HIV Pre-Exposure Prophylaxis (PrEP)
The Future of PrEP

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Disclosures

December 2023: only FTC/TDF (Truvada), FTC/TAF (Descovy), and CAB-LA (Apretude) are approved by the U.S. Food and Drug Administration (FDA) and only for use in some, but not all, populations.

This talk will include discussion of non-FDA approved strategies for HIV prevention.
Funding for this presentation was made possible by U1OHA29296 from the Human Resources and Services Administration HIV/AIDS Bureau. The views expressed do not necessarily reflect the official policies of the Department of Health and Human Services nor does mention of trade names, commercial practices, or organizations imply endorsement by the U.S. Government. Any trade/brand names for products mentioned during this presentation are for training and identification purposes only.
### What to prescribe as PrEP (December 2023)

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<thead>
<tr>
<th>IAS-USA (2022)</th>
<th>HHS/CDC (2021)</th>
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<tr>
<td><strong>FTC/TDF</strong></td>
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<td>All persons at risk from sexual or injection exposures.</td>
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<td><strong>FTC/TAF</strong></td>
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<td>- Preferred if eCrCl 30-60 mL/min or known osteoporosis</td>
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<td>- Limited to anyone whose risks do not include receptive vaginal or neovaginal sex or exclusive IDU</td>
<td>- Recommended for men and TGW who have sex with men.</td>
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<td><strong>CAB</strong></td>
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<td>All persons at risk from sexual exposures and PWID with sexual risk.</td>
<td>All persons at risk from sexual exposures.</td>
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Why do we need more PrEP studies and PrEP options?

- Not all PrEP options are approved in all populations
- Daily pill-taking is challenging for many people
- Easier accessibility at home or other locations
- Side effects
- More options = better choices
- More options = more competition = lower costs?
- Avoiding drug resistance in first line antiretroviral therapy?
The Future of PrEP

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<thead>
<tr>
<th>Prevention Product</th>
<th>2022</th>
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<td><strong>Vaginal Ring</strong></td>
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<td><strong>Long-Acting Injectable</strong></td>
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<td>Oral intramuscular injection</td>
<td>(3ml) every 2 months</td>
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<td><strong>Oral PrEP</strong></td>
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<td>F/TAF daily</td>
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<td>Phase 3: part of PURPOSE 1</td>
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<td>Possible Go/No-Go Decision for Phase 3 in Q1 2025</td>
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<td><strong>Dual Prevention Pill</strong></td>
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<td>Co-formulated TDF/FTC and ethinyl estradiol/levonorgestrel oral contraceptive pill daily</td>
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<td>Pilot bioequivalence (BE) study</td>
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<td>Acceptability Study: HPTN 104</td>
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- Demonstrated modest efficacy
- Unclear demand & limited initial supply
- Initial price ~$180 per year
- Oct 2023: PopCouncil licensed Kiara Health in SA to mfg.; volumes and prices unknown
- Opportunity to build market and platforms for vaginal rings

- Demonstrated high efficacy
- Unclear demand & limited initial supply
- Initial LMIC price ~$240/yr; in 2024 ~$170/yr
- March 2023: MPP & ViV licensed to 3 generics that need 7 years to market
- Opportunity to build market and platforms for injectables

Vaginal ring for sustained delivery of ARV drugs
Dapivirine ring

27% ↓

40% ↓

NEJM 2016; 375: 2121-32 (Baeten et al) and 2133-2143 (Nel et al.)
Adapted from Dr. Sharon Hillier’s presentation at the Annual Principles of STI/HIV Research Course
Vaginal ring for sustained delivery of ARV drugs
Future products

• Longer duration vaginal rings
  - Dapivirine ring 004 (30 days) v 008 (90 days) (Phase I, enrolling)

• Other medications
  - TDF/FTC ring (Phase I, active)

• Multipurpose rings (PrEP + contraception)
  - Dapivirine 200mg + Levonorgestrel 320mg (Phase I/II, enrolling)
  - TDF + Levonorgestrel
Capsid inhibitors

Attachment Inhibitor
Post-attachment Inhibitor
Coreceptor Antagonist
Fusion Inhibitor
Protease Inhibitors
Capsid Inhibitor

1 ENTRY
2 CYTOPLASMIC TRANSPORT & NUCLEAR IMPORT
3 REVERSE TRANSCRIPTION
4 INTEGRATION
5 TRANSCRIPTION
6 TRANSLATION
7 ASSEMBLY
8 BUDDING & MATURATION
HOST CELL
NUCLEUS
Mature HIV virion
HIV Gap polyprotein
HIV Gap-Pol polyproteins
HIV intron
Envelope glycoproteins gp120/gp41
CD4 receptor
CCR5 co-receptor

Illustration: Cognition Studio, Inc. and David H. Spach, MD.
National HIV Curriculum: https://www.hiv.uw.edu/
Lenacapavir as PrEP

- Lenacapavir as PrEP in an IV HIV challenge macaque model
  (Swanstrom et al., EBioMedicine 2023)
- Lenacapavir as PrEP in a rectal SHIV challenge macaque model
  (Bekerman et al., J Clin Invest 2023)

Prevention dosing:
Oral LEN 600mg day 1 and 2, then
Subcutaneous LEN 927mg q26 weeks (i.e. every 6 months)
PURPOSE: lenacapavir

- PURPOSE 1: lenacapavir v FTC/TAF in girls and women phase III, n=5639, South Africa and Uganda, 1° completion 2024

- PURPOSE 2: lenacapavir v FTC/TDF in cisMSM, transgender/GNB persons phase III, n=3000, US/ex-US sites, 1° completion 2025

- PURPOSE 3: lenacapavir v FTC/TDF in cisgender women in US (HPTN 102) phase II, n=250, 1° completion 2027

- PURPOSE 4: lenacapavir v FTC/TDF in PWID in US (HPTN 103) phase II, n=250, 1° completion 2027

- PURPOSE 5: lenacapavir persistence in UK and France

Clinicaltrials.gov, https://www.purposestudies.com/
Long-acting oral formulations

- MK-8591 = islatravir, no longer being studied for prevention

- MK-8527 taken monthly
  NRTTI = nucleoside reverse transcriptase translocation inhibitor
  phase IIa (safety, tolerability, PK) in low-risk participants
  n=350, completion 2025
Dual Prevention Pill (DPP): PrEP + Contraception

- Generic maker is co-formulating
  - FTC/TDF + Levonorgestrel (0.15mg) + Ethinyl Estradiol (0.03mg) in blister pack
  - 21 combo pills + 7 peach-colored PrEP only pills

- Two crossover adherence/acceptability studies – study completion 2023

- FDA submission?
Questions?
Acknowledgment

This Mountain West AIDS Education and Training (MWAETC) program is supported by the Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services (HHS) as part of an award totaling $3,333,289 with 0% financed with non-governmental sources.

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