Newer PrEP Options: The Future of HIV Prevention

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Newer PrEP Options: The Future of HIV Prevention

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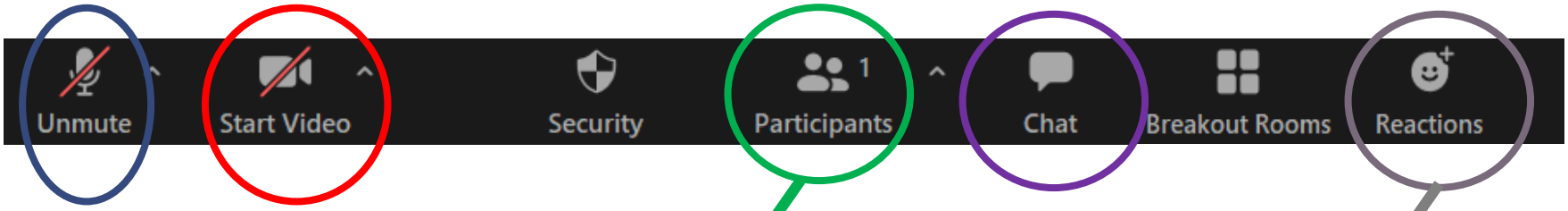

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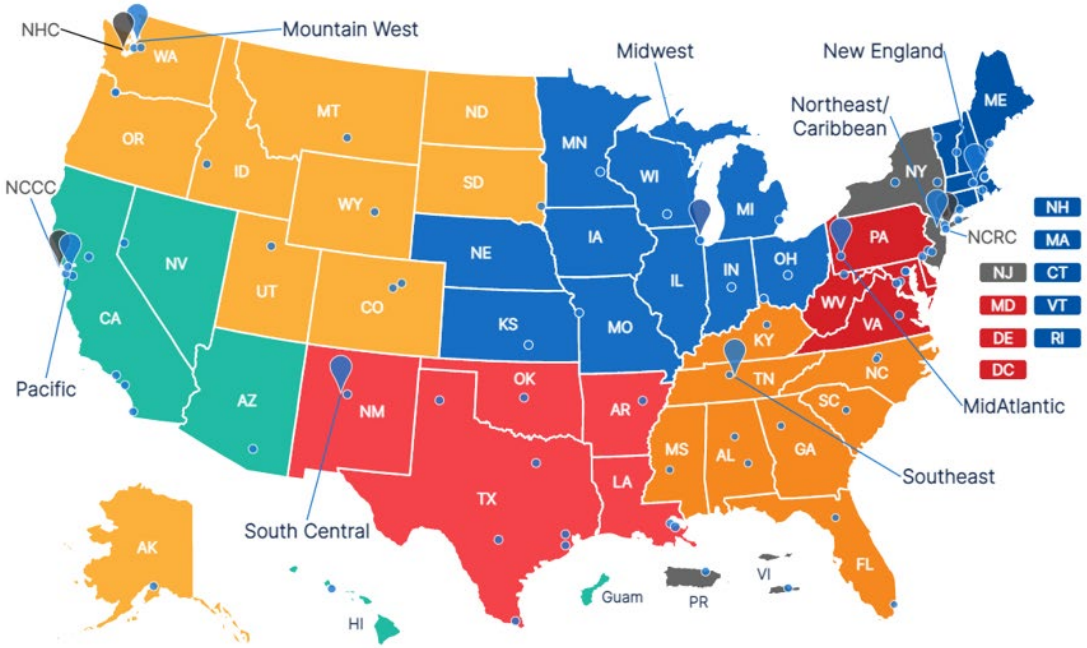
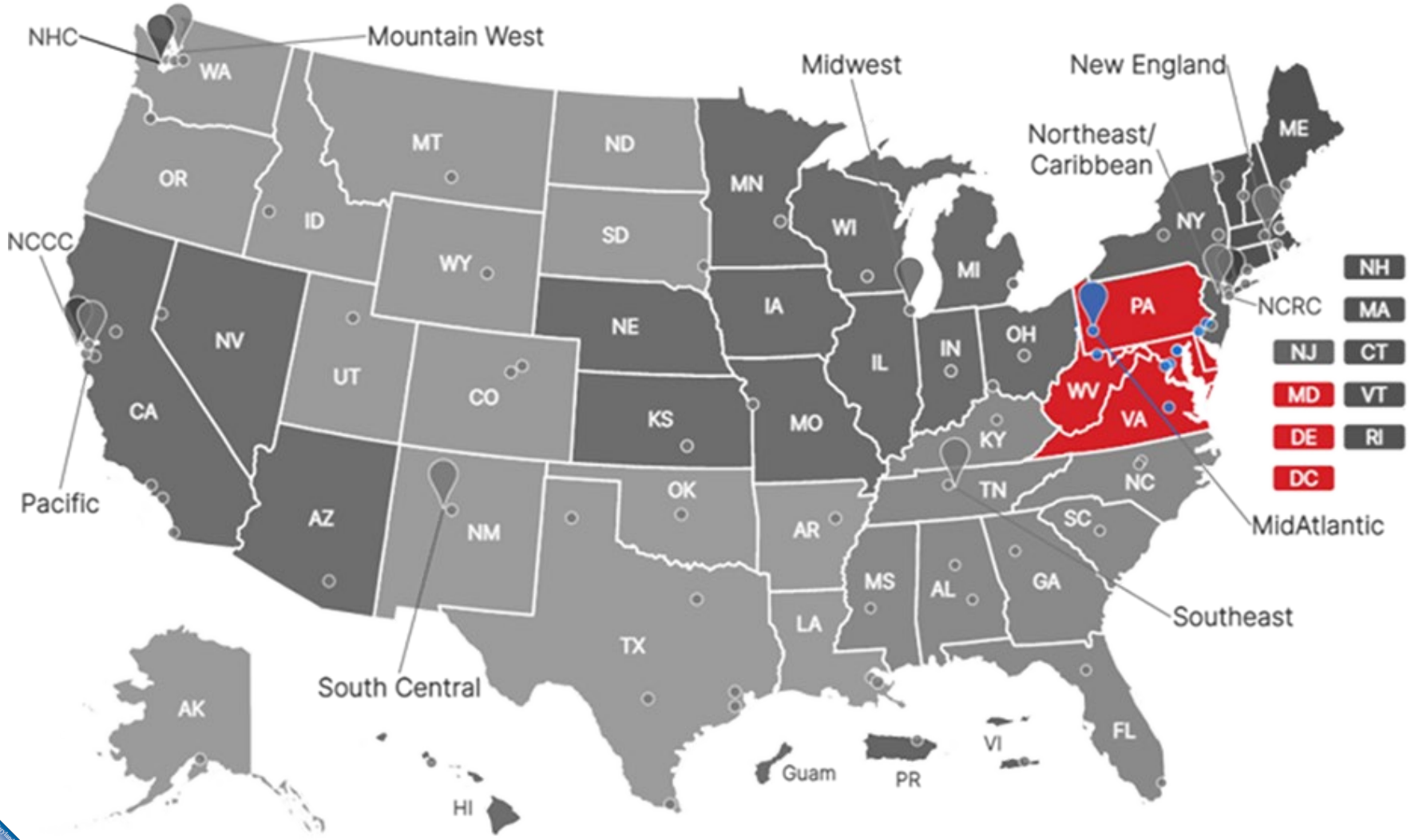
Nationwide AETC Network

AETC Program Regions and Centers



AETC AIDS Education & Training Center Program

MidAtlantic AIDS Education and Training Center



AETC Program – National Centers and National HIV Curriculum

- **National Coordinating Resource Center –** serves as the central web-based repository for AETC Program training and capacity building resources; its website includes a free virtual library with training and technical assistance materials, a program directory, and a calendar of trainings and other events. Learn more: https://aidsetc.org/
- **National Clinician Consultation Center** – provides free, peer-to-peer, expert advice for health professionals on HIV prevention, care, and treatment and related topics. Learn more: https://nccc.ucsf.edu
- **National HIV Curriculum** – provides ongoing, up-to-date HIV training and information for health professionals through a free, web-based curriculum; also provides free CME credits, CNE contact hours, CE contact hours, and maintenance of certification credits. Learn more: www.hiv.uw.edu

Planning Disclosure

The staff involved with the planning of today's event **do not** have any conflicts of interest to disclose.

Speaker Disclosure

- Speaker's Bureau: ViiV Healthcare

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- Please contact the coordinator of the event or maaetc@pitt.edu with any questions.

Today's Objectives

As a result of attending this program, participants should be able to:

1. Describe the newest options for biomedical HIV prevention
2. Review clinical trial findings of new PrEP formulations in development
3. Incorporate quality improvement measures with your team to increase PrEP implementation at your site

Agenda

- Background
  - HIV Prevention
  - Currently Available PrEP Options
- PrEP Formulations in Development
- PrEP Best Practices
- Self-Assessment Questions
- Q&A

Background

HIV Prevention

- Approximately 1.2 million people living in the US are at high risk for HIV and could benefit from comprehensive HIV prevention strategies, including PrEP
  - Only 36% were accessing PrEP in 2022
  - 2/3 of those who could benefit are African-American or Latino
- ~93% of all PrEP users are men
  - 14x more male PrEP users than female
  - Men account for ~81% of all new HIV diagnoses
- ~64% of all PrEP users were 25 to 44 years old
  - This age group represents ~54% of all new HIV diagnoses
- The South accounts for more than 50% of new HIV diagnoses, yet only accounts for 30% of all PrEP users

Kaiser Family Foundation, 10/9/2024, The HIV/AIDS Epidemic in the United States: The Basics
https://www.kff.org/hivaids/fact-sheet/the-hiv-aids-epidemic-in-the-united-states-the-basics/

Why HIV Prevention Matters

- Approximately 1.2 million people in the US have HIV
  - About 13% don't know it and need testing
- In 2022, an estimated 31,800 new HIV infections occurred in the United States
  - The highest rates of new diagnoses continue to occur in the South
  - In 2022, there were 24,886 people living with HIV in Virginia
  - In 2022, 834 people were newly diagnosed with HIV
  - Rates are much higher in D.C.
- PrEP is simple and safe to prescribe
  - In 2022, there were 9,785 PrEP users in Virginia

https://www.hiv.gov/hiv-basics/overview/data-and-trends/statistics, 8/15/2024

PrEP Overview

- Three medications FDA-approved for PrEP
  - TDF 300 mg/FTC 200 mg = Truvada®
  - TAF 25 mg/FTC 200 mg = Descovy®
  - Injectable CAB 200 mg/mL = Apretude® (Approved after the latest guidelines were released but still addressed in the guidelines)
- Taken correctly, PrEP can be up to 99% effective in preventing HIV transmission through sex
  - Reduces risk by at least 74% in injection drug users (IDU)
  - Much less effective when not taken as prescribed
- PrEP does not prevent other STIs and should be part of a comprehensive prevention approach, including consistent condom use
- Takes 1-3 weeks to reach maximum protection
  - For receptive anal sex → 7 days of daily use
  - For receptive vaginal sex & IDU → 21 days of daily use
  - The time from initiation of CAB to maximal protection against HIV-1 infection is unknown

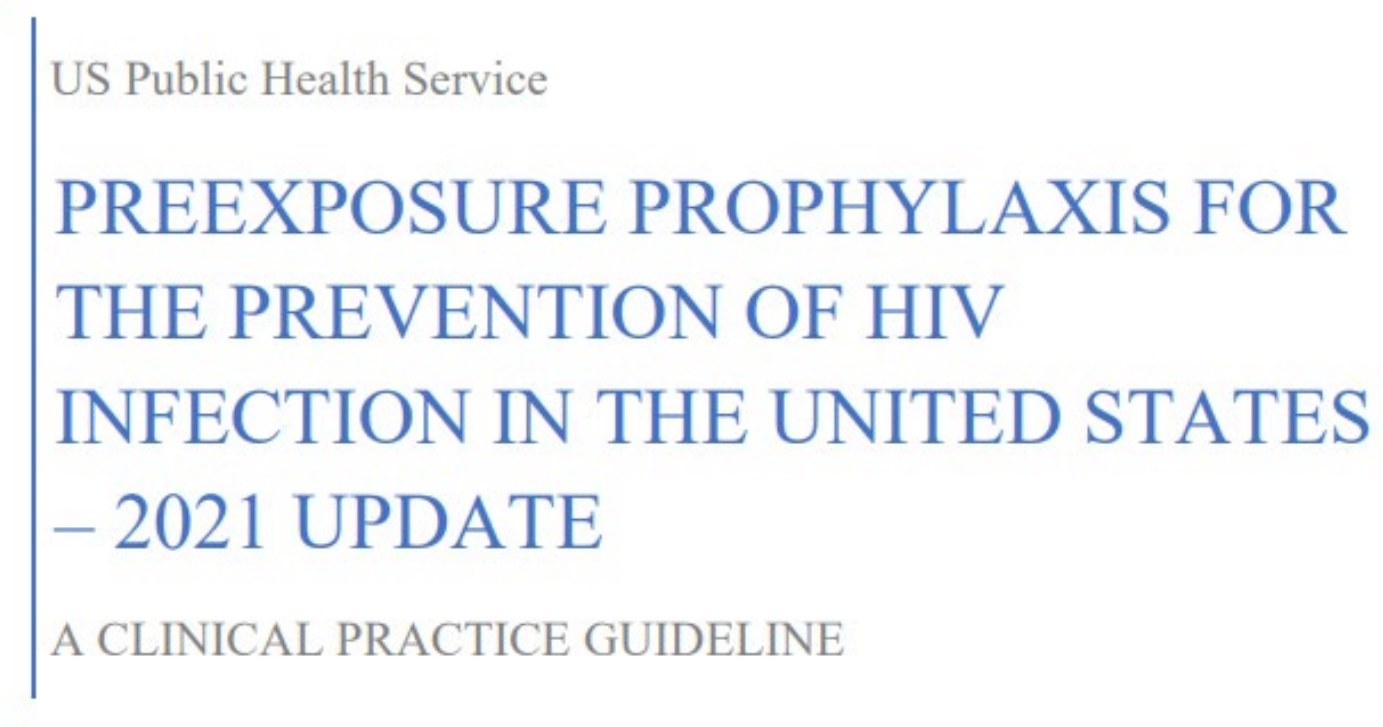
Who will benefit?

- The first step in prescribing PrEP is identifying individuals at risk for HIV
  - This requires taking a detailed sexual and drug use history

- PrEP should be considered in patients with one or more of the following characteristics:

STI diagnosis or request for testing for STIs	Inconsistent or infrequent condom use	Recent nPEP usage
Request for HIV testing	Partner with HIV infection	Transactional sex
Sexual activity in high-prevalence areas or networks	Multiple partners or in a non-monogamous relationship	Use of drugs or alcohol, especially in relation to sexual activity
Use of IV drugs	Incarceration of individual or their partner	

Guidelines on Prescribing PrEP



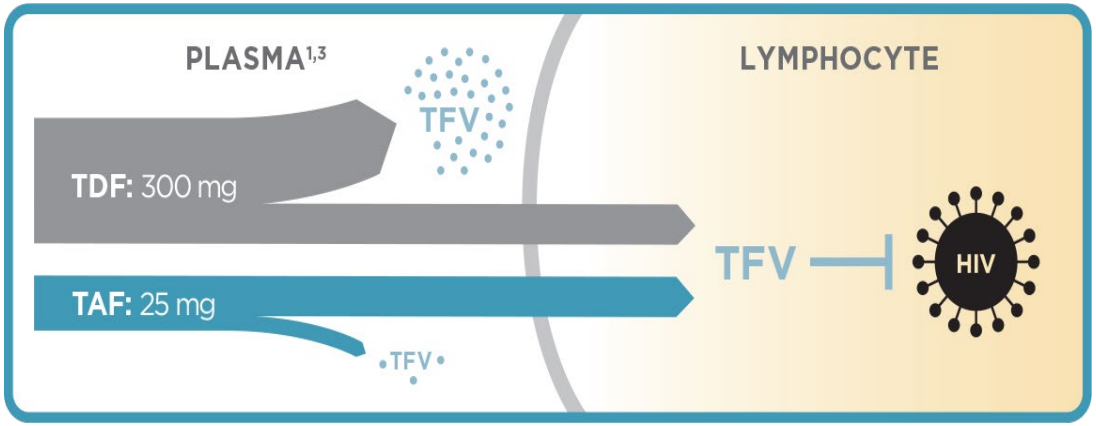
https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf

Currently Available Oral PrEP Medications

FTC/TDF	FTC/TAF
200 mg emtricitabine + 300 mg TDF	200 mg emtricitabine + 25 mg TAF
1 tablet by mouth once daily	1 tablet by mouth once daily
Approved for all patients (male or female)	Approved for men and transgender women (not cisgender women)
CrCl >60 mL/min	CrCl >30 mL/min
Pro-drug that is converted to TFV in the plasma → more renal and bone toxicity	Pro-drug that is converted to TFV in the lymphocyte → less renal and bone toxicity
Brand and generic available	Brand only

Tenofovir Formulations

Tenofovir disoproxil fumarate (TDF)	Tenofovir alafenamide (TAF)
Truvada®, Atripla®, Stribild®, Complera®	Descovy®, Genvoya®, Odefsey®
Greater risk for kidney and bone toxicity	Lower risk for kidney and bone toxicity
Lower risk of metabolic side effects	Higher risk of metabolic side effects



Alternative Dosing Schedules

	DAILY PrEP	PrEP 2-1-1
Who can use it?	Anyone	People having anal sex. Not shown to be effective for receptive vaginal or front hole sex
When to use it?	Every day	Every time you have sex
Works best	If you take one pill every day	If you take it with every partner
Effectiveness	Extremely effective when used daily	Extremely effective when used every time you have sex
Taking pills	Take one pill every day	Requires planning and reminders to take 2-1-1 doses
Missing doses	Not advised, but may be OK if you take at least 4 or more pills per week for anal sex	Important not to miss doses
Side effects	Same as PrEP 2-1-1	Same as daily PrEP
Planning	No planning needed around sex	Need at least 2 hours of notice to take pills before sex
Hepatitis B	Can take daily with chronic hepatitis B	Potentially dangerous to use with chronic hepatitis B
Cost (assuming you pay for meds)	May be more expensive than PrEP 2-1-1	May be less expensive than daily PrEP
Hormones (testosterone & estradiol)	Effective with hormone use	May be less effective with hormone use

A note on FDA review: Once-daily Truvada® is currently the only FDA-approved strategy for PrEP. There is an additional strategy called PrEP 2-1-1 for anal sex, where you take Truvada® only when you have sex. This additional strategy has not been reviewed by the FDA, as Gilead, the pharmaceutical company, has not submitted this strategy for FDA approval. However, there is substantial published evidence this dosing strategy will work, requiring less lifetime exposure to Truvada® compared to once-daily dosing. The San Francisco Department of Public Health, the World Health Organization (WHO), the New York City Department of Public Health, and the International AIDS Society in the USA (professional medical society) endorse PrEP 2-1-1.

San Francisco AIDS Foundation.

Medications for PrEP

- Three medications FDA-approved for PrEP
  - TDF 300 mg/FTC 200 mg
  - TAF 25 mg/FTC 200 mg
  - Injectable CAB 200 mg/mL -- Approved *after* the latest guidelines were released but still addressed in the guidelines

Cabotegravir

- Cabotegravir 200 mg/mL
  - First and only long-acting, injectable for PrEP
    - Not the same product as Cabenuva (cabotegravir/rilpivirine) which is approved for HIV treatment
  - Cabotegravir is an INSTI structurally similar to dolutegravir
  - Cabotegravir was shown to be 69-90% more effective than TDF in their initial Phase III studies
    - Likely due to lack of perfect adherence to TDF
  - Administered ventrogluteally by a healthcare professional
  - Can be acquired through specialty pharmacy or buy and bill
    - Insurance coverage varies
      - Some plans require medical billing rather than pharmacy billing
    - Either way, medication is shipped directly to prescribers' office rather than to the patient or a retail pharmacy
  - Oral lead in is optional

. Cabotegravir for the prevention of HIV-1 in women: results from HPTN 084, a phase 3, randomised clinical trial. 2022 May 7;399(10337):1779–1789. doi: 10.1016/S0140-6736(22)00538-4 https://pmc.ncbi.nlm.nih.gov/articles/PMC9077443/

Guidelines on Prescribing Injectable PrEP

- Initially given as an injection ventrogluteally one time every month for the first 2 months
  - Then continue as an injection every 2 months
  - May prescribe 1 oral cabotegravir tablet 1 time a day for 1 month (at least 28 days) to assess tolerability
- Counsel on risk reduction
- Monitor closely
  - Every 2 months (i.e. each injection): HIV test, risk assessment, side effects, and adherence counseling (i.e. missed dose instructions)
  - Every 3-6 months: STI screening
  - Every 6-12 months: Screen creatinine level

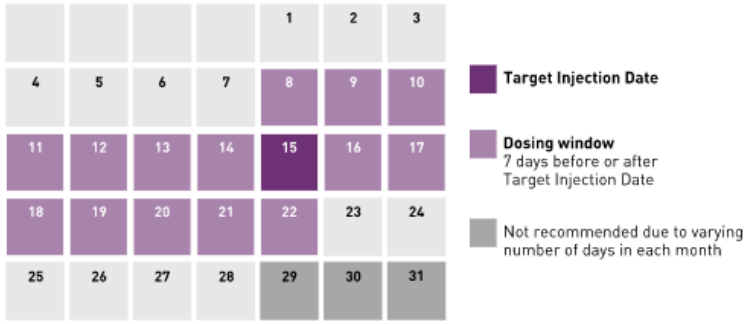
https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2017.pdf

Guidelines on Prescribing Injectable PrEP

- Dosing schedule:
  - ➢ Before starting: Confirm HIV Negative Status
  - ➢ Initiation: Dose in Month 1, Month 2
  - ➢ Continuation: Dose Month 4, Month 6, Month 8

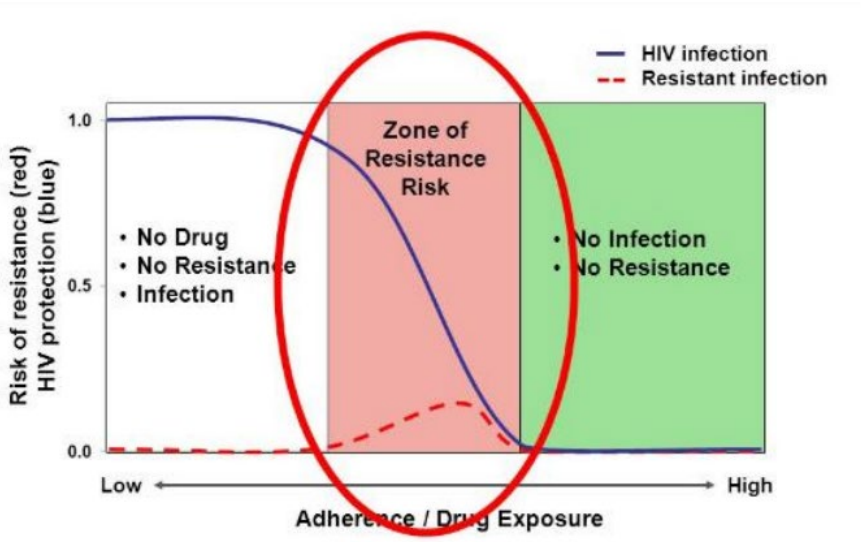
    – Example: Injection #1 in January, Injection #2 in February, Injection #3 in April, Injection #4 in June

- Dosing window: +/- 7 days
  - – Give on same date of each month (i.e. always the third of the month)



Guidelines on Prescribing Injectable PrEP

- Discontinuing CAB
  - CAB can delay seroconversion by 6-17 weeks
  - Change to oral medication within 8 weeks of last injection and continue for, ideally, 12 months



Special Populations

- Pregnant women?
  - Yes, PrEP can be used in pregnant women who have a partner with HIV
    - Only TDF at this time
    - Probably fine with TAF or CAB but not enough data
- Women (who are not pregnant)?
  - Yes, TDF or CAB may be used
  - TAF does not have enough data but theoretically there is no problem with using it in female patients
- Adolescents?
  - Yes, all three PrEP drugs are approved for use by adolescents who weigh at least 75 lbs (35 kg)
- Lots of other medications?
  - Oral options: no major drug interactions, including with contraceptives or hormone replacement therapy
  - CAB contraindicated with some anticonvulsants but otherwise not many drug interactions

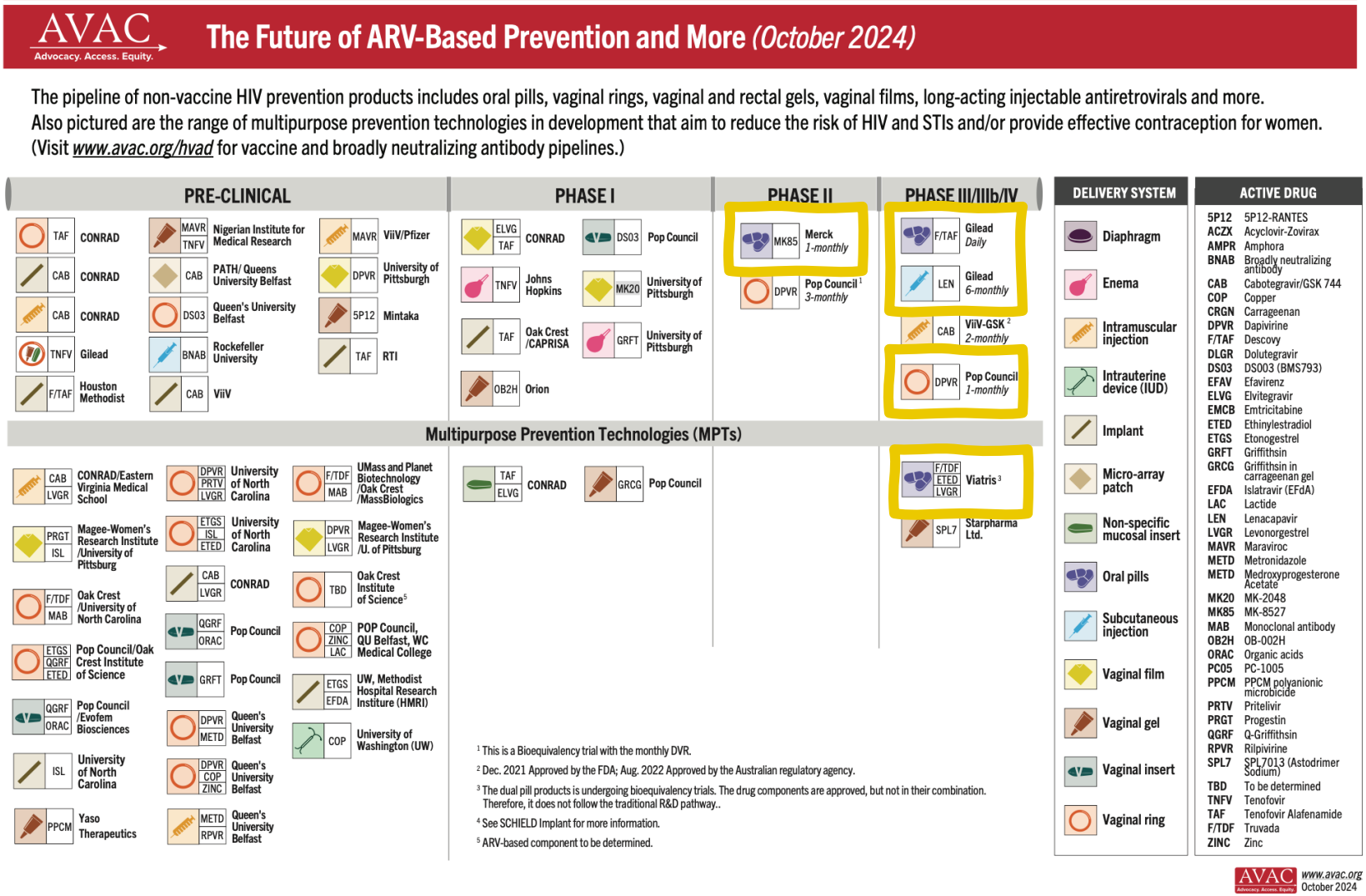
PrEP Quick Guide, National Clinical Consultation Center, University of California, San Francisco, 1/31/2023, https://nccc.ucsf.edu/clinical-resources/prep-resources/prep-quick-guide/

Counseling Points

- Adherence, adherence, adherence!!!
  - Missed dose instructions
    - If monthly injections are missed or delayed by >7 days and oral therapy has not been administered, if ≤2 months since first injection: Administer cabotegravir 600 mg injection as soon as possible for every other month injections
- Time to efficacy
  - No specific data from the drug company, however we know that it reaches adequate concentrations within 7 days
- Still need to use condoms to protect from other STIs
  - ONE Brand are specifically FDA approved for anal sex
- S/S of an acute HIV infection, such as: Acute flu-like symptoms (fatigue, fevers, headache, body aches), rash

PrEP Formulations in Development

The HIV Prevention Pipeline



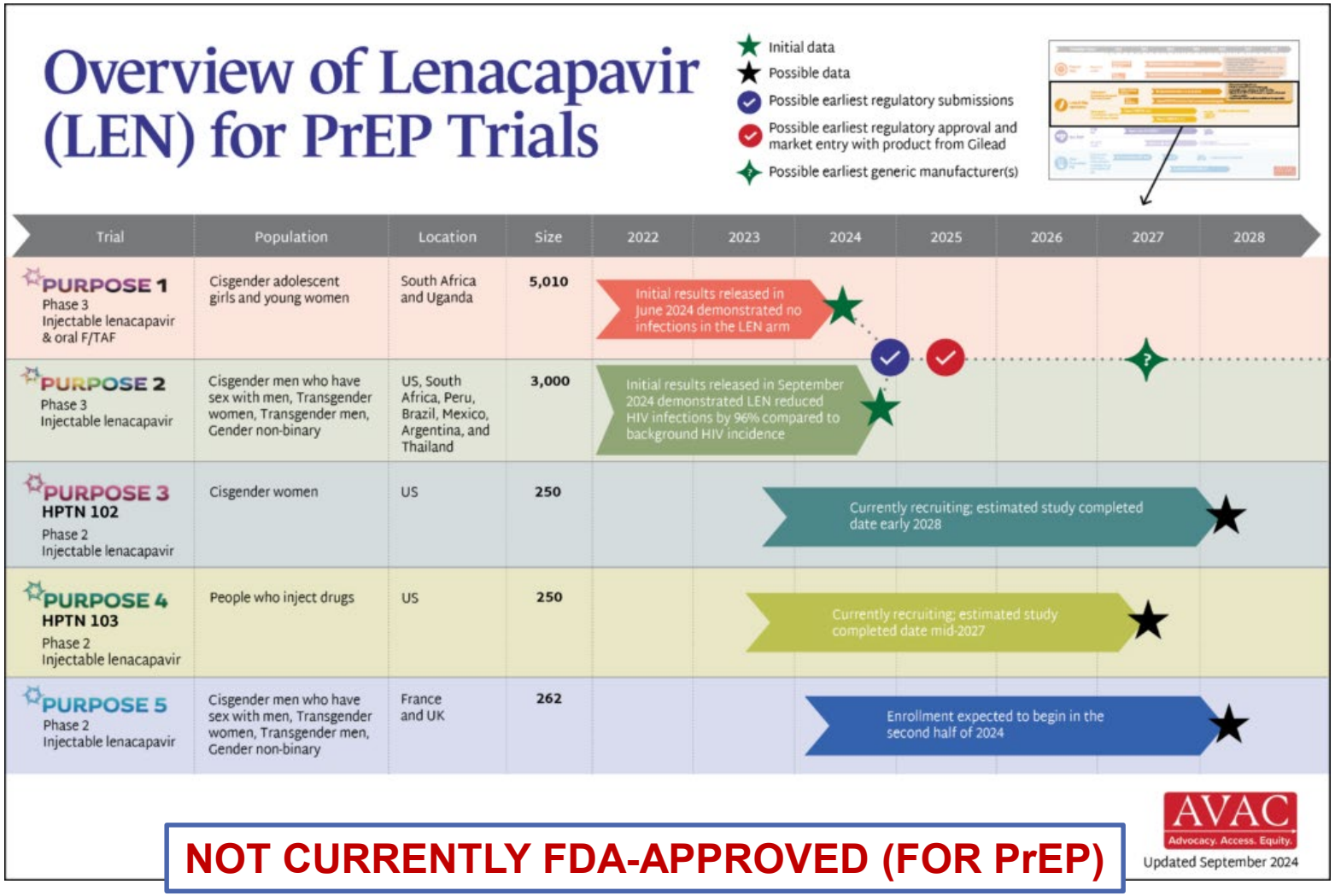
Lenacapavir (LEN)

- Already FDA approved for salvage therapy in HIV treatment under brand name Sunlenca®
- Administered every 6 months as two subcutaneous injections given on the same visit in the abdomen
- Studied for use as prevention in two large Phase III clinical trials: PURPOSE 1 and PURPOSE 2
  - Submitted to FDA for approval for PrEP on December 19, 2024
  - Was previously granted by the FDA for PrEP Breakthrough Therapy Designation
- Three smaller Phase II clinical trials (PURPOSE 3, PURPOSE 4, and PURPOSE 5) are investigating safety and efficacy in populations not included in PURPOSE 1 or PURPOSE 2

NOT CURRENTLY FDA-APPROVED (FOR PrEP)

https://pubmed.ncbi.nlm.nih.gov/39046157/ and https://pubmed.ncbi.nlm.nih.gov/39602624/

Lenacapavir (LEN)



NOT CURRENTLY FDA-APPROVED (FOR PrEP)

PURPOSE 1

- Conducted among approximately 5,000 cisgender women in South Africa and Uganda
- Testing the efficacy of both LEN for PrEP and the daily pill emtricitabine/tenofovir alafenamide (F/TAF) in preventing HIV
- In June 2024, the trial was unblinded after meeting its primary endpoint of superiority to oral PrEP (TDF/FTC) and background HIV incidence
- Scheduled to run until July 2027
- The first Phase III clinical trial to include pregnant and lactating people from the start—which could make it easier to get approval for use in this population if found to be effective and safe

NOT CURRENTLY FDA-APPROVED (FOR PrEP)

PURPOSE 2

- Conducted among 3,000 men who have sex with men, gay men, transgender men, transgender women, and gender non-binary people in Argentina, Brazil, Mexico, Peru, Puerto Rico, South Africa, Thailand, and the USA
- In September 2024, the trial was unblinded after meeting its primary endpoint of superiority to oral PrEP (TDF/FTC) and background HIV incidence
- Scheduled to run until April 2027

NOT CURRENTLY FDA-APPROVED (FOR PrEP)

Lenacapavir (LEN)

- NOT currently FDA approved, but anticipated to be reviewed early 2025
- Brand name for PrEP indication unknown
- Risk for nodules
  - Very common in the clinical trials
  - Most are mild-moderate, but can be severe
  - Typically last several months
  - Palpable, but not usually visible
- Cost and coverage
  - TBD

NOT CURRENTLY FDA-APPROVED (FOR PrEP)

TAF/FTC for People AFAB

- Studies of TAF/FTC for PrEP did not include women, transgender men, or injection drug users
  - DISCOVER Trial studied cisgender men and transgender women only
  - Theoretical concern about TAF/FTC not reaching appropriate concentrations in vaginal tissue to confer protection
- PURPOSE trials included cisgender women and adolescent girls and they were assigned to the FTC/TAF groups
  - Similar results to FTC/TDF

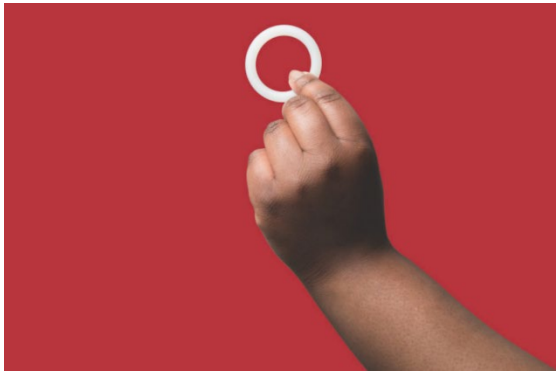
NOT CURRENTLY FDA-APPROVED (FOR PEOPLE AFAB)

MK-8527

- MK-8527 is an investigational antiretroviral (ARV) drug that is being studied as a potential PrEP product
- Oral pill given once a month
- An ARV from a class of drugs first tested by another drug known as islatravir
  - Islatravir studies for prevention were discontinued when a fall in white blood cell counts (sometimes referred to as lymphocyte levels) was detected after the drug was administered
  - MK-8527 has a different chemical structure than islatravir, and studies so far show no safety risk.
- Currently under investigation for use as prevention in a small Phase II clinical trial.
  - Conducted among approximately 350 HIV-negative adults in Israel, South Africa, and the USA
  - Testing safety, tolerability, and pharmacokinetics
  - Scheduled to run until December 2024
- Also under investigation as a once-weekly pill for treatment

NOT CURRENTLY FDA-APPROVED

Dapivirine Vaginal Ring (DVR)



- The dapivirine vaginal ring (DVR) is the first long-acting, user-controlled, non-systemic, HIV prevention product to be approved
- A flexible silicone ring that is inserted in the vagina and slowly releases dapivirine over the course of one month
- Approved in several African countries
  - At this time it has not been submitted for approval outside of Africa
  - First approved in 2021 by the Medicines Control Authority of Zimbabwe
- Not widely available at the present time outside of implementation studies
- Only for use by people assigned female at birth
- A three-month version of the ring is currently under investigation
  - Early data has shown that it delivers dapivirine at higher levels than the one-month ring

https://popcouncil.org/media/3-month-dapivirine-vaginal-ring-for-hiv-prevention-demonstrates-superior-drug-release-compared-to-1-month-ring/

NOT CURRENTLY FDA-APPROVED

DVR Safety & Efficacy

- Topical drugs such as the DVR are locally-acting, which means the ring only protects against HIV through vaginal sex
  - Very little dapivirine will be absorbed elsewhere in the body, making it unlikely to be found in high concentrations in the bloodstream and other body tissues
  - This may reduce side effects as well as the risk of development of HIV resistance.
- Clinical trials showed 35% reduced risk of HIV infection, while later studies found risk reduced by as much as 50%
- Does not prevent pregnancy, though multipurpose rings which also prevent pregnancy are currently being investigated
- Well-established tolerability with long-term use, including by adolescents
  - Side effects can include vaginal discharge, itching, urinary tract infections, and pelvic and lower abdominal pain
- Favorable safety profile for pregnant and lactating people and their infants

https://popcouncil.org/media/3-month-dapivirine-vaginal-ring-for-hiv-prevention-demonstrates-superior-drug-release-compared-to-1-month-ring/

NOT CURRENTLY FDA-APPROVED

Dual Prevention Pill

- The Dual Prevention Pill (DPP) is currently being developed for daily use to prevent both HIV and pregnancy
  - It is one of several multipurpose prevention technologies (MPTs) in the pipeline
- Combines two already-approved products—oral PrEP (tenofovir disoproxil fumarate and emtricitabine, or TDF/FTC) and oral contraception (ethinyl estradiol and levonorgestrel, or EE/LNG)
- Manufacturer could submit the DPP for regulatory approval in 2024, with first approval as early as late 2025
  - Planned for initial introduction in East and Southern Africa, where 68% of new HIV infections are amongst women of reproductive age (WRA), and 15% of WRA have unmet need for family planning
- Could increase oral PrEP uptake and help mitigate PrEP stigma by combining PrEP with contraception, which is more commonly used
- If approved, the DPP will be the first commercially-available MPT since condoms and the first MPT containing PrEP

NOT CURRENTLY FDA-APPROVED

Best Practices

Best Practices and Other Considerations

- Consider prescribing DoxyPEP in addition to PrEP
- Medications should be combined with other safe-sex practices
- Long-acting injectables
  - Prepare for high patient demand of these products
  - Billing and reimbursement practices for long-acting injectables vary
  - In my professional experience, it is ideal to have a dedicated team member who focuses on PrEP and/or long-acting injectables to be able to offer these medications when requested

Best Practices and Other Considerations

- How to pick the best PrEP medication?
  - Patient preference
  - Transportation concerns
  - Route (by mouth, intramuscular, subcutaneous, topical, etc.)
  - Kidney function (eGFR or creatinine clearance)
  - Current medications taken by the patient
  - Insurance coverage (or lack of insurance)

Summary

- FDA-Approved medications include:
  - FTC/TDF by mouth once daily
  - FTC/TAF by mouth once daily in persons AMAB
  - CAB IM every 30 days x2 doses then every other month thereafter
- There are several interesting medications in the pipeline for PrEP
  - LEN was submitted to the FDA for review in December 2024
- Medications for PrEP should be used in conjunction with safe-sex practices
  - Choice of PrEP agent should be individualized and account for several patient-specific factors

Self-Assessment Questions

Self-Assessment Question 1

- Which of the following are medications that are currently FDA-approved for PrEP and are recommended in the CDC guidelines?
  A. FTC/TDF once daily
  B. FTC/TAF once daily
  C. CAB IM every 30 days x 2 doses, then every other month thereafter
  D. Lenacapavir (LEN) subcutaneously every 6 months
  E. Doravirine vaginal ring inserted every 30 days

Self-Assessment Question 2

- Which of the following is NOT an appropriate counseling point for a patient newly starting on CAB for PrEP?
  A. You no longer need to use condoms since PrEP protects you from all STIs
  B. You will be tested for HIV status at each injection visit
  C. Injection site reactions are common, but you may treat them with OTC pain relievers, ice, or heat
  D. This medication has a lower risk of kidney damage compared to oral PrEP medications

Self-Assessment Question 3

- Which of the following statements is TRUE regarding lenacapavir (LEN)?
  A. It is currently FDA-Approved for PrEP
  B. There are no known side effects of the medication
  C. In clinical trials, lenacapavir was very effective and shown to be superior (more effective) than oral PrEP agents
  D. In clinical trials, it was administered as an intramuscular injection every 60 days

Self-Assessment Question 4

- Which of the following factors should be utilized when deciding on the best PrEP medication for a patient?
  A. Patient preference
  B. Transportation concerns
  C. Route (by mouth, intramuscular, subcutaneous, topical, etc.)
  D. Kidney function (eGFR or creatinine clearance)
  E. Current medications taken by the patient
  F. Insurance coverage (or lack of insurance)
  G. All the above

Questions?

Thank You

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