Global PrEP Learning Network

Updated WHO Guidance on Laboratory Monitoring for PrEP and the GEMS Project's HIV Drug Resistance Monitoring

September 30, 2021

PEPFAR
USAID FROM THE AMERICAN PEOPLE
EpiC Meeting Targets and Maintaining Epidemic Control
RISE Reaching Impact, Saturation, and Epidemic Control

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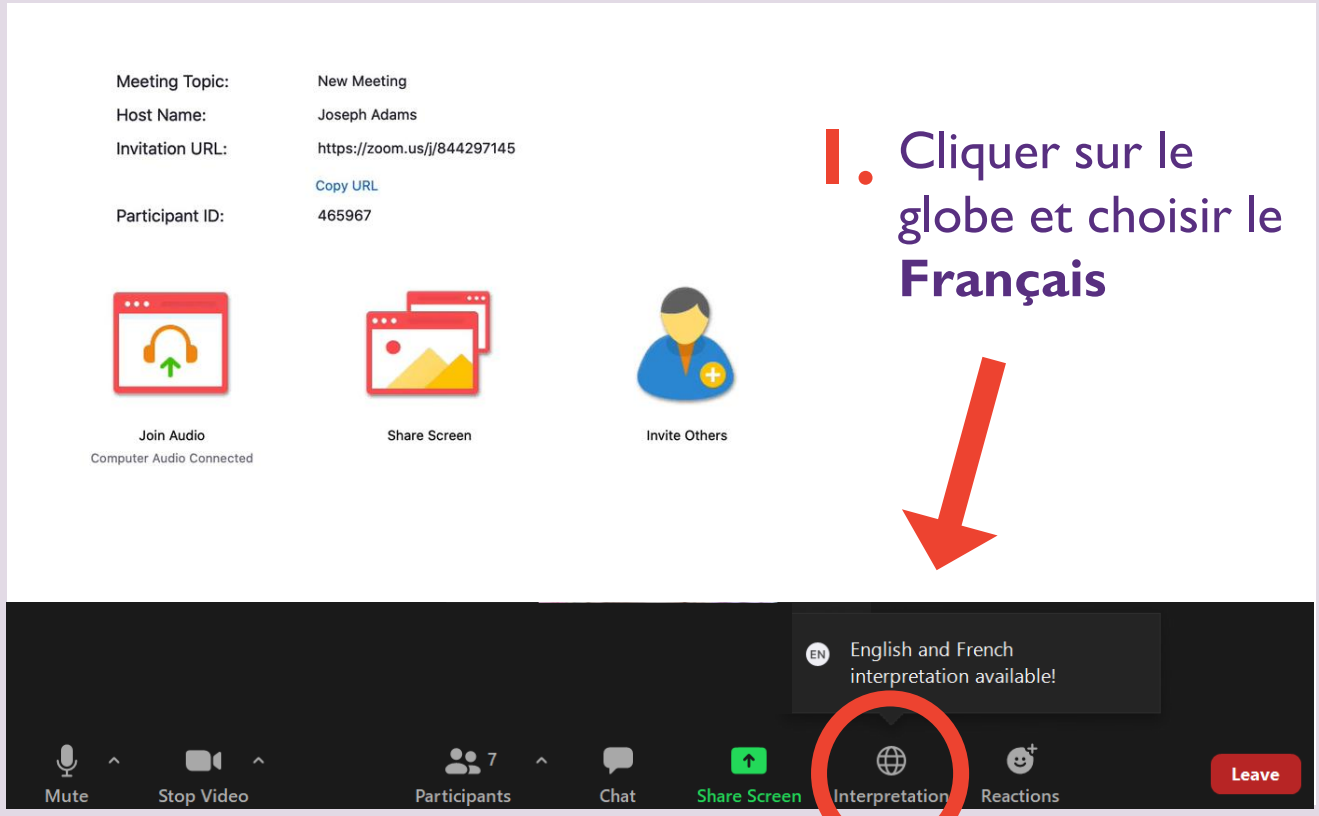
Accès à l'interprétation vers le Français



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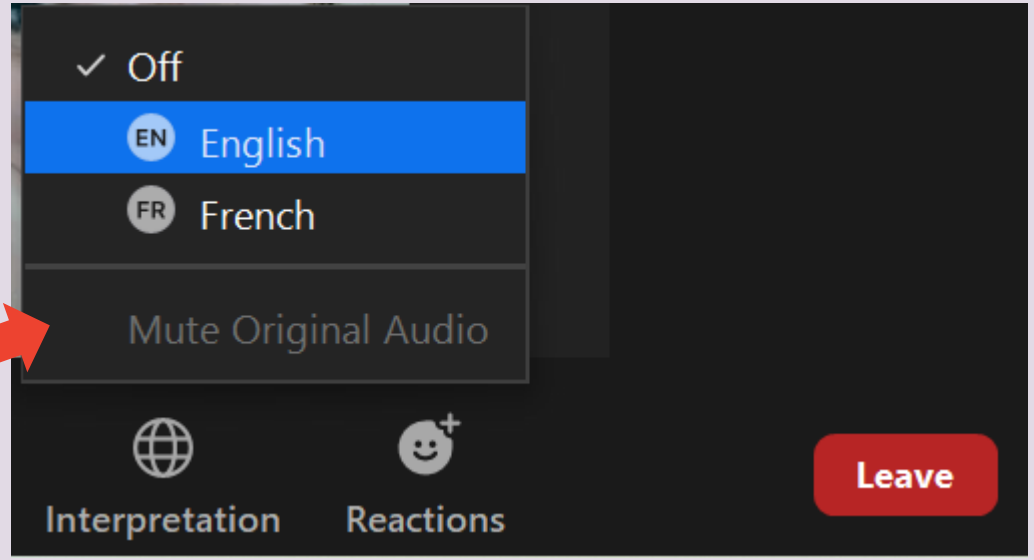

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Updates from the 2021 WHO Consolidated HIV Guidelines

HIV Drug Resistance (HIVDR) and PrEP: Key Concepts

Panel Discussion: Country Experiences with Implementing a National HIV Drug Resistance Monitoring Protocol

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Q&A

Up Next

Today's Speakers

Urvi Parikh, University of Pittsburgh

Urvi Parikh, PhD is an Assistant Professor of Medicine in the Division of Infectious Diseases at the University of Pittsburgh and the Associate Director of the Virology Core Microbicide Trials Network. She was the co-lead for the GEMS project.

Robin Schaefer, World Health Organization (WHO)

Robin Schaefer works for the Testing, Prevention, and Populations Unit of the Global HIV, Hepatitis, and STIs Programmes of the World Health Organization. He works on PrEP for HIV prevention with a particular focus on simplified service delivery and new PrEP products. He holds a PhD in infectious disease epidemiology and has worked on a range of global health issues, including sexual and reproductive health and malnutrition.

Anita Hettema, FHI 360

Anita Hettema, RN, MA is a Technical Advisor for FHI 360's biomedical prevention product portfolio in Eswatini. She was the GEMS project lead for the Eswatini HIVDR project.

Bhavna Chohan, Kenya Medical Research Institute, Nairobi

Bhavna Chohan, PhD, MSc is a Senior Research Scientist in the Center for Virus Research at the Kenya Medical Research Institute, Nairobi, and a Clinical Assistant Professor in the Department of Global Health at University of Washington. She also holds a Visiting Scientist and Honorary Lecturer position at University of Nairobi. She was the GEMS project lead for the Kenya HIVDR project.

Everline Bosek, University of Pittsburgh

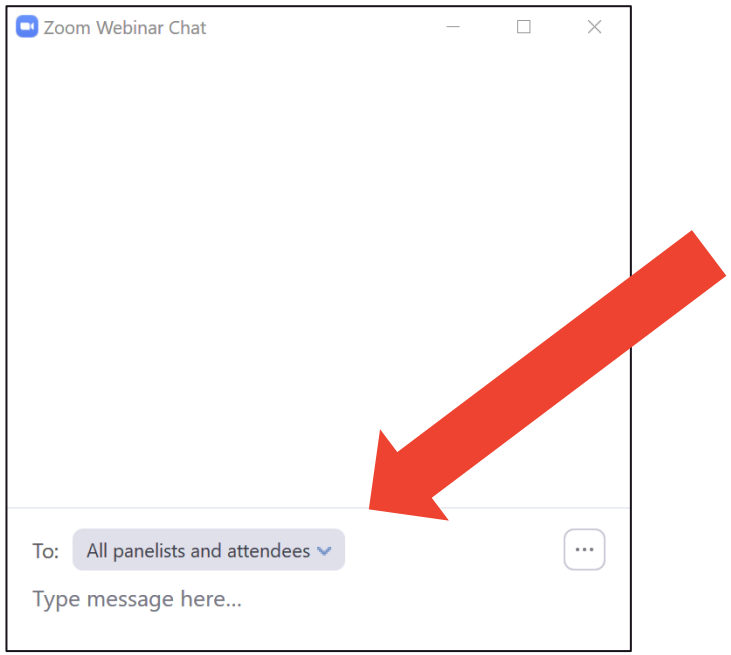
Everline Bosek, MsC, MPH is a project management professional with experience in implementation science, community health, and mobile projects. She was the GEMS project manager for the Kenya HIVDR project.

Lisa Levy, FHI 360

Lisa Levy, MPH is the Associate Project Director for the MTN (Microbicide Trials Network) and IMPAACT(International Maternal Pediatric and Adolescent AIDS Clinical Trials) Network with the Science Facilitation department at FHI 360. She also led the policy team for the GEMS project.

Reminder: Use "Chat" Function

Please feel free to ask questions and add comments to the chat box at any point during today's presentations. At the end of the session, we will dedicate time to Q&A.



Choose *"all panelists and attendees"* from the drop-down menu when adding a question or comment to the chat box.

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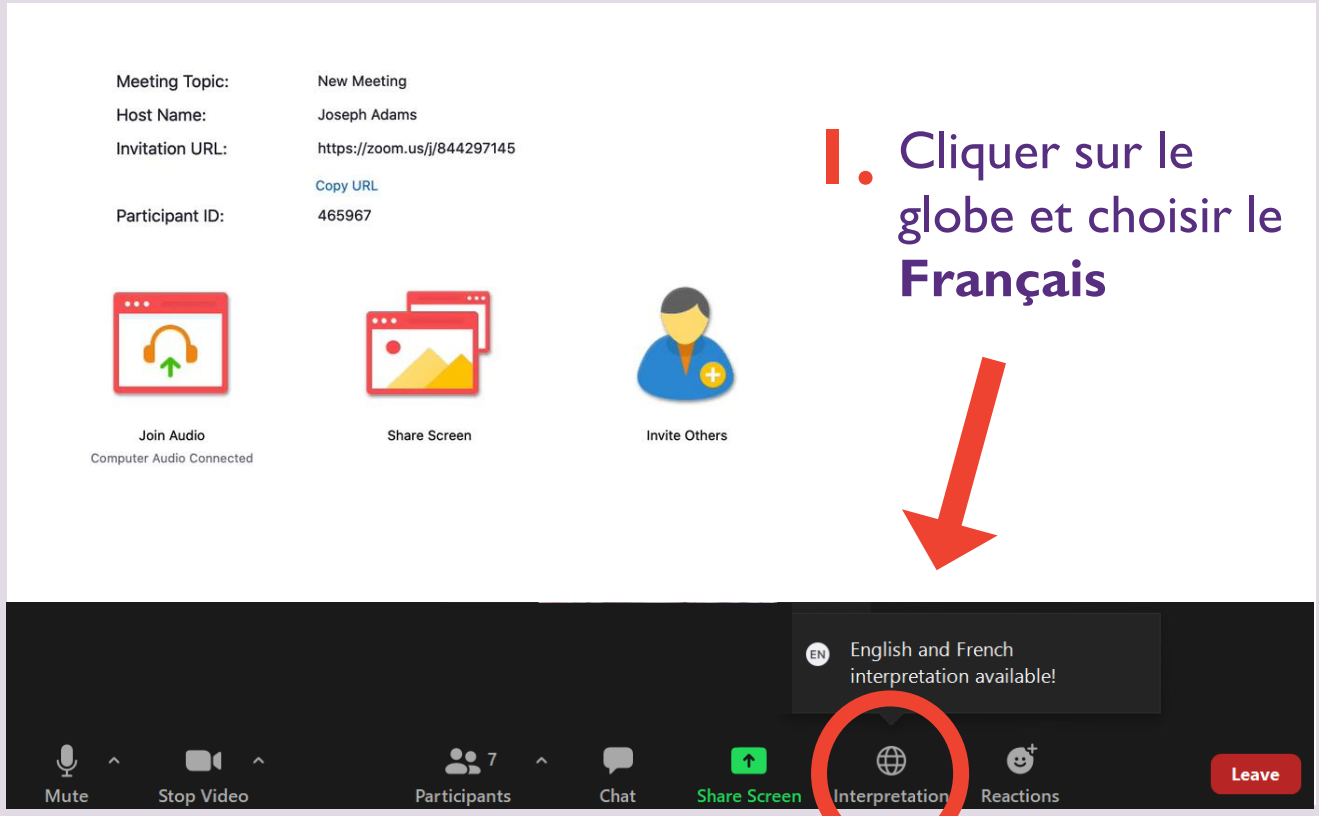

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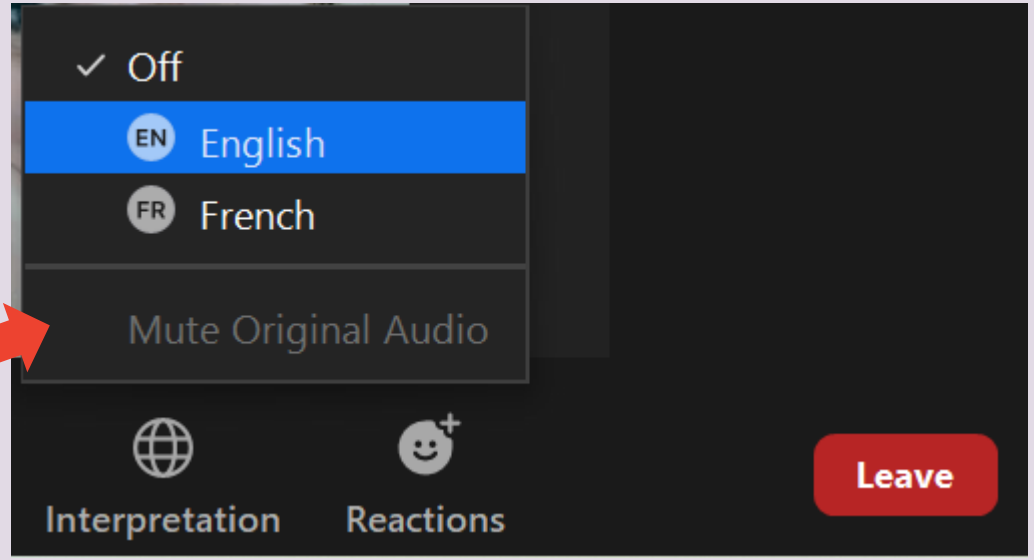

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World Health Organization

Photo credit: Project PrEP - Unitaid

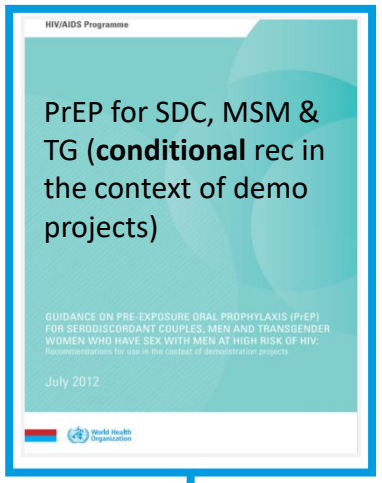
Updates from the 2021 WHO Consolidated HIV Guidelines on laboratory monitoring and testing for oral PrEP

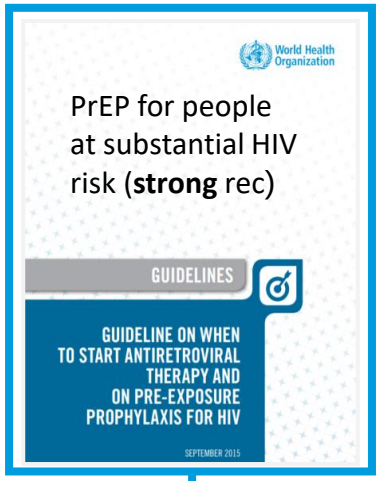
30 September 2021

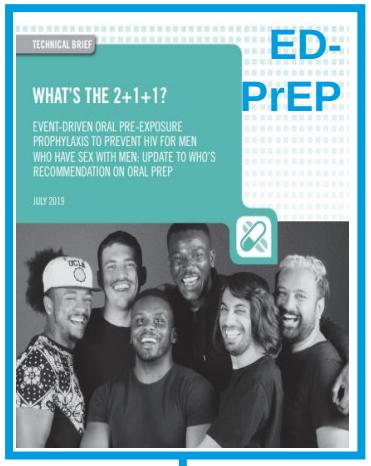
Robin Schaefer | Global HIV, Hepatitis and STIs Programmes | World Health Organization

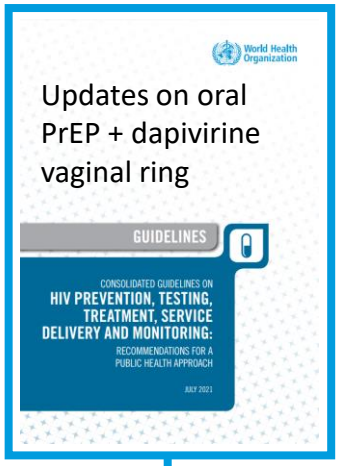
www.who.int

WHO PrEP recommendations and guidance



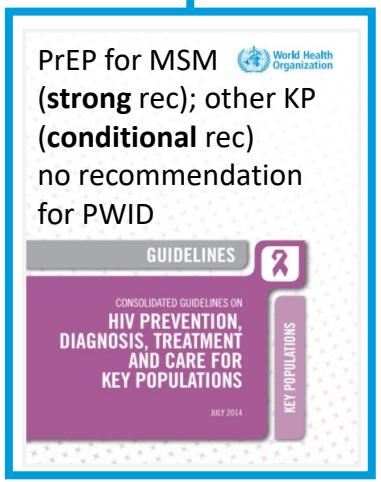


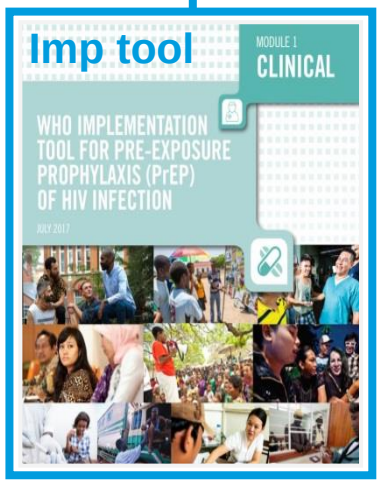




Revised PrEP implementation guidance, including for simplified PrEP service delivery

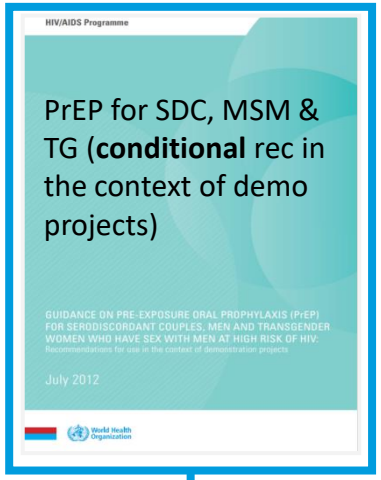
2012 2014 2015/16 2017 2019 2021 2021/22

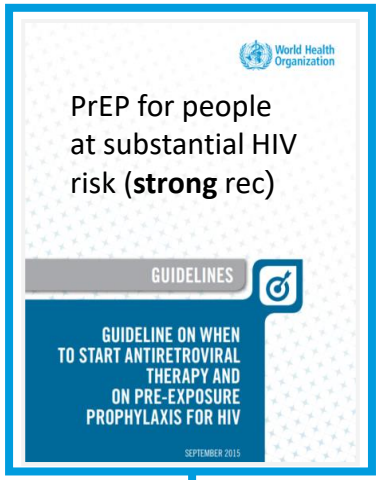




WHO recommendation on CAB-LA

WHO PrEP recommendations and guidance





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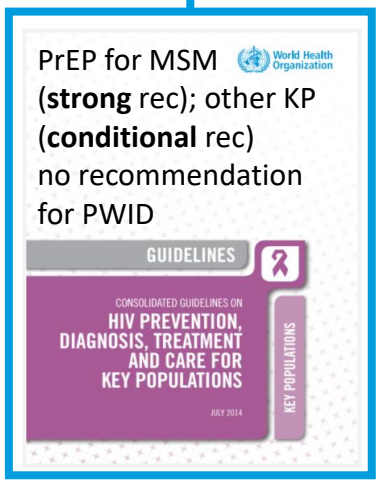
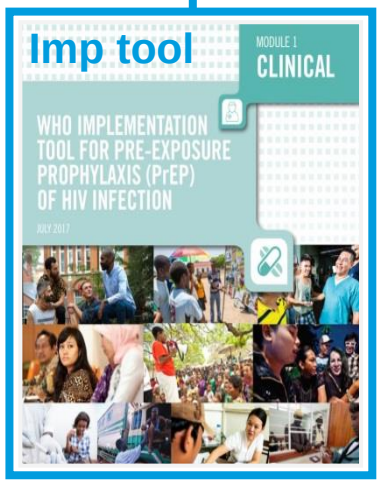
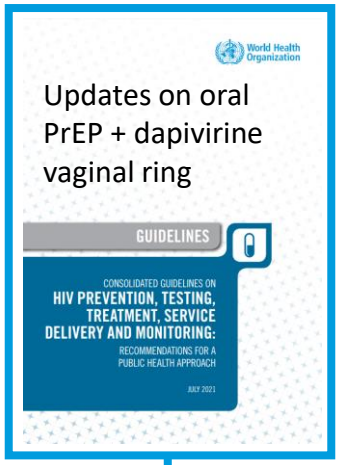




WHO guidance in 2015-17

Rationale	Issues
"Cautious": Limited implementation outside of HIC and pilots **"Do not harm" principle: Reassure countries anxious about new product for people without HIV**	**Guidance was "suggestions"** **Not based on evidence per see but on "practice" – what was done in the trial and pilots and consensus from experts**

WHO PrEP recommendations and guidance



Revised PrEP implementation guidance, including for simplified PrEP service delivery

2021 → **2021/22**

DPV-VR

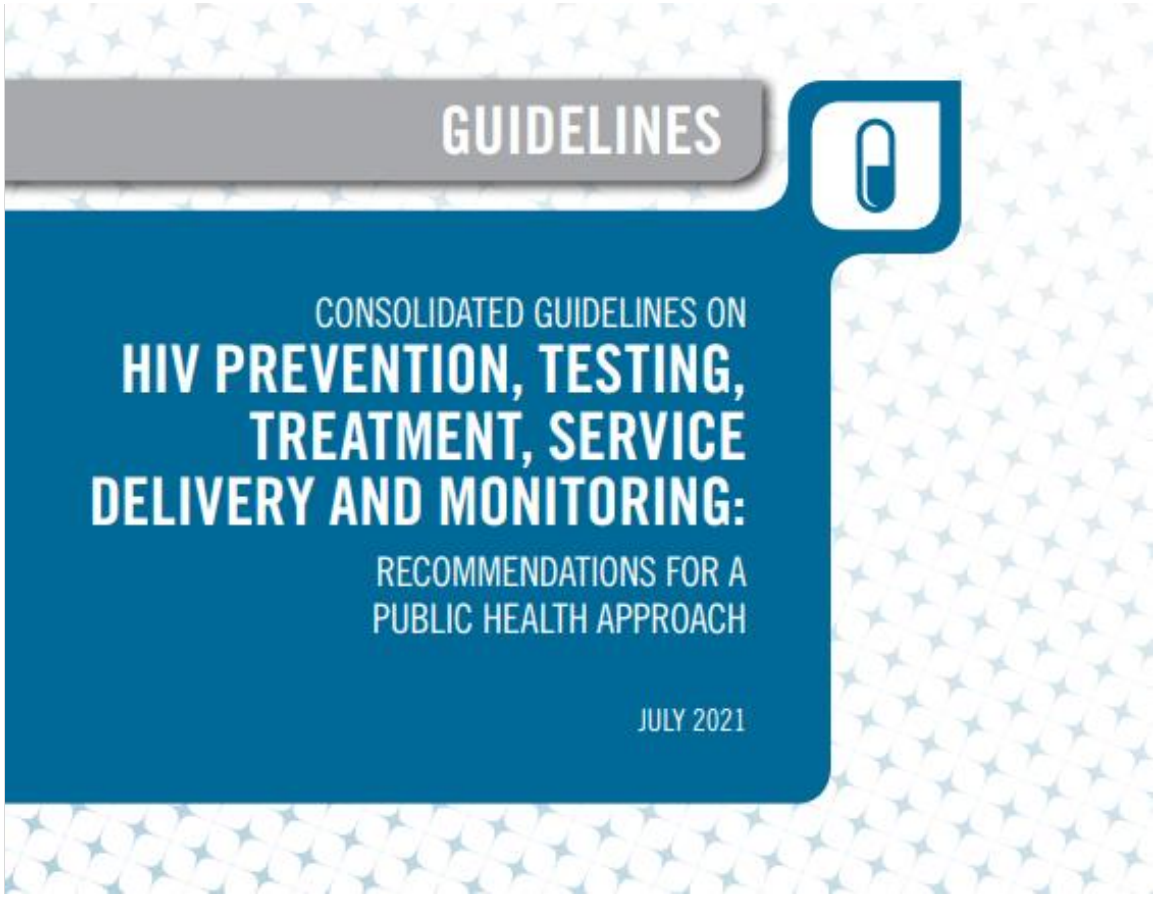
WHO recommends the dapivirine vaginal ring as a new choice for HIV prevention for women at substantial risk of HIV infection

WHO recommendation on CAB-LA

WHO guidance going forward

Rationale	Issues
Much more experience **Current WHO guidance is seen as a barrier to implementation** • Criticism from global funders • Some countries ignore • Some countries use it as an 'excuse' not to implement • Many people accessing PrEP informally without any 'checks' • C-19 has led to necessary adaptations • Community and pharmacy delivery are proposed	**Lack of RCTs to make usual WHO "recommendations"** **WHO reviewing current practice** **WHO seeking expert opinion** **Balance of benefits vs harms** **A menu of options?**

Highlights from the 2021 WHO HIV Guidelines



- Guidance on the **dapivirine vaginal ring** as an additional PrEP option for cisgender women
- Updates on testing and monitoring for oral PrEP:
  - **Renal function monitoring**
  - **HIV self-testing**
  - **Viral hepatitis**

Renal function monitoring for oral PrEP

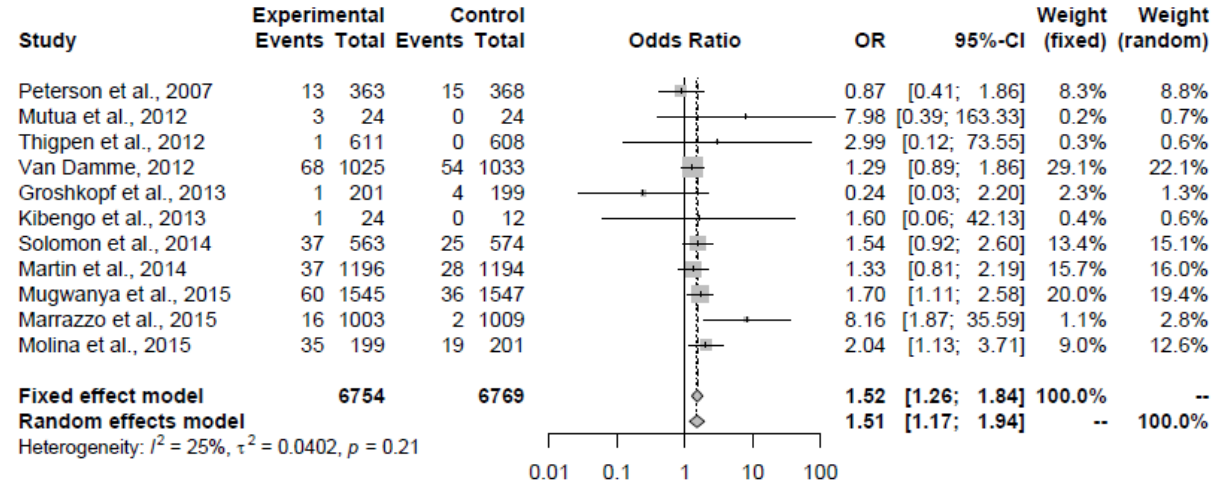
Impaired kidney function, indicated by a creatinine clearance of <60ml/min, is a contraindication for using oral PrEP containing TDF.

Systematic review of published literature

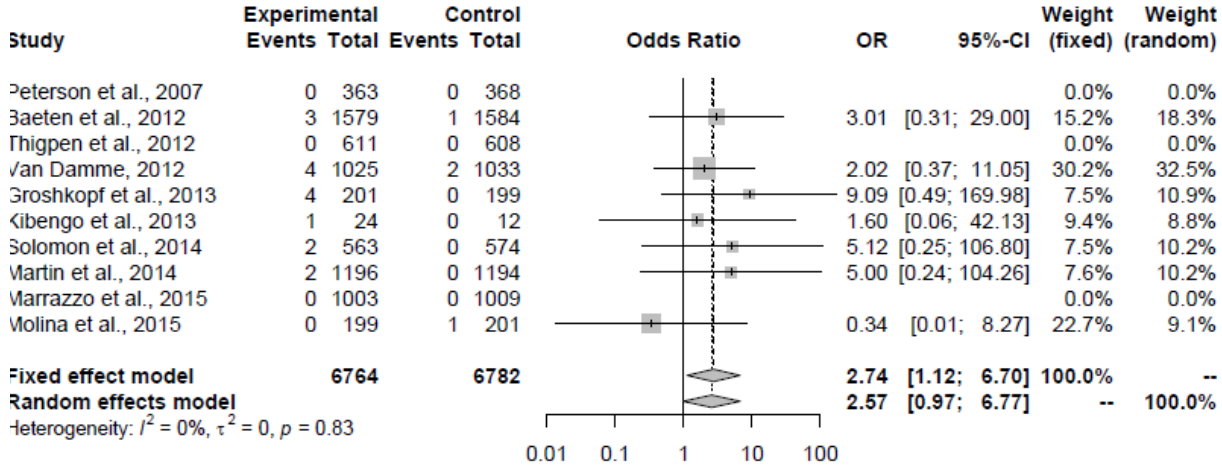
In 11 different RCTs, significant increase in risk of kidney-related adverse events

Risks are small and grade 2+ adverse events are rare (16 grade 2+ events among 6764 PrEP users vs. 4 events among 6782 control).

Grade 1+ adverse events (mild +)



Grade 2+ adverse events (moderate +)



Renal function monitoring for oral PrEP

Impaired kidney function, indicated by a creatinine clearance of <60ml/min, is a contraindication for using oral PrEP containing TDF.

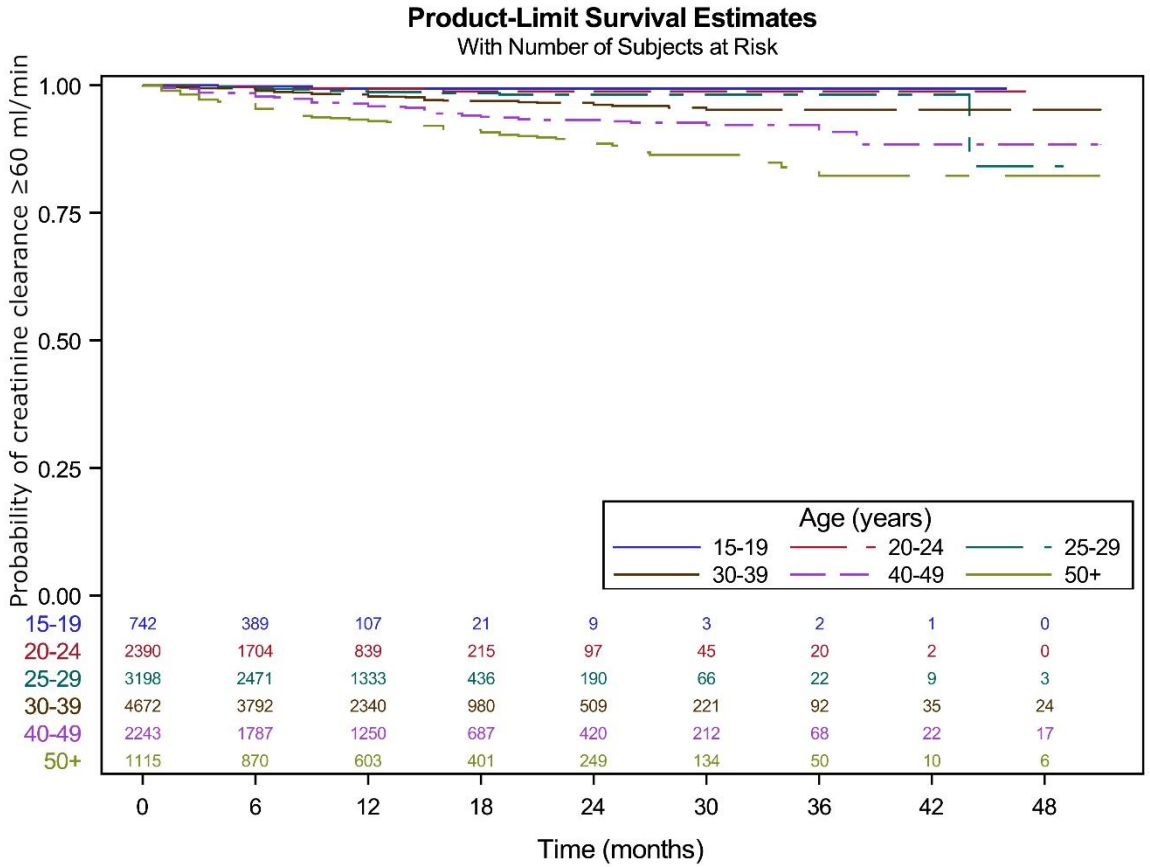
Global data analysis

Data on 18,676 individuals screened for PrEP initiation across 15 countries

79 out of 18,676 (0.42%) individuals who were screened for PrEP had CrCl <60ml/min

Among 14,368 individuals who initiated PrEP and had follow-up measurements, 349 (2.43%) developed <60ml/min CrCl

Baseline CrCl of <90ml/min and increasing age associated with increased risk



Renal function monitoring for oral PrEP

Impaired kidney function, indicated by a creatinine clearance of <60ml/min, is a contraindication for using oral PrEP containing TDF.

Population		Initiation	Follow-up
Kidney-related comorbidities	**Age**		
No	<30	Optional	Optional (until age 30 or kidney-related comorbidities develop) If baseline done and CrCl <90ml/min, conduct follow-up ever 6-12months
No	30-49	Conduct once within 1-3 months after oral PrEP initiation	If CrCl ≥90ml/min, optional (until age 50 or kidney-related comorbidities develop) If CrCl <90ml/min, screening every 6-12 months
Yes	Any age	Conduct once within 1-3 months after oral PrEP initiation	Screening every 6-12 months
No	50+		

Renal function monitoring for oral PrEP

Impaired kidney function, indicated by a creatinine clearance of <60ml/min, is a contraindication for using oral PrEP containing TDF.

Suggested procedure **applies to daily and event-driven oral PrEP use**.

Waiting for creatinine screening result should not delay starting oral PrEP and results can be reviewed at follow-up visit.

Abnormal creatinine clearance results of <60ml/min should be repeated on a separate day before stopping oral PrEP.

Abnormal creatinine clearance usually returns to normal levels after stopping oral PrEP.

Oral PrEP can be **restarted if creatinine clearance is confirmed to be ≥90ml/min** 1-3 months after stopping PrEP.

If creatinine clearance does not return to normal levels after stopping PrEP, **other causes of renal insufficiency should be evaluated.**

HIV testing for oral PrEP

HIV testing is required prior to starting or restarting PrEP and should be conducted regularly (e.g., every 3 months) during PrEP use.

- Use WHO **serial testing strategies, within a validated testing algorithm**, using WHO prequalified assays.
- Individuals may be tested at POC following the **national testing algorithm**, usually a combination of 3rd generation RDTs
- If the initial HIV test -ve and no history or signs/ symptoms of an acute viral syndrome, **offer same day initiation**
- Once initiated on PrEP, HIV testing is suggested every 3 months and whenever restarting PrEP after a gap in use.
- Additional HIV testing 1 month after starting or restarting PrEP may also be beneficial

HIV testing for oral PrEP

HIV testing is required prior to starting or restarting PrEP and should be conducted regularly (e.g., every 3 months) during PrEP use.

HIV self-testing

Current guidance: HIV ST suggested for **demand creation** but not for monitoring during oral PrEP use

March 2020 WHO guidance for maintaining essential health services during COVID-19 suggested **HIV ST to sustain PrEP programmes**

Numerous programmes were adapted to include HIV ST during COVID-19

Several trials ongoing looking at HIV ST in PrEP programmes

Blood-based HIV ST may be preferable over oral fluid-based HIV ST

WHO simplification of PrEP guidance late 2021/early 2022 and HTS update end 2022.

PrEP and viral hepatitis

In many settings, populations at risk of HIV are also at high risk of hepatitis B and C infection.

PrEP services provide a unique opportunity to screen for hepatitis B and hepatitis C infection and address multiple public health issues

Hepatitis B

Testing oral PrEP users for **hepatitis B surface antigen (HBsAg) once**, around PrEP initiation, is suggested.

Rapid point-of-care tests are available for HBsAg, and WHO has prequalified several rapid diagnostic tests.

Consider people with detectable HBsAg for treatment

People at risk of acquiring hepatitis B with non-reactive HBsAg test may be considered for hepatitis B vaccination depending on endemicity and country recommendations.

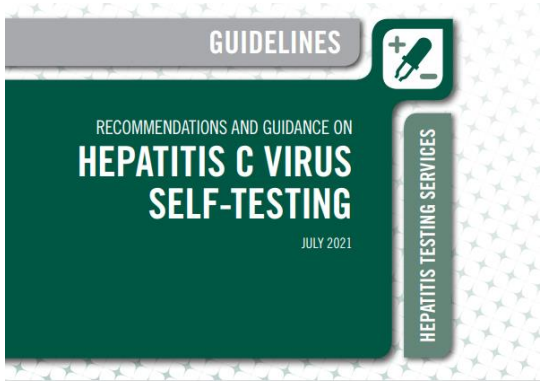
Current guidance suggests that hepatitis B infection is a contraindication for event-driven oral PrEP use. **This guidance is currently under review.**

Hepatitis C

Hepatitis C antibody testing can be considered **at PrEP initiation and every 12 months**, especially when PrEP services are provided to men who have sex with men, people who use drugs and people in prisons and other closed settings.

Individuals with reactive serology test results should be referred for further assessment and treatment for hepatitis C infection.

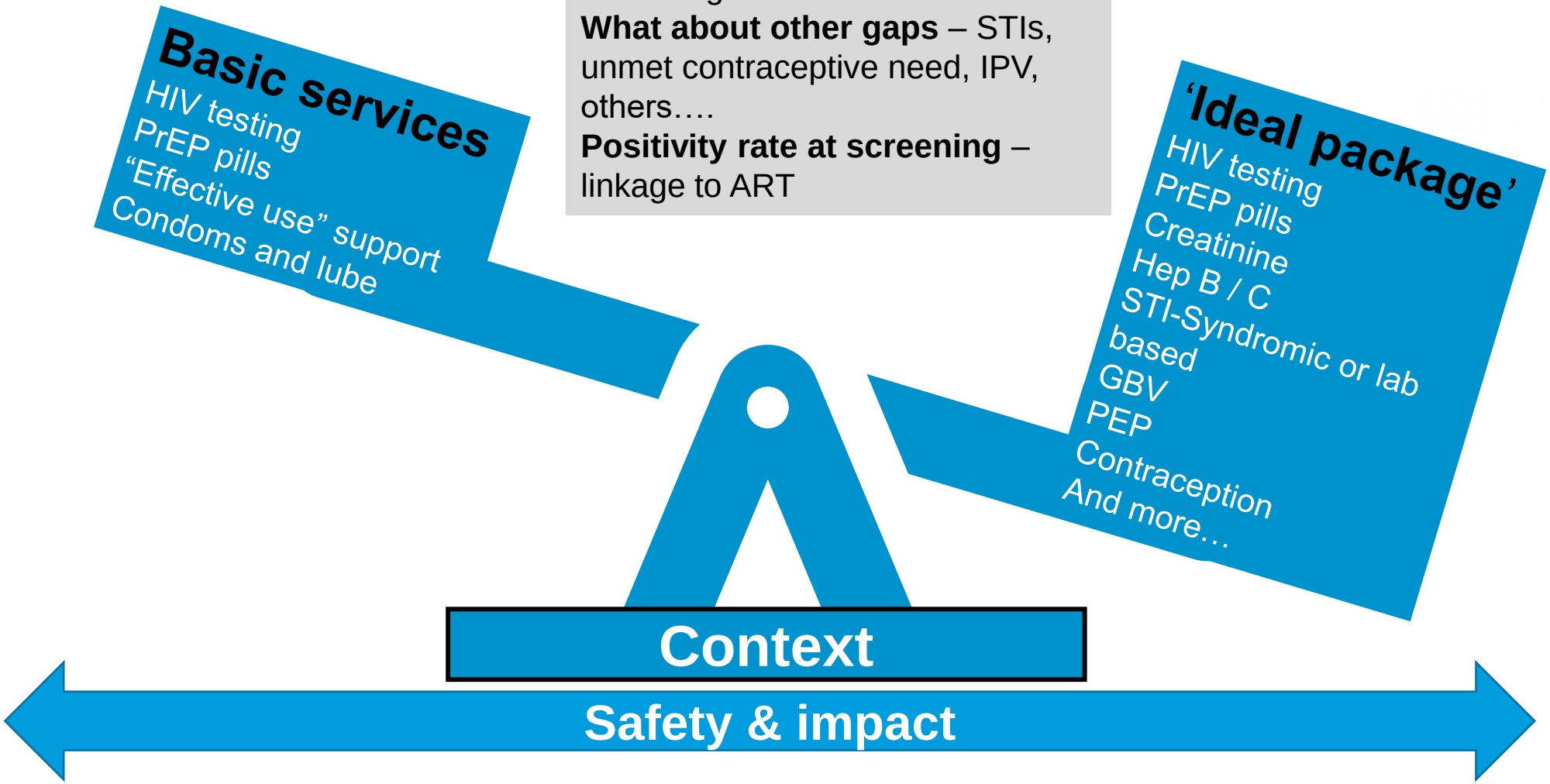
Hepatitis C infection is not a contraindication for daily or event-driven oral PrEP use, and PrEP can be initiated before hepatitis C test results are available.



WHO has recently released guidelines on hepatitis C self-testing

Making PrEP more efficient and effective: Balancing costs, efficiency, and impact

HIV risk and incidence matters – screening tools?
What about other gaps – STIs, unmet contraceptive need, IPV, others….
Positivity rate at screening – linkage to ART



Upcoming WHO guidance

Simplification of oral PrEP: end 2021/early 2022

- Renal function monitoring
- Viral hepatitis
- HIV self-testing
- Community-based delivery of PrEP, including telehealth for PrEP
- M&E

Updates to the WHO PrEP Implementation Tool: 2022

Thank you!

World Health Organization

I thank the **Testing, Prevention, and Populations** team for contributions to this presentation.

Contact me for questions or comments: Robin Schaefer, **schaeferr@who.int**

WHO Global HIV, Hepatitis and STIs Programmes:
https://www.who.int/teams/global-hiv-hepatitis-and-stis-programmes/overview

WHO Global PrEP Network:
https://www.who.int/groups/global-prep-network

Q&A

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PrEP and Risk of HIV Drug Resistance:

Key Concepts

Urvi M Parikh, PhD
University of Pittsburgh

Topics

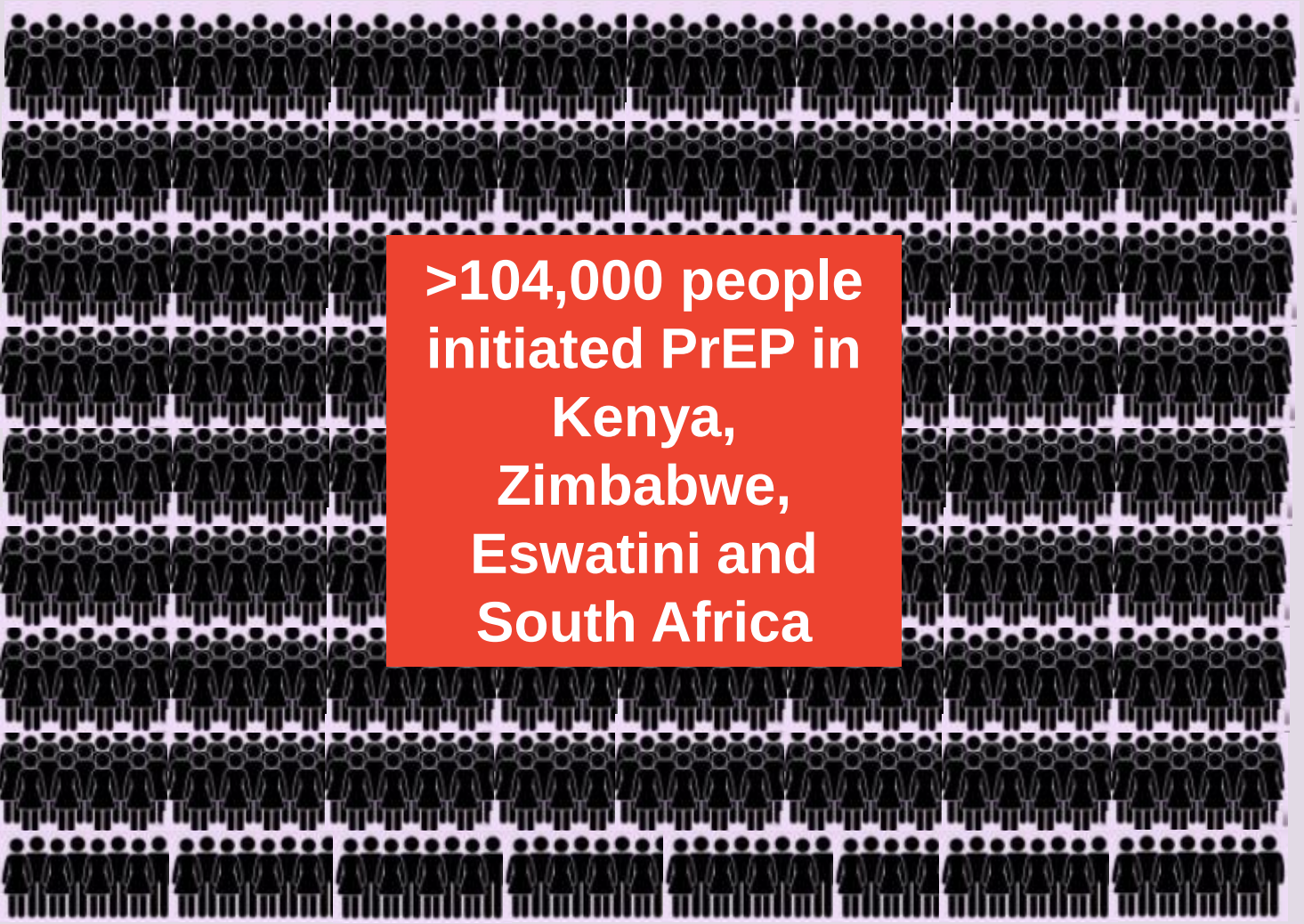
- How does a PrEP user get drug resistant HIV?
- What can PrEP programs and projects do to monitor for HIV drug resistance?
- What have we learned from PrEP resistance monitoring in the countries that have implemented it?

PrEP Prevents HIV

NO INFECTION = NO RESISTANCE

An HIV negative person cannot have HIV drug resistance

Concern about HIVDR should not be a reason to limit use of PrEP



229 reported seroconversions over 4 years in the GEMS project

The rate of HIV infection on PrEP is low

No infection = no drug resistance

Parikh et al. IAS 2021

Resistance Risk with Seroconversion on PrEP

Transmitted Drug Resistance

- A PrEP user could get infected with drug resistant HIV from a partner

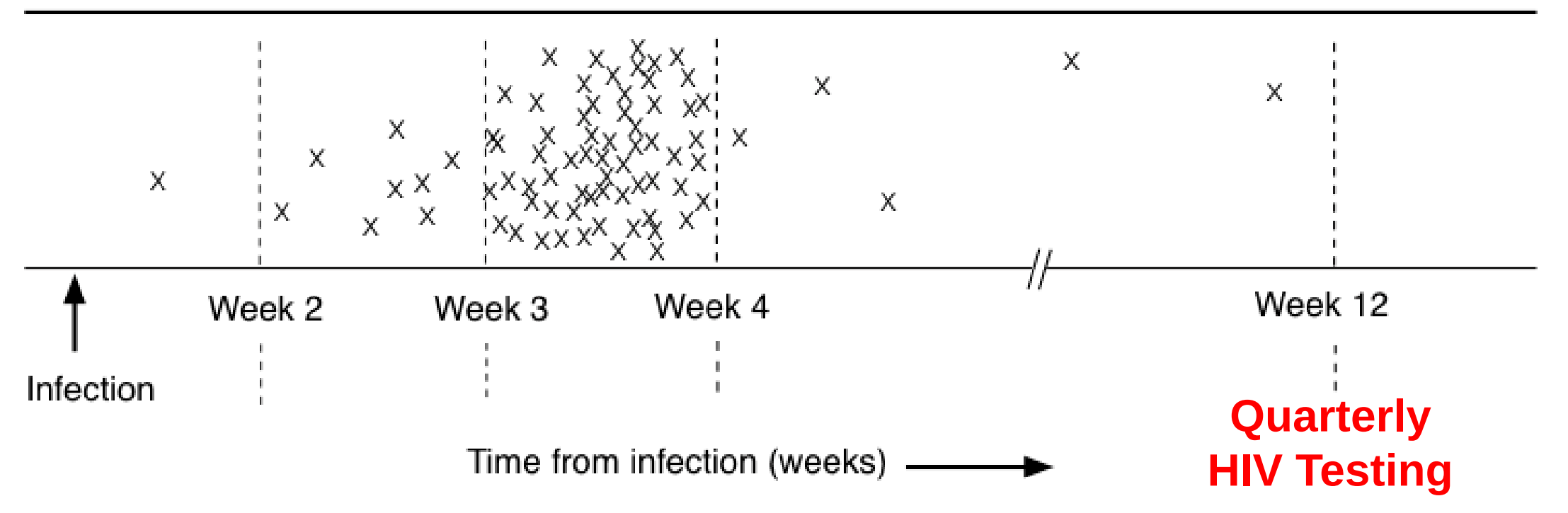
Resistance Risk with Seroconversion on PrEP

Acquired Drug Resistance

- An HIV positive person could keep using PrEP before they know their HIV status
  - If they started PrEP before realizing they were HIV infected
  - If they stopped PrEP, became infected, and re-started PrEP
  - If they didn’t have enough PrEP doses to prevent infection
  - If PrEP didn't work (rare)

HIV testing is important

“Window” period before HIV is detected by diagnostic tests



X represents when a person’s HIV test result is positive

Image: https://i-base.info/guides/testing/what-is-the-window-period

HIVDR monitoring with PrEP is important

- Ensure effectiveness of National PrEP program and to understand if additional support is needed for PrEP adherence and/or routine HIV testing
- Assess whether the frequency of HIV testing is adequate to capture seroconversions as quickly as possible
- Support national HIV prevention and treatment programs by understanding the HIVDR frequency with PrEP use

Monitoring Strategies for HIVDR

Implement national research protocol to assess HIVDR in PrEP seroconverters

Partner with existing PrEP Demo Projects to add DRM to their protocol or procedures

Expand national surveillance for PDR and ADR to include PrEP DRM specifically

Monitoring Strategies for HIVDR

Implement national research protocol to assess HIVDR in PrEP seroconverters

KENYA

ESWATINI

ZIMBABWE

Procedures for HIVDR Monitoring with PrEP

PROTOCOL

Establish resistance monitoring protocol

SAMPLE COLLECTION

Collect blood from consenting HIV positive individuals who had been prescribed PrEP in the last 3 months

TESTING

Test for PrEP drug levels and HIV resistance mutations

GEMS monitored HIV drug resistance (HIVDR) in PrEP rollout programs in Sub-Saharan Africa

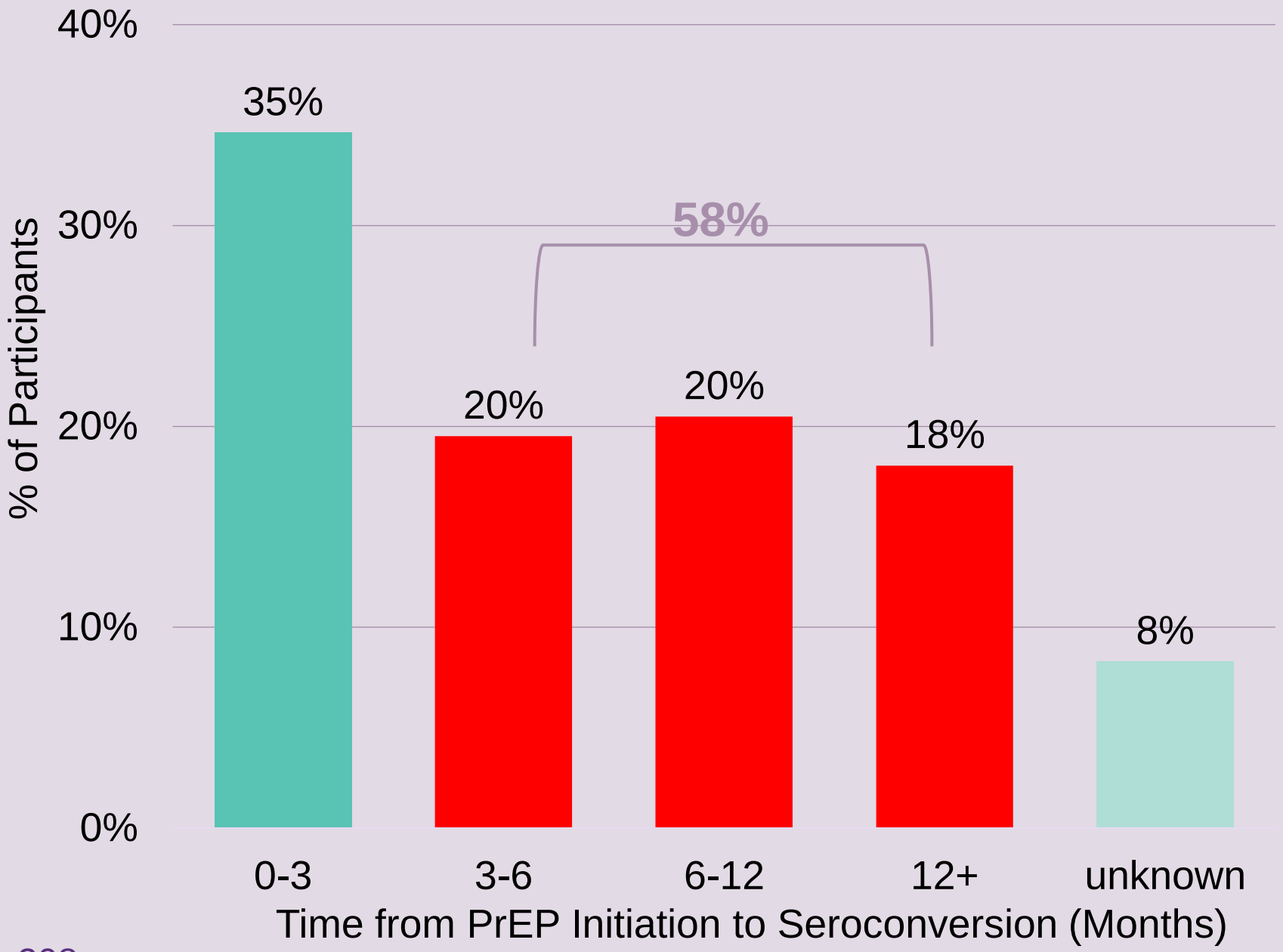
GEMS
GLOBAL EVALUATION OF MICROBICIDE SENSITIVITY

- Observational Cross-Sectional Study (Dec 2017 – Jul 2019)
- Current PrEP user (collected initial supply or resupply of PrEP)
- Identified as HIV positive per national HIV testing algorithm **after** PrEP initiation
- Provided informed consent
- **Samples collected from 208 HIV positive individuals**

Parikh et al. IAS 2021

Participants were mostly young, female, and in varied populations

Characteristic	N = 208
Female	155 (75%)
Age at Seroconversion	
16 – 24	108 (52%)
25+	95 (46%)
unknown	5 (2%)
Population	
Adolescent Girl/Young Woman	87 (42%)
Serodifferent Couple	50 (23%)
Female Sex Worker	20 (10%)
Men Who Have Sex with Men	15 (7%)
Transgender Woman	12 (6%)
Pregnant or Lactating	8 (4%)
Incarcerated	1 (<1%)



N = 208

The majority of participants initiated PrEP more than 3 months prior to becoming HIV positive

Key Findings – HIV Drug Resistance

MUTATION PROFILE	# PARTICIPANTS
No resistance mutations	65/118 (55%)
Not associated with PrEP	26/118 (22%)
PrEP-associated (K65R, K70E, M184IV)	**27/118 (23%)**

LIMITATIONS

- Timing of taking PrEP and HIV infection not known
- There may be a gap in seroconversion and sample collection for some participants

TRANSMITTED RESISTANCE

ACQUIRED OR TRANSMITTED RESISTANCE

118 out of 208 samples (57%) were successfully tested for HIVDR

Summary

- **PrEP WORKS!** The number of reported infections (229) was very small compared to the estimated number of people who initiated PrEP (>104,000)
- Resistance is a risk for people who become HIV positive on PrEP.
- Improved HIV diagnostics to detect HIV earlier, and monitoring for HIVDR are important for both PrEP and treatment programs.

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Bhavna Chohan, PhD, MSc
Kenya HIVDR Team Lead

Everline Bosek, MSc, MPH
Kenya HIVDR Program Manager

Anita Hettema, RN, MA
Eswatini HIVDR Team Lead

PANEL DISCUSION: Country Experiences with HIVDR Monitoring with PrEP Rollout

Resistance Monitoring Set-up

- Talk about the process of including HIVDR monitoring in your country's PrEP program

Resistance Monitoring Structure

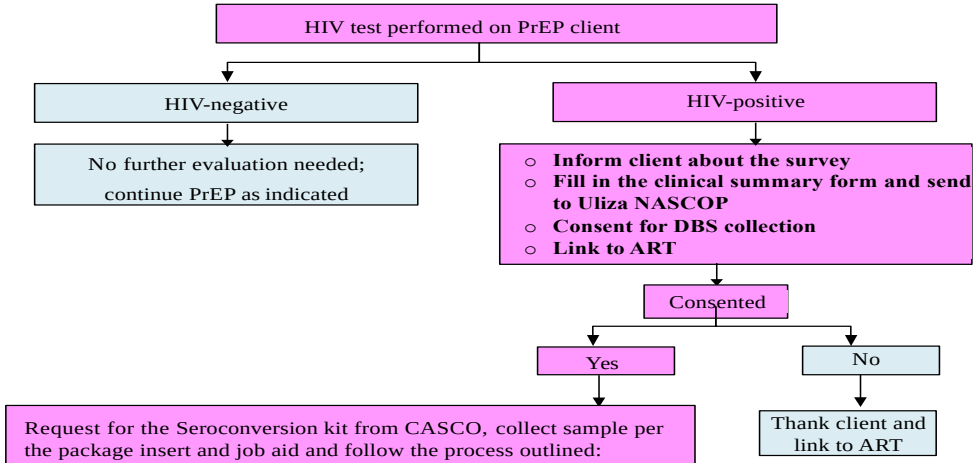
- Why did you decide to use a research protocol to conduct monitoring rather than adding to an existing surveillance program?

Resistance Monitoring Logistics

- Were there any in-country systems for specimen collection and shipment that you were able to utilize?

MINISTRY OF HEALTH

PrEP Seroconverter HIV Drug Resistance Test Flowchart



Request for the Seroconversion kit from CASCO, collect sample per the package insert and job aid and follow the process outlined:

- **Complete Lab Requisition Form (LRF)**
- **Collect blood via venipuncture**
- **Prepare two DBS cards**
- **Package dried DBS cards**
- **Call G4S to ship sample to Kisumu KEMRI lab** (addressed envelope in the kit)

sample must be shipped within 3 days

Return of HIV Drug Resistance Test Results:

- Results returned from KEMRI Lab to requesting PrEP sites
- Results sent to *Uliza NASCOP (ulizanascop@gmail.com)*

NB: PrEP sites are encouraged to seek guidance from their *County HIV Clinical TWG/PrEP or Uliza NASCOP* for management of PrEP seroconverter if mutations detected.

Abbreviations:
ART - Antiretroviral Treatment;
DBS - Dried Blood Spot;
LRF - Lab requisition form;
PrEP - Pre-exposure Prophylaxis

Contact:
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Version 1.1 November 2018

Resistance Monitoring Procedures at PrEP Sites

- What were the steps taken by health care workers after identifying a PrEP user who seroconverted?

Appendix II *Version 1.0 June 2018*

MINISTRY OF HEALTH

NATIONAL AIDS AND STI CONTROL PROGRAMME

LABORATORY REQUISITON FORM FOR PrEP SEROCONVERTORS

Name of Facility		**MFL Code**	
Client PrEP barcode no. (*do not write name*)		**Date of Request:**	
Blood collection Date		**Time**	
DBS Preparation Date		**Time**	
Client Details	**Year of Birth:** _____ **Gender:** _____ **PrEP initiation Date:** _____ **Date PrEP bottle was last collected:** _____ **Date PrEP was last taken:** _____ **Date of first HIV positive test:** _____ **Date of last HIV negative test:** _____		
Clinician's Name			
Facility Contacts	**Tel:**	**Email:**	

High-risk assessment criteria for reason on PrEP:

Discordant couple ☐ **Adolescent/Young women** ☐ **MSM** ☐ **FSW** ☐

Sex with unknown partner ☐

Other (specify) ☐

Is sexual Partner HIV positive: Yes ☐ **No** ☐ **Don't know** ☐

If partner HIV positive, what ARV regimen is the partner currently taking:

☐ **Don't know** ☐

Adherence Evaluation: Per client report, was the client adherent to PrEP?

☐ **Good, missed 0-3 doses in past month**
☐ **Fair, missed 4-5 doses in past month**
☐ **Bad, missed 6-7 doses (or more) in part month**

BARC

Global Central Laboratory

BARC SOUTH AFRICA PTY LTD A Joint venture between Lancet Laboratories and BARC NV (a division of Cerba European Laboratories)

JOHANNESBURG 11 Napier Road Richmond Johannesburg, 2092 +27 11 242-7044
DURBAN 2nd Floor, Block A, Capital Haematology Hospital Complex, 65 King Cetshwayo Highway, Westridge, Durban 4001 +27 31 309-6617
PRETORIA Persuedia Building, 1st Floor 509 Pretorius Street, Arcadia, Pretoria, 0083 +27 12 480 0255/6/7
CAPE TOWN Waverley Business Park Unit 7 Bldg 23D, Wycroft Rd, Mowbray, Cape Town, 7700 +27 21 448-4311

ESWATINI GEMS PrEP - DBS

PARTICIPANT DEMOGRAPHICS

Patient Initials ☐☐☐☐

PT ID ☐☐☐☐☐☐☐☐☐☐☐☐☐☐

Date Of Birth ☐☐ ☐☐ ☐☐☐☐ (D D M M Y Y Y Y)

Gender M F TGM TGF OTHER

Collection Date ☐☐ ☐☐ ☐☐☐☐ (D D M M Y Y Y Y)

Collection Time ☐☐ : ☐☐ (24-hour clock)

Blood

Collected by _____ (Initials)

SPONSOR DETAILS

Sponsor : USAID / PEPFAR / GEMS
Trial : GEMS
Kit : GEMS1

INVESTIGATOR DETAILS / SITE STAMP

ctGEMS8
Principal Investigator:
Dr. Rudo A. P. Kuwengwa
Ministry of Health
Eswatini

Site Contact:
Contact Person:
Telephone Numbers:

PLEASE MARK APPLICABLE VISIT TYPE:

Date of PrEP Initiation ☐☐ ☐☐ ☐☐☐☐ (D D M M Y Y Y Y)

☒ *Seroconversion Visit (SCV)*

Date of PrEP last taken ☐☐ ☐☐ ☐☐☐☐ (D D M M Y Y Y Y)

Please state date of the first Positive HIV test:

☐☐ ☐☐ ☐☐☐☐ (D D M M Y Y Y Y)

Per client report, was the client adherent to PrEP?

Yes	☐	usually used medication as instructed
Somewhat adherent	☐	used medication but not daily
No	☐	mostly did not use medication as instructed
Discontinued	☐	stop taking PrEP completely

BARC LAB USE ONLY

BARC Receiving: *Log the visit as SCV*

Received Date & Time: *See Date and Time stamp*

Received By:

Record quantity of specimens received:

DBS LASEC	DBS WHATMAN
10ml EDTA	Other

Logged By:

Lab MRI Number:

Demo Checked By:

CLINIC INSTRUCTIONS:

Mix tubes immediately by gentle inversion (8-10 times). Keep at room temperature prior to DBS preparation in the clinic. DBS to be prepared on DBS card within 4 hrs of blood collection. Prepare two DBS cards. Dry the DBS cards for at least 3 hours and once DBS cards are dry, send to NRL with regular national sample transport. In case NSTS will not collect within 1 day, contact Anita Hettema 76751498 or Dr. Rudo Kuwengwa 76027775 to arrange alternative sample pick-up. PLEASE SEND REMAINING BLOOD SAMPLE IN EDTA TUBE AFTER DBS SPOTTING, ALONG WITH SHIPMENT.

CLINICAL SITE TO DO - Please record each DBS card spotting time below:

BARC BARCODE	LOGGING CODES	SPECIMEN	TESTS	TEST REQUIRED	PERFORM SITES
	BARC		ADMIN		
LAB NO. BARCODE 1 AFFIX BARCODE LABEL HERE	Z111	1 x DBS CARD (PCR)	HIV DBS Drug Resistance (preparation done on DBS card) Card 1 (Resistance) : ____ : ____	X	3113
	DBSUCT	1 x DBS CARD (UCT)	Storage for PK Analysis Card 2 (PK) : ____ : ____	X	3300

Resistance Monitoring Training Approach

- How did you approach training for the health care workers interacting with PrEP clients and other stakeholders?

Implementation Best Practices

- What procedures did you use to ensure successful implementation of resistance monitoring?

Adaptation during COVID lockdowns

- How did you adapt so resistance monitoring could still occur during COVID (taking into account lockdowns and restrictions on gatherings)?

Successes of HIVDR monitoring

- What is one component of HIVDR monitoring with PrEP that you thought went really well?

Challenges of HIVDR monitoring

- What were some challenges of implementing HIVDR monitoring with PrEP?

Key Takeaways

- What are some key takeaways from your experience implementing HIVDR monitoring with PrEP?

Opening & Introductions

Updates from the 2021 WHO Consolidated HIV Guidelines

HIV Drug Resistance (HIVDR) and PrEP: Key Concepts

Panel Discussion: Country Experiences with Implementing a National HIV Drug Resistance Monitoring Protocol

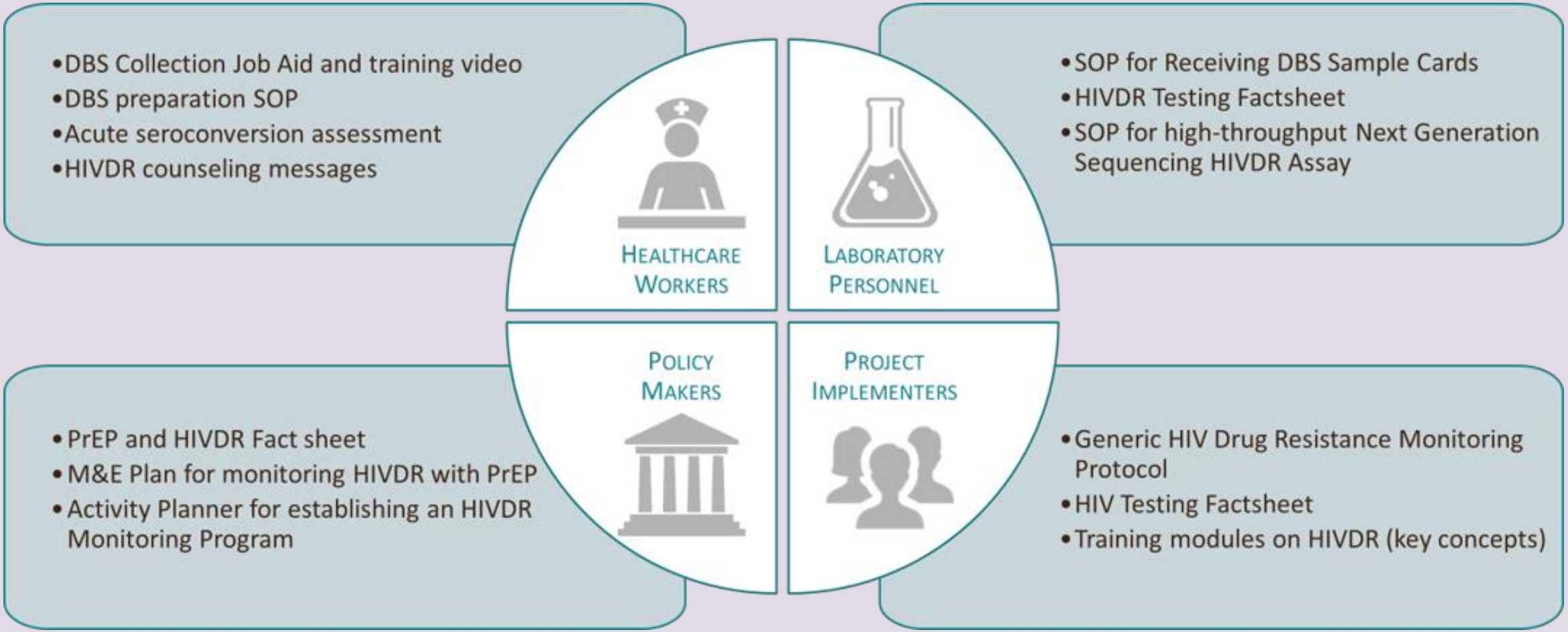
Overview of GEMS Toolkit Materials

Q&A

Up Next

HIVDR Monitoring Tools and Resources

https://www.prepwatch.org/gems/



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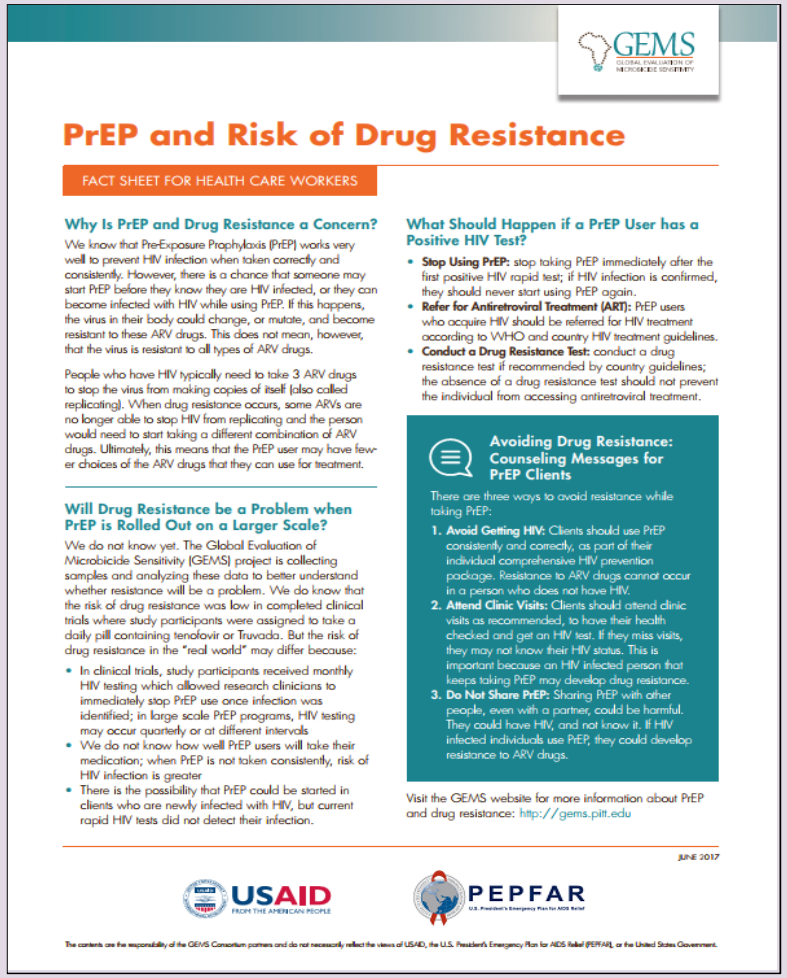

GEMS
GLOBAL EVALUATION OF MICROBICIDE SENSITIVITY

PrEP and Risk of Drug Resistance

FACT SHEET FOR HEALTH CARE WORKERS

Why Is PrEP and Drug Resistance a Concern?

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People who have HIV typically need to take 3 ARV drugs to stop the virus from making copies of itself (also called replicating). When drug resistance occurs, some ARVs are no longer able to stop HIV from replicating and the person would need to start taking a different combination of ARV drugs. Ultimately, this means that the PrEP user may have fewer choices of the ARV drugs that they can use for treatment.

Will Drug Resistance be a Problem when PrEP is Rolled Out on a Larger Scale?

We do not know yet. The Global Evaluation of Microbicide Sensitivity (GEMS) project is collecting samples and analyzing these data to better understand whether resistance will be a problem. We do know that the risk of drug resistance was low in completed clinical trials where study participants were assigned to take a daily pill containing tenofovir or Truvada. But the risk of drug resistance in the "real world" may differ because:

- In clinical trials, study participants received monthly HIV testing which allowed research clinicians to immediately stop PrEP use once infection was identified; in large scale PrEP programs, HIV testing may occur quarterly or at different intervals
- We do not know how well PrEP users will take their medication; when PrEP is not taken consistently, risk of HIV infection is greater
- There is the possibility that PrEP could be started in clients who are newly infected with HIV, but current rapid HIV tests did not detect their infection.

What Should Happen if a PrEP User has a Positive HIV Test?

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- **Conduct a Drug Resistance Test:** conduct a drug resistance test if recommended by country guidelines; the absence of a drug resistance test should not prevent the individual from accessing antiretroviral treatment.

Avoiding Drug Resistance: Counseling Messages for PrEP Clients

There are three ways to avoid resistance while taking PrEP:

1. **Avoid Getting HIV:** Clients should use PrEP consistently and correctly, as part of their individual comprehensive HIV prevention package. Resistance to ARV drugs cannot occur in a person who does not have HIV.
2. **Attend Clinic Visits:** Clients should attend clinic visits as recommended, to have their health checked and get an HIV test. If they miss visits, they may not know their HIV status. This is important because an HIV infected person that keeps taking PrEP may develop drug resistance.
3. **Do Not Share PrEP:** Sharing PrEP with other people, even with a partner, could be harmful. They could have HIV, and not know it. If HIV infected individuals use PrEP, they could develop resistance to ARV drugs.

Visit the GEMS website for more information about PrEP and drug resistance: http://gems.pitt.edu

JUNE 2017

USAID FROM THE AMERICAN PEOPLE

PEPFAR U.S. President's Emergency Plan for AIDS Relief

The contents are the responsibility of the GEMS Consortium partners and do not necessarily reflect the views of USAID, the U.S. President's Emergency Plan for AIDS Relief (PEPFAR), or the United States Government.

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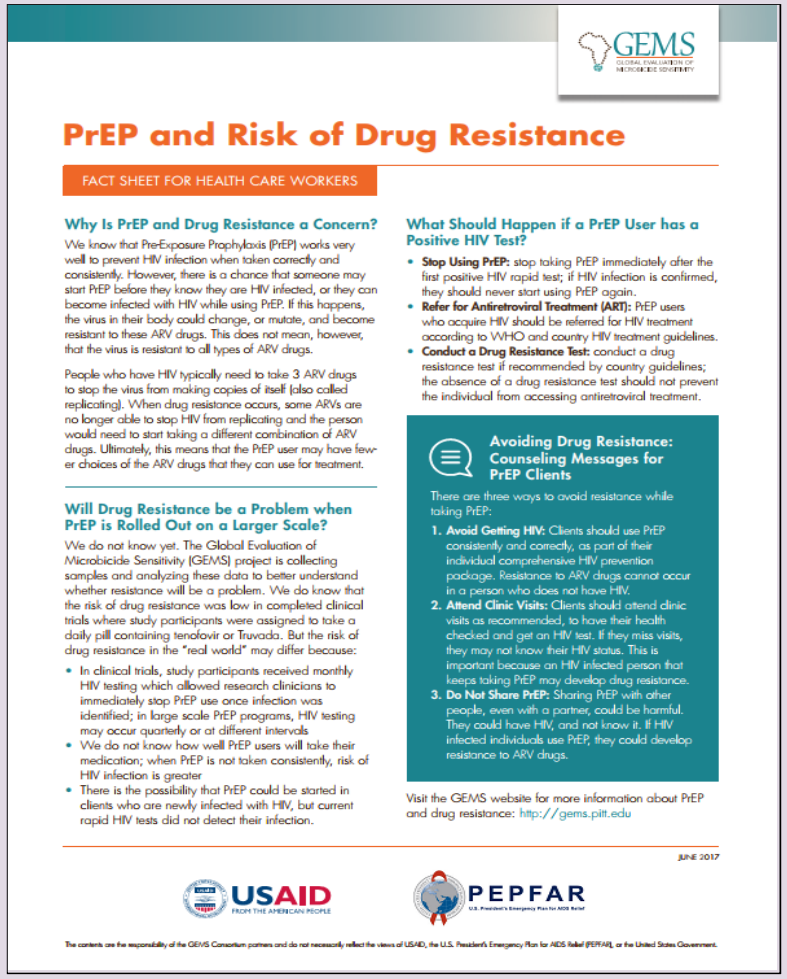

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3. **Do Not Share PrEP:** Sharing PrEP with other people, even with a partner, could be harmful. They could have HIV, and not know it. If HIV infected individuals use PrEP, they could develop resistance to ARV drugs.

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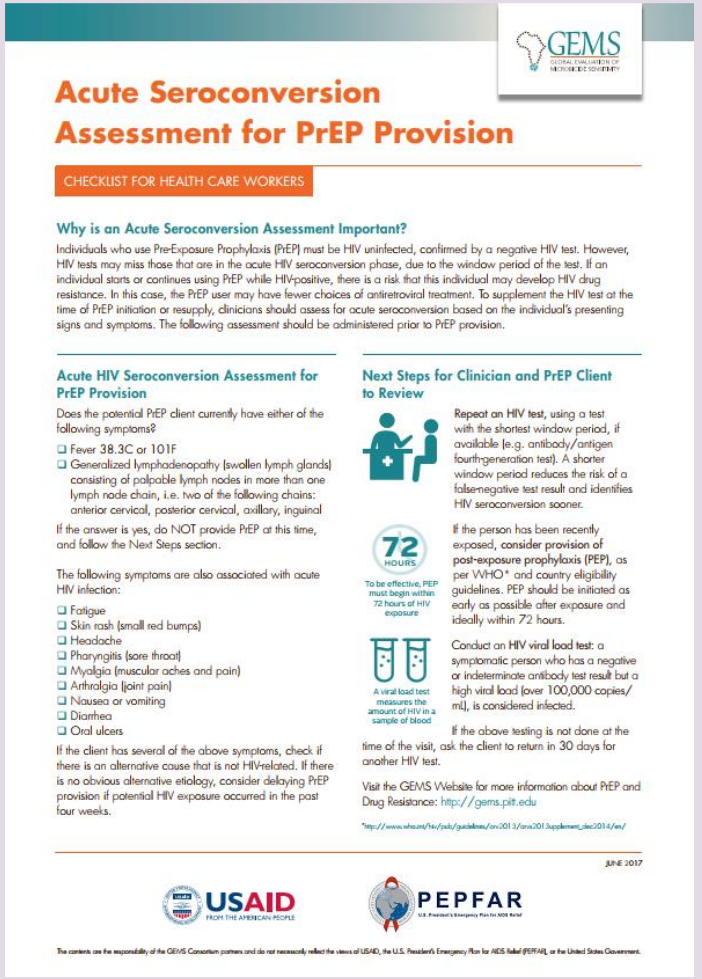
How do clinically assess for acute seroconversion?



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Acute Seroconversion Assessment for PrEP Provision

CHECKLIST FOR HEALTH CARE WORKERS

Why is an Acute Seroconversion Assessment Important?

Individuals who use Pre-Exposure Prophylaxis (PrEP) must be HIV uninfected, confirmed by a negative HIV test. However, HIV tests may miss those that are in the acute HIV seroconversion phase, due to the window period of the test. If an individual starts or continues using PrEP while HIV-positive, there is a risk that this individual may develop HIV drug resistance. In this case, the PrEP user may have fewer choices of antiretroviral treatment. To supplement the HIV test at the time of PrEP initiation or resupply, clinicians should assess for acute seroconversion based on the individual's presenting signs and symptoms. The following assessment should be administered prior to PrEP provision.

Acute HIV Seroconversion Assessment for PrEP Provision

Does the potential PrEP client currently have either of the following symptoms?

- ❑ Fever 38.3C or 101F
- ❑ Generalized lymphadenopathy (swollen lymph glands) consisting of palpable lymph nodes in more than one lymph node chain, i.e. two of the following chains: anterior cervical, posterior cervical, axillary, inguinal

If the answer is yes, do NOT provide PrEP at this time, and follow the Next Steps section.

The following symptoms are also associated with acute HIV infection:

- ❑ Fatigue
- ❑ Skin rash (small red bumps)
- ❑ Headache
- ❑ Pharyngitis (sore throat)
- ❑ Myalgia (muscular aches and pain)
- ❑ Arthralgia (joint pain)
- ❑ Nausea or vomiting
- ❑ Diarrhea
- ❑ Oral ulcers

If the client has several of the above symptoms, check if there is an alternative cause that is not HIV-related. If there is no obvious alternative etiology, consider delaying PrEP provision if potential HIV exposure occurred in the past four weeks.

Next Steps for Clinician and PrEP Client to Review

Repeat an HIV test, using a test with the shortest window period, if available (e.g. antibody/antigen fourth-generation test). A shorter window period reduces the risk of a false-negative test result and identifies HIV seroconversion sooner.

72 HOURS

To be effective, PEP must begin within 72 hours of HIV exposure

If the person has been recently exposed, **consider provision of post-exposure prophylaxis (PEP),** as per WHO* and country eligibility guidelines. PEP should be initiated as early as possible after exposure and ideally within 72 hours.

A viral load test measures the amount of HIV in a sample of blood

Conduct an **HIV viral load test:** a symptomatic person who has a negative or indeterminate antibody test result but a high viral load (over 100,000 copies/ml), is considered infected.

If the above testing is not done at the time of the visit, ask the client to return in 30 days for another HIV test.

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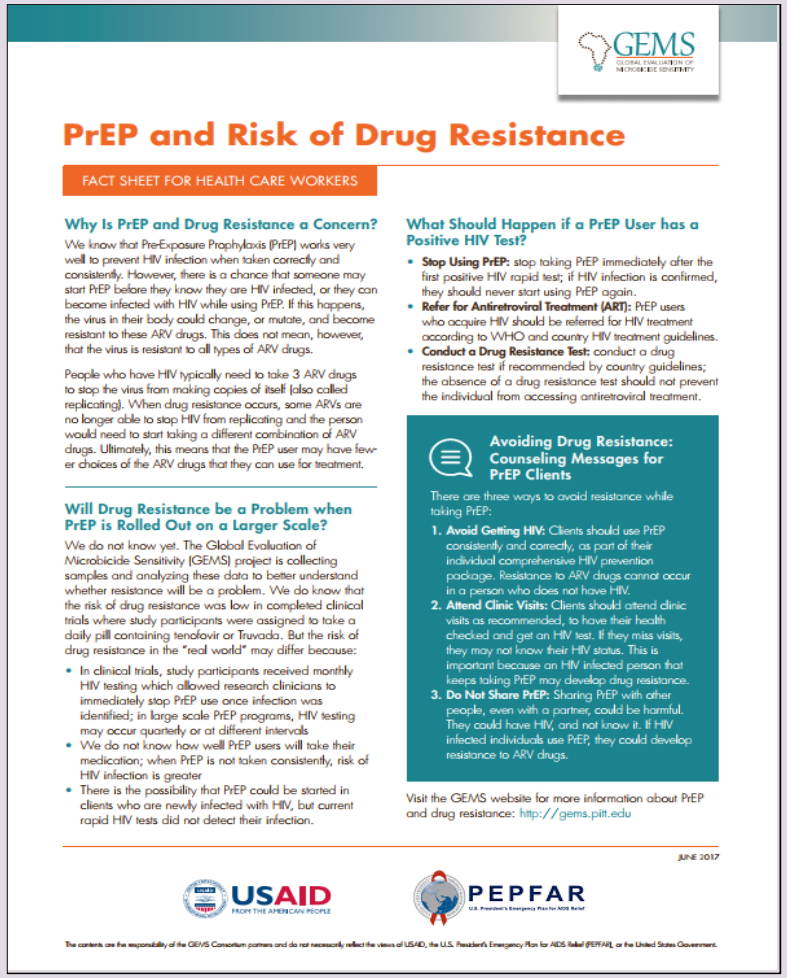

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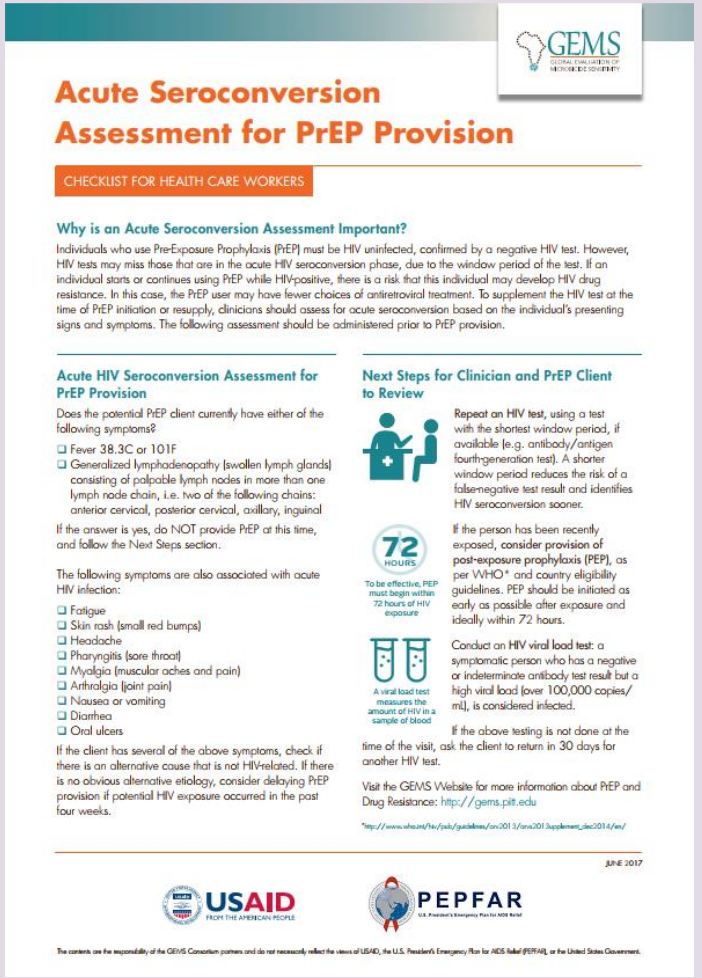

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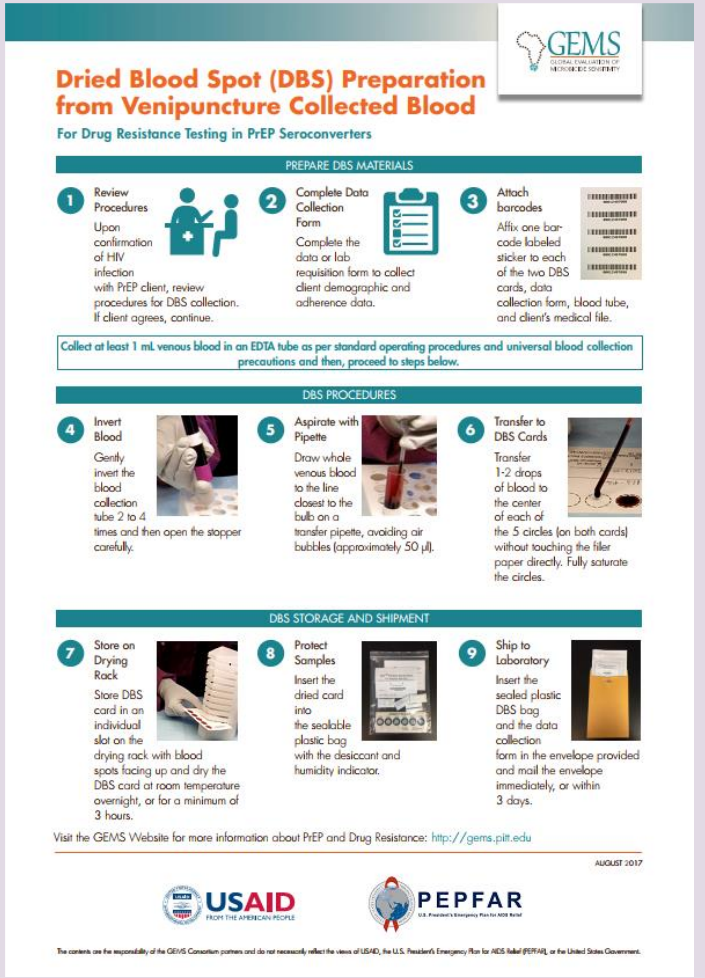
What are the steps needed to collect a sample and in what order?



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Dried Blood Spot (DBS) Preparation from Venipuncture Collected Blood

For Drug Resistance Testing in PrEP Seroconverters

PREPARE DBS MATERIALS

1. **Review Procedures** — Upon confirmation of HIV infection with PrEP client, review procedures for DBS collection. If client agrees, continue.
2. **Complete Data Collection Form** — Complete the data or lab requisition form to collect client demographic and adherence data.
3. **Attach barcodes** — Affix one bar-code labeled sticker to each of the two DBS cards, data collection form, blood tube, and client's medical file.

Collect at least 1 mL venous blood in an EDTA tube as per standard operating procedures and universal blood collection precautions and then, proceed to steps below.

DBS PROCEDURES

4. **Invert Blood** — Gently invert the blood collection tube 2 to 4 times and then open the stopper carefully.
5. **Aspirate with Pipette** — Draw whole venous blood to the line closest to the bulb on a transfer pipette, avoiding air bubbles (approximately 50 µl).
6. **Transfer to DBS Cards** — Transfer 1-2 drops of blood to the center of each of the 5 circles (on both cards) without touching the filer paper directly. Fully saturate the circles.

DBS STORAGE AND SHIPMENT

7. **Store on Drying Rack** — Store DBS card in an individual slot on the drying rack with blood spots facing up and dry the DBS card at room temperature overnight, or for a minimum of 3 hours.
8. **Protect Samples** — Insert the dried card into the sealable plastic bag with the desiccant and humidity indicator.
9. **Ship to Laboratory** — Insert the sealed plastic DBS bag and the data collection form in the envelope provided and mail the envelope immediately, or within 3 days.

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AUGUST 2017

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How do you create dried blood spots (DBS)?

gems.pitt.edu/sites/default/files/DBS Venipuncture_08.06.18.mp4

And much more!

- Template protocol
- Training slides
- M&E indicators
- Standard Operating Procedures
- HIV testing factsheet
- Policy brief on HIVDR modeling findings

Acknowledgements

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PEPFAR

CeSHHAR Zimbabwe

GOVERNMENT OF ZIMBABWE
Ministry of Health & Child Care

REPUBLIC OF KENYA
MINISTRY OF HEALTH

NASCOP

MINISTRY OF HEALTH
KINGDOM OF SWAZILAND

fhi360
THE SCIENCE OF IMPROVING LIVES

lvct health
healthy societies

innovating to save lives
Jhpiego
an affiliate of Johns Hopkins University

UCL

PZAT
PANGAEA ZIMBABWE AIDS TRUST

UNIVERSITY OF WASHINGTON
INTERNATIONAL CLINICAL RESEARCH CENTER

University of Pittsburgh

CLINTON HEALTH ACCESS INITIATIVE

psi

University of Cape Town · Universiteit van Kaapstad · iYunivesithi yaseKapa

University of the Witwatersrand
WITS RHI

KENYA MEDICAL RESEARCH INSTITUTE
KEMRI

World Health Organization

MTN
microbicide trials network

OPTIONS
OPTIMIZING PREVENTION TECHNOLOGY INTRODUCTION ON SCHEDULE

POWER
Prevention Options for Women Evaluation Research

CHARISMA
Agency in Relationships & Safer Microbicide Adherence

BARC
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Upcoming Sessions – Join us virtually at ICASA!

DEC 6 11:35 SAST

Pathway to PrEP: Expanding Access to HIV Prevention Options for Adolescent Girls and Young Women in Kenya through Integration with Family Planning Services

DEC 6 12:25 SAST

Meet the Ring: Product overview and provider/user perspectives on the dapivirine vaginal ring

DEC 6 13:20 SAST

Launching PrEP-it 2.0 – a multi-functional online tool for planning, monitoring, and evaluation of all forms of PrEP

DEC 6 14:15 SAST

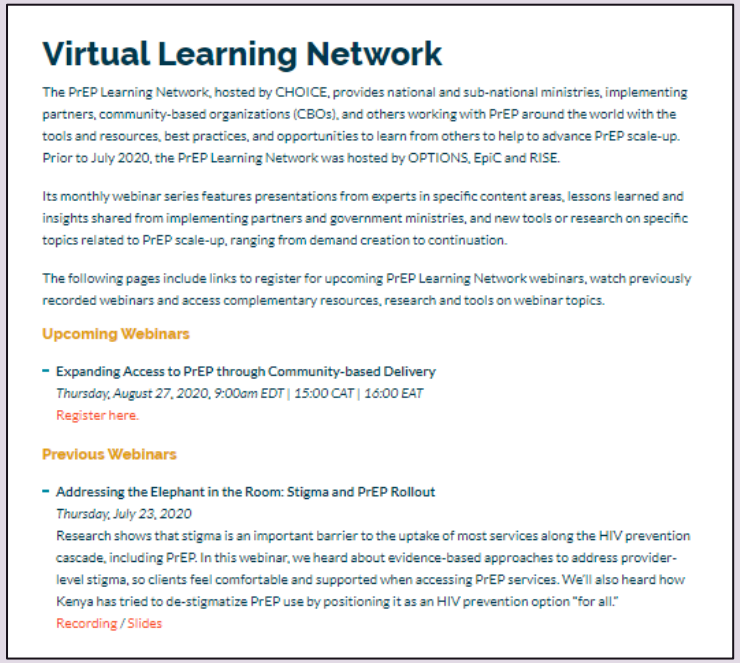
The Dapivirine Vaginal Ring: National planning experience from three countries

DEC 9 12:36 SAST

PrEP for Pregnant and Breastfeeding Women

Visit PrEPWatch

- All **webinars are recorded** and will be accessible on PrEPWatch within a week post-presentation date.
- Complementary **resources** will also be shared on PrEPWatch—including relevant research articles and tools.
- Registration for **upcoming webinars** is also located on PrEPWatch.



Virtual Learning Network

The PrEP Learning Network, hosted by CHOICE, provides national and sub-national ministries, implementing partners, community-based organizations (CBOs), and others working with PrEP around the world with the tools and resources, best practices, and opportunities to learn from others to help to advance PrEP scale-up. Prior to July 2020, the PrEP Learning Network was hosted by OPTIONS, EpiC and RISE.

Its monthly webinar series features presentations from experts in specific content areas, lessons learned and insights shared from implementing partners and government ministries, and new tools or research on specific topics related to PrEP scale-up, ranging from demand creation to continuation.

The following pages include links to register for upcoming PrEP Learning Network webinars, watch previously recorded webinars and access complementary resources, research and tools on webinar topics.

Upcoming Webinars

- **Expanding Access to PrEP through Community-based Delivery**
  Thursday, August 27, 2020, 9:00am EDT | 15:00 CAT | 16:00 EAT
  Register here.

Previous Webinars

- **Addressing the Elephant in the Room: Stigma and PrEP Rollout**
  Thursday, July 23, 2020
  Research shows that stigma is an important barrier to the uptake of most services along the HIV prevention cascade, including PrEP. In this webinar, we heard about evidence-based approaches to address provider-level stigma, so clients feel comfortable and supported when accessing PrEP services. We'll also heard how Kenya has tried to de-stigmatize PrEP use by positioning it as an HIV prevention option "for all."
  Recording / Slides

Visit www.prepwatch.org/virtual-learning-network for up-to-date information.

Thank You!