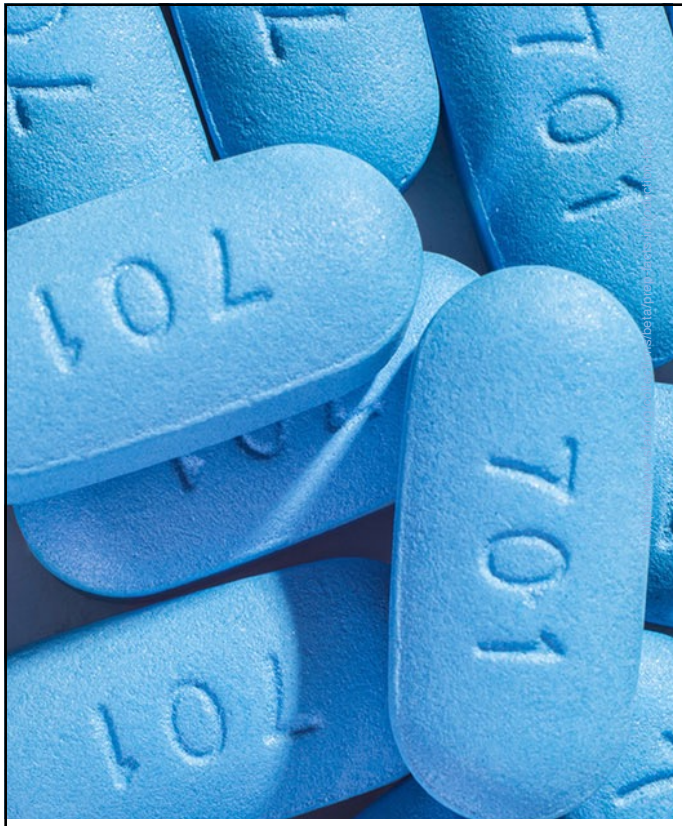


PrEP in 2023

An Update for OCHD

AETC AIDS Education & Training Center Program Southeast

NCHTEC
North Carolina HIV Training & Education Center at the UNC School of Medicine

AETC Program – National Resources

- **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 director, 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

Disclosures

- This program is supported by the Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services (HHS) under grant number U1OHA30535 as part of an award totaling $4.2m. The contents are those of the author(s) and do not necessarily represent the official views of, nor an endorsement, by HRSA, HHS, or the U.S. Government. For more information, please visit: https://www.hrsa.gov

- Funding for this presentation was made possible by cooperative agreement U1OHA30535 from the Health 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.

Christopher B. Hurt, MD, FIDSA

Associate Professor of Medicine

Associate Chief for Clinical Operations, UNC Division of Infectious Diseases
Director, North Carolina HIV Training & Education Center
Site PI, Ryan White HIV/AIDS Program Part D, UNC ID Clinic

Institute for Global Health & Infectious Diseases
University of North Carolina at Chapel Hill
School of Medicine

Dr. Hurt is supported by the Health Resources and Services Administration (HRSA-17-039, U1OHA30535) and the National Institute of Allergy and Infectious Diseases (P30AI50410, R61AI174285, UM1AI069423, UM1AI068619).

The views expressed are not necessarily those of HRSA or the NIH.

Objectives

- Critically appraise the 2021 CDC/USPHS PrEP guideline's recommendations for HIV testing.
- Name at least two differences between delivery of oral versus injectable PrEP.
- Compare and contrast current options for oral PrEP in terms that a client can understand.
- Outline an approach to counseling and managing PrEP for an adult under age 25.

Who should be offered PrEP?

Take a step back and try to look at the whole picture before deciding someone doesn't "qualify" for PrEP.

US Public Health Service

PREEXPOSURE PROPHYLAXIS FOR THE PREVENTION OF HIV INFECTION IN THE UNITED STATES – 2021 UPDATE

A CLINICAL PRACTICE GUIDELINE

Preexposure Prophylaxis for the Prevention of HIV Infection in the United States – 2021 Update Clinical Practice Guideline
Page 1 of 108

HIV uninfected, plus:

Any condomless anal or vaginal sex in past 6m

Any partner(s) with HIV or unknown HIV status in past 6m

Any bacterial STI in past 6m

Shared injection equipment in past 6m

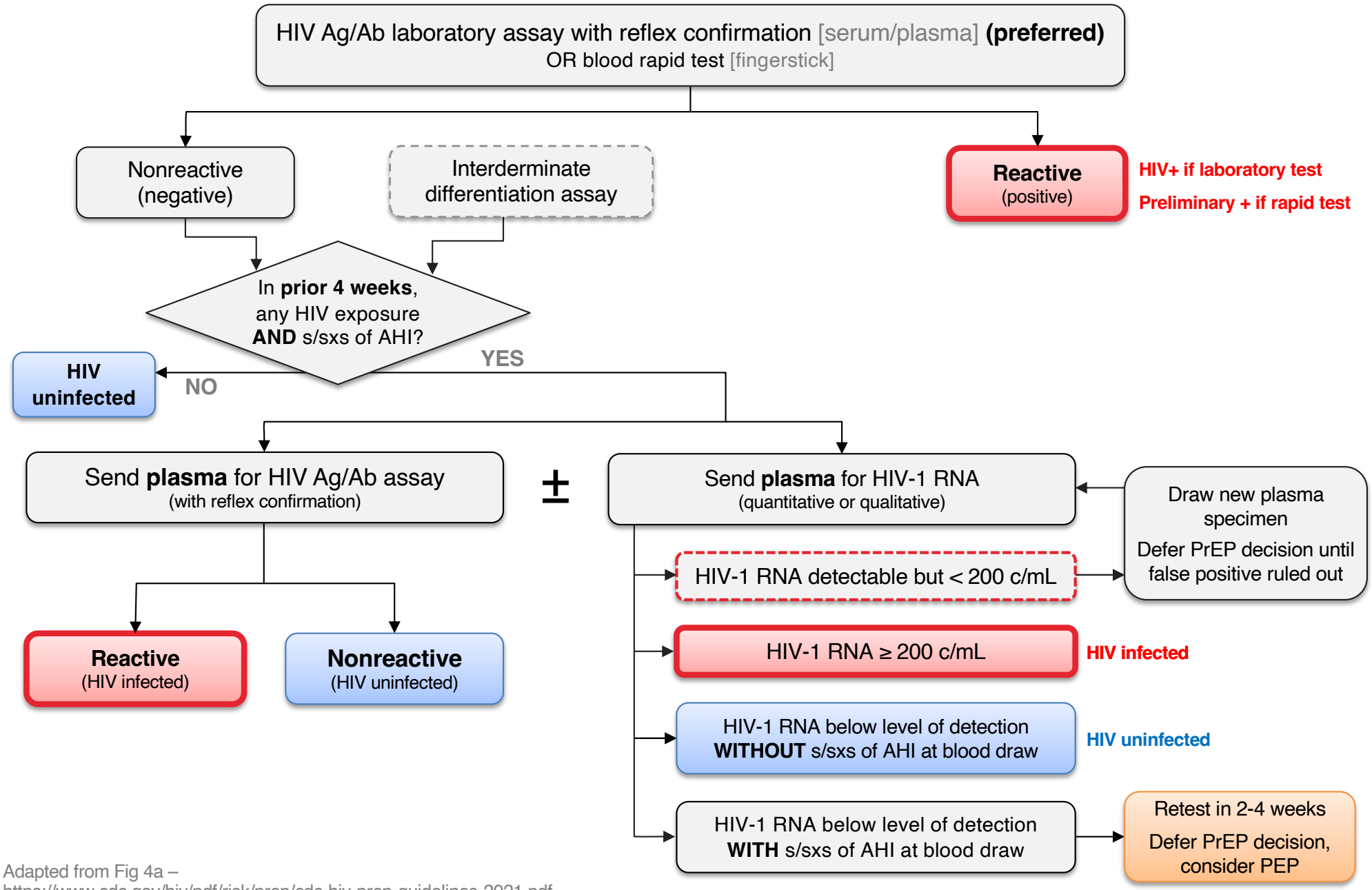
Injecting partner(s) with HIV

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

HIV testing for PrEP

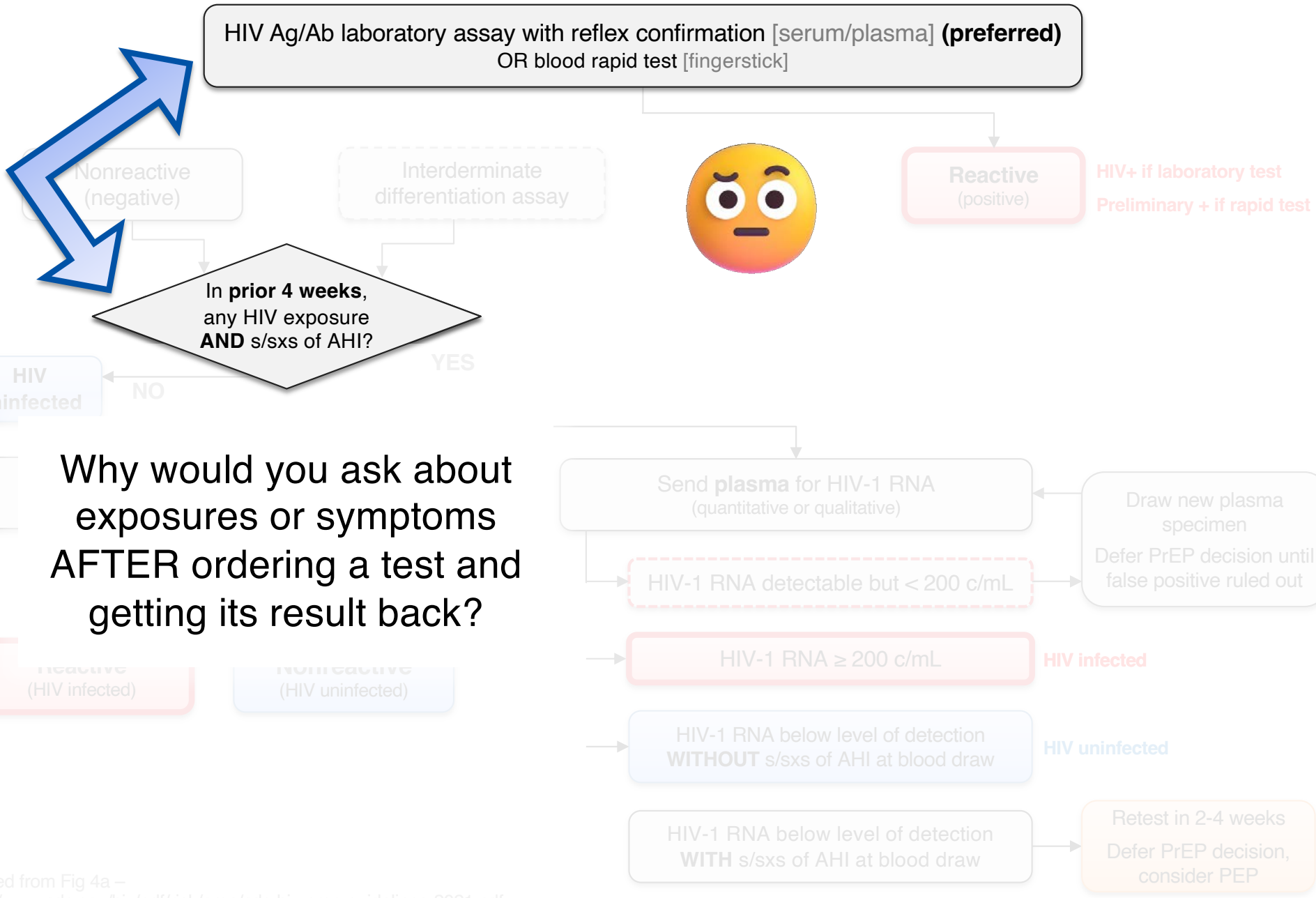
AETC AIDS Education & Training Center Program Southeast

2021 guidelines: persons without ARV exposure



Adapted from Fig 4a –
https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf

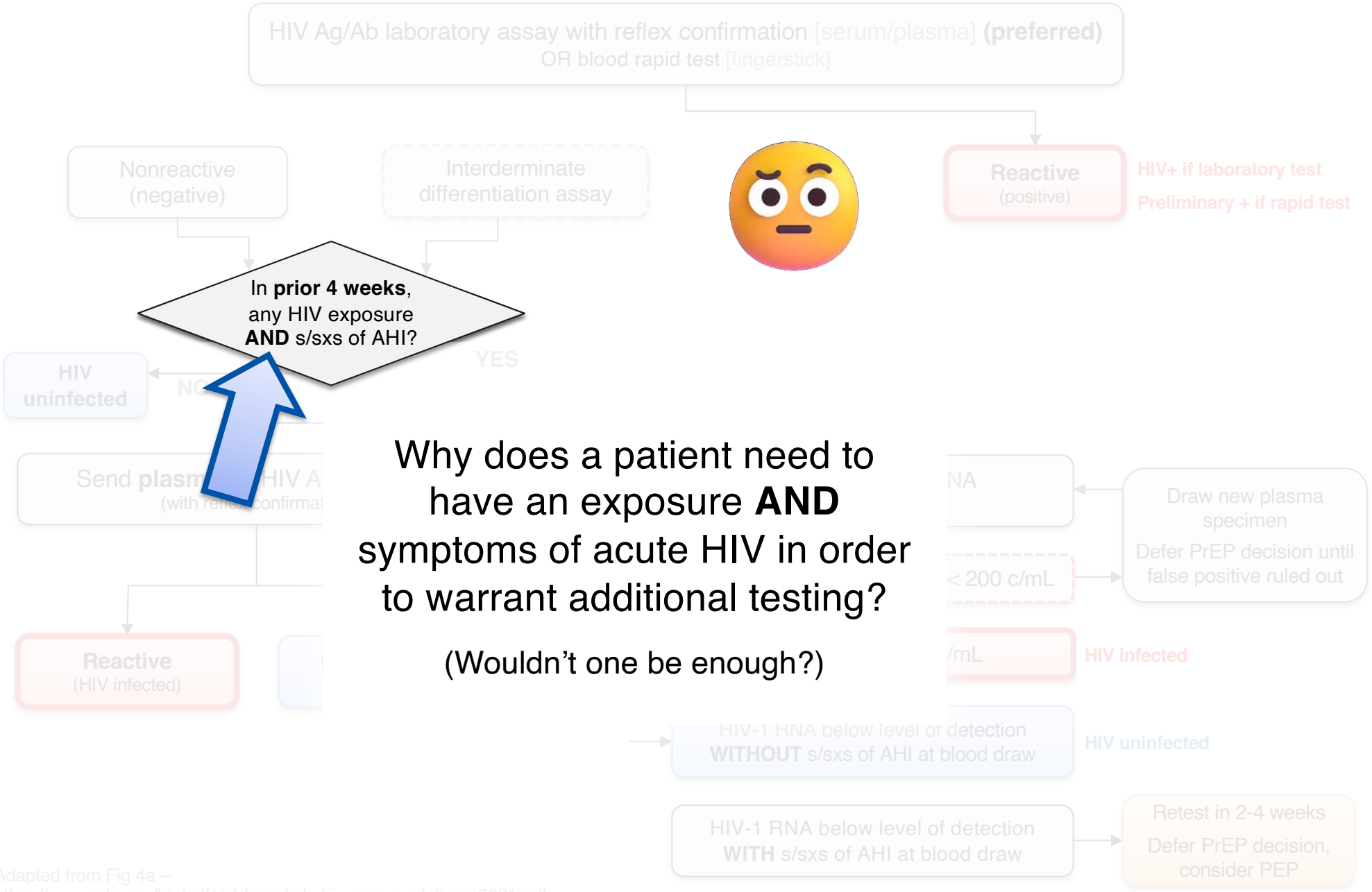
2021 guidelines: persons without ARV exposure



Why would you ask about exposures or symptoms AFTER ordering a test and getting its result back?

Adapted from Fig 4a – https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf

2021 guidelines: persons without ARV exposure

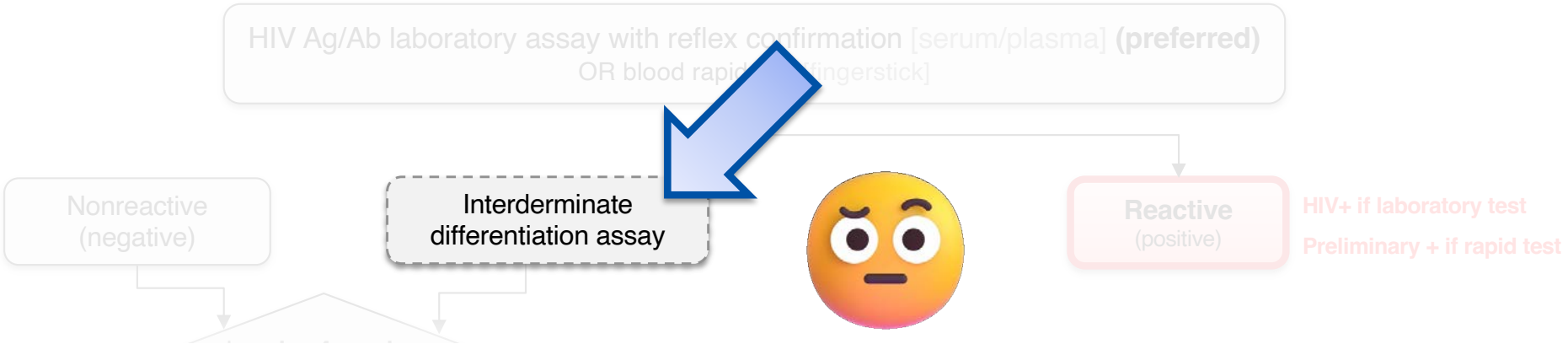


Why does a patient need to have an exposure **AND** symptoms of acute HIV in order to warrant additional testing?

(Wouldn't one be enough?)

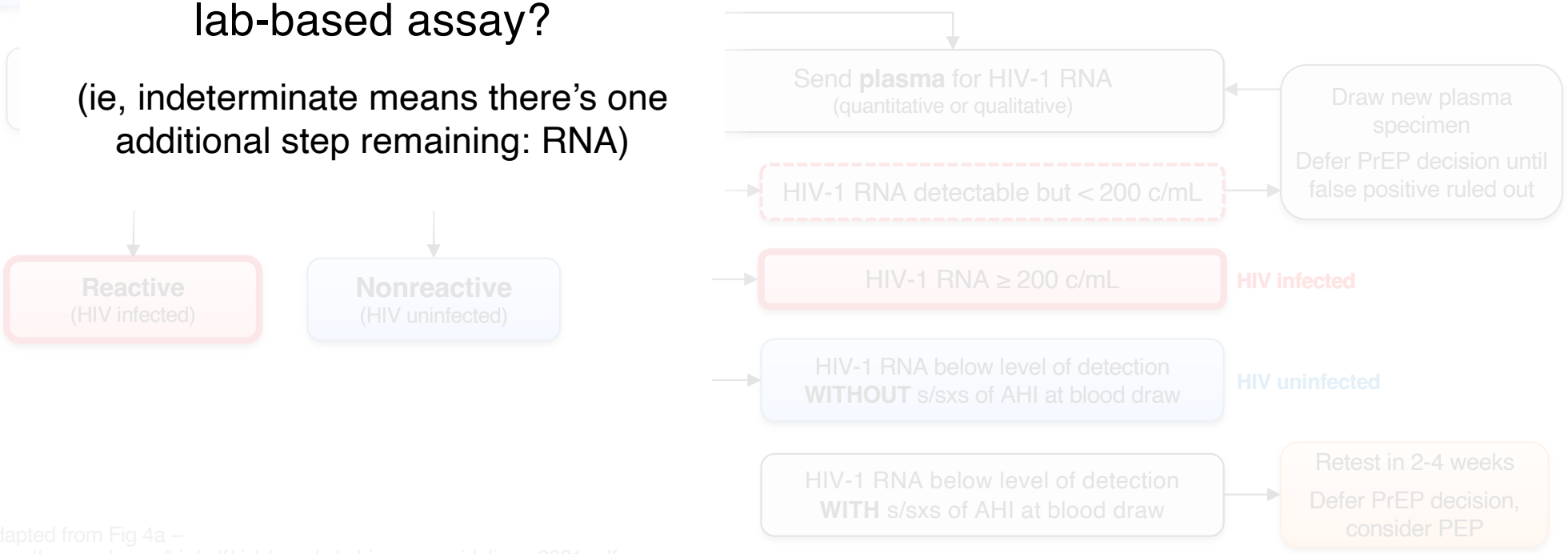
Adapted from Fig 4a – https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf

2021 guidelines: persons without ARV exposure



Why would you act on an **interim** result from a lab-based assay?

(ie, indeterminate means there's one additional step remaining: RNA)



Adapted from Fig 4a –
https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf

2021 guidelines: persons without ARV exposure

In what circumstances should an HIV RNA assay be used in conjunction with an Ag/Ab assay?

HIV Ag/Ab laboratory assay with reflex confirmation [serum/plasma] **(preferred)**
OR blood rapid test [fingerstick]

Reactive (positive)

HIV+ if laboratory test

Preliminary + if rapid test

Send **plasma** for HIV Ag/Ab assay (with reflex confirmation)

±

Send **plasma** for HIV-1 RNA (quantitative or qualitative)

Reactive (HIV infected)

Nonreactive (HIV uninfected)

HIV-1 RNA detectable but < 200 c/mL

Draw new plasma specimen

Defer PrEP decision until false positive ruled out

HIV-1 RNA ≥ 200 c/mL

HIV infected

HIV-1 RNA below level of detection **WITHOUT** s/sxs of AHI at blood draw

HIV uninfected

HIV-1 RNA below level of detection **WITH** s/sxs of AHI at blood draw

Retest in 2-4 weeks

Defer PrEP decision, consider PEP

Adapted from Fig 4a – https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf

SUGGESTION: persons without ARV exposure

How likely is it that the patient may have acquired HIV in the past 4-6 weeks?

Consider the patient and their risk environment

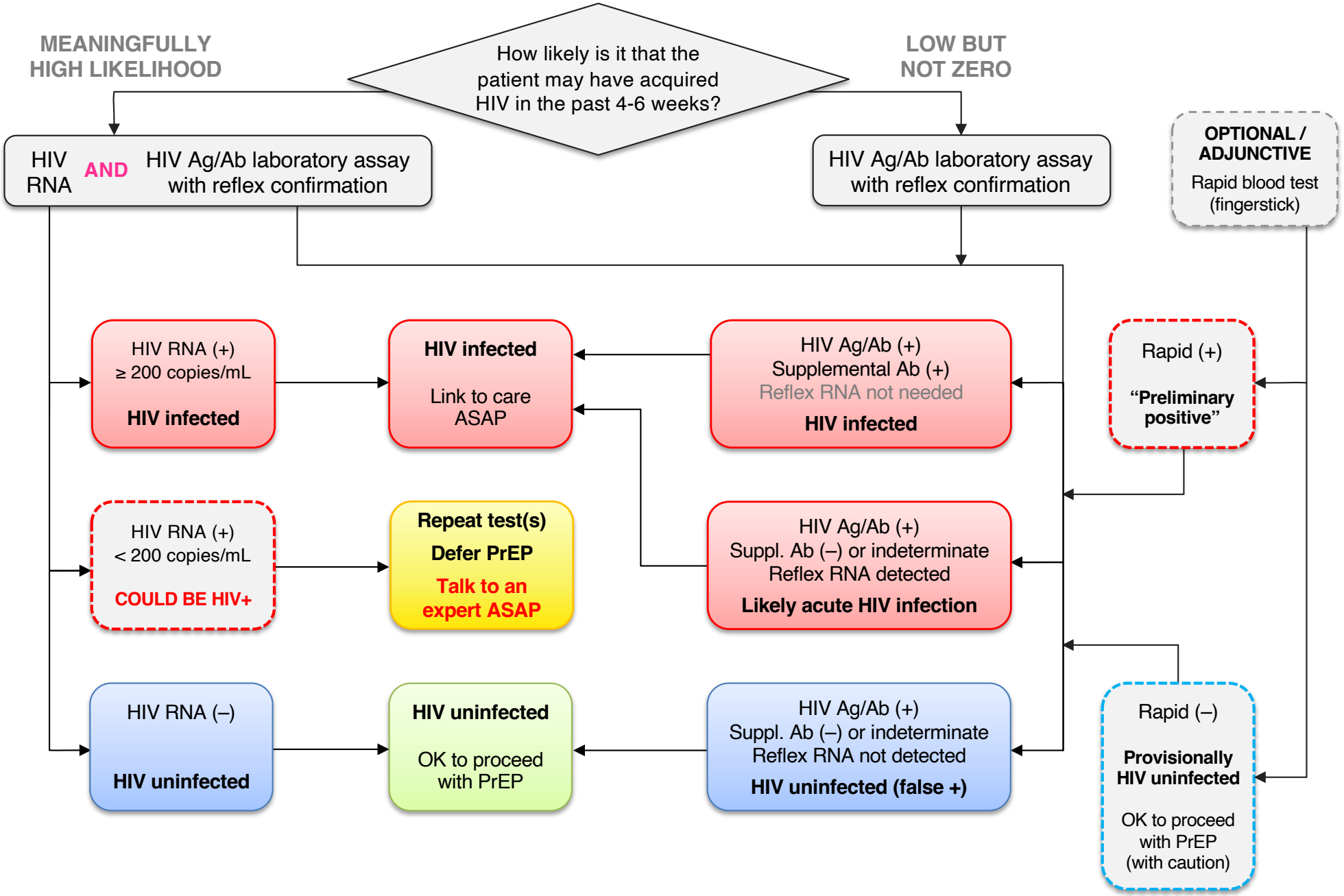
HIGHER

LOWER

Receptive anal sex	Black & has anal sex	25-34	Syphilis	Southeast
Shares needles and/or works	Hispanic/Latinx & has anal sex	Under 24	Herpes	US Dependent Areas
Receptive vaginal sex	White & has anal sex	35-44	Gonorrhea	Northeast
Insertive anal or vaginal sex	Black & has vaginal sex	45-54	Chlamydia	West
	Hispanic/Latinx & has vaginal sex	Over 55	Trichomonas	Midwest
	White & has vaginal sex			

Risk factors as described → https://www.cdc.gov/hiv/statistics/overview/ataglance.html

SUGGESTION: persons without ARV exposure



ARVs alter the timeline for Ag/Ab positivity

HPTN 083

Worldwide; Dec 2016-May 2020

4566
at-risk persons
2282 cabotegravir LAI
2284 oral FTC/TDF

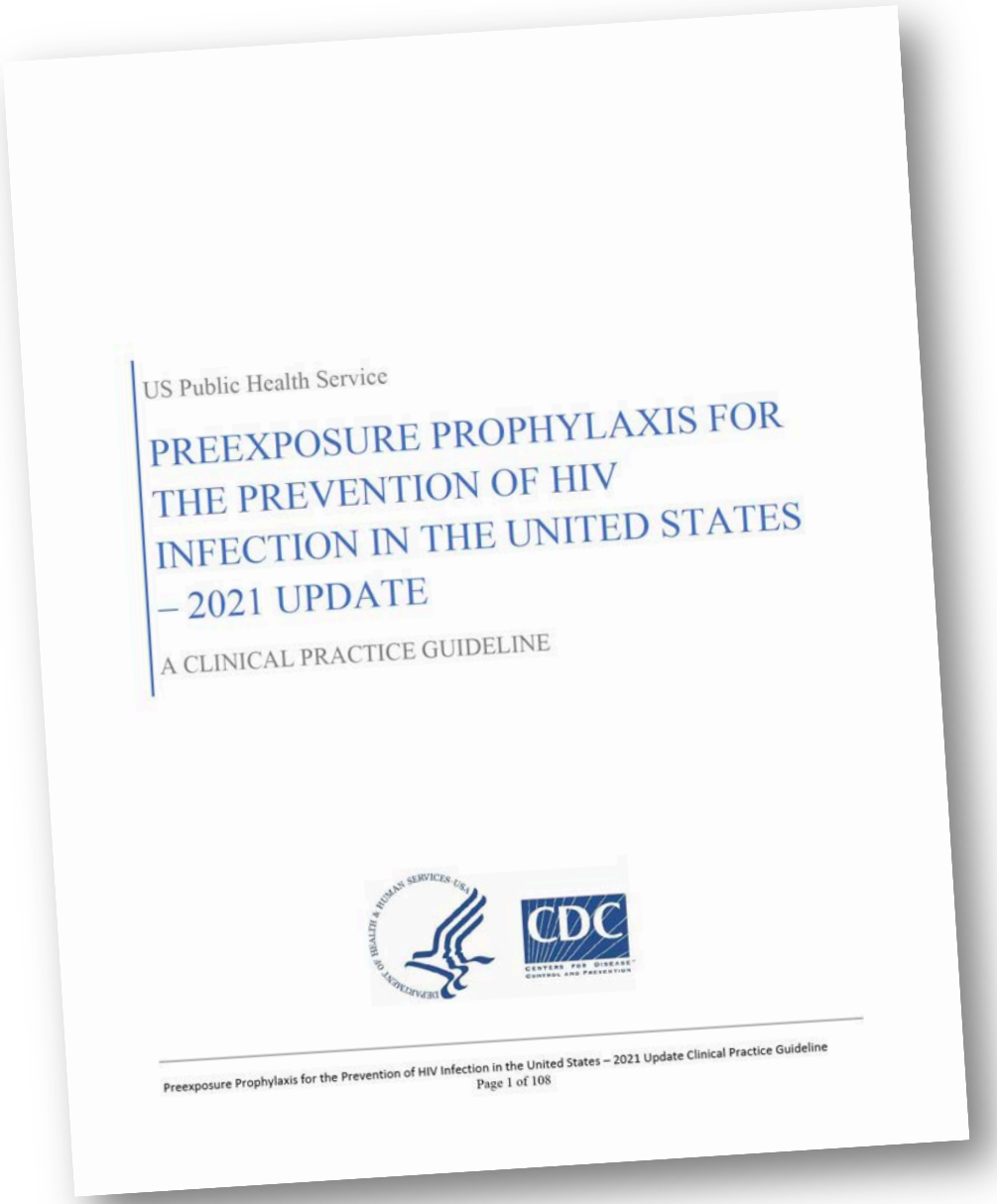
51
seroconversions
5 had no recent CAB
3 during oral lead-in
4 on CAB-LA
39 on FTC/TDF

37
of 39 infections on F/TDF arm had low-to-no drug level detected

31 **day delay in incident HIV detection on FTC/TDF** (range, 7-68 d)

98 **day delay in incident HIV detection on CAB-LA** (range, 35-185 d)

Marzinke MA, et al. J Infect Dis. 2021;224(9):1581-92



US Public Health Service

PREEXPOSURE PROPHYLAXIS FOR THE PREVENTION OF HIV INFECTION IN THE UNITED STATES – 2021 UPDATE

A CLINICAL PRACTICE GUIDELINE

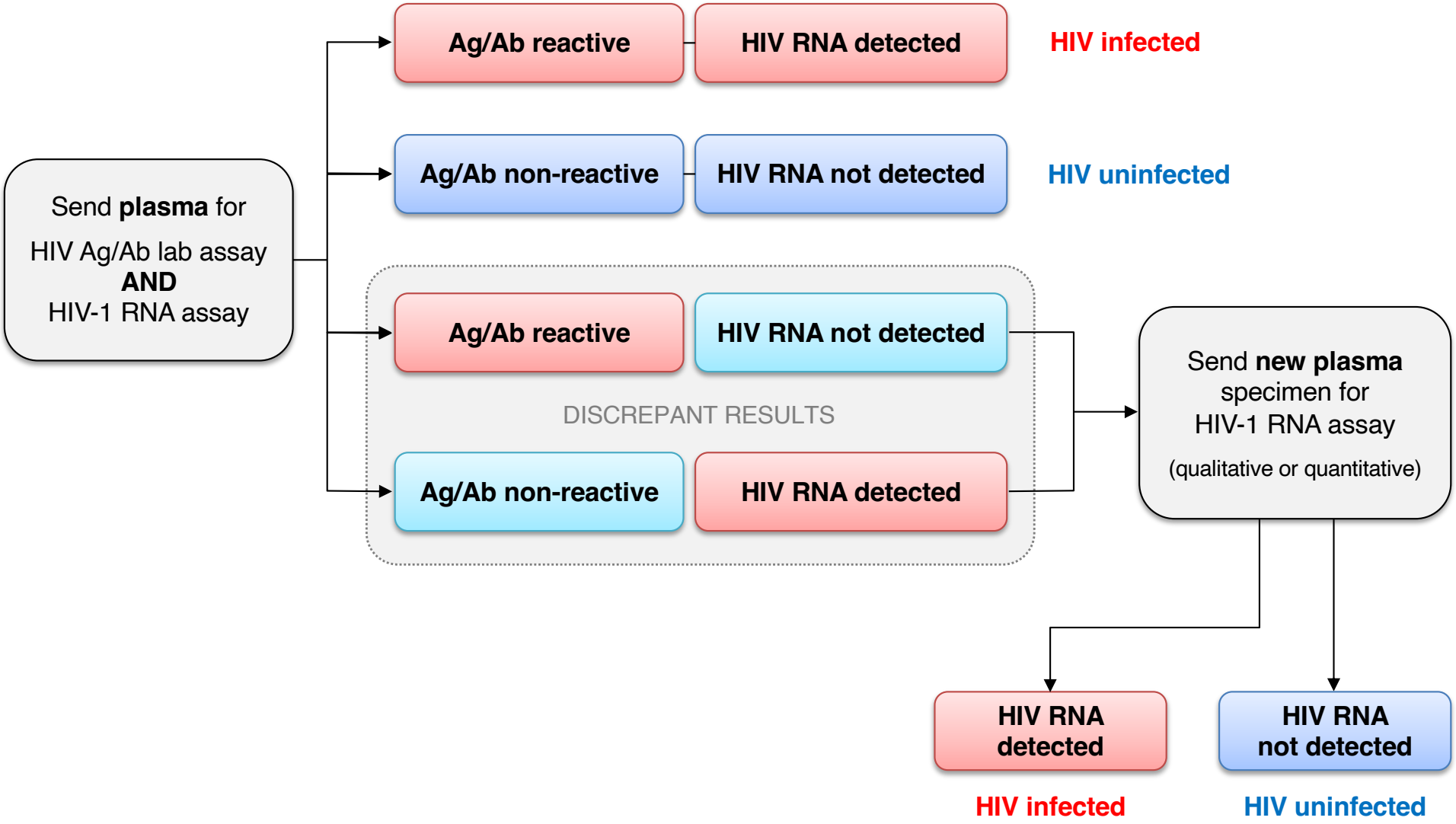
Preexposure Prophylaxis for the Prevention of HIV Infection in the United States – 2021 Update Clinical Practice Guideline
Page 1 of 108

The 2021 PrEP guidelines radically changed HIV testing recommendations for people who were already on PrEP.

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

2021 guidelines: persons with ARV exposure

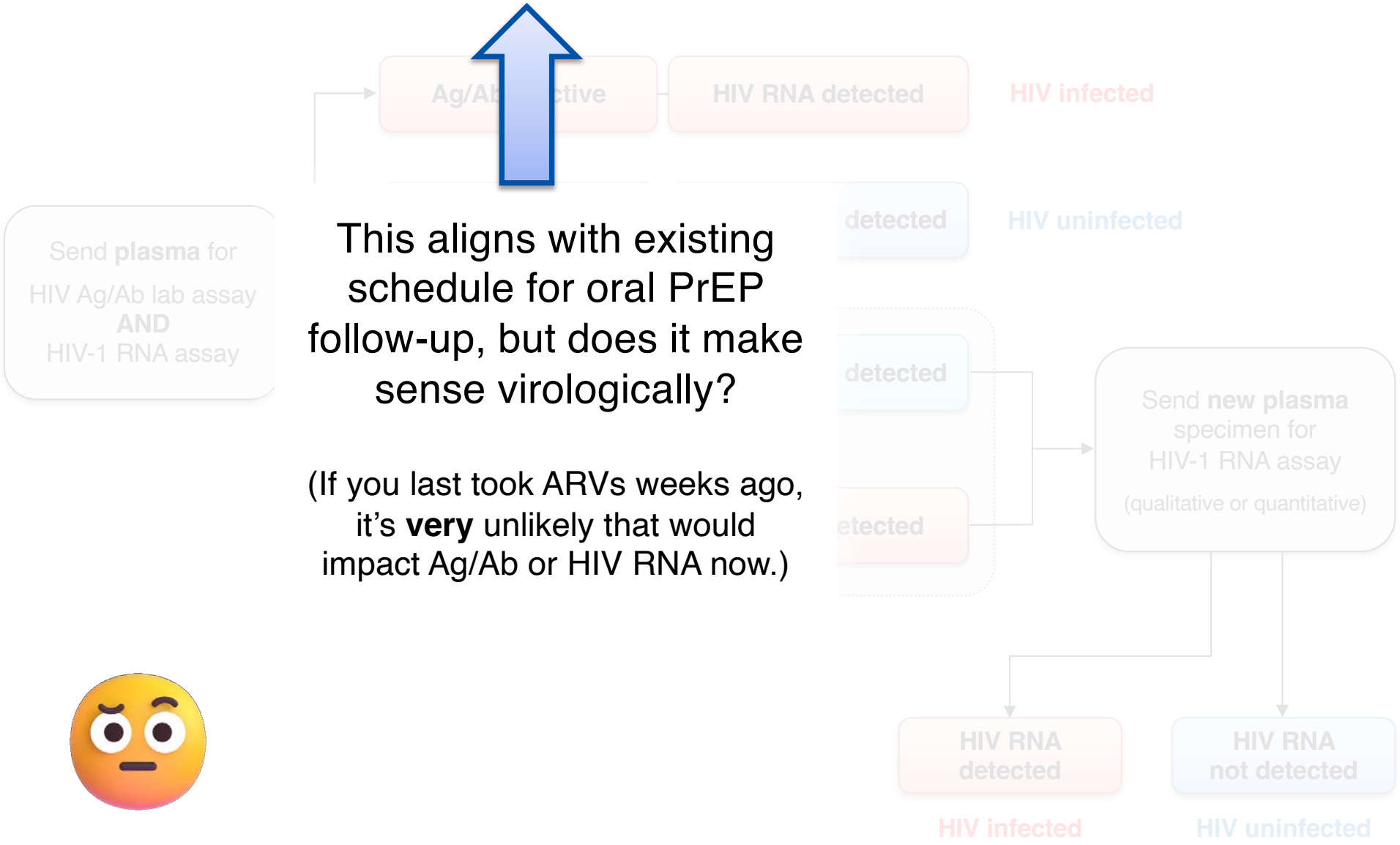
Oral PEP or PrEP in prior 3 months **OR** cabotegravir IM in prior 12 months



Adapted from Figure 4b– https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf

2021 guidelines: persons with ARV exposure

Oral PEP or PrEP in prior 3 months **OR** cabotegravir IM in prior 12 months



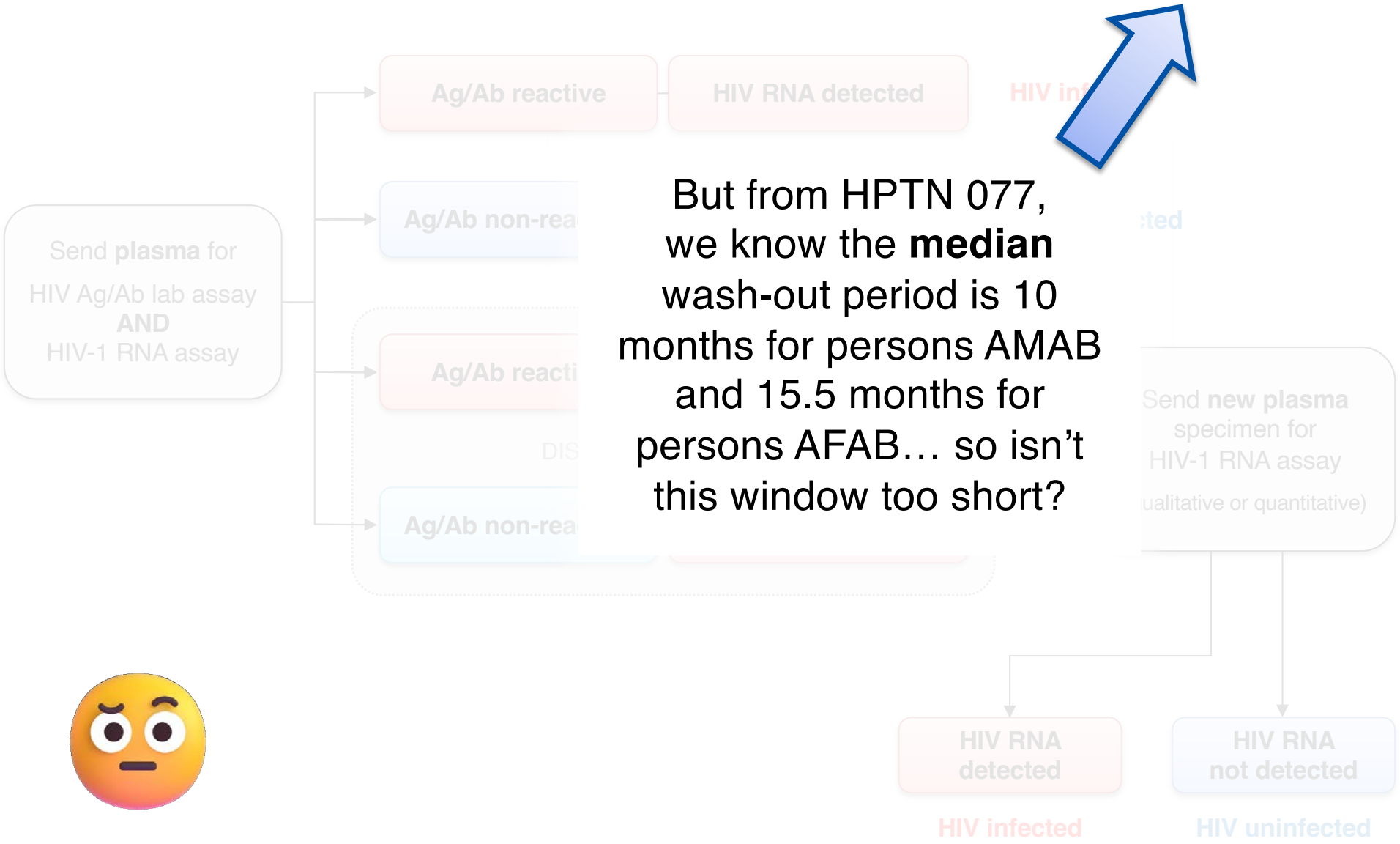
This aligns with existing schedule for oral PrEP follow-up, but does it make sense virologically?

(If you last took ARVs weeks ago, it's **very** unlikely that would impact Ag/Ab or HIV RNA now.)

Adapted from Figure 4b– https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf

2021 guidelines: persons with ARV exposure

Oral PEP or PrEP in prior 3 months **OR** cabotegravir IM in prior 12 months

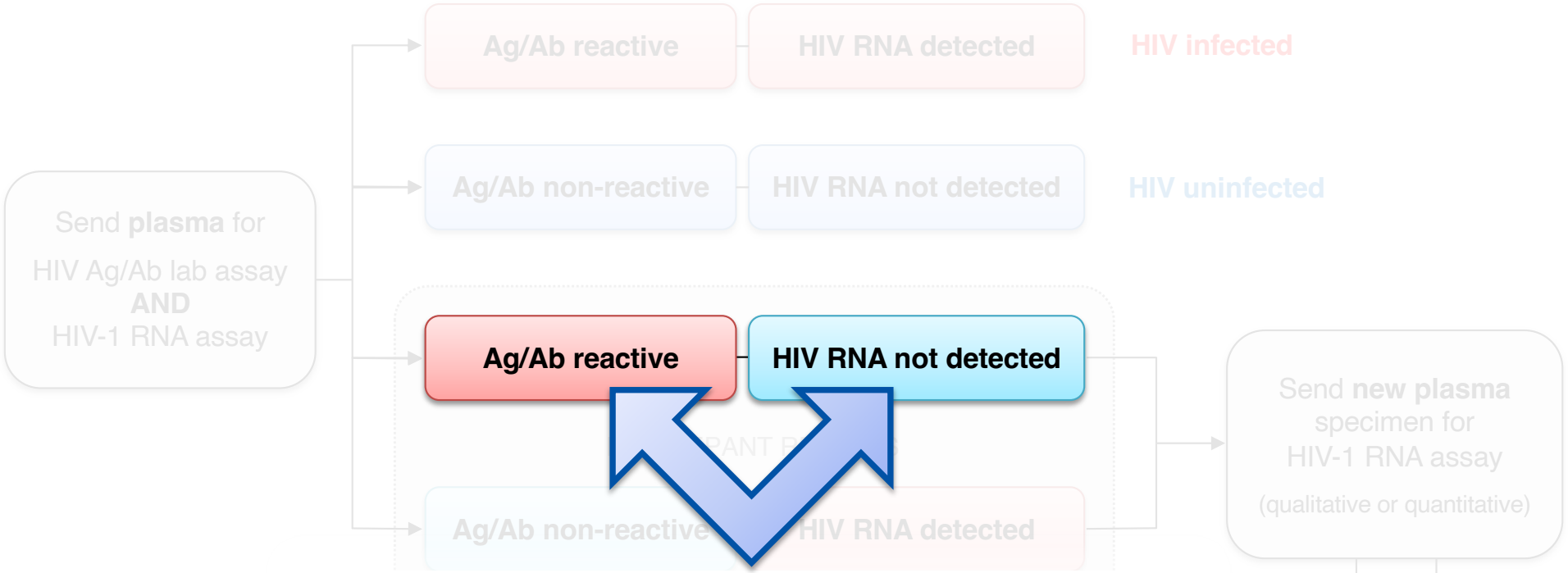


But from HPTN 077, we know the **median** wash-out period is 10 months for persons AMAB and 15.5 months for persons AFAB… so isn't this window too short?

Adapted from Figure 4b– https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf

2021 guidelines: persons with ARV exposure

Oral PEP or PrEP in prior 3 months **OR** cabotegravir IM in prior 12 months



This particular combination is essentially impossible.

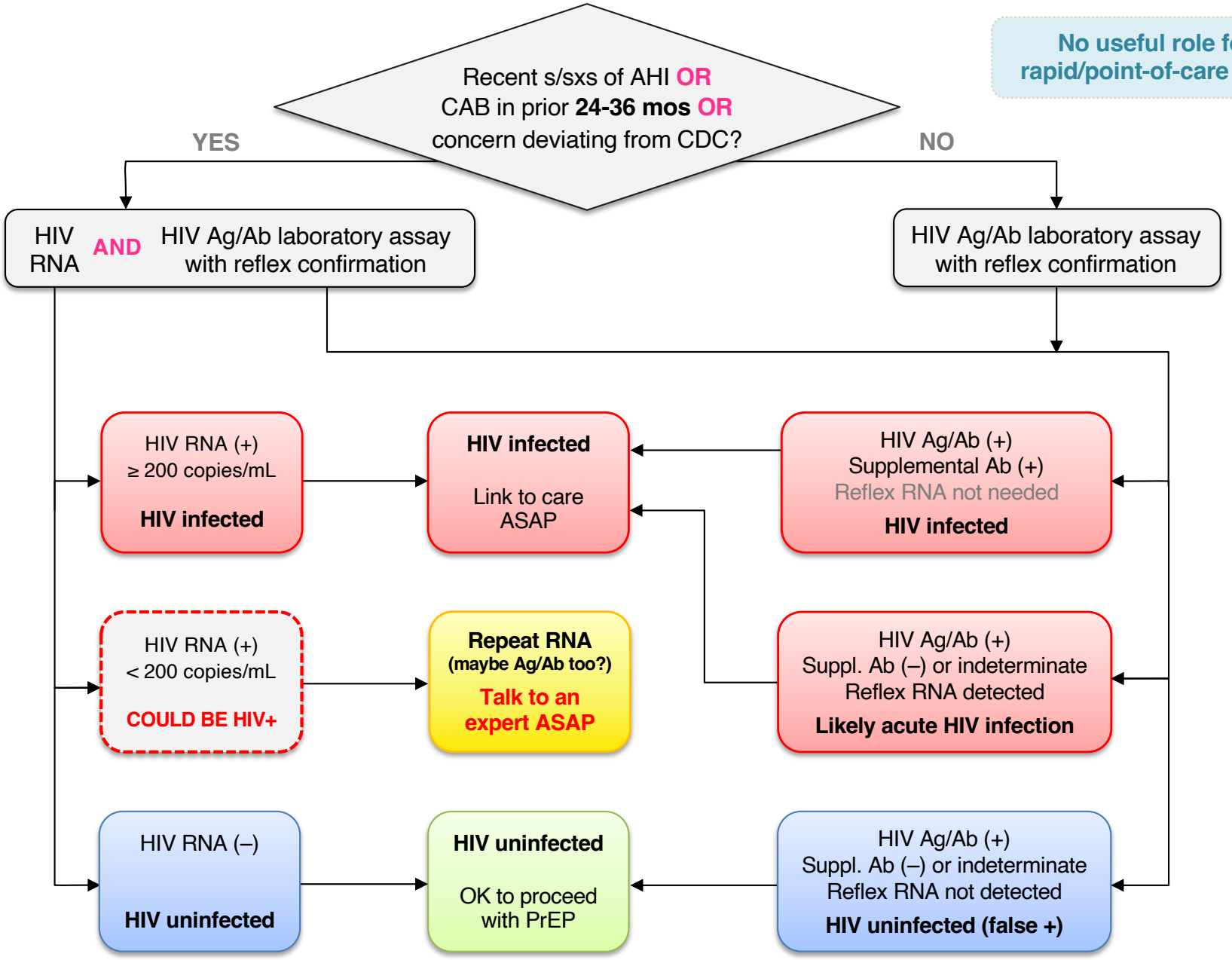
Lab-based Ag/Ab reactivity would prompt a supplemental assay, and if it was negative or indeterminate, an HIV RNA is used to adjudicate.

Adapted from Figure 4b– https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf

What's the big picture?

- Poor adherence means low(er) drug levels that permit infection but delay Ag/Ab conversion.
- Seroconversion delays are extreme with CAB, so using RNA with Ag/Ab makes sense.
- Why not just use RNA for everything?
  - Only one assay is FDA-approved for HIV diagnosis.
  - False positive RNA results are unfortunately common.
- Expert opinion (including Dr. Hurt's) is that checking Ag/Ab **and** RNA assays for **every** patient on PrEP adds complexity and cost without clear benefit.

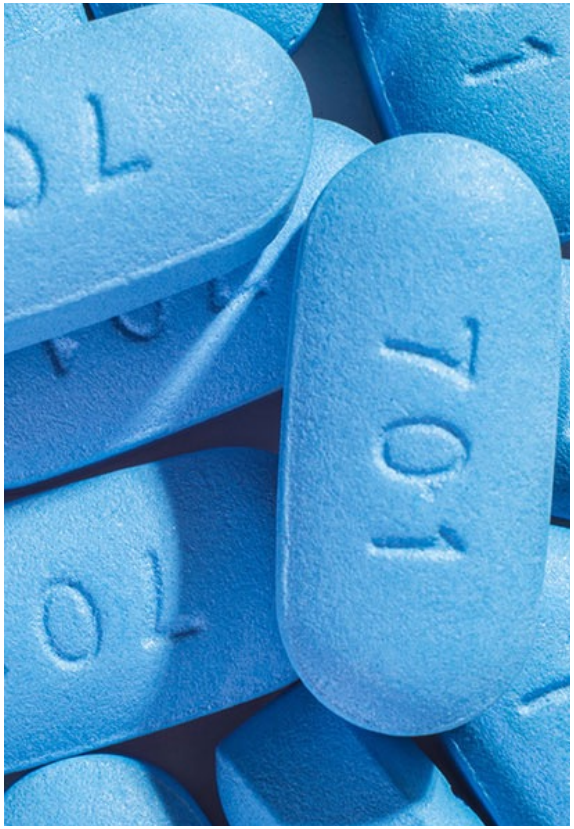
SUGGESTION: persons with ARV exposure



Assessing the options

AETC AIDS Education & Training Center Program Southeast

Three options are available for PrEP



FTC/TDF

emtricitabine / tenofovir disoproxil fumarate

Approved in 2012

FTC/TAF

emtricitabine / tenofovir alafenamide fumarate

Approved in 2019

CAB

cabotegravir long-acting injectable

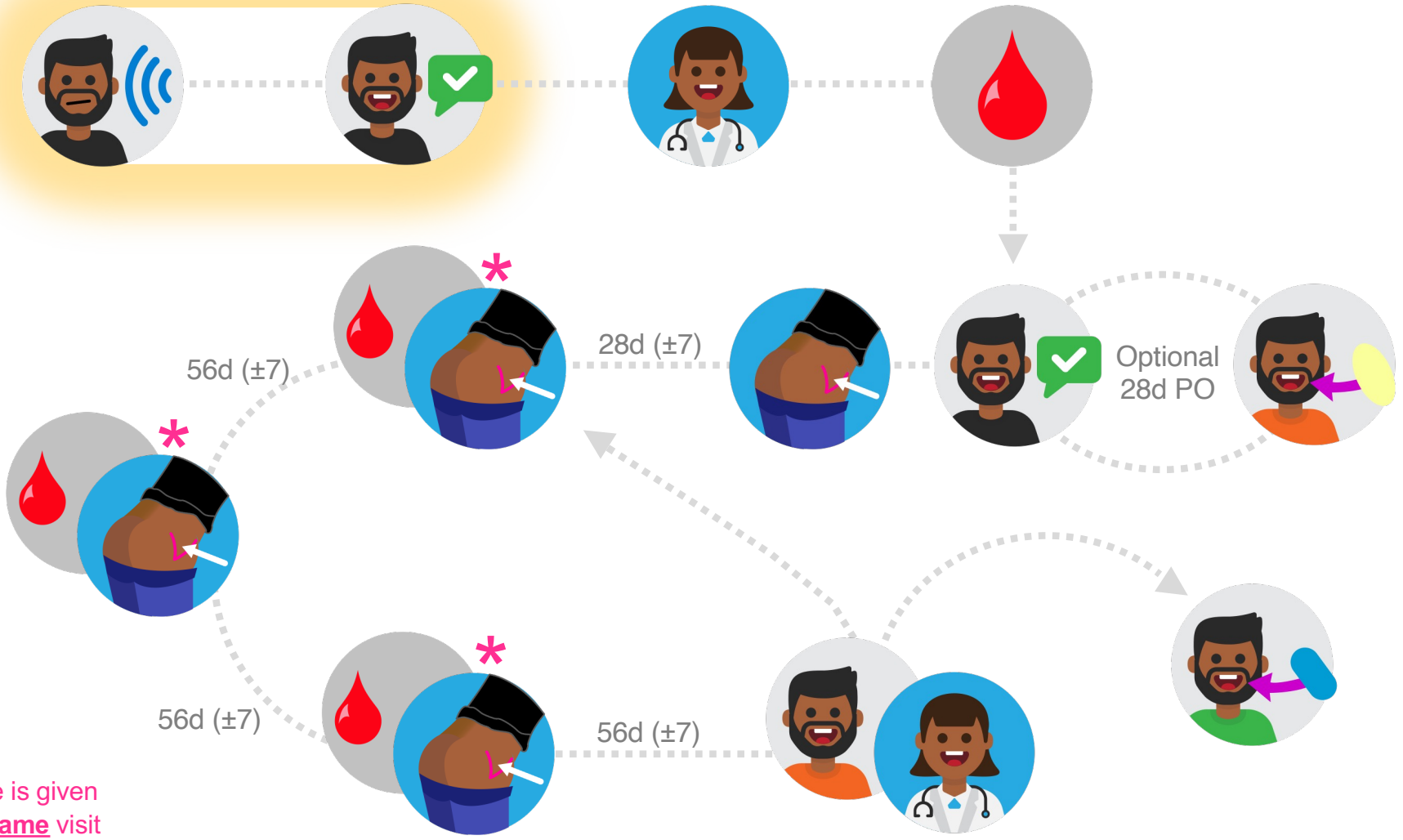
Approved in 2021

Cabotegravir

AETC AIDS Education & Training Center Program Southeast

What does PrEP service delivery look like?

For injectable cabotegravir

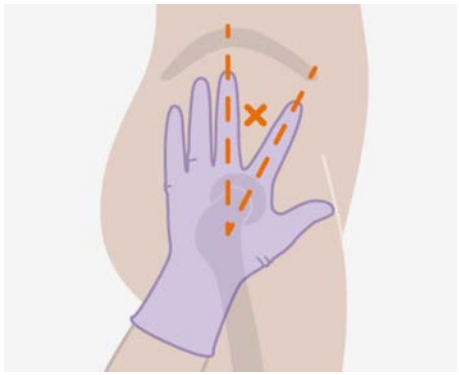


* IM dose is given at the **same** visit as the blood draw for HIV testing

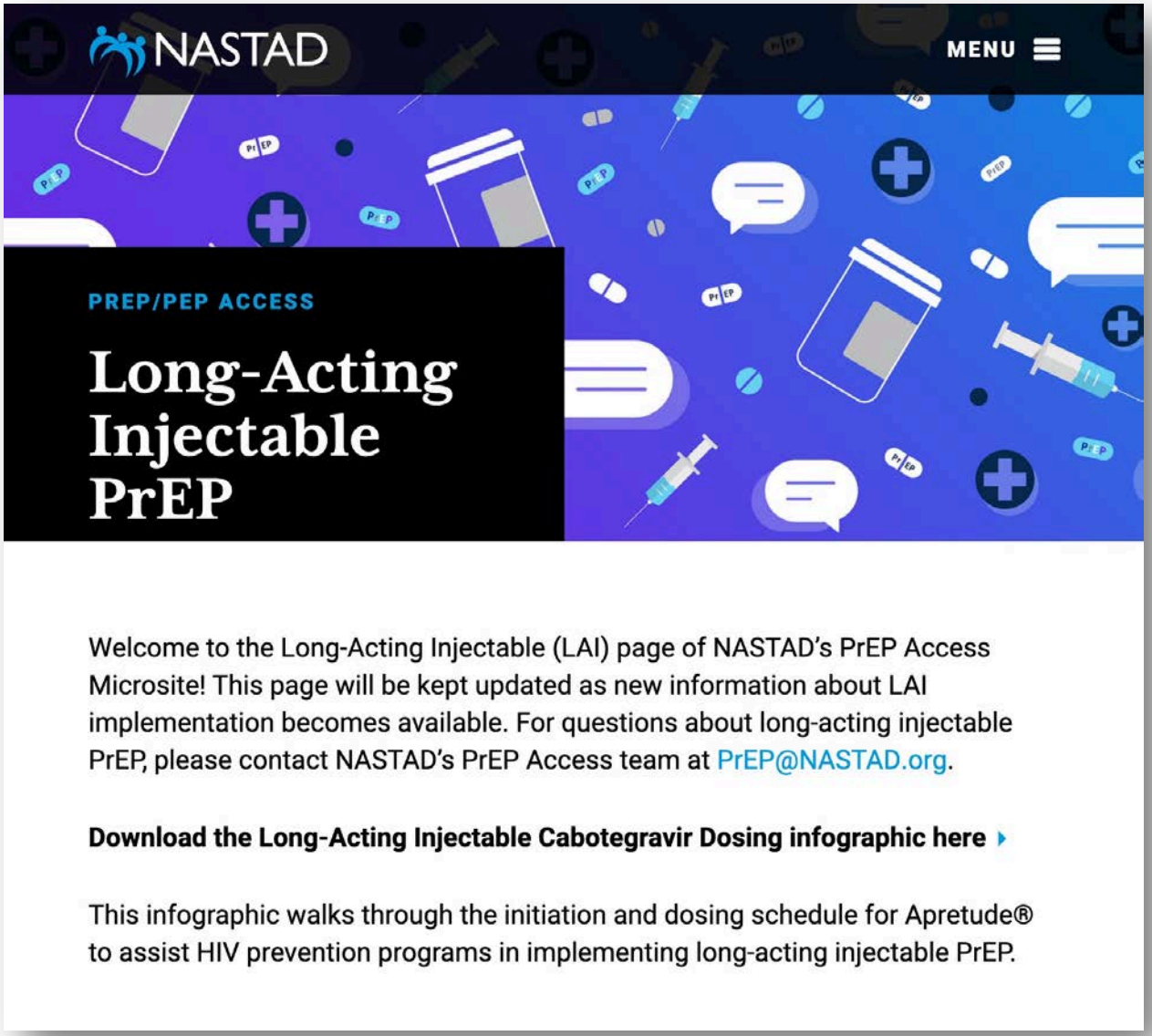
What is pre-exposure prophylaxis (PrEP)?

Long-acting, injectable cabotegravir (CAB) was approved for PrEP by FDA in December 2021

- Statistically superior to oral FTC/TDF in two large clinical trials
- Single dorso- or ventro-gluteal IM injection every 56 days (2 mos.)



The logistics for CAB are formidable



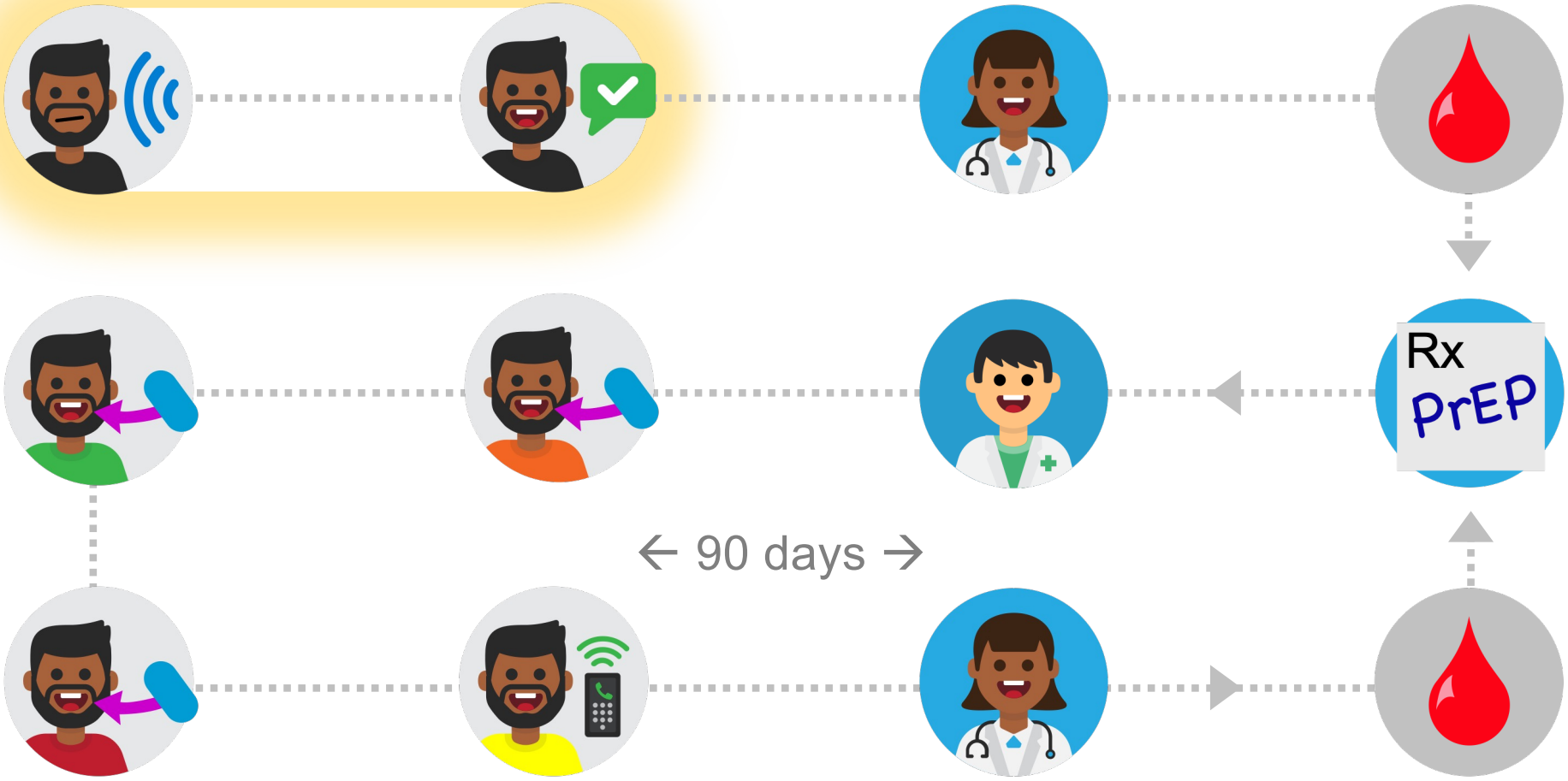
https://nastad.org/long-acting-injectable-prep

Oral PrEP

AETC AIDS Education & Training Center Program Southeast

What does PrEP service delivery look like?

For oral FTC/TDF or oral FTC/TAF

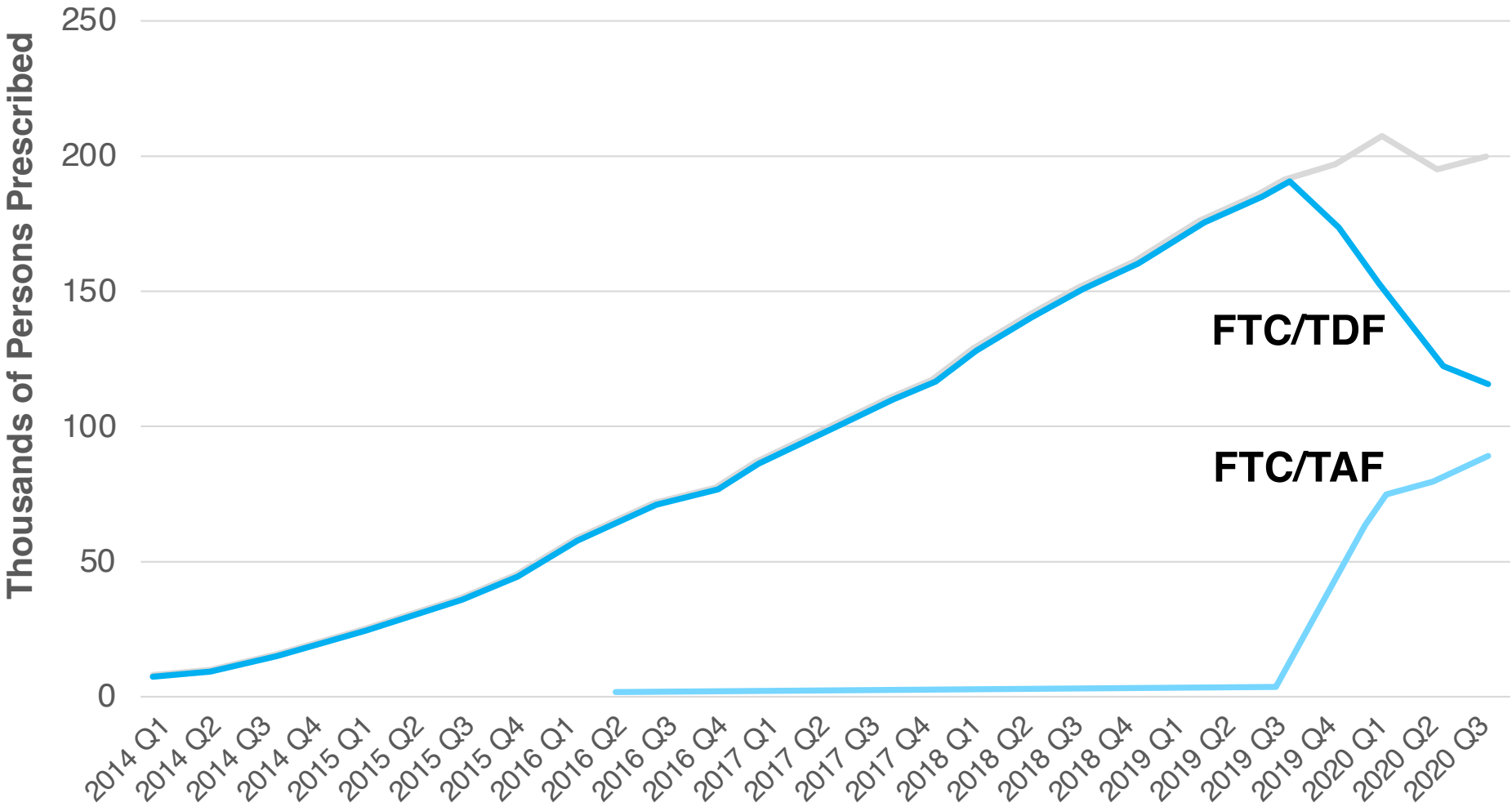



701


225

???

FTC/TAF's market share is rising rapidly



Hoover KW, et al. CROI 2021, Abstract 696 – https://www.aidsmap.com/news/mar-2021/large-numbers-now-descovy-prep-united-states

Comparing the two oral options

Truvada[TDF]

emtricitabine / tenofovir disoproxil fumarate

Approved in 2012

Proven to protect people during:
Injection drug use
Insertive vaginal sex
Insertive anal sex (topping)
Receptive vaginal sex
Receptive anal sex (bottoming)

Descovy[TAF]

emtricitabine / tenofovir alafenamide fumarate

Approved in 2019

Proven to protect people during:
~~Injection drug use~~
~~Insertive vaginal sex~~
Insertive anal sex (topping)
~~Receptive vaginal sex~~
Receptive anal sex (bottoming)

Comparing the two oral options

Truvada[TDF]

emtricitabine / tenofovir disoproxil fumarate

Generics available

Negligible weight loss within first 6m of use, then return to baseline

Asymptomatic, reversible renal dysfunction in ~2 of 100 users

Descovy[TAF]

emtricitabine / tenofovir alafenamide fumarate

No generics available

Significant weight gain (1.1 kg = 2.5 lbs.) after 2Y

No significant adverse effects on renal function

Comparing the two oral options

Truvada[TDF]

emtricitabine / tenofovir disoproxil fumarate

Can be used “on demand”

Bone density loss of ~1.5% within 3-6 months of initiation among persons **who have achieved peak bone mass**

Lowers HDL and LDL
(“good” and “bad” cholesterol levels)

Descovy[TAF]

emtricitabine / tenofovir alafenamide fumarate

CANNOT be used “on demand”

No significant adverse effects on bone density / health

Elevated triglycerides observed in DISCOVER trial

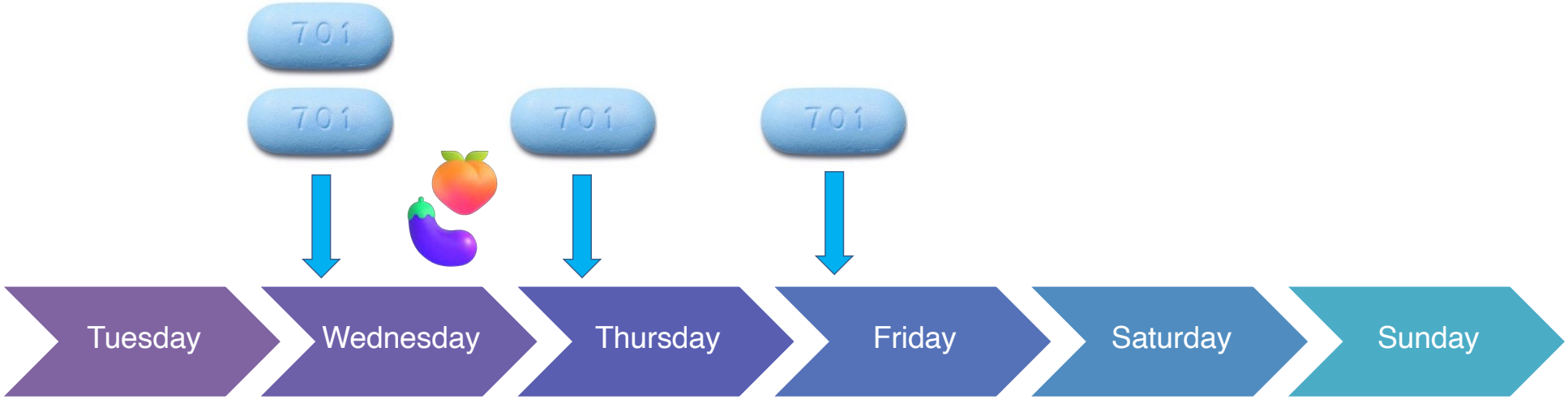
Daily or “on-demand” FTC/TDF?

ONLY studied with FTC/TDF to-date

- 2 tablets 2-24 hours before sex
- 1 tablet 24 hours later
- 1 tablet 48 hours after first intake

ipergay
ANRS
Intervention Préventive de l’Exposition aux Risques avec et pour les Gays

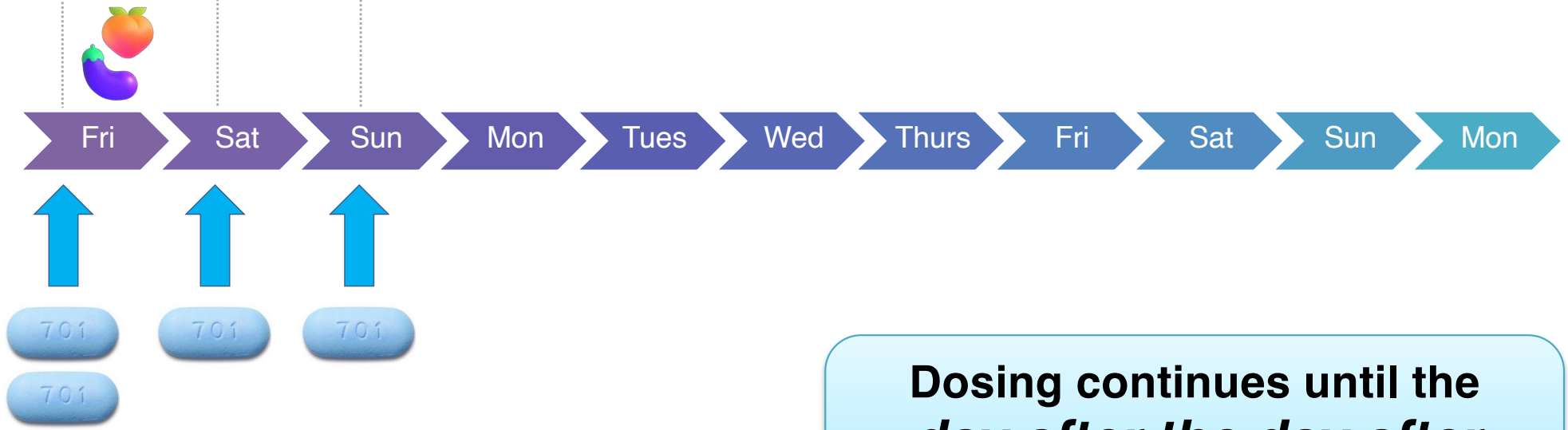
Prévenir
ANRS



IPERGAY → Molina JM, et al. N Engl J Med. 2015;373:2237-2246. Molina JM, et al. Lancet HIV. 2017;4:e402-e410. Antoni G, et al. Lancet HIV. 2020 Feb;7(2):e113-e120.
Prévenir → Molina JM, et al. CROI 2021. Abstract 148. http://www.croiwebcasts.org/p/2021croi/croi/148 https://www.natap.org/2021/CROI/croi_55.htm

“2-1-1” is simpler with less frequent sex

- Two FTC/TDF tablets 2-24h before sex
- One FTC/TDF tablet 24h after first two tablets
- One FTC/TDF tablet 48h after first two tablets



Dosing continues until the *day after the day after* the last “sex day”

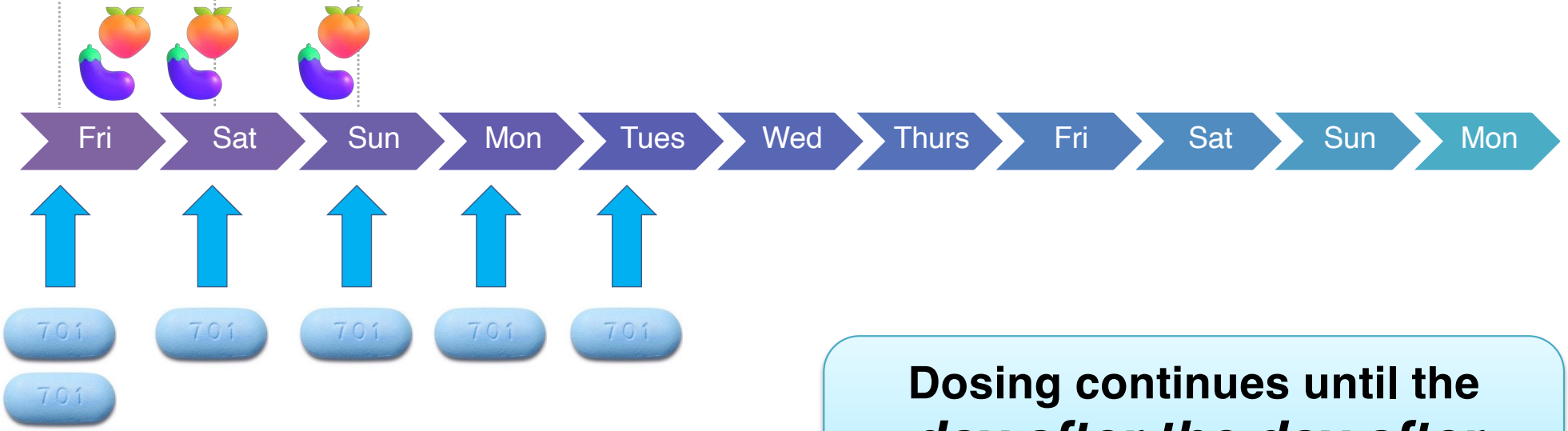
Adapted from → Saberi, P., Scott, H.M. *J Gen Intern Med* 35, 1285–1288 (2020)

Scenario 2: weekend in bed*

* or wherever…
who am I to judge?

- Two FTC/TDF tablets 2-24h before sex
- One FTC/TDF tablet 24h after first two tablets
- One FTC/TDF tablet 48h after first two tablets

Continue taking one tablet every 24h until the day after the day after the last sex day (Sun → Tues)



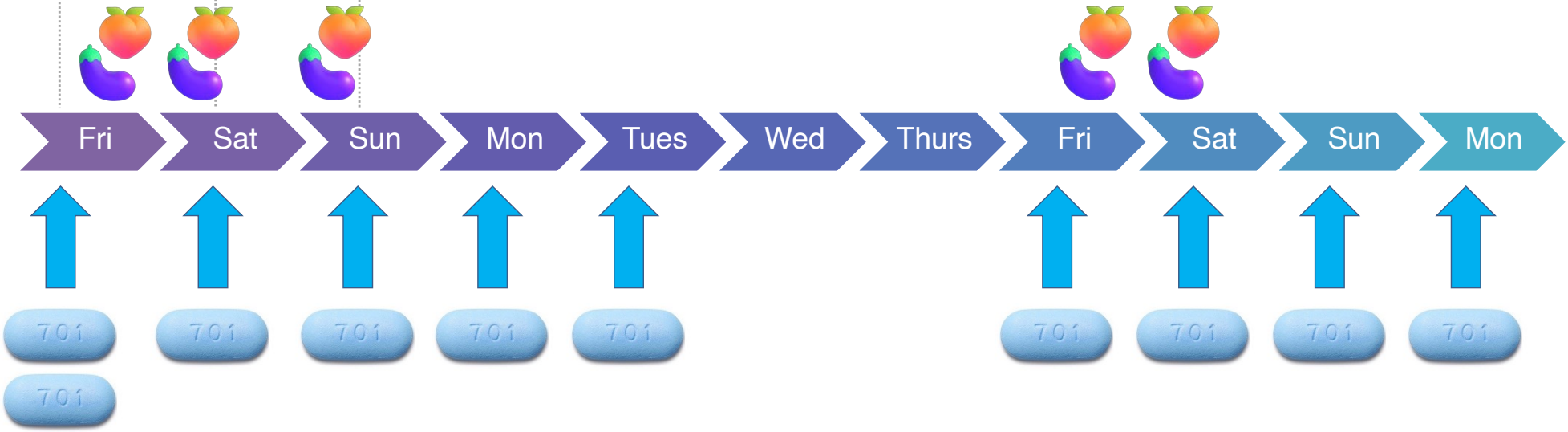
Dosing continues until the *day after the day after* the last "sex day"

Adapted from → Saberi, P., Scott, H.M. *J Gen Intern Med* 35, 1285–1288 (2020)

Scenario 3: two weekends in a row

- Two FTC/TDF tablets 2-24h before sex
  - One FTC/TDF tablet 24h after first two tablets
    - One FTC/TDF tablet 48h after first two tablets

If LESS THAN 7 DAYS elapse between end of one dosing period & start of next, <u>ONE</u> tablet to restart

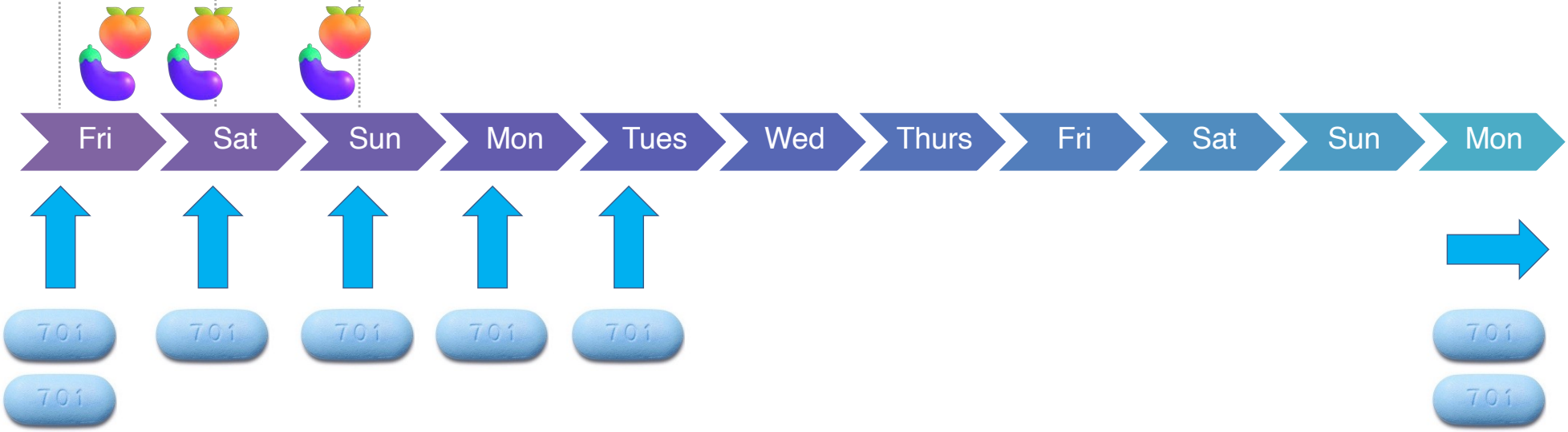


Adapted from → Saberi, P., Scott, H.M. *J Gen Intern Med* 35, 1285–1288 (2020)

Scenario 4: see you when I see you

- Two FTC/TDF tablets 2-24h before sex
  - One FTC/TDF tablet 24h after first two tablets
    - One FTC/TDF tablet 48h after first two tablets

If MORE THAN 7 DAYS elapse between end of one dosing period & start of next, TWO tablets to restart



Adapted from → Saberi, P., Scott, H.M. *J Gen Intern Med* 35, 1285–1288 (2020)

Special considerations

AETC AIDS Education & Training Center Program Southeast

Coming back to bone health…

Truvada[TDF]

emtricitabine / tenofovir disoproxil fumarate

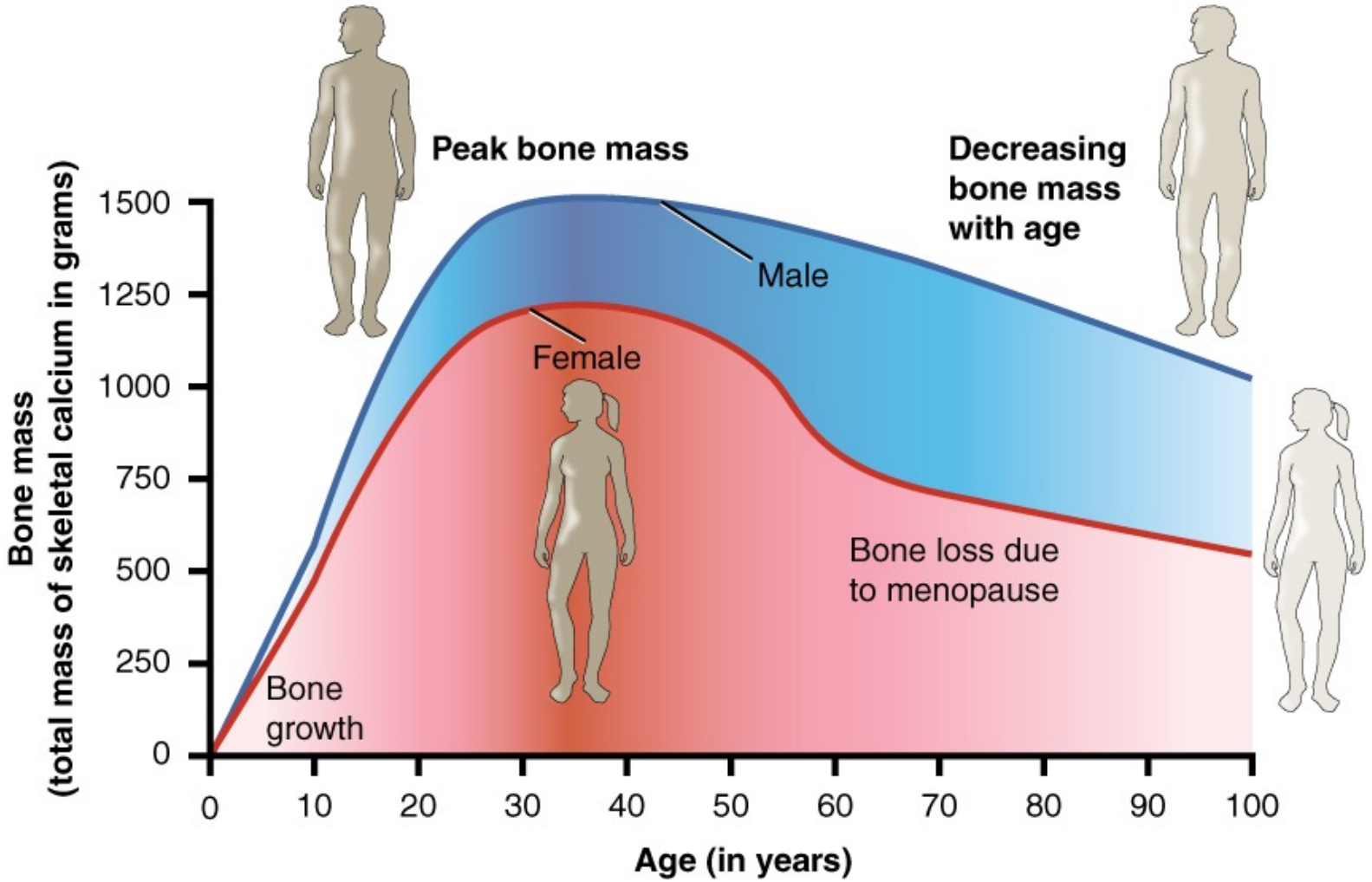
Bone density loss of ~1.5% within 3-6 months of initiation among persons **who have achieved peak bone mass**

Descovy[TAF]

emtricitabine / tenofovir alafenamide fumarate

No significant adverse effects on bone density / health

Peak density by age 21-25, for most

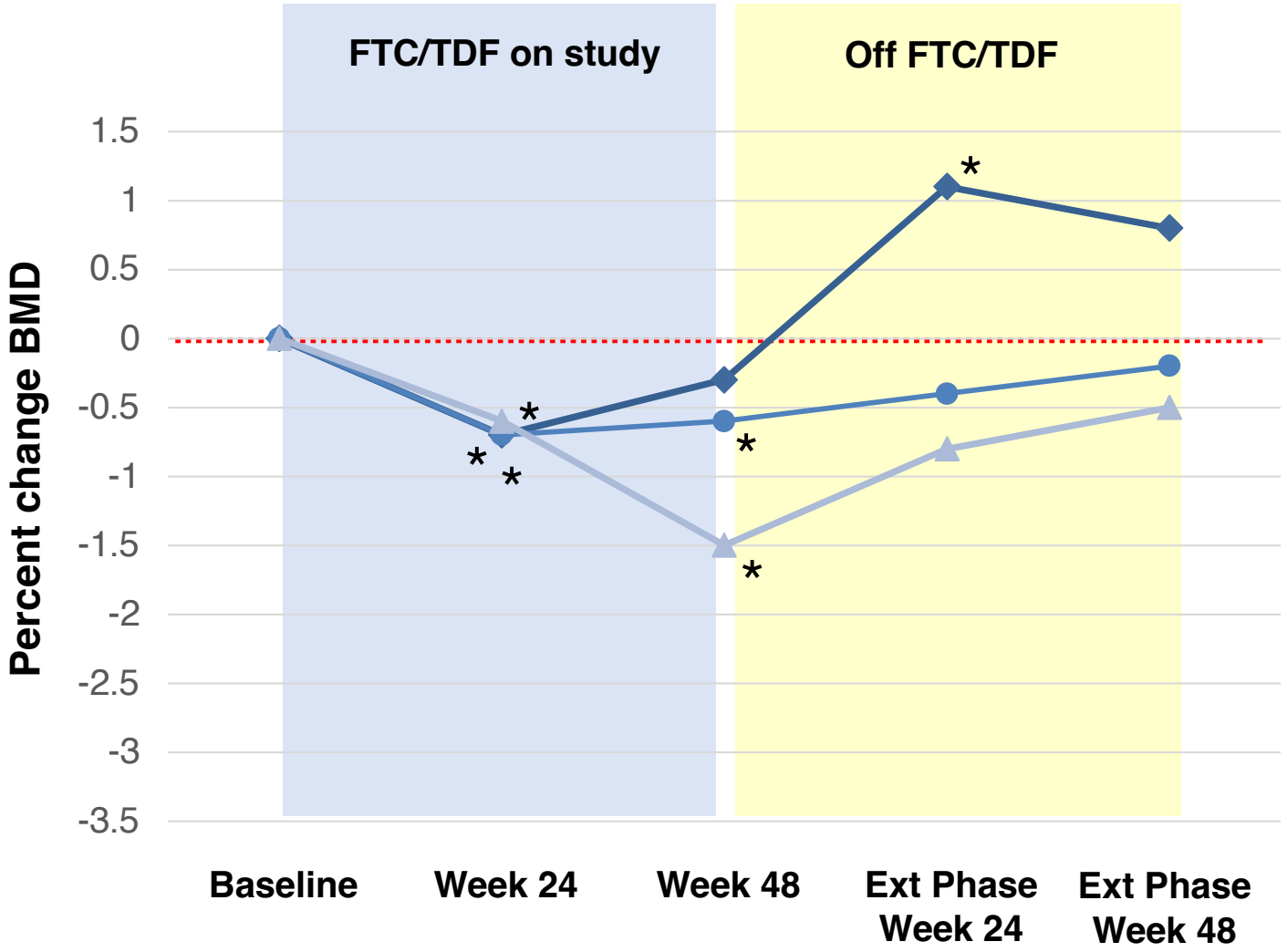


Graphic from → https://www.physio-pedia.com/Bone_Density

Chevalley T, Rizzoli R. Best Pract Res Clin Endocrinol Metab. 2022 Mar;36(2):101616
Gordon RJ, Misra M, Mitchell DM. Endotext.org (via NLM) – https://www.ncbi.nlm.nih.gov/books/NBK593436/

Bone health has largely been overlooked

Project PrEPare 2 (ATN 110), 72 who stopped FTC/TDF



18-22
years old

Spine
P=0.03 vs W48
P=0.04 vs BL

Whole Body
P=0.01 vs W48
P=0.7 vs BL

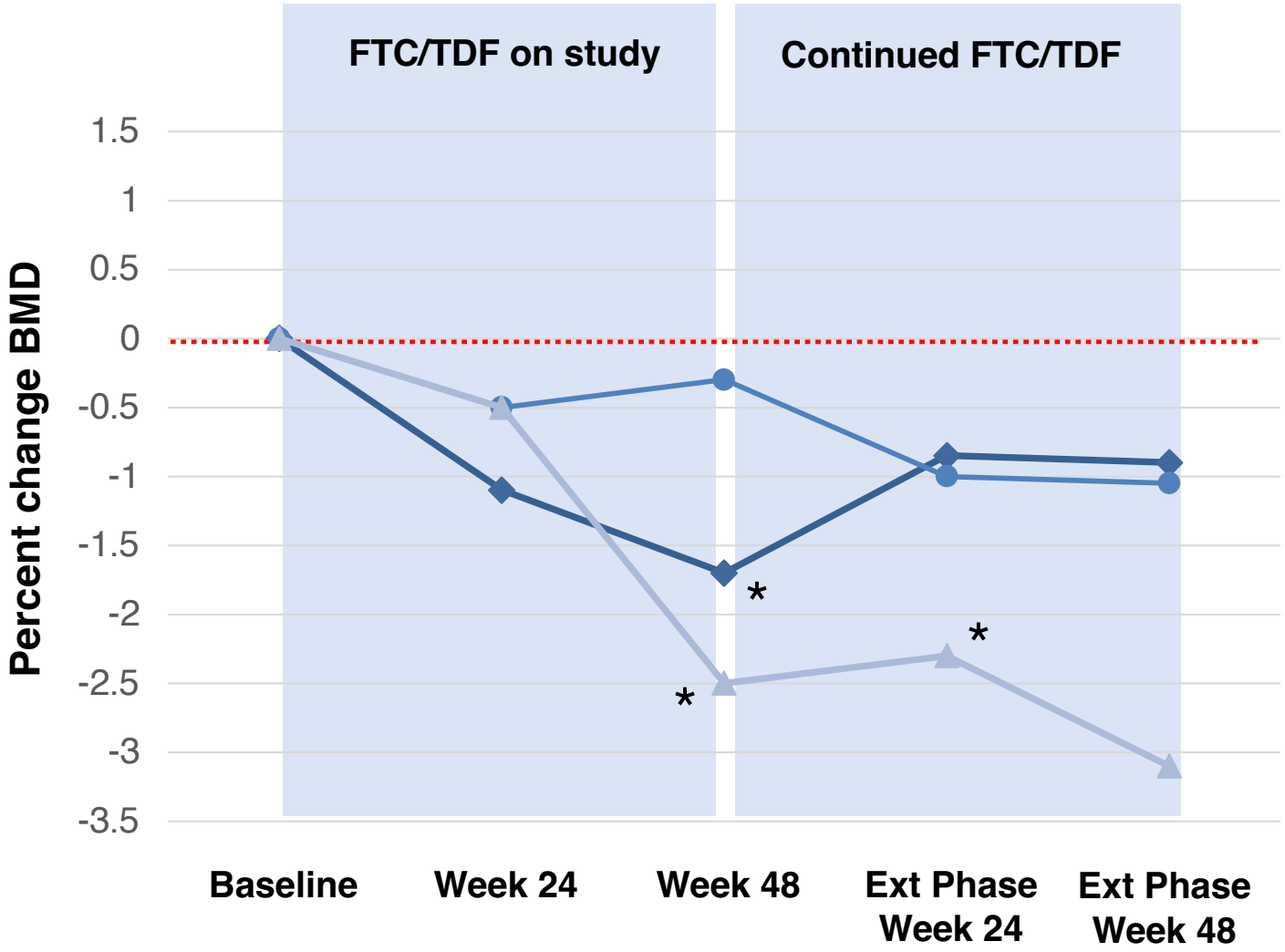
Hip
P=0.04 vs W48
P=0.5 vs BL

* $P < 0.05$ vs BL

Mulligan K, et al. 18th Int'l Workshop on Comorbidities and Adverse Drug Reactions in HIV. 12-13 Sept 2016. NYC, NY. Abstract 001
https://www.natap.org/2016/AdverseReactComor/AdverseReactComor_04.htm

Bone health has largely been overlooked

Project PrEPare 2 (ATN 110), 15 who continued FTC/TDF



18-22
years old

Spine
P=0.15 vs W48
P=0.44 vs BL

Whole Body
P=0.25 vs W48
P=0.17 vs BL

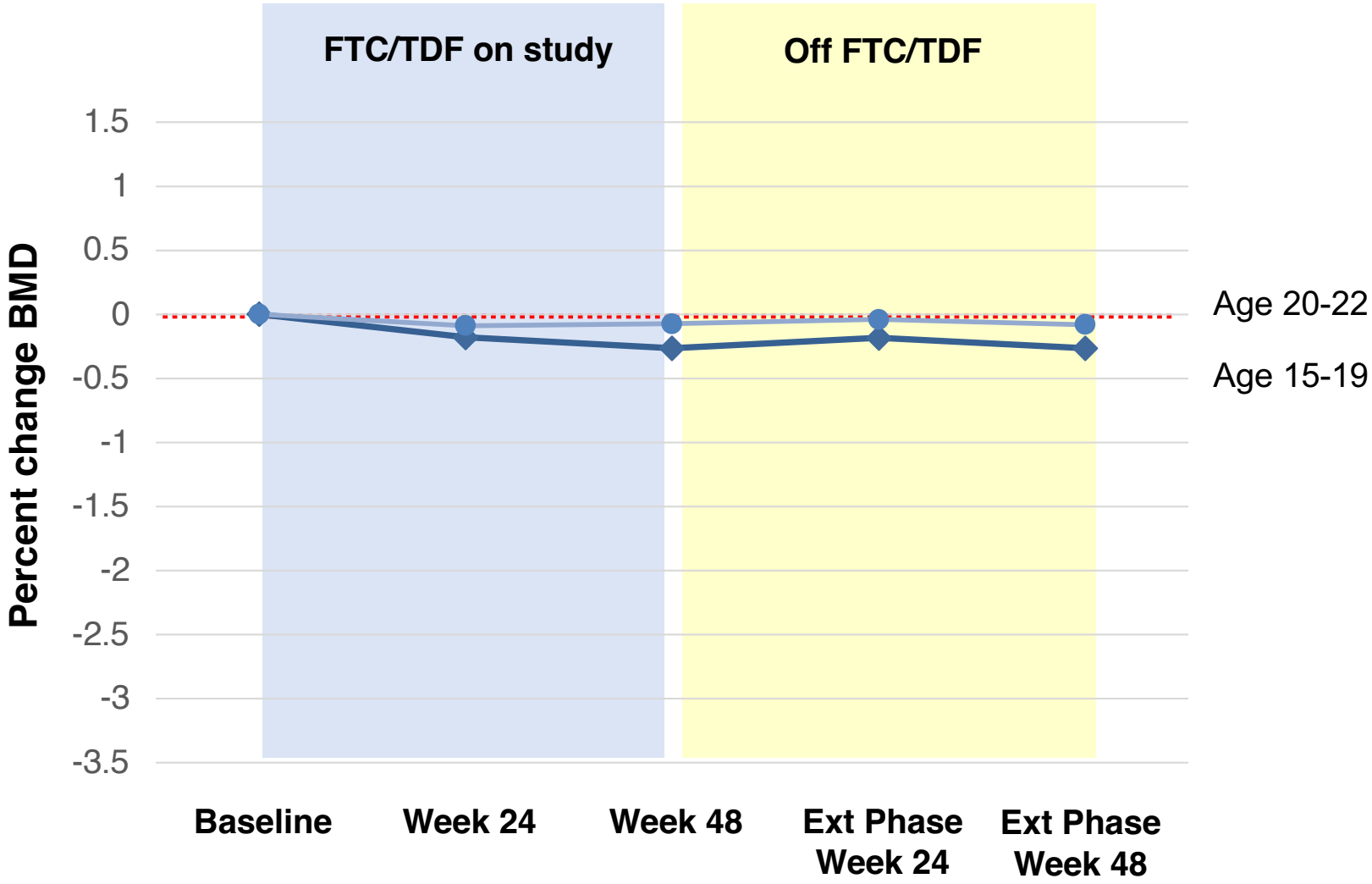
Hip
P=0.57 vs W48
P=0.001 vs BL

* $P < 0.05$ vs BL

Mulligan K, et al. 18th Int'l Workshop on Comorbidities and Adverse Drug Reactions in HIV. 12-13 Sept 2016. NYC, NY. Abstract 001 https://www.natap.org/2016/AdverseReactComor/AdverseReactComor_04.htm

BMD recovery after PrEP, all ages

Projects PrEPare 1 (ATN 113) and 2 (ATN 110)

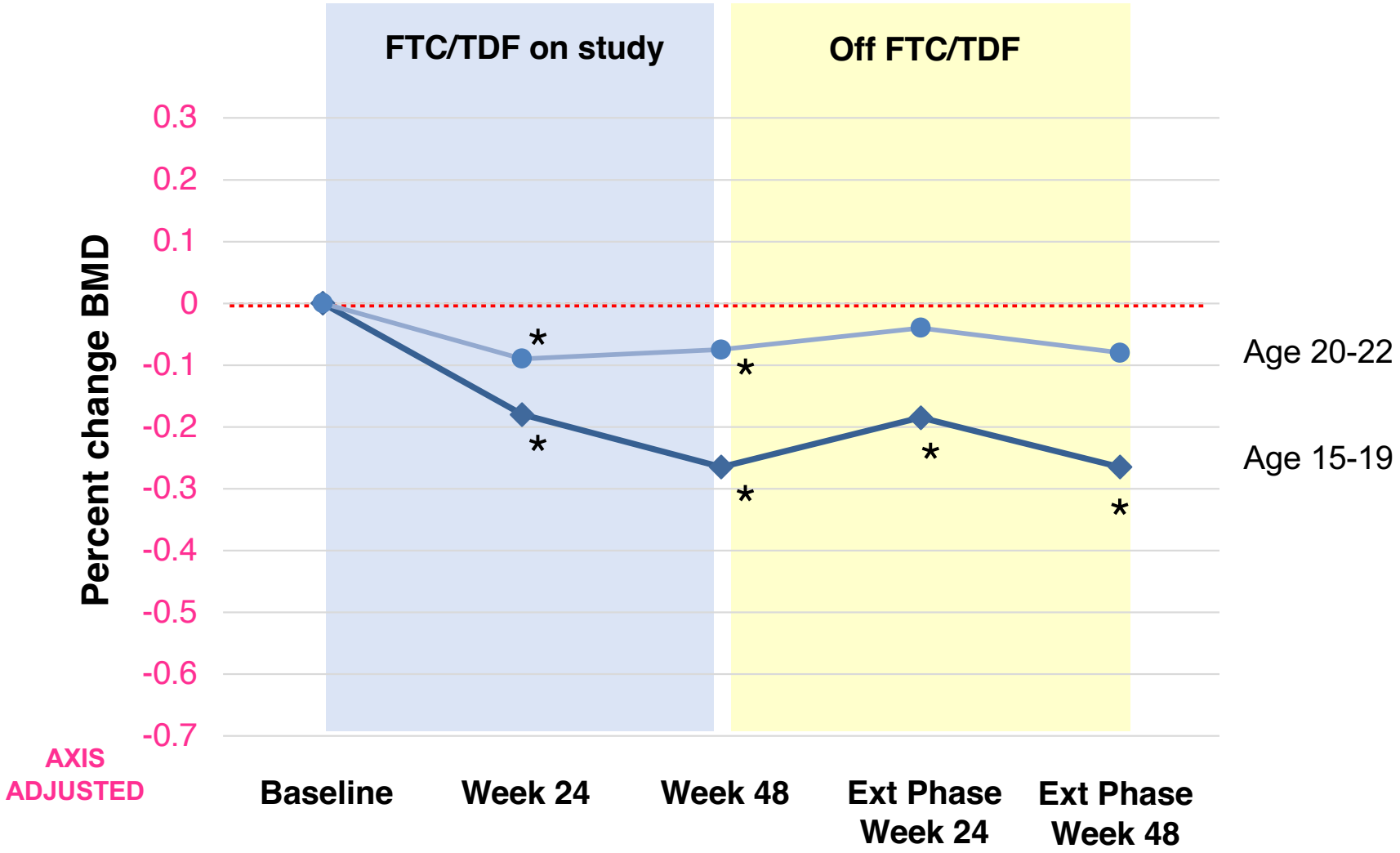


* $P < 0.05$ vs BL

Havens PL, et al. Clin Infect Dis. 2020 Feb 3;70(4):687-691. PMID: 31179503; PMCID: PMC7319267.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7319267

Teenage start = persistent, slight BMD loss

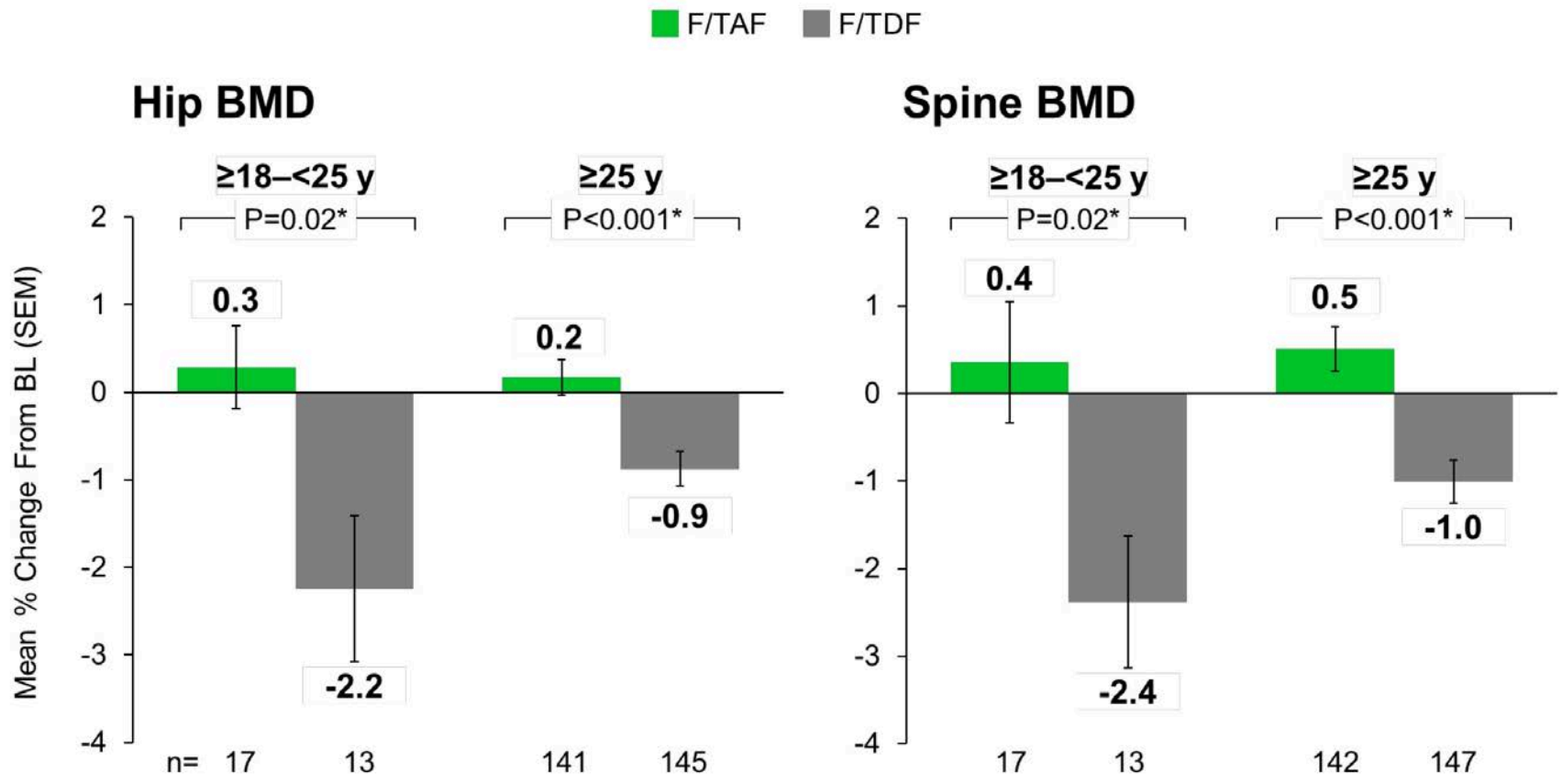
Projects PrEPare 1 (ATN 113) and 2 (ATN 110)



Havens PL, et al. Clin Infect Dis. 2020 Feb 3;70(4):687-691. PMID: 31179503; PMCID: PMC7319267.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7319267

So you should just use FTC/TAF, right?

Figure S6. Bone Safety at Week 48 for Participants Aged ≥18 to <25 and ≥25 Years

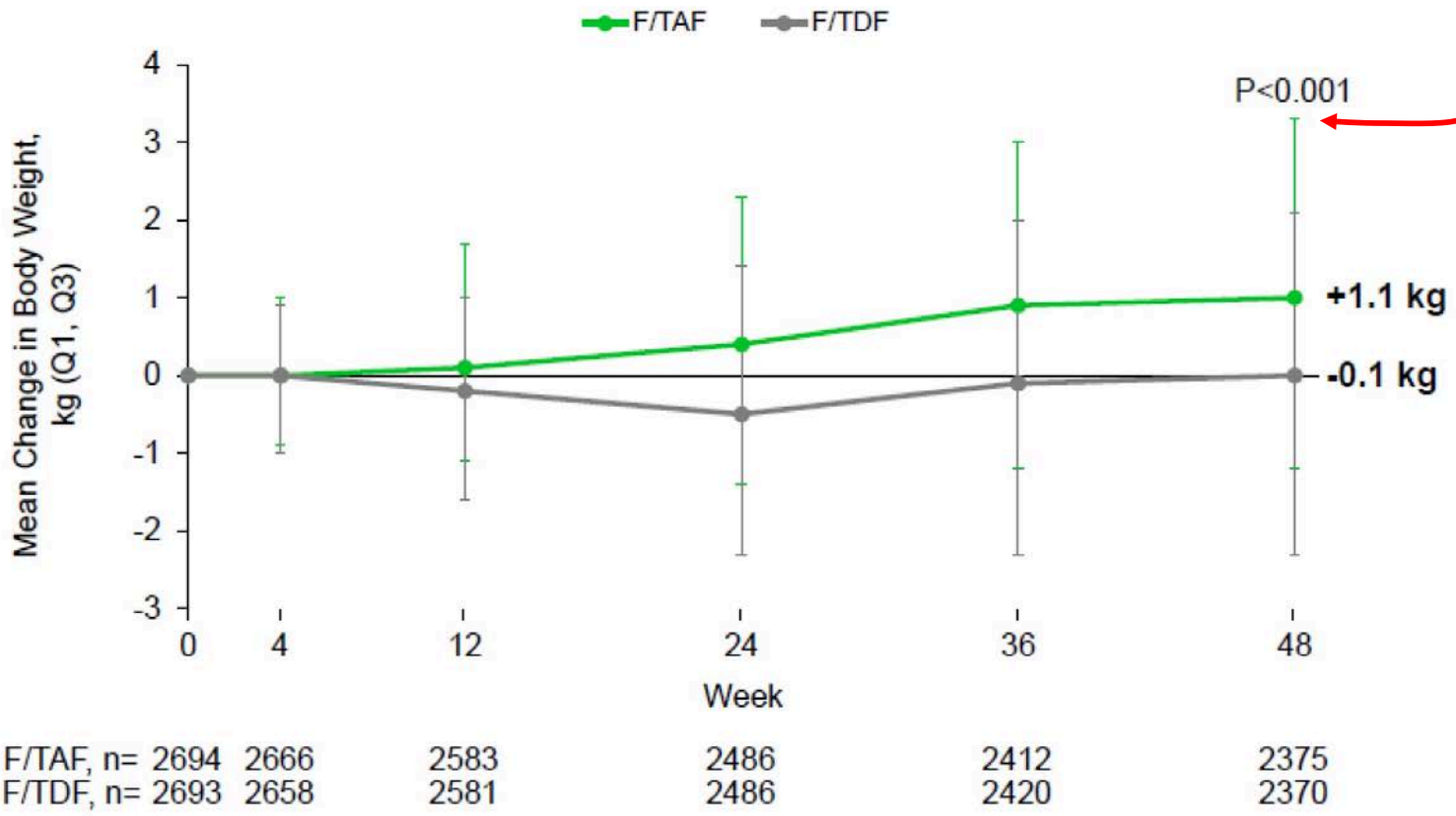


*P-values from analysis of variance model with BL F/TDF for PrEP and treatment as fixed effects.

SUPPLEMENTARY MATERIAL from → Mayer KH, et al. Lancet. 2020 Jul 25;396(10246):239-254. PMID: 32711800

So you should just use FTC/TAF, right?

Figure S12. Body Weight Change through Week 48



P-value from analysis of covariance model including baseline F/TDF for PrEP and treatment as fixed effects and baseline weight as a covariate.

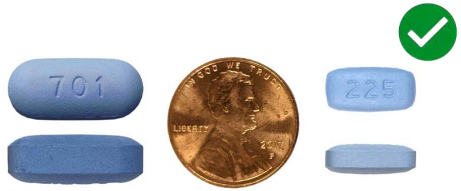
SUPPLEMENTARY MATERIAL from → Mayer KH, et al. Lancet. 2020 Jul 25;396(10246):239-254. PMID: 32711800

What would Christopher do?

1. Lay out the key data as objectively as possible

Track Record

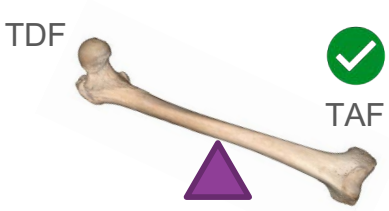
Pill size



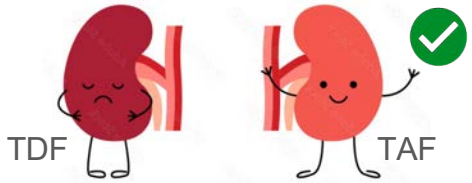
Weight change

TDF	TAF
- 0.1 kg	+1.1 kg

Bone health



Kidney health



2. Ask the patient which of these is most important to them

What would Christopher do?

3. Describe what most experts recommend…

+

±

FTC/TDF
one tablet daily

Vitamin D_3 (or D_2)
4,000 IU daily

Calcium
1,000 mg daily

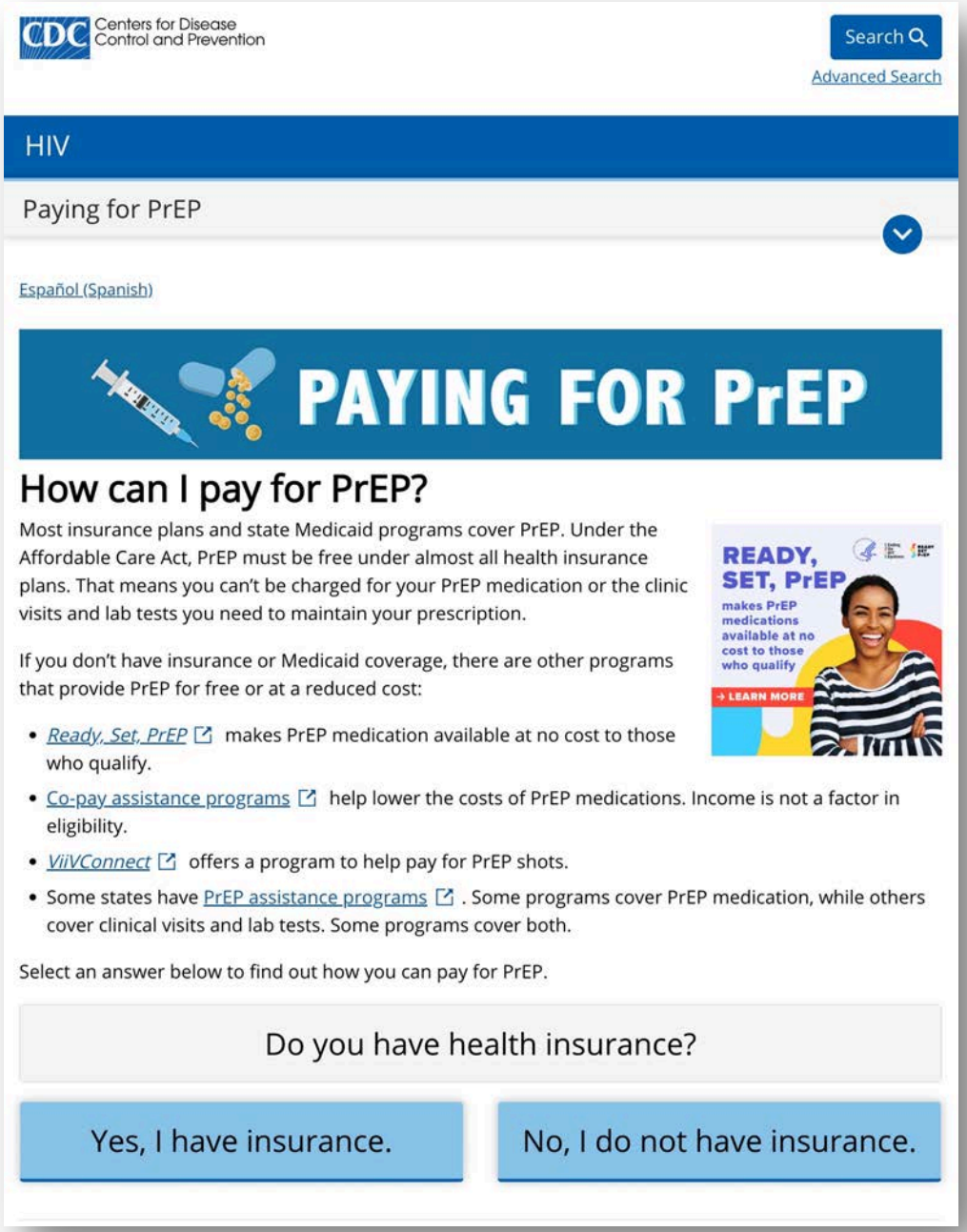
4. Let the patient make a final decision

5. Prescribe and proceed

Paying for PrEP

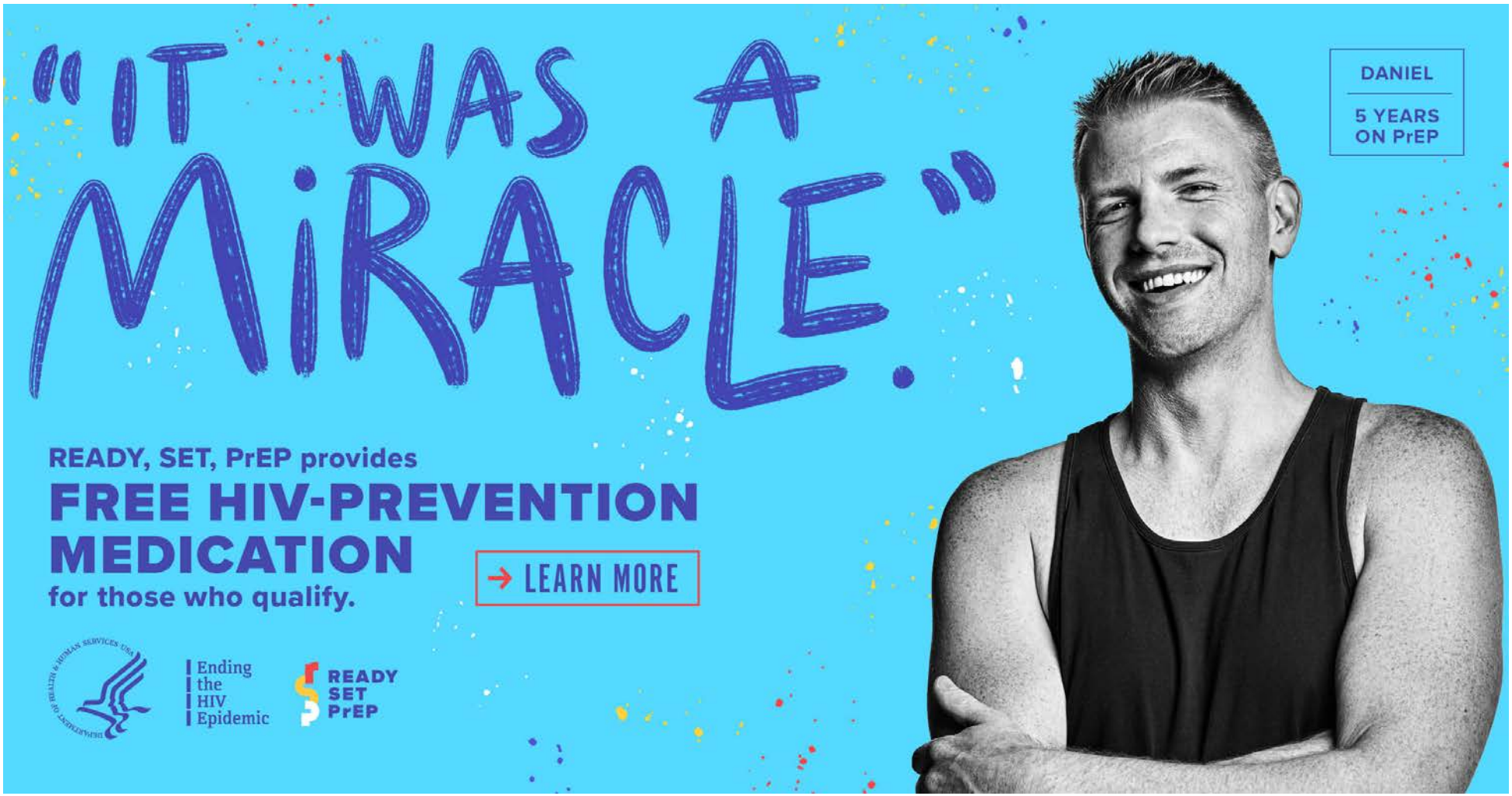
AETC AIDS Education & Training Center Program Southeast

CDC has an excellent starting point…



https://www.cdc.gov/hiv/basics/prep/paying-for-prep/

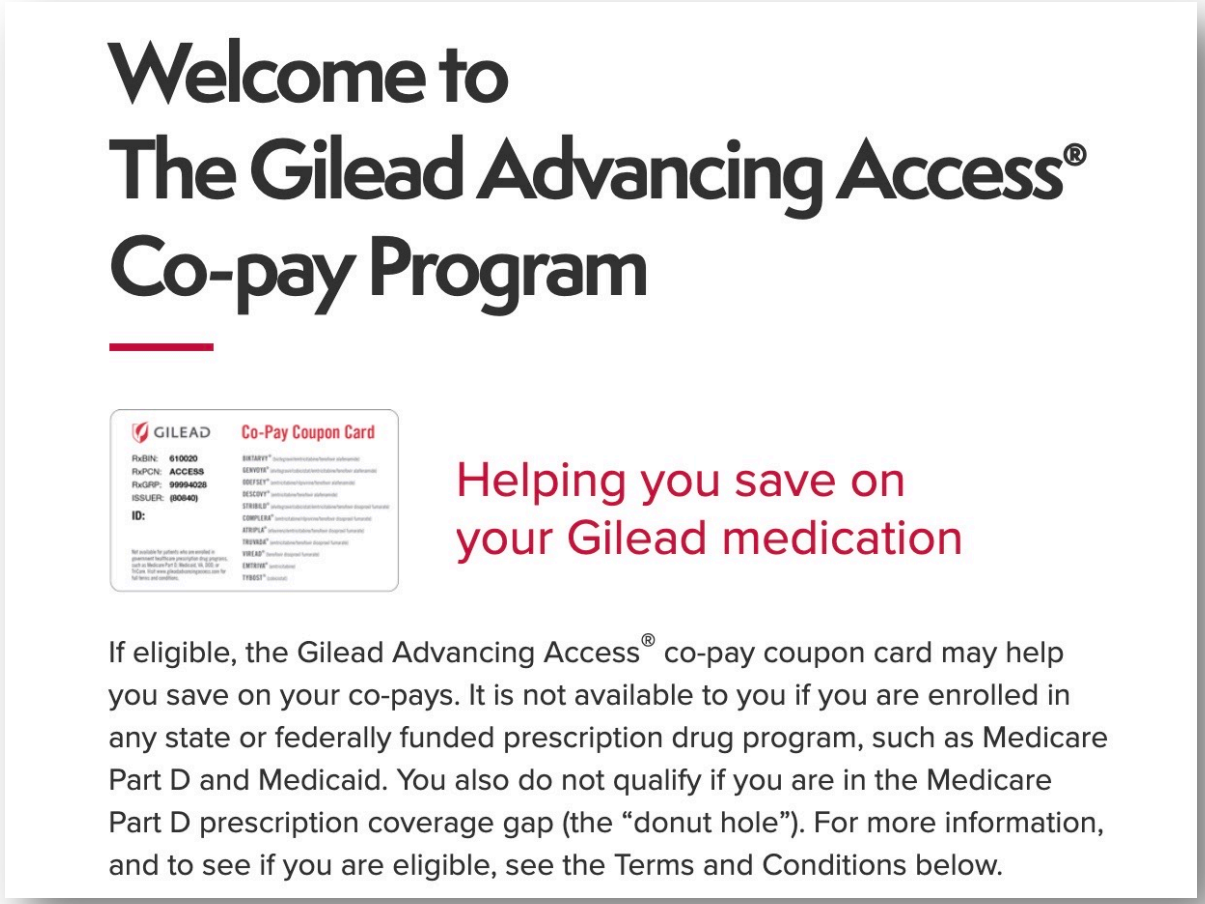
Patients may be eligible for free medication



https://www.getyourprep.com/

https://www.hiv.gov/federal-response/ending-the-hiv-epidemic/prep-program-resources

Copay assistance available for brand-name



Welcome to The Gilead Advancing Access® Co-pay Program

Helping you save on your Gilead medication

If eligible, the Gilead Advancing Access® co-pay coupon card may help you save on your co-pays. It is not available to you if you are enrolled in any state or federally funded prescription drug program, such as Medicare Part D and Medicaid. You also do not qualify if you are in the Medicare Part D prescription coverage gap (the "donut hole"). For more information, and to see if you are eligible, see the Terms and Conditions below.

- Up to $7,200 per year
- No monthly limit
- Not available for generics

https://www.gileadadvancingaccess.com/copay-coupon-card

Questions?

Christopher Hurt, MD

churt@med.unc.edu

https://www.wikiart.org/en/keith-haring/stop-aids-1989