Recommendations for Monitoring and Evaluation of Seroconversions and Drug Resistance in a PrEP Program

AUGUST 2024

Monitoring seroconversions and HIV drug resistance within PrEP programs and understanding ways to reduce the risk of resistance will help to ensure the long-term effectiveness of both PrEP and antiretroviral treatment options. The World Health Organization recommends that PrEP programs be accompanied by surveillance to detect HIV drug resistance (HIVDR) that may compromise the effectiveness of first-line antiretroviral therapy (ART) among PrEP users who acquire HIV. The following tables will assist program implementers to effectively monitor for drug resistance in their PrEP programs.

Table 1 provides a sample monitoring and evaluation (M&E) framework that lists program activities that will lead to intended program outcomes. Suggested inputs required to perform the activity, as well as direct outputs, intermediate outcomes, and the overall project outcome, are included.

Table 1. Sample M&E Framework to Monitor Drug Resistance in People Who Seroconvert During PrEP Rollout

Activities	Inputs	Outputs	Outcomes	Overall Outcome
Identify PrEP clients who seroconvert.	▪ HIV tests ▪ Staff to perform the test	HIV test results	Clients know their HIV status.	Long-term effectiveness of PrEP and ART programs.
Collect a blood sample from the PrEP client for resistance testing on the same day the client gets a positive HIV test result.	▪ Blood collection supplies ▪ Staff time for collection ▪ Access to a lab with capability to perform resistance tests	Resistance test results *(note: results are not expected to be returned for client care)*	Program has data to understand if PrEP client who seroconverted has HIV drug resistance.	

Suggested indicators to be collected monthly are included in Table 2. Each PrEP client who seroconverts would be tested for resistance only once near the time of identification of seroconversion, so numerators and denominators for all the indicators could be summed over time for quarterly or annual rates of resistance. When these data are combined with analyses of programmatic indicators for PrEP effective use and retention, programs will better understand the factors associated with resistance. Table 3 provides next steps and further analyses needed to understand the HIVDR results.

MOSAIC is made possible by the generous support of the American people through the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) and the U.S. Agency for International Development (USAID) cooperative agreement 7200AA21CA00011. MOSAIC is led by FHI 360 with core partners Jhpiego, LVCT Health, Pangaea Zimbabwe, Wits RHI, and AVAC. The contents of this resource are the responsibility of MOSAIC and do not necessarily reflect the views of PEPFAR, USAID, or the U.S. Government.

PEPFAR USAID FROM THE AMERICAN PEOPLE MOSAIC Maximizing Options to Advance Informed Choice for HIV Prevention

Table 2. Suggested Indicators for HIV Drug Resistance Monitoring and Evaluation

Indicator	Definition	Recommended Disaggregation	Data Source	Entity Responsible
1. Total # of current PrEP users who seroconverted during the data collection period	Current PrEP users who test HIV positive. Current users are defined as those who collected an initial supply of PrEP agents or a resupply of PrEP agents in the last three months prior to an HIV positive diagnosis (for oral PrEP and PrEP ring) or in the last twelve months prior to an HIV positive diagnosis (for CAB PrEP).	▪ By PrEP product ▪ Timing of PrEP initiation ▪ Length of time on PrEP (uninterrupted) ▪ Age ▪ Sex/Gender	PrEP register	PrEP clinician, counselor
2. # of those reported under indicator 1 who had a blood sample collected for resistance testing	Of those current PrEP users who seroconvert, the number of clients who had a blood sample collected for resistance testing on the same day as confirmation of HIV seroconversion	▪ Time of sample collection (prior to or after ART initiation) ▪ Age ▪ Sex/gender	PrEP register	PrEP clinician, counselor
3. # of those reported under indicator 2 whose resistance test results indicate PrEP-related resistance*	The number of clients who have drug resistance related to the PrEP agent taken, as defined by the testing platform used.	▪ By PrEP product ▪ Length of time on PrEP (uninterrupted) ▪ Drug with associated resistance ▪ Level of resistance ▪ Age ▪ Sex/gender	Resistance test result Facility or lab register	Lab technician, PrEP clinician, counselor

*PrEP-related resistance is defined as the client having HIV drug resistance mutations that could be associated with the medications in PrEP agents: for example, NRTI mutations with oral PrEP, NNRTI mutations with the PrEP ring, or INSTI mutations with CAB PrEP. Drug resistance results may be related to PrEP use, other naturally occurring polymorphisms, or transmitted resistance.

Other Potential Indicators to Consider

- **Past PrEP use**. To monitor future risk for resistance related to previous PrEP use, ART registers or electronic medical records could capture whether a client failing first-line treatment was a PrEP user in the past.
- **PrEP stock-outs.** Stock-outs of PrEP drugs will have a negative impact on PrEP continuation, which may increase the risk of drug resistance. Programs should measure the total number of days per month any facility experiences a PrEP drug stock-out.
- **HIV test kit stock-out.** PrEP can be initiated or resupplied only with a negative HIV test result. Stock-outs of tests could lead to interruptions in PrEP initiation and resupply, putting clients at increased risk of seroconversion and/or drug resistance. As with PrEP drug stock-outs, the number of days a facility is without HIV tests should be measured.
- **Pre-treatment HIVDR data.** Programs should collect pre-treatment HIVDR data to better understand background rates of transmitted resistance circulating in the population of potential PrEP users.

Table 3. Interpreting Seroconversions and HIVDR Results and Evaluating Next Steps

Results	Interpretation	Evaluation and Next Steps for the Program
Seroconversions occurring within the first month of PrEP initiation, regardless of HIVDR result	Client may have initiated PrEP during the acute HIV infection phase.	If the program identifies several PrEP clients who had an HIV positive test within the first month of PrEP initiation, review acute seroconversion assessment procedures and utilize more sensitive screening HIV tests, if available.
No HIVDR *(susceptible)*	No drug resistance indicated	If the program identifies several PrEP clients who test positive for HIV but do not have any evidence of resistance, evaluate them for acute HIV infection and review PrEP effective use counseling procedures within the program.
Any level of HIVDR related to a PrEP agent	PrEP use possibly a factor	In addition to assessing for acute HIV infection, review the following: ❖ If **PrEP**-related resistance is associated with gaps in PrEP continuation (missed doses, ring removal, or missed injections): ○ Review effective use counseling procedures. Additional client support and reminders may be necessary. ○ Review client retention. ❖ Review recent pre-treatment drug resistance surveillance conducted in country to consider alternative cause of resistance, such as transmitted drug resistance. ❖ Review the health system's ability to meet demand, including reliability of HIV testing supplies, PrEP product supply, and adequate facility staffing to allow for on-time resupply.
Any level of HIVDR ***not*** related to PrEP agent	Likely transmitted resistance	Review most recent pre-treatment drug surveillance conducted in country. Consider additional surveillance as per WHO guidelines.

Reference

[1]HIV drug resistance surveillance in countries scaling up pre-exposure prophylaxis. Geneva: World Health Organization; 2020. License: CC BY-NC-SA 3.0 IGO.