Monitoring Strategies for HIV Drug Resistance in PrEP Rollout Settings

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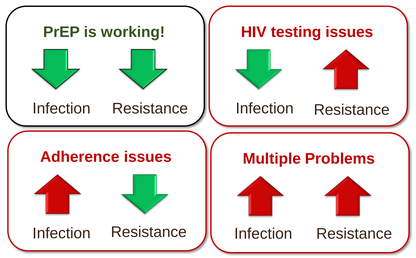
Background

- HIV drug resistance (HIVDR) among pre-exposure prophylaxis (PrEP) seroconverters is a concern as some antiretrovirals (ART) are used for both HIV prevention and treatment.
  - Breakthrough infection and subsequent selection of resistance with continued use of PrEP during acute infection could compromise the effectiveness of first-line ART.
  - Efficacy of PrEP could be reduced if the transmitted variant is from a partner failing an ART regimen with virus that is cross-resistant to PrEP.
- Evidence on HIVDR in PrEP seroconverters is limited and comes from PrEP efficacy studies with different HIV testing intervals and adherence support strategies compared to PrEP rollout.

Why monitor for HIVDR with PrEP?

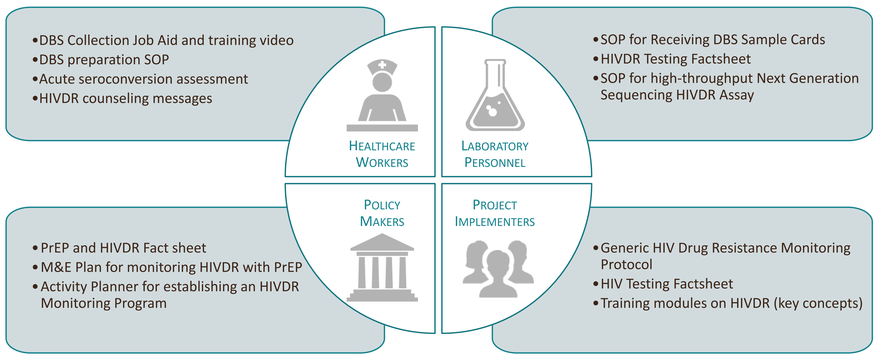
Potential Outcomes of PrEP Programs



- Low PrEP retention could result in initial exposure to PrEP drug, if a person then seroconverts with inadequate drug levels in their system they could develop HIVDR
- Limited funding for PrEP in some programs could result in drug stock outs and clients going on/off PrEP during times of HIV risk

More data are needed to understand the risk of HIVDR in real-world implementation.

GEMS HIVDR Monitoring Toolkit



Key Considerations for Drug Resistance Monitoring (DRM) Strategies

	OPTION 1 Standalone Study Protocol	OPTION 2 Demonstration Project	OPTION 3 National PrEP Guidelines	OPTION 4 National Surveillance Program
	Implement research protocol to assess drug resistance in PrEP seroconverters	Partner with existing PrEP Demonstration Projects to add DRM to their protocol or procedures	Work with MOH & TWG to include DRM as part of National PrEP Guidelines and Policies	Expand national surveillance for ART failures or pre-treatment surveillance to include PrEP DRT
Key Advantage	**Results may inform long-term national planning for resistance monitoring and PrEP programs**	**Added value to original demonstration project by further understanding HIVDR with PrEP seroconversions**	**Larger number of samples to inform long-term policy decisions, for both PrEP and ART**	**Common understanding of overall HIVDR surveillance and implications for country; whether from PrEP or ART**
Budget	• Need for external sponsor/funding	• Reduce cost by sharing resources with existing demo project	• Allocation of funds/staffing/coordination within MOH needed for implementation	• Minimal burden if DR surveillance infrastructure is established and funded
Infrastructure	• Capacity for research implementation at PrEP clinics must exist or be developed • Study team with local primary investigator and partners must be created	• Utilize existing infrastructure of study-specific sites providing PrEP within existing demo project	• May be challenging to reach all facilities providing PrEP including remote areas • Consider targeting subset based on regional HIV prevalence or high-volume sites	• Utilize existing surveillance infrastructure to coordinate with specimen collection, testing and reporting systems already in place
Timeline	• Limited to duration of protocol	• Limited to duration of demo project	• Indefinite, unless set forth in guidelines or national policy changes	• No distinct timeline, unless aligned with ART surveillance timeline
Implementation Decisions	• Opportunity to assess other components of interest such as drug level testing or behavioral assessments • Must ensure GCP is followed • May be easier to publish data with informed consents and ethics approvals in place	• Add a single blood sample collection at visit of seroconversion identification • Develop standard operating procedures and guidance to ensure seamless integration of resistance testing with other project procedures	• Identify PrEP populations of interest; key populations or nationwide sample • May not require a separate informed consent process, if considered standard of care for national program • Assess training needs and changes to be made to training curricula to support resistance testing	• Establish intervals of specimen collection • Integrate within HIVDR surveillance protocol, including, study procedures, data collection forms, sample analysis description, statistical analysis plan • Requires mechanism to disaggregate and possibly prioritize testing specimens (PrEP versus ART)
GEMS Global Evaluation of Microbicide Sensitivity	SOUTH AFRICA: Protocol to assess HIVDR among MSM and FSW KENYA ZIMBABWE: Protocols to assess HIVDR among a national sample of PrEP users	KENYA SOUTH AFRICA: DRT incorporated into existing demo projects for AGYW, MSM and serodiscordant couples	While Kenya and Zimbabwe are conducting national HIVDR monitoring, both countries are doing so through a protocol mechanism	No countries, that GEMS is working with, are currently using Option 4

Lessons Learned

- HIVDR monitoring for PrEP seroconverters is feasible with a **one-time dried blood spot specimen** collection at seroconversion.
- Countries have varying degrees of resources and stakeholder engagement for integrating DRT for PrEP delivery, impacting monitoring strategy. Approaches to monitoring will vary and may evolve as new data are analyzed.
  - Advantages and limitation of monitoring strategies should be weighed in context of **DR testing capacity, program cost, PrEP rollout stage, and levels of pretreatment HIV drug resistance.**
  - Currently, **countries are supportive** of conducting a time-limited evaluation of drug resistance in the absence of clear data and during early stages of PrEP rollout.
- As DR laboratory testing technology evolves, **more efficient and effective options** could impact monitoring.
- These proposed methods and **GEMS implementation support materials** will assist countries in developing policies that best fit their PrEP program needs and resources.
- Information learned from DR monitoring protocols and demonstration projects are anticipated in 2020. These data will inform efforts by MOHs **to maximize preventive impact of PrEP, while maintaining effectiveness of ART.**

For more information, and additional implementation support materials, visit: www.gems.pitt.edu/toolkit

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