). Using latent-class models, 2 underlying groups emerged, including "low-risk perceivers" (67%) who selected low perceived risk for HIV and that testing had not been recommended by health care workers, and "stigma avoiders" (33%) who were worried about HIV stigma and were afraid of being HIV positive. Additionally, Black participants were more likely to cite

distrust and lack of peer recommendations as barriers to testing than White participants.

Patel and colleagues (Abstract 1120) evaluated the impact of the COVID-19 pandemic on racial/ethnic and regional disparities in HIV testing. They analyzed monthly HIV testing rates using data from the National Clinical Cohort Collaborative (N3C), the largest harmonized EHR dataset in the US covering 71 clinical sites across all census regions. Before the COVID-19 pandemic (January 2018 to February 2020), HIV testing rates remained stable across all regions and racial/ethnic groups. During the early phase of the pandemic (March to August 2020), HIV testing rates dropped significantly nationwide, with particularly sharp declines among the Black population in the US Northeast (decline of 50.34 tests/10,000 persons). In contrast, the White population in the Midwest saw a modest decline of 8.19 tests per 10,000 persons. Testing rates fluctuated in the early pandemic phase before beginning a slow and uneven recovery during the late pandemic period (September 2020 to December 2022). The Black population in the Midwest, despite higher prepandemic HIV testing rates, continued to experience disparities in the recovery period.

Substance Use and Mental Health

In the N'Galy-Mann lecture, Kamarulzaman (Abstract 15) discussed the intersection of drug use, public health, and policy in Malaysia. Like many countries around the world, Malaysia had subscribed to the "war on drugs."

In the first 7 years of implementing a harm-reduction program in Malaysia, more than 12,000 new HIV cases were averted

Through a US NIH Comprehensive International Program of Research on AIDS (CIPRA) grant, she was able to demonstrate the intersection between HIV and drug use and used it to advocate for HIV prevention programs. She pointed to data from 2004 indicating that 80% of PWID in Malaysia injected 3 times a day, 81% shared needles with more than 5 others, and HIV prevalence was 70% among PWID. After years of criminalization of drug use, stigma was pervasive, even among medical students and doctors. She described how 2 allies played an important role in supporting her work to promote needle exchange programs and opiate agonist therapy, including the Inspector General of the Police and a religious scholar who helped garner government support for harm reduction programs. Due to success implementation of these programs, there was a marked decline in new HIV infections due to drug use from the early 2000s to 2022 in Malaysia. In a study funded by the World Bank, in the first 7 years of the harm-reduction program, more than 12,000 new HIV cases were averted, and by 2050, the program is estimated to avert 103,717 infections and save 909 million Malaysian Ringgit (approximately $205 million) in health care costs. Despite this success, the laws in Malaysia have not changed. If found to be in possession of drugs or have a positive urine drug test, an individual could be put in jail for 2 years or more. A study done with Altice demonstrated that compulsory detention centers do not work — people who leave detention centers relapse very quickly, with 50% relapsing within one month. The median time to relapse in this setting is 31 days vs 352 days for those in community-based treatment. UNAIDS has called for closure of these compulsory centers, but they continue to proliferate.

Despite scientific evidence of the effectiveness of drug use treatment, the approach to drug use continues to be dominated by punitive and coercive policies and practices, with drug use or possession being considered a criminal offence in about 40% of 94 countries where data are available. Prisons are overcrowded and are sites of infectious diseases outbreaks. She noted that 8% of people who use drugs have active tuberculosis in one prison, with late initiation of treatment. When people leave prison, there a high risk of death, due to overdose, HIV-related complications, and despair. A study showed prescribing methadone in prison increases linkage to care after release. Unfortunately, many people who need access to harm reduction and opiate agonist treatment around the world do not have access. In March 2019, a joint statement from the UN endorsed decriminalization of possession and use of drugs, and several countries are now moving in that direction. She ended by highlighting the Helping to End Addiction Long-term (HEAL) Initiative, an NIH-funded cluster randomized trial testing an intervention featuring community engagement and coalition forming, and implementation of evidence-based practices, including medications for opiate use disorder, harm reduction services, stigma reduction campaigns. This study is being implemented in 67 communities in 4 states heavily impacted by the opioid crisis in the US.

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Shoptaw and colleagues (Abstract 183) described the preliminary efficacy of integrated strategies for PWID enrolled across 5 US sites in the HPTN 094 study. This study randomly assigned PWID with an opiate use disorder to 26 weeks of "1 stop" integrated health services supported by peer navigation delivered via a mobile unit vs peer health navigation only. The study enrolled 409 people without HIV (PWoH) and 38 people with HIV (PWH), more than half of whom were marginally housed or experiencing homelessness. Study retention was high, with 86% of PWH and 82% of PWoH completing their 26-week visit. At this visit, there was no difference in the proportion of participants using medications for opiate use disorder (7.4% intervention vs 7.8% active control) or PrEP use (5.4% intervention vs 2.9% active control). However, there was a 70% reduction in all-cause mortality at 6 months in the intervention arm (3 deaths; incidence rate, 2.8 deaths/100 py) vs active control arm (10 deaths; incidence rate, 9.7 deaths/100 py), resulting in an estimated HR of 0.30 (0.08-1.08; $P = .067$), which was a nonstatistically significant signal. These findings support additional implementation science follow-on studies of this care delivery model for PWID.

The HIV incidence rate among daily methamphetamine users who reported unstable housing was 8 per 100 py

Chan and colleagues (Abstract 1144) reported on methamphetamine use and group sex among MSM with acute HIV infection (AHI) in Bangkok, Thailand. From 2009 to 2023, 726 individuals with AHI enrolled in the RV254 study. More than a fifth of participants reported methamphetamine use and group sex prior to AHI. Compared with nonusers, methamphetamine users had higher frequencies of group sex (51% vs 17%; $P < .001$), previous syphilis (38% vs 23%; $P = .035$), and any PrEP use (17% vs 6%; $P = .022$). Additionally, there was an increase in detection of concurrent syphilis and hepatitis C virus infection particularly among methamphetamine users, highlighting the need for integrated services to address substance use, HIV, and STIs.

Javanbakht and colleagues (Abstract 1145) examined the impact of housing instability and methamphetamine use on HIV incidence in a longitudinal cohort of 274 racial and ethnic minority men in Los Angeles, California. Overall, 47% identified as Black/African American and 38% Hispanic/Latine; 34% reported unstable housing; and 32% reported methamphetamine use in the past 6 months at baseline. Based on regression analysis, both daily methamphetamine use (HR, 5.0; 95% CI, 1.8-13.7) and unstable housing (HR, 3.0; 95% CI, 1.3-7.4) were independently associated with HIV seroconversion. The HIV incidence rate was 2.7 per 100 py among daily methamphetamine users with stable housing, 2.3 per 100 py for nonusers with unstable housing, and highest among daily methamphetamine users who reported unstable housing (8.0/100 py; 95% CI, 3.3-16.2), highlighting a synergistic effect. The authors conclude that intervening on both housing instability and substance use concurrently is crucial for reducing HIV transmission.

Loeb and colleagues (Abstract 1148) evaluated the impact of residing or injecting in testing center catchments on HIV testing in Churachandpur, India. Free HIV testing has been available in India through government-supported integrated care and testing centers (ICTCs), and beginning in 2013, PWID-focused integrated care centers (ICCs) were established to provide free HIV testing along with other services, including medication for opioid use disorder. Among 752 PWID recruited through respondent-driven sampling from November 2022 to February 2023, the median age was 27 years, 84% reported injecting daily in the past 6 months, and 72% did not self-report with HIV. Overall, 66% reported living or regularly injecting within a catchment area for the ICCs, and 70% were within the catchment for ICTCs. Being within a 30-minute walking catchment of an ICC doubled the odds of testing within the past 6 months (aOR, 1.97; 95% CI, 1.03-3.76), however being in close proximity to an ICTC did not significantly increase the odds of testing (aOR, 1.51; 95% CI, 0.80-2.84). These findings suggest that centers specifically oriented toward PWID may facilitate HIV testing.

As alcohol use is a risk factor for nonretention in HIV prevention and care, Ayieko and colleagues (Abstract 1301) evaluated the impact of person-centered care on status-neutral outcomes among persons with alcohol use in East Africa. Among 47,844 adults enrolled in the Sustainable East Africa Research in Community Health (SEARCH) trial and screened for HIV, 10% had HIV, and 18% reported any alcohol use in the past 3 months at baseline. PWH who had or were at risk for viral non-suppression were referred to the Life Events Assessments Program (LEAP), which included brief alcohol counseling for those with unhealthy alcohol use; people without HIV but reporting HIV risk and were

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referred to Dynamic Choice Prevention (DCP), which offered biomedical prevention product choice, clinic or off-site visits, and self- or clinician-based HIV testing. Among 661 people with HIV, alcohol use was associated with increased risk of untreated HIV (aRR, 1.6) and a decreased likelihood of viral suppression (aRR, 0.6) at baseline. At 1 year, 66% of participants were retained, and 90% were virally suppressed, with no significant associations between alcohol use and retention (relative risk [RR], 1.0) or viral suppression (RR, 0.8; 95% CI, 0.5-1.2). Among the 43,128 persons without HIV at baseline, alcohol use was associated with self-reported HIV risk (aRR, 2.3; 95% CI, 2.1-2.5). Among the 2260 participants who received the DCP intervention, 48% were retained at year 1. There was no significant association between alcohol use and reported HIV risk (aRR, 1.0) or retention in DCP (aRR, 1.0) at 1-year follow-up. These findings suggest that person-centered interventions may mitigate the risks of alcohol use among people with or at risk for HIV.

Coelho and colleagues (Abstract 1302) reported on depression and suicide risk among sexual and gender minorities in the ImPrEP CAB (Implementation of Pre-exposure Prophylaxis of Injectable Cabotegravir) Brazil study. Among 1200 participants (91% MSM; 62% aged 25 to 30 years; 61% non-White) enrolled and received a long-acting cabotegravir (CAB-LA) injection, 11% had moderate/severe depression on the Patient Health Questionaire-9 and 9.6% had suicide risk using the Columbia-Suicide Severity Rating Scale. Transgender women had higher rates of depression (24.2%) and suicide risk (16.7%) than cisgender MSM (9.9% rate of depression; 8.9% rate of suicide risk), and transgender men had the highest rate of depression and suicide risk (30.8% for both). Depression and suicide risk were greater in those with less than 12 years of education (16.1% and 12.5%, respectively), and suicide risk was highest among those aged 18 to 20 years (21.8%). These findings underscore the need to integrate mental health interventions into PrEP programs.

Jaetoo and colleagues (Abstract 1300) evaluated the impact and cost-effectiveness of screening and treatment for alcohol use and depression as strategies to reduce HIV burden in KwaZulu-Natal, South Africa. Using an HIV compartmental transmission model, they compared prevention as usual with scale-up of screening and treatment for alcohol use disorder (AUD) and major depressive disorder (MDD) using the Alcohol Use Disorders Identification Test (AUDIT-C) and Patient Health Questionnaire-9 for screening. Treatment included culturally tailored motivational interviewing and problem-solving therapy for AUD, and cognitive behavioral therapy for MDD. AUD accounts for 28.3% of new HIV infections, and MDD accounts for 11.8% of new infections, together accounting for 33.6% of new infections in KwaZulu-Natal. Screening and treatment for AUD could reduce new infections by 14.3% at $2000 per infection averted and $2900 per quality-adjusted life year (QALY), and screening and treatment for MDD could reduce new infections by 5.8% at $1900 per infection averted and $2600 per QALY. Combined AUD and MDD interventions could reduce new infections by 25.8% at $1600 per infection averted and $2500 per QALY. The most efficient groups to target for the interventions include female sex workers ($450/infection averted and $620/QALY), MSM ($880/infection averted and $1220/QALY), and adolescent girls and young women ($950/infection averted and $1320/QALY). These results demonstrate the cost-effectiveness of integrated AUD and MDD screening and treatment for priority populations in KwaZulu-Natal.

Preexposure Prophylaxis

The PURPOSE-1 (Pre-Exposure Prophylaxis Study of Lenacapavir and Emtricitabine/Tenofovir Alafenamide in Adolescent Girls and Young Women at Risk of HIV Infection) study was the first randomized clinical trial (RCT) in which the efficacy of TAF coformulated with emtricitabine (FTC) for protection against HIV acquisition was tested in cisgender women. Kiweewa and colleagues (Abstract 194) assessed the efficacy of TAF/FTC in women in PURPOSE-1, based on adherence rates to daily oral PrEP. TAF/FTC was not statistically different from background rates of HIV infection nor against tenofovir disoproxil fumarate (TDF) coformulated with FTC. However, adherence to daily oral PrEP in this study was poor: a 10% random subsample of tenofovir (TFV) in dried blood spots indicated that at 8 weeks, only 67%

In the PURPOSE-1 study, the odds of HIV acquisition were 89% lower among women who took 2 or more pills of TAF/FTC per week

of women took 2 or more pills per week, dropping to 16% by week 52. Retrospective testing indicated that only 2 of the women who seroconverted had high levels of TFV. One of these women had likely transmitted drug resistance with both a K65R (resistance to TFV) and a M184V (resistance to FTC) as well as a nonnucleoside analogue reverse transcriptase resistance mutation. The other woman had declining TFV levels. Their analysis found the odds of HIV acquisition was 89% lower among women who took 2 or more pills per week (OR, 0.11; 95% CI, 0.012-0.49; $P = .0006$). This suggests that TAF/FTC could be an effective prevention tool in women with moderate to high adherence.

It took more than 24,000 HIV RNA level test results to uncover 4 true positives in HPTN 084

Hanscom and colleagues (Abstract 193) presented an elegant analysis to determine the plasma concentration of CAB-LA from the HPTN 083 study that determined the superior efficacy of CAB-LA compared with oral TDF/FTC among MSM and transgender women. Having 4-times the protein-adjusted 90% inhibitory concentration (PA-IC_{90}) provided 93% protection against HIV acquisition (95% CI, 77-98), and that having CAB-LA concentrations that were 1 or more times the PA-IC_{90} but less than 4-times the PA-IC_{90} provided 79% protection (95% CI, -20 to 96). These targets may be helpful in future studies of other formulations of CAB-LA, such as a formulation under development that would be given every 4 months.

Delany-Moretlwe and colleagues (Abstract 195) evaluated the utility of RNA screening in the HPTN 084 study, an RCT that demonstrated the superiority of CAB-LA over TDF/FTC in preventing HIV acquisition in cisgender women. Data from the HPTN 083 and 084 studies demonstrated that persons acquiring HIV while on CAB-LA may experience delayed seroconversion. In the open-label extension of HPTN 084, where women were allowed to choose whether to receive CAB-LA or TDF/FTC, 78% of the women chose CAB-LA. For the open-label extension, in addition to screening using rapid HIV Ab tests and laboratory-based Ag/Ab tests, RNA screening was performed at visits every 8 weeks. A total of 1927 women on CAB-LA had more than 20,000 RNA tests and 535 women on TDF/FTC had nearly 4000 RNA tests. Of all of these, 8 persons were confirmed to have acquired HIV, of whom 4 had had an isolated RNA positive test; 3 of these had received CAB-LA and 1 had received TDF/FTC. For those on CAB-LA, quantitative testing could not differentiate true from false positives. But, 77 additional persons with at least 1 reactive test were later determined to be HIV uninfected, including 12 with an isolated HIV RNA positive test. That means that 3-times as many people had false-positive RNA test results than true-positive test results (12 vs 4, respectively), and it took more than 24,000 RNA tests to uncover 4 true positives. In addition, of the 12 false positives with an isolated positive RNA test, 5 (42%) ended up having injection delays of more than 10 weeks while sorting out their HIV infection status, leaving them susceptible to acquiring HIV. The authors suggest that consideration be given to the costs and risks associated with HIV screening for people on CAB-LA. An earlier analysis from Landovitz[1] and colleagues in HPTN 083 in MSM and transgender women found a positive predictive value of HIV positive RNA tests to be only 9%, suggesting that RNA screening may cause more harm than good for the overall population using CAB-LA because of its high efficacy.

Preexposure Prophylaxis Roll-Out and Persistence

Tao and colleagues (Abstract 1348) discussed data on socioeconomic disparities and geographic variations in PrEP practitioners throughout the US using the IQVIA Longitudinal Access and Adjudication Dataset claims database. Using data from 2021 to 2023, they found that PrEP was most commonly prescribed by nurse practitioners or physician assistants (37%) and family physicians (30%). Overall, 65% of clinicians worked in neighborhoods with mostly White people and only 13% worked in low-income neighborhoods. The ratio of clinicians who offer PrEP to people using PrEP was low in Southern states and Ending the HIV Epidemic regions, suggesting these places do not have enough clinicians offering PrEP.

Ma and colleagues (Abstract 1350) reported on PrEP uptake among Latinx and Black transgender women in Los Angeles from 2019 to 2023. They found that the proportion of Latinx transgender women using PrEP increased from 23% to 42% over that period, but PrEP use remained relatively level for Black transgender women (21%-19%). These data suggest that prevention efforts targeting Latinx communities appear to have

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been effective, but that the lack of progress among Black transgender women points to the urgent need for racially and culturally tailored interventions for this population.

The proportion of Latinx transgender women using PrEP in Los Angeles, California, increased from 23% to 42% from 2019 to 2023 but PrEP use remained level (21% to 19%) among Black transgender women

Hoover and colleagues (Abstract 1216) used MarketScan data to evaluate adherence to CDC testing guidelines at initiation and follow-up of oral PrEP and CAB-LA. Using data from 2022 and 2023, only 38% of more than 35,000 oral PrEP users received laboratory-based HIV testing at initiation and only 56% of more than 12,000 individuals with a follow-up prescription had laboratory-based HIV testing. Only 55% of 453 CAB-LA PrEP users received laboratory-based HIV testing at initiation and 82% received laboratory-based HIV testing at follow-up. Adherence to testing for bacterial STIs was less than 40% for both oral and CAB-LA PrEP but was substantially higher (66%-83%) for individual STIs at follow-up. The authors concluded that although some PrEP users may have received HIV testing with a point-of-care test, the CDC recommendation is to confirm the result with laboratory-based testing. They suggest that clinical decision supports using automated laboratory order sets could improve adherence to CDC guidelines.

Every 3-month testing for HIV and STIs and in-clinic visits can be burdensome. To evaluate whether less frequent monitoring (every 6 months) and online mediated monitoring (vs clinic-based monitoring) would be noninferior to traditional clinic-based monitoring every 3 months on self-reported adherence, Bruinderink and colleagues (Abstract 1206) conducted a 2x2 factorial, open-label, multicenter, randomized, controlled, noninferiority trial at 4 sexual health clinics in the Netherlands. In total, 469 participants were randomly assigned to either in-clinic or online-mediated monitoring and to monitoring every 3 or 6 months. In evaluating the number of condomless anal sex acts with a casual partner not covered by PrEP, they found that monitoring online and every 6 months were both noninferior to traditional monitoring every 3 months. The authors suggest that this less intensive monitoring can be implemented.

Huang and colleagues (Abstract 1200) evaluated the persistence of oral PrEP use in the US based on the IQVIA Real World Data database of commercial prescriptions. They evaluated persons aged 16 years and older who were newly prescribed oral PrEP for more than 30 days, and compared the 2017 to 2018 cohort with the 2021 to 2022 cohort, following up on each for 12 to 36 months after initiation. Of 183,584 new PrEP starts in 2017 to 2018, median duration of oral PrEP use was only 4 months (IQR, 1-12 months), and only 42.4% persisted for 6 months. The data for the 321,224 new PrEP starts in 2021 to 2022 was no better: the median duration on PrEP was only 3 months (IQR, 2-10) and only 37.9% persisted for 6 months. Factors associated with nonpersistence across cohorts included being female (aHR, 1.62); being younger than those aged 55 to 64 years (16-24 years: aHR, 1.65; 25-34 years: aHR 1.28; 35-44 years: aHR 1.10; 45-54 years: 1.02); being Black (aHR, 1.18), Hispanic (aHR, 1.09), or other race/ethnicity (aHR, 1.05) compared with White; having public health insurance (aHR, 1.35), or paying cash (aHR, 1.63) compared with commercial health insurance; and being in the Northeast (aHR, 1.03), South (aHR, 1.06), or West (aHR, 1.08) compared with the Midwest. The 2021-to-2022 cohort was also more likely to not persist (aHR, 1.06) compared with the 2017-to-2018 cohort. The authors recognized that the decline in persistence (defined as continuous PrEP use until a gap of more than 30 days) might reflect the increased use of on-demand PrEP or transition to injectable PrEP.

Median duration of PrEP use in the US was only 4 months in 2017 to 2018 and only 3 months in 2021 to 2022

Almost 20% of all new HIV diagnoses in 2022 were in youth less than 25 years old, yet there are few data on PrEP uptake in youth. Venturelli and colleagues (Abstract 1076) used the Marketscan Commercial Claims database to evaluate PrEP uptake among US youth aged 13 to 21 years meeting a PrEP indication from 2018 to 2022, based on International Classification of Diseases

(ICD)-10 codes for gonorrhea, chlamydia, syphilis, or high-risk sexual behavior. In a multivariable analysis, factors associated with PrEP fill included male sex (aHR, 15.6); aged 18 to 19 years (aHR, 2.82), and aged 20 to 21 years (aHR, 3.38) compared with 13 to 17 years; year of PrEP indication 2019 (aHR, 1.24), 2020 (aHR, 1.17), 2021 (aHR, 1.59), 2022 (aHR, 1.64) compared with 2018; ICD-10 code of high-risk sexual behavior (aHR, 2.36), syphilis (aHR, 4.52), or gonorrhea (aHR, 2.47); mental health condition (aHR, 2.00), and substance use (aHR, 0.66). Of note, there was no significant association with coming from a state with minor consent laws for HIV treatment but there was a significant association in those coming from states with strong legal protections as measured by the LGBTQ+ equality index (aHR, 1.36). The authors also found that family medicine physicians prescribed PrEP in approximately 5-times greater numbers than pediatricians. These data suggest that prescribing may be increasing over time, but that more work may need to be done to train pediatricians and in states with less progressive laws. Mann and colleagues (Abstract 1077) used IQVIA Real-World Data to evaluate the types of PrEP taken up by those aged 13 to 24 years from 2019 to 2023. The annual number of adolescents and young adults prescribed PrEP increased from 14,209 in 2019 to 66,612 in 2023. In 2023, only 2.3% of prescriptions were for CAB-LA, although the number had doubled from 2022.

US urban PrEP users traveled a median distance of 6.2 miles to a practitioner; rural PrEP users traveled a median of 36.0 miles

Zhu and colleagues (Abstract 1223) discussed data comparing urban with rural PrEP users in the US in 2023 using IQVIA Real-World Data. They reported that in 2023, more than 472,000 urban PrEP users were prescribed PrEP by more than 86,000 practitioners; more than 28,000 rural users were prescribed PrEP by more than 16,000 practitioners. Urban PrEP users were more likely to receive care from a physician (58.8%) but rural users were more likely to receive care from a nurse practitioner or physician assistant (56.3%). Urban PrEP users traveled a median distance of 6.2 miles; rural PrEP users traveled a median of 39.0 miles to an urban clinician and 36.0 miles to a rural clinician. The authors concluded that lack of convenient access may be a barrier to PrEP use among rural populations, and that PrEP delivery models that use telehealth and local pharmacies may be able to improve access.

Espinoza and colleagues (Abstract 1231) described data on breakthrough infections in a PrEP program in British Columbia. From 2018 through 2023, more than 12,000 persons were prescribed PrEP, 96% of whom were cisgender men and 84% of whom had no prior PrEP experience. Over 6 years of follow-up, 73 MSM seroconverted with an incidence of 0.19 per 100 py. Based on dispensing records, only 5 (7%) had a PrEP medication supply at the time of diagnosis, and 37% were diagnosed 18 months after their prescription run-out date. Persons who seroconverted were more likely to have a higher HIRI-MSM risk score (41% vs 19%; $P < .001$); use substances (16% vs 2%; $P < .001$), have syphilis infection during follow-up (32% vs 9%; $P < .001$), and to have fewer days covered by PrEP medication (median 22% vs 60%; $P < .001$). Although overall incidence in this cohort was low, the authors call for strategies to improve persistence among those with ongoing risk.

Lindsay and colleagues (Abstract 1217) reported on a program whereby HIV-negative incarcerated persons in Zambia were offered PrEP and followed up for 12 months from incarceration through release into the community. Of 706 persons approached for this project, 326 (46%) began PrEP. Those initiating PrEP were more likely to be sentenced vs awaiting trial (OR, 1.7), had previously heard of PrEP (OR, 2.4), had greater worry about acquiring HIV in prison (OR, 1.2), self-reported an STI in the previous 3 months (OR, 2.6), and reported condomless sex (OR, 1.5). Of those who declined PrEP but had a follow-up visit, 13% chose to initiate PrEP later. Of 198 who initiated PrEP at enrollment with at least 1 follow-up in the community, 34% had at least 1 PrEP refill in the community with a median of 8.9 months of follow-up from enrollment. Persons who reported they had been sexually active in the past 3 months were significantly less likely to have received a community refill (aOR, 0.38), and people who reported that they were neutral or less likely to acquire HIV than their peers were more likely to get a community refill (aOR, 5.78). In addition, only 24% of those reporting to persist on PrEP had urine TFV levels consistent with adequate adherence. This suggests that this vulnerable population may need interventions to reduce their risk of HIV acquisition.

PrEP in Thailand is offered as a daily regimen, and one of the main priority populations is MSM with frequent condomless sex. Salvadori and colleagues (Abstract

1225) point out that MSM with less frequent risk may not be offered PrEP. The authors tested MSM 18 years or older at 4 anonymous testing sites in northern Thailand and excluded those already diagnosed with HIV or on PrEP. They categorized men as having frequent (more than 6), infrequent (1-6) or no (0) condomless sex acts in the past 3 months. HIV prevalence was measured by confirming positive rapid Ab tests, and HIV incidence was estimated using an HIV limited Ag avidity assay. Among the frequent group, HIV prevalence was 7% and estimated incidence was 4 per 100 py. Among the infrequent group, HIV prevalence was 10% and estimated incidence was 11 per 100 py. Even among the group reporting no condomless sex in the past 3 months, HIV prevalence was 5% and estimated HIV incidence was 4 per 100 py. The authors recommend that all MSM should be offered PrEP, including event-driven PrEP for those with less frequent sexual contact.

At 2 large integrated health care systems in the US, CAB-LA accounted for only 0.8% of all PrEP prescriptions

Several presentations focused on PrEP roll-out with CAB-LA. Traeger and colleagues (Abstract 191) discussed data on CAB-LA rollout at 2 large integrated health care systems serving more than 5.4 million health plan members combined. CAB-LA was licensed as PrEP in December 2021 and rolled out in Kaiser Permanente (KP) Northern California in May 2022 and in KP mid-Atlantic (Washington, DC, Maryland, Virginia) in March 2023. They extracted data from the EHR system from December 2021 through June 2024. Of 23,311 PrEP users, only 180 (0.8%) were prescribed CAB-LA. Compared with oral PrEP users, CAB-LA users were less likely to have commercial insurance (82% vs 89%; $P = .04$) and more likely to be Black (19% vs 10%) and Latino (34% vs 24%; $P < .001$); to have had a previous bacterial STI (45% vs 28%; $P < .001$); and to have hypertension (22% vs 13%; $P < .001$). Of CAB-LA users, 24% had no prior history of oral PrEP. Most CAB-LA injections were on-time (87%) or early (10%), with only 4% being late. Persistence was 88% at 6 months and 75% at 12 months, with 34% of those discontinuing going onto oral PrEP with no HIV infections seen. The authors concluded that although CAB-LA uptake is quite low in these health plans, they seem to be reaching an underserved population with high adherence and persistence.

Khan and colleagues (Abstract 196) described data from the PILLAR (A Study Evaluating Implementation Strategies for the Delivery of Cabotegravir in Low and High-Volume PrEP Site in the United States) CAB-LA demonstration project at 17 sites across the US. Of 201 cisgender and transgender MSM participants who enrolled, 26% were Black, 38% were Latino, and 6% were transgender men, exceeding their target goals. Overall, 22% had no oral PrEP use in the last 6 months, suggesting that CAB-LA can increase the population of people on PrEP. At 12 months of follow-up, 72% completed all injections with an additional 3% receiving oral CAB or other PrEP during the hiatus. Of those receiving injections, 85% received their injections on time (± a 7-day window) by 12 months. Only 5% discontinued because of an adverse event related to CAB-LA, most commonly injection-site pain (3%). On survey, 94% stated that they did not find the every-2-month visits difficult. There were no detected seroconversions throughout follow-up. The authors cite the high adherence and persistence along with high efficacy in this real-world setting as evidence that CAB-LA is feasible to roll out among diverse populations.

Loubriel and colleagues (Abstract 1344) reported on CAB-LA discontinuations at a peer specialist-led program in Washington, DC. Of 130 CAB-LA PrEP users, 67% were adherent to the 14-day window (of whom half adhered to the 7-day window) and 23% discontinued CAB-LA by 9 months (the sixth injection visit). In a multivariable model including race, ethnicity, age, sex, being an MSM, and insurance status, Black CAB-LA users were significantly less likely to discontinue CAB than White CAB-LA users (aOR, 0.24). Adverse effects (43%) and insurance coverage gaps (23%) were the most common causes of discontinuations. Of those who discontinued CAB but remained at risk for HIV, 93% (27 of 29) were transitioned to oral daily or on-demand PrEP. The authors pointed out concerns with insurance coverage gaps as undermining CAB-LA implementation efforts.

LoVullo and colleagues (Abstract 1351) presented data from early PEPFAR implementation of CAB-LA at 110 facilities in 45 districts across Zambia, Malawi, Zimbabwe, Eswatini, and Ukraine in 2024. There were 6623 individuals who initiated CAB-LA from February to September 2024, with a 2-fold increase from July to September compared with the previous quarter. Of the 5811 clients eligible for a second dose of CAB-LA, 75% returned after 1 month. The authors found these data to

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be promising and suggested the importance of expanding PrEP options and scale-up of LA agents.

LaBrot and colleagues (Abstract 1292) modeled the impact of PrEP use on new sexually acquired HIV infections in the US. They predicted that use by 1 million and 10 million persons would prevent about 4200 and about 15,900 cases, respectively, when distributed optimally. They suggest that increases in PrEP uptake, substantially beyond prior CDC targets may be required to achieve HIV elimination goals. However, Scott and colleagues (Abstract 1295) modeled ways to achieve the EHE goal of 90% reduction in HIV acquisition by 2030 among US MSM. In their model, the status quo would not meet these goals. The most successful individual intervention would be to increase engagement in HIV care to 98% at 2 years, which would achieve a 67% reduction in transmission. The only strategy that would meet the EHE goals in the next 20 years would be increasing combined testing and care with increased PrEP among MSM at higher risk. In this model, a 90% reduction could be achieved by 2038.

The only strategy that would meet the EHE goals in the next 20 years would be increasing combined testing and care with increased PrEP among MSM at higher risk

Preexposure Prophylaxis Choice

Naidoo and colleagues (Abstract 1354) reported on PrEP preferences among 1326 HIV-negative women 15 years or older in 22 public health clinics in Lesotho, South Africa, Uganda, and Zimbabwe. In stage I, participants were offered oral PrEP or the monthly dapivirine vaginal ring. In stage II, they were also offered CAB-LA. Among 808 women enrolled in stage I, 62% switched to CAB-LA in stage II, and among 518 new enrollees in stage II, 86% chose CAB-LA. Overall, CAB-LA was chosen by 71%, followed by oral PrEP (20%), vaginal ring (7%), and no method (2%). In multivariable analysis, CAB-LA was more likely to be chosen by sex workers (aOR, 1.6; $P < .001$), persons with multiple partners (aOR, 1.5; $P = .03$), persons using any family planning method (aOR, 1.4; $P = .02$), and being divorced, separated, or widowed than those never married (aOR, 1.9; $P=.001$). Those selecting CAB-LA were less likely to be married vs never married (aOR, 0.6; $P = .004$) and to have previously chosen oral PrEP or the ring vs no method (aOR, 0.5; $P < .001$). Month 1 continuation was 83% for CAB-LA, 42% for oral PrEP, and 31% for vaginal ring. The authors concluded that there is high demand for CAB-LA among women when offered in the context of a multimethod PrEP market, particularly among women who were new to PrEP, and that adherence was best in this group.

There is high demand for CAB-LA among women when offered in the context of a multimethod PrEP market

Shahmanesh and colleagues (Abstract 1342) discussed data on patterns of PrEP use among rural South African youth given the choice of PrEP modality. They note that even provision of free oral PrEP has limited population effect due to challenges of taking oral daily pills, especially among youth at most risk. They evaluated the effect of offering choice of oral PrEP, CAB-LA, dapivirine vaginal rings, or packs of 28 days of PEP to those who were aged 15 to 30 years and attending mobile sexual health clinics in rural KwaZulu-Natal. In the 2 years prior to the introduction of choice, 1015 (64%) of youths offered oral PrEP initiated its use; half were cisgender women. In the 9 months after introduction of choice, 701 (95%) of those seen initiated PrEP, 57% of whom were cisgender women, and 77% chose CAB-LA. None of the women chose the dapivirine vaginal ring, and 5% switched between PrEP modalities. Of those who started PEP, 40% transitioned to either oral or injectable PrEP. Among those seen after the introduction of choice, 25% were diagnosed with either gonorrhea or chlamydia and 2% were diagnosed with syphilis, indicating that this is a population at some risk of acquiring HIV. The authors suggest that mobile sexual and reproductive health services can be used to provide PrEP to adolescents and youth with substantial sexual health and HIV needs.

Mansoor and colleagues (Abstract 1230) evaluated preferences for twice-yearly injections vs daily pills

among women enrolled in the PURPOSE 1 trial assessing the efficacy of LEN vs daily TAF/FTC or TDF/FTC. All participants received both twice-yearly injections and daily pills as part of this double-blind placebo-controlled RCT. At baseline, 67% preferred an injection, 4% had no preference, and 29% preferred the pill, with two-thirds of those with preferences stating that their preference was strong. Among participants who received at least 1 dose of PrEP and completed the baseline and the week 52 questionnaires, approximately half of those who reported no preference at baseline and half of those who reported a preference for daily pills at baseline shifted their preference to twice-yearly injections. Overall, 75% of those who stated a preference for twice-yearly injections and 49% of those who stated a preference for daily pills at baseline maintained their baseline preference. In addition, approximately 60% of participants reported greater confidence in their ability to remain adherent and to feel more protected with twice-yearly injections vs daily pills. The authors cited the importance of choice for PrEP uptake and persistence but suggest that LEN could increase uptake of, adherence to, and persistence on PrEP among cisgender women in sub-Saharan Africa. This study was augmented by a qualitative study conducted by Montgomery and colleagues (Abstract 1234) among PURPOSE 1 participants. In this study, participants reported that, compared with oral PrEP, LEN afforded both freedom from daily dosing and the ability to enjoy and not worry about sexual activity. Participants appreciated not having to conceal or remember medication, or to be judged for using PrEP. They often preferred the lifestyle fit of a twice-yearly injectable over a daily pill and found pain or injection site reactions to be acceptable because of these benefits. The authors also reiterated the importance of choice and highlighted the acceptability and preference for twice-yearly injections among many women.

Among MSM, transgender, and nonbinary persons in a PrEP choice study in Brazil, 83% chose CAB-LA

Grinsztejn (Abstracts 192 and 1356) discussed data on a PrEP choice study in Brazil. MSM, transgender, and nonbinary persons, aged 18 to 30 years who were PrEP naive but seeking HIV testing or PrEP at 1 of 6 PrEP public clinics in 6 Brazilian cities were enrolled in the study. Participants were randomly assigned to a mobile health intervention plus standard-of-care counseling vs standard-of-care counseling alone and allowed to choose CAB-LA or oral PrEP. Overall, 1447 participants enrolled and were compared with 2411 participants who sought care at any of 14 Brazilian public health clinics that offered only oral PrEP (comparison group). Overall, 83% of participants chose CAB-LA and 17% chose oral PrEP. Those randomly assigned to the mobile health intervention were more likely to choose CAB-LA (OR, 2.5). Among those who chose CAB-LA, 38% were 18 to 24 years old, 91% were MSM, 60% were Black or mixed race, and 96% had 12 or more years of education. This did not differ substantially from those who chose oral PrEP or the comparison group, except the latter were substantially less likely to have a secondary education (69%). Those choosing CAB-LA had 94% on-time injections through 13 months of follow-up. They had 95% of their follow-up days covered by PrEP, whereas those choosing oral PrEP had only 58% coverage (defined as having sufficient PrEP to cover 4 or more days/week) and those in the comparison group having only 48% coverage. HIV incidence was 0 in the CAB-LA choice cohort compared with 1.0 per 100 py (95% CI, 0.0-5.6) in the oral PrEP choice cohort and 1.5 per 100 py (95% CI, 0.7-2.8) in the comparison group. Of the CAB-LA group, 6% were lost to follow-up, which was more common among those with lower education levels and those who were transgender or nonbinary. Four percent of CAB-LA users switched to oral PrEP, largely because of injection-site pain and 9% of oral PrEP users switched to CAB-LA, largely because they did not like taking daily pills. The authors concluded that CAB-LA substantially improved PrEP coverage and protection, underscoring its potential as a tool to address adherence challenges with daily oral PrEP for young people.

Magno and colleagues (Abstract 1203) discussed data on patterns of choice, switching, and discontinuation of oral and injectable PrEP among adolescents in Brazil from April to September 2024. In this study, 15- to 19-year-old MSM, transgender people, and nonbinary persons assigned male at birth were recruited in 3 Brazilian cities and offered oral PrEP and CAB-LA. Of 261 participants enrolled, 69% initially chose oral PrEP and 31% CAB-LA. CAB-LA was more likely to be chosen by Black than White participants (35% vs 20%; $P = .02$), and by those with up to a high school education than those with higher levels of education (35% vs 19%; $P = .02$).

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No significant differences were observed by gender, income, or prior experience with oral PrEP. By the end of the study, 14% had switched from oral PrEP to CAB-LA and 2% had switched from CAB-LA to oral PrEP.

Among salon clients in Lesotho, many were comfortable receiving oral HIV self-testing (93.5%), PrEP (83.3%), or PEP services (86.4%) from their hair stylists

Ony 5% in the oral PrEP group and 3% in the LA injectable PrEP group discontinued in this 6-month study. The authors emphasized the importance of PrEP choice for this population.

Watson and colleagues (Abstract 1353) reported on HIV PrEP method preferences among transgender and gender-diverse adults in the US. In an online survey with 304 HIV-negative transgender and gender-diverse adults from April to June 2022, 33% preferred a monthly oral pill, 28% an implant, 22% an injection every 6 months, 13% a daily oral pill, and only 4% an injection every 2 months. Those preferring a twice-yearly injection were more likely to be non-Latinx Black (aOR, 2.77; $P = .03$) or Latinx of any race (aOR, 2.39; $P = .02$). The authors point to the importance of comprehensive low-barrier services for this population and access to LEN when available.

Gottert and colleagues (Abstract 1256) discussed data from a discrete choice experiment in 2105 women in all 50 US states on preferences for a multipurpose vaginal ring. The mean age of the women was 31 years, and 4.5% were currently on PrEP. Current contraceptive methods were condoms (43%), oral contraceptives (32%), withdrawal (27%), and tracking fertile days (13%). The characteristic most important to users was effectiveness of pregnancy prevention; the importance of HIV prevention was approximately half that of the importance of the effectiveness of pregnancy prevention, and the effectiveness against STI infection was half that of HIV prevention. When shown a vaginal ring with hypothetical 80% effectiveness for pregnancy prevention and 50% effectiveness each for HIV and STI prevention, 33% stated they would be very likely and 41% likely to use the vaginal ring. Among those unlikely to use the ring, the most common reasons were happiness with current method(s) (55%) and wanting higher pregnancy (42%) or HIV/STI (21%) effectiveness.

Alternative Delivery Models

Kopeka and colleagues (Abstract 1314) surveyed 157 hair stylists and 308 female clients in Lesotho to determine the feasibility of using hair stylists to deliver HIV self-testing, PrEP, and PEP. Hair salons were ranked as being more accessible than the nearest health care center in terms of cost and time. Overall, 10.8% of stylists thought that offering HIV and sexual and reproductive health services would negatively impact their business. Among salon clients, 93.5% were comfortable receiving oral HIV self-testing, 88.3% PrEP, and 86.4% PEP services from their hair stylist. These data suggest that hair salons may be an alternative delivery location for distributing HIV prevention products.

Given that 90% of the US population lives within 5 miles of a pharmacy and 10 states allow pharmacists to prescribe PrEP, Tran and colleagues (Abstract 1235) evaluated the cost-effectiveness of community pharmacy-based PrEP for MSM in Atlanta. In their base case model, compared with the status quo, pharmacy-based PrEP decreased new HIV diagnoses by 13.3% and decreased costs by 0.02%. Depending on the assumptions related to adherence, persistence, and delivery method (including pharmacy-based telehealth PrEP), PrEP could be cost-saving or cost-effective, suggesting that this method of PrEP delivery should be explored. However, Lukose and colleagues (Abstract 1315) conducted a mixed-methods study to evaluate the feasibility of delivering PrEP through pharmacies in Baltimore. Maryland, and San Diego, California. They contacted 418 pharmacies, 61% of which completed an assessment in Baltimore (n = 148) and San Diego (n = 86). Six of the pharmacies in San Diego already initiated PrEP. Among these pharmacies, only 58% had private space available, although 81% offered PrEP and HIV counseling. But less than 3% had point-of-care testing available, less than 2% had STI test results available, and less than 1% had renal function test results available. The average number of pharmacists on staff was 2 and the average number of pharmacy technicians was 3. Based on these surveys and interviews with 20 pharmacists and 6 clinicians who provide PrEP, they found that pharmacy-initiated PrEP may serve as a complementary strategy for expanding PrEP access, but that implementation challenges exist. They concluded that effective implementation of pharmacy-initiated PrEP may require standardized workflows and checklists,

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testing and referral systems, pharmacist training, financial sustainability, electronic records, additional staff, and community awareness.

Preexposure Prophylaxis Uptake and Adherence Interventions

Kuguyo and colleagues (Abstract 1202) reported on a pilot study comparing optional pharmacy-based refills with escalating incentives vs standard of care (clinic-based refills) among 8 key population program outreach sites serving young and adult women who sell sex. For the 4 programs randomly assigned to the pharmacy-based refill arm, participants were given incentives of the equivalent of $5 at month 1, $6 at month 3, $7 at month 6, and no incentive at month 9. Among the 100 women recruited in the intervention arm, PrEP continuation was 78% at 1 month, 68% at 3 months, 60% at 6 months, and 49% at 9 months. In the standard-of-care arm among 62 women recruited, PrEP continuation was 26% at 1 month and 0% at all subsequent visits. The authors recognize that they are unable to tease apart the contribution of pharmacy refills from incentives, although high retention continued after incentives ceased. They are planning a larger trial that can differentiate between the contributions of these 2 types of interventions.

Ortblad and colleagues (Abstract 1322) conducted a cluster-RCT in Central Kenya. Index peers were adolescent girls and young women aged 16 to 24 years who had used PrEP in the past 12 months. These index peers were then randomly assigned to enhanced peer referral (in-person group training on referral strategies, HIV self-test kits for delivery, and self-testing and PrEP educational brochures) or standard peer referral (informal referral strategies). Although HIV self-testing increased in the intervention vs the control arm (91% vs 54%; risk difference, 39%), there was no difference in PrEP initiation (30% vs 41%) or PrEP continuation (13% vs 11%) between the arms. The authors hypothesized that it is possible that because referred peers each got 2 self-test kits, they may have learned their partner was HIV negative and did not require PrEP, or that those recruited in the standard arm were ones with greater PrEP need. They called for future research into additional implementation strategies to improve PrEP engagement in this population.

Davey and colleagues (Abstract 166) discussed data from an RCT on the impact of counseling based on point-of-care (POC) urine TFV testing on oral PrEP adherence in pregnant women in South Africa. This urine TFV test is a lateral flow assay rapid test strip in which results are available in 2 minutes and in previous studies correctly classified more than 98% of participants who took a dose of TDF/FTC in the past 4 days as adherent. They randomly assigned 750 pregnant women 1:1 to counseling based on urine testing or to standard-of-care counseling. Testing was performed at enrollment, 1 month, and 3 months, and adherence was assessed at 6 months based on the urine testing. Retention was 58% at 6 months in the intervention arm and 50% in the standard-of-care arm. Evaluating all 750 participants and counting those lost-to-follow-up as nonadherent, the intervention arm had higher adherence rates (32% vs 24%; RR, 1.32), suggesting this type of intervention may improve PrEP adherence. Among those who self-reported taking at least 1 PrEP pill in the last week, 92% of the intervention arm vs 81% of the standard-of-care arm had a positive urine TFV test, suggesting that this intervention may also improve self-reported adherence.

Spinelli and colleagues (Abstract 1212) conducted a pilot test of POC urine TFV testing with online counseling among young US MSM to evaluate its impact on PrEP adherence. They enrolled 49 MSM younger than 30 years and randomly assigned them 2:1 to POC drug-level feedback counseling vs standard of care. The counseling consisted of two 30-minute motivational interviewing informed sessions over a 4-week period delivered by psychology or post-doctoral students, where the first session focused on reflections on PrEP use and developing an action plan to improve or maintain adherence and the second on the participant's choice of focus on relevant contributors to adherence (eg, navigating primary partnerships, mental health, substance use). Hair samples at 3 months determined adherence levels. All 31 participants in the intervention arm successfully administered the urine test and reported the intervention was somewhat/very acceptable. They found a 0.01 ng/mg increase in hair TFV levels in the intervention group compared with the control group ($P = .04$), equivalent to a 1 or 2 dose per week increase in pill taking. Among those with fewer than 4 doses per week at baseline, 6 of 8 in the intervention arm and 0 of 4 in the control group increased above 4 doses per week. The authors call for future studies to evaluate long-term adherence and to use different types of counselors (eg, clinicians, nurses, case managers) to conduct the counseling.

Niu and colleagues (Abstract 1213) evaluated whether oral fluids could be used for assessing adherence. They provided TDF/FTC on 2, 4, or 7 doses per week to HIV-negative adults and measured drug concentrations using liquid chromatography tandem mass spectrometry with a limit of detection of 5 ng/mL. Among 165 oral fluid samples from 22 adults, TFV concentrations in oral

fluids were low and not associated with nonadherence, making it unsuitable for monitoring PrEP adherence. However, FTC was detectable in oral fluids, and levels less than 7.5 ng/mL may serve as a reliable marker of recent PrEP nonadherence (1 or more missed doses or time since last dose more than 24 hours). However, this methodology for measurement of adherence islaboratory intensive, unlike the urine test outlined above that is a POC test.

Among 47 MSM and transgender women exposed to CAB-LA in the HPTN 083 trial who became HIV infected, 76.6% achieved viral suppression on their first ART regimen, including 71.4% on an InSTI regimen

Liu and colleagues (Abstract 1305) compared 2 mobile health tools in 3 clinic-based settings. PrEPmate, a bidirectional texting platform used weekly check-in messages and daily pill reminders, and DOT Diary was an app promoting self-management of PrEP use through pill-taking/sexual diary with feedback on PrEP protection levels. PrEP adherence was measured by having protective TFV levels consistent with at least 4 doses per week in dried blood spots at 6 and 12 months. Across timepoints, 75% of samples in the PrEPmate arm and 81% of samples in the DOT Diary arm showed protective levels ($P = .34$). Among PrEPmate users, 62% would use the tool in the future and 72% would recommend it to a friend; these values were 60% and 66% for DOT Diary (no significant difference). The authors concluded that both tools can support PrEP adherence and persistence in real-world clinical settings.

Treatment After Breakthrough Infection

Landovitz and colleagues (Abstract 197) evaluated ART treatment outcomes in 47 MSM and transgender women exposed to CAB-LA in the HPTN 083 trial who became HIV infected. The ART regimens were chosen locally and genotyping was available for some participants. In this analysis, they included those diagnosed after at least 1 CAB-LA injection with more than 30 days of follow-up on treatment. Overall, 76.6% had viral suppression (defined as HIV RNA level <50 copies/mL) on their first ART regimen, including 71.4% suppression on an integrase strand transfer inhibitor (InSTI) regimen and 80.8% on a non-InSTI regimen. Of those started on a non-InSTI regimen, 5 were switched to an InSTI-regimen, 2 who were not virally suppressed at the time of switch. Four of these participants achieved viral suppression on an InSTI regimen, including both who were not suppressed at the time of switch; data were unavailable for the fifth participant. In evaluating central laboratory testing for genotyping, 9 of 41 participants had InSTI resistance prior to initiating treatment, all of whom suppressed on their initial regimen, including one started on an InSTI in the setting of an R263K mutation. Two of 3 participants who did not have genotyping results did not achieve viral suppression, 1 on an InSTI regimen and the other on a non-InSTI regimen. The authors pointed out that there was incomplete information about what guided site-based treatment choices and that there were no adherence data. However, they note that in these rare cases of infection in people previously treated with CAB-LA, there were similar short-term treatment outcomes between those initiated on InSTI vs non-InSTI regimens. They point to the need for more data to define optimal treatment regimens in this setting.

A single injection of once-yearly LEN administered intramuscularly achieved drug concentrations higher than those seen in studies of twice-yearly LEN through 56 weeks of follow up

Koss and colleagues (Abstract 1228) reported on the largest analysis to date of breakthrough infections in routine clinical care on CAB-LA. This US national study analyzed 7 persons with breakthrough infections on CAB-LA. They found that 6 (86%) had breakthrough infections after on-time CAB-LA injections, with a median of 7 injections prior to detection of infection. All participants had HIV RNA monitoring at most CAB-LA injection visits but 4 of 7 had nonreactive HIV Ag/Ab results at first detected HIV RNA results. The CAB concentration in plasma at the time of diagnoses was

greater than 4-times the $PAIC_{90}$ in 5 of 6 persons (83%), indicating protective CAB levels at the time of testing. One of 6 had high-frequency major resistance-associated mutations (RAMs) against InSTIs detected by population sequencing and 4 of 6 were detected by single genome sequence only, indicating low-frequency levels. All participants were initially treated with darunavir-based therapy and achieved HIV RNA levels below 200 copies/mL. Three participants with low-frequency major InSTI RAMs switched from darunavir to practitioner-selected InSTI-based ART and maintained viral suppression at 13 to 31 weeks. The authors suggest that additional follow-up is needed to determine the clinical significance of low-frequency InSTI RAMs and the durability of viral suppression on InSTI-based ART in these cases.

A pharmacokinetic model of event-driven TDF/FTC in cisgender women predicted that 2-1-1 dosing would provide 85% protection for 5 days after sex and would increase by 8% to 15% if stretched to 2-1-1-1

Novel Preexposure Prophylaxis Agents

Singh and colleagues (Abstract 154) discussed data from a trial of a single injection of once-yearly LEN administered intramuscularly in 2 cohorts of 20 adults without HIV at low risk of HIV acquisition. Both cohorts received 5000 mg of LEN administered as two 5 mL gluteal injections. The formulation for cohort 1 used 5% ethanol and for cohort 2, 10% ethanol. For both cohorts, drug concentrations were higher than have been seen in studies of twice-yearly LEN through 56 weeks, and trough concentrations for all participants were similar to or higher than for twice-yearly LEN. Injections were safe and well-tolerated, with the most common adverse event being injection-site pain, which was most often mild, although 1 participant experienced grade 3 pain with syncope. There were no grade 4 adverse events or laboratory abnormalities. Pain was reduced by pretreatment with ice. The authors noted that preliminary pharmacokinetic modeling suggests that a lower dose of once-yearly LEN may be used and they are currently planning a phase III trial of once-yearly LEN.

Jamieson and colleagues (Abstract 1229) conducted a cost-effectiveness analysis to determine the threshold price at which twice-yearly LEN or CAB-LA would be as cost-effective as TDF/FTC scale-up in South Africa. Despite similar effectiveness, LEN leads to higher impact than CAB-LA due to higher uptake and longer effective use, according to their model. Under their model assumptions, LEN could avert 27% to 41% of new HIV infections and CAB-LA 21% to 35%, compared with 8% averted by TDF/FTC. Because of its higher impact, LEN can be accepted at a higher price than CAB-LA, with a threshold of $117 to $225 per person per year compared with $88 to $144 per person per year for CAB-LA. They also determined that under high uptake, LEN could reduce HIV incidence to below 0.1% by 2032 instead of 2042, helping to eliminate HIV in South Africa 10 years earlier. Given that South Africa has historically bought 20% of the world's PrEP, the authors state that they should not accept a LEN price higher than $225 per year.

Cottrell and colleagues (Abstract 157) described data from a pharmacokinetic/pharmacodynamic model of event-driven oral PrEP for cisgender women. Based on their model, they predicted that 2-1-1 dosing would provide 85% protection for 5 days after sex, but that would increase by 8% to 15% if stretched to 2-1-1-1. They called for clinical trials to evaluate alternative dosing regimens for women.

King and colleagues (Abstract 1236) described data on a novel multipurpose technology (MPT): an in-situ forming implant (ISFI) containing CAB and medroxyprogesterone acetate (MPA). ISFIs were administered subcutaneously to mice, and plasma concentrations of CAB and MPA were determined following depot removal at day 90, 180, and until time to completion. CAB concentrations were maintained above the 4-times $PAIC_{90}$ level for 210 days, and MPA maintained therapeutic plasma concentrations for 180 days. Following removal of the ISFIs at days 90 and 180, all animals had undetectable plasma CAB levels within 2 to 3 weeks. Plasma MPA was undetectable at day 1 following implant removal for all animals. The implants were able to be visualized via X-ray imaging for at least 180 days with no signs of implant migration. Similarly, Benhabbour and colleagues from the same group (Abstract 199) reported on data using the same ISFI in 6 pigtail macaques. They removed the ISFI at 3 months in 3 animals and assessed the other 3 animals at 6 months. All animals had complete suppression of ovulation; those

with removal at 3 months returned to ovulation within 2-3 weeks. CAB was released at or above the 4-times $PAIC_{90}$ level up until the time of removal, with rapid drop to below the level of quantitation. The ISFI was well tolerated in 5 of the animals; a sixth animal had recurrent local adverse events that resolved with nonsteroidal antiinflammatory drugs and antibiotics. The ISFI was able to be completely removed at 3 months and did not migrate over 6 months in the remaining animals. Both authors suggest that these data suggest this as a promising modality for discrete and reversible MPTs for women and girls.

Benhabbour and colleagues (Abstract 1238) presented data on another potential MPT, this one as a 3D-printed intravaginal ring (IVR) containing islatravir, a nucleoside reverse transcriptase translocation inhibitor (NRTTI) that was found to cause lymphopenia in a dose-dependent manner in clinical studies. They administered the IVRs containing 15, 30, and 60 mg islatravir in pigtail macaques, and based on the total amount of islatravir released over a 90-day period, selected the 60 mg dose for a vaginal SHIV challenge study. The frequency of CD4+ and CD8+ cells remained stable over time with no statistically significant changes over 90 days. All 6 animals with the 60 mg islatravir IVR were completely protected against 12 weekly low-dose simian-human immunodeficiency virus (SHIV) 162p3) vaginal inoculations and remained uninfected for an additional 10 weeks after the IVR was removed. Two untreated controls and 6 historic controls were all infected within 10 weeks, with all but 1 infected by 5 weeks. The authors suggest this approach could be advanced to incorporate hormones as an MPT.

Kim and colleagues (Abstract 1233) described data on islatravir implants in rhesus macaques. In this study, islatravir implants placed in 6 animals provided complete protection in up to 8 SHIV rectal challenges. The implants achieved similar plasma islatravir concentrations to those observed in humans with once-daily oral dosing over a 28-week period. The implants were well-tolerated, with minimal implant site reactions and no impact on total lymphocytes. The authors concluded that their study supports the development of islatravir implants for ultra-long-acting HIV prevention.

MK-8527 is a novel NRTTI that is currently being developed as a monthly PrEP agent. Kapoor and colleagues (Abstract 1232) discussed data on its use on a weekly basis to prevent SHIV infection after rectal challenge in rhesus macaques when administered weekly. After receiving 0.1 to 6 mg/kg of oral MK-8527 weekly, 0 of 8 challenged animals were infected with SHIV compared with 7 of 8 control animals. Based on this study, phase I clinical data, and comparison to other oral PrEP agents, the pharmacokinetic efficacy threshold of MK-8527 triphosphate (the pharmacologically active form) was set at 0.03 pmol/10^6 peripheral blood mononuclear cells for prevention. This led to the selection of 3, 6, and 12 mg administered monthly for the phase II study to assess safety and tolerability in people with low likelihood of HIV exposure.

Postexposure Prophylaxis

Nonoccupational PEP (nPEP) can lower the risk of HIV acquisition but should be initiated within 72 hours after a potential exposure and continued for 28 days. Harold and colleagues (Abstract 1323) reported on a 24-hour, 7-day-a-week (24/7) PEP hotline in Washington, DC, launched in April 2021. Callers speak with a clinician and if nPEP is indicated, receive a 5-day supply of nPEP from a partnering pharmacy. PEP users are supposed to be seen at a clinic within 5 days to receive laboratory testing, the remainder of their medications, and follow-up care, including transition to PrEP if desired. In the first 30 months of operation, the Washington, DC, PEP hotline received 838 calls, and 632 (75%) of the callers initiated PEP and attended an initial appointment at the clinic. Of these, 391 (62%) came for a post-PEP appointment within 45 days, and 272 (43%) transitioned to PrEP. The hotline attracted a diverse population, with 35% Black, 40% White, 13% Asian, and 17% Latino. Overall, 79% identified as cisgender men, 19% as cisgender women, 1.4% as transgender women, and 0.3% as transgender men and 1.0% as genderqueer. No seroconversions were identified during PEP but 1 person acquired HIV 4 months after completion of PEP. The authors conclude that a 24-hour hotline can expand access to PEP beyond emergency departments (EDs) and traditional medical settings and can assist in transitioning persons from PEP to PrEP.

Sexually Transmitted Infections

Given that some people only access medical care through EDs, Stanford and colleagues (Abstract 160) discussed data on a syphilis and HIV screening program implemented in a hospital ED. They looked at data 2 years after implementation of a universal opt-out testing program, in which all persons under 65 years of age received a trigger message through the electronic medical record to conduct syphilis and HIV testing. They determined active cases through review of test results and the medical record. Of more than 37,000 persons

screened, they found 624 syphilis diagnoses and 83 newly diagnosed cases of HIV. Had they limited screening to only those with a blood test otherwise ordered, they would have missed 17% of syphilis cases and 24% of HIV cases. Had they only tested people with gonorrhea or chlamydia testing, they would have missed 76% of syphilis cases and 69% of HIV diagnoses. The authors recommend universal screening practices in EDs for improved diagnosis of syphilis and HIV.

Pregnant women treated for syphilis infection with at least one 9-day interval between penicillin doses had 3.7-times the rate of congenital syphilis as women with 6 to 8 days between penicillin doses

Johnson and colleagues (Abstract 161) described data on appropriate intervals for the 3 doses of benzathine penicillin G (BPG) in pregnant women to prevent congenital syphilis. She pointed out that there has been a 10-fold rise in the number of congenital syphilis cases from 2012 to 2022, making treatment of syphilis in pregnant women an urgent issue. They have previously shown that a 6 to 8 day window between doses of BPG was noninferior to the recommended 7-day interval, but current CDC guidelines suggest that even 9-day intervals are adequate and do not require restarting the series of 3 injections. Using California surveillance data from 2016 to 2023, they found that women who had all 6- to 8-day intervals had a congenital syphilis rate of 5.6%. However, those with at least one 9-day interval had a congenital syphilis rate of 18.2% (OR, 3.7; $P = .01$) compared with 6- to 8-day intervals. Those with no or inadequate treatment had a congenital syphilis rate of 36.8%, (OR, 9.8) not significantly different from the 9-day interval rate. Despite limitations of their retrospective analysis, they recommend that pregnant women with syphilis be treated with 3 doses of BPG 6 to 8 days apart.

More than 700,000 cases of congenital syphilis occur worldwide each year and the World Health Organization recommends combined HIV/syphilis rapid tests in antenatal settings to address gaps in both HIV and syphilis testing among pregnant women. Monroe-Wise and colleagues (Abstract 1247) reported on data from the Global Fund on the uptake of the dual HIV/syphilis test from 2021 to 2023. They found that pregnant women in countries reporting dual test uptake were 58% more likely to be tested for syphilis than countries not procuring these tests. Syphilis testing in pregnant women increased by 51% in Uganda, 48% in Kenya, and 137% in India over that time. They called for further scale-up of dual HIV/syphilis testing in low- and middle-income countries.

Two studies had conflicting results on the need for screening for neurosyphilis among people with HIV with high Venereal Disease Research Laboratory (VDRL) titers but without neurologic symptoms. Otth and colleagues (Abstract 1242) evaluated 220 people with HIV with VDRL titers at or higher than 1:32 in Chile. There was no association of CD4+ cell count or viral load with initial VDRL titers or their decline. Because of COVID-19, they did not screen them for neurosyphilis with a lumbar puncture (LP), which was their previous practice. After treatment with BPG, none developed neurologic symptoms. Six underwent subsequent LPs because of persistently high VDRL titers after treatment, but none had cerebrospinal fluid positive for VDRL and all had fewer than 5 cells/μL. They concluded that LPs are not necessary for asymptomatic people with HIV with high VDRL titers. Navarro-Lara and colleagues (Abstract 1243) evaluated their screening program among 1267 people with HIV at a tertiary-care hospital in Mexico. Only 62% were screened for syphilis, and 14% of the total number had a VDRL titer of 1:32 or greater. Of these, only 2 of 3 underwent ophthalmologic exams and or LPs. Of the 123 undergoing such testing, 47 (43%) were found to have ocular or neurosyphilis and underwent inpatient treatment. They called for more effective screening programs. Although the US CDC does not recommend LPs for asymptomatic persons with HIV with VDRL titers at or greater than 1:32 because there are no data indicating that such persons benefit clinically from standard BPG treatment, a difference of opinion among experts remains. Current European guidelines do recommend LP in people with HIV with high VDRL titers and CD4+ counts less than 350 cells/mL.

Several studies reported on high rates of STIs among women and men in Africa. Nuwagaba-Biribonwoha and colleagues (Abstract 1266) reported on STI prevalence and incidence in the HPTN 084 study. Among nearly 3200 women aged 18 to 45 years, 28% were diagnosed with an STI at baseline: 19% with chlamydia, 7% with gonorrhea, 8% with trichomonas vaginalis. Of the 93% who had follow-up data, STI incidence was 35 events

per 100 py on semiannual testing. Multivariable models found STI incidence was independently associated with being aged 18 to 24 years; having secondary education or less; not with a primary main partner or being single, divorced, or widowed; and any alcohol use. They call for novel, multipurpose, scalable interventions to address STI and HIV incidence. Nyemba and colleagues (Abstract 1265) reported on STI prevalence among 1261 women older than 15 years who had chlamydia/gonorrhea testing at baseline and follow-up on pregnancy outcomes. The prevalence of STIs was 28% (24% with chlamydia and 8% with gonorrhea). Those who had POC testing were significantly more likely than those with laboratory-based testing to have immediate treatment (84% vs 15%) and significantly less likely to have delayed (12% vs 65%) or no treatment (4% vs 22%). On multivariable analysis, having a miscarriage or stillbirth was significantly more likely in those without treatment than in those with immediate treatment (aOR, 4.6), although the authors call for larger studies to evaluate causal relationships. Tonzel and colleagues (Abstract 1270) reported on 3-site screening (urine, oropharyngeal, and rectal) among 405 women and men aged 14 to 55 years in western Kenya. Eligible participants reported vulnerability to HIV acquisition as measured by self-report in the last 24 weeks of a diagnosed STI, transactional sex, condomless sex with a person with HIV or of unknown serostatus, injection drug use, or anal or neovaginal sex with multiple partners. At baseline, they report 35% were found to have gonorrhea or chlamydia. Risk was increased in those 24 years or younger ($P = .01$), female ($P = .013$), or those reporting transactional sex ($P = .035$). However, on multivariable analysis, no demographic or behavioral factors were associated with a baseline STI. Among 117 persons with anorectal STI diagnosed, only 14% reported receptive anal sex on a computer-assisted self-interview. The authors called for universal 3-site STI screening in this population.

Doxycycline Postexposure Prophylaxis

Doxycycline administered as PEP within 72 hours after sex has been shown to dramatically decrease rates of syphilis and chlamydia and modestly reduce rates of gonorrhea in MSM and transgender women. Martinson and colleagues (Abstract 1358) reported on a national survey of 827 MSM with HIV from 46 states, Washington, DC, and Puerto Rico conducted from October 2023 to October 2024 on doxy-PEP awareness and use. Overall, 59% were aware of doxy-PEP, 13% were on doxy-PEP, and of the 46% aware but not on it, 84% stated they would start it if offered at their HIV clinic. Among the 41% who had not heard of doxy-PEP, 89% were interested in it. Doxy-PEP awareness was greater in those with a recent bacterial STI (aOR, 1.15), and individuals with an annual income at or above $25,000; awareness was lower in the South, Midwest, and Mountain regions than in the West (aOR, 0.81). DoxyPEP uptake was greater in those with a recent bacterial STI (aOR, 1.11) and lower among those in the South, Midwest, and Mountain regions (aOR, 0.86). The authors point to the socioeconomic and geographic disparities in the rollout of doxy-PEP, but with high interest, suggest substantial opportunities for expanding access. Nassau and colleagues (Abstract 1276) discussed data from the 2023 National HIV Behavioral Surveillance study in Philadelphia. Among 326 persons who had sex with men in the past 12 months and was assigned male at birth or identifying as a transgender man, 36.5% had heard of doxy-PEP, 12.6% discussed doxy-PEP with a practitioner, and 5.5% had used doxy-PEP in the last 12 months. Awareness was higher in those with more than a high school education than not (42% vs 30%, respectively), or with a recent history of gonorrhea (60% vs 31%, respectively) or chlamydia than not (64% vs 32%, respectively). Discussion of doxy-PEP with a practitioner was more common in those with a recent STI test (15% vs 3%) and those on PrEP (18% vs 7%). Despite these low proportions, many participants were interested in doxy-PEP with racial/ethnic differences: 82% in non-Hispanic White, 63% in non-Hispanic Black, and 52% in Hispanic persons. Gender, age, insurance status, housing, and HIV status were not associated with any step in the doxy-PEP continuum. Among those not on doxy-PEP, 45% stated they thought it was not needed, 30% needed more information, and 12% were concerned about adverse effects. The authors pointed to the need for education about doxy-PEP.

Among doxy-PEP users in a sexual health clinic in San Francisco, there was an 89% reduction in syphilis cases, an 81% reduction in chlamydia cases, and a 44% reduction in gonorrhea cases

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Barry and colleagues (Abstract 164) reported on the doxy-PEP cascade among clients seen at a sexual health clinic in San Francisco. Of the nearly 7500 clients who met local doxy-PEP guidelines, 59% were prescribed doxy-PEP, 36% initiated doxy-PEP, and 22% self-reported being adherent to doxy-PEP. Overall, the doxy-PEP cascade was worst among those with HIV, persons 14 to 29 years old, Black/African Americans, and those with unstable housing or experiencing homelessness. The authors call for special attention to these populations to eliminate disparities in doxy-PEP roll out.

Doxy-PEP may reduce overall use of antibiotics because of its protective effects against bacterial STIs

Scott and colleagues (Abstract 163) presented data on doxy-PEP impact on STIs among PrEP users in that same sexual health clinic. Doxy-PEP rollout began in November 2022 and they compared STI rates in the 5 quarters before vs 5 quarters after doxy-PEP initiation. Of nearly 4600 PrEP clients, 55% took doxy-PEP at some point during 2-year follow-up. Among doxy-PEP users, there was an 89% reduction in syphilis infection ($P = .006$), an 81% reduction in chlamydia infection ($P < .001$), and a 44% reduction in gonorrhea infection ($P < .001$). There was no significant decline in bacterial STIs among non–doxy-PEP users over this period. The impact on bacterial STIs seen in this clinical setting mirror those seen in RCTs of doxy-PEP.

Balkus and colleagues (Abstract 1281) compared results of a doxy-PEP survey conducted at the King County, Washington, annual pride event in 2023 to 2024 among MSM and transgender women. The Public Health – Seattle and King County issued doxy-PEP guidelines in June 2023. Overall, 92% of respondents were HIV negative, 43% were on PrEP, and 13% reported an STI in the past year. Overall knowledge of doxy-PEP increased from 48% to 59% and use of doxy-PEP increased from 15% to 30% from 2023 to 2024. Similarly, among MSM on PrEP, there was considerably more knowledge of doxy-PEP (67% to 88%) and those who took doxy-PEP (18% to 35%) from 2023 to 2024. Awareness declined among transgender women between samples (60% to 27%) with uptake similar to that in MSM on PrEP (17% to 33%). The authors called for increased community and clinician education focused on transgender women.

Raccagni and colleagues (Abstract 1284) conducted a retrospective analysis of MSM with HIV or on PrEP in Milan. They offered doxy-PEP to those with at least 1 STI or condomless sex, and then quantified antibiotic use as days of therapy (DOT) after doxy-PEP was prescribed and compared that to the anticipated DOT had doxy-PEP not been prescribed, based on pre-prescription STI rates. Of 754 MSM prescribed doxy-PEP, 222 (29%) ended up using doxy-PEP. There were 401 STIs before and 146 STIs after doxy-PEP was prescribed. In their calculations, after doxy-PEP was prescribed, they needed 1.26 DOT per 1000 person-days of ceftriaxone, 0.37 DOT per 1000 person-days of penicillin, and 3.21 DOT per 1000 person-days for doxycycline. However, they would have expected 4.85, 1.86, and 24.71 DOT per 1000 person-days, respectively, for each of those antibiotics in the absence of doxy-PEP. Therefore, they suggest that doxy-PEP may reduce overall use of antibiotics because of its protective effects against bacterial STIs.

Gómez-Ayerbe and colleagues (Abstract 1275) presented data from a single center study in Spain of 197 MSM on PrEP. They evaluated 2 periods of time, the pre–doxy-PEP period from PrEP initiation to doxy-PEP prescription (mean, 18 months of follow-up), and the post-doxy-PEP period from doxy-PEP initiation to August 2024 or discontinuation of doxy-PEP (mean, 14 months of follow-up). Doxy-PEP was offered to HIV PrEP users who had had at least 1 STI in the past year or who, in the past 6 months, reported condomless sex or more than 3 partners. Over follow-up, 9 persons discontinued doxy-PEP, 4 for adverse reactions. Participants underwent STI screening every 3 to 4 months. STI levels dropped significantly for chlamydia infection (31.4 to 7.8/100 py; $P < .0001$) and for syphilis infection (21.5 to 3.2/100 py; $P < .001$) in the pre- vs post-periods. Gonorrhea fell from 41.5 to 28.9, but this did not achieve statistical significance ($P = .1$). There was no increase in extended-spectrum beta lactamase (ESBL) *Escherichia coli*, or methicillin-resistant *Staphylococcus aureus* at week 48. There was no cephalosporin resistance among gonorrhea isolates and tetracycline resistance was similar in the pre- vs post-periods (46% vs 42%). The authors emphasized the significant effects of doxy-PEP on STIs in a real-world setting for more than 48 weeks of follow-up, but suggest further data are needed to evaluate antimicrobial resistance.

Secco Torres da Silva (Abstract 1279) reported on doxy-PEP awareness among 8217 sexual and gender minority persons in Brazil. In this online survey, 33%

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were aware of doxy-PEP. In multivariable analysis, increased awareness was associated with secondary or post-secondary education (aOR, 1.3); HIV knowledge (aOR, 1.2); or having more than 5 sex partners in the last 6 months (aOR, 1.45), condomless anal sex (aOR, 1.3), chemsex (aOR, 1.3), or at least 1 STI (aOR, 1.3). They call for targeted efforts to increase knowledge in this population and for doxy-PEP integration into sexual health services.

A novel vaginal insert containing doxycycline protected 8 pigtail macaques against chlamydia challenge compared with 5 of 6 control animals that acquired chlamydia infection

Grennan and colleagues (Abstract 1288) evaluated changes to the rectal microbiome among 52 MSM and transgender women enrolled in a study in Vancouver, Canada taking doxycycline PrEP (doxy-PrEP). In the immediate arm, 22 participants received doxy-PrEP (100 mg doxycycline/day) at baseline; in the deferred arm, 19 participants received doxy-PrEP starting at 24 weeks. Both arms were followed up through 48 weeks. There was no significant difference in beta-diversity within or between study arms. In the immediate arm, there were no changes in alpha-diversity at the genus or family level, but at the order, class, and phylum level, there was a modest decrease in alpha-diversity. The authors concluded that there was minimal impact on the rectal microbiome of doxy-PrEP at 48 weeks, and particularly no changes in diversity at the genus level. They recommended long-term data to further explore any effects of doxycycline PrEP on the rectal microbiome.

Garber and colleagues (Abstract 1283) tested a novel vaginal insert containing doxycycline in pigtail macaques to protect against chlamydia infection. Four animals each were administered 10 mg or 50 mg of doxycycline 4 hours after vaginal challenge with chlamydia infection. There was no systemic absorption of doxycycline but vaginal levels remained above the IC_{90} for more than 11 days. All 8 animals were protected against chlamydia infection whereas 5 of 6 control animals with no insert developed vaginal chlamydia infection. The authors state this is a promising intervention for PEP, and could be coformulated with TAF/elvitegravir that is currently being developed as an HIV prevention product.

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Additional Reference Cited in Text

1. Landovitz RJ, Voldal E, Hanscom B, et al. Site-based HIV testing assay performance for cabotegravir and TDF-FTC PrEP failure in HPTN 083 [Abstract 128]. In Special Issue: Abstracts From the 2024 Conference on Retroviruses and Opportunistic Infections. *Top Antivir Med*. 2024;32(1):24-25.

Top Antivir Med. 2025;33(2):508-535