HIV PrEP: Empowering PCPs to End the Epidemic

56th Annual Primary Care Review

February 10, 2024

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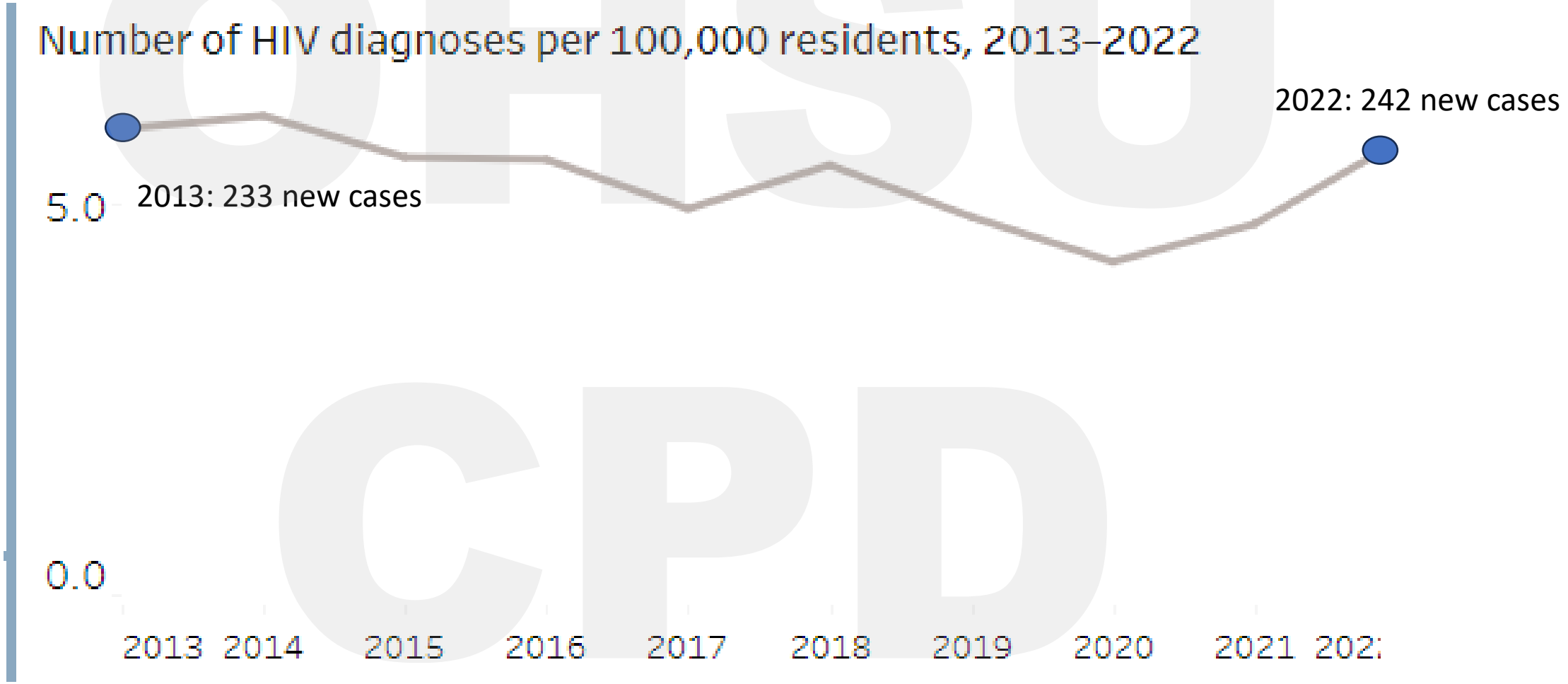
Learning Objectives

Identify	Initiate	Provide
Identify people at risk for HIV in rural and urban settings	Initiate PrEP with the appropriate dosing strategy	Provide longitudinal management for patients on PrEP

Agenda

- Why PrEP
  - HIV epidemic
  - PrEP efficacy
- What is PrEP?
  - Pharmacotherapies
  - Dosing strategies
- How to PrEP
  - Indications
  - Counseling
    - Follow up
    - Adverse Effects
  - Disparities
- Summary

Oregon's Persistent Epidemic



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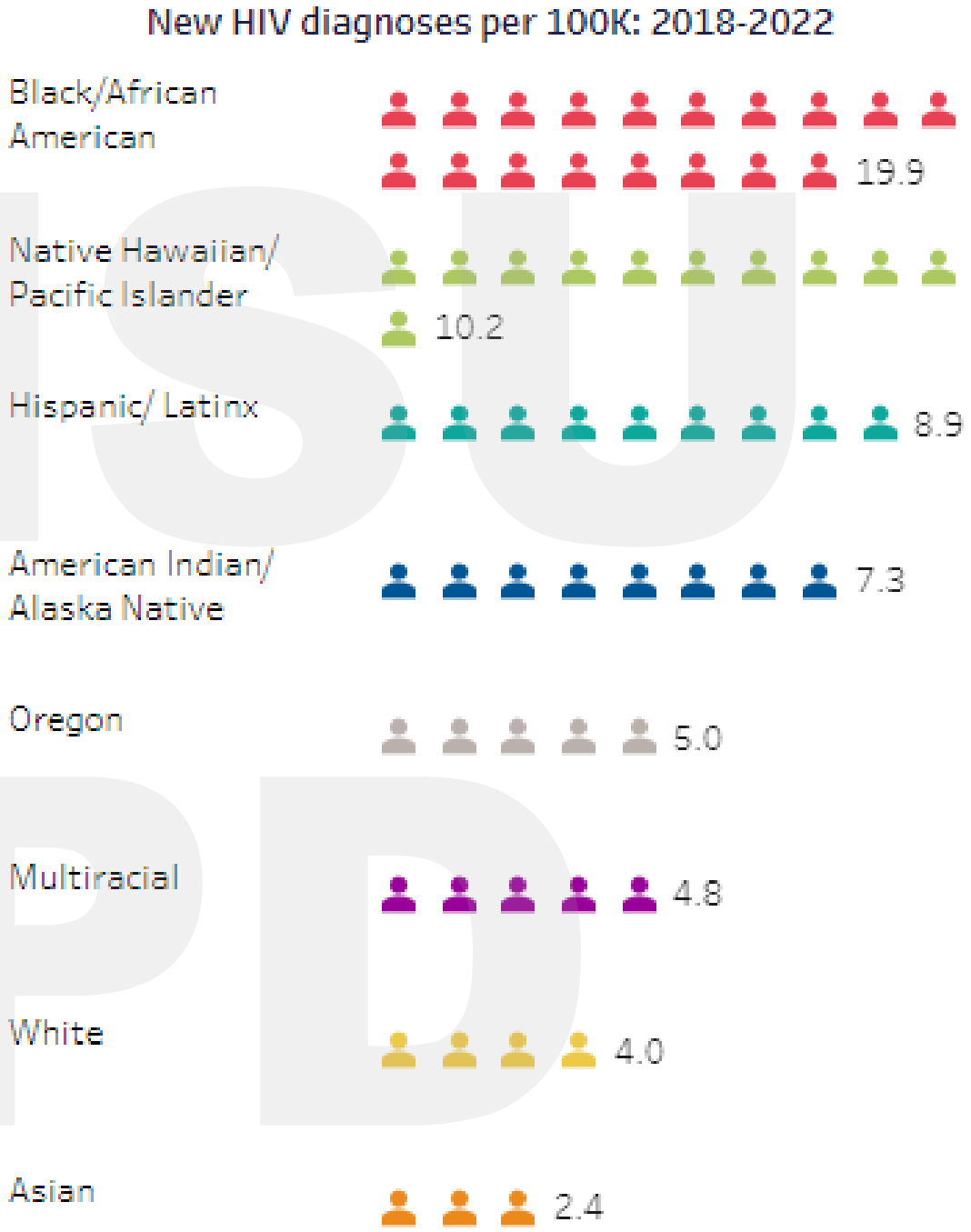
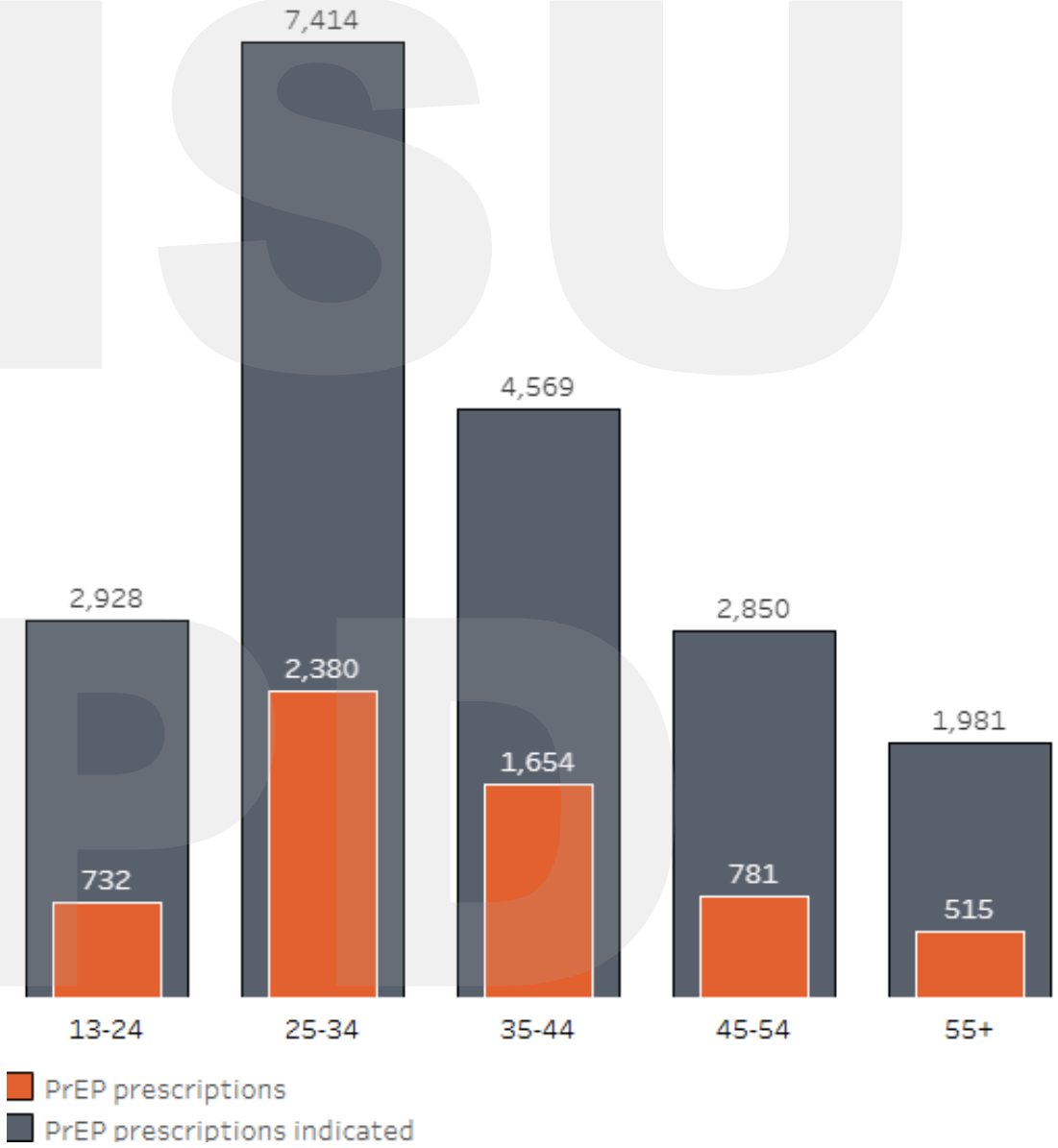
Inequity in new HIV Diagnosis

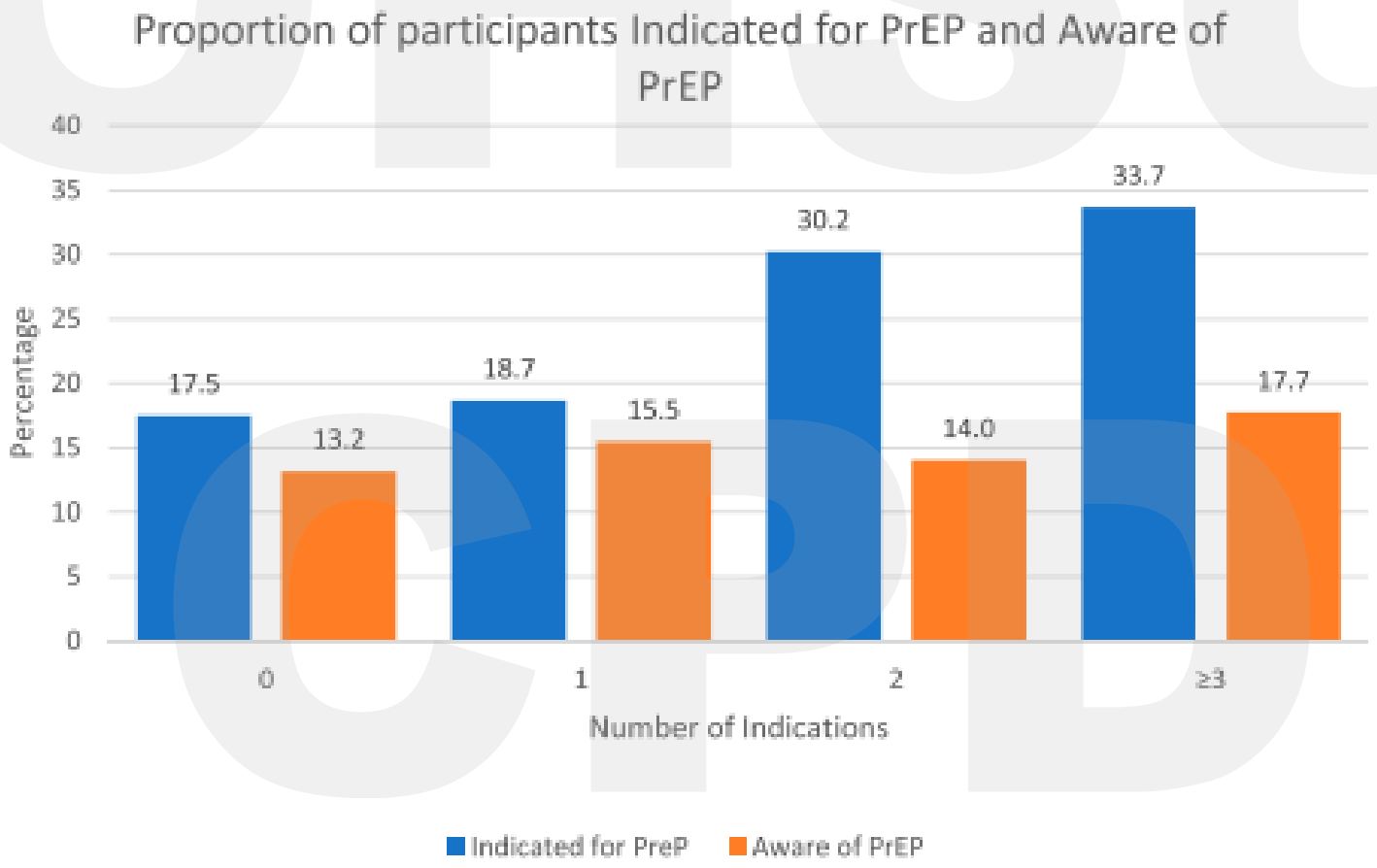


Insufficient PrEP Utilization

PrEP Prescriptions vs Number Indicated for PrEP, 2022



PrEP need is high among PWID



Spencer HC, et al. Int J STD AIDS. 2023 doi:10.1177/09564624231154302.

Missed Opportunities

- Of 243 HIV diagnoses in 2023
  - 12.3% were ever on PrEP
  - 13.1% were diagnosed with STI in the two years prior

PrEP Works

- 20 RCTs (N = 36,57518,837)
- Global MSM, HET, PWID
- Decreased risk of HIV infection
  - RR = 0.46 (0.33-0.66)
  - ARR= −2.0% (95% CI, −2.8% to −1.2%)
  - NNT=50
- Greater adherence was associated with greater efficacy
  - RR with adherence ≥70% = 0.27 (0.19-0.39)

US Preventive Services Task Force | Evidence Report

FREE

August 22/29, 2023

Preexposure Prophylaxis for the Prevention of HIV

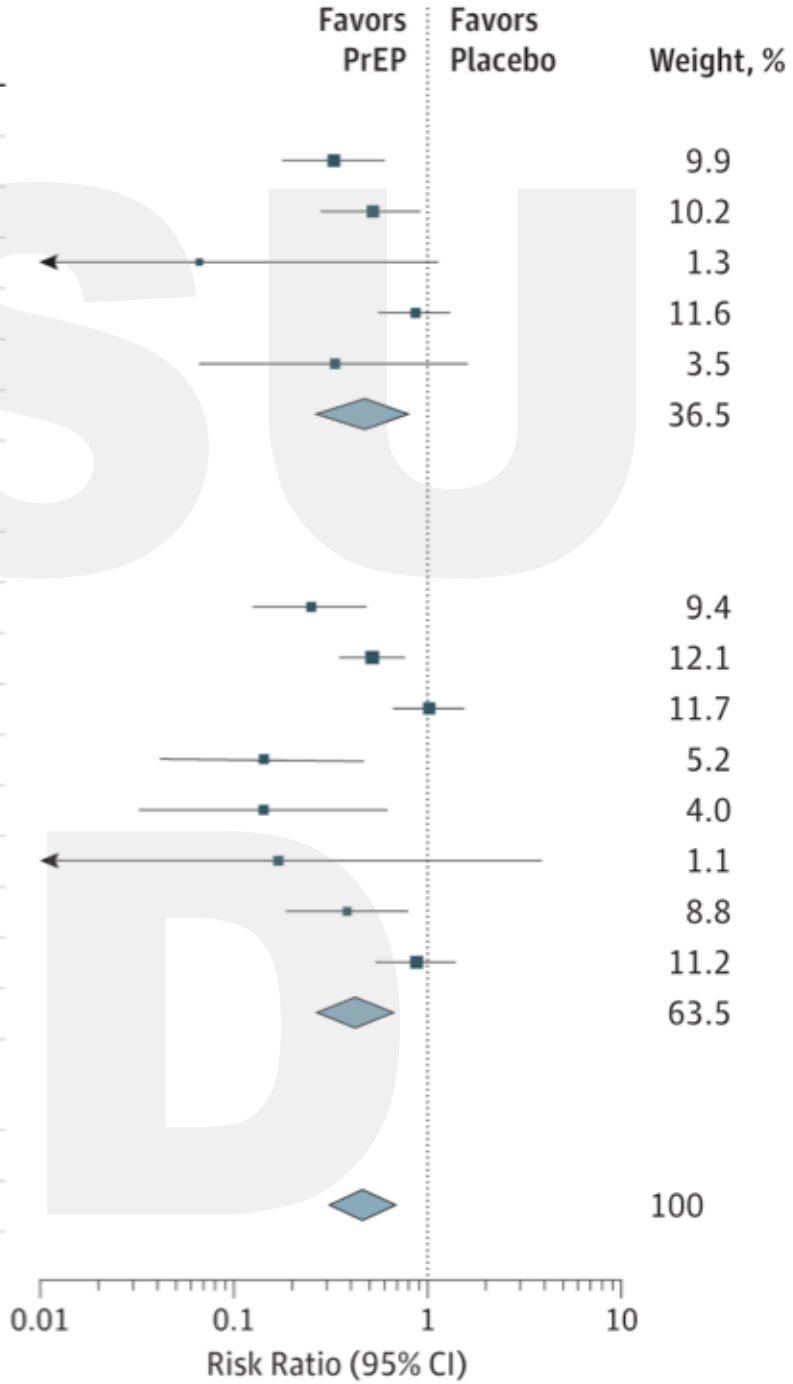
Updated Evidence Report and Systematic Review for the US Preventive Services Task Force

Roger Chou, MD[1,2]; Hunter Spencer, DO[2]; Christina Bougatsos, MPH[1]; et al

» Author Affiliations | Article Information

JAMA. 2023;330(8):746-763. doi:10.1001/jama.2023.9865

Source	No. of Events/Total PrEP	Placebo	Risk Ratio (95% CI)	Weight, %
Tenofovir disoproxil fumarate				
Baeten et al,[12] 2012[a]	17/1572	26/793	0.33 (0.18-0.60)	9.9
Choopanya et al,[14] 2013	17/1204	33/1207	0.52 (0.29-0.92)	10.2
Grohskopf et al,[18] 2013[b]	0/201	7/199	0.07 (0.00-1.15)	1.3
Marrazzo et al,[27] 2015[a]	52/1007	30/504	0.87 (0.56-1.34)	11.6
Peterson et al,[40] 2007	2/427	6/432	0.34 (0.07-1.66)	3.5
Subtotal	88/4411	12/3135	0.49 (0.28-0.84)	36.5
$I^2 = 58\%$; $\chi^2_4 = 9.50$ for heterogeneity, $P = .05$; $\tau^2 = 0.19$				
Overall effect: $z = 2.60$, $P = .009$				
Tenofovir disoproxil fumarate/emtricitabine				
Baeten et al,[12] 2012[c]	13/1568	26/793	0.25 (0.13-0.49)	9.4
Grant et al,[17] 2010	38/1251	72/1248	0.53 (0.36-0.77)	12.1
Marrazzo et al,[27] 2015[c]	61/1003	30/505	1.02 (0.67-1.56)	11.7
McCormack et al,[31] 2016[b]	3/268	20/255	0.14 (0.04-0.47)	5.2
Molina et al,[33] 2015[b]	2/199	14/201	0.14 (0.03-0.63)	4.0
Mutua et al,[39] 2012	0/48	1/24	0.17 (0.01-4.03)	1.1
Thigpen et al,[42] 2012	10/601	26/606	0.39 (0.19-0.80)	8.8
Van Damme et al,[43] 2012	31/1024	35/1032	0.89 (0.55-1.44)	11.2
Subtotal	158/5962	224/4664	0.44 (0.27-0.72)	63.5
$I^2 = 74\%$; $\chi^2_7 = 27.08$ for heterogeneity, $P < .001$; $\tau^2 = 0.30$				
Overall effect: $z = 3.31$, $P < .001$				
Overall				
Subtotal	246/10373	326/7799	0.46 (0.33-0.66)	100
$I^2 = 67\%$; $\chi^2_{12} = 36.59$ for heterogeneity, $P < .001$; $\tau^2 = 0.22$				
Overall effect: $z = 4.34$, $P < .001$				
Subgroup differences: $I^2 = 0\%$; $\chi^2_1 = 0.07$ for heterogeneity, $P = .79$				



Why Prescribe PrEP in Primary Care?

- HIV is uncontrolled in our communities
- PrEP works
- Many of your patients are indicated for PrEP

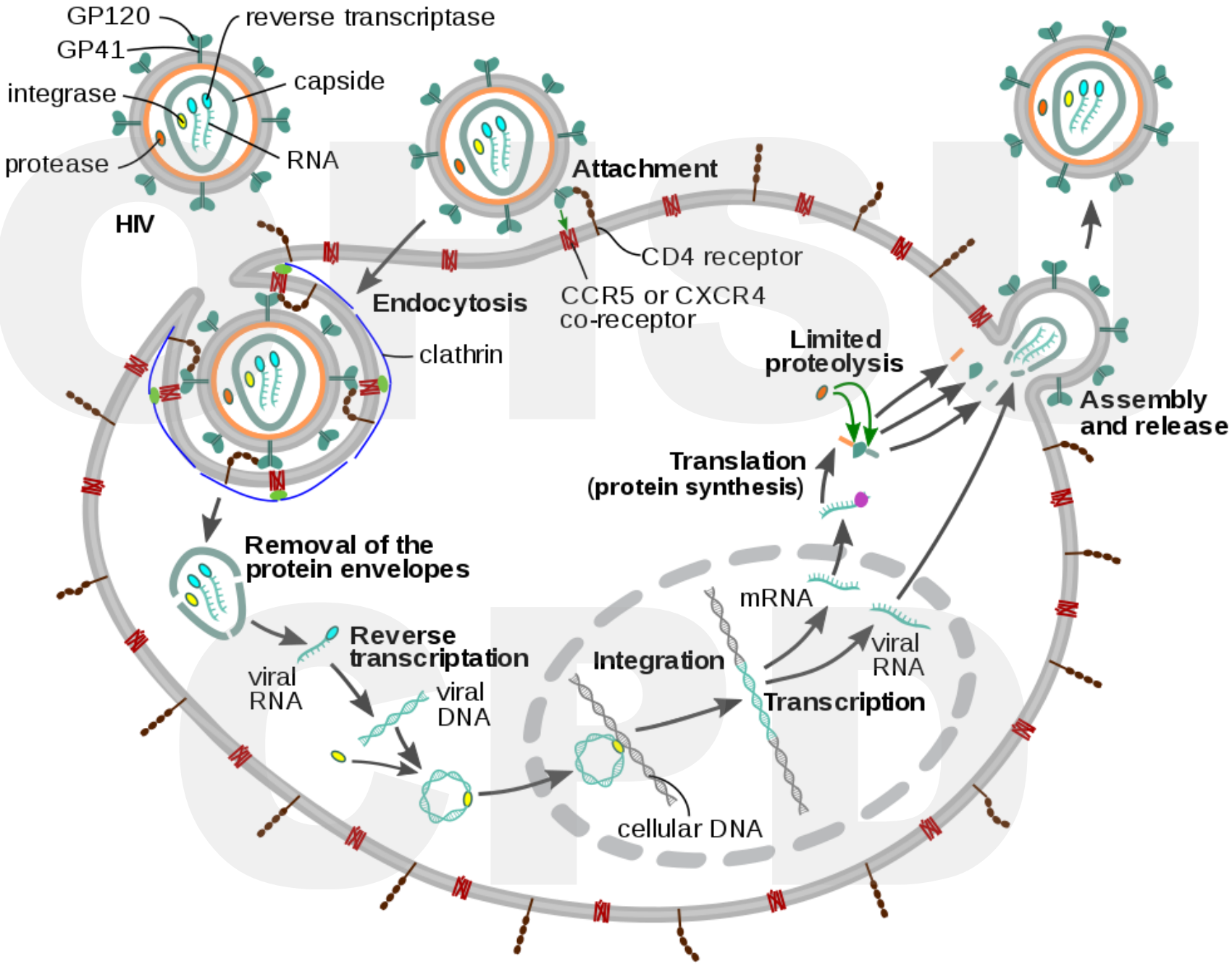
Population	Recommendation	Grade
Persons at high risk of HIV acquisition	The USPSTF recommends that clinicians offer preexposure prophylaxis (PrEP) with effective antiretroviral therapy to persons who are at high risk of HIV acquisition. See the Clinical Considerations section for information about identification of persons at high risk and selection of effective antiretroviral therapy.	A

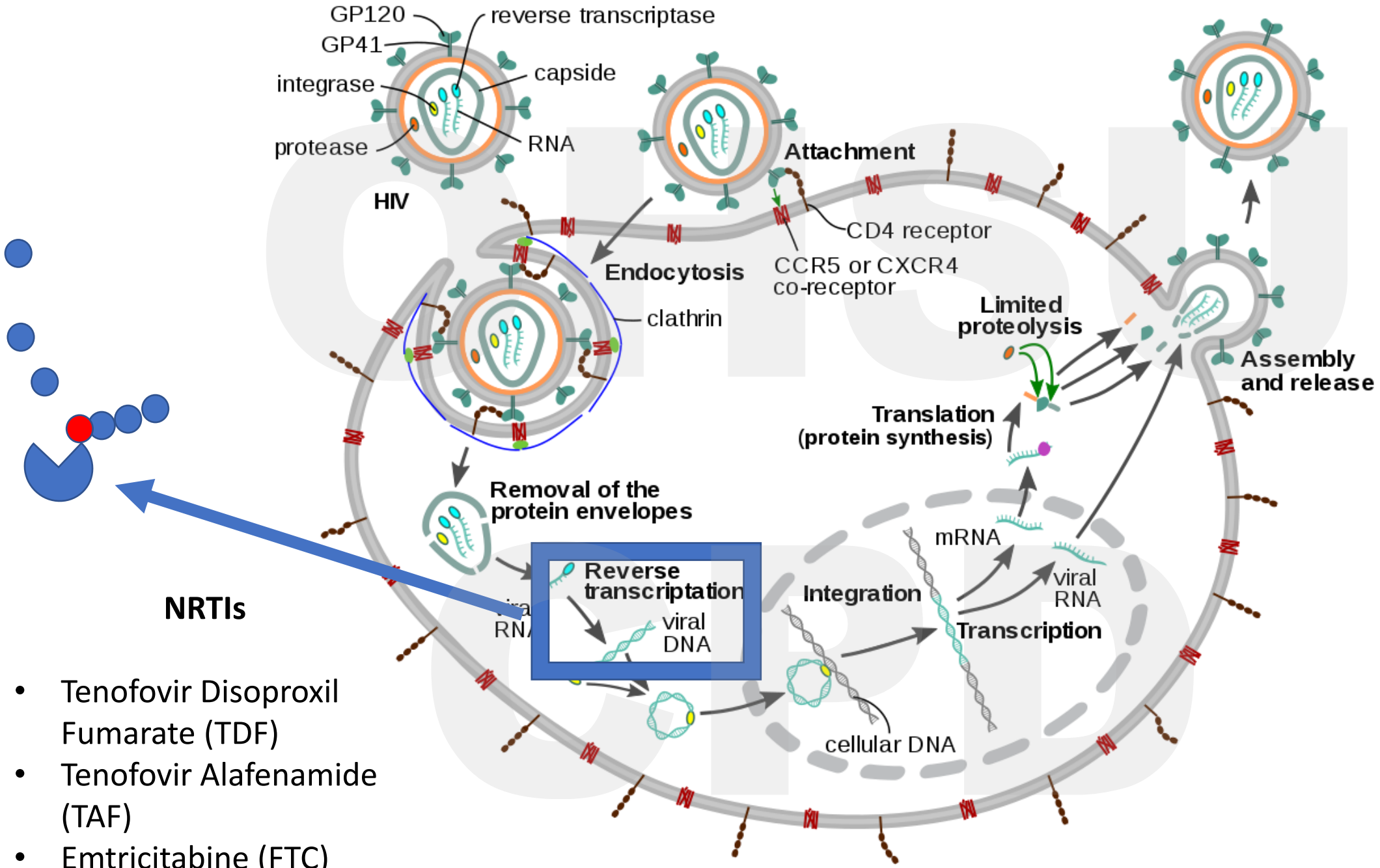
CDC Guidelines

	Sexually-Active Adults and Adolescents[1]
Identifying substantial risk of acquiring HIV infection	Anal or vaginal sex in past 6 months AND any of the following: • HIV-positive sexual partner (especially if partner has an unknown or detectable viral load) • Bacterial STI in past 6 months[3] • History of inconsistent or no condom use with sexual partner(s)

Persons Who Inject Drug[2]
HIV-positive injecting partner OR Sharing injection equipment

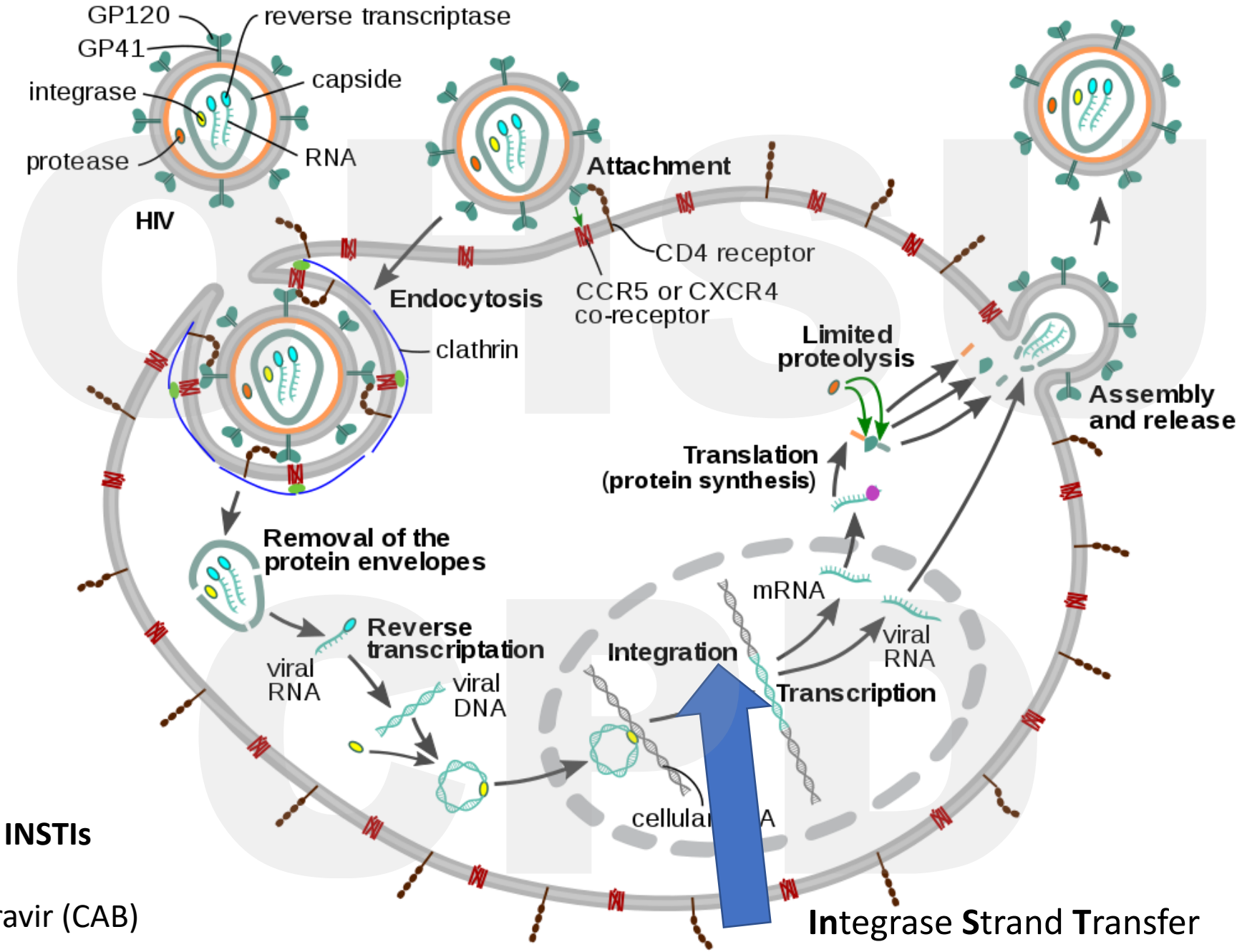
	Tenofovir disoproxil fumarate – Emtricitabine *The Original*	Tenofovir Alafenamide-Emtricitabine *New (and improved?)	Cabotegravir *The Paradigm Shifter*
Abbreviation	TDF-FTC	TAF-FTC	CAB
Brand Name	Truvada	Descovy	Apretude
Route	PO	PO	IM
Strategy	Daily or “On-demand” aka 2-1-1	Daily	Long Acting
Mechanism	NRTI	NRTI	INSTI
Approved Population	Daily: General 2-1-1: MSM	MSM / TGW	General





NRTIs

- Tenofovir Disoproxil Fumarate (TDF)
- Tenofovir Alafenamide (TAF)
- Emtricitabine (FTC)



INSTIs

- Cabotegravir (CAB)

Integrase **S**trand **T**ransfer Inhibitor= **INSTI**

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Brand Name	Truvada	Descovy	Apretude
Route	PO	PO	IM
Strategy	Daily or "On-demand" aka 2-1-1* * *Off-label use*	Daily	Long Acting
Mechanism	NRTI	NRTI	INSTI
Approved Population	Daily: General 2-1-1: MSM	MSM / TGW	Sexual transmission

TAF vs TDF

- Prodrugs metabolized to TFV
  - TAF metabolized more efficiently
  - Higher intracellular concentration
  - Lower dose
- Decreased Change in Cr, decreased change in BMD
- TDF has better metabolic profile
- Approved for eGFR>30
- Under patent

Bottom Line: Use TAF only for a compelling indication

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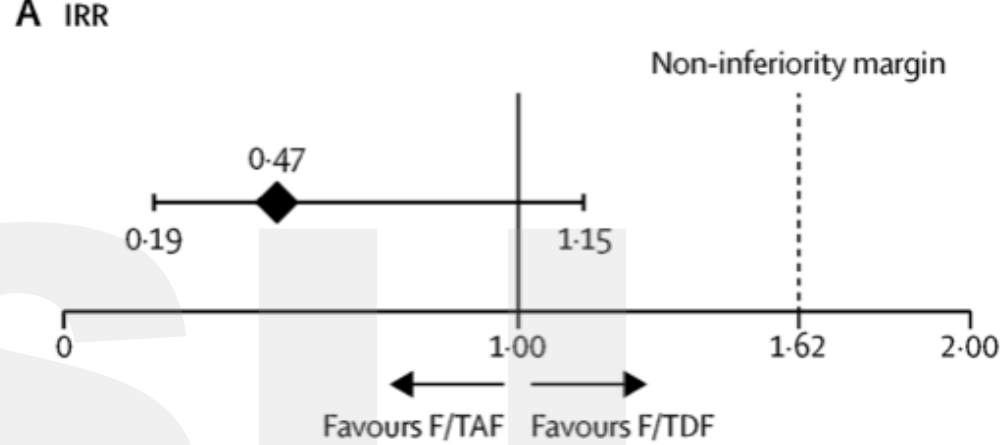
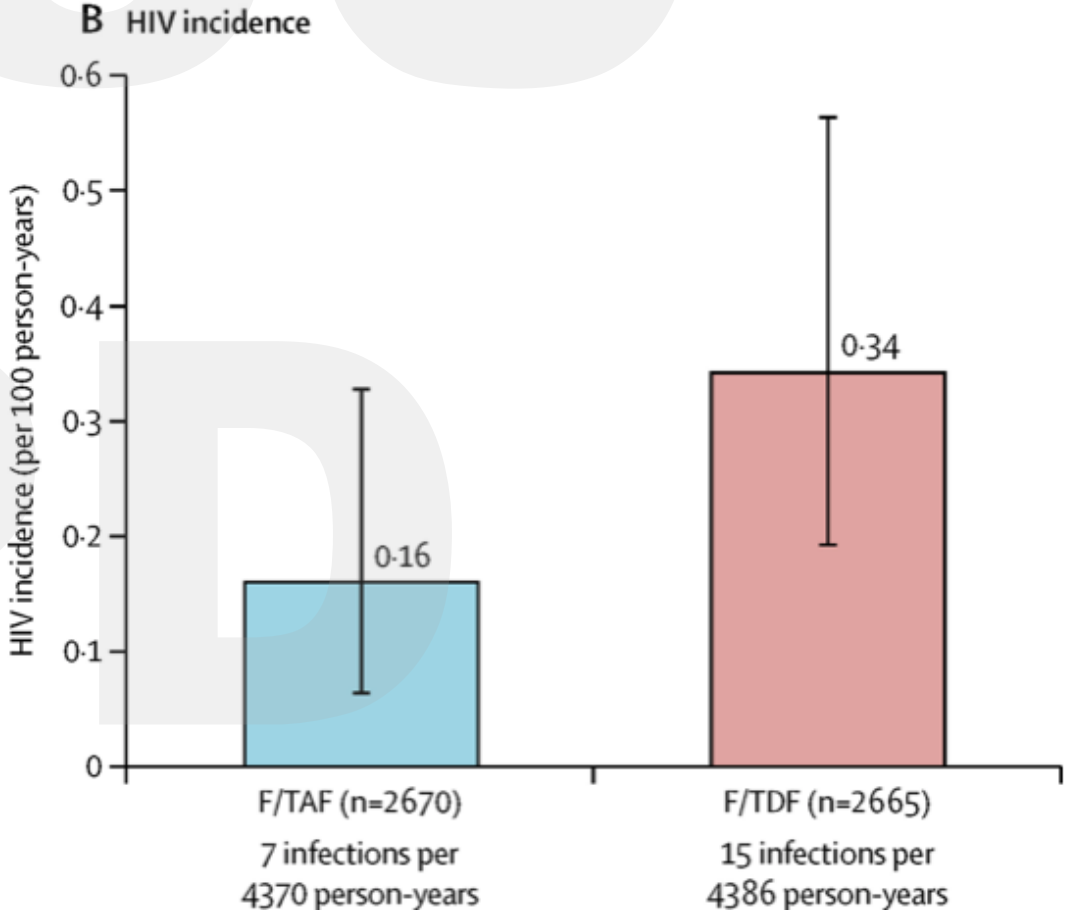
Articles

Emtricitabine and tenofovir alafenamide *vs* emtricitabine and tenofovir disoproxil fumarate for HIV pre-exposure prophylaxis (DISCOVER): primary results from a randomised, double-blind, multicentre, active-controlled, phase 3, non-inferiority trial

Prof Kenneth H Mayer MD [a, b], Prof Jean-Michel Molina MD [c], Melanie A Thompson MD [d], Prof Peter L Anderson PharmD [e], Karam C Mounzer MD [f], Joss J De Wet MD [g], Edwin DeJesus MD [h], Heiko Jessen MD [i], Prof Robert M Grant MD [j], Peter J Ruane MD [k], Pamela Wong MPH [l], Ramin Ebrahimi MSc [l], Lijie Zhong PhD [l], Anita Mathias PhD [m], Christian Callebaut PhD [n], Sean E Collins MD [o], Moupali Das MD [o] ✉, Scott McCallister MD [o] ... C Bradley Hare MD [t]

- N=5,857
- 98% MSM, 2% TGW
- Europe and North America
- Daily TDF-FTC or TAF-FTC
- Industry funded





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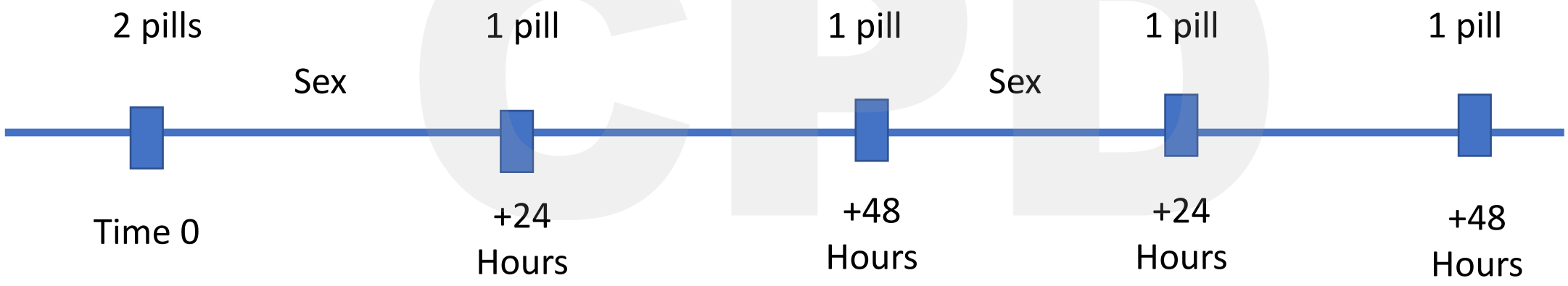
Mechanism	NRTI	NRTI	INSTI
Approved Population	Daily: General 2-1-1: MSM	MSM / TGW	General

Daily vs 2-1-1 Dosing

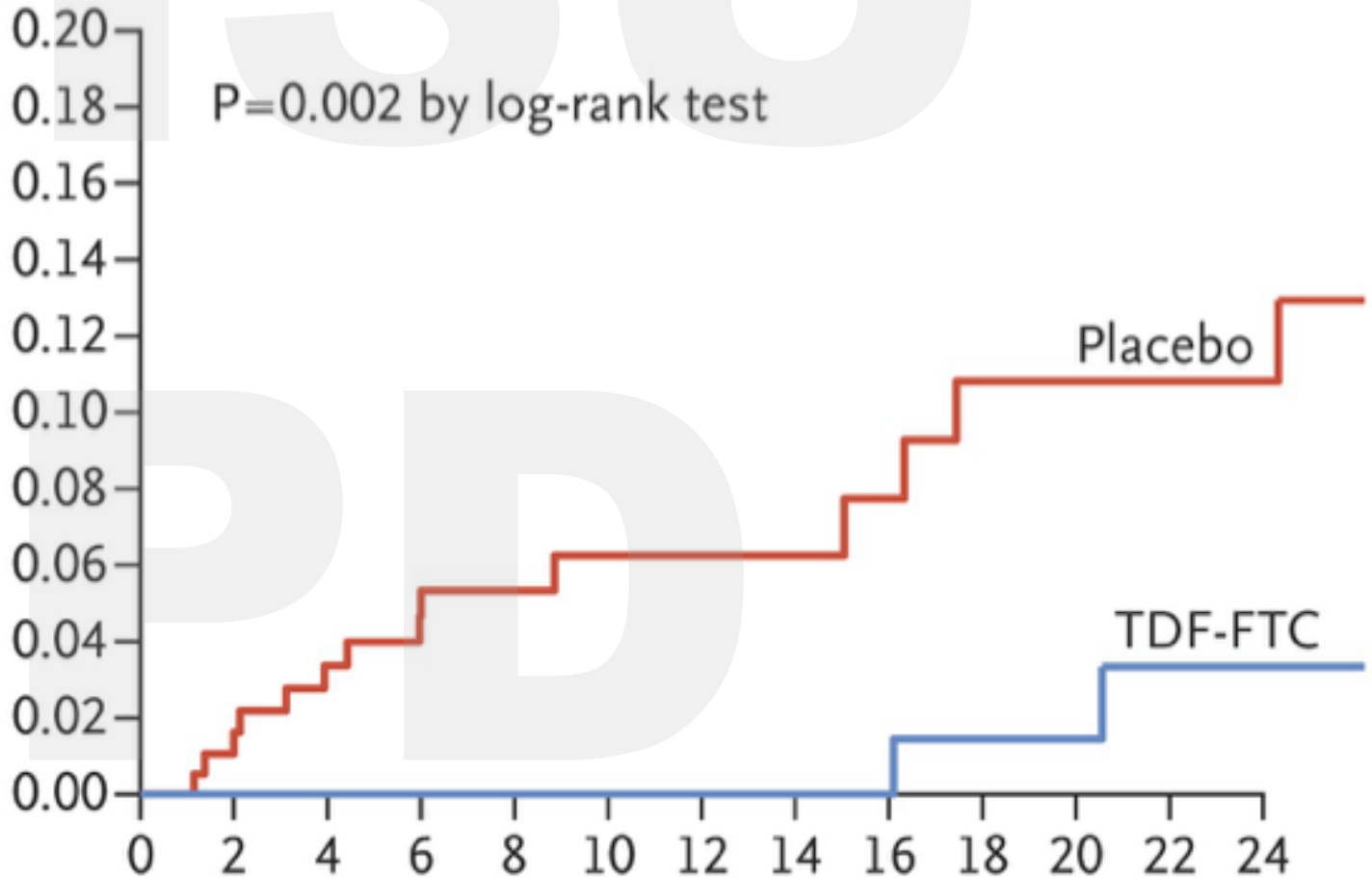
- On-demand, event driven
- Effective in MSM
- TDF-FTC



On-Demand Preexposure Prophylaxis in Men at High Risk for HIV-1 Infection

Jean-Michel Molina, M.D., Catherine Capitant, M.D., Bruno Spire, M.D., Ph.D., Gilles Pialoux, M.D., Laurent Cotte, M.D., Isabelle Charreau, M.D., Cecile Tremblay, M.D., Jean-Marie Le Gall, Ph.D., Eric Cua, M.D., Armelle Pasquet, M.D., François Raffi, M.D., Claire Pintado, M.D., et al., for the ANRS IPERGAY Study Group*

- N=400
- MSM
- France and Canada
- TDF-FTC with 2-1-1 vs placebo
- RRR=86% (40%-98%)
- Average doses=15 per month
- Similar efficacy in lower-utilization subgroup



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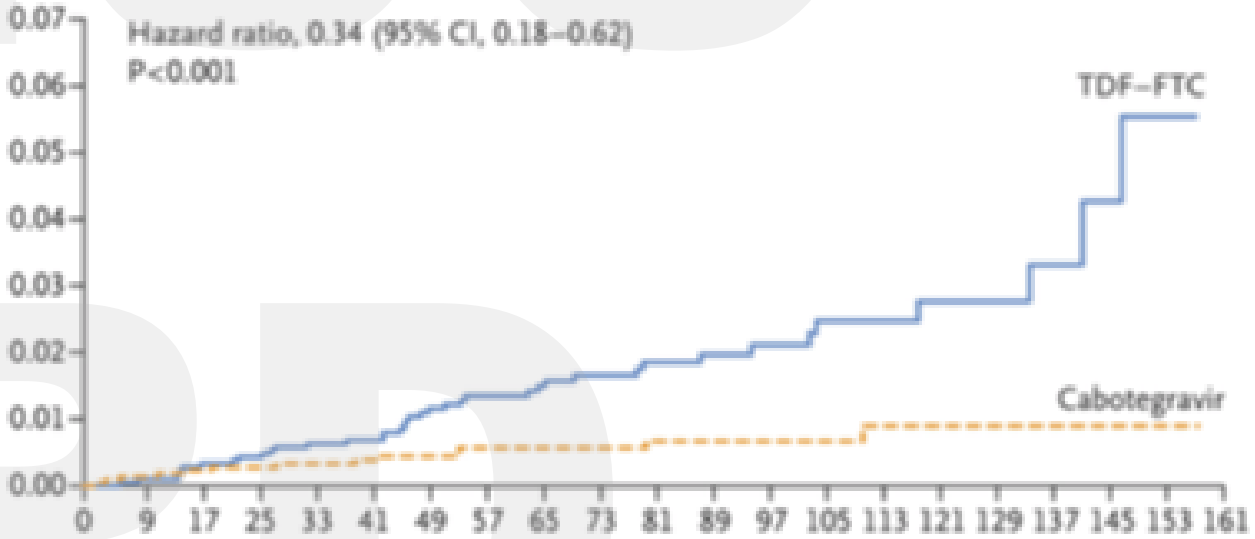
Long-Acting Injectable PrEP

- Adherence is the primary driver of efficacy
- 2021 Cabotegravir approved as part of the first long-acting injectable ART regimen
- 2022 Cabotegravir approved as first long-acting injectable PrEP
- Schedule: 0→ 4 weeks → q8weeks
- Anterogluteal IM injection
- Half Life = 40 days

Cabotegravir for HIV Prevention in Cisgender Men and Transgender Women

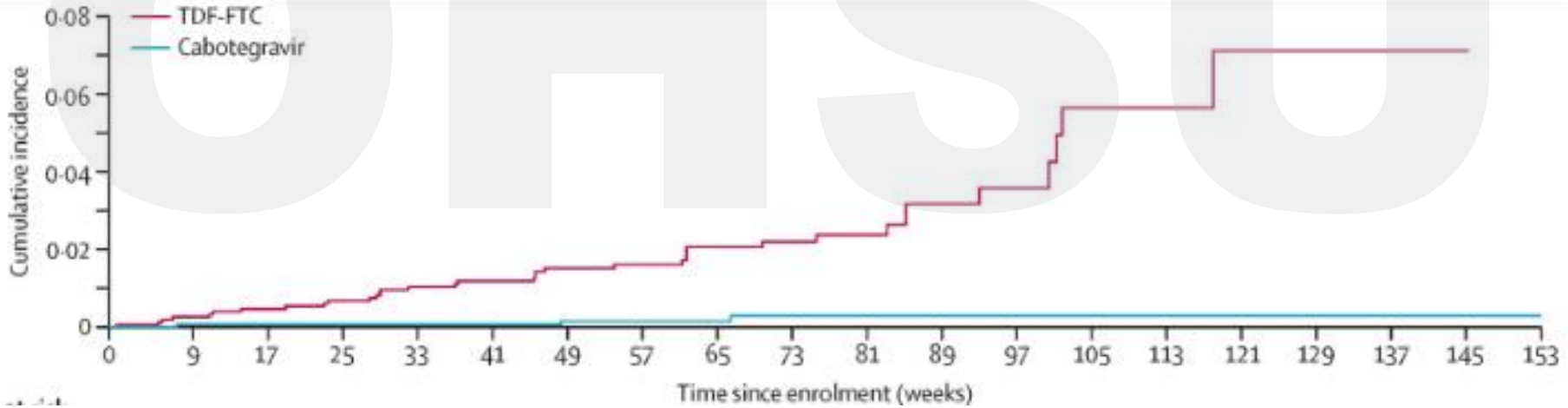
Raphael J. Landovitz, M.D., Deborah Donnell, Ph.D., Meredith E. Clement, M.D., Brett Hanscom, Ph.D., Leslie Cottle, B.A., Lara Coelho, M.D., Robinson Cabello, M.D., Suwat Chariyalertsak, M.D., Dr.P.H., Eileen F. Dunne, M.D., M.P.H., Ian Frank, M.D., Jorge A. Gallardo-Cartagena, M.D., Aditya H. Gaur, M.D., et al., for the HPTN 083 Study Team*

- Double blind, double-dummy RCT
- Daily TDF-FTC
- N=4,566
- MSM, TGW; Global
- HR= 0.34 (0.18-0.62)
- 4 breakthrough infections
- INSTI resistance



Cabotegravir for the prevention of HIV-1 in women: results from HPTN 084, a phase 3, randomised clinical trial

Prof Sinead Delany-Moretlwe, PhD • Prof James P Hughes, PhD • Prof Peter Bock, PhD • Samuel Gurrion Ouma, MD • Portia Hunidzarira, MBChB • Dishiki Kalonji, FCPHM • et al. Show all authors



- Double blind, double dummy RCT
- Daily TDF-FTC
- N=3,224
- Women; Sub-Saharan Africa

- HR=0·12 (0·05–0·31)
- Incident HIV associated with delayed dose
- No INSTI mutations

IM Cabotegravir

- High adherence to dosing interval
- Resistance is rare, but consequential
- Coverage through the “pharmacokinetic tail”
- Administration and administrative burden

Bottom Line: Default to oral PrEP unless you can develop a multi-disciplinary program.

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Route	PO	PO	IM
Strategy	Daily or “On-demand” aka 2-1-1	Daily	Long Acting
Mechanism	NRTI	NRTI	INSTI
Approved Population	Daily: General 2-1-1: MSM	MSM / TGW	General

Indications

1. Sexually Active, >35Kg with:
    1. Inconsistent condom use
    2. STI in the last 6 months*
    3. Known HIV+ partner who is not stably undetectable
2. PWID who:
    1. Have shared injection equipment
    2. Have an HIV+ injection partner

*Gonorrhea or syphilis in Heterosexuals. Gonorrhea, syphilis or chlamydia in MSM

Initiation

- Exclude Acute HIV
  - Clinical history
  - 4th Gen Ag/Ab within 1 week
  - Consider more recent exposures
- STI Screening
  - Syphilis
  - HCV
  - Hep B serologies
  - Triple site G/C
- Creatinine
- Hep B serologies
- Vaccines

Initiation: PrEP ≠ PEP

- If recent high risk exposure within 72 hours, start PEP instead
  - 3 drug HIV treatment regimen for 28 days, then transition to PrEP

Counseling

- Choose strategy
  - Medical history
  - eGFR
  - Historical/anticipated sexual behavior
- **≤ 90-day supply**
- Adverse Effects: GI upset, kidney disease, BMD

Follow up

Every 3 months

- 4th generation HIV Ag/Ab
- STI screening
  - Syphilis
  - HCV
  - Hep B serologies
  - Triple site G/C
- Harm Reduction

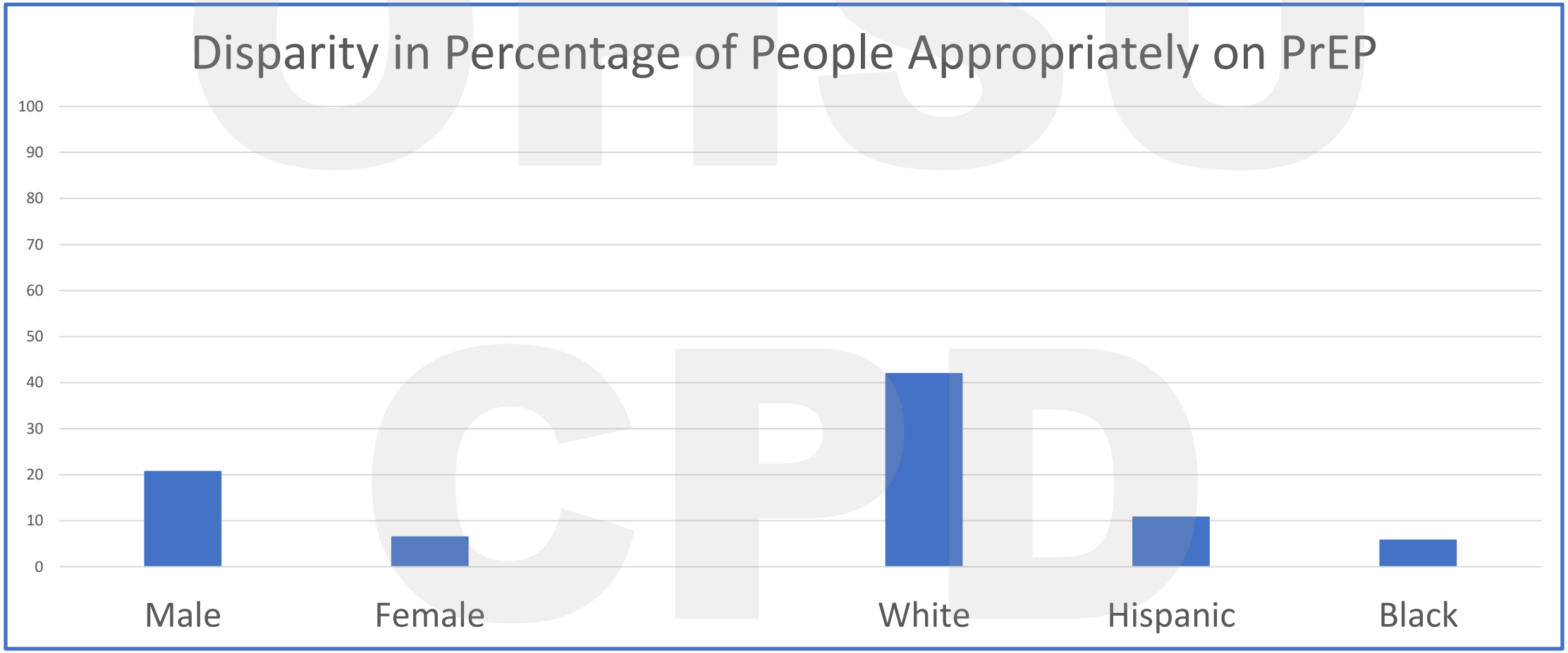
Every 6 months

- BMP (if impaired clearance or age >50)

Every 12 months

- Lipids
- BMP (all patients)

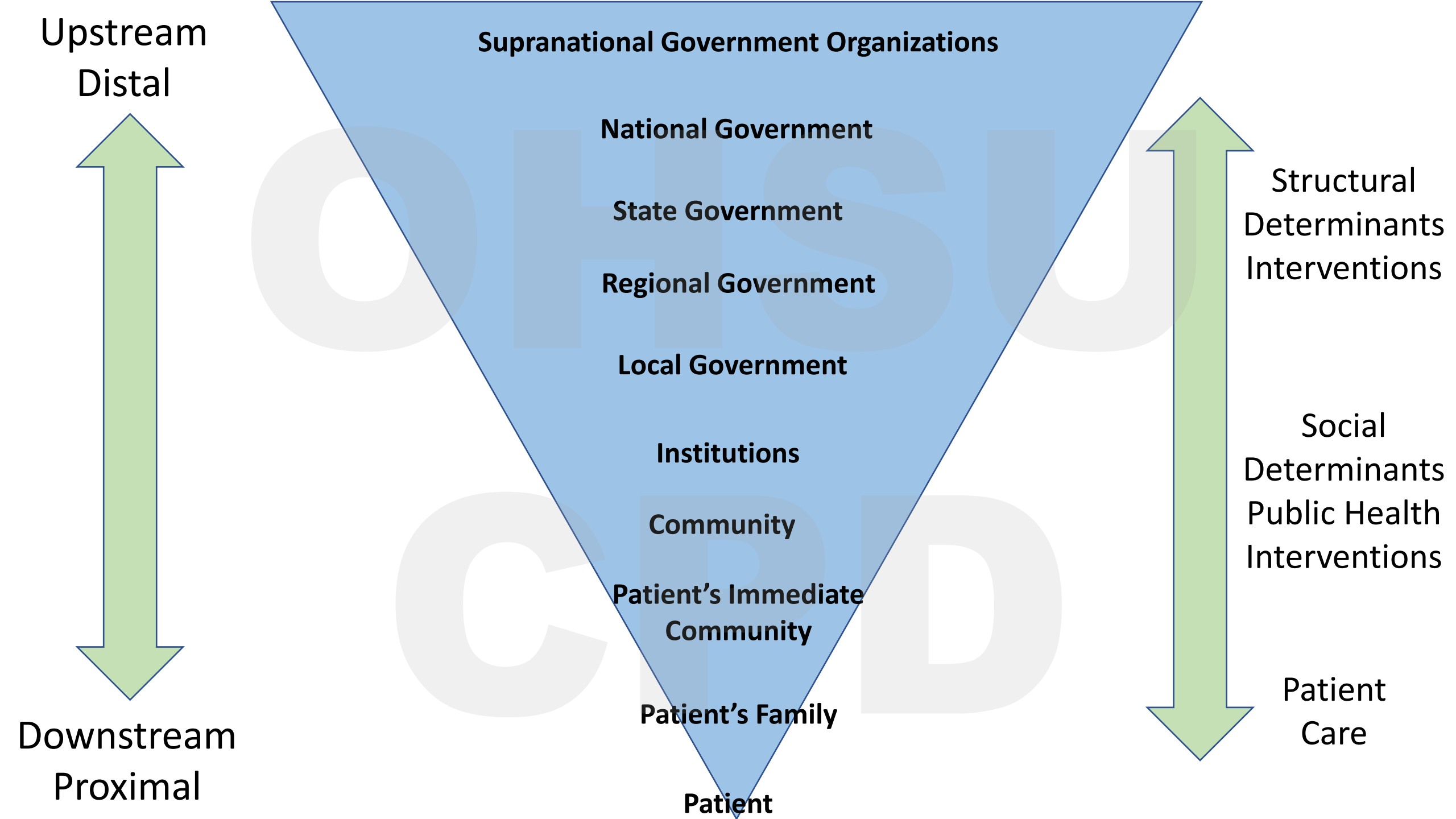
Disparities in Utilization



Kanny D, Jeffries WL 4th, Chapin-Bardales J, Denning P, Cha S, Finlayson T, Wejnert C; National HIV Behavioral Surveillance Study Group. Racial/Ethnic Disparities in HIV Preexposure Prophylaxis Among Men Who Have Sex with Men - 23 Urban Areas, 2017. MMWR Morb Mortal Wkly Rep. 2019 Sep 20;68(37):801-806. doi: 10.15585/mmwr.mm6837a2. PMID: 31536484; PMCID: PMC6755820.

Disparities in Utilization

- PWID: 0-3% PrEP use in SR of 10 studies (Mistler)
- Youth: Age, change in adherence per 5 years aOR=1.15 (1.07 to 1.24) (Mannheimer)
- Transgender: TG vs MSM aPR 0.52 (0.32-0.85) (Schumacher)


Upstream
Distal
Downstream
Proximal
Supranational Government Organizations
National Government
State Government
Regional Government
Local Government
Institutions
Community
Patient's Immediate Community
Patient's Family
Patient
Structural Determinants Interventions
Social Determinants Public Health Interventions
Patient Care

Call to Action: End HIV

- Universal screening for HIV
- Discuss PrEP routinely and broadly
- Many of your patients have indications!
- You can resolve many barriers in your office

Summary

- Uncontrolled HIV epidemic
- PrEP: Proven efficacy
- Dosing strategies
  - TDF/FTC po daily or 2-1-1
  - TAF/FTC po daily in MSM/TGW
  - LA IM CAB
- Practical Guidance
  - **Exclude acute HIV**
  - ≤90-day Rx
  - HIV RNA
  - Triple site G/C

Additional Resources

- PrEP Line: 1-855-448-7737 (8-3pm)
- Mountain West AIDS Education and Training Center
- https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf
- Refer to OHSU TelePrEP

- Centers for Disease Control and Prevention: US Public Health Service: Preexposure prophylaxis for the prevention of HIV infection in the United States—2021 Update: a clinical practice guideline. https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf. Published XXX 2021.
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