Updates on PrEP & PEP Guidelines

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CONTEXT

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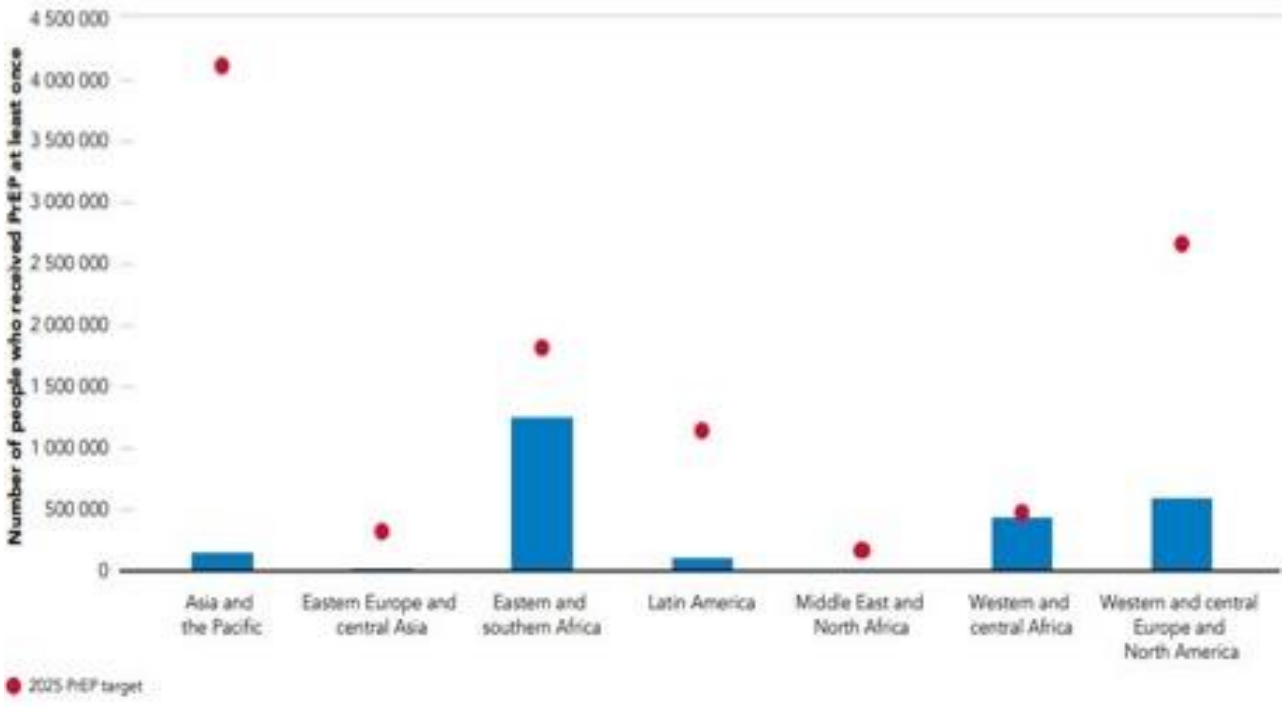
Full potential of PrEP not being recognized – target (2025) and users (2022) by the region

Except for one region, PrEP use trails very far behind the estimated need

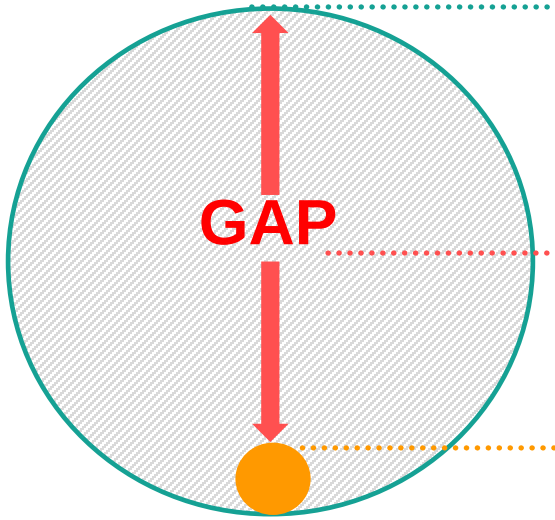
Figure 2.6 Number of people who received PrEP at least once during the reporting period, by region, 2022, and 2025 target



Source: UNAIDS Global AIDS Monitoring, 2023 (https://aidsinfo.unaids.org/); Stover J, Glaubius R, Teng Y, et al. Modeling the epidemiological impact of the UNAIDS 2025 targets to end AIDS as a public health threat by 2030. PLoS Med. 2021;18(10):e1003831.

Source: Prepared by www.aidsdatahub.org based on Global AIDS Monitoring; Information from national programmes; and National Commitments and Policy Instrument

PrEP Uptake in Asia-Pacific is too slow to impact the HIV epidemic



4 000 000+

2025 PrEP target

96%

to reach 2025 target

150 000+

estimated PrEP users in 2022

4% of the 4M target for 2025

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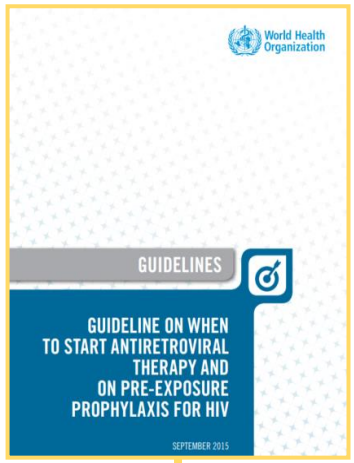
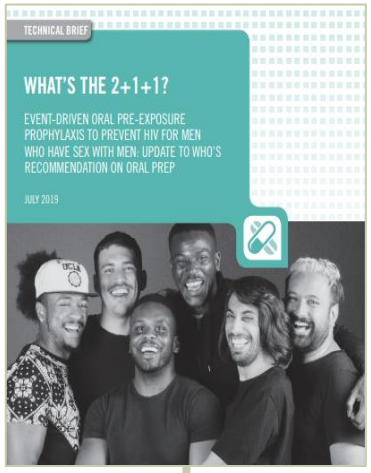
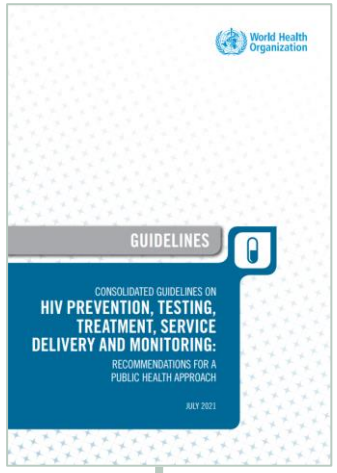
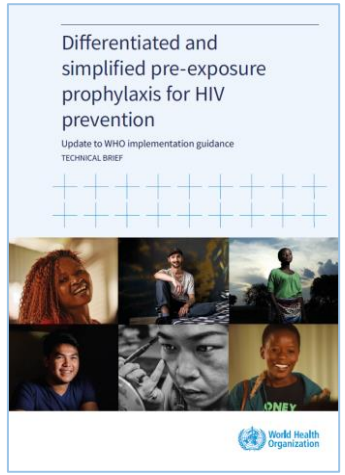
PrEP: Over a decade of integrating evidence into guidelines



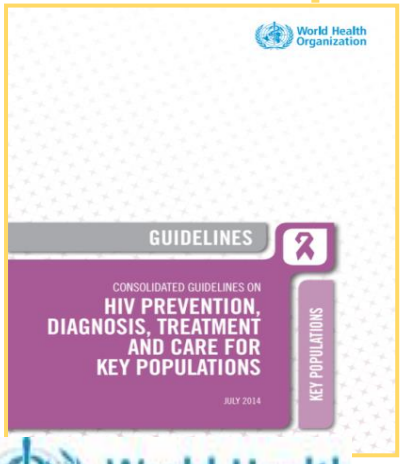


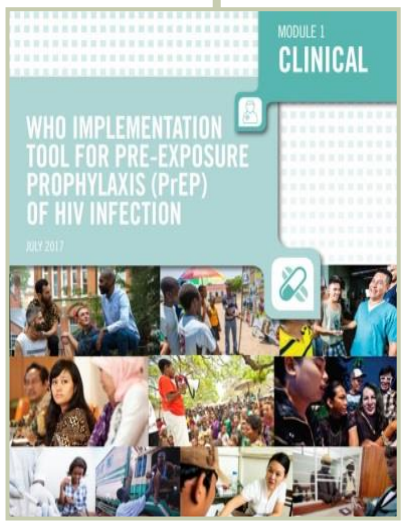




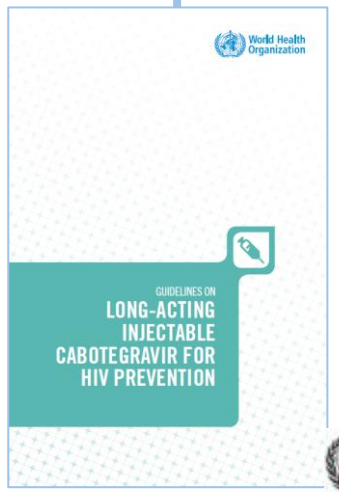
PrEP Implementation tool for HCP

2012 2014 2015/16 2017 2019 2021 2022 2023/24





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



Updated guidelines on PEP implementation

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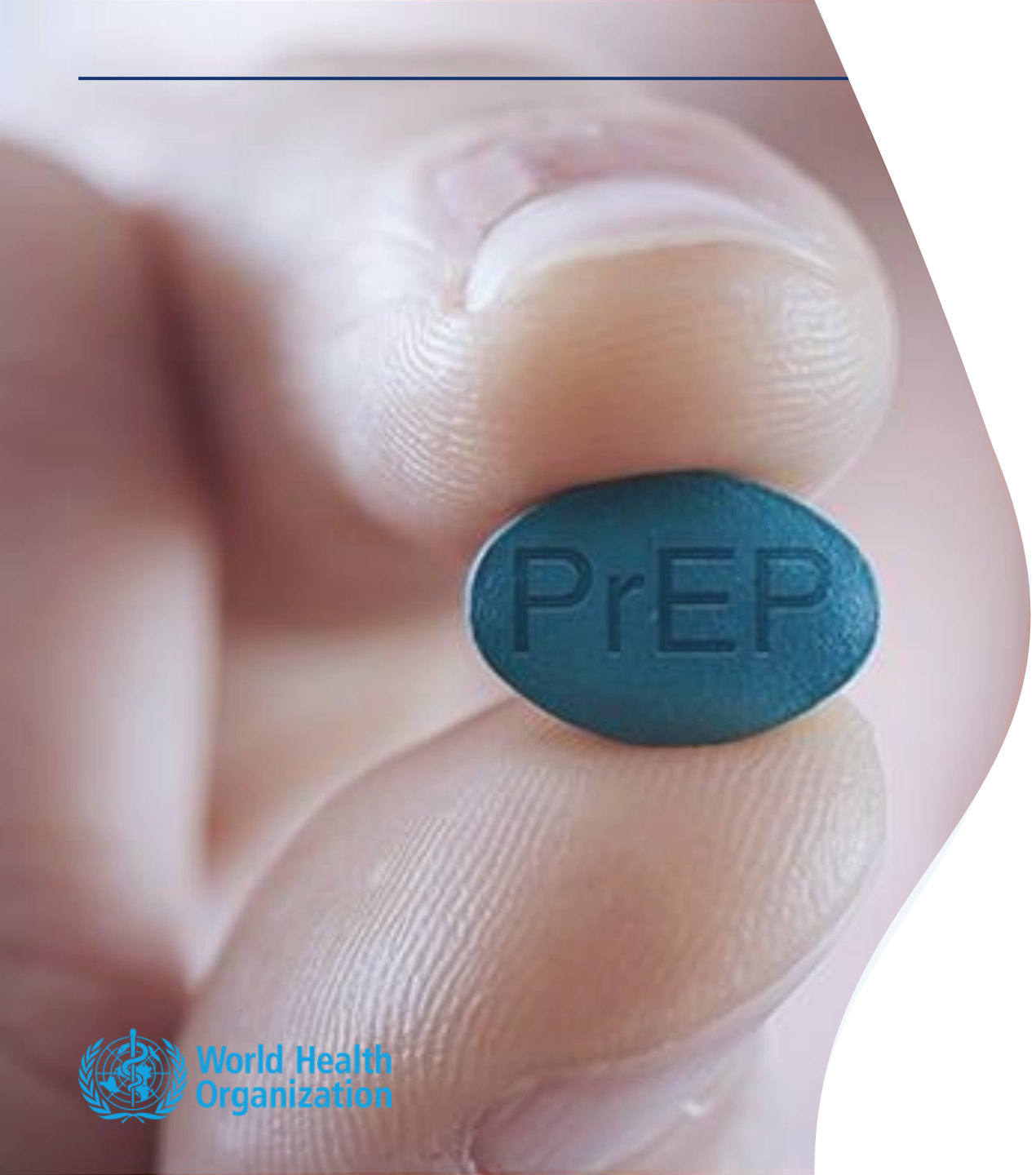

Updated guidance on oral PrEP

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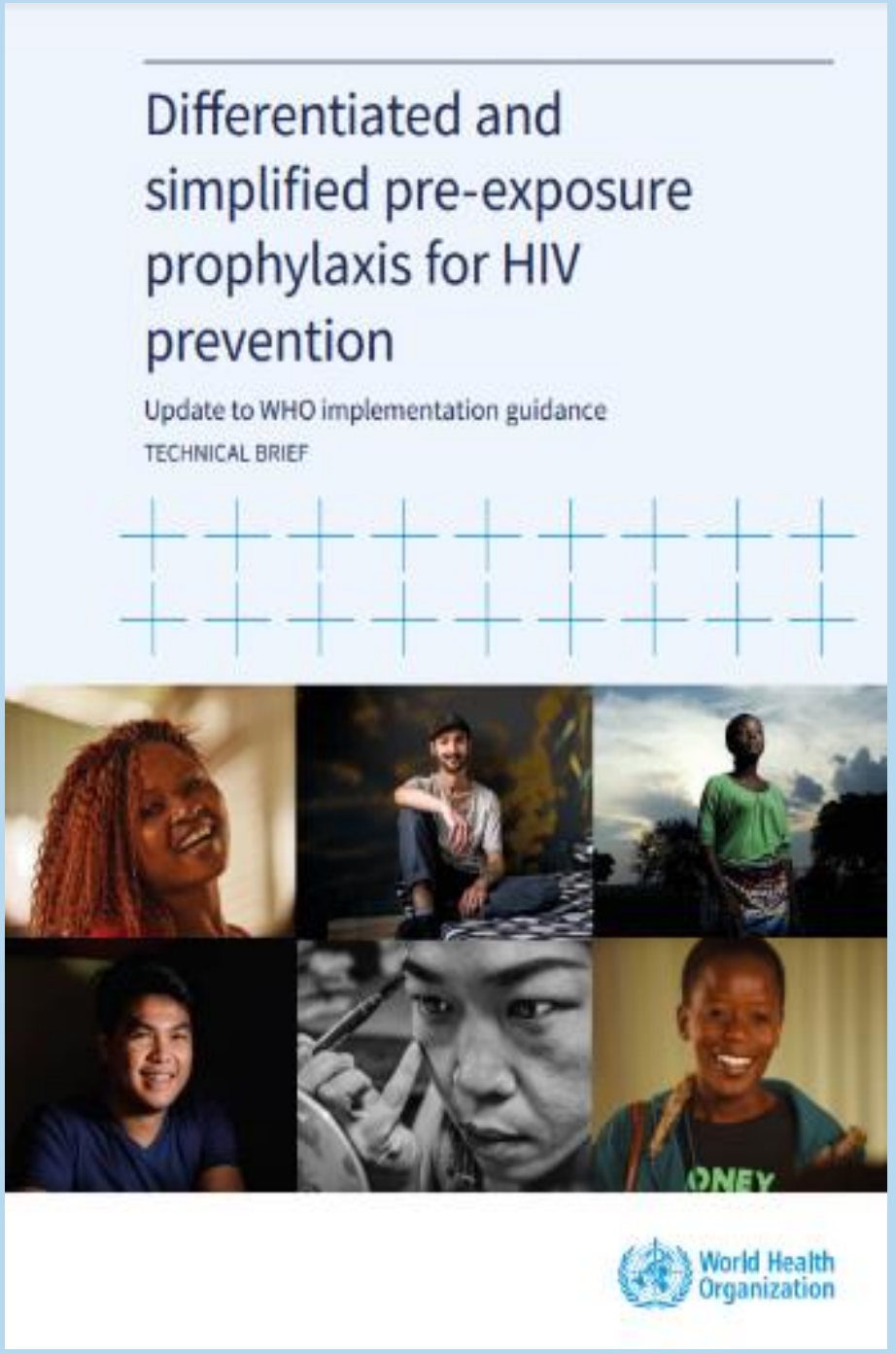
WHO Guidance for Simplified & Differentiated PrEP - 2022

1. PrEP and kidney function
2. PrEP and hepatitis B and C
3. HIV self-testing (HIVST) for PrEP
4. Starting, using, and stopping oral PrEP
5. Differentiated PrEP service delivery: WHEN, WHERE, WHO and WHAT to deliver

Focus of the technical brief is oral PrEP, with considerations for DVR and CAB-LA



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Oral PrEP and Kidney Function

Population	Initiation	Follow-up
Individuals <30 years with no kidney-related comorbidities	Optional	If no test at initiation or Cr CL ≥90 mL/min, follow-up is optional. If baseline test result is <90 mL/min, conduct follow-up screening every 6 to 12 months, if available.
Individuals 30–49 years with no kidney-related comorbidities	Optional/ Conduct once within 1 - 3 months of oral PrEP initiation, if available.	If baseline test Cr Cl ≥90 mL/min, further screening is optional until age 50 or kidney-related comorbidities develop. If the baseline test result is <90 mL/min, conduct follow-up screening every 6 - 12 months, if available.
Individuals 50 years and older **-OR-** **Individuals of any age with kidney-related comorbidities** **-OR-** **Individuals with previous creatinine screening of <90 mL/min**	Conduct once within one to three months of oral PrEP initiation, if available.	Conduct follow-up screening every six to 12 months, if available.

Waiting for kidney function test results should not delay starting PrEP

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Oral PrEP and Viral Hepatitis B and C

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

- **TDF-based daily or ED PrEP and the Dapivirine vaginal ring can be safely offered to persons with HBV or HCV infection.**

- **HBV and HCV testing should not be a barrier to PrEP initiation or use. Not a requirement for PrEP use.**

- **Hepatitis B**: Testing oral PrEP users for Hepatitis B once, at or within 1-3 months of PrEP initiation, is strongly encouraged where feasible.
  - If the test is positive, referral for management and treatment of hepatitis B
  - If the test is negative, complete the vaccination schedule

- **Hepatitis C**: A diagnostic test for HCV is strongly encouraged at or within 3 months of PrEP initiation and every 12 months thereafter where PrEP services are provided to those at high risk of HCV infection.
  - If the test is positive should be referred for further assessment and treatment for hepatitis C infection.

CAB-LA should not be initiated in people with advanced liver disease or acute viral hepatitis
It should be discontinued if hepatoxicity is confirmed.

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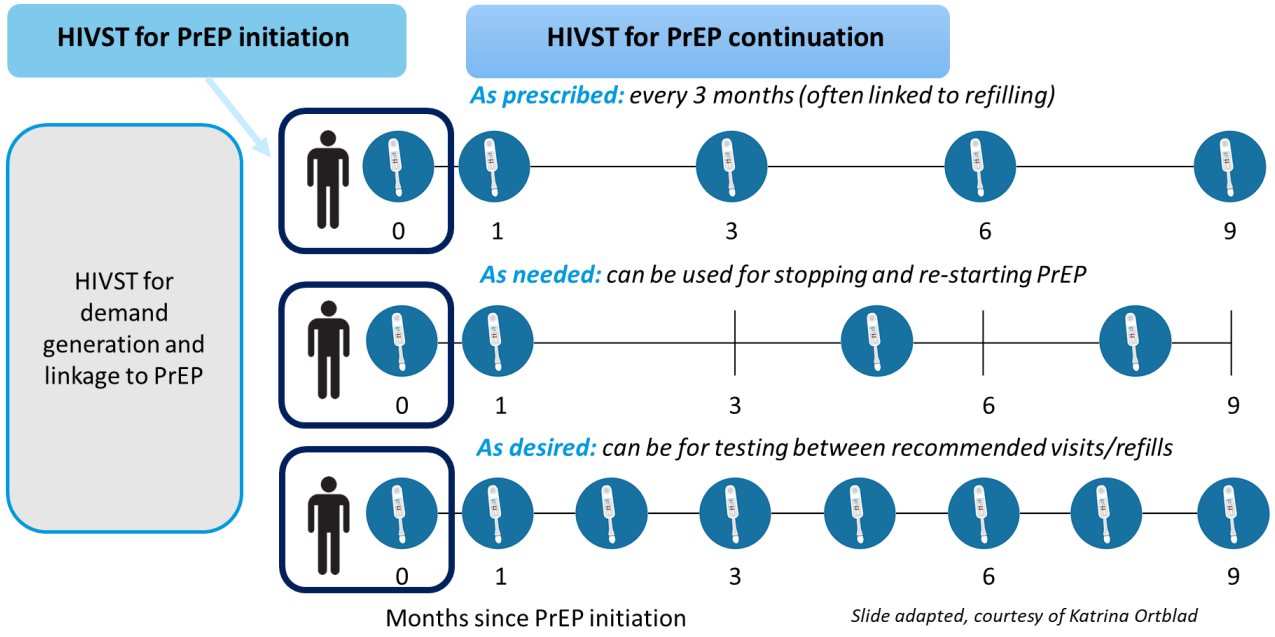
WHO recommends HIVST may be used for PrEP initiation, re-initiation and continuation

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

New recommendation:
HIV self-testing may be used to deliver pre-exposure prophylaxis, including for initiation, re-initiation and continuation (conditional recommendation, low certainty evidence)

- HIVST: additional testing choice, that can **complement existing HIV testing strategies** for **oral PrEP and DVR**, and may:
  - **reduce clinic visits**
  - be preferred for **convenience, privacy, self-managed care**
  - Improve uptake, persistence, and effective use of PrEP
- **Role of HIVST with CAB-LA is currently unclear.**
- Programmes can consider HIVST for oral PrEP and DVR users when starting, re-starting, and/or continuing PrEP
  - **Clear and concise messaging**
- Where HIVST-supported PrEP delivery models reduce clinic visits, important that **comprehensive services** to address the diverse needs of PrEP users still provided
- HIVST can be used to increase confidence in oral PrEP by showing that your HIV status remains negative during PrEP use.
- **Operational research on HIVST-supported PrEP delivery, e.g. optimizing delivery, understanding impact, and costs.**

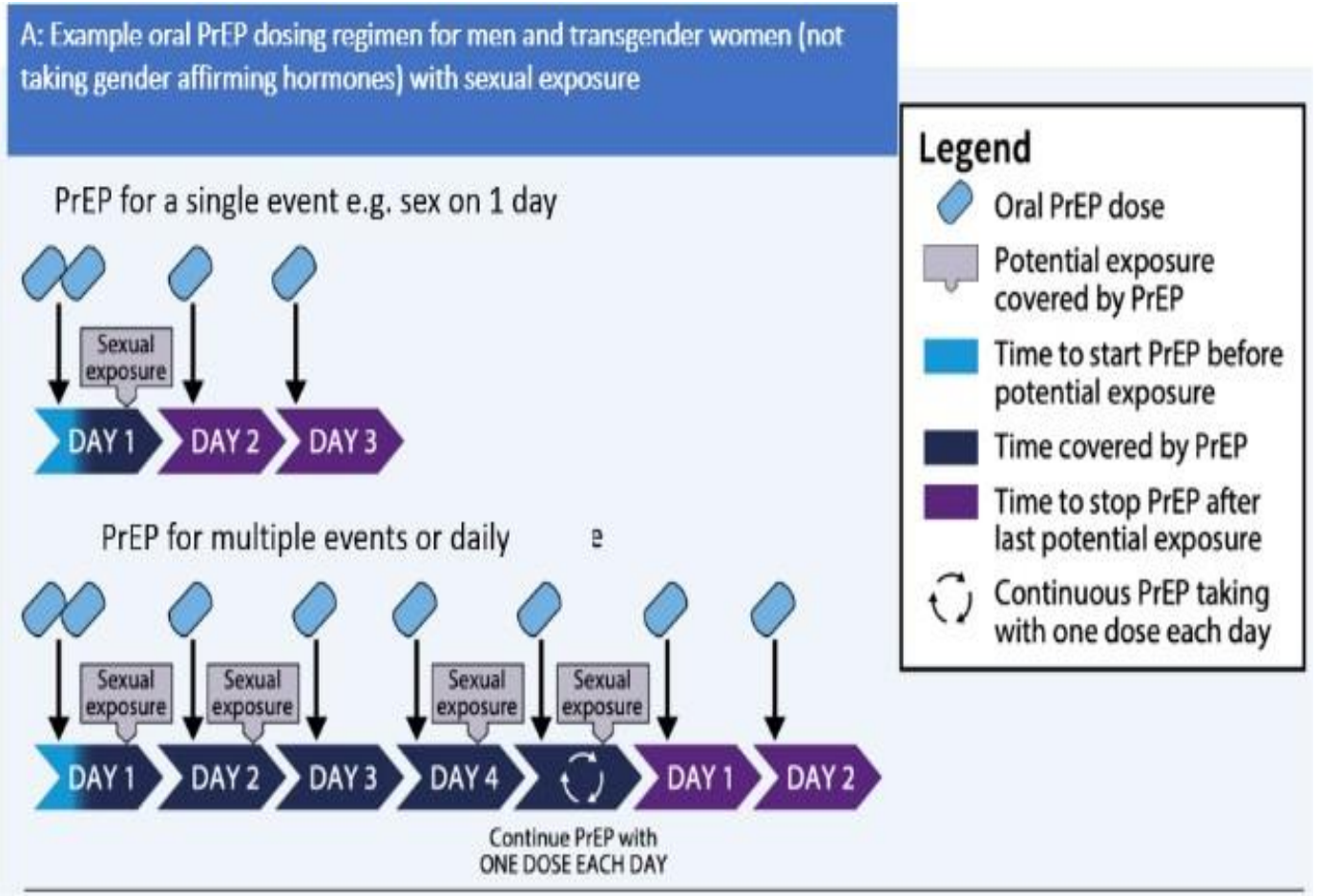


Role for HIVST with CAB-LA currently unclear

https://www.who.int/news/item/22-07-2023-who-recommends-optimizing-hiv-testing-services

Oral PrEP dosing regimen: All men* and transgender women not taking gender-affirming hormones

- **How do you take it?**
  - **Starting: Two doses** 2–24 hours before potential exposure
  - **Using:** Continue to take **one dose** per day while having potential exposures
  - **Stopping:** Stop using **two days** after the last potential exposure
- **What else?**
  - This dosing is **only** effective for sexual exposure
  - This is **only** for TDF based PrEP
  - Hepatitis B infection is **not** a contraindication
  - Can be used for one event **or** continued use



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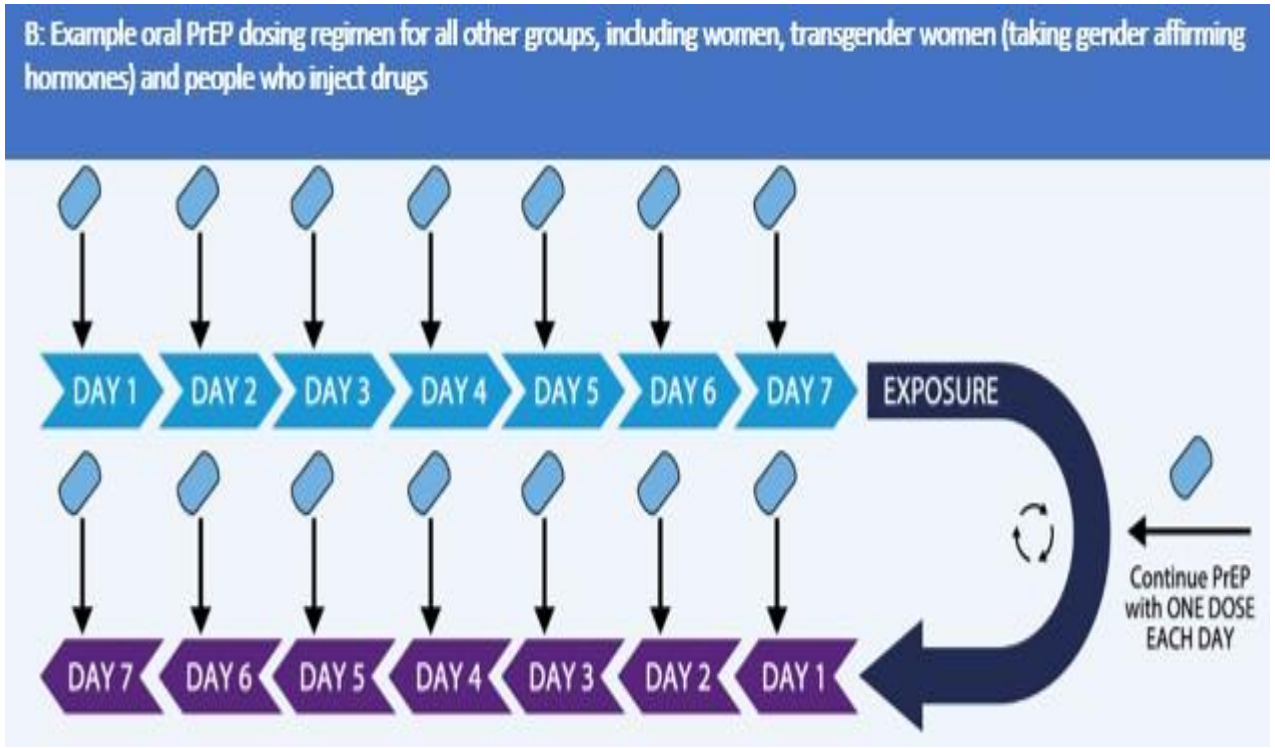
*The term men applies to cisgender men and trans and gender diverse people assigned male at birth.

Oral PrEP dosing regimen: Everyone else

(e.g. women**, transgender men, transgender women using gender affirming horomnes, people who use drugs, and people who do not gender identify

- **How do you take it?**
  - **Starting: One dose** per day for **7 days** before potential exposure
  - **Using:** Continue to take **one dose** per day while having potential exposures
  - **Stopping: One dose** per day for **7 days** after last potential exposure

- **What else?**
  - Is effective for sexual exposure and exposure through injecting drug use



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**The term women applies to cisgender women and trans and gender-diverse people assigned female at birth.

Initiation, continuation & stopping of oral PrEP among different populations

Population	Starting oral PrEP	Using oral PrEP	Stopping oral PrEP
Cisgender men (includes MSM, MSW) and transgender women who are not taking estradiol-based (gender-affirming) hormones (Hepatitis B is not a contra-indication)	Take a double dose 2–24 hours before potential sexual exposure (ideally closer to 24 hours before potential exposure)	One tablet daily	Take one dose per day until two days after the day of the last potential sexual exposure
Cisgender women (includes Female Sex Workers), transgender men and transgender women taking estradiol-based hormone	Take one dose daily for seven days before potential exposure	One tablet daily	Take one dose daily for seven days after the last potential sexual exposure
Persons using oral PrEP to prevent HIV acquisition from injecting drug use (PWID)			

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Differentiated services for PrEP support scale-up, access & acceptability

Differentiated PrEP services:

- Person- and community-centred (i.e. adapted to needs & preferences)
- Support making services more accessible and acceptable
- May improve uptake, persistence, effective use, and health system efficiency
- **Task sharing/shifting** makes the best use of available human resources
- **Supported by:**
  - Appropriate clinical oversight and referral pathways
  - Logistics systems
  - Adequate infrastructure
  - Integrated data systems

Building block	PrEP initiation, initial follow-up (0–3 months), and re-initiation			PrEP continuation (3+ months)	
	Initiation	Initial follow-up (0–3 months) (if required)	Re-initiation after discontinuation	PrEP refill	Follow-up
Where: Service location (e.g., primary health care facility, community setting, virtual setting)	Locations for PrEP assessment and initiation	Locations for initial follow-up	Locations for PrEP re-initiation	Locations where PrEP refills can be collected	Locations where follow-up services will be provided
Who: Service provider (e.g., physician, nurse, pharmacist, peer)	Service provider/s authorized to assess for and initiate PrEP	Service providers who can carry out initial follow-up visit/s	Service provider/s authorized to re-initiate PrEP	Service provider/s who can dispense PrEP refills	Service provider/s who conduct follow-up
When: Service frequency (e.g., monthly, every 3 months)	Timing of PrEP assessment and initiation	Timing of initial follow-up	Timing of PrEP re-initiation	Frequency of PrEP refill visits (length of supply)	Frequency of follow-up services
What: Service package (including HIV testing, clinical monitoring, PrEP prescription and dispensing, and comprehensive services)	Service package for PrEP assessment and initiation	Service package at initial follow-up	Service package for PrEP re-initiation	Service package with PrEP refill	Service package with follow-up

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Integration of STI and PrEP services: an opportunity

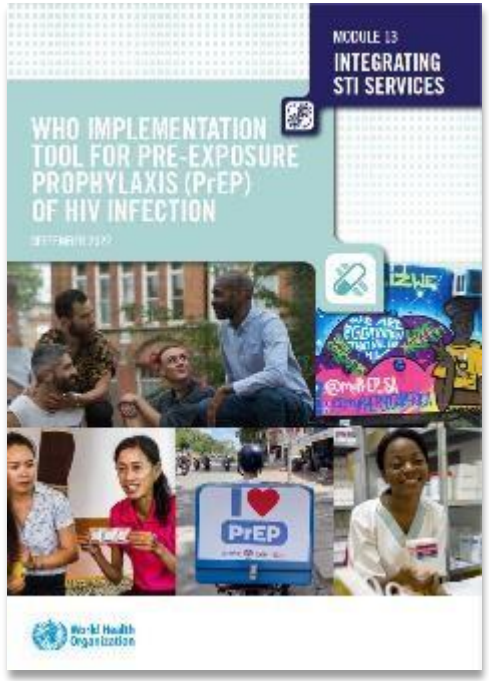

Fig. 4.

Schematic summary of optimal STI services and case management for people who access HIV PrEP

Information
- Modes of transmission and cure
- Prevention
- Self-recognition of signs and symptoms
- Places to seek care
- Informing partners in case of infection

Jump to section

Counselling
- Information sharing
- Support for vaccination, testing, treatment completion and linkage to care
- Assist notifying partners, including EPT
- Prompting for STI symptoms and signs at first and follow-up visits

Counselling to change behaviours is ineffective to decrease HIV/STI incidence

Jump to section

Prevention

Provision of:
- female condoms
- male condoms
- lubricants
- vaccination for hepatitis A and B, and HPV when appropriate

Jump to section

Testing

Provision of:
- rapid testing for syphilis or syphilis/HIV
- confirmatory test for syphilis
- provider-collected or self-sampling from all three anatomical sites for NG/CT testing
- molecular testing for NG/CT

Jump to section

Partners services
- Offer options to notify and treat sexual partners, including EPT

Treatment of sexual partners prevents reinfection and interrupts the chain of transmission

Jump to section

Clinical consultation
- Assure private space and client consent
- Take sexual history
- Conduct physical examination for STI manifestations on:
  - Lymph node
  - Inside the mouth
  - Genital and anal areas
  - Skin (include palms and soles)
  - Speculum exam and anoscopy, if feasible

Jump to section

Treatment and follow-up
- Etiologically treat common STIs or, if not possible, use syndromic approach
- Follow-up persistent symptoms
- Assess for treatment failure (adherence, reinfection, AMR, other STIs)

Jump to section

Referrals and linkages
- If possible, refer complicated conditions
- Have a pre-established mechanism to assure linkage to care and to provide feedback to the referral facility

Jump to section

Acronyms

CT *Chlamydia trachomatis*
EPT Expedited partner treatment
HPV Human papillomavirus
NG *Neisseria gonorrhoeae*

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New PrEP products: DVR and CAB-LA

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Dapivirine vaginal ring (DVR)

Important to have choices

Recommendations (2021)

The dapivirine vaginal ring may be offered as an additional prevention choice for women[a] at substantial risk of HIV infection as part of combination prevention approaches *(conditional recommendation, moderate-certainty evidence).*

[a] For the recommendation on the dapivirine vaginal ring, the term women applies to cisgender women, meaning women assigned female at birth. There is no research at this time to support the dapivirine vaginal ring for other populations.

Source: *Guidelines: updated recommendations on HIV prevention, infant diagnosis, antiretroviral initiation and monitoring (12).*

- **Women-initiated, easy-to-use, silicone vaginal ring** containing dapivirine (NNRTI)
- Dapivirine is released slowly into the vagina over 1 month (continuous protection if left in situ)
- **The risk of HIV-1 infection is reduced 24 hours after ring insertion**
- Current evidence suggests that oral daily PrEP, when taken as prescribed, has greater efficacy for HIV prevention than DVR
    - High safety, rare adverse effects and no interactions with contraceptives
    - Phase III trials demonstrate safety and efficacy (~30%)
    - Open-label studies suggest higher efficacy (~50 – 70%)
    - Safety and efficacy during pregnancy and lactation
- Regulatory approval or import authorization in 11 several African countries
- Acceptability and feasibility assessment underway in 4 Asia-Pacific countries (UNAIDS, funded by DFAT)
- This is only for cisgender women

26 January 2021 | Departmental news

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

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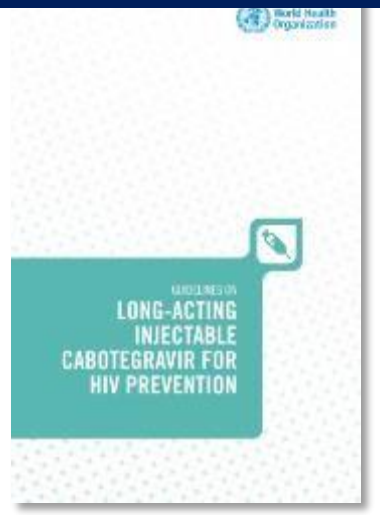
Long-acting injectable cabotegravir (CAB-LA)

Important to have choices

Long-acting injectable cabotegravir may be offered as an additional prevention choice for people at substantial risk of HIV infection, as part of combination prevention approaches *(conditional recommendation; moderate certainty of evidence)*.



- Intramuscular injection every 8 weeks (with first two, 4 weeks apart)
- Phase III trials (HPTN 083 and 084) showed high efficacy
- Values and preferences from potential users show CAB-LA provides an opportunity to address adherence related challenges of oral PrEP
- Regulatory approval in 13 countries* including Philippines and Malaysia
- Voluntary license agreement with Medicine Patent Pool for generic manufacturing

Outstanding critical issues

- Drug resistance
- Safety during pregnancy and breastfeeding
- HIV testing strategies, frequency
- Limited representation of some KP (TGM, SW)

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*https://viivhealthcare.com/content/dam/cf-viiv/viivhealthcare/en_GB/pdf/cab-prep-wwrs-27oct2023-for-external-use.pdf

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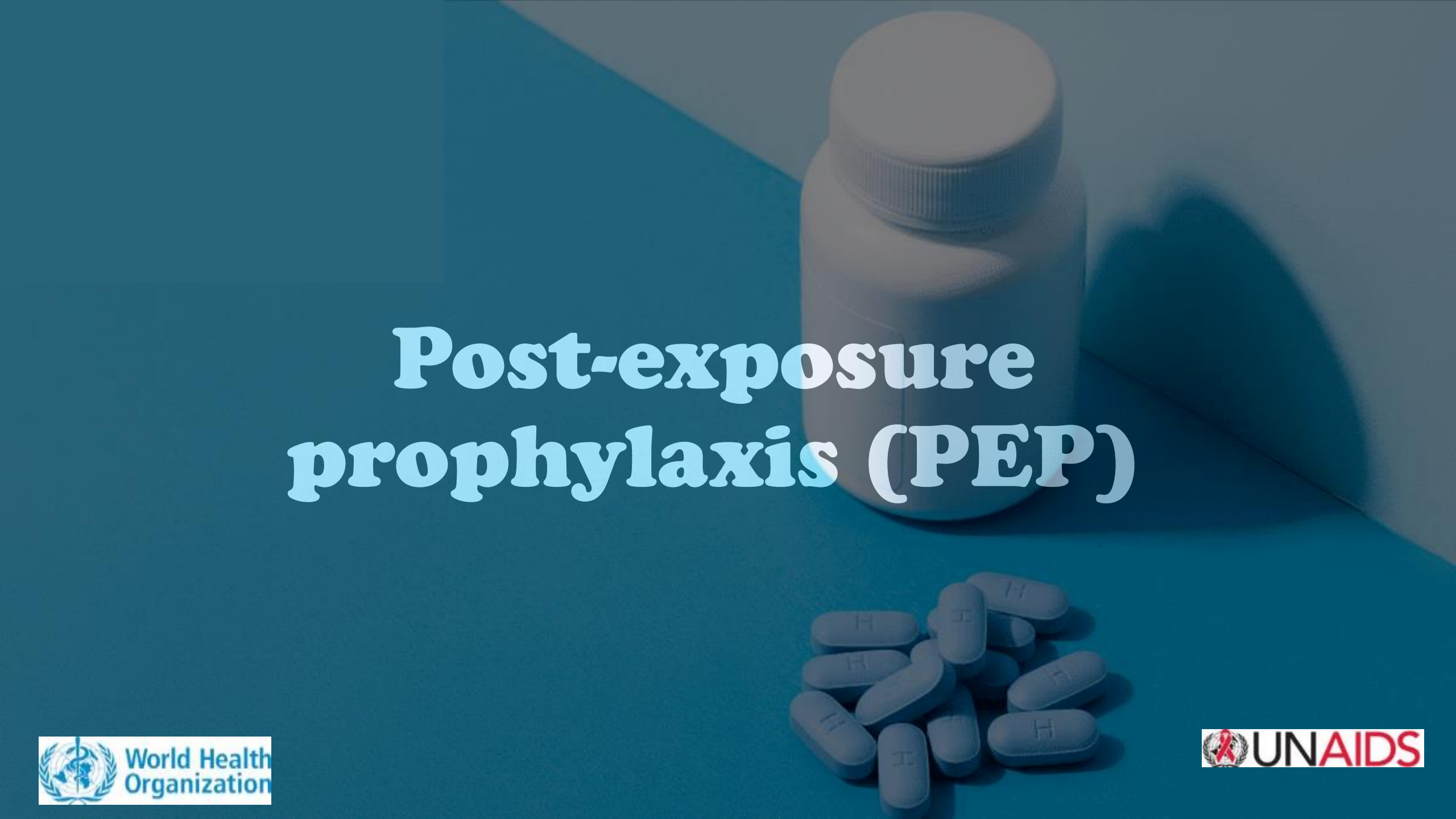
Post-exposure prophylaxis (PEP)



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Post-exposure prophylaxis (PEP)

Recommendations (2016)

Overall

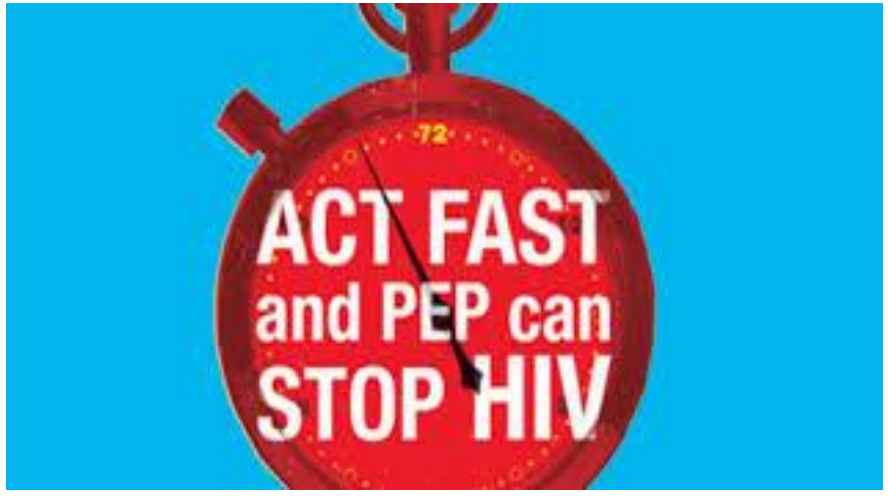
An HIV PEP regimen with two ARV drugs is effective, but three drugs are preferred *(conditional recommendation, low-certainty evidence).*[a]

Adults and adolescents

TDF + 3TC (or FTC) is recommended as the preferred backbone regimen for HIV PEP *(strong recommendation, low-certainty evidence).*[a]

DTG is recommended as the preferred third drug for HIV PEP *(strong recommendation, low-certainty evidence).*

When available, ATV/r, DRV/r, LPV/r and RAL may be considered as alternative third drug options for PEP *(conditional recommendation, low-certainty evidence).*



- PEP should be offered and initiated as early as possible for all individuals with exposure that has the potential for HIV transmission, preferably within 72 hours

Issues with use of PEP in HIV prevention

- Knowledge about PEP is low in groups affected by HIV
- Limited and medicalized access
- PEP is under-utilized
- PEP is often started late
- Completion rate is sub-optimal

To improve the completion rate

- Adherence support and a full 28-day course of medication during the first clinic visit should be provided

When thinking about PEP

- Think about STIs and emergency contraception
- Using a “PEP contact” to think about longer-term prevention, incl. **PEP to PrEP**

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PEP and PrEP

- Transitioning from PEP to PrEP
  - Some people on PEP may have repeated exposure to HIV
  - Discuss with clients if they may benefit from transitioning to PrEP
  - Clients who complete the 28-day PEP regimen and wish to use PrEP can start PrEP without a gap with a negative HIV test result
  - Eligibility and management remain the same as other PrEP clients
  - Immediate transition to PrEP is preferable for individuals with ongoing exposure to HIV.

- Transitioning from PrEP to PEP
  - Clients who take PrEP as prescribed don't need PEP
  - If PrEP is not used as directed or stopped, there may be a risk of acquiring HIV if exposed, PEP can be an important HIV prevention strategy during these periods.
  - To assess if PEP is needed, consider the type of exposure, timing, time since PrEP was last taken or # the of missed PrEP doses

DSD options for PEP is gaining attention

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SUMMARY

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What's next?

WHO PrEP guideline updates

- Incorporate all three WHO-recommended PrEP products
- Includes simplified and differentiated PrEP guidance
- Includes simplified testing and dosing
- Includes new recommendations on HIV testing
- Promotes integrated service delivery

PEP: simplified and differentiated guidance

- Under utilized prevention option (difficulties accessing it in many countries)
- Strengthen PEP to PrEP
- Investigating the package and looking at differentiated models

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Thank you!

Thanks to the **WHO HHS Testing, Prevention, and Populations** team and **UNAIDS-RST** (Brigitte Quenum) for contributions to this presentation.

Contact the WHO PrEP team for questions or comments:

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WHO's global work on PrEP:
https://www.who.int/teams/global-hiv-hepatitis-and-stis-programmes/hiv/prevention/pre-exposure-prophylaxis
WHO Global PrEP Network webinars:
https://www.who.int/groups/global-prep-network

- **WHO technical brief on PrEP implementation guidance:**
- https://www.who.int/publications/i/item/9789240053694
- **WHO guidelines on CAB-LA:**
- https://www.who.int/publications/i/item/9789240054097
- **WHO consolidated key population guidelines:**
- https://www.who.int/publications/i/item/9789240052390
- **WHO consolidated HIV guidelines:**
- https://www.who.int/publications/i/item/9789240031593
- **WHO PrEP Implementation Tool:**
- https://www.who.int/tools/prep-implementation-tool
- **STI module of WHO PrEP Implementation Tool:**
- https://www.who.int/publications/i/item/9789240057425
- **Further updates to WHO PrEP Implementation Tool expected in 2024** (starting with provider module)
- **Updated PEP Guideline in 2024**

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