30 SEPTEMBER 2021

HIV Drug Resistance & Laboratory Monitoring: Highlights from GEMS and an Update from WHO

PrEP Learning Network Webinar Series

Thank you to our guests Robin Schaefer from the World Health Organization (WHO), Urvi Parikh and Everline Bosek of the University of Pittsburgh, Anita Hettema and Lisa Levy of FHI 360, and Bhavna Chohan of the Kenya Medical Research Institute and University of Washington, who presented during the September PrEP Learning Network webinar. In this webinar, we discussed the new consolidated HIV guidelines on laboratory monitoring and testing for oral PrEP, the Global Evaluation of Microbicide Sensitivity (GEMS) experience from Kenya and Eswatini on setting up HIV drug resistance (HIVDR) monitoring in individuals who seroconvert while using PrEP, and shared related job aids and resources. In case you missed it, you can access the webinar recording here.

Top Questions and Key Messages

Below is a highlight of the discussion and Q&A for those seeking more information. Learn more by listening to the webinar recording, accessing complementary resources including the webinar slides in English and French, signing up for future webinars, or visiting the PrEP Virtual Learning Network page.

Updated WHO Guidelines

Which estimated glomerular filtration rate (eGFR) calculation formula is preferable, CG or MDRD, for Asians?

The Cockcroft-Gault (CG) equation is most widely used to estimate creatinine clearance as a measure of kidney function because it is simple and can be implemented in any setting. However, both Modification of Diet in Renal Disease (MDRD) and Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equations are likely to be more accurate than CG. While CKD-EPI is possibly the best formula, it has not been validated in all settings and the equation includes a “race” term (originally developed to describe differences by race in the US).). Some authors have suggested to drop "race" from the equation and that it can be used in any setting, but this is an ongoing debate. CG will be fine for PrEP programs, particularly because a measurement of <60ml/min CrCl should be repeated before stopping PrEP. In most scenarios, national guidelines will specify the formula to be used and should be followed.

Upcoming event:

UNAIDS Global HIV Prevention Coalition: Pre-Exposure Prophylaxis Webinar

Join representatives from WHO, UNAIDS, and Avenir Health for a session exploring tools available for PrEP implementation planning, including target setting using PrEP-it 2.0.

27 October 2021
9:00-10:30 EDT
16:00-17:30 EAT

Register Here

How is the WHO now describing populations who should be prioritized for PrEP?
In an effort to ensure that PrEP rollout was cost effective, "substantial risk" was previously described as an incidence of 3 per 100 person years. However, there is a variation of HIV prevention needs within populations that may be masked by population-level metrics such as incidence per person years. WHO is now encouraging programs to consider local context and population heterogeneity to ensure that those who need PrEP have access. Overall, individuals who request PrEP should be considered for PrEP provision because this request is an indicator that the individual could benefit from HIV prevention methods such as PrEP.

Will there be any simplification in the guidance on PrEP for transgender populations?
WHO recommends offering tenofovir disoproxil fumarate (TDF)-based oral PrEP to all populations at substantial risk of HIV infection, including transgender populations. During revisions of implementation guidance, WHO will consider all populations, including transgender women, transgender men, and non-binary individuals. Current WHO guidance on event-driven oral PrEP (ED-PrEP) states that it is only appropriate for cisgender men. While there is some evidence that suggests that ED-PrEP is inappropriate for transgender women taking gender-affirming hormones, there is also some research that suggest that there is no difference in ED-PrEP effectiveness between these two populations. ED-PrEP is likely appropriate for transgender women not taking gender-affirming hormones, although what constitutes gender-affirming hormones varies across settings and may include medications informally acquired. We will consider this in the upcoming guidance on simplifying PrEP service delivery (to be released early 2022). This document will also include revised guidance on safely starting and stopping PrEP for all populations.

Are there any specific risks regarding oral PrEP use for people engaged in injection drug use?
PrEP is appropriate for all populations in need of HIV prevention methods, including people who use and inject drugs (PWID). However, there is limited evidence on PrEP use among PWID, and limited implementation of programs focusing on this population.

HIV Drug Resistance – Update from GEMS

Key Messages:

- GEMS monitored for HIV drug resistance in PrEP rollout programs in Kenya, Zimbabwe and Eswatini through national programs, and in South Africa through project partners using a study protocol that tested for HIVDR in a blood sample from consenting HIV positive participants.
- GEMS confirmed that seroconversion on PrEP is a rare event; therefore, concern about HIVDR should not be a reason to limit PrEP use. Both PrEP drug-associated and transmitted resistance was observed in seroconversions on PrEP, highlighting outcomes. Results from the GEMS studies highlight the importance of HIVDR surveillance with PrEP rollout.
- The experiences in Kenya and Eswatini demonstrated that it was feasible to monitor for drug resistance and adherence with seroconversions on PrEP. The GEMS project led to increased training and support for healthcare providers around acute HIV infection identification, dried blood spot preparation, and drug resistance risk.

Does the work conducted through GEMS include those who were initiated on PrEP while experiencing acute HIV infection (AHI) or does it only include those who acquired HIV after PrEP initiation?
Samples were not collected or stored from when a person started PrEP to determine if they had undiagnosed AHI. Some people seroconverted within three months of starting PrEP while the majority seroconverted more than three months after starting PrEP, suggesting that this monitoring likely included both clients who initiated PrEP with undiagnosed AHI and those who acquired HIV after PrEP initiation.

Did GEMS produce any data on treatment regimen and HIV suppression during antiretroviral therapy?
Most people who acquired HIV while using oral PrEP received first line ART (such as TDF/3TC and DTG, as in Eswatini) according to national guidelines. GEMS does not have any follow up data on these individuals.

Has there ever been legal action from clients who seroconverted under the impression that oral PrEP was 100% effective?
GEMS has not encountered any legal action from clients in any of our projects. Although oral PrEP is highly effective, it does not provide 100% protection from HIV, so it is very important to provide adequate client counseling on the benefits and limitations of PrEP. A key counseling message is that PrEP effectiveness will improve with correct use but will not be 100%.

What improvements in HIV diagnostics do you see as most important in preventing resistance, and what trade-offs do you see in terms of more expensive or complex HIV testing reducing PrEP reach and impact?
Fourth-generation HIV diagnostic tests have provided modest improvement in detecting HIV earlier, and nucleic acid testing like viral load would help identify acute HIV infection before starting PrEP – but would present too much of a barrier to PrEP implementation with cost and turnaround time for results. Rates of infection are very low among oral PrEP users and the chances of acquired resistance can be mitigated by regular HIV testing during PrEP use.

How does the frequency of drug resistance among PrEP users compare with frequency of resistance among people who acquired HIV when not using PrEP?
There was not a concurrent group of non-PrEP using seroconverters who were followed as part of the GEMS study to provide a direct data comparison. However, comparisons can be made to resistance results from ECHO trial participants from South Africa and Kenya who texted positive for HIV and reported no prior PrEP use. The frequency of NNRTI resistance, which is not associated with PrEP, was similar between seroconverters in the ECHO trial and in the GEMS study. At the same time, rates of NRTI resistance – transmission of which is uncommon in the communities where ECHO and GEMS were conducted – among seroconverters in the GEMS study were higher than in the ECHO trial.

What fora are available to continue the discussion on 4th generation HIV diagnostic testing?
In 2022, WHO will release new guidelines on HIV testing and the topic of 4th generation tests will be included in this update.

Additional Resources

For further information on PrEP and HIVDR, please see the following resources:

- **GEMS Toolkit:** Materials to assist ministries of health, project implementers and policymakers to develop HIVDR monitoring strategies and support the collection and testing of samples for HIVDR testing
- **WHO Guidance on HIVDR Surveillance for PrEP:** World Health Organization guidance for HIV drug resistance surveillance in countries scaling up pre-exposure prophylaxis
- **WHO Consolidated HIV Guidelines:** 2021 update on the World Health Organization's guidelines on HIV prevention, testing, treatment, service delivery and monitoring.

Join us virtually at ICASA 2021 on December 6th and 9th to discuss multiple topics related to expanding access to HIV prevention, an introduction to the dapivirine vaginal ring, the launch of PrEP-it 2.0 and further discussion on PrEP for pregnant and breastfeeding women.

Visit the PrEP Virtual Learning Network for more information on previous or upcoming sessions.