

Recommendations for Monitoring and Evaluation (M&E) Drug Resistance in a PrEP Program

Monitoring HIV drug resistance among pre-exposure prophylaxis (PrEP) users who have seroconverted, and understanding ways to reduce the risk of resistance, will help to ensure the long-term effectiveness of both PrEP and antiretroviral treatment options. Also important for resistance risk reduction, is for PrEP users to adhere to PrEP medication and the HIV testing schedule, as per WHO and country guidelines.

The following tables will assist program implementers effectively monitor for drug resistance in their PrEP programs:

Table 1: Sample M&E framework to Monitor Drug Resistance in Seroconverters during PrEP Roll-Out

Listed here are 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 also listed.

Activities	Inputs	Outputs	Outcomes	Overall outcome
Identify PrEP clients that seroconvert	<ul style="list-style-type: none"> HIV tests Staff to perform the test 	HIV test results	Clients know their HIV status	Optimal care for the client and long term effectiveness of the PrEP intervention for key populations ensured.
Collect a blood sample from the PrEP client for future resistance testing on the same day the client gets a positive HIV test result	<ul style="list-style-type: none"> Resistance test sample collection mechanism Staff time for collection Access to a lab with capability to perform resistance tests 	Resistance test results	Program has data to understand if PrEP client who seroconverted has HIV drug resistance	

Table 2: Suggested Indicators for HIV Drug Resistance Evaluation

Suggested indicators that should be collected monthly are listed here. As each PrEP client who seroconverts would likely be tested for resistance only once around the time of identification of seroconversion, numerators and denominators for all the indicators could be summed over time to get quarterly or annual rates of resistance. When combined with analyses of programmatic indicators for PrEP adherence and retention, programs would better understand factors associated with resistance.

Indicator	Definition	Recommended Disaggregation	Data Source	Entity Responsible
1. Total # of current PrEP users who seroconverted during the data collection period	Count only current PrEP users. Current PrEP users are those who have collected an initial supply of PrEP agents or a resupply of PrEP agents in the last three months, independent of self-reported adherence.	<ul style="list-style-type: none"> By adherence level Age Gender 	PrEP Register	PrEP Clinician, Counsellor

Indicator	Definition	Recommended Disaggregation	Data Source	Entity Responsible
2. # of those reported under indicator 1 who had a blood sample collected for resistance testing upon seroconversion	Of those PrEP clients who seroconvert, those who had a blood sample collected for resistance testing upon the same day as confirmation of HIV seroconversion.	<ul style="list-style-type: none"> • Sample for resistance test collected on the same day as first positive HIV test • Sample for resistance test collected within three months of the first positive HIV test • Sample for resistance collected more than three months after first positive HIV test • Age • Gender 	PrEP Register	PrEP Clinician, Counsellor
3. # of those reported under indicator 2 whose resistance test results indicate PrEP-related resistance	<p>The number of PrEP seroconverting clients who have ARV drug resistance related to the PrEP agent (tenofovir or truvada).</p> <ul style="list-style-type: none"> • Resistance is defined as low, intermediate, or high-level resistance to any drug. • Susceptible is not counted as resistance for the purpose of this indicator. • PrEP-related resistance is defined as the client's HIV genotype result having the mutation K65R, K70E and/or M184I or V if Truvada was used as PrEP, and K65R and/or K70E if tenofovir was used as PrEP. 	<ul style="list-style-type: none"> • Drug with associated resistance • Age • Gender 	Resistance test result Clinic/ facility register or lab database	Lab technician, PrEP clinician, Counsellor

Other Considerations

Table 2 does not list all possible indicators to monitor PrEP-related drug resistance, but rather, outlines those that might not be collected elsewhere in a project. If not part of the standard M&E indicators for a PrEP program, programs should consider collecting additional data on:

- **Past PrEP use.** To monitor future risk for resistance related to previous PrEP use, anti-retroviral treatment registers or electronic medical records could record whether a client failing first line treatment was a PrEP user in the past.
- **Communication of results to clients.** As part of high quality of care, programs should set a target for and measure how quickly test results are communicated back to clients.
- **PrEP stockout.** Stockouts of PrEP drugs will have a negative impact on client adherence, which may increase the risk of drug resistance. Programs should measure the total number of days per month any facility experiences a PrEP drug stockout.
- **HIV test stockout.** Stockouts of HIV tests are also important to measure due to the risk of drug resistance when PrEP is initiated or continued with a client who is already HIV infected. As with PrEP drug stockouts, the number of days a facility is without HIV tests should be measured.

Recognizing that HIV drug resistance testing is not routinely available in some low- and middle-income countries, WHO provides additional recommendations for drug resistance surveillance in locations where resistance testing is not available (<http://www.who.int/hiv/topics/drugresistance/en/>).

Table 3: Interpreting Results and Evaluating Next Steps

Outlined here are suggested next steps and further analyses needed to more fully understand the overall drug resistance results.

Drug Resistance Test Results	Interpretation	Evaluation and Next Steps for the Program
No resistance (susceptible)	No drug resistance indicated	If the program identifies several seroconverters but no resistance, evaluate adherence and counselling procedures within the program; however, likely no need to change resistance monitoring program
Any level of resistance related to PrEP agent (tenofovir or truvada)	PrEP use a likely factor	<p>Assess adherence among clients with these resistance test results. If several cases of PrEP-related resistance are associated with poor adherence:</p> <ul style="list-style-type: none"> • Review adherence counselling procedures; additional client support and reminders may be necessary • Review client retention; ensure clinic procedures adequately retain clients so that they return on time for their HIV tests and PrEP resupply <p>Assess timing of seroconversion in relation to PrEP Initiation:</p> <ul style="list-style-type: none"> • If several seroconversions occur within the first 3 months of PrEP initiation, consider establishing routine drug resistance monitoring during acute seroconversion phase; review acute seroconversion assessment procedures
Any level of resistance NOT related to PrEP agent (tenofovir or truvada)	PrEP use not a factor, likely pre-treatment drug resistance (transmitted resistance).	Review most recent pre-treatment drug surveillance conducted in country; consider additional surveillance as per WHO guidelines.