



HIV in the Era of Covid-19: PrEP (Pre-exposure Prophylaxis)

The Theory, Practice and Results

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What is PrEP?

- One pill once a day to reduce risk of contracting HIV
- $\geq 90\%$ protective against sexually acquiring HIV
- Reduces HIV acquisition risk in intravenous drug users (IVDU)
- Currently only two agents approved for PrEP

What are we trying to accomplish? A Case Study

Herman, a 54-year-old man (HIV-negative) comes into the hospital unable to talk normally. He is the longtime partner of Bill, a 35-year-old man who is HIV-positive, compliant with anti-retroviral therapy and whose HIV-1 RNA (viral loads) are nearly always non-detectable.

Bill was hospitalized for 10 for diabetes mellitus, neuropathy and renal failure. He came to clinic weeks later; his HIV-1 viral load was >3,000 copies of RNA.

Herman was hospitalized 1 month later slurring his speech and could move his tongue only to the right. The HIV-1 RNA was >1,000,000 copies and the platelets <30,000/dL.

Herman was treated with plasmapheresis and ART. He is doing well and compliant with ART.

Another Case Study

- Roger is a 56-year-old man (MSM) who has "come out" two months ago. He was an insurance executive with a good income and no sexual activity with women or men for years. In the past he occasionally had HIV tests and they were all negative. (The testing was done at his place of work.)
- He had one male partner 3 weeks ago and was primarily the partner on the bottom. He now complains of fever, skin rash and a sore throat.
- On physical examination he has oral-pharyngeal thrush, tender lymphadenopathy and a macular rash on the extremities and abdomen.
- The HIV-1 RNA was >2,000,000 copies and the RPR was negative.
- He was started on ART and has done well.



Truvada (FTC/TDF)

- Single pill containing two medications
 - Emtricitabine (FTC) 200 mg
 - Tenofovir disoproxil (TDF) 300 mg
- One tablet once a day
 - No more than 90-day prescription provided
- Can be taken with or without food
- Take missed doses as soon as remembered
 - If close to next dose, wait until then and take 1 tablet



Descovy (FTC/TAF)

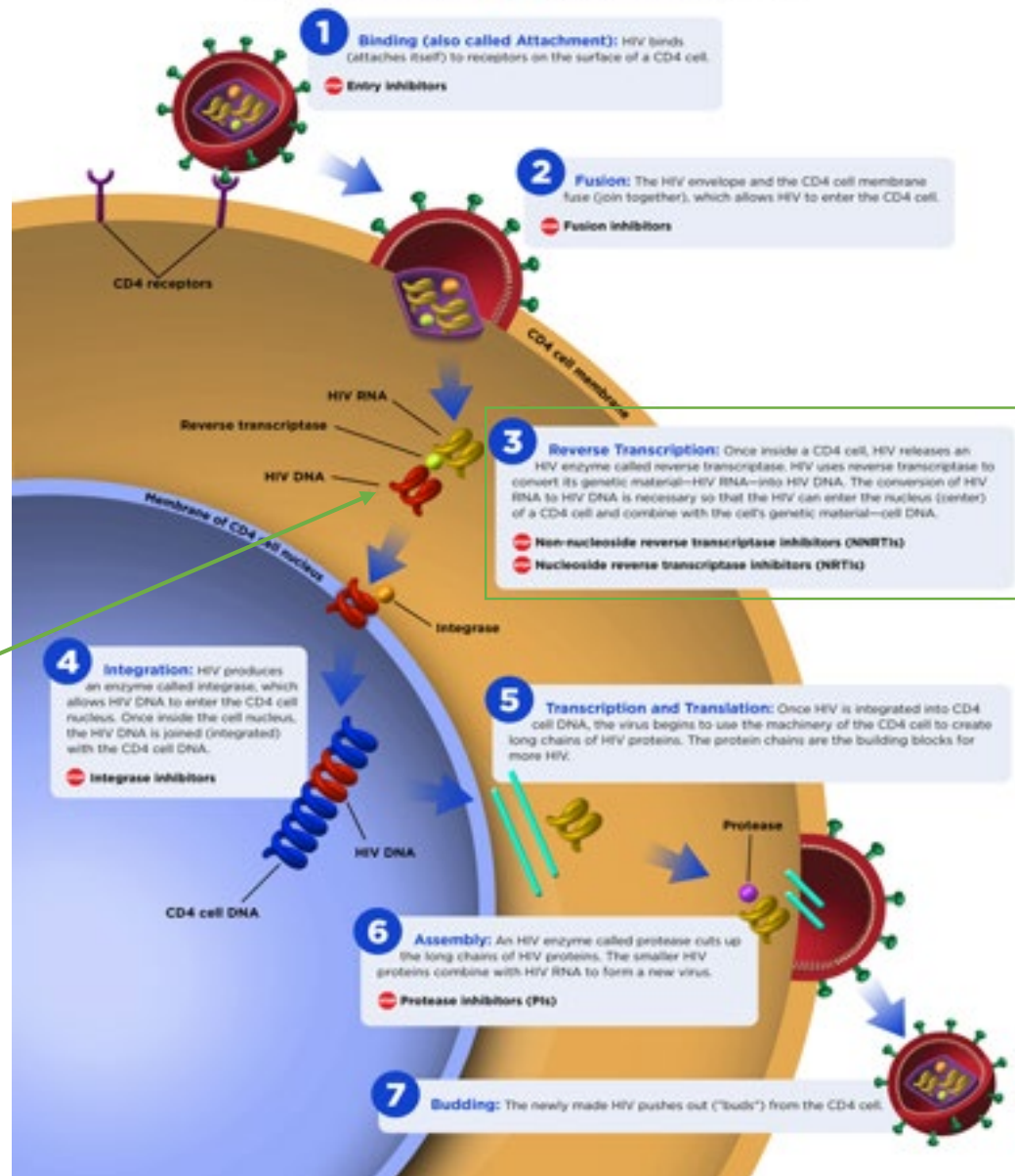
- Single pill containing two medications
 - Emtricitabine (FTC) 200 mg
 - Tenofovir alafenamide (TAF) 25 mg
- Same instructions for use as Truvada
- ONLY studied in MSM and transgender women
 - Not recommended for use in cisgender women or for IVDU

NRTIs Nucleoside/Nucleotide Reverse Transcriptase Inhibitors

Indirectly inhibits enzyme
required to copy viral RNA to
DNA.

The HIV Life Cycle

HIV medicines in six drug classes stop HIV at different stages in the HIV life cycle.



Side Effects of PrEP

May experience nausea, bloating upon initiation

Usually resolves within 2-3 weeks

Headache

Increased risk of decreased renal function

Uncommon but known adverse effect from TDF

Increased risk of decreased bone mineral density

Renal function usually returns to normal if PrEP stopped

Tenofovir Disoproxil Drug Issues

Primarily
known for its
potential
renal issues

Risk of renal
dysfunction
may be
multifactorial

- Age
- Addition of other nephrotoxic agents

May also lead
to decreased
bone mineral
density

- Possibly 1-3% greater loss with TDF
- Calcium/vitamin D supplementation may help

Tenofovir
Alafenamide
Drug Issues

Same concerns as TDF but appears to be lower risk

- Improved renal/bone adverse effect profile

Not as well studied for PrEP

- Only recently approved
- Effects of missing doses less clear than with TDF regimen

Descovy for PrEP

- DISCOVER study looked at MSM and transgender women
 - Found to be equivalent to Truvada
- Major concerns again relate to female use
 - A previous PK study with TAF found poor tissue levels
 - 11-fold lower in cervicovaginal fluid
- Uncertain how important adherence is for use

When PrEP is NOT Recommended

- Do not begin Truvada if CrCl < 60 mL/min
- If CrCl declines to < 50 mL/min, stop Truvada
 - FTC and TDF have recommended dose adjustments
 - Renally-adjusted doses were not studied for PrEP
- Descovy should be stopped if CrCl < 30 mL/min
 - An option for PrEP in patients with mild-moderate CKD

PrEP (Truvada) Drug Interactions

Table 11: PrEP Medication Drug Interactions ^{6,80}

	TDF	FTC
Buprenorphine	No significant effect. No dosage adjustment necessary.	No data
Methadone	No significant effect. No dosage adjustment necessary.	No data
Oral contraceptives	No significant effect. No dosage adjustment necessary.	No data
Acyclovir, valacyclovir, cidofovir, ganciclovir, valganciclovir, aminoglycosides, high-dose or multiple NSAIDs or other drugs that reduce renal function or compete for active renal tubular secretion	Serum concentrations of these drugs and/or TDF may be increased. Monitor for dose-related renal toxicities.	No data
Ledipasvir/sofosbuvir	Serum concentrations of TDF may be increased. Monitor for toxicities.	No significant effect



PrEP (Descovy) Drug Interactions

- Descovy more likely to have interactions than Truvada
- TAF more susceptible to p-glycoprotein effects
 - Efficacy may be compromised with select agents
- Avoid use with:
 - Barbiturates
 - Carbamazepine/oxcarbazepine
 - Phenytoin
 - Rifamycins
 - St John's Wort


PrEP Activity

Truvada deposits at varying rates into different tissues

Estimate ~7 days for maximal rectal tissue levels

Estimate ~20 days for maximal vaginal tissue/blood levels

This data is not yet known for Descovy



On-Demand PrEP (Truvada)

- Recent evidence supports this potential approach
 - 2 tablets 2-24 hours before sexual encounter
 - 1 tablet 24 hours after sexual encounter
 - 1 tablet 48 hours after sexual encounter
- Missing doses here may not be as forgiving
- Reliant on anticipation of a sexual encounter
- Not officially recommended as of yet

Vaginal Exposures and Adherence

- Far less clear how levels are affected in this tissue
- DOES appear to be much more susceptible to missed doses
- Would avoid on-demand PrEP in this group

Indications - MSM

BOX B1: RECOMMENDED INDICATIONS FOR PREP USE BY MSM²

- Adult man
- Without acute or established HIV infection
- Any male sex partners in past 6 months (if also has sex with women, see Box B2)
- Not in a monogamous partnership with a recently tested, HIV-negative man

AND at least one of the following

- Any anal sex without condoms (receptive or insertive) in past 6 months
- A bacterial STI (syphilis, gonorrhea, or chlamydia) diagnosed or reported in past 6 months

Indications - Heterosexuals

Box B2: RECOMMENDED INDICATIONS FOR PrEP USE BY HETEROSEXUALLY ACTIVE MEN AND WOMEN

- Adult person
- Without acute or established HIV infection
- Any sex with opposite sex partners in past 6 months
- Not in a monogamous partnership with a recently tested HIV-negative partner

AND at least one of the following

- Is a man who has sex with both women and men (behaviorally bisexual) [also evaluate indications for PrEP use by Box B1 criteria]
- Infrequently uses condoms during sex with 1 or more partners of unknown HIV status who are known to be at substantial risk of HIV infection (PWID or bisexual male partner)
- Is in an ongoing sexual relationship with an HIV-positive partner
- A bacterial STI (syphilis, gonorrhea in women or men) diagnosed or reported in past 6 months

Indications - IVDU

BOX B3: RECOMMENDED INDICATIONS FOR PREP USE BY PERSONS WHO INJECT DRUGS

- Adult person
- Without acute or established HIV infection
- Any injection of drugs not prescribed by a clinician in past 6 months

AND at least one of the following

- Any sharing of injection or drug preparation equipment in past 6 months
- Risk of sexual acquisition (also evaluate by criteria in Box B1 or B2)

Patient Visits

Typically PrEP patients are seen every 3 months

Visits should be focused around:

- Risk reduction counseling
- Assessment of HIV status/signs and symptoms of acute infection
- STI screening as recommended or needed
- Medication adherence counseling

Virtual Visits

Patients Access:

Telephone needed for phone consults

Smartphone or Computer with working camera needed for video consults

Telemedicine Coordination:

- Confirm patient's appointment type
- Coordinate necessary lab work and access to virtual consults
- Make sure patient has a clear understanding of follow up plan, provide in writing if possible
- Make sure patient has access to all necessary testing, including STI swabs

Baseline Testing

HIV screening test

Estimated creatinine clearance

Hepatitis B serologies (HBsAb, HBcAb, HBsAg)

- Follow up with HBV DNA if HBsAg is positive

Hepatitis C screening

Bacterial STI testing

Every 3 Month Monitoring

HIV testing (preferably 4th generation)

Pregnancy testing for women who may become pregnant

Bacterial STI testing if signs/symptoms present

Bacterial STI testing for asymptomatic MSM patients

- If history of STI or multiple partners

Every 6
Month
Monitoring

Monitor estimated
creatinine clearance

Bacterial STI testing
for all sexually active
patients

HIV 4th Generation Screening Test

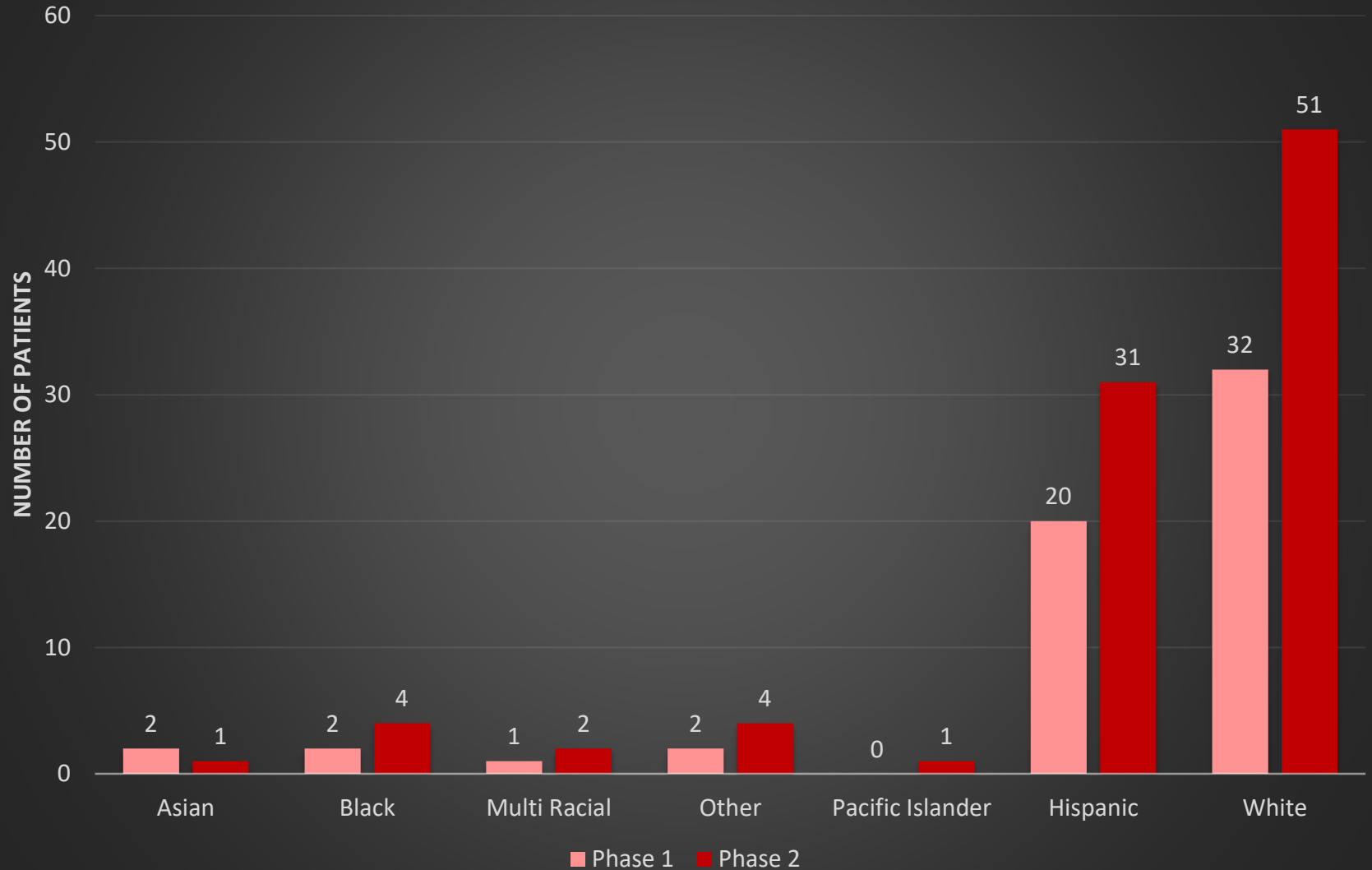
Preferred test, quickest
identification on HIV

Can detect a new infection
10-14 days after exposure

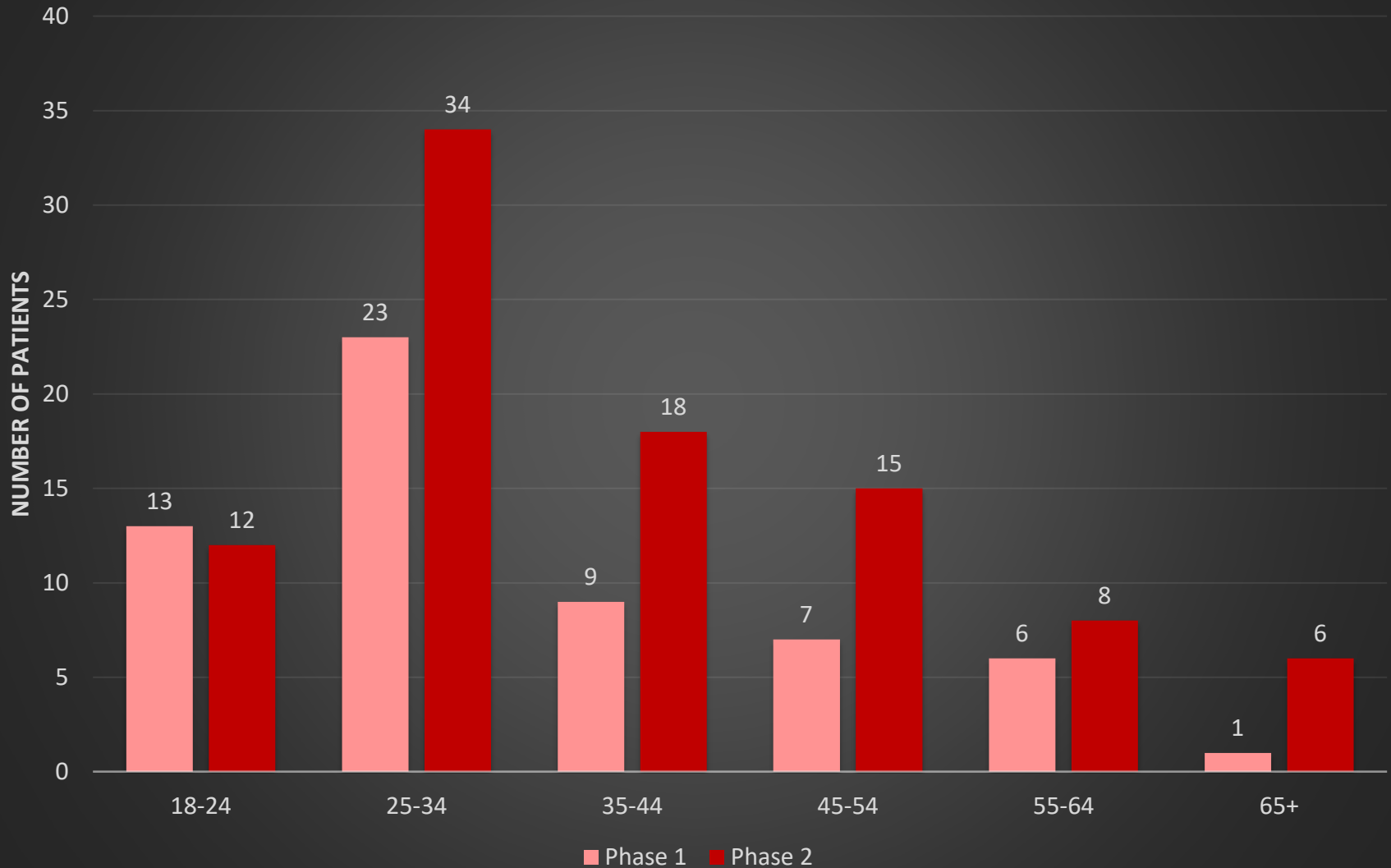
May affect decision to
initiate PrEP

- If unprotected encounter within 2-week period, may repeat test

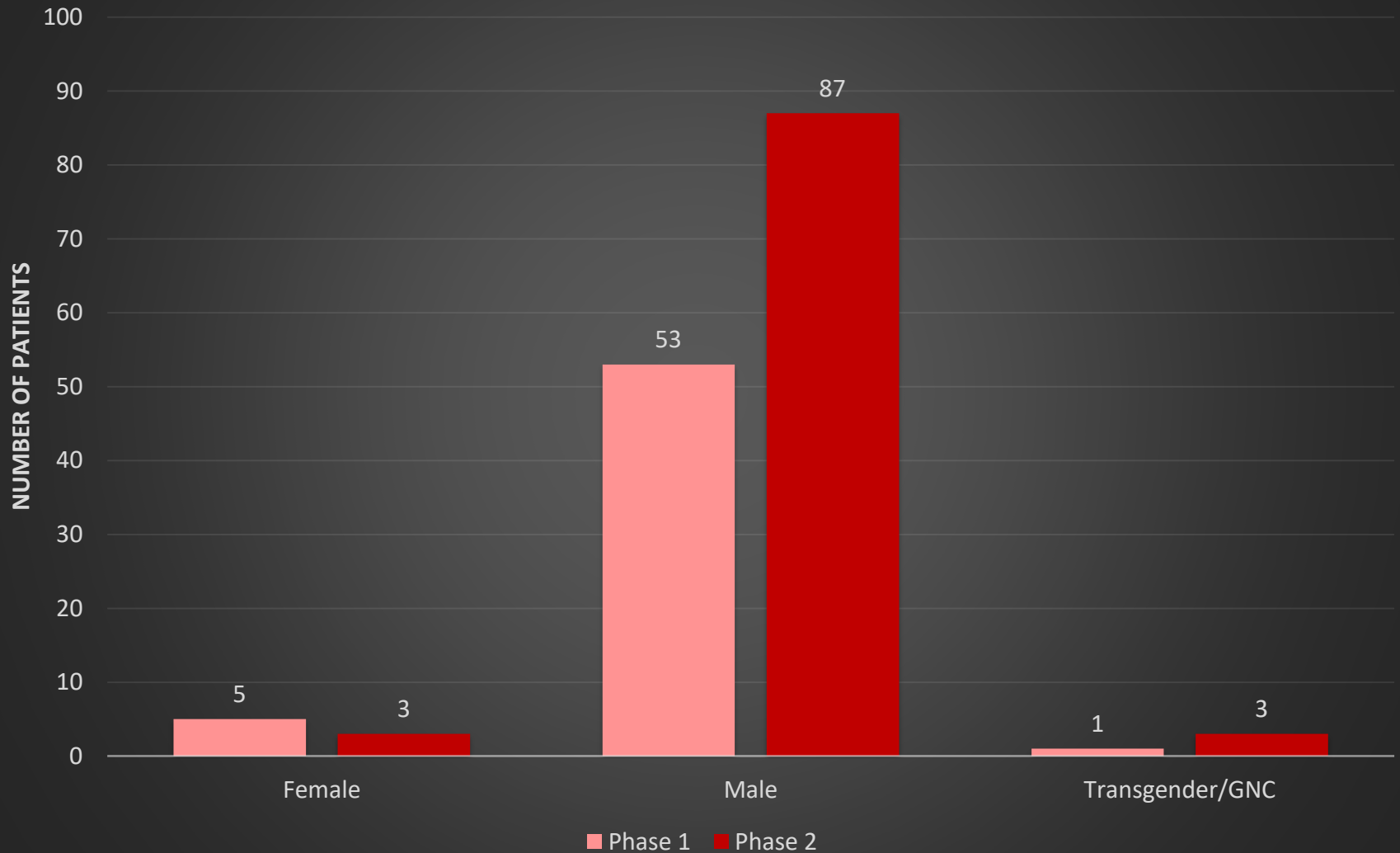
PrEP Initiation by Race/Ethnicity



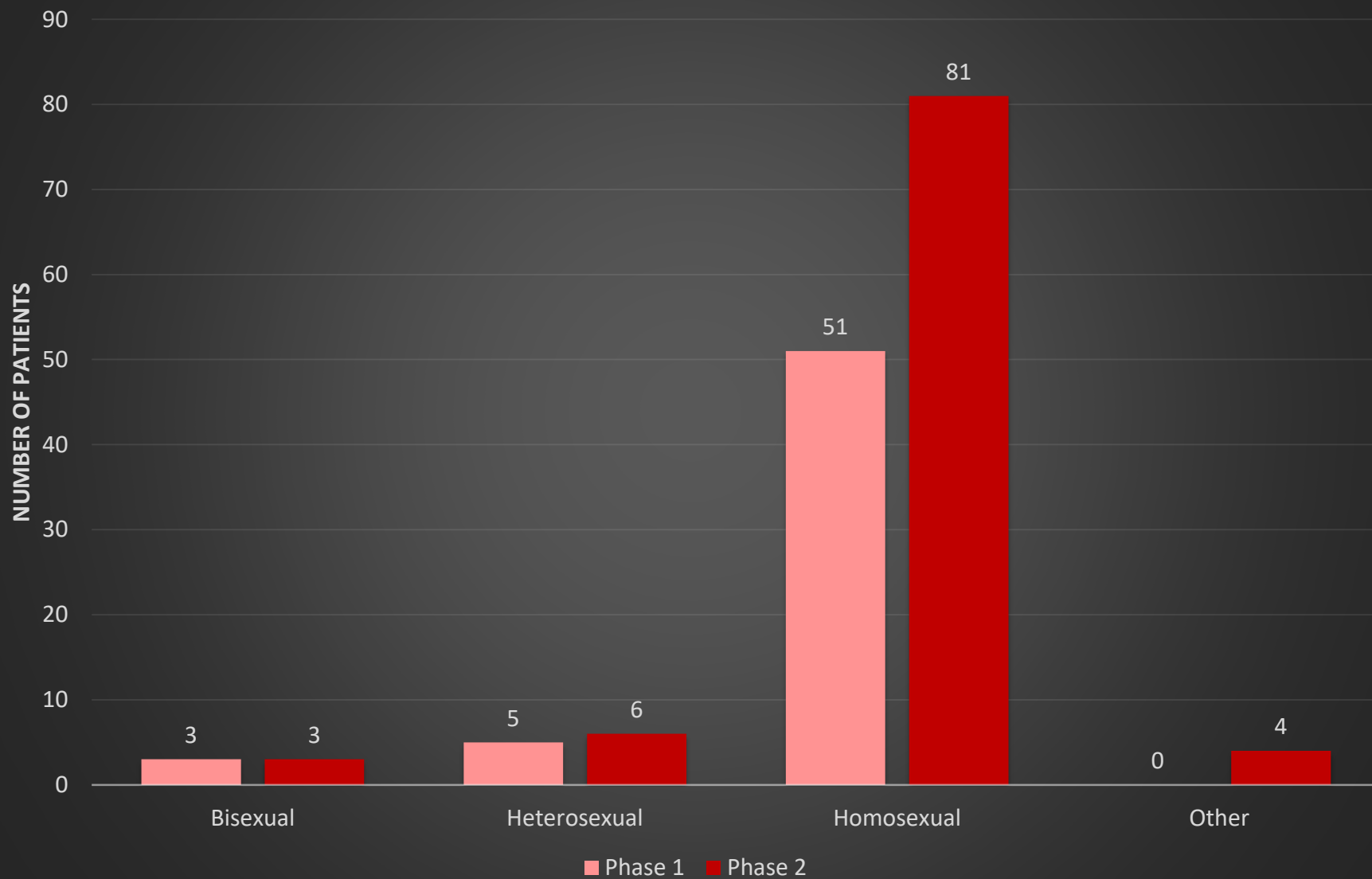
PrEP Initiation by Age Category



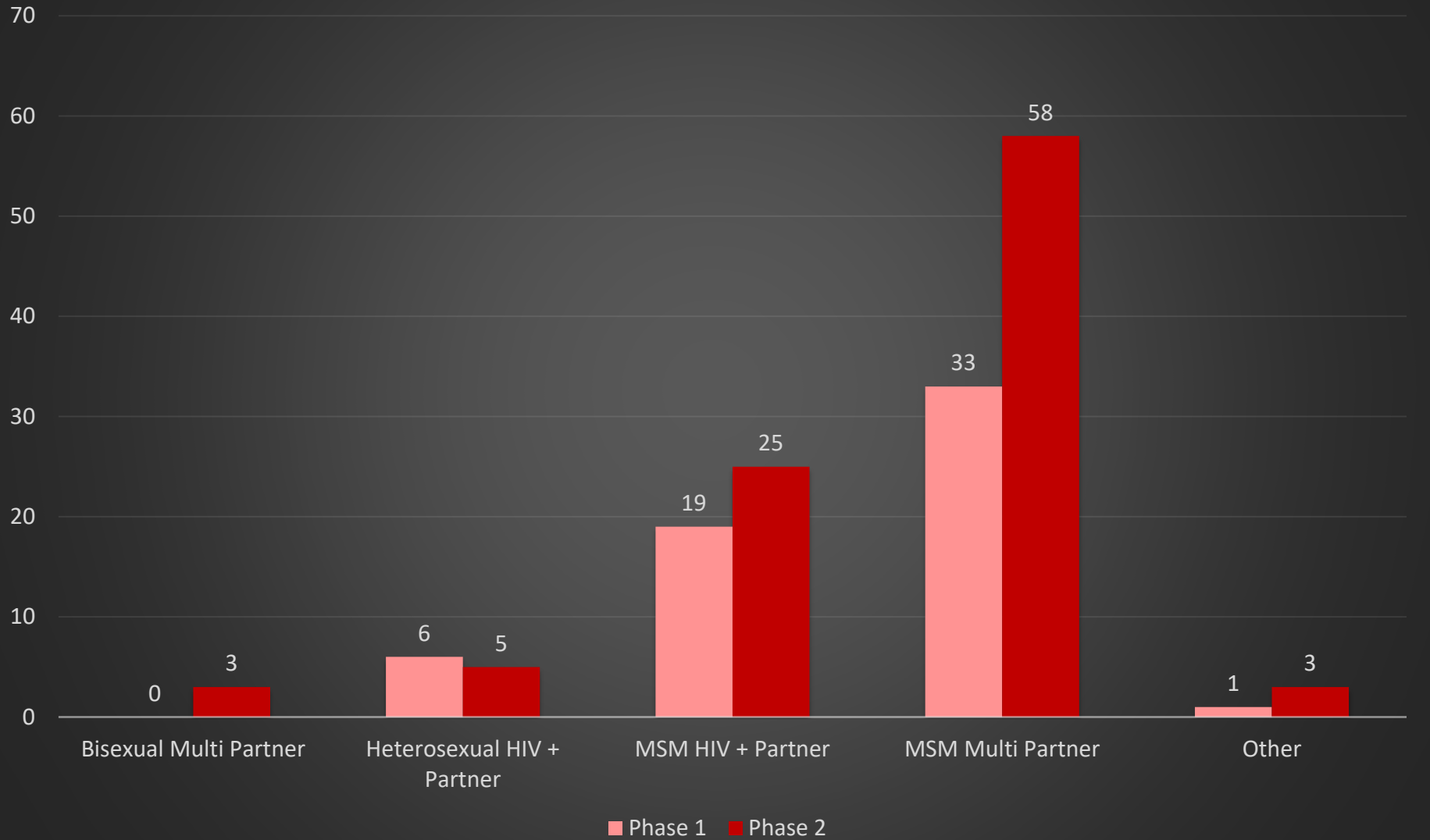
PrEP Initiators by Gender

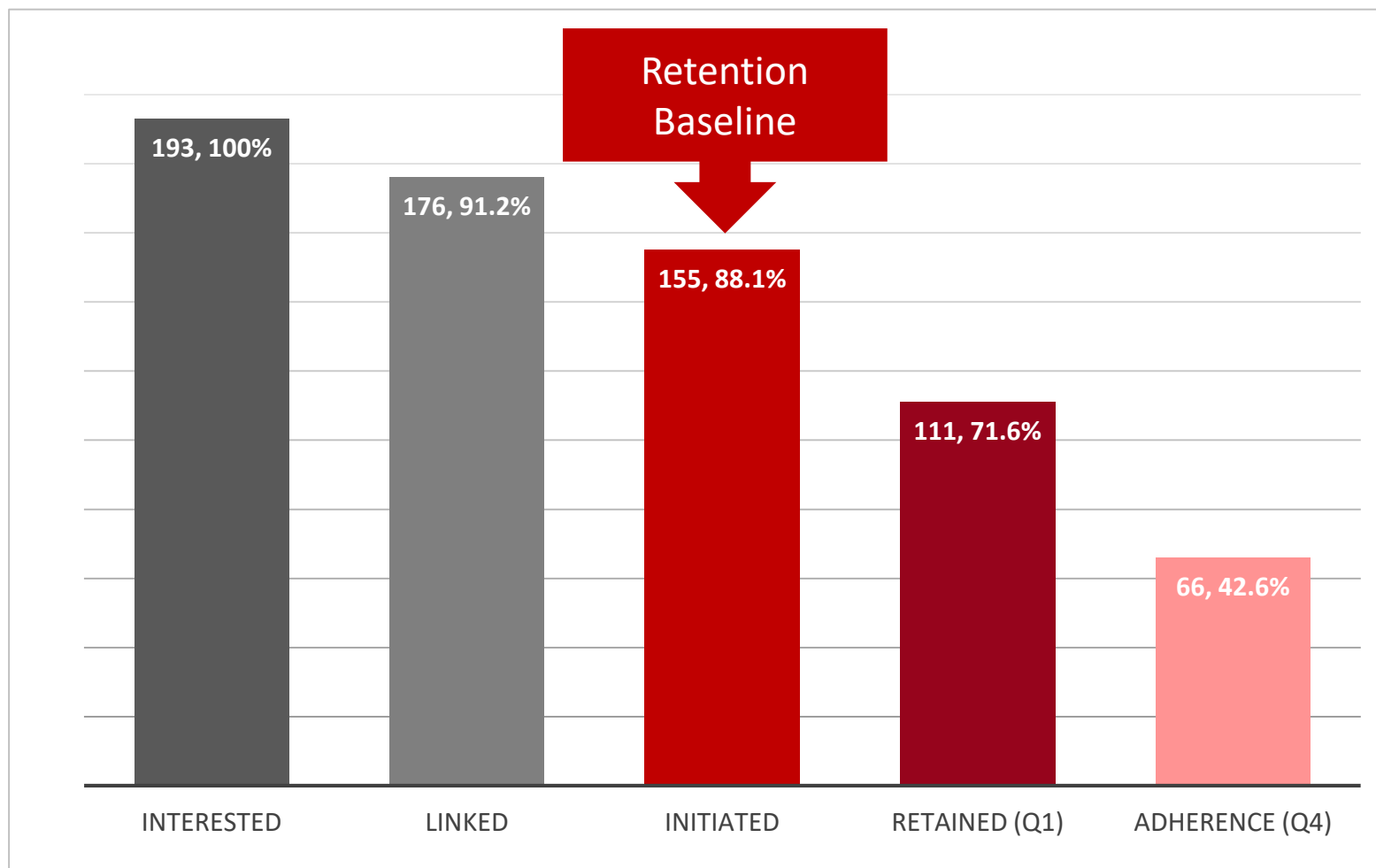


PrEP Initiation by Sexual Orientation

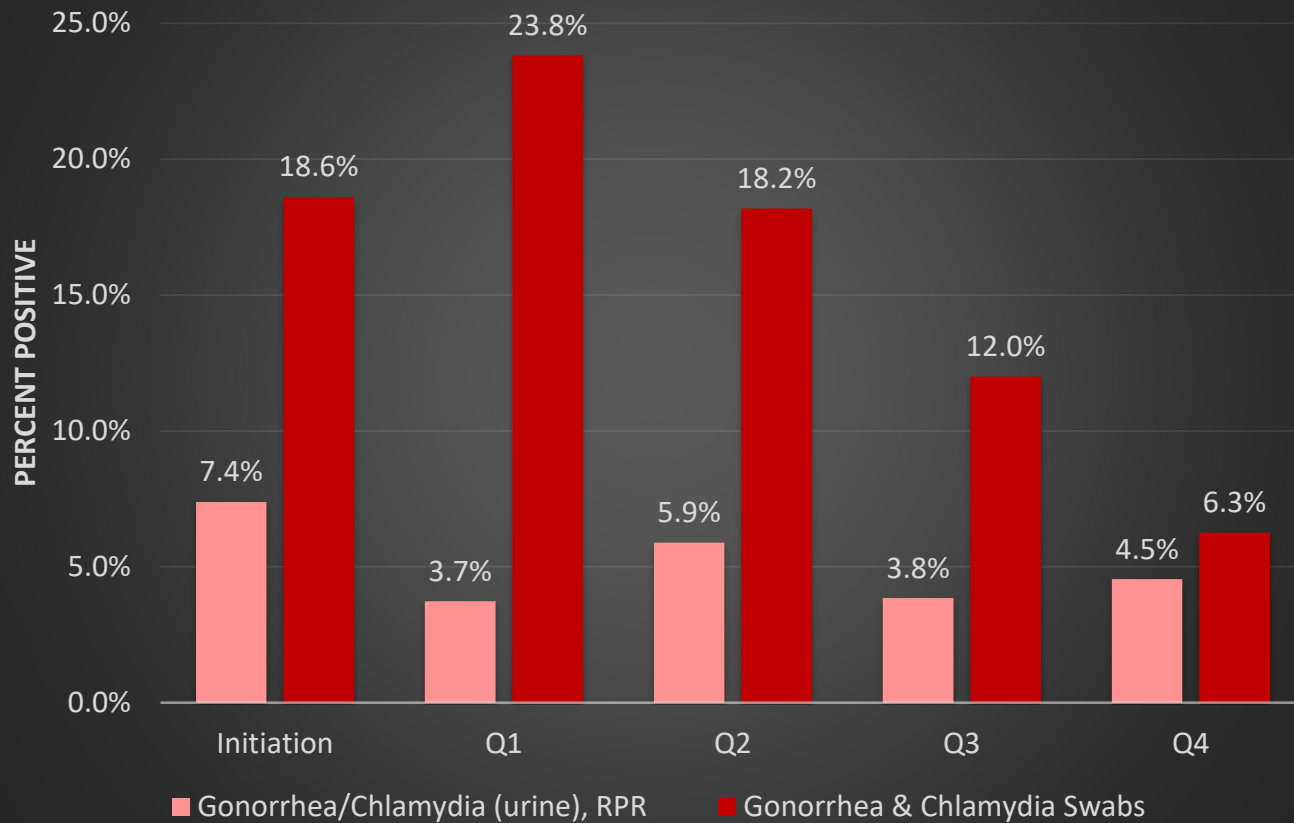


PrEP Initiators by Risk Group





STI Positivity Rate



Increased Risk of STI Acquisition?

A recent meta-analysis suggests increased STIs with PrEP

Unclear association as even newer data refutes this

Arguably, STI rates have increased for all MSM despite PrEP

- However, PrEP clearly has reduced the rate of HIV acquisition

U=U: Need
for PrEP?

Undetectable =
Untransmittable

Recent CDC initiative to raise
awareness

- If HIV RNA < 200 copies/mL, do not sexually transmit HIV

If patient in a monogamous,
sero-discordant relationship:

- PrEP may not be warranted
- Discussion with patient regarding desire for use

Paying for PrEP

AWP per tablet = \$70.32

If high copays:

- Gilead offers a copay card good for several thousand dollars/year

If insurance will not cover or a PA appeal is denied:

- Gilead may pay for medication

THANK YOU!