“PrEParing” Primary Care!

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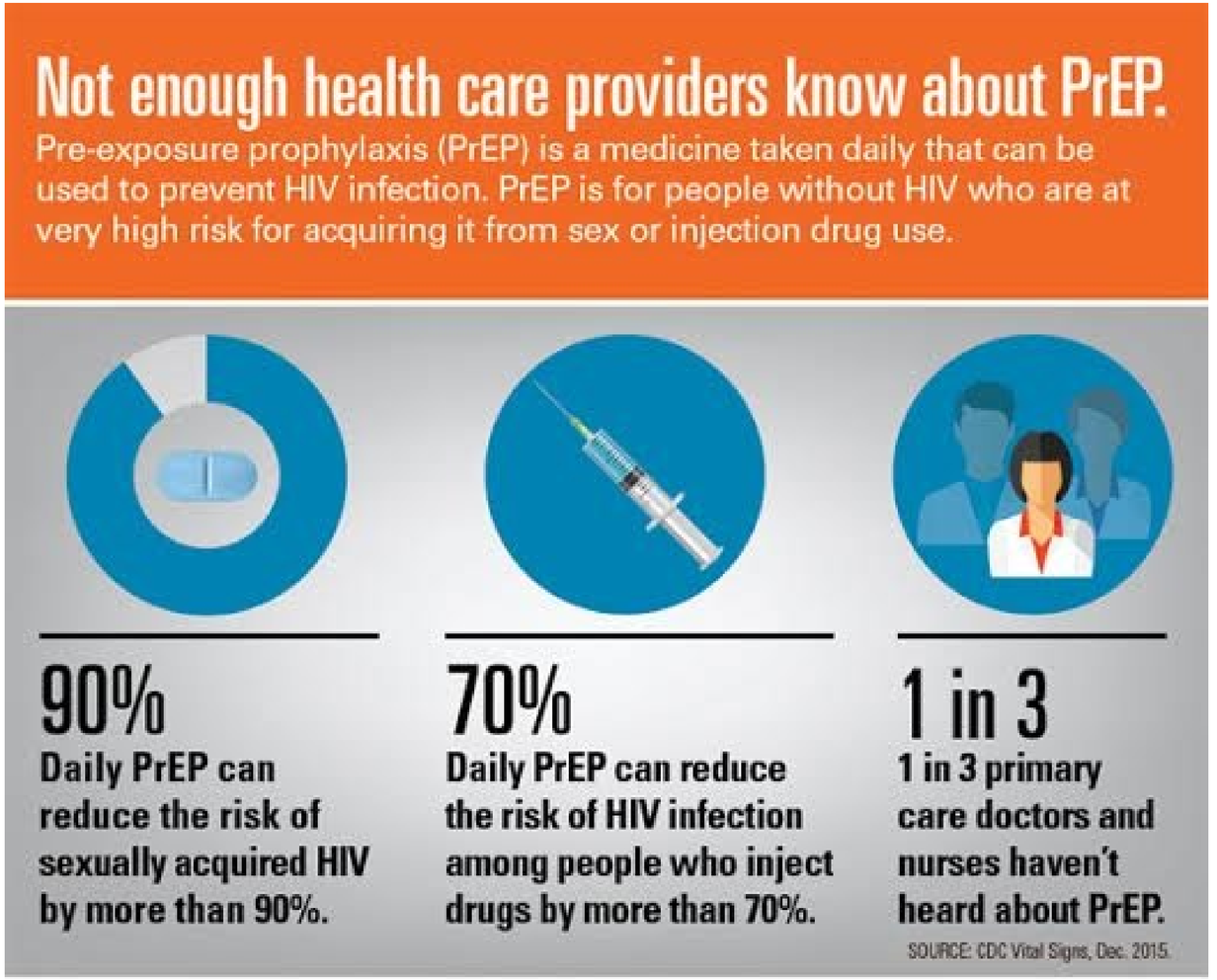

https://www.cdc.gov/hiv/policies/dear-colleague/dcl/092421.html

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Let's talk about history

- July 2012: FDA approves F/TDF for PrEP
- May 2018: approval for F/TDF extended to adolescents and young adults
- June 2019: USPSTF "A" rating
- October 2019: FDA approves F/TAF for MSM and transgender women (women/transgender men not included in efficacy and safety trial)
- 2021: DHHS→ oral PrEP medications, lab tests and clinic visits must be provided by most commercial insurers and some Medicaid programs at no out-of-pocket cost
- December 2021: FDA approves injectable long-active cabotegravir for PrEP

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

https://www.fda.gov/news-events/press-announcements/fda-approves-first-injectable-treatment-hiv-pre-exposure-prevention

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“Status Neutral Approach”

- CDC: “…facilitates the integration of prevention and treatment services so that both become part of the fabric of comprehensive primary care and address the needs of the whole person while mitigating HIV -related stigma.”

https://www.cdc.gov/hiv/policies/dear-colleague/dcl/092421.html

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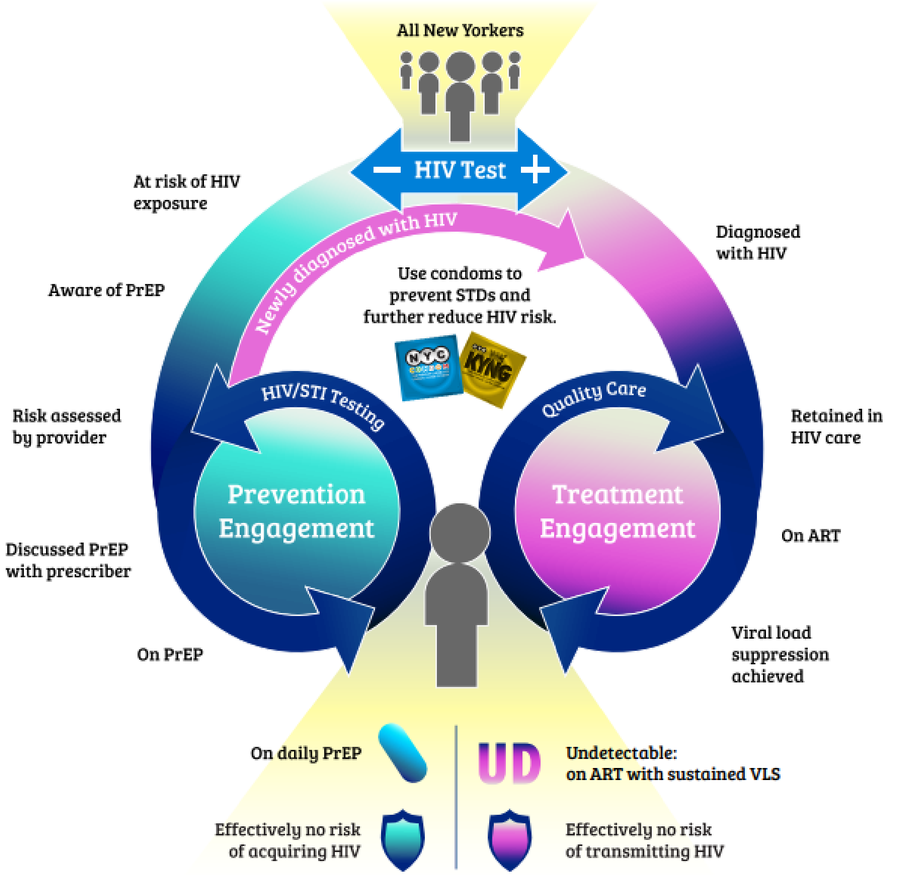
New York City's HIV Status Neutral Prevention and Treatment Cycle



People at risk of HIV exposure taking daily PrEP and people with HIV with sustained viral load suppression do not acquire or transmit HIV.

NYC Health

https://www1.nyc.gov/assets/doh/downloads/pdf/ah/neutral-prevention-treatment-cycle.pdf

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Why should we prescribe PrEP?

- When taken as prescribed, oral PrEP reduces risk of HIV infection by 99%
- Less evidence for PWID, but reduces risk of HIV infection by at least 74%
- MSM/transgender women: injectable PrEP had 69% less risk of HIV infection compared to F/TDF
- Heterosexual women: injectable PrEP had 90% less risk of HIV infection compared to F/TDF
- Compare to consistent condom use: 80% risk reduction in heterosexual couples, 70% in MSM

https://www.cdc.gov/hiv/basics/prep/prep-effectiveness.html#:~:text=How%20effective%20is%20PrEP%3F,99%25%20when%20taken%20as%20prescribed.
https://www.fda.gov/news-events/press-announcements/fda-approves-first-injectable-treatment-hiv-pre-exposure-prevention
https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf

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Type of exposure	Estimated risk of HIV transmission per exposure from a known HIV-positive individual not on ART	References
Receptive anal intercourse	1 in 90	10-16
Receptive anal intercourse with ejaculation	1 in 65	10-17
Receptive anal intercourse no ejaculation	1 in 170	17
Insertive anal intercourse	1 in 666	10,12,13,18
Insertive anal intercourse not circumcised	1 in 161	17
Insertive anal intercourse and circumcised	1 in 909	17
Receptive vaginal intercourse	1 in 1000	10,15,19-15
Insertive vaginal intercourse	1 in 1219	14,15,19-25
Semen splash to eye	<1 in 10,000	26
Receptive oral sex (giving fellatio)	<1 in 10,000	13,20,25,27
Insertive oral sex (receiving fellatio)	<1 in 10,000	12,25
Blood transfusion (one unit)	1 in 1	28
Needlestick injury	1 in 333	27,29,30
Sharing injecting equipment (includes chemsex)	1 in 149	26
Human bite	<1 in 10,000	31,32

ART: antiretroviral therapy.

https://www.researchgate.net/figure/Risk-of-HIV-transmission-per-exposure-from-a-known-HIV-positive-individual-not-on-ART_tbl1_301539090

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Show me the numbers

- Estimated 1.2 million people have an indication (25% prescribed in 2020 compared to 3% in 2015)
- Helped to decrease new HIV infections by 8% from 2015 -2019 after stable interval of time
- Fundamental component of the U.S. government's *Ending the HIV Epidemic in the U.S.* policy initiative: goal of 50% update by 2030
- How has the COVID-19 pandemic impacted PrEP use?

https://www.cdc.gov/nchhstp/newsroom/fact-sheets/hiv/PrEP-for-hiv-prevention-in-the-US-factsheet.html#:~:text=Notable%20gains%20have%20been%20made,only%20about%203%25%20in%202015

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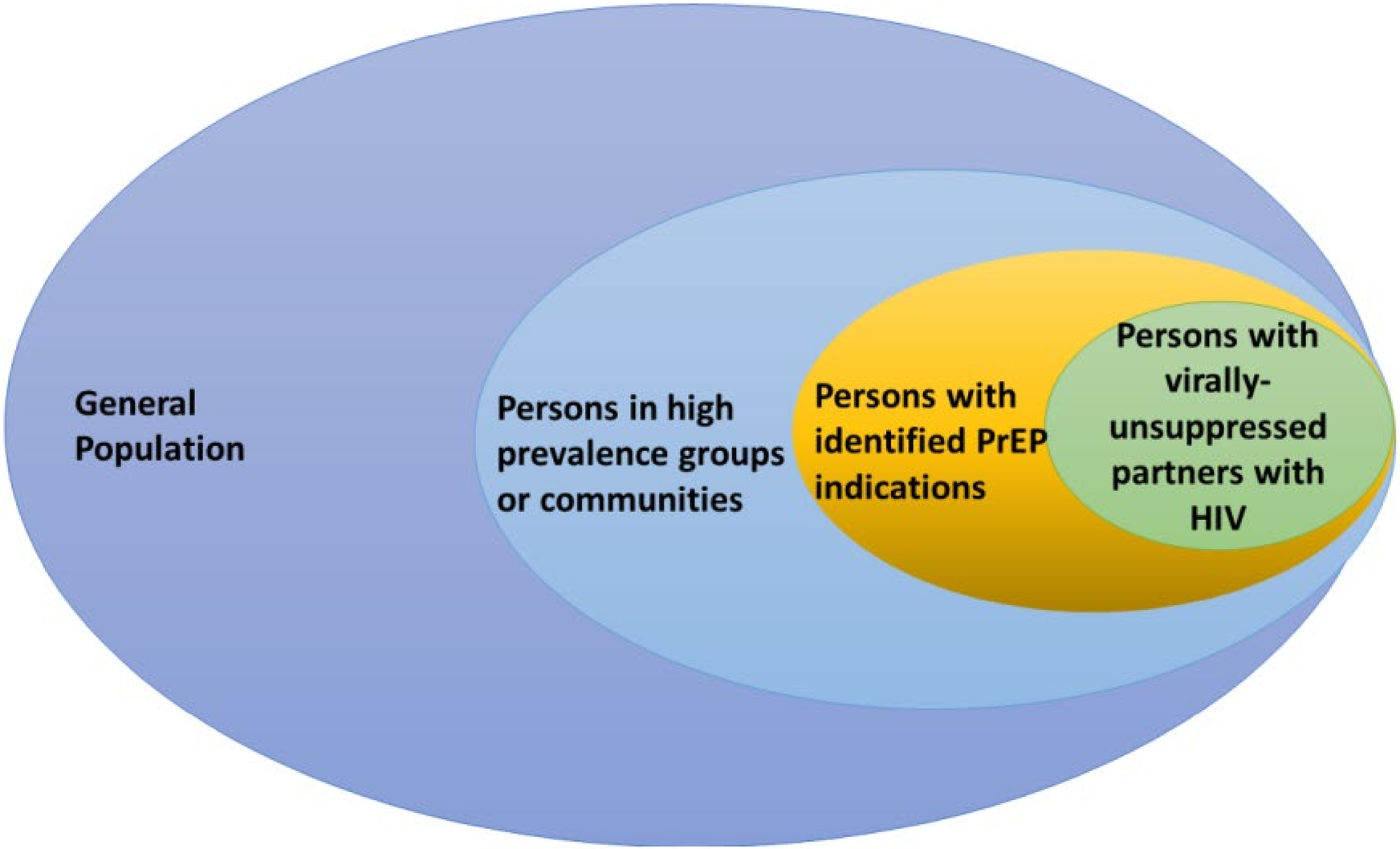

https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf

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It’s important to talk about sex (and drugs)

- Brief, targeted sexual history recommended for all adults and adolescents
- Patient often do not disclose stigmatized sexual or substance use behaviors
- Often deferred because of provider or anticipated patient discomfort
- Don’t limit sexual history to only selected patients: everyone is at risk
- Who patient is having sex with and what kind of sexual behaviors they are engaging in
- Ask about gender identity
- Ask about substance use and practices, shared needles/equipment?

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

What's the indication for PrEP?

- All sexually active adult and adolescent patients should be informed about PrEP
- Indications the same for both oral and injectable PrEP
- If someone has an HIV-positive partner, anal or vaginal sex (especially unknown or detectable viral load)
- Bacterial STI in the last 6 months: gonorrhea, chlamydia and syphilis
- Risky sexual behavior, inconsistent or no barrier protection
- PWID who share equipment or have an HIV-positive injecting partner

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

"Patients may request PrEP because of concern about acquiring HIV but not feel comfortable reporting sexual or injection behaviors to avoid anticipated stigmatizing responses in health care settings. For this reason, after attempts to assess patient sexual and injection behaviors, patients who request PrEP should be offered it, even when no specific risk behaviors are elicited."

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

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How do we help?

- If partner(s) of unknown HIV status, testing should be offered (https://gettested.cdc.gov/)
- If HIV-positive partner: understand ART regimen, adherence and viral load
- Offer comprehensive STI screening and treatment
- Help to connect to drug -related behavioral support programs, mental health services, medication -assisted therapy, 12-step programs

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

Who can get PrEP?

- Negative HIV ag/ab test within one week of initiation
- No signs or symptoms consistent with acute HIV infection
- Estimated creatinine clearance ⩾30 mL/min (F/TAF), ⩾60 mL/min (F/ TDF)
- No interacting or contraindicated drugs

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

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Table 2: Clinical Signs and Symptoms of Acute (Primary) HIV Infection[71]

Features	Overall (n = 375) %	Sex		Route of transmission	
		Male (n = 355) %	Female (n = 23) %	Sexual (n = 324) %	Injection Drug Use (n = 34) %
Fever	75	74	83	77	50
Fatigue	68	67	78	71	50
Myalgia	49	50	26	52	29
Skin rash	48	48	48	51	21
Headache	45	45	44	47	30
Pharyngitis	40	40	48	43	18
Cervical adenopathy	39	39	39	41	27
Arthralgia	30	30	26	28	26
Night sweats	28	28	22	30	27
Diarrhea	27	27	21	28	23

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

What should we prescribe?

- Daily oral F/TDF
- Daily oral F/TAF (men and transgender women)
- Injectable cabotegravir (one injection per visit, gluteal muscle)
  - 600 mg initial dose → 4 weeks later dose #2 → every 8 weeks

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

PrEP pharmacokinetics

- HIV risk reduction efficacy: 99% for 7 doses/week, 96% for 4 doses/week, 76% for 2 doses/week
- Significant protection for lower vaginal tract tissues required 6 -7 doses per week (>85% adherence), colorectal tissues 2 doses per week (28% adherence)
- Maximum tissue levels of protection:
  - Rectal: 7 days
  - Cervicovaginal: 20 days
- Data for penile tissue, F/TAF and injectable cabotegravir not available
- IAS-USA: double dose (2 pills) of F/TDF can be given on the first day (for MSM)

https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf
https://jamanetwork.com/journals/jama/fullarticle/2771873

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F/TDF

- HIV nucleoside/nucleotide reverse transcriptase inhibitor combination
- At risk through sex or injection drug use
- 200/300 mg once daily
- Headache, abdominal pain and weight loss
- Renal function:
  - Estimated creatinine clearance ⩾60 mL/min
  - Small decreases in renal function observed in PrEP trials (mostly reversed when discontinued) HIV treatment: rare cases of ARF, Fanconi's syndrome
- Bone density:
  - iPrEX trial demonstrated ~1% decline in BMD in first few months of PrEP use that either stabilized or returned to normal (~3-4% declines seen in patients on combination ART)
  - No increase in fragility fractures over 1-2 years of observation
- Hepatitis B, including potential for flare on discontinuation
- Drug interactions: https:/ / www.hiv-druginteractions.org/

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

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F/TAF

- HIV nucleoside/nucleotide reverse transcriptase inhibitor combination
- At risk through sex, men and transgender women only
- 200/25 mg once daily
- Diarrhea
- Renal function:
  - Estimated creatinine clearance ⩾30 mL/min
  - No decrease in renal function observed in single PrEP trial evaluating this
- Lipid profile:
  - Higher rates of weight gain and triglyceride elevation versus F/ TDF (which is associated with reductions in both HDL and LDL cholesterol)
- Bone density:
  - Slight increase in BMD at the hip and spine through 96 weeks of the DISCOVER trial, no difference in frequency of fractures versus F/ TDF
- Hepatitis B, including potential for flare on discontinuation

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

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Which medication should I prescribe for PrEP?

TDF/FTC

EFFECTIVENESS
- ✓ for multiple populations

SAFETY
- Small ↓ in eGFR and BMD

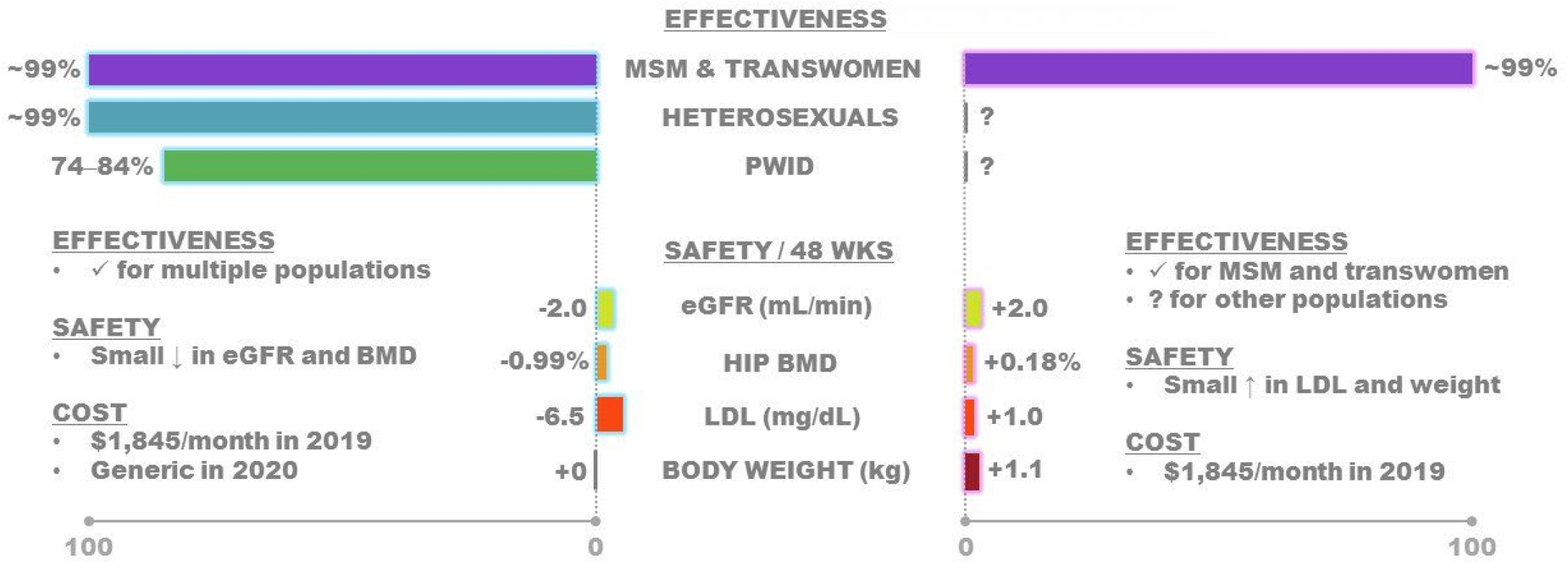
COST
- $1,845/month in 2019
- Generic in 2020

TAF/FTC

EFFECTIVENESS
- ✓ for MSM and transwomen
- ? for other populations

SAFETY
- Small ↑ in LDL and weight

COST
- $1,845/month in 2019



Sources: fda.gov/media/129607/download; fda.gov/media/129609/download; cdc.gov/hiv/risk/estimates/preventionstrategies.html Created by: @JuliaLMarcus

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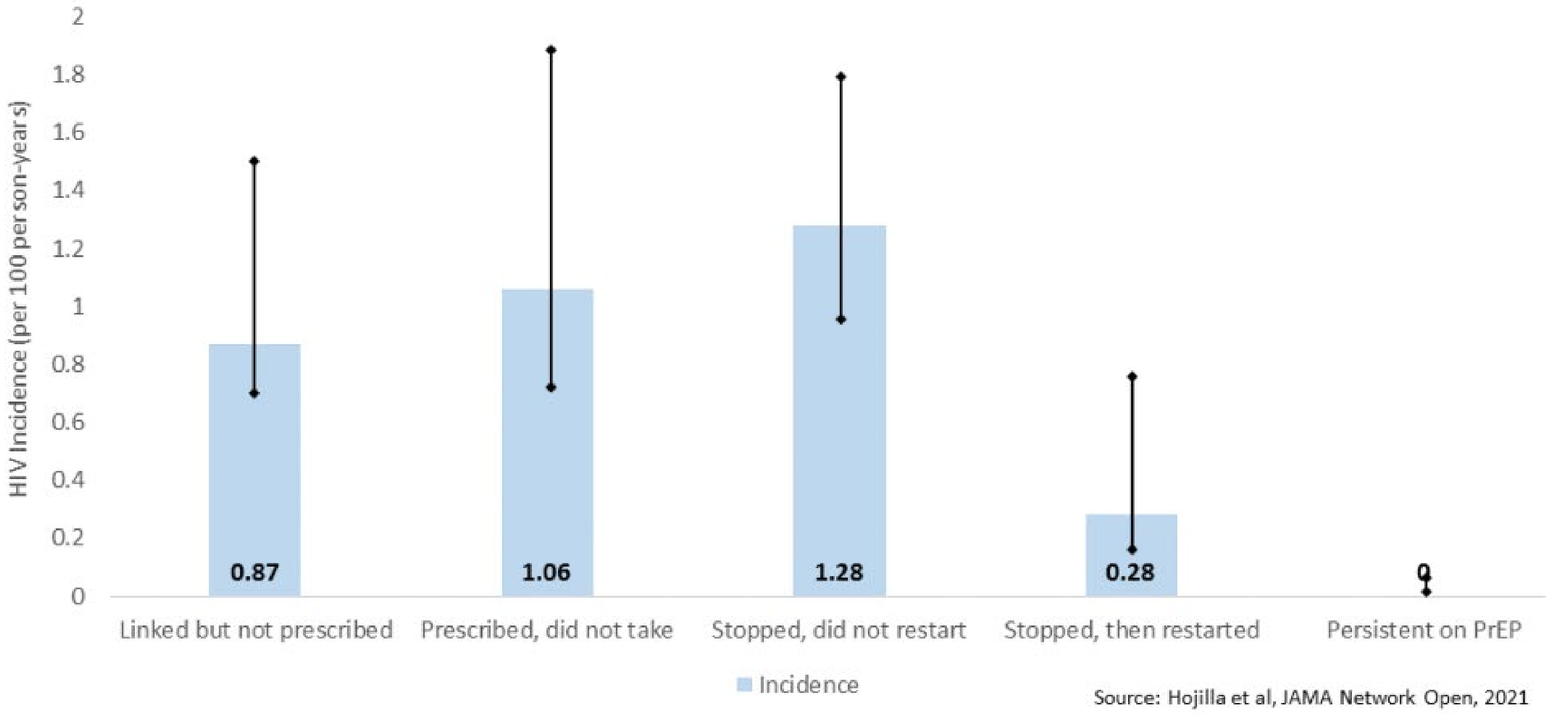
Discontinuing oral PrEP: protections wanes after ~7 -10 days

Figure 6 HIV Incidence in MSM Before, While Taking, and After Discontinuing F/TDF PrEP Use[140, 141]



Source: Hojilla et al, JAMA Network Open, 2021

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

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Cabotegravir

- HIV integrase strand transfer inhibitor
- At risk through sex
- 600 mg injected into gluteal muscle q2 months
- 30 mg daily oral lead -in x 4 weeks is optional
- NOT indicated: creatinine/clearance, hepatitis B serology, lipids, hepatic panel
- BMI <30 use 1.5 inch needle, BMI ≥30 use 2 inch needle
- Injection site reactions generally mild or moderate, lasted a few days

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

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Discontinuing injectable PrEP

- Discuss cabotegravir “tail” and implications of declining drug levels: risk of resistance
  - Median time to undetectable CAB plasma levels was 44 weeks for men and 67 weeks for women
- Educate regarding continuing HIV risk and prevention
- Can prescribe oral PrEP within 8 weeks of last injection if risk factors persist (consider nPEP)
- Quarterly HIV testing for 12 months: continued follow-up appointments

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

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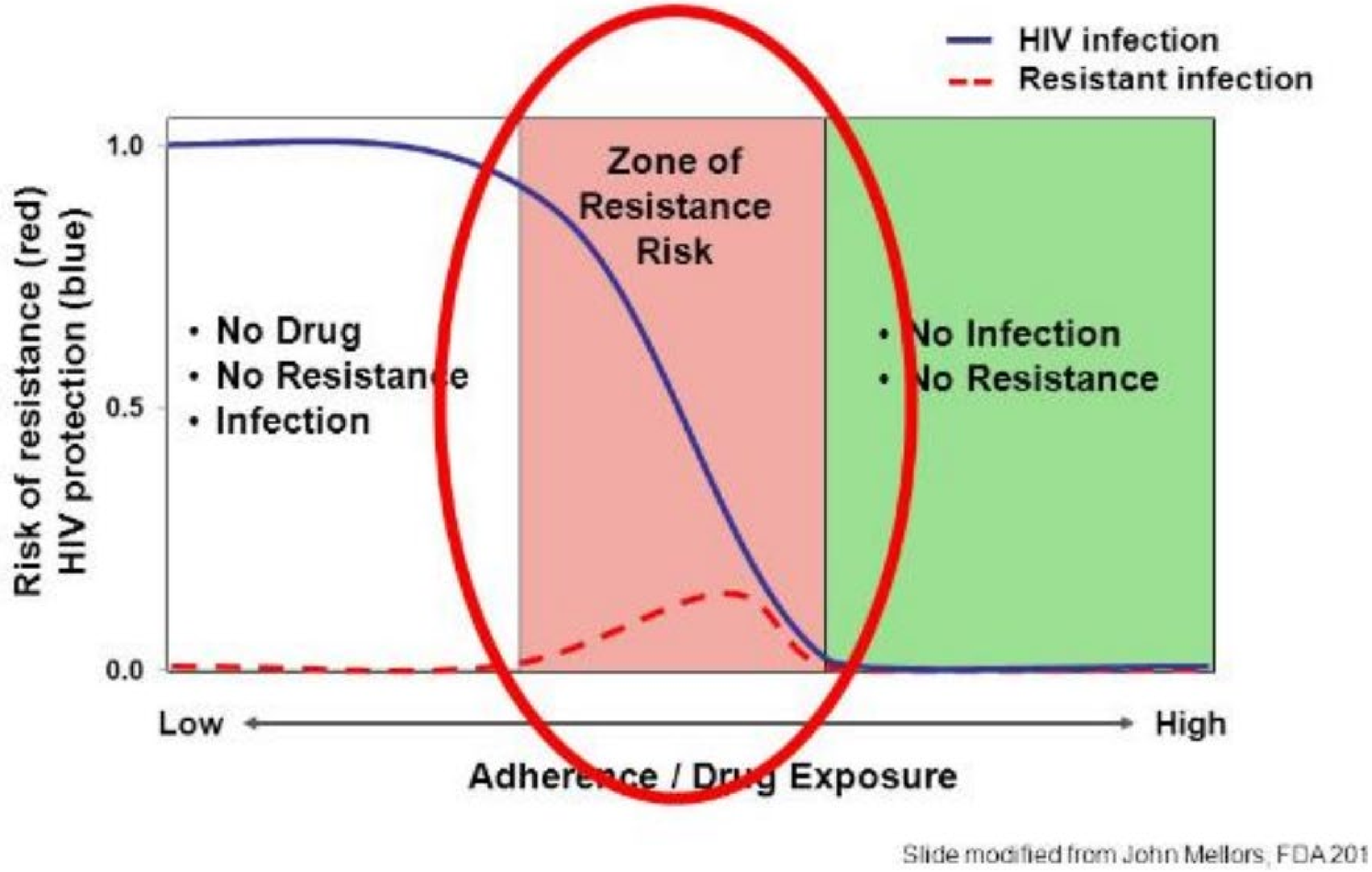
PrEP and HIV resistance



Slide modified from John Mellors, FDA 201

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

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Monitoring on PrEP

- HIV ag/ab testing and HIV -1 RNA assay
  - Oral: Baseline and q3 months
  - Injectable: Baseline, at 1 month and q2 months
- Gonorrhea, chlamydia and syphilis testing
  - Oral: q3-6 months
  - Injectable: q4 -6 months
- Renal function
  - Oral: Baseline, q6 months for age ⩾50 years or estimated creatinine clearance <90 mL/min, otherwise yearly
  - Injectable: n/a
- Access to clean needles and drug treatment services
- Assess desire to continue: PrEP allows for flexibility

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

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Ambiguous HIV test results

- National Clinician's Consultation Center PrEPline: 855-448-7737
- Assess PrEP adherence since last negative testing and draw new ag/ab and RNA testing
- Options
  - Continue PrEP: good effectiveness if adherent
  - Provide PEP: add third agent x 28 days
  - Discontinue PrEP x 1-2 weeks, then recheck HIV testing
  - Injectable CAB: hold until final determination is made

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

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“Same Day PrEP”

- Convenience and increased uptake
- Ability to check POC HIV testing (antigen/antibody fingerstick)
  - Draw lab creatinine and HIV testing
- Same-day lab-based antigen/antibody or HIV -1 RNA test

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

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“2-1-1” PrEP regimen

- “Event-driven,” “intermittent,” “on -demand”
- Nondaily dosing regimen given in relation to sexual intercourse events in MSM
- IPERGAY andPrevenir trials (Paris and Canada): ⩾86% preventive efficacy (although men took ~3-4 doses per week)
- Not FDA-approved
- Recommended by IAS-USA

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

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Conception and pregnancy

- Elevated risk of HIV infection occurs during time of conception, pregnancy and breastfeeding
- Offer F/TDF to women attempting contraception, pregnant or breastfeeding whose sexual partner has HIV:
  - Especially unknown viral load, detectable viral load, undocumented viral load
- If sexual partner has HIV -1 viral load <200 copies/mL there is essentially no risk of sexual transmission (U=U)
- Antiretroviral Pregnancy Registry provides no evidence of adverse effects with F/TDF (TAF also found to be safe but not well -studied)
- Likely limited exposure through breast milk

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

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Primary care considerations

- Opportunity to engage in preventive health screenings and measures
- Overall sexual health
- Vaccinations: hepatitis A, hepatitis B, HPV, meningococcal
- Screenings for hepatitis C, depression, substance use, intimate partner violence
- Cancer screenings: mammography, cervical cancer, prostate cancer, lung cancer

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

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References

- https://www.cdc.gov/hiv/basics/prep/prep-effectiveness.html#:~:text=How%20effective%20is%20PrEP%3F,99%25%20when%20taken%20as%20prescribed
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- https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf
- https://www.cdc.gov/hiv/policies/dear-colleague/dcl/092421.html
- https://www.cdc.gov/nchhstp/newsroom/fact-sheets/hiv/PrEP-for-hiv-prevention-in-the-US-factsheet.html#:~:text=Notable%20gains%20have%20been%20made,only%20about%203%25%20in%202015
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- https://www.researchgate.net/figure/Risk-of-HIV-transmission-per-exposure-from-a-known-HIV-positive-individual-not-on-ART_tbl1_301539090
- https://stacks.cdc.gov/view/cdc/38856

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