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CROI 2023: Epidemiologic Trends and Prevention for HIV and Other Sexually Transmitted Infections

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Abstract: *At the 2023 Conference on Retroviruses and Opportunistic Infections (CROI), several investigators used tests of recent HIV infection to track which populations are currently most heavily impacted by HIV and to estimate HIV infection rates in those populations. Assisted partner notification for HIV was successfully applied for spouses of persons with HIV and sexual and injection partners of people who inject drugs; however, delays in linkage to care were seen for non-spousal partners in one study. Lack of awareness of HIV positive status remains an issue in various populations; several presentations focused on novel strategies for improving HIV testing uptake in these populations. Doxycycline administered as 200 mg post sexual exposure significantly reduced the risk of syphilis, chlamydia, and gonorrhea infection in men who have sex with men but did not prevent bacterial sexually transmitted infections (STIs) in cis-gender women; reasons for this discrepancy are currently being explored. Although oral HIV preexposure prophylaxis (PrEP) is increasingly being used in populations in greatest need of prevention tools, PrEP uptake and persistence remain low in a number of key populations, including people who inject drugs. Several innovative delivery models show early promise in addressing gaps along the PrEP continuum. The successful use of injectable cabotegravir PrEP in several populations was presented at this conference, although uptake remains low globally. The pipeline of novel long-acting and rapid-onset PrEP agents appears to be robust, including implants, vaginal rings, and topical inserts, with several presentations focusing on preclinical and early clinical trials.*

Keywords: HIV, testing, prevention, transmission, PrEP, PEP, STI, doxycycline, doxy-PEP

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Recent HIV Infections and HIV Incidence

The Recent Infection Testing Algorithm (RITA) is a tool that differentiates recent from chronic HIV infection. Suthar and colleagues used the RITA algorithm to compare factors associated with HIV infection with those associated with recent infection in Cambodia (Abstract 848). Of more than 53,000 individuals tested for HIV infection from August 2020 to August 2022 in 68 facilities, 6868 (13%) tested HIV positive, and 192 of these (3.1%) tested RITA-recent. Compared with the general population, men who have sex with men (MSM) had a nearly 2-fold higher adjusted odds for testing RITA-recent than for being newly diagnosed with longer-term HIV infection (adjusted odd ratio [aOR], 27.4 vs 15.5, respectively). Transgender women (TGW) were also substantially more likely to be deemed recently infected than for being newly diagnosed (aOR, 19.2 vs 11.0, respectively), as were entertainment workers (aOR, 6.1 vs 3.5, respectively). Persons who inject drugs (PWID) were less likely to test RITA-recent than newly diagnosed (aOR, 13.9 vs 26.3, respectively). These data might suggest that MSM, TGW, and entertainment workers are acquiring their infections more recently than other groups, and PWID may have HIV for longer periods of time prior to being diagnosed. The authors suggest that these data may help point to populations in need of greater prevention and testing interventions.

Recency testing was also used by Stephens and colleagues to understand patterns of HIV acquisition and testing in Malawi (Abstract 849). Of more than 8300 newly diagnosed persons aged 15 to 24 years diagnosed from September 2019 to March 2022 across 251 sites in Malawi, 4.9% were recently infected overall, although 8.2% of diagnoses among breastfeeding women were recent. Most males aged 15 to 18 years (>50%) and females aged 15 to 16 years (55%) reported they had never previously tested for HIV, although the largest proportion of recent infections were in persons aged 17 to 18 years (7.3%). These data suggest that most young people with HIV in Malawi have been infected for longer than 12 months at the time of diagnosis. Improved HIV testing uptake and prevention interventions are needed among this population.

Saito and colleagues examined recency testing paired with partner notification services in 60 health facilities in all 5 provinces in Rwanda (Abstract 199). From August 2021 to October 2022, data were analyzed on routine recency testing and sexual partner notification at these sites. Recent infections using the rapid test for recency assays (RTRI) were designated as less than 6 to 12 months in duration, and long-term infections were those designated to be greater than 12 months in duration. Of the 1238 index cases aged 15 years and older, 7.9% were found to be recent. Recent cases were more likely than long-term cases to be younger than 35 years (72% vs 60%; P = .008), female (79% vs 62%; P = .001), single (38% vs 30%; P = .008), and a female sex worker (FSW) (20% vs 8%; P = .001). Overall, 45% of the sexual contacts listed were tested, and the HIV prevalence in this group was 15.5% (20% among recently infected index cases vs 15.1% among long-term infected index cases). The recency yield was 4% among sexual

contacts linked to recently infected index cases vs 0.8% among sexual contacts linked to long-term infected persons (P = .045). These data found that newly diagnosed index cases with recent infection were more likely than those with long-term infection to have sexual contacts with recent infection. The authors suggest that HIV recency testing paired with partner notification provides important opportunities to identify new infections earlier and tailor prevention efforts to groups at high risk.

Poirot and colleagues reported on the impact of returning recency test results on intimate partner violence (IPV) in Rwanda (Abstract 940). The authors point out that the President's Emergency Plan for AIDS Relief (PEPFAR) does not recommend returning recency results to persons newly diagnosed with HIV due in part to lack of safety information about whether such information might trigger IPV. They conducted a prospective cohort study of newly diagnosed persons with HIV from August 2021 to October 2022 in 60 health facilities in Rwanda. Over a 6-month period, persons were asked at 4 study visits about experiences of control, economic, emotional, physical, or sexual violence from a current partner in the prior 4 weeks. Of 932 persons newly diagnosed with HIV who had IPV data from 1 or more visits after return of recency test results, they found higher rates of IPV at baseline before HIV diagnosis compared with after HIV diagnosis (29.8% vs 17.6%; P < .001). Prevalence of IPV did not increase after return of HIV recent infection test results (17.6% vs 16.1%; P = .40), nor did they see a difference in IPV between those with recent vs longer-term infection. One participant did report that their recency result was a reason for the violence they experienced, although there were other reasons as well. The authors conclude that programs returning results can adopt strategies to mitigate IPV risks.

Hallmark and colleagues reported on HIV time-space alerts among PWID and MSM in the United States from 2018 to 2021 (Abstract 851). The Centers for Disease Control and Prevention (CDC) issues alerts when the number of diagnoses in the most recent 12-month period is greater than 2 standard deviations and more than 2 diagnoses above the mean in the preceding 12-month period, as a way of potentially identifying clusters or outbreaks of HIV. During this period, the CDC issued 308 quarterly alerts in 4.9% of counties for PWID and 777 quarterly alerts among 14.2% of counties for MSM. Alerts among PWID occurred in a higher percentage of large central metro areas (41.2%), whereas for MSM, a higher percentage of alerts occurred in large fringe (29.1%) and medium (27.4%) metro areas. There were steep declines in alerts, especially among MSM, in the period immediately following the start of the COVID-19 pandemic, likely due to decreased testing. These numbers rebounded for MSM but not for PWID. Numerous subsequent alerts occurred in 29.9% of counties with alerts among PWID and 19.3% of counties with alerts among MSM. The authors raise concerns about the occurrence of alerts for PWID among 41% of central metro areas, which may suggest expanding transmission among PWID in these urban areas as well as sustained alerts in many counties.

Torres and colleagues used RITA testing to calculate an annualized HIV infection rate among MSM and TGW seeking HIV testing

who were not on preexposure prophylaxis (PrEP) or postexposure prophylaxis (PEP) at 6 sites in Brazil and 12 sites in Peru (Abstract 850). They enrolled more than 7000 participants into the study, with 97% acceptance rate of those who were eligible. HIV prevalence was 10.0% in Brazil and 20.7% in Peru. Overall annualized incidence was 3.3 per 100 person-years in Brazil and 7.6 per 100 person-years in Peru. Incidence was highest in 18 to 24 year olds in both countries (4.1 per 100 person-years in Brazil and 10.5 per 100 person-years in Peru). Transgender women had a higher incidence in Brazil than MSM (4.0 vs 3.3 per 100 person-years, respectively), whereas in Peru, MSM had a higher infection rates than TGW (8.2 vs 5.7 per 100 person-years, respectively). These data highlight the urgency of expanding PrEP services to young MSM and TGW in both countries.

McFall and colleagues reported on HIV incidence among MSM and PWID attending care centers in India from 2014 to July 2022 (Abstract 863). In this study, clients who were HIV negative on their first test and had 1 or more subsequent tests were included. The study enrolled more than 5700 MSM and more than 7300 PWID. The HIV incidence rate was 1.9 per 100 person-years among MSM and 4.1 per 100 person-years among PWID. These high infection rates occurred despite being engaged in a community-based clinic where prevention services are free. The authors called for more focus on prevention for key populations in low- and middle-income countries, including long-acting PrEP.

Risk Factors for HIV Acquisition and Transmission

Tate and colleagues presented data from the National HIV Behavioral Surveillance (NHBS) survey of PWID in San Francisco to characterize the status of the HIV epidemic for this population (Abstract 864). Despite decreases in new HIV infections overall in San Francisco during this time, new diagnoses among PWID rose by 48%, accounting for 27% of all new diagnoses in San Francisco in 2021. Of the 95-95-95 targets for the proportion of people diagnosed, proportion on antiretroviral treatment (ART), and proportion virally suppressed, the NHBS survey suggested that none of these landmarks had yet been met. In NHBS in San Francisco in 2022, 80% of PWID with HIV knew their HIV status, 92% of these were on ART, and 71% of these were fully virally suppressed. Of the PWID with a new HIV positive test result, 75% had had a health care visit in the previous 12 months, and only 22% of them had been offered an HIV test. Participants with new HIV positive test results tended to be Black/African American (42%), male (50%), heterosexual (83%), and over age 50 years (50%). The authors suggest that San Francisco is not on course to get to zero HIV infections among PWID, with substantial progress needed to reach the 95-95-95 2030 goals. They called for increased HIV testing of PWID in health care settings, as well as more support for PWID with HIV to achieve viral suppression.

Goodreau and colleagues reported on changes in sexual practices among cis-gender MSM who were not on PrEP, as reported in the American Men’s Internet Survey from 2014 to 2019 (Abstract 866). They found that young (15 to 24 years old) MSM not on PrEP saw a 5 percentage

point year-on-year increase in condomless anal sex; this year-on-year percentage increase was 13 percentage points for young Hispanic MSM. Most of this sexual practice was with partners of perceived negative or unknown status, so this is not attributable to undetectable equals untransmittable (U=U). The authors call for more messaging around risk for MSM who cannot or do not want to take PrEP.

Edun and colleagues modeled the potential impact of persons with low-level viremia (51-1000 viral copies/mL) on HIV transmission, using data from Population-based HIV Impact Assessment (PHIA) surveys in 14 sub-Saharan African countries from 2015 to 2019 (Abstract 868). They found that persons with low-level viremia were not more likely to report high-risk behavior than those with undetectable viral loads, but that persons with undiagnosed HIV and those diagnosed but untreated were more likely to report high-risk behavior. In their model, undiagnosed and diagnosed but untreated persons with HIV contributed to 72% of transmissions, and less than 1% of transmissions occurred from persons with low-level viremia. The authors call for improved HIV testing and linkage services to address this source of new HIV infections.

Kroidl and colleagues report ecologic data on changes in HIV incidence following mass drug administration to eliminate lymphatic filariasis (*Wuchereria [W] bancrofti* infection) in southwest Tanzania (Abstract 869). Previously, *W bancrofti* was associated with a 2.3-fold increase in HIV incidence. The Tanzanian government distributed ivermectin and albendazole once annually from 2009 to 2015, resulting in a reduction of *W bancrofti* prevalence from 35.1% to 1.7%. The same individuals whose data were collected from 2007 to 2011 were revisited in 2019 and screened for *W bancrofti* and HIV. Among those who were *W. bancrofti*-uninfected, HIV incidence declined only from 0.72 to 0.64 per 100 person-years over this period. However, among those who were originally *W bancrofti* infected, HIV incidence decreased from 1.9 to 0.76 per 100 person-years. The authors postulate that treatment of *W bancrofti* led to this more substantial decline in HIV incidence.

Singogo and colleagues reported on venue-based vs clinic-based recruitment for HIV testing in Malawi (Abstract 1087). They conducted cross-sectional biobehavioral surveys of representative samples of individuals seeking care in government clinics (n=2313) and social venue patrons (n = 1802) from January to March of 2022. Clinics were randomly selected from government clinics providing HIV testing, and venues were randomly sampled from urban and rural strata, with an oversampling of rural venues. They found that compared with the clinic population, the venue population was more likely to be male (69% vs 28%), aged greater than 25 years (61% vs 51%), unmarried (62% vs 40%), drink alcohol daily (44% vs 8%), have more sexual partners in the last year (mean, 16 vs 2), report a new sex partner in the past 4 weeks (42% vs 15%), and report transactional sex (52% vs 12%). HIV prevalence was higher among the venue population (19% vs 9%), although more than three-quarters in each group were virally suppressed. At venues, HIV prevalence among women increased from 0% among 15 to 17 year olds to 43% among 18 to 21 year olds. At venues, factors associated with HIV infection included being female (39% vs 10%),

having a new partner in the past 4 weeks (28% vs 13%), and transactional sex (25% vs 12%). Acute (0% vs 0.6%) and recent infections (4.7% vs 9.7%) were uncommon in clinics and in venues, respectively. The authors suggest that outreach to venues, particularly to young women, is important for HIV prevention and viral suppression.

Partner Notification

Parthasarathy and colleagues presented data from the high-burden state of Telengana in India (Abstract 152). With 2.3 million persons with HIV, India has the second-highest HIV burden in the world. The team contacted spouses, nonspousal sex partners, and children or parents of 9863 index cases. Of the 15,253 contacts reached, median age was 32 years and 47% were male. Overall, 33% were spouses, 51% were nonspousal sex partners, and 16% were children or parents of the index case. Of this group, 87% received test results, 20% were found to be HIV positive, and 92% of them initiated antiretroviral therapy (ART). However, the speed with which they were notified and began ART was substantially longer for nonspousal sex partners than spouses. The vast majority of spouses received same-day testing and notification of test results, and 31% of the nonspousal sex partners took more than 1 week for testing and notification of test results. Of this 31%, the median delay was 41 days (interquartile range, 17-92 days). In evaluating time of initial contact to beginning ART, 75% of spouses achieved this on the same day or within 1 week, but this was only true of 43% of sex partners. The authors point to the importance and success of index testing but highlight the need for more expedited methods for the nonspousal sex partners of index persons.

Monroe-Wise and colleagues presented data from a study of Assisted Partner Services (APS) in Kenya (Abstract 153). They pointed out that PWID have a 22-fold higher prevalence of HIV infection than the general population, similar to that seen in MSM, but that there are substantial barriers to HIV testing and care for this population. The team used community-embedded peer educators to locate persons with HIV infection in the community, locate their injecting and sexual partners, and find the people with HIV and partners testing positive for HIV or hepatitis C virus (HCV) after 6 months for follow-up interviews. The team found 485 women and 504 men with HIV. These PWID had been injecting for an average of 5.4 years, and 10.8% reported sharing equipment in the past month. Of this group, 16.4% were HCV positive and 67.9% were HIV virally suppressed. Nearly three-quarters reported 1 to 5 sexual partners, with the remainder reporting 6 or more. Of the 4705 partners reported, 97% were located and 100% of these were enrolled in the study, a testament to the skill of the peer educators. Of these, 70.5% were injecting partners, 18% were sexual partners, and 11.5% were injecting and sexual partners. Among the partners, HCV prevalence was 18%, HIV prevalence was 18%, and 69.9% of these were virally suppressed. HIV prevalence was highest (32.5%) in participants who were sexual and injecting partners. Of the partners found to have HIV, 85% were known to be positive, 91% of those were on

ART, but only 77% of those were virally suppressed. Only 26% of HCV-positive partners were known to be HCV positive, and only 2% of those who were PCR positive had been previously treated. The authors calculated that the number needed to interview to find a partner with HIV was 11.24, but to find a partner with HIV who was either unaware of their status, not on ART, or not virally suppressed was 4.14. On follow-up, of 189 of the index participants not virally suppressed at baseline, 71.9% were virally suppressed at 6 months; 71.8% of partners not virally suppressed at baseline were suppressed at 6 months. Of those reporting IPV at baseline, 22% reported IPV at 6 months, and 4% of those reporting no IPV at enrollment reported IPV at 6 months, although none attributed the IPV to study procedures. This appeared to be a successful program to identify and link to care PWID and their injecting and sexual partners.

HIV Testing

Singh and colleagues presented data from 21 jurisdictions in the National HIV Surveillance System on the proportion of persons who tested positive who had ever had a previous HIV negative test from 2014 to 2019 (Abstract 934). They found that for all races and ethnicities, the proportion who ever had a previous negative HIV test before HIV diagnosis decreased significantly (from 63% to 54%; estimated annual percent change [EAPC], -2.7). This decrease was greatest for Hispanic/Latino persons (from 63% to 52%; EAPC, -3.2), then White persons (from 68% to 57%; EAPC, -3.0), and then Black/African Americans (from 62% to 54%; EAPC, -2.2). Significant decreases occurred for males and females among Black/African American persons, but males only among Latino and White persons. The authors postulate that this decrease in HIV testing before diagnosis may be associated with trends in uptake of HIV testing and prevention strategies, reminding us that annual HIV testing should be promoted among all persons with HIV risk factors.

Patel and colleagues evaluated the association between the amount of HIV testing and the areas with greatest needs for HIV testing, as defined by the rate of persons with undiagnosed HIV infection in 2019 (Abstract 935). They found a significant association between the amount of testing and the areas with greatest needs for testing (Rho, 0.59; $P < .001$), but found that jurisdictional associations varied. For instance, those with the greatest need (higher undiagnosed HIV infection per capita and lower CDC-funded HIV tests per capita) included Miami-Dade County, FL; Prince George’s County, MD; Hudson County, NJ; Bronx County, NY; and Hamilton County, OH. Those with the lowest need (lower undiagnosed HIV infection per capita and higher CDC-funded HIV tests per capita) were San Francisco County, CA; Tarrant County, TX; Suffolk County, MA; and Missouri and Alabama. The authors suggest that those areas with greater unfulfilled testing needs could use these data to identify gaps and barriers to their testing services and improve or expand upon their testing programs. Those with fewer unfulfilled needs may also be areas with more robust

PrEP programs, which may both increase knowledge of HIV serostatus and increase the number of HIV tests being done.

Guardiola and colleagues reported on directed screening for HIV infection in 10 emergency departments (EDs) in Catalonia, Spain (Abstract 942). They recommended HIV testing in the EDs for any of 6 specific clinical scenarios: presence of sexually transmitted infection (STI), PEP, chemsex, mononucleosis-like syndrome, and community pneumonia or herpes zoster in those under the age of 65 years. After 60 weeks of follow-up from June 2021 through August 2022, 6180 HIV tests were performed with 55 new HIV diagnoses (0.9%) identified. Persons reporting chemsex had an HIV seroprevalence of 5.4%, and patients with community-acquired pneumonia or mononucleosis-like syndromes had an HIV prevalence close to 2%. The authors suggest that these clinical scenarios provide efficient criteria for ED screening.

Kailembo and colleagues reported on factors associated with lack of awareness of HIV infection among Tanzanians with HIV (Abstract 936). Using data from the Tanzania HIV Impact Survey conducted in 2016 to 2017, they found that of 1779 survey participants with HIV, 39% were unaware of their HIV status. On multivariable analysis, factors associated with unawareness included male sex (adjusted prevalence ratio [aPR], 1.47), younger age (15-24 years compared with those 50 years or older; aPR, 1.43), having low HIV knowledge (aPR, 1.2), and not using condoms (aPR, 1.42). Widowed persons were significantly less likely to be unaware of positive status (aPR, 0.74). The authors state that this reinforces the need for targeted interventions to increase safe and ethical index testing, social network testing, and HIV self-testing, with a focus on young adults and men.

Leslie and colleagues reported on the prevalence of overreporting of recent HIV testing and underreporting of positive HIV serostatus based on a population-based survey conducted in a rural setting of Ehlanzeni District in South Africa (Abstract 937). They found that 69% reported recent testing, but reporting was confirmed in only 34% of survey respondents after correcting for potential under-documentation. They also found that HIV prevalence was estimated at 16% based on self-report but was actually 28% in this population. They suggest that survey-based measures must be interpreted with caution, given the inaccuracies found in this survey.

Shaikh and colleagues point to the importance of offering non-HIV services for TGW as a method for increasing HIV testing (Abstract 941). They evaluated data from 3 clinics in India from February 2021 to July 2022. During this time, 2276 individuals registered at the clinics, 87% of whom identified as a TGW, and 54% of whom had never received services through the government’s targeted interventions program. The most utilized service was laser therapy, followed by HIV services. Of 883 clients screened for HIV, 48 were newly diagnosed with HIV infection, although only 20 completed confirmatory testing and 13 initiated ART. The authors concluded that integrating non-HIV services desired by the community enabled these clinics to reach clients not previously engaged in local or national HIV programming and served as an entry point to HIV testing and care. Additional

efforts are needed to increase confirmatory testing and ART initiation.

Polk and colleagues reported on the impact of the mpox outbreak on increased HIV testing and diagnosis in a large integrated health care system (Abstract 944). They reported on 17 EDs and 44 Urgent Care clinics across the Charlotte region in North Carolina in the period pre-mpox (July 2021 to June 2022) to testing during the mpox outbreak (July 2022-October 2022). Overall, total HIV tests increased from 2.3 per 1000 encounters per month to 3.8 per 1000 encounters per month ($P < .05$) and the total number of new diagnoses per month increased from 1.4 to 3.9 ($P < .05$). They plan to use this information to continue to educate clinicians in these settings on the need and opportunities for HIV testing.

Armstrong-Hough and colleagues reported on a randomized controlled trial to increase HIV testing uptake among household contacts of persons with tuberculosis (TB) (Abstract 1050). They point out that up to half of household contacts decline HIV test offers during routine TB contact investigation in Uganda and South Africa. Community health workers visited the homes of TB index patients to screen contacts for TB symptoms and to offer free, optional oral HIV testing. Households were randomly assigned 1:1 to standard-of-care or a socio-behavioral intervention to make HIV testing the norm. In total, 328 contacts in 99 index patient households were randomly assigned to the intervention and 224 contacts in 86 patient households were randomly assigned to the standard-of-care arm. Completion of HIV testing was higher in the intervention than the control arm (98% vs 92%; $P = .006$). Out of these tests, 2.1% of those tested in the intervention arm were found to be HIV positive, as were 0.6% in the control arm ($P = .22$). Community health workers reported that the norming strategy took equivalent or less time than the standard strategy. These results suggest that this simple, brief strategy could increase HIV testing uptake among contacts of persons diagnosed with TB.

Terwilliger and colleagues reported on attempts to isolate HIV from municipal wastewater (Abstract 947). They used samples from 6 wastewater treatment plants in the Houston area, and were able to identify DNA, but not RNA in these samples. They suggest that wastewater monitoring could be a new tool to understand the epidemiology of HIV in near real time.

HIV Self-Testing

Ekwunife and colleagues evaluated the impact of removal of subsidies for HIV online self-testing kit ordering in Kenya (Abstract 930). They evaluated periods before subsidy removal (cost of oral-fluid and blood-based kits was $2.30 USD) to periods after subsidy removal (cost of oral-fluid tests was $4.30 USD and cost of blood-based kits was $6.90 USD), using sales of an emergency contraceptive product during those periods as a control. They found that ordering of oral-fluid self-test kits declined 1.5-fold after subsidy removal (with 357 fewer test kits per month), and blood-based self-collection

kits declined by 27-fold (with 226 fewer test kits per month) compared with the control. These data suggest that subsidies are effective at increasing the demand for HIV self-test kits.

Pines and colleagues evaluated PWID willingness to use and deliver HIV self-test kits to peers at the San Diego-Tijuana border region (Abstract 932). Of the 539 HIV-negative PWID completing the survey, 81% stated that they would want to use HIV self-test kits, with more than 90% reporting reasons that they would be able to test for HIV more regularly, that it would be more convenient than going to a clinic or community-based organization, and that it would give them more privacy and confidentiality. Of the 19% stating they would not want to use self-test kits, 24% each reported that they would be worried that self-tests are less accurate, that they would be worried about using the test incorrectly, and that they would be worried about misinterpreting the test results. Individual characteristics associated with willingness to use self-test kits included more years of education (aPR, 1.02), prior HIV testing (aPR, 1.24), prior HIV self-test kit use (aPR, 1.27), and hazardous alcohol consumption (aPR, 1.12). The following were less likely to want to use a self-test kit: persons who injected drugs several times per day in the past 6 months (aPR, 0.87); receptive syringe sharing (aPR, 0.92); and perceived HIV risk (aPR, 0.83). Among the 366 participants who consented to the social network substudy, willingness to distribute self-test kits was increased with years of education (aPR, 1.02), prior HIV testing (aPR, 1.27), prior HIV self-test kit use (aPR, 1.25), willingness to use self-test kits themselves (aPR, 8.31), network size (aPR, 1.04), proportion of network that ever had unstable housing (aPR, 1.5), proportion of network that had ever been detained or arrested (aPR, 1.57), and proportion of network that offered drugs or encouraged drug use (aPR, 1.29). Those who reported a higher proportion of the network with whom they were very close were less likely to be willing to distribute HIV self-test kits (aPR, 0.8). The authors conclude that there is high potential for HIV self-test kits and their distribution among PWID, which could address undertesting in this population.

Effect of COVID on HIV Testing and Prevention Services

Viguerie and colleagues attempted to isolate the effect of COVID–19-related disruption of HIV testing on HIV diagnoses in the United States in 2020 (Abstract 158). Prior to 2020, the US saw a 2% to 3% annual decline in new diagnoses per year, but found a 17% decline in 2021. The authors wanted to differentiate decreased diagnoses because of decreased testing vs decreased infections due to behavior changes related to COVID-19 (eg, social distancing). Using 3 different mathematical techniques, they found that 3200 to 3300 new HIV diagnoses were missed in the US in 2020 due to decreased testing, or approximately 18% fewer diagnoses than expected. The absolute number of missed infections was highest among persons assigned male at birth, MSM, persons in the South, and Black persons. However, the proportion of missed infections was highest in Hispanic/Latino persons (22%), females at birth (24%), heterosexuals (24%), and MSM/PWID (30%). These

are likely the lower bound of estimates for missed infections because they do not take into account either very new missed infections or very old missed infections. These data suggest that the substantial decrease in new HIV diagnoses in 2020 in the US were not attributable to incidence changes, but rather decreases in HIV testing services.

Nassau and colleagues presented data on changes in prevention services for PWID in Philadelphia in 2022 compared with 2018 to assess the impact of COVID-19 on service disruption (Abstract 1100). Using data from NHBS, they compared HIV testing, medical care, syringe service program access, drug treatment, and PrEP use in the year prior to interview. There were baseline differences in the participants sampled in the 2 years by age, race/ethnicity, housing stability, and primary injecting drug. After adjusting for these differences, they found an 18% decrease in recent HIV testing was observed between these 2 times (aPR, 0.82; $P < .001$). Although a significantly smaller proportion of PWID accessed each service in 2022 than in 2018, they did not see statistically significant differences in access to HIV services in adjusted models. PrEP awareness was higher in 2022 (approximately 38% in 2018 vs 54% in 2022; $P = .001$); however, this did not translate into improved PrEP use (both arms <5%). The authors concluded that harm reduction services should be co-located with HIV prevention and care services in nontraditional, nonclinical settings.

HIV Prevention Interventions

Cowan and colleagues presented the results of the Amethist trial, a cluster randomized trial investigating the effect of risk-differentiated care for FSW in Zimbabwe (Abstract 123). In southern Africa, FSW have a high burden of HIV, and although community-led FSW programs in Asia have shown benefit on HIV and STI incidence, these interventions have not been widely used nor tested in Africa. The investigators nested this study into a larger study, the Sisters' study (not described in the presentation). The Amethist intervention consisted of a peer educator providing risk-differentiated peer support, as well as self-help groups, although few of these groups took place. The intensity of the intervention varied depending on the amount of risk reported by the FSW (ie, risk determined by age under 25 years, new to sex work [ie, for <6 months], high client burden of >10 per week, inconsistent condom use, problematic drinking and/or drugs, and problematic violence). In all, 22 clusters were randomly assigned in a 1:1 ratio to the Sisters' program alone or the Sisters' program with Amethist. Outcomes were assessed after 28 months using respondent-driven sampling in all 22 clusters. In total, approximately 2200 FSW were recruited from each arm, and more than 2100 per arm contributed to the final analysis. There was no significant difference in the proportion of HIV-negative FSW with risk of HIV acquisition (defined as condomless sex by Y chromosome or gonorrhea on vaginal specimen without adequate PrEP use [700 fmol/punch on dried blood spot]); 92.1% of the intervention group and 92.2% of the control group were at risk for HIV acquisition. However, there was a significant decrease in the risk of HIV transmission from FSW with HIV (defined as

condomless sex as described above in someone not virally suppressed); 5.8% of the intervention arm vs 10.4% of the control arm ($P < .001$). The results for FSW at risk for HIV infection were disappointing, and more is needed to determine how to reach this population with effective interventions. The authors also concluded that self-report did not correlate well with biomarkers, either for condomless sex or for PrEP use.

Buchbinder and colleagues presented interim data from the Mosaico trial, a phase III trial of a combination adenovirus 26 mosaic vaccine and a mosaic and clade C gp140 vaccine among 3887 MSM and transgender persons in the US, Latin America, and Europe (Special Session 1). This trial had a novel design in how PrEP was handled: participants were first navigated to low- or no-cost PrEP, and if they declined PrEP, were offered to be screened for the study. Participants were not on PrEP when they enrolled, but if they were counseled and offered PrEP throughout the trial, and if they took up PrEP, remained in the trial. PrEP uptake was approximately 10% by month 24 in the study. The vaccine had no effect on HIV infection rates, which were 4.1 per 100 person-years in both arms in the modified intent-to-treat analysis. HIV infection rates were highest among younger study participants and participants enrolled in Latin America. This presentation was followed by a presentation by Corey, who laid out the future of HIV vaccine research, which is focused on many strategies to develop vaccines that induce broadly neutralizing antibodies as well as infusion of broadly neutralizing antibodies.

Sexually Transmitted Infections

Several studies evaluated the use of doxycycline-PEP (doxy-PEP) for the prevention of STI. Haaland and colleagues presented on the mucosal pharmacology of doxycycline following oral dosing in 11 men and 9 women (Abstract 118). They conducted a single-dose pharmacology study in which participants were administered 200 mg of a delayed release formulation of doxycycline hyclate and a single dose of tenofovir alafenamide/emtricitabine/bictegravir, followed by collection of rectal or vaginal and cervical biopsies and urethral swabs at 24 hours, and blood and rectal or vaginal swabs for up to 7 days. Rectal secretion doxycycline concentrations peaked at 48 hours, compared with 8 hours in vaginal secretions, and 4 hours in plasma. Doxycycline exposure in mucosal secretions was higher than in plasma, with an area-under-the-curve ratio of 2.17 for rectal secretions to plasma and 1.72 for vaginal secretions to plasma. Additionally, plasma and rectal doxycycline concentrations did not differ between men and women. The maximum concentration (C_{max}) of doxycycline in mucosal secretions reached 10- to 20-times (x) the minimum inhibitory concentration (MIC) for *Chlamydia trachomatis*; these concentrations remained above the MIC for about 4 days and above 4x the MIC for up to 2 days after dosing. For *Treponema pallidum*, C_{max} reached 7x to 12x the MIC and remained above the MIC for approximately 3 days and above 4x MIC for up to 2 days. For *Neisseria gonorrhoeae*, C_{max} only reached 3x to 5x the MIC, remained above the MIC for approximately 2 days but above 4x MIC for

less than 12 hours. Tissue concentrations of doxycycline were 3x to 9x the MIC for *Chlamydia trachomatis* and *Treponema pallidum* but only 1x to 2x MIC for *Neisseria gonorrhoeae,* and doxycycline concentrations in male urethral secretions were 11x to 18x MIC for *Chlamydia trachomatis* and *Treponema pallidum* but only 4x MIC for *Neisseria gonorrhoeae*. These findings suggest that doxycycline efficiently distributes to mucosal sites and persists at concentrations exceeding reported MIC values for *Chlamydia trachomatis* and *Treponema pallidum* to a greater extent than for sensitive *Neisseria gonorrhoeae*.

Molina and colleagues reported results from the ANRS 174 Doxyvac study, an open-label randomized trial to prevent STIs among MSM on PrEP (Abstract 119). Participants who had an STI in the past 12 months were randomly assigned in a 2x2 factorial design to receive doxy-PEP (200 mg doxycycline taken within 24-72 hours post sex) or no PEP in a 2:1 ratio, and 2 injections of the 4CmenB vaccine or no vaccine in 1:1 ratio. Based on results from the DoxyPEP trial[1] demonstrating a 65% reduction in STI incidence, in September 2022, the Doxyvac Data Safety Monitoring Board requested an unblinded analysis of 502 participants enrolled from January 2021 to July 2022. At baseline, the median age was 39 years, 81% were White, and participants had a median of 42 months of PrEP use and 10 sex partners in the last 3 months. There was no interaction between doxy-PEP and the 4CmenB vaccine for the primary endpoints. The incidence of first episode of chlamydia or syphilis was 5.6 vs 35.4 per 100 person-years in the doxy-PEP vs no PEP arms (adjusted hazard ratio [aHR], 0.16; 95% confidence interval [CI], 0.08-0.30), with an 89% reduction in time to first chlamydia and 79% reduction in time to first syphilis. There were also significant reductions in time to first gonorrhea (aHR, 0.49; 95% CI, 0.32-0.76) and *Mycoplasma genitalium* (aHR, 0.55; 95% CI, 0.34-0.89) infection with doxy-PEP. Among 65 cultures available for gonorrhea resistance testing, 100% (7/7) were tetracycline resistant at baseline, with no difference between arms during follow-up (67% and 81% tetracycline resistant in the doxy-PEP and no PEP arms, respectively). No chlamydia resistance was observed among samples tested. In a microbiome analysis, there was no difference in methicillin-resistant *Staphylococcus aureus* (MRSA) in throat swabs or extended spectrum beta-lactamase (ESBL) *Escherichia coli* in anal swabs between arms. For the 4CmenB vaccine evaluation, the incidence of first episode of gonorrhea was 9.8 vs 19.7 per 100 person-years in the 4CmenB vaccine vs no vaccine arms (aHR, 0.49; 95% CI, 0.27-0.88). There were no drug-related serious adverse events reported for either doxycycline or 4CmenB; drug-related adverse events were uncommon in those receiving doxy-PEP and were mostly gastrointestinal events; approximately one-third of participants receiving 4CmenB had a drug-related adverse event, mostly pain at the injection site, which was short lived.

Luetkemeyer and colleagues examined antimicrobial resistance among MSM and transgender women in the DoxyPEP trial[1] (Abstract 120). In this study, 637 participants were randomly assigned 2:1 to receive 200 mg doxycycline within 72 hours of condomless sex or no doxycycline. Among 320 gonorrhea cases detected at baseline and follow-up, 49% of cases had culture collected, and of those, 42% had

culture growth. At baseline, 4 of 17 gonorrhea cases (24%) had tetracycline resistance, and during follow-up, 6 of 20 cases (30%) had tetracycline resistance in the doxy-PEP arm, compared with 11% in the standard-of-care arm, suggesting that doxy-PEP may be less protective against gonorrhea strains with existing tetracycline resistance. Doxy-PEP was associated with a 14% absolute reduction in *Staphylococcus Aureus* colonization and an 8% absolute increase in doxycycline resistance compared with baseline. MRSA prevalence was low (6%) and was unchanged with doxy-PEP use. For nonpathogenic *Neisseria* species, which may serve as a reservoir for drug-resistant genes that can transmit to pathogenic bacteria, nearly two-thirds of isolates had preexisting doxycycline resistance; however, there were no significant changes associated with doxy-PEP use. Luetkemeyer recommended longer-term monitoring during doxy-PEP implementation to understand the trajectory and clinical importance of microbial susceptibility patterns associated with doxy-PEP.

Stewart and colleagues reported results on doxycycline PEP among 449 cisgender women in Kenya (Abstract 121). Participants taking daily oral PrEP were randomly assigned 1:1 to receive 200 mg doxycycline hyclate taken within 72 hours of sex or standard of care and followed for 12 months. The median age was 24 years, and the median time on PrEP was 7 months; the prevalence of STIs at baseline was 18%. Retention was high in the cohort, and women assigned to doxy-PEP reported coverage of 78% of sex acts. The overall STI incidence was 27 per 100 person-years. There were 109 incident STI events detected: 50 in the doxy-PEP arm, and 59 in the standard-of-care arm (relative risk [RR], 0.88; 95% CI, 0.60-1.29; P = .51), and results were also not statistically significant for chlamydia and gonorrhea alone. When censoring follow-up once participants became pregnant, there was no difference in STI incidence rates between arms (RR, 0.91; 95% CI, 0.62-1.35); results were also similar in subgroup analyses by age, hormonal contraception use, transactional sex, and STI detected at baseline. There were no severe adverse reactions related to doxycycline use and no incident HIV infections in either arm; however, 4 participants reported social harms related to doxy-PEP use. High levels of tetracycline-resistant *Neisseria gonorrhoeae* (100%; 6/6 samples) were detected at baseline and at follow-up visits (100%; 22/22 samples). There was no resistance to *Chlamydia trachomatis* detected among 66 samples tested. The researchers proposed several possible explanations for the negative results, including: (1) anatomy: whether endocervical tissue may differ from urethral, rectal, and pharyngeal tissues; (2) resistance: high levels of gonorrhea resistance were observed in Kenya; however, there are no known cases of resistance chlamydia globally; and (3) adherence: although the trial was designed to maximize adherence, and self-reported adherence was high, it was imperfect in the study. Given the high burden of STIs among cisgender women, they highlighted the need for effective STI prevention interventions in this population.

Traeger and colleagues modeled the potential impact and efficiency of prescribing doxy-PEP among people with or at risk of HIV infection, using data from a Boston-based lesbian, gay, bisexual,

transgender, queer, and intersex (LGBTQI+) health center (Abstract 122). They tested 10 different hypothetical strategies for targeting doxy-PEP, 3 of which targeted populations: (1) all persons accessing care; (2) persons with HIV and PrEP users; (3) PrEP users only); and 7 of which included only persons with a diagnosed bacterial STI in the past 12 months: (1) any STI; (2) rectal STI; (3) 2 STIs in past 12 months; (4) 2 STIs in past 6 months; (5) 2 STIs in the same visit; (6) syphilis; and (7) gonorrhea). They then applied a counterfactual using efficacy data from the US DoxyPEP study to assess the number of persons requiring doxy-PEP, the number of STIs averted, and the number needed to treat (NNT) for a year to avert 1 STI. They drew data from more than 10,000 patients followed up for more than 28,000 person-years from 2015 to 2020. They found that treating population groups averted more STIs, but at the cost of requiring treatment of larger populations of patients. Most efficient was treating persons with previous STIs. For example, using doxy-PEP just for persons with an STI in the previous year would require treating 41% of the cohort but averting 42% of the infections. The NNT was lowest for averting chlamydia and gonorrhea for persons with 2 STIs in the past 12 months (2.8 and 4.1, respectively), 2 STIs in the past 6 months (2.5 and 3.6, respectively), and 2 concurrent STIs (2.5 and 3.4, respectively). For syphilis, the most efficient strategy was to treat persons with prior syphilis infection (NNT, 6.0). The authors concluded that guidelines should incorporate having a recent STI diagnosis as an indication for doxy-PEP, recognizing that treating a larger population would reduce more infections, but at the cost of treating a larger proportion of people. They also recommended that persons with an STI, regardless of whether they had HIV or were on PrEP, be offered doxy-PEP, as restricting to these 2 subpopulations did not improve the NNT. They further suggested that local epidemiology could be used to target specific STIs. For example, treating persons with prior syphilis with doxy-PEP would require that only 9% of the population be treated while averting 25% of syphilis cases. They recognize that there are numerous assumptions with their model, including the population on which it is based, so different results could come from other populations.

Atkins and colleagues reported on the incidence of syphilis, HIV, and HCV among people reporting sex work from a Birmingham, Alabama-based AIDS service organization from May 2008 to June 2022 (Abstract 1025). Of more than 20,000 clients served, 950 (4.6%) reported sex work in the prior 5 years. Sex work was associated with older age (mean, 32 years vs 31 years; $P = .002$), being a cis-gender woman (45.8% vs 42.5%; $P < .001$), and identifying as non-Hispanic White (71.5% vs 44.2%; $P < .001$). Persons reporting sex work were also more likely to report injection drug use (57% vs 8%), other drug use (19% vs 3%), having a PWID partner (41% vs 5%), and sharing noninjection drug equipment (12% vs 1%). Sex work was associated with 3.42x the odds of syphilis diagnosis and 1.75x the odds of HCV diagnosis. Among the subgroup of MSM, sex work was associated with 4.57x the odds of HCV diagnosis and 2.49x the odds of HIV diagnosis. The authors concluded that targeted prevention and treatment programming is needed for persons reporting sex work.

Brown and colleagues reported on patterns of STI among TGW with and without HIV in 6 eastern and southern cities in the US (Abstract 1027). Of 1018 TGW studied, median age was 31 years, 29% self-identified as Black and 27% as Latinx, and 27% had HIV. TGW with HIV were significantly more likely to be diagnosed than TGW without HIV with 1 or more bacterial STIs (aPR, 1.96) including syphilis (aPR, 2.7) and to have herpes simplex virus (HSV)-2 IgG antibody (aPR, 1.53). Among TGW without HIV, correlates of having 1 or more bacterial STIs included being from Baltimore/Washington DC (aPR, 2.3), being Black (aPR, 5.47) or Latino (aPR, 3.87), self-identifying as genderqueer/nonbinary (aPR, 1.68), and having more than 1 sex partner (aPR, 1.87); having non-cisgender male partners exclusively was associated with decreased risk (aPR, 0.10). Among TGW with HIV, having one or more bacterial infections was less likely with increasing age (aPR, 0.91), hazardous alcohol use (aPR, 0.54), and having a lifetime history of sexual violence (aPR, 0.60). The authors concluded that the prevalence and correlates of bacterial STIs differs substantially between TGW with and without HIV, highlighting differential needs of these populations. They speculated that the relative lack of individual level correlates of bacterial STIs among TGW living with HIV may suggest macro-level factors in conferring risk among this population and called for an effort to elucidate the drivers of bacterial STIs among TGW to facilitate more targeted prevention and treatment strategies optimally suited for these populations.

Moscicki and colleagues reported on rates of STIs among young people with perinatally acquired HIV and those exposed perinatally but without HIV in the US-based Pediatric HIV/AIDS Cohort Study network (Abstract 1028). Youth in this cohort study were screened annually for chlamydia, gonorrhea, and trichomoniasis; young women were also tested for human papilloma virus (HPV). The incidence of gonorrhea, chlamydia, trichomoniasis, and HPV among youth with HIV was 49, 111, 75, and 135 per 1000 person-years, respectively; the rates for youth without HIV were 33, 95, 54, and 52 per 1000 person-years, respectively. The authors concluded that rates of gonorrhea, chlamydia, and trichomoniasis were high and similar between these 2 populations, underscoring the need for STI prevention strategies, including promotion of condom use and counseling, which clinicians may mistakenly believe has already happened. They also called for robust triage for cervical abnormalities in young women with HIV to avoid over-referral to colposcopy.

Syndromic management substantially underestimates the prevalence of STIs. Truong and colleagues reported on the prevalence of chlamydia and gonorrhea among adolescents in Kisumu, Kenya (Abstract 1026). They reported on STI testing among 1159 boys and girls aged 15 to 19 years on whom STI testing had interpretable results. Overall prevalence was 9.6%, and higher among girls (odd ratio [OR], 2.13; $P < .001$), those reporting last sexual activity 1 month ago or more recently (OR, 1.69; $P = .01$), having more than 1 partner (OR, 2.14; $P = .19$), having experienced forced sexual contact (OR, 1.6; $P = .02$), having engaged in transactional sex (OR, 1.68; $P = .01$), and having ever experienced STI symptoms (OR, 1.77; $P = .007$), although the latter was only

reported by 13.8% of youth diagnosed with an STI. The authors point out that undiagnosed or misdiagnosed STIs can result in onward transmission and impact the reproductive health of adolescents; they suggest STI testing should be made available for adolescents with risk factors.

PrEP

Long-Acting Injectable PrEP

Marzinke and colleagues evaluated cabotegravir (CAB) pharmacology among participants with delayed injections in the HIV Prevention Trials Network (HPTN) 084 study (Abstract 159). This is an ongoing phase III trial that demonstrated the superiority of long-acting injectable CAB (CAB-LA) compared with daily oral tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) in individuals assigned female at birth. In the injection phase of the study, the first 2 injections were administered 4 weeks apart, followed by injections given every 8 weeks thereafter. The CAB-LA regimen was targeted to achieve concentrations greater than 4x the protein-adjusted 90% inhibitory concentration (PA-IC_{90}) (0.664 µg/mL) in 80% of individuals, and more than 8x the PA-IC_{90} (1.33 µg/mL) in 50% of individuals. They classified delayed injections as type 1 if the second injection occurred 8 to 14 weeks after the first injection and as type 2 if any subsequent injection took place 12 to 18 weeks after the last injection. Among 1614 participants randomly assigned to the CAB-LA arm, 194 participants (12%) had at least 1 delayed injection, with a total of 224 delays observed: 19 type 1 and 205 type 2 delays. For type 1 delays in which the second injection was given 8 to 10 weeks after the first injection, 100% and 91% had CAB trough concentrations more than 4x the PA-IC_{90} and more than 8x the PA-IC_{90}, respectively; however, 75% were less than 4x the PA-IC_{90} when the interval was 12 to 14 weeks between injections. For type 2 delays in which the injection was administered 12 to 14 weeks apart, 98% and 87% of CAB trough concentrations were more than 4x the PA-IC_{90} and more than 8x the PA-IC_{90}, respectively; 90% and 62% remained more than 4x the PA-IC_{90} and more than 8x the PA-IC_{90} when the injections were 16 to 18 weeks apart. Participants with a body mass index less than the median of 26.3 kg/m^2 were more likely to have concentrations more than 8x the PA-IC_{90} following a delay. One participant seroconverted in the setting of delayed injections in the blinded phase of HPTN 084, with HIV first detected after a 16.1-week delay between the 8^{th} and 9^{th} injections; the CAB concentration was less than 4x the PA-IC_{90} at the first HIV-positive visit. In parallel with these analyses, population pharmacokinetic modeling was conducted using data from 16 clinical trials and nearly 24,000 injection events and demonstrated that CAB concentrations were 28% lower after the first injection but 32% higher at steady state among women than among men. Additionally, CAB concentrations were 30% lower after the first injection and 5% lower at steady state among participants with body mass index at or above 30 kg/m^2 vs below 30 kg/m^2. These data suggest that there may be up to 6

weeks of forgiveness in persons assigned female at birth who received delayed CAB-LA injections.

Eshleman and colleagues described the long-acting early viral inhibition (LEVI) syndrome occurring in individuals with early HIV infection in the setting of CAB-LA PrEP (Abstract 160). Among the 2282 cisgender men and TGW randomly assigned to CAB-LA PrEP in the HPTN 083 trial, 6 infections occurred despite on-time injections, 16 infections occurred with no CAB exposure within the past 6 months, 4 had HIV infection at enrollment, 3 were infected while receiving oral CAB, 3 were infected after 1 or more delayed injections, and 2 were infected near the time of CAB reinitiation. In these cases, HIV rapid tests and antigen/antibody tests often failed to detect HIV infection in the setting of CAB-LA PrEP, and viral suppression and delayed or diminished antibody expression can persist for months after infection. In HPTN 083, detection of infection was delayed in approximately half of the CAB arm infections but was rarely observed when infection occurred over 6 months after CAB administration. She presented a case study from HPTN 083 in which there was a 3-month delay in detecting HIV infection by antigen/antibody testing (qualitative RNA was positive at the first HIV positive visit with viral load of 6.1 copies/mL). Although genotyping failed at the first HIV-positive visit, integrase strand transfer inhibitor (InSTI) resistance was detected at a visit 9 months later. This participant had assay reversion in which rapid, antigen/antibody, and qualitative RNA test results switched from reactive to nonreactive and back to reactive during the first year after infection. Eshleman compared acute HIV infection (AHI) as a phase of natural HIV infection to infections occurring in the setting of LEVI (infection during PrEP use or initiation of PrEP during acute/early infection). Although viral replication in AHI is explosive and associated with various symptoms, viral replication in the setting of LEVI is smoldering and symptoms are usually minimal or variable. Assay reversion is rare in AHI but common in LEVI. Although AHI usually lasts 1 to 2 weeks until antibody detection, LEVI can persist for months after the antiviral agent is discontinued. Viral transmission is very likely during AHI, but it is unlikely during LEVI. Drug resistance is unlikely in AHI but can emerge early in the LEVI syndrome when viral load is low. In HPTN 083, InSTI resistance emerged in 10 of 18 cases when CAB was administered within 6 months of the first HIV-positive visit; however, InSTI resistance was not observed when the first HIV-positive visit occurred more than 6 months after the last CAB injection. In most cases, retrospective testing using a sensitive RNA assay detected HIV infection prior to the emergence of InSTI resistance. RNA testing can be used to screen for HIV infection in individuals on CAB-LA PrEP, as recommended by the US Centers for Disease Control and Prevention and in the US Food and Drug Administration package insert, and the pros and cons of RNA screening are being evaluated in the ongoing HPTN 083 and 084 open-label studies.

Scott and colleagues presented data on HIV incidence and prevention efficacy of CAB-LA PrEP among US Black men and TGW who have sex with men in HPTN 083 (Abstract 161). Among 1698 participants

enrolled at US sites, 844 (50%) self-identified as Black (or mixed race including Black), most were MSM (93%), and the median age was 27 years; a lower proportion of Black vs non-Black participants had a college education or higher (68% vs 83%). At enrollment, Black and non-Black participants reported a similar number of sex partners in the past month (median, 2), Black participants were less likely to report recreational drug use in the past 6 months (63% vs 73%); however, prevalent STIs were more common among Black participants at baseline (syphilis, 4% vs 1.9%; rectal gonorrhea, 5.7% vs 3.4%; urine gonorrhea, 1.1% vs 0.4%). Among Black MSM and transgender women, HIV incidence was 2.11 per 100 person-years in the TDF/FTC arm (15 infections) and 0.58/100 person-years in the CAB-LA arm (4 infections), with a hazard ratio (HR) of 0.28 (95% CI, 0.096-0.834). Among non-Black MSM and transgender women, HIV incidence was 0.63 per 100 person-years in the TDF/FTC arm (5 infections) and 0/100 person-years in the CAB-LA arm (0 infections), with HR of 0.086 (95% CI, 0.004-2.060). Adherence to TDF/FTC was somewhat lower among Black vs non-Black participants using dried-blood spot assessments, with 65% of Black vs 81% of non-Black participants having drug levels consistent with taking 4 or more doses per week. On-time CAB-LA injections were high among Black and non-Black participants (83% vs 90%), and injection site reactions were slightly less common among Black participants (56% vs 65%). These findings highlight the potential of CAB-LA to increase access to PrEP and address continued racial disparities in HIV incidence in the US.

Clement and colleagues reported on PrEP product choice among HPTN 083 participants enrolled in the US (Abstract 994). In the open-label extension of this study, participants were offered the choice of open-label CAB-LA or daily oral TDF/FTC. Among 803 participants in whom regimen choice data were available, 96% chose CAB-LA and 4% chose TDF/FTC. Choice did not differ by age, cohort, race, ethnicity, or education status. The most common reasons for choosing CAB-LA included preferring injections and/or not liking pills (70%), superiority of CAB-LA to TDF/FTC for HIV prevention (15%), and CAB being more convenient, discreet, or easier to adhere to (5%); the most common reasons for choosing TDF/FTC included not liking injections and/or preferring pills (52%), potential adverse effects of TDF/FTC are better understood or preferable to those of CAB-LA (12%), concerns about resistance if injectable PrEP fails (21%), and scheduling constraints or difficulties with visits (12%).

Brown and colleagues reported on bone mineral density (BMD) changes with CAB-LA or TDF/FTC PrEP in MSM and TGW in HPTN 083 (Abstract 987). Among 254 participants (median age, 27 years) who received at least 10 bimonthly injections over 18 months from enrollment, BMD was 0.2 to 0.6 standard deviations lower than an age-, sex-, and race-matched population at baseline, with 15% having a Z-score 2.0 or lower at the lumbar spine, femoral neck, or total hip. BMD decreased by 0.5% to 1.0% in the TDF/FTC arm and increased 0.5% to 1.5% in the CAB-LA arm. After adjusting for age and race, BMD was significantly higher among participants receiving CAB-LA than those receiving TDF/FTC (Z-score difference, 0.09-0.20 at week 105). The

researchers suggest that individuals interested in PrEP and at higher risk of fracture because of older age, lower BMD, or other osteoporosis risk factors may consider CAB-LA to maintain bone health.

Hosek and colleagues reported on the safety, tolerability, and acceptability of CAB-LA in African female adolescents enrolled in the HPTN 084-01 study (Abstract 162). This single-arm, open-label, phase IIb safety study enrolled 55 adolescents below the age of 18 years in Uganda, Zimbabwe, and South Africa. The mean age of participants was 16 years; 25% had 1 or more sex partners with HIV, 22% reported transactional sex, 31% had chlamydia, and 36% reported significant depressive symptoms at baseline. Three participants had neuropsychiatric events (depression, anxiety, and suicidal behavior/attempt) during follow-up, all of which resolved with counseling. Among 55 participants enrolled, 2 discontinued during the oral CAB lead-in phase due to unrelated adverse events, and 53 participants entered the injection phase. There were no product-related serious adverse events, no product discontinuations due to adverse events, and no incident HIV infections during follow-up. CAB-LA injections were well tolerated, with only 17% reporting injection-site reactions at week 5 that decreased over time, and no participants discontinued injections early due to intolerability. Adherence to injections was very high, with only 1 participant discontinuing injections due to pregnancy, and 100% of expected injections given over 33 weeks of injection phase follow-up. When asked what they liked about the injectable method, participants liked that CAB-LA protected them against HIV (55%), was easier to use than other methods (42%), provided longer-term protection than other methods (23%), and can be used discreetly (19%). Overall, 36% did not have any concerns about the injectable method; however, some raised concerns that injections may be painful (28%), may cause harmful adverse effects (19%), and once injected, cannot be reversed (13%). After completing the injection phase, most participants (92%) chose to continue CAB-LA over oral TDF/FTC when given a choice in the HPTN 084 open-label extension.

Hazra and colleagues reported on a breakthrough HIV-1 infection in the setting of real-world CAB-LA PrEP administration (Abstract 981). This was a 28-year-old gender-diverse patient assigned male at birth who had HIV-1 detected 91 days after transitioning from TAF/FTC to CAB-LA, despite on-time dosing. He reported condomless oral and anal sex with a primary partner and 20 to 30 unique partners monthly, had recently engaged in anal fisting, and was also diagnosed with syphilis and mpox in the 6 months prior to HIV infection. The primary partner had HIV resistant to nucleoside reverse transcriptase inhibitors (nRTIs) (K65R, Y118I) and InSTIs (E92G) and had an undetectable HIV-1 RNA for more than 24 months on treatment. The patient had on-time injections at days 0, 27, and 91; on day 91, the HIV-1/HIV-2 antigen/antibody was nonreactive, but an HIV RNA-PCR test was detected at 1.48 $\log_{10}$ copies/mL. At repeat testing on day 100, his HIV-1/HIV-2 antigen/antibody test was reactive, HIV-1 antibody was detected on differentiation assay, and HIV RNA-PCR was detected at 1.30 $\log_{10}$ copies/mL, and standard HIV-1 sequencing was unable to be performed. HIV DNA qualitative PCR was below the lower limit of

quantitation and HIV-1 proviral DNA resistance could not be performed. Plasma CAB concentration on day 128 (37 days following the most recent injection) was 1180 ng/mL. The patient was started on a fully suppressive ART regimen (darunavir/cobicistat + dolutegravir) with undetectable RNA at day 128. This case highlights diagnostic and management challenges in the setting of CAB-LA PrEP failure and the need to better understand HIV-1 reservoirs in breakthrough infections.

Novel PrEP and PEP Agents

Young and colleagues presented data on an ultra-LA in situ forming implant (ISFI) with CAB (Abstract 991). This implant, comprised of a biodegradable-polymer, water-miscible solvent, and CAB, generates a liquid syringeal suspension that undergoes a phase inversion when injected into the subcutaneous space and releases drug over time via diffusion. Although this ISFI is biodegradable, it can also be removed early if needed, and can also be co-formulated to include multiple drugs in a single injection. Prior studies demonstrate the safety, ultra-LA pharmacokinetics (PK), and complete protection after several simian human immunodeficiency virus (SHIV) rectal challenges in female macaques. In this study, the researchers demonstrated that CAB plasma concentrations following 50 to 100 µL injections in mice were well above the PK benchmark of protection (4x PA-IC_{90}) for 11 to 12 months. When the implant was removed after 180 days, CAB plasma concentrations declined substantially, but complete CAB elimination was not achieved. After 180 days, the CAB ISFIs were easily retrievable, with 25% CAB remaining and 15% polymer remaining across all doses. When co-formulated with barium sulfate to assess implant migration, the ISFIs were visible with X-ray imaging for more than 210 days after a single injection with minimal implant migration. Young highlighted some potential benefits of ISFIs, including ability to be self-administered as a subcutaneous injection, reduced dosing frequency, reversibility, and potential for a shorter PK tail after removal.

Grattoni and colleagues presented data on an ultra-LA refillable islatravir implant tested in nonhuman primates (Abstract 165). They developed a titanium implant that uses a silicon nano-fluidic membrane to control drug release from a reservoir. This nanochannel acts like an hourglass and uses an electrostatic interaction to allow for sustained islatravir release at a constant rate, and the implant has ports that can be loaded and refilled transcutaneously. This implant was inserted into 4 rhesus macaques and achieved sustained islatravir and islatravir triphosphate concentrations in plasma, peripheral blood mononuclear cells (PBMCs), and rectal tissue over 12 to 20 months, with no changes in safety parameters, including levels of creatinine, aspartate aminotransferase, alanine aminotransferase, and lymphocyte, and CD4+ and CD8+ cell counts. In a repeated challenge model with SHIV ($SHIV_{SF162P3}$), the implant provided 100% protection to 10 weekly rectal or vaginal challenges in 6 male and 6 female macaques, respectively, whereas all control animals became infected. The implants were well tolerated; however, mild swelling was noted within the first 15 days of implantation and some local tissue inflammation was observed.

Although none of the implants had migrated, the researchers noted that 1 implant flipped and turned upside down, which resulted in severe inflammation at the implant site, suggesting that directionality of release is key to tolerability of the implant.

Daly and colleagues evaluated the safety and vaginal efficacy of a biodegradable islatravir implant in female pigtailed macaques (Abstract 989). This matchstick-sized implant consists of an extruded tube with polycaprolactone walls loaded with islatravir. Two implants were inserted into arms of 6 macaques and safety and PK were assessed over 5 weeks, followed by twice weekly vaginal SHIV challenges for 6 weeks; 1 islatravir implant was then removed to assess efficacy at a lower dose, and procedures were repeated. There were minimal implant-site reactions over 33 weeks, with only 1 of 12 implants with mild erythema, and no sign of inflammation or necrosis in skin biopsies after implant removal. Plasma islatravir concentrations were similar to once-daily dosing in humans, with 2 implants corresponding to 0.75 mg oral islatravir, and 1 implant corresponding to 0.25 mg oral islatravir. Overall, 5 of 6 animals were protected from repeated vaginal SHIV challenges, with clinically relevant plasma islatravir levels (median, 1.4-3.9 nM); the 1 breakthrough infection was associated with low plasma islatravir concentrations (median, 0.8 nM).

Bunge and colleagues reported on the safety of the dapivirine vaginal ring during pregnancy in the DELIVER/Microbicide Trials Network (MTN) 042 study (Abstract 127). This study was conducted in a stepwise fashion enrolling 1 of 3 cohorts at a time, beginning with later gestational age to minimize risks of drug exposure. Cohort 1 included women at 36 to 38 weeks gestation; cohort 2 at 30 to 35 weeks; and cohort 3 at 12 to 29 weeks. Data from cohort 1 (150 participants) and cohort 2 (157 participants) were presented in which participants were randomly assigned 2:1 to use either the monthly dapivirine ring or daily oral TDF/FTC until delivery; pregnancy outcomes were reported up to 6 weeks post delivery and compared with local background rates obtained through a systematic chart review. For both cohorts, the most common outcome was a full-term birth (≥37 weeks), 98% in cohort 1 and 94% in cohort 2. There was 1 stillbirth in cohort 1 (in the TDF/FTC arm) and 1 stillbirth in cohort 2 (in the dapivirine arm), with a rate lower than background. In both cohorts, pregnancy complications were rare, with hypertensive disorders of pregnancy being the most commonly reported, and similar to local background rates. In cohort 2, there was 1 case of chorioamnionitis in the dapivirine ring arm. No HIV seroconversions have been observed to date, and there have been no maternal deaths. There were 2 infant deaths, 1 in each cohort, assessed as not related to study product. With approval of an independent review panel, enrollment into cohort 3 began in July 2022 and was completed in January 2023.

Owor and colleagues reported on dapivirine ring safety and drug detection in 197 breastfeeding mother-infant pairs in the MTN-043 study (Abstract 785). In this open-label trial, exclusively breastfeeding mother-infant pairs were randomized 3:1 to receive the dapivirine ring or oral PrEP for 12 weeks. Most adverse events were mild or moderate, and only a few serious adverse events or grade 3 or

higher events occurred among mothers and infants, all of which were assessed as unrelated to study product. Similar to prior studies, dapivirine concentrations in breastmilk were higher than in maternal plasma; however, infant plasma concentrations remained extremely low, with drug detected in 5% to 15% of samples, and mean dapivirine concentrations ranging from 10.7 to 14.5 pg/mL. In the oral PrEP arm, tenofovir diphosphate (TFV-DP) concentrations from infant dried blood spots were all below the lower limit of quantitation. These data support updates to World Health Organization and national guidelines to include breastfeeding people in recommendations for the dapivirine vaginal ring for HIV prevention.

Riddler and colleagues presented data on the safety and PK of a fast-dissolving tenofovir alafenamide/elvitegravir (TAF/EVG) insert administered rectally in the MTN-039 study (Abstract 164). Prior studies in nonhuman primates have demonstrated the efficacy of this insert in vaginal and rectal simian HIV challenge models. In this 2-period study, 23 participants (17 male, 6 female) were enrolled and received rectal administration of one TAF/EVG insert (20/16 mg), followed by a washout period, then rectal administration of 2 inserts. The TAF/EVG insert was well tolerated, with 17 adverse events reported for 9 participants, and only 1 related adverse event of mild anal erythema. EVG, TAF, and TFV were present in plasma at 1 hour after insertion, at concentrations substantially lower than that seen with oral dosing. EVG was present in rectal tissue at 2 hours and exceed 1 ng/mg at most time points decreased by 24 hours. TFV concentrations in rectal fluid and tissue were high, with sustained levels in the majority of participants for 48 to 72 hours, and almost all participants had TFV-DP concentrations in rectal tissue from 2 to 72 hours that exceeded levels observed in the HPTN 066 PK study with daily oral TDF dosing. In an ex vivo challenge model, compared with baseline, the postdose cumulative $\log_{10}$ copies/mL HIV 24 levels were significantly reduced through 72 hours for both 1 and 2 inserts ($P <$ .032 and $P <$ .020, respectively). These results support the continued evaluation of the TAF/EVG insert for rectal protection.

Makarova and colleagues evaluated the window of PEP efficacy of TAF/EVG inserts against SHIV vaginal infection in pigtailed macaques (Abstract 990). Prior studies demonstrated the TAF/EVG insert provided 92% and 100% efficacy against vaginal SHIV exposure when given 4 hours before and 4 hours after exposure, respectively. In this study, TAF/EVG inserts were administered 8 or 24 hours after 13 weekly vaginal SHIV exposures. The 8-hour PEP insert protected 5 of 6 macaques (94% efficacy), and the 24-hour PEP insert provided 77% efficacy. These results extend the window of high postexposure protection of the insert to 8 hours and support the clinical development of the TAF/EVG insert for on-demand PEP against HIV.

Bekerman and colleagues evaluated the PK and efficacy of the HIV capsid inhibitor lenacapavir in macaques (Abstract 992). Based on in vitro testing in activated human and rhesus PBMCs, lenacapavir was predicted to be 4.4-fold less potent against SHIV vs HIV. After a single high-dose SHIV rectal challenge, 3 of 11 treated animals became infected (27%) vs 10 of 16 untreated controls (63%). In animals with

lenacapavir plasma concentrations above the rhesus-adjusted target exposure of 70 nM, lenacapavir demonstrated complete protection and was superior to the untreated group (*P* = .012). These data support the ongoing phase III clinical studies of LA lenacapavir for HIV PrEP.

Oral PrEP in Cisgender and Transgender Women

Marrazzo and colleagues presented pooled data on real-world PrEP effectiveness among 6296 cisgender women enrolled across 11 TDF/FTC demonstration projects in 6 counties over an 8-year period (2012-2020) (Abstract 163). Most participants were enrolled in Africa, with 21% from India. The mean age was 25 years, half were married, one-quarter had a primary education or less, 44% had 1 or more children, and 21% reported commercial sex work. There were only 32 incident HIV infections across all studies, with an HIV incidence of 0.72 (95% CI, 0.51-1.01) per 100 person-years. Adherence was assessed in a subset of 237 participants with objective adherence data (drug levels in dried blood spots or plasma) and 2887 participants with subjective data (electronic pill-cap monitoring, pill counts, or self-report). Substantially higher adherence was reported with subjective vs objective adherence measures, and overall adherence declined over time by both measures. Using group-based trajectory modeling to identify longitudinal patterns of adherence, the researchers found that 17% of women had consistently daily adherence, 22% had consistently high (4-6 doses/week) adherence, 39% had high but declining adherence, and 21% had consistently low (<2 doses/week) adherence. HIV incidence was 0 and 0.13 per 100 person-years in the consistently daily and consistently high groups, respectively; 0.49 per 100 person-years in the high but declining group; and 1.27 per 100 person-years in the consistently low group. Unlike prior PK modeling studies suggesting high adherence (6-7 doses/week) is required for high efficacy in women, these findings suggest that the effectiveness of TDF/FTC was similar in cisgender women who demonstrated consistently high (>4 tablets/week) or daily (7 tablets/week) adherence.

Remera and colleagues evaluated the effectiveness of PrEP among FSWs in Rwanda (Abstract 993). In a retrospective cohort study of 2544 HIV-negative FSWs seen in 22 health facilities in Kigali, Rwanda, 45% participated in the PrEP program. At 12 months, 79% of FSWs were retained in the PrEP program and 64% not on PrEP were retained in the HIV prevention program. Overall, 0.56% of FSWs in the PrEP program and 1.69% of those not in the PrEP program became HIV positive, resulting in a 69% lower risk of HIV infection among FSWs actively followed in the PrEP program (aOR, 0.31; 95% CI, 0.11-0.87).

Hiransuthikul and colleagues evaluated drug-drug interactions between feminizing hormone therapy (FHT) and oral TAF/FTC PrEP among 20 transgender women in the iFact 3 study (Abstract 996). TGWs who had not received injectable FHT within the past 3 months were enrolled and prescribed estradiol valerate and cyproterone acetate at baseline until week 9; PrEP was initiated at week 3 until week 12, and intensive PK sampling was performed at week 3 (FHT only), week 9 (FHT + PrEP), and week 12 (PrEP only). Plasma estradiol, FTC, and tenofovir

exposures trended lower when TAF/FTC was administered with FHT, however the areas under the curve and C_{max} geometric mean ratios of FTC and TFV were between 0.92 and 1.14, within the bioequivalence range, indicating no clinically significant drug-drug interactions from FHT toward TAF/FTC PrEP. The geometric mean ratio for area under the curve and C_{max} for estradiol at week 3[1] and week 9 was 0.80 (**90% CI,** 0.72-0.90; *P* = .002) and 1.11 **(**90% CI, 257; *P* = .23).

PrEP in Pregnancy

Gómez and colleagues evaluated perinatal outcomes following maternal PrEP use in a subsample of women enrolled in a cluster randomized controlled trial in Kenya (Abstract 766). They included 3608 mother-infant pairs in the analysis, including a random sample of 103 PrEP initiators who had detectable TFV-DP in pregnancy (18% of all PrEP initiators), and 3505 women who were unexposed to PrEP. Compared with those not exposed to PrEP, PrEP-exposed women were slightly older (median age, 27 years vs 24 years), were more likely to have a partner living with HIV (30% vs 2%), were less likely to be primigravida (11% vs 28%), and were more likely to have an STI diagnosis (8% vs 2%). Compared with PrEP unexposed women, women with confirmed PrEP exposure during pregnancy experienced similar frequencies of stillbirth (4% vs 3%; aPR, 1.1; 95% CI, 0.1-9.4), preterm birth (16% vs 19%; aPR, 0.9; 95% CI, 0.6-1.5), small for gestational age (13% vs 10%; aPR, 1.4; 95% CI, 0.8-2.5), and neonatal death (1% vs 2%; aPR, 0.7; 95% CI, 0.1-5.0). At 9 months post partum, there was no association between prenatal PrEP exposure and frequency of underweight (*P* = .68), stunting (*P* = .38), or wasting (*P* = .80). Similar to prior data that relied on self-reported PrEP use, the researchers found no difference in adverse perinatal outcomes among women with prenatal PrEP exposure confirmed with a pharmacologic measure.

Nyemba and colleagues presented data on the integration of PrEP into an antenatal care for pregnant women in South Africa (Abstract 768). Among 1200 women without HIV enrolled in the PrEP-PP (Pre-exposure Prophylaxis in Pregnancy & Postpartum) study at their first antenatal visit, 1013 (84%) accepted a PrEP prescription at baseline, and 829 (69%) returned at 1 month and had confirmed to have initiated PrEP. Among the 829 who initiated PrEP, PrEP continuation was 58% at 3 months, 42% at 6 months, and 35% at 9 months. Less than half of women continued PrEP after 6 months when in the postpartum period, and more than half of the 187 women who initially declined PrEP at enrollment initiated PrEP later (n = 104; 56%). These results highlight the need for interventions to improve PrEP continuation, particularly during the postpartum period.

Within the same study, Voux and colleagues conducted a randomized controlled trial to evaluate the impact of point-of-care STI testing on PrEP use in pregnancy (Abstract 970). Pregnant women seen at a regular antenatal care visit were offered PrEP and randomly assigned to standard-of-care (syndromic STI management) or point-of-care STI testing with self-collected vaginal swabs tested for *Chlamydia trachomatis, Neisseria gonorrhoeae,* and *Trichomonas vaginalis.* Among

268 pregnant women enrolled, 28% of women in the intervention arm were diagnosed with 1 or more STIs and 20% of women in the standard-of-care arm were treated for a symptomatic STI. Overall, 64% initiated PrEP at baseline, 67% in the intervention and 62% in the standard-of-care arm (P = .42). PrEP initiation was higher among STI-diagnosed/symptomatic women than among undiagnosed/asymptomatic women (adjusted relative risk [aRR], 1.24; 95% CI, 1.04-1.47), and PrEP persistence at 1 month was somewhat higher among STI-diagnosed/symptomatic women (aRR, 1.14; 95% CI, 0.98-1.33). These findings highlight the importance of integrated STI testing and care in PrEP programs among pregnant women.

Mogaka and colleagues reported on the acceptability of STI testing and expedited partner therapy among pregnant women initiating PrEP at 5 antenatal clinics in Kenya (Abstract 767). From February to September 2022, women were offered syphilis (RPR or rapid test) and chlamydia and gonorrhea testing using rapid assay for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* with same-day results and immediate directly observed treatment and expedited partner therapy provided to women diagnosed with chlamydia or gonorrhea. Among 177 women offered STI testing, 93% accepted testing, with 12% testing positive for an STI (chlamydia, 7%; gonorrhea, 4%; syphilis, 2%). The frequency of STIs was higher among those younger than 20 years of age than among women 20 years of age or older (25% vs 8%; P = .009), and the STIs were often asymptomatic. Among those testing positive for chlamydia or gonorrhea, 94% accepted same-day treatment and expedited partner therapy, with all male partners accepting treatment within 1 month and no social harms reported. These findings suggest that same-day STI testing with expedited partner therapy may be a high-yield intervention, which can benefit women and their infants and partners.

Anand and colleagues evaluated PrEP continuation among peri-conception, pregnant, and lactating women in Kenya (Abstract 769). In the Partners Scale-up Project, a stepped wedge cluster-randomized trial of PrEP delivery in 25 public HIV clinics in Kenya, 2640 women initiated PrEP, most of whom (80%) were in serodifferent relationships; 44% reported inconsistent condom use and 12% reported multiple sexual partners. At baseline, 11% were pregnant and 16% were breastfeeding, and among nonpregnant women at baseline, 15% were actively trying to conceive, 25% had future pregnancy intention, and 33% had no pregnancy intention. PrEP continuation at 1, 3, and 6 months was 59%, 45%, and 36%, respectively, and was higher among those actively trying to conceive vs those with future or no plans to conceive (P < .01), whereas PrEP continuation did not differ by breastfeeding or pregnancy status.

Pintye and colleagues evaluated PrEP adherence among 198 women who initiated PrEP during pregnancy in the PrIMA (PrEP Implementation for Mothers in Antenatal Care) study, a cluster randomized trial in 20 antenatal clinics in Kenya (Abstract 771). Among 454 visits where participants continued with PrEP, 94% reported any PrEP use in the last 30 days. Among dried blood spots from these visits, 48% had detectable TFV-DP, of which 28% had TFV-DP concentrations indicating fewer than 2 doses/week, 64% indicating 2 to 6 doses/week, and 8% indicating 7 doses/week. Having detectable TFV-DP exposure at follow-

up visits was more likely during the pregnant vs postpartum period (69% vs 31%; aRR, 1.87; 95% CI, 1.38-2.53), among women with a primary partner with HIV than among those with an HIV-negative primary partner (aRR, 2.03; 95% CI, 1.33-3.09), and was lower among those who had experienced PrEP adverse effects (aRR, 0.68; 95% CI, 0.47-0.99). These results point to the need for interventions to support adherence in the postpartum period and to increase knowledge of partner HIV status.

From the same study, Marwa and colleagues reported on HIV risk perception and PrEP use among 2249 Kenyan women during and after pregnancy (Abstract 773). Using a validated risk score to predict HIV acquisition among perinatal women, they identified 617 women (27%) at high HIV risk, corresponding to 8.9 HIV infections per 100 person-years; of these, most women (57%) perceived themselves to be at low risk for HIV. Women who perceived high risk were more likely to have a partner known to have HIV (21% vs 5%; prevalence ratio, 1.5) and more likely to initiate PrEP (40% vs 18%; prevalence ratio, 2.2). Additionally, perceived high HIV risk was associated with age older than 24 years, prior pregnancy, polygamous marriages, and syphilis diagnosis during pregnancy. Among 9 women who acquired HIV during follow-up, only 4 had high perceived HIV risk and only 3 reported ever taking PrEP, all of whom discontinued PrEP prior to seroconversion. The researchers suggest that improving knowledge of partner HIV status in PrEP delivery programs may help improve risk perception and encourage PrEP uptake, particularly among younger women.

Also in the PrIMA cohort, Wu and colleagues reported on the correlation between hair and dried blood spot PrEP levels during pregnancy and post partum (Abstract 770). They evaluated 34 hair-dried blood spot paired samples, with 12 from pregnancy visits at a median of 32 weeks gestation and 22 from postpartum visits at a median of 3.5 months after birth. Tenofovir levels in hair were strongly correlated with TFV-DP levels in dried blood spot ($r = 0.77$; $P < .001$), with stronger correlation during the postpartum period ($r = 0.82$) compared with pregnancy ($r = 0.57$). Based on dried blood spot benchmarks from the IMPAACT 2009 study in pregnant and postpartum women, 44% of dried blood spot samples had TFV-DP levels consistent with 2 or more doses per week, and 41% of hair samples had tenofovir levels consistent with 2 or more doses per week based on benchmarks in nonpregnant women. These results suggest that unlike blood-based measures, which are more influenced by physiologic changes during pregnancy, hair metrics may not need adjustment for PK differences in the perinatal period.

Tenofovir Adherence Assays

Ngure and colleagues assessed the acceptability and feasibility of a point-of-care urine-based tenofovir adherence assay among women in Kenya (Abstract 973). They conducted in-depth interviews with 20 women on PrEP enrolled in the point-of-care assay arm of the PUMA (Point-of-care Urine Monitoring of Adherence) study and their 8 clinicians. Most participants reported less worry of acquiring HIV due to a positive urine assay result and believed the urine assay improves PrEP

adherence since they always wanted to receive positive results. Clinicians reported that real-time feedback facilitates counseling tailored to individual needs, but stated that the test would be more feasible if test kits were widely available and marketed for clinical use. Some participants reported embarrassment with providing a urine sample, and clinicians reported concerns that the kit not measuring long-term adherence may affect retention of clients with low adherence. Overall results suggest the point-of-care urine tenofovir assay to be highly acceptable and feasible for women on PrEP and their clinicians.

Mustanski and colleagues evaluated the predictive value of the urine point-of-care tenofovir test among 73 young MSM PrEP users in the RADAR cohort (Abstract 979). Self-reported adherence was over-reported (87% for ≥4 doses in the last 7 days) compared with urine tenofovir (69%) and FTC-triphosphate (68%) and TFV-DP (67%) in dried blood spot. Urine TFV and dried blood spot FTC-TP performed similarly well in predicting longer-term adherence, with positive and negative predictive values of 94% and 93% for dried blood spot FTC-TP and 91% and 87% for urine TFV, respectively, compared with dried blood spot TFV-DP. In multivariable analyses, the urine assay was significantly predictive of TFV-DP in dried blood spot (OR, 30.2; $P < .001$). These findings support the utility of the urine point-of-care tenofovir test in real-world clinical settings.

Trends in the PrEP Continuum

Zhu and colleagues reported on trends in oral and injectable PrEP use in the US (Abstract 980). Using the IQVIA Real-World Data–Longitudinal Prescription Database, they assessed trends in PrEP prescriptions from January 2013 through September 2022. From 2013 to 2020, the number of persons prescribed branded TDF/FTC increased, then decreased markedly after TAF/FTC and generic TDF/FTC became available. By September 2022, 50% were prescribed generic TDF/FTC, 45% TAF/FTC, and only 3.8% branded TDF/FTC. From January 2022 through August 2022, a total of 1951 persons picked up a CAB-LA prescription, of which 84% received a prescription for a second dose within 1 month of the first prescription. A larger proportion of women were prescribed CAB-LA than oral PrEP, with women accounting for 13% of injectable PrEP prescriptions, but only 7% of oral PrEP prescriptions. These findings highlight the need to better understand reasons for low uptake of CAB-LA.

Hoover and colleagues evaluated trends in PrEP prescriptions in the US among persons enrolled in Medicaid by race and ethnicity from 2015 to 2020 (Abstract 986). Based on Centers for Medicare and Medicaid Services data for all 50 states and the District of Columbia, the number of Medicaid enrollees prescribed PrEP increased from 7932 in 2015 to 41,325 in 2020, with an EAPC of 31%. In 2020, 23% of Medicaid enrollees prescribed PrEP were Black, 18% were Hispanic, 40% were White, and 19% were women. From 2015 to 2020, racial and ethnic disparities in PrEP use increased among men, and more men continue to use PrEP than do women, with only 2976 Black women prescribed PrEP in

2020. The researchers call for interventions to increase PrEP use in populations with high rates of HIV diagnoses, particularly in Black cisgender women and transgender women.

Huang and colleagues assessed trends in PrEP use among US veterans using Veterans Health Administration (VHA) services between 2017 and 2022 (Abstract 997). The number of VHA patients prescribed PrEP increased from 1910 in 2017 to 6023 in 2022, with an EAPC of 23%. During this period, the number of Black veterans prescribed PrEP increased from 373 in 2017 to 1491 in 2022, with an EAPC of 27%, and the proportion of Black persons who comprised PrEP users increased from 20% to 25%. As PrEP prescriptions from the VHA are excluded from the IQVIA database, these data fill an important gap in monitoring PrEP use in the US.

Suprasert and colleagues reported on trends in PrEP use among PWID in San Francisco from 2018 to 2022 (Abstract 983). From 2019 to 2021, new HIV infections among PWID rose by 48% and now account for 27% of new HIV diagnoses in San Francisco. In 2022, the NHBS surveyed 479 PWID, of whom 81% experienced homelessness in the past year, 77% had a usual source of health care, and 75% had health care visits in the past year. Only 55% were aware of PrEP, 5.9% discussed PrEP with a health care practitioner, and 1.5% used PrEP in the past 12 months. These PrEP indicators were comparable or significantly worse than those of 2018: 54% had heard of PrEP ($P = .796$), 13% had discussed PrEP with a practitioner ($P < .001$), and 2.9% had used PrEP ($P = .147$). Factors associated with low PrEP awareness among PWID in 2022 were Black race/ethnicity, household income below the federal poverty level, and not testing for HIV, hepatitis C, or STIs. In contrast, among MSM surveyed in 2021, 66% had discussed PrEP with a practitioner and 65% had used PrEP in the past year. The researchers suggest that public health interventions to increase HIV testing and PrEP discussions from health care practitioners for PWID may have the greatest potential to improve PrEP uptake among PWID.

Factors Influencing PrEP Engagement

Andrzejewski and colleagues examined barriers to and facilitators of retention in PrEP care among 170 transgender women enrolled in the iMPrEPT (iTAB plus Motivational Interviewing for PrEP Adherence in Transgender Individuals) demonstration project (Abstract 985). Compared with participants who were retained at 24 weeks, those not retained were more likely to report engaging in sex work (18% vs 7%) and substantial/severe drug use (18% vs 8%) and were less likely to be taking gender-affirming hormone treatment (56% vs 71%). In qualitative interviews, 2 subcategories of sex work emerged: “non-survival sex work,” in which individuals had stable housing, sought clients from online sources, accessed gender-affirming hormones through practitioners, and had little difficulty staying in PrEP care, and “survival sex work,” in which individuals had unstable housing, sought street-based clients, used black-market hormones, and had more difficulty staying in PrEP care. TGW cited financial incentives as a strategy to help with retention in PrEP care and highlighted the

importance of privacy and discretion when working with TGW engaged in sex work. Additionally, TGW often prioritized medical gender affirmation over PrEP, although acknowledging that taking PrEP could facilitate adherence to gender-affirming hormones, and PrEP made TGW feel safer during sex work. Substance use was seen as a barrier to PrEP care for some TGW, often in the context of sex work.

Javanbakht and colleagues evaluated the role of methamphetamine use on PrEP care engagement among MSM enrolled in the mSTUDY, a cohort study of substance use and HIV in racial/ethnic minority MSM (Abstract 982). Among 149 participants (48% Black, 36% Latinx) who reported PrEP use in this cohort, lapses in PrEP use and inconsistent care engagement were reported in 26% of visits. Inconsistent PrEP care was associated with unemployment ($P < .01$), gonorrhea positivity ($P = .04$), and higher levels of methamphetamine use for the participant and the partner ($P < .01$). In a multivariable analysis, inconsistent engagement in PrEP care was nearly 4x higher when both the participant and their partner reported methamphetamine use (aOR, 3.82; 95% CI, 1.8-8.0) than in visits where no methamphetamine use was reported by the participant or partner.

Lankowski and colleagues reported on retention-in-care rates among Peruvian MSM and TGW enrolled in a real-world PrEP program (Abstract 1071.5). In PrEP PERU, a multi-site cohort study evaluating PrEP implementation in 4 nongovernment clinics in Lima, Peru, TDF/FTC PrEP is provided free of charge, and participants pay for laboratory testing plus a small service fee for clinic visits. Among 351 participants who initiated PrEP between January 2017 and March 2020, 91% attended at least 1 PrEP follow-up visit and 77% attended at least 2 PrEP follow-up visits within 6 months. Additionally, 85% of participants had favorable adherence, defined as having proportion of days covered above 0.8 based on pharmacy records. Age 30 years or older, bisexual identity, and higher income were associated with retention in care but not adherence; those who cited a healthcare practitioner recommendation as a motivator to taking PrEP were more likely to be retained in care and have higher adherence. Overall, there were 6 confirmed HIV seroconversions over 510 person-years of follow-up (HIV incidence, 1.2/100 person-years).

Mugwanya and colleagues assessed appropriateness of PrEP discontinuations in a large PrEP program in Kenya (Abstract 1074). They interviewed 300 clients (63% female, 42% in a serodifferent partnership) in the Partners Scale-Up Project, a large cluster-randomized trial of PrEP delivery integrated in public HIV clinics within Kenya’s national PrEP roll-out program. At PrEP initiation, 85% had high perceived risk of acquiring HIV, and 57% had used PrEP for at least 3 months. Nearly three-quarters of all PrEP discontinuations were appropriately aligned with self-reported low HIV risk states, and less than 1% of discontinuations were attributed to clinic-level factors such as wait time and staff attitudes. Additionally, nearly all clients were satisfied with their HIV prevention choice at the time of the survey. The researchers suggest that using client-level PrEP continuation rates alone without considering dynamic individual

risk and use of other prevention options is not an appropriate measure of real-world PrEP program success.

Wu and colleagues reported on the alignment of PrEP use with HIV risk among young women and their male partners in Uganda (Abstract 998). From 2018 to 2021, 88 young women and 125 male partners were enrolled in linked longitudinal studies, with a median age of 24 years for men and 20 years for women. In women and men, PrEP refills were more common when they or their partners self-reported multiple sex partners.

Zia and colleagues evaluated structural influences on the PrEP continuum among adolescent girls and young women (AGYW) in postabortive care in Kenya (Abstract 1073). Among 6877 AGYW seen across 14 postabortion clinics in Kenya, 25% were offered PrEP and 14% accepted PrEP. Most clinics were private (57%), had low client flow (57%), had some but not all clinicians trained (57%), had engaged leadership (64%), and had challenges with staff numbers (86%) and space (57%). Most AGYW were seen in postabortion clinics that had experienced PrEP commodities stock-outs (75%), had high clinic volume (63%), and had highly engaged administrative leadership (56%). Frequency of PrEP offers and uptake was higher in clinics that never experienced PrEP or HIV medication stock-outs, in public vs private clinics, and in clinics in which all clinicians were trained and had sufficient staffing for PrEP delivery. These findings point to the importance of investing in human resources and PrEP/HIV commodities to facilitate greater PrEP coverage in AGYW.

Ntabadde and colleagues reported on the PrEP continuum among Lake Victoria fisherfolk in Southern Uganda, a community with 40% HIV prevalence (Abstract 1072). Among 1401 HIV-seronegative participants assessed between 2018 and 2020 as part of surveillance in the Rakai Community Cohort study, 97% reported ever receiving an HIV test result, 86% had heard of PrEP, and 40% were eligible for PrEP, but only 14.5% ever used PrEP. PrEP discontinuation was reported by nearly half (48%) of individuals who had ever used PrEP. PrEP use was associated with a higher perceived HIV risk, having more sexual partners, and a recent HIV test in the past year. Additionally, women who engaged in transactional sex and those who reported intimate partner violence were also more likely to report PrEP use.

Thomas and colleagues evaluated the effect of intimate partner violence on adherence to PrEP and ART in HIV-serodifferent couples in Uganda (Abstract 984). Among 149 heterosexual couples enrolled, 81% were married or cohabitating, and 64% of partners with HIV were female. Low adherence was more common when PrEP or ART users reported intimate partner violence. Ashipala and colleagues evaluated the relationship between depression and PrEP use among key populations in Namibia (Abstract 1075). In surveys of 500 PrEP users (including MSM, male sex workers, AGYW, and FSW) accessing services at 13 health care facilities in Namibia, 11% and 5% had Patient Health Questionnaire (PHQ-9) scores suggesting moderate and acute depression, respectively; 3 in 10 clients reported suicidal ideation; and 6 in 10 screened as having a potential alcohol use disorder. Depression was associated with PrEP holidays, defined as taking a break from PrEP for at least 3

consecutive days (*P* = .03) and missing pills on weekends (*P* = .02). PrEP holidays were also associated with alcohol use disorder (*P* = .010) and illicit drug use (*P* < .01). These results suggest that clients accessing PrEP services in these settings may be at greater risk for mental health issues and highlight the need for tailored interventions in key populations facing mental health challenges.

Novel PrEP and PEP Delivery Models

Kakande and colleagues presented the results of a cluster-randomized trial of a dynamic choice HIV prevention intervention delivered by community health workers in southwest Uganda and western Kenya (Abstract 124). They randomly assigned 16 villages 1:1 to the dynamic choice intervention or to a standard-of-care control condition that included referral to HIV prevention services at local health facilities. The dynamic choice intervention allowed participants to choose their preferred product (PrEP or PEP pill in pocket), service location (clinic, home/community site, phone/virtual visit), HIV testing (rapid test, self-test), and refill frequency (up to 3 months for PrEP refills). Persons in the intervention arm also had access to patient-centered care, including phone access to clinicians 24 hours a day, 7 days a week; structured assessments of barriers to prevention services with development of personalized plans; referral to clinics with integrated reproductive health and STI services; and referrals for treatment for trauma and gender-based violence. They screened approximately 500 persons per arm and enrolled approximately 200 persons per arm; lack of risk was the primary reason for non-enrollment. The primary outcome was self-reported PrEP and PEP use. In the intervention arm, 58% chose PrEP at least once and 58% chose PEP at least once. From baseline to week 48, PrEP selection increased from 40% to 48% and PEP selection declined from 46% to 25%. Condom choice increased over time. Self-testing increased from 52% at baseline to 71% at week 48. Nearly all people chose off-site locations for prevention services at each visit. The average proportion of follow-up covered with PrEP or PEP was 28% in the intervention group and 0.5% in the control arm (*P* < .001). During periods of HIV risk, PrEP or PEP uptake was 36.6% of follow-up time in the intervention arm, compared with 0.9% in the control arm (*P* < .001). This represents a substantial improvement in the intervention compared with the control. Next, the investigators plan to Integrate lo—-acting injectable cabotegravir as PrEP as one of the intervention choices.

Koss and colleagues presented results of an individually randomized trial of the same dynamic choice prevention intervention implemented in outpatient departments in rural Kenya and Uganda (Abstract 975). Overall, 403 participants (61% women; median age, 27 years) enrolled in the study, with 197 in the dynamic choice prevention arm and 206 in the standard-of-care arm. In the dynamic choice prevention arm, 86% ever chose PrEP and 15% chose PEP over 48 weeks; the choice of HIV self-testing increased from 26% to 51%, and choice of out-of-facility visits increased from 8% to 52% during follow-up. The proportion of follow-up time covered by PrEP or PEP was

47.5% in the dynamic choice prevention arm and 18% in the standard-of-care arm (29% difference; *P* < .001), with similar results among men and women. When follow-up was restricted to time of self-reported risk of HIV exposure, PrEP or PEP coverage was 65% in the dynamic choice arm and 26% in the standard-of-care arm (39% difference; *P* < .001). The researchers are currently studying a dynamic choice model offering a product choice of CAB LA, oral PrEP, and PEP.

Shahmanesh and colleagues reported results of a trial of community-based sexual reproductive health and peer support among youth in rural Kwazulu Natal, South Africa (Abstract 976). In this 2x2 factorial trial, 1743 participants aged 16 to 29 years were randomly assigned to 1 of 4 groups: (1) enhanced standard of care comprised of mobile adolescent youth friendly services (AYFS) including condoms, universal test and treat, and PrEP; (2) sexual and reproductive health (SRH), which included home-based self-collected specimens for STI testing and referral to AYFS for integrated SRH and HIV prevention; (3) peer support, which included referral to peer navigator for a needs assessment to tailor health and support; and (4) SRH plus peer support. Overall, 43% of participants were linked to AYFS by 60 days, and 21% were eligible and started PrEP. Among 832 participants assigned to SRH, 29% of women and 16% of men had an STI. Although SRH increased linkage to AYFS within 60 days (aOR, 1.61; 95% CI, 1.32-1.95), peer support had no effect on linkage to AYFS. At 12 months, 19% tested positive for HIV, of which 185 (82%) had a suppressed HIV viral load. After adjustment for age, sex, and rural/urban area, there was no difference in transmissible HIV by either intervention.

Bardon and colleagues assessed the effects of 6-month PrEP dispensing on sexual behaviors in Kenya (Abstract 977). In the JiPime-JiPrEP trial, 495 participants, including women and men in serodifferent relationships and single women, were randomly assigned to 6-month PrEP dispensing with interim HIV self-testing and biannual clinic visits or standard-of-care 3-month PrEP dispensing with clinic-based HIV testing and quarterly clinic visits. Results from this study were previously presented that demonstrated that biannual clinic visits supported with 6-monthly PrEP dispensing resulted in non-inferior PrEP continuation outcomes, including HIV testing, PrEP refills, and PrEP adherence. In this secondary analysis, the researchers evaluated whether sexual behaviors differed between the intervention and standard-of-care arms at 6 and 12 months of follow-up. They found that inconsistent condom use and number of sex partners in the past month did not differ between arms at either point, further emphasizing the safety of this differentiated service delivery model and supporting its use to help simplify PrEP delivery in Kenya and similar settings.

Roche and colleagues presented data from a pilot study extension of pharmacy-based PrEP delivery in Kenya (Abstract 978). In this stepped care-delivery model, pharmacists are trained to screen for PrEP and PEP eligibility using a standardized checklist, with a remote clinician available for support. In a 6-month extension of a pilot study, PEP services were added to the model, and the patient fee was eliminated. During this period, 12 participating pharmacies were able

to initiate 670 clients on PrEP and 161 on PEP, many of whom were young, unmarried men not in known serodifferent relationships. Among those who initiated PEP, 37% returned and tested HIV negative, and 20% transitioned to PrEP after PEP completion. At 4 months, 51% were still on PrEP, and PrEP continuation, defined as having refilled PrEP at least once at a pharmacy over the 6-month period, was 73%. Acceptability of pharmacy delivered PrEP was high, with 96% to 100% of clients and clinicians reporting they liked getting or delivering PrEP/PEP at a pharmacy, and 94% to 100% agreed that pharmacies are a good way to reach people who are at risk for HIV. The research team will soon be launching a community randomized clinical trial of pharmacy-based PrEP/PEP delivery across 60 pharmacies.

Kuo and colleagues reported on client preferences for PrEP refills at facilities vs pharmacies in Kenya (Abstract 1091). Clients initiating PrEP at 2 public health facilities in Kenya were given the option to refill PrEP at a public clinic for free or at 1 of 3 nearby private pharmacies for a fee of 300 KES (approximately $2.50 USD). Among 106 clients enrolled, 55% preferred getting refills at public clinics and 45% preferred a private pharmacy location. Over 292 client-months of follow-up, 44 clients (42%) refilled PrEP at least once, with only 3 clients (3%) refilling PrEP at a pilot pharmacy. In in-depth interviews, clients already engaged in clinic-based PrEP services preferred delivery in this setting and had perceived concerns with pharmacy-delivered PrEP, including mistrust of pharmacy providers, perceived lower quality of services, lack of privacy, and increased client costs. The investigators recommend additional research to understand drivers of PrEP refill location choice and implementation strategies that might facilitate clients in selecting their preferred refill site. Kuo and colleagues also assessed the costs of providing pharmacy-initiated PrEP in Kenya through time-and-motion studies (Abstract 1090). The median financial cost of pharmacy-based PrEP delivery was $7.70 per month at initiation and $19.86 per 3 months at continuation visits, with PrEP drugs accounting for the greatest proportion (61%) of costs. They found that financial costs of pharmacy-based PrEP delivery may be comparable to facility-based PrEP delivery and that improved efficiencies may further decrease costs.

Bassett and colleagues presented data from a pilot randomized clinical trial assessing the uptake of contraception and PrEP in 3 hair salons in Durban, South Africa (Abstract 999). In this model, a stylist introduces the study and refers potentially interested participants to a nurse who provides HIV, STI, and pregnancy testing, risk-reduction counseling, and dispenses contraception (oral or injectable) and oral PrEP. Among 97 female intervention participants enrolled in the study, 70% report going to the salon at least every 2 months, with 43% spending at least 2 hours at the salon during their visit. Overall, 31% of women thought their primary sex partner had other partners, 8% reported intimate partner violence, and 36% were diagnosed with an STI. Uptake of contraception was 89%, and uptake of PrEP was 37%. In a multivariable model, only intimate partner violence was associated with PrEP uptake (aOR, 1.54; 95% CI, 1.7-140; P = .02).

Future directions include incorporating injectable PrEP as a prevention option.

Silverberg and colleagues conducted a cluster randomized trial leveraging electronic health record data to increase PrEP uptake (Abstract 1089). Adult primary care practitioners within Kaiser Permanente San Francisco were randomly assigned to usual care (60 practitioners, including 6 HIV practitioners) or a low-intensity clinical decision support intervention (61 practitioners, including 6 HIV practitioners) in which providers were notified via a secure email message prior to an upcoming visit when a patient had an elevated HIV risk prediction (3-year risk of HIV, ≥0.2%). There was a nonsignificant increase in PrEP linkage in the intervention arm vs control condition (6% vs 4.5%; hazard ratio [HR], 1.32; 95% CI, 0.84-2.06); however, PrEP linkage was increased in the intervention arm among HIV practitioners (HR, 2.59; 95% CI, 1.30-5.16). The researchers suggest that more intensive interventions may be needed for practitioners less familiar with PrEP and HIV care.

Fisher and colleagues presented results of a PEP-in-pocket (PIP) program of on-demand HIV PrEP in 2 HIV prevention clinics in Toronto, Canada (Abstract 972). Patients referred for PrEP or PEP were offered a full 28-day prescription for PEP if they reported a low-frequency (0-4 per year) of higher-risk HIV exposures of any type. Patients receiving PIP were provided counseling on when to initiate medications and where to seek follow-up care. From January 2016 to December 2022, 111 people were prescribed PIP, of which 35 initiated PIP for sexual exposures (16 used PIP once, 19 used PIP more than once). Overall, a total of 69 PIP courses were initiated, with 98.6% follow-up at 6 months, and no HIV seroconversions detected. Switching between PIP and PrEP was common, with 29% of participants switching from PrEP to PIP, and 31% switching from PIP to PrEP.

Modeling the Impact and Cost-Effectiveness of PrEP and PEP

Stansfield and colleagues compared the population impact of expanding PrEP use in South Africa based on 3 HIV transmission models (Abstract 969). Synthesis is a stochastic, individual-based model targeting PrEP to 9% of adults with a PrEP indication; EMOD-HIV is a stochastic, individual-based model targeting PrEP to 3.5% adults at high risk and 20.5% at low risk; and Thembisa is a deterministic, compartmental model targeting PrEP to 22% of women and 32% of men at high risk. In baseline scenarios, HIV prevalence was about 17% in all models and median PrEP coverage remained below 2%. Expanding PrEP coverage to 5% with CAB-LA by 2027 may avert 46% of new infections over 20 years in the Synthesis model, 35% in the EMOD-HIV model, and 12% in the Thembisa model. Increasing PrEP coverage to 20% may increase the impact by 12 percentage points (Synthesis), 18 percentage points (EMOD-HIV), and 23 percentage points (Thembisa). Compared with 5% CAB coverage, achieving 5% coverage with oral TDF/FTC would be expected to reduce impact on new infections averted by 16 percentage points (Synthesis), 21 percentage points (EMOD-HIV), and 3 percentage points (Thembisa). They projected that 5% CAB-LA coverage would be highly

efficient in 2 models with 14 (Synthesis) and 13 (EMOD-HIV) additional person-years on CAB-LA needed to prevent 1 infection. They concluded that expanding PrEP access with CAB-LA in South Africa may be highly effective and efficient if it is used during periods of substantial risk.

Cox and colleagues assessed the impact of HIV self-testing vs provider HIV testing for PrEP scale-up in Kenya (Abstract 1051). In the EMOD-HIV model, they compared 4 HIV testing scenarios: (1) provider-administered nucleic acid technique (NAT); (2) clinician-administered rapid diagnostic tests detecting antibodies (Ab-RDT); (3) capillary whole blood-based HIV self-testing (blood HIVST); and (4) oral-fluid HIV self-test (oral HIVST). In all testing scenarios, PrEP coverage was about 29%, which was projected to avert 50% of HIV infections and 14% of HIV-related deaths over a 20-year period. The percentage of HIV infections with PrEP-associated nRTI-associated resistance was 0.5% and 0.7% in the blood and oral HIVST scenarios, respectively, compared with 0.1% and 0.2% in the NAT and Ab-RDT scenarios, respectively, due to a low projected number of people with HIV inappropriately started on PrEP. They attributed the low population prevalence of nRTI resistance across testing scenarios to the reduction in HIV and HIV-related drug resistance in the PrEP scenarios compared with the no PrEP scenario.

Milali and colleagues evaluated the cost-effectiveness of a dual prevention pill for contraception and HIV prophylaxis in sub-Saharan Africa (Abstract 967). Using an agent-based model in Kenya, Zimbabwe, and South Africa, they found the dual prevention pill likely to be a cost-effective alternative to oral PrEP among users needing contraception and likely cost-saving in sex workers and serodifferent couples not currently on oral PrEP. They also found that the dual prevention pill is unlikely to be cost-effective in oral contraceptive users aged 25 to 49 years without further targeting of subgroups at higher risk of HIV, and could be net harmful if it reduced contraceptive adherence. They highlight the need for effective counseling and decision-support tools to facilitate informed choice and effective use of the dual prevention pill.

Phillips and colleagues assessed the potential cost-effectiveness of availability of community tenofovir-lamivudine-dolutegravir (TLD) for HIV PEP and treatment in sub-Saharan Africa (Abstract 968). Using the HIV Synthesis model, they evaluated the impact of making TLD widely and freely available in communities without prescription (along with HIV self-tests, condoms, and emergency contraception) as a strategy to enhance PEP access. In the short term (over 3 years), they projected that community TLD availability would increase PEP and PrEP use by 10% among people with a PrEP/PEP indication, and a mean of 3% to 4% increase in the percent of people living with HIV who are on ART. In the longer term (over 20 or 50 years), community TLD availability increased viral suppression among people with HIV by 4% and reduced HIV incidence by 36% over 20 years. There was not predicted to be a detrimental effect on prevalence of integrase resistance. Overall costs were lower with community TLD in 97% of

setting scenarios, with a $24 million saving per year over 50 years due to fewer people requiring ART and lower ART-related clinic visits.

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Additional Reference Cited in the Text

1. Luetkemeyer AF, Donnell D, Dombrowski JC, et al. Postexposure doxycycline to prevent bacterial sexually transmitted infections. *N Engl J Med.* 2023;388(14):1296-1306. 10.1056/NEJMoa2211934 [doi].