AETC AIDS Education & Training Center Program Southeast

Update on PrEP: Focus on the Medications

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Disclosures

- The activity planners and speakers do not have any financial relationships with commercial entities to disclose.

- This slide set has been peer-reviewed to ensure that there are no conflicts of interest represented in the presentation

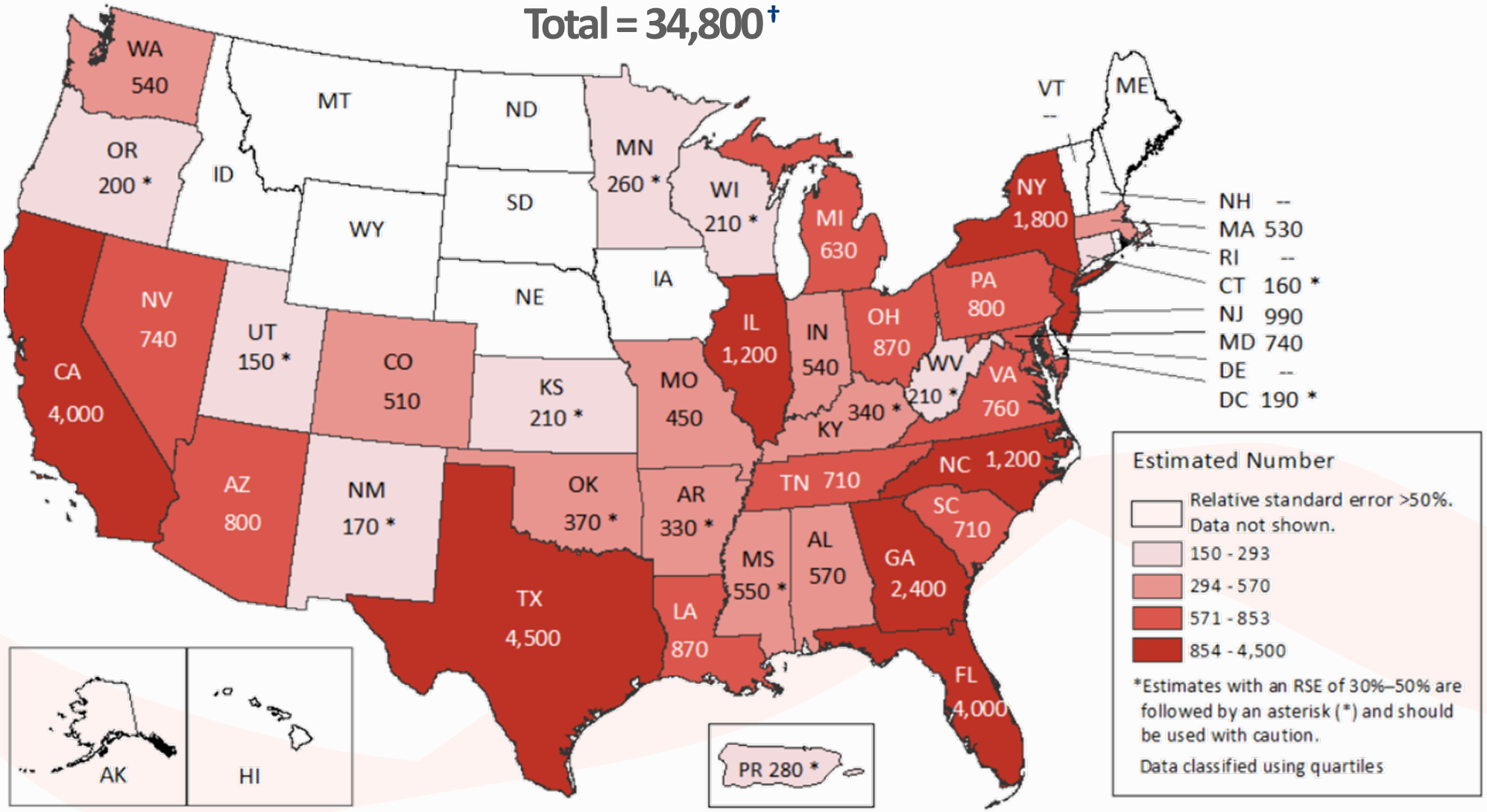
Objectives

- Describe PrEP and its role in preventing HIV
- Discuss efficacy and safety of current PrEP options
- Discuss medications in development for the indication of PrEP

INTRODUCTION: PrEP

Estimated HIV Incidence among Persons Aged ≥13 Years, by Area of Residence 2019—United States and Puerto Rico

Total = 34,800†

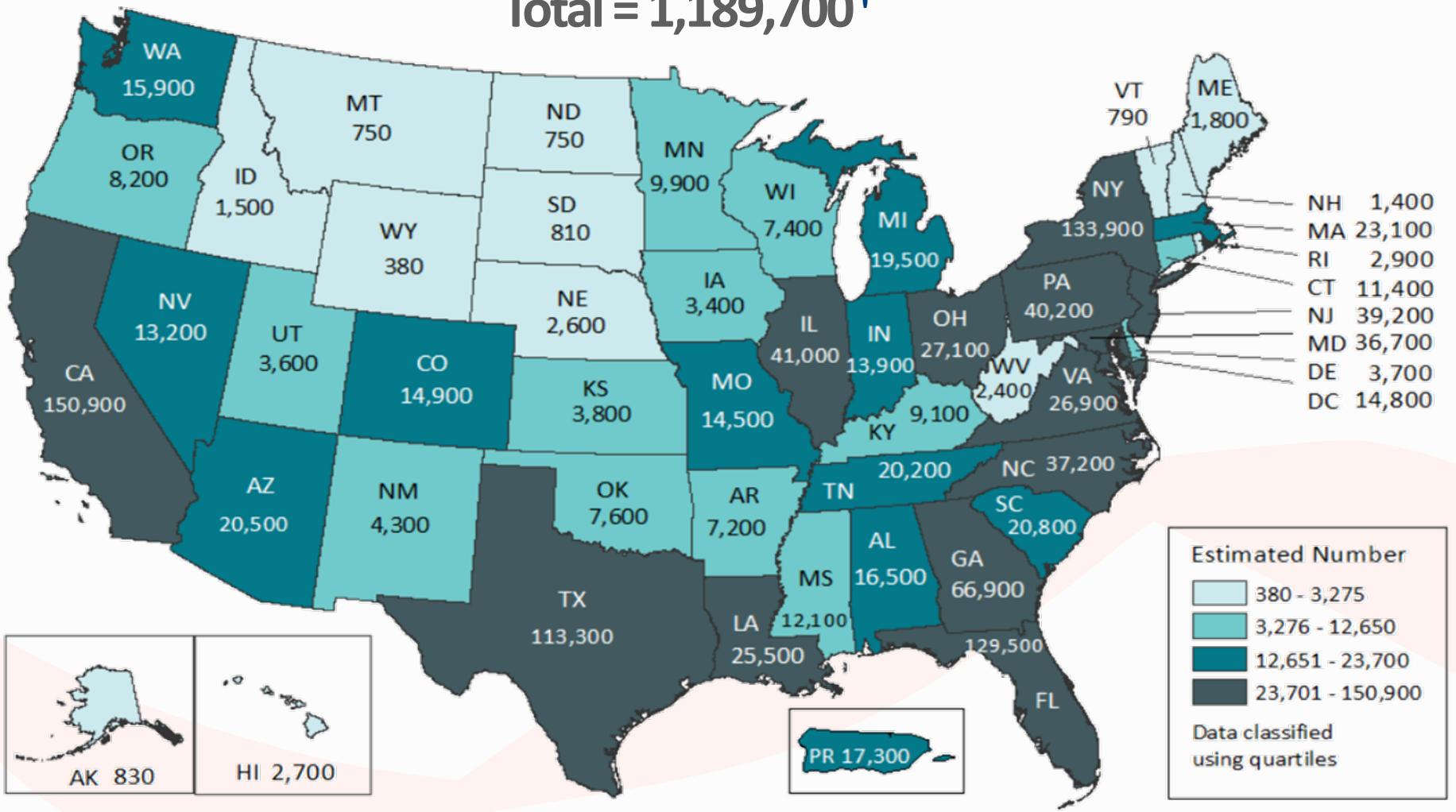


Note. Estimates were derived from a CD4 depletion model using HIV surveillance data. Estimates rounded to the nearest 100 for estimates >1,000 and to the nearest 10 for estimates ≤1,000 to reflect model uncertainty.

†Total estimate for the United States does not include data for Puerto Rico.

Estimated HIV Prevalence among Persons Aged ≥13 years, by Area of Residence 2019—United States and Puerto Rico

Total = 1,189,700†



Note. Estimates were derived from a CD4 depletion model using HIV surveillance data. Estimates rounded to the nearest 100 for estimates >1,000 and to the nearest 10 for estimates ≤1,000 to reflect model uncertainty. Estimates for the year 2019 are preliminary and based on deaths reported to CDC through December 2020. Estimates should be interpreted with caution due to incomplete death ascertainment for Kansas, Massachusetts, Mississippi, Nevada, North Dakota, and Vermont.

†Total estimate for the United States does not include data for Puerto Rico.

Pre-Exposure Prophylaxis (PrEP) for HIV Prevention

What is PrEP?

- PrEP is when people without HIV take HIV antiretroviral medications to prevent HIV
- If taken as prescribed, PrEP medications prevent getting HIV during sex by up to 99%
- Medications are taken daily, used before and during periods of risk
- HIV PrEP for people without HIV and treatment as prevention (U=U*) for people with HIV work together to reduce new HIV infections in the US

*Undetectable=Untransmittable

CDC, USPHS. Preexposure prophylaxis for the prevention of HIV infection in the United States – —2017 Update: a clinical practice guideline. https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2017.pdf. Published March 2018.

Pre-Exposure Prophylaxis (PrEP) for HIV Prevention

- Use of antiretroviral meds by *uninfected* patients to **prevent HIV infection**
- Used before and during periods of risk
- Tenofovir disoproxil fumarate (DF)/emtricitabine was the first ARV FDA approved and CDC recommended for PrEP
  - Now also TAF/emtricitabine has received FDA approval
  - Cabotegravir (injectable) has not yet received FDA approval for this indication

CDC, USPHS. Preexposure prophylaxis for the prevention of HIV infection in the United States – —2017 Update: a clinical practice guideline. https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2017.pdf. Published March 2018.

How do patients take PrEP?

- **Must be taken DAILY, one pill once a day**
- The exact time from initiation of daily oral doses of TDF/FTC to maximal protection against HIV infection is unknown
- PrEP medications reach maximum intracellular concentrations in rectal tissue for **receptive anal sex** at about **7 days** of daily use.
- For **all other activities**, including insertive anal sex, vaginal sex, and injection drug use, PrEP reaches maximum protective concentrations at about **20 days** of daily use.

CDC, USPHS. Preexposure prophylaxis for the prevention of HIV infection in the United States – 2017 Update: a clinical practice guideline. https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2017.pdf. Published March 2018.

Who is PrEP for?

Consider for anyone who is HIV negative but at increased risk for HIV infection:

- Anyone in a relationship with a HIV positive partner
- Anyone with more than one STI in the last year
- Anyone with multiple partners and inconsistent condom use
- Those receiving nPEP (non-occupational), especially more than once

Indicators of risk for HIV infection

Adults and adolescents* 15 yrs+ at substantial risk of HIV acquisition:

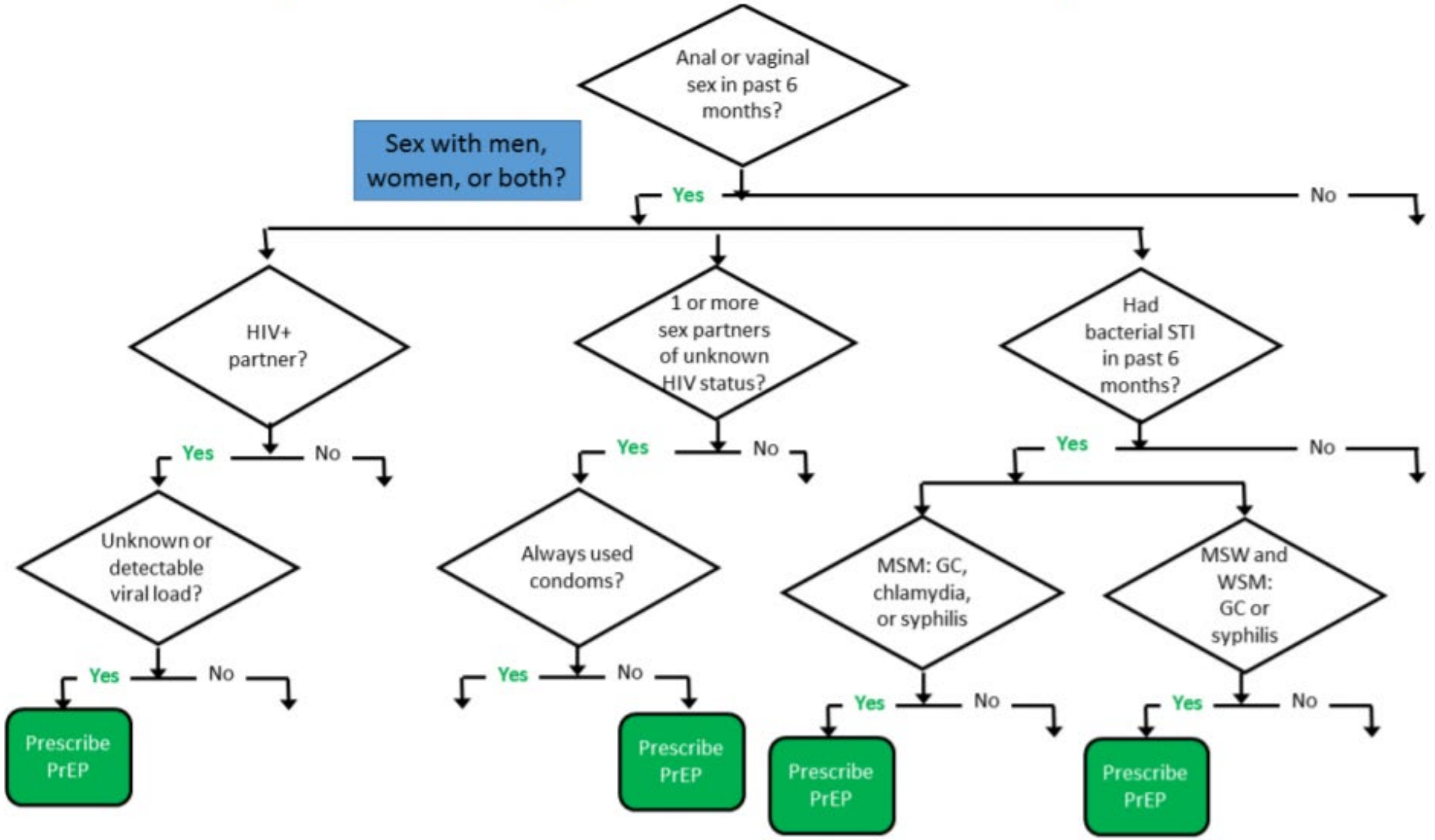
	MSM (Sexually-active)	**Heterosexual Women and Men (Sexually-active)**	**Injection Drug Users**
Detecting substantial risk of acquiring HIV infection	▪ HIV-positive sexual partner ▪ Recent bacterial STI ▪ High number of sex partners ▪ History of inconsistent or no condom use ▪ Commercial sex work	▪ HIV-positive sexual partner ▪ Recent bacterial STI ▪ High number of sex partners ▪ History of inconsistent or no condom use ▪ Commercial sex work ▪ In high-prevalence area or network	▪ HIV-positive injecting partner ▪ Sharing injection equipment
Recent, *in past 6 months*, bacterial STI	Gonorrhea, chlamydia, syphilis	Gonorrhea, syphilis	Gonorrhea, syphilis

*Adult or adolescent person weighing at least 35kg (77lbs)

Adapted from: CDC, USPHS. Preexposure prophylaxis for the prevention of HIV infection in the United States – —2017 Update: a clinical practice guideline. https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2017.pdf. Published March 2018.

CDC Draft Document

Figure 2 Assessing Indications for PrEP in Sexually Active Persons

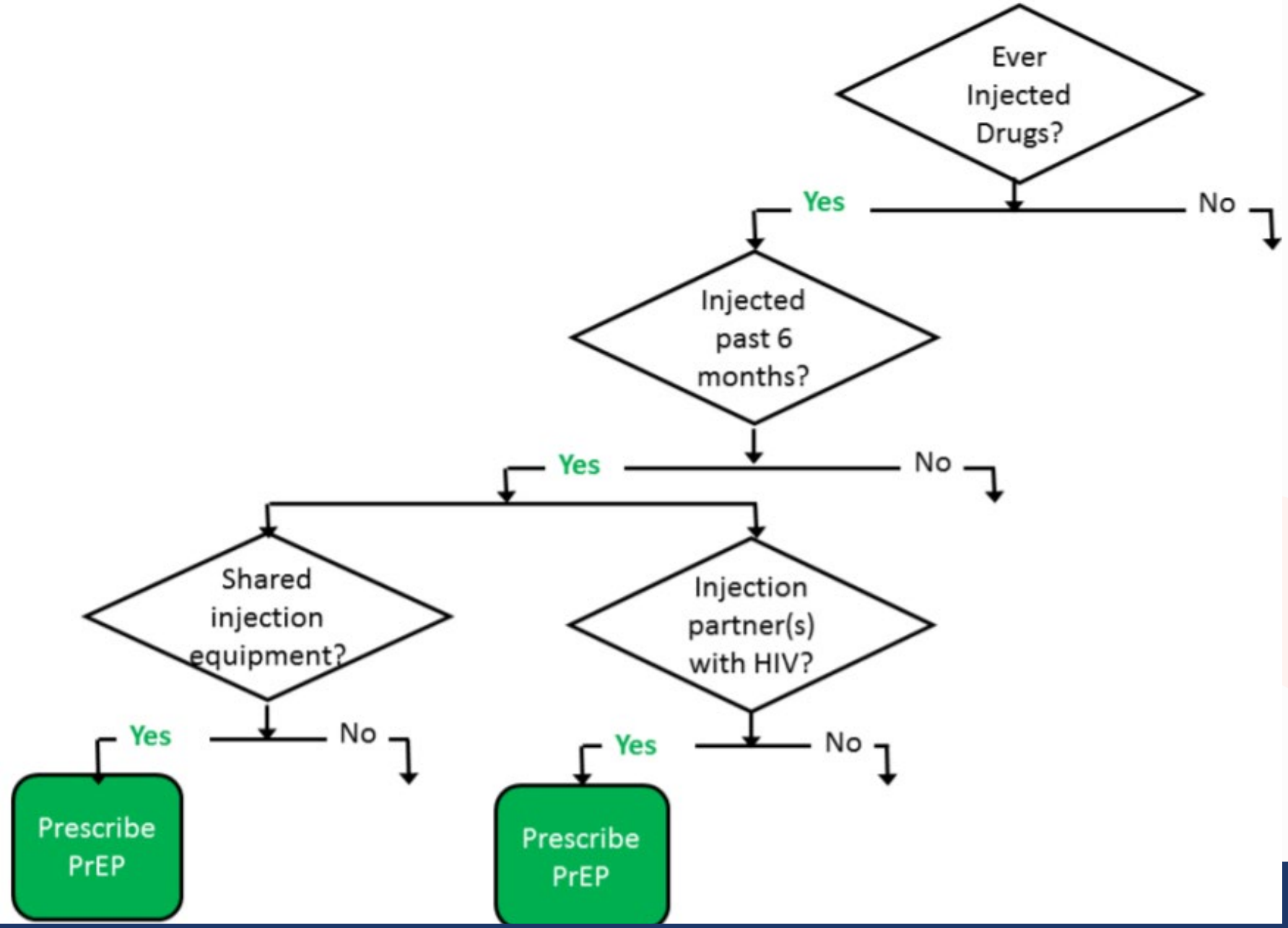


Patients may request PrEP because of concern about acquiring HIV infection but not feel comfortable reporting sexual or injection behaviors to avoid anticipated stigmatizing responses in health care settings.[33-36] For this reason, after attempts to assess patient sexual and injection behaviors, patients who request PrEP should be offered it, even when no specific risk behaviors are elicited.

https://www.cdc.gov/hiv/pdf/programresources/cdc-hiv-PrEP-GL-Webinar-2021-Presentation.pdf

CDC Draft Document

Figure 3 Assessing Indications for PrEP in Persons Who Inject Drugs



https://www.cdc.gov/hiv/pdf/programresources/cdc-hiv-PrEP-GL-Webinar-2021-Presentation.pdf

Effectiveness Estimates

For sexual transmission:	• With daily PrEP use the risk of acquiring HIV is reduced by an estimated 99%
For injection drug use transmission:	• With consistent PrEP use the risk is estimated to be reduced by 74-84%

https://www.cdc.gov/stophivtogether/library/prescribe-hiv-prevention/brochures/cdc-lsht-php-brochure-prep-faq.pdf

PrEP Medication Options in *Draft* of New Guidelines

Tenofovir disoproxil fumarate (TDF)/ emtricitabine was the only ARV FDA approved and CDC recommended for PrEP until October 2019

- Truvada or TDF/FTC oral tablet once daily

Now, tenofovir alafenamide(TAF)/ emtricitabine has received FDA approval, CDC draft guidelines have Descovy (TAF/emtricitabine) for men/TGW only

- Descovy (TAF/FTC) oral tablet once daily

On November 17, 2020 FDA designated long-acting, **injectable cabotegravir for PrEP** as a break-through therapy, expediting consideration for approval. A final FDA approval decision is expected in 2021. CDC draft guidelines recommend this for both men and women.

- Injectable cabotegravir intramuscularly every 8 weeks

https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf Accessed May 24, 2021

ADME of Oral PrEP medications

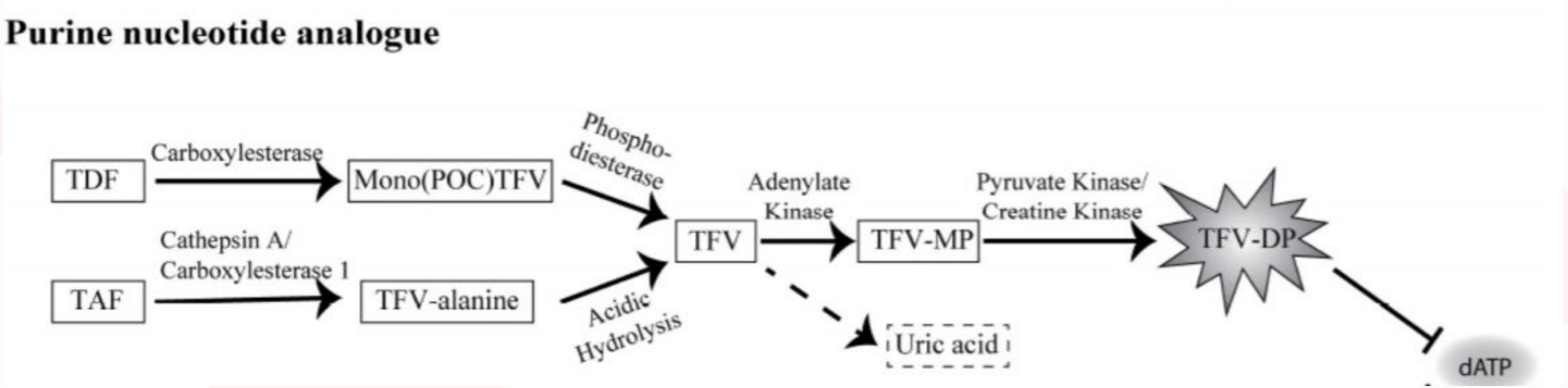
PARAMETER	TENOFOVIR *	EMTRICITABINE
Oral bioavailability, %	25	93
Effect of meals on AUC	↑ 40% (high fat)	↔
Plasma $t_{1/2}$, h	14–17	10
Intracellular $t_{1/2}$ of triphosphate, h	60–100	39
Plasma protein binding, %	<8	<4
Metabolism, %	--	13
Renal excretion of parent drug, %	70–80	86

* tenofovir disoproxil fumarate (TDF), TAF has improved bioavailability and increased potency as reflected in the dose

Adapted from: Chapter 64 Antiretroviral Agents and Treatment of HIV Infection, Brunton LL, Hilal-Dandan R, Knollmann BC. *Goodman & Gilman's: The Pharmacological Basis of Therapeutics, 13e;* 2017. Available at: https://accesspharmacy.mhmedical.com/content.aspx?sectionid=172486528&bookid=2189 Accessed: November 1, 2020

Formation of the triphosphate

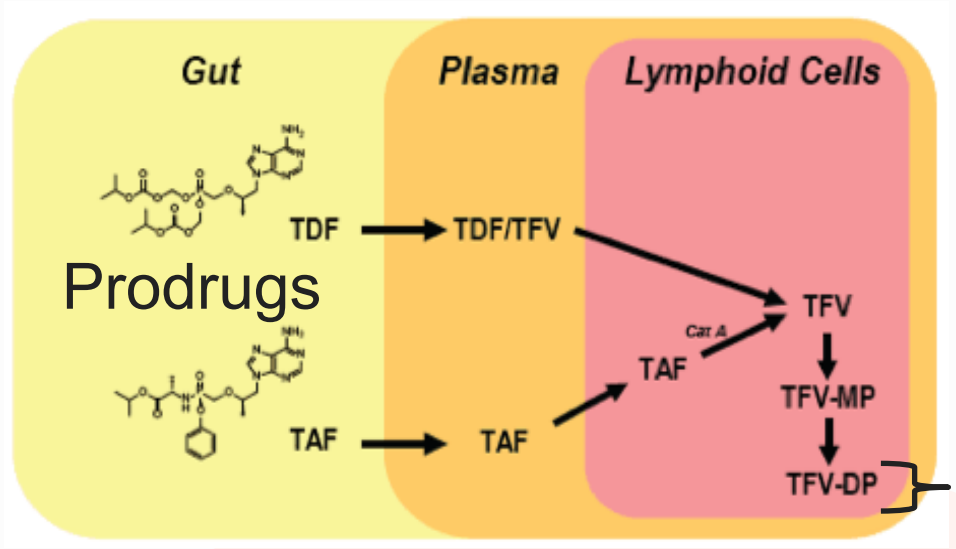
- Both TDF and TAF are prodrugs that eventually convert to a nucleotide analogue



Holec et al. Curr HIV Res. 2017 ; 15(6): 411–421.

TDF vs. TAF

- TAF has improved HIV activity at lower doses than TDF
- TAF 25mg vs. TDF 300mg
- TAF results in 5-7 fold increase in intracellular TFV-DP (active form) in the cell and in lower circulating plasma TFV levels



- TFV is metabolized intracellularly to its active form TFV-DP
- TAF delivers ↑ TFV levels into the cell (vs. TDF) & is able to achieve ↑ TFV-DP levels

TDF: tenofovir disproxil fumarate; TAF: tenofovir alafenamide; TFV: tenofovir; TFV-MP: tenofovir monophosphate; TFV-DP: tenofovir diphosphate

Photo: http://blogs.nature.com/spoonful/2013/07/gilead-under-pressure-to-produce-stand-alone-version-of-new-hiv-drug.html

DISCOVER

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

- Enrolled MSM and TGW in North America and Europe, who were HIV-negative and at high risk for acquiring HIV
- Participants were randomized to receive either **daily oral** F/TAF or F/TDF and were followed for 48-96 weeks
- 5335 participants (2670 in the F/TAF group and 2665 in the F/TDF group)

Mayer et al. Lancet 2020; 396: 239–54

Long-term safety and efficacy of emtricitabine and tenofovir alafenamide *vs* emtricitabine and tenofovir disoproxil fumarate for HIV-1 pre-exposure prophylaxis: week 96 results from a randomised, double-blind, placebo-controlled, phase 3 trial

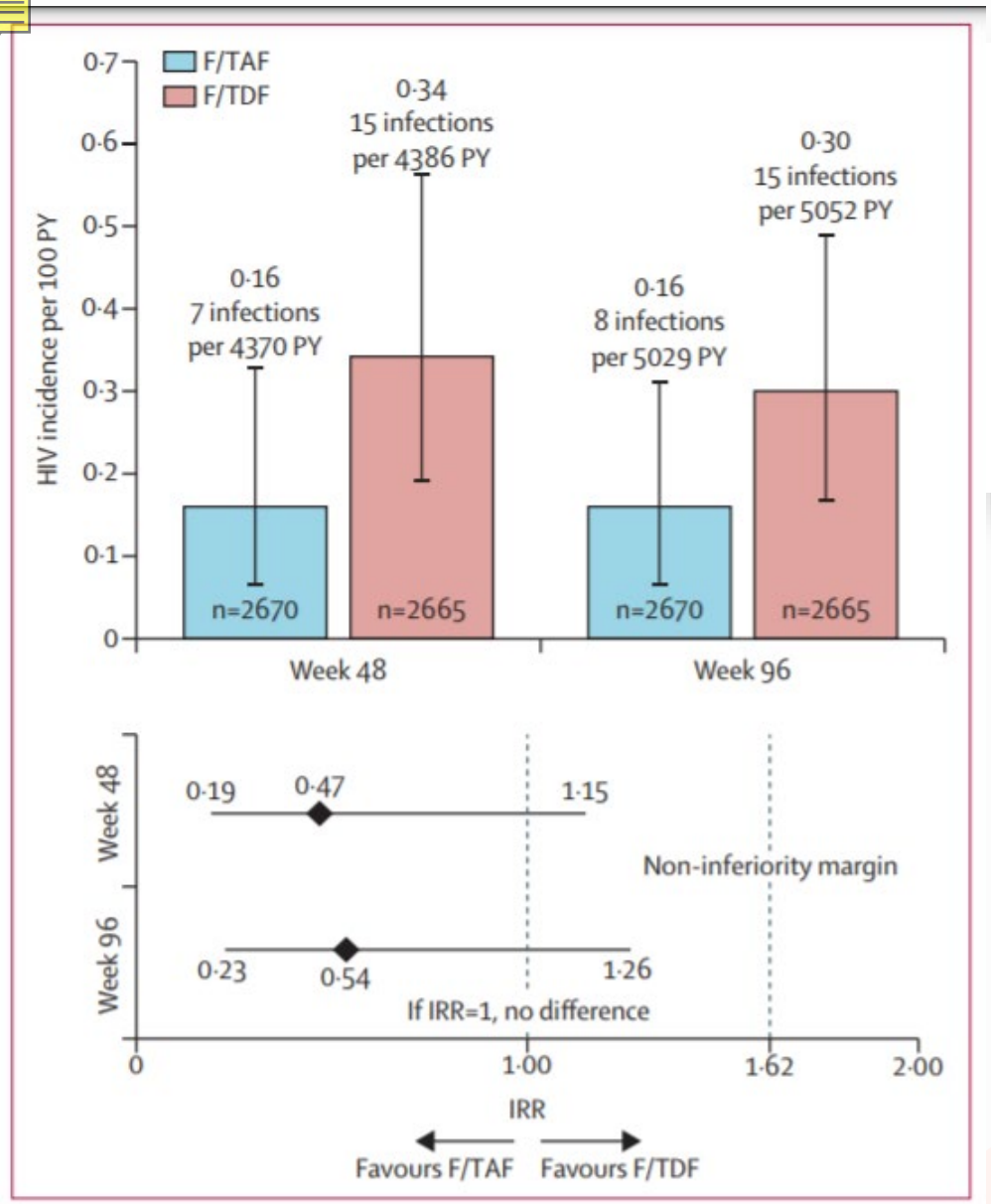


***Figure 2*: HIV incidence and IRR at weeks 48 and 96**
Incidence of HIV per 100 PY in the F/TAF and F/TDF groups and IRR (F/TAF divided by F/TDF). Error bars represent 95% CIs. F/TAF=emtricitabine and tenofovir alafenamide. F/TDF=emtricitabine and tenofovir disoproxil fumarate. IRR=incidence rate ratio. PY=person-year.

- F/TAF non-inferior to F/TDF for prevention of HIV
  - After 10 081 person-years of follow-up, 23 participants were diagnosed with HIV, 8 in F/TAF group and 15 in F/TDF group
  - TAF had more favorable biomarkers of renal safety and bone mineral density

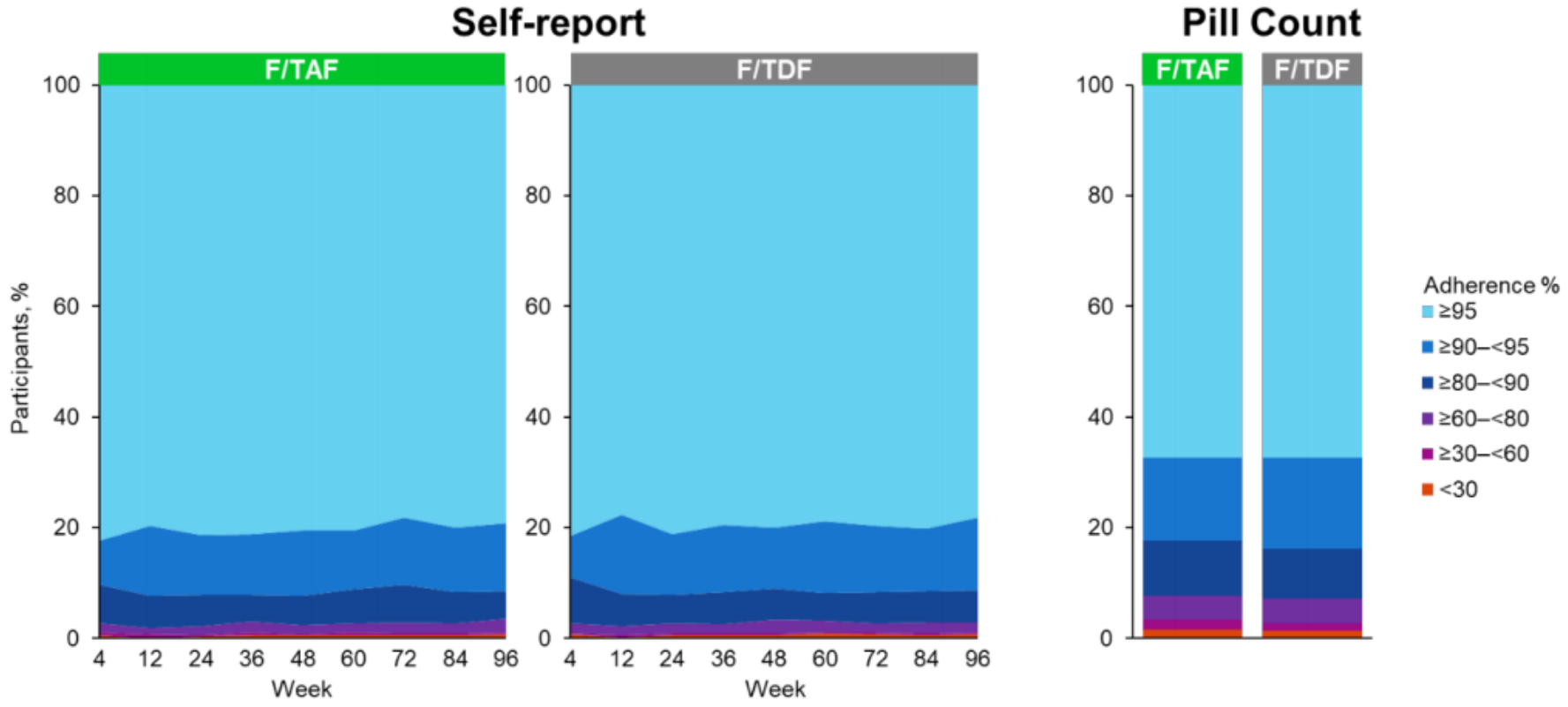
Ogbuagu, Onyema et al. Lancet HIV 2021; 8: e397–407

Adherence to daily regimen in DISCOVER

Compared to the early (placebo controlled) trials looking into PrEP efficacy, the adherence to daily PrEP in the DISCOVER study was better

*Approximately 78–82% of participants reported taking study medication more than 95% of the time across all study visits

Appendix Figure 1. Adherence by self-report and pill count



F/TAF=emtricitabine and tenofovir alafenamide, F/TDF=emtricitabine and tenofovir disoproxil fumarate

Ogbuagu, Onyema et al. Lancet HIV 2021; 8: e397–407

Sexually transmitted infections while on PrEP

- Rates of sexually transmitted infections **remained high and similar across groups** (21 cases per 100 person-years for rectal gonorrhea and 28 cases per 100 person-years for rectal chlamydia).

- Reminder:
  - PrEP can only prevent HIV, and is not effective at preventing bacterial STIs

STI	TAF/F	TDF/F
Rectal chlamydia	890 (33%)	902 (33%)
Oropharyngeal gonorrhea	871 (32%)	838 (31%)
Rectal gonorrhea	805 (30%)	797 (30%)
Syphilis	413 (15%)	392 (15%)
Urethral chlamydia	346 (13%)	314 (12%)
Urethral gonorrhea	259 (10%)	255 (9%)

Ogbuagu, Onyema et al. Lancet HIV 2021; 8: e397–407

DISCOVER: Renal Adverse Events

Table S5. Renal Adverse Events

Participants, n (%)	F/TAF (N=2694)	F/TDF (N=2693)
Any renal-specific AE	263 (10)	266 (10)
Study drug-related renal AEs	14 (1)	26 (1)
Grade ≥3 renal AEs	2 (<1)	3 (<1)
Renal AEs leading to discontinuation	2 (<1)	6 (<1)
Proximal renal tubulopathy	0	1 (<1)

AE, adverse event.

- Renal Adverse Events were seen in 10% of patients, although most were not considered to be related to study drug

Mayer et al. Lancet 2020; 396: 239–54

DISCOVER 96 week data

- Of the 9 patients who discontinued study drug due to renal endpoints
  - 2 were in TAF
  - 7 were in TDF

Appendix Table 4. Renal Discontinuation Cases

Emtricitabine and tenofovir alafenamide (N=2694)					Emtricitabine and tenofovir disoproxil fumarate (N=2693)				
AE	**Grade**	**Related**	**Age Range, y**	**Contributing Factors**	**AE**	**Grade**	**Related**	**Age Range, y**	**Contributing Factors**
Acute kidney injury	1	No	40–49	Myocardial infarction, contrast nephropathy	Fanconi syndrome	3	Yes	40–49	None identified
Acute kidney injury	2	Yes	30–39	Hypertension, FSGS on renal biopsy	Renal impairment	1	Yes	40–49	None identified
					Acute kidney injury	2	Yes	40–49	None identified
					Glomerular proteinuria	2	Yes	60–69	Hypertension
					Acute kidney injury	2	Yes	60–69	History of kidney disease, hypertension, NSAID use
					Renal impairment	2	Yes	60–69	Baseline kidney disease, NSAID use
					Renal impairment	2	Yes	50-59	None identified

FSGS, focal segmental glomerulosclerosis; NSAID, nonsteroidal anti-inflammatory drugs

Lancet HIV. 2021 Jul;8(7):e397-e407. doi: 10.1016/S2352-3018(21)00071-0.

What is the kidney toxicity associated with TDF?

- Fanconi syndrome (renal tubular injury with severe hypophosphatemia)
  - Extremely rare, only 1 patient in the DISCOVER trial
- Reduced eGFR
  - may result in increased serum creatinine, increased urinary protein loss (particularly tubular)

Mayer et al. Lancet 2020; 396: 239–54

Comparison of two oral options

TDF/FTC: *preferred option for most PrEP patients**

- Now has generic available
  - Should be available at NO cost for patients if plan complies with ACA requirements
- More clinical experience and research in cis-women/IVDU
- Very rare AKI risk
- Changes to BMD
  - clinical relevance?
- Not recommended for CrCl<60 mL/min

TAF/FTC

- Newly approved for PrEP in MSM/TGW
- More $$$, most insurance options require Prior Authorization
  - Considerations for CKD and/or osteoporosis risks
- Not recommended for CrCl < 30 mL/min

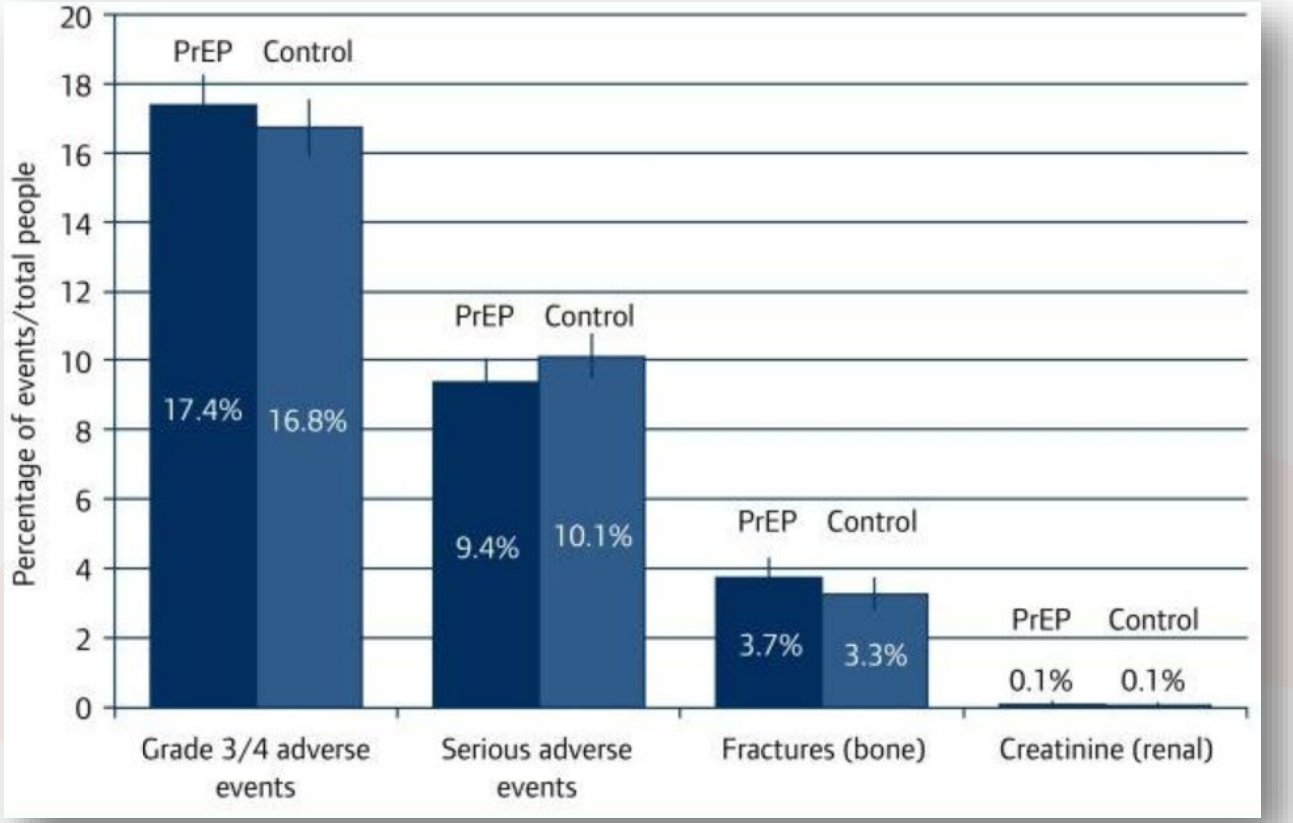
*guidelines have not been finalized since new TAF/FTC PrEP indication

Summary of TDF and TAF considerations

- TDF:
  - Generally safe, and studied in all approved PrEP populations
  - Not associated with weight gain
    - In the DISCOVER study, there was more weight gain, although overall small, among participants who had received emtricitabine and tenofovir alafenamide (median weight gain 1·7 kg vs 0·5 kg, p<0·0001)
- TAF:
  - Could consider in male patients with an already reduced eGFR, possibly in patients with reduced BMD whom further reduction could lead to osteoporosis

PrEP Safety Compared to Placebo

- In meta-analysis of 13 RCTs of 15,678 participants of PrEP with TDF/FTC
- PrEP is safe
- No significant differences
  - Bone fractures
  - Grade 3/4 ADEs
  - Serious ADEs



Pilkington et al. J Virus Erad. 2018 Oct; 4(4): 215–224.

Counsel Patient on Side Effects

- Headache, nausea, flatulence “start-up syndrome”
  - Can use over the counter medications to manage (ie. simethicone, APAP, ibuprofen)
- Other side effects were uncommon in PrEP trials
  - ***The above SEs often resolved in first month***
- Counsel patients about symptoms indicating need for urgent evaluation
  - Acute renal injury, acute HIV infection

Summary of Oral PrEP

- Oral PrEP with either TDF/FTC or TAF/FTC are currently available and effective at preventing HIV infection when taken daily
- Current oral options are safe with very few side effects
- PrEP must be covered by insurance
  - The US Preventive Services Task Force (USPSTF) gave PrEP an “A” recommendation, placing it on the list of preventive services that health plans must cover at no cost to the patient.
- PrEP medications only protect against HIV, so condoms are still important to prevent other sexually transmitted infections

INJECTABLE PrEP with Cabotegravir: Currently under FDA review for approval

Cabotegravir

- Cabotegravir (CAB) is an integrase strand transfer inhibitor (INSTI), it is formulated as a long-acting injectable nanosuspension
  - Second generation INSTI, similar to dolutegravir and bictegravir with a higher barrier for resistance compared to first generation INSTIs
- Generally well tolerated
  - Common SEs noted were injection site reactions(ISRs)
    - Most participants continued with injections despite the temporary ISRs
  - No renal adjustments or kidney function monitoring necessary

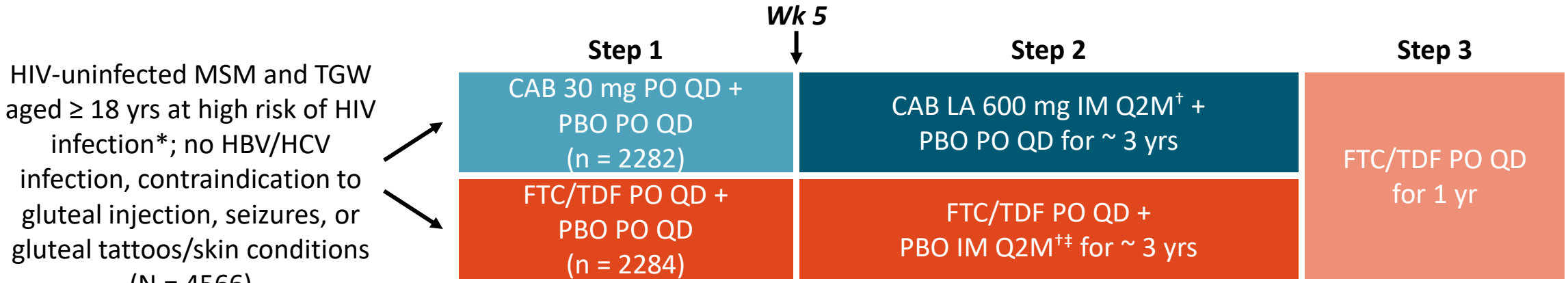
1. Thornhill and Orkin. Curr Opin Infect Dis. 2021 Feb 1;34(1):8-15. doi: 10.1097/QCO.0000000000000701 2. Diana Canetti & Vincenzo Spagnuolo (2021) An evaluation of cabotegravir for HIV treatment and prevention, Expert Opinion on Pharmacotherapy, 22:4, 403-414, DOI: 10.1080/14656566.2020.1843635

HPTN Study 083 and 084

- HPTN 083 (CAB for PrEP in cisgender men and transgender women who have sex with men) published
- HPTN 084 (CAB for PrEP in women) peer reviewed results pending
  - Link for more information: https://www.hptn.org/research/studies/hptn084
- These studies are investigating the use of long-acting injectable cabotegravir (CAB LA) vs. daily oral Truvada (TDF/FTC)
  - Cabotegravir was administered daily by mouth for 5 weeks and then via intramuscular injection at 8-week intervals after an initial 4-week interval load

HPTN 083: Study Design

- International, randomized, double-blind phase IIb/III study
  - At interim analysis on May 14, 2020, with 25% of endpoints accrued, DSMB recommended termination of blinded study due to crossing of prespecified O'Brien-Fleming stopping bound



*Any noncondom receptive anal intercourse, > 5 partners, stimulant drug use, incident rectal or urethral STI or incident syphilis in past 6 mos; or SexPro Score ≤ 16 (US only). †First 2 doses given in Wks 5 and 9, then every 2 mos thereafter. ‡PBO for CAB injection was a 20% intralipid solution.

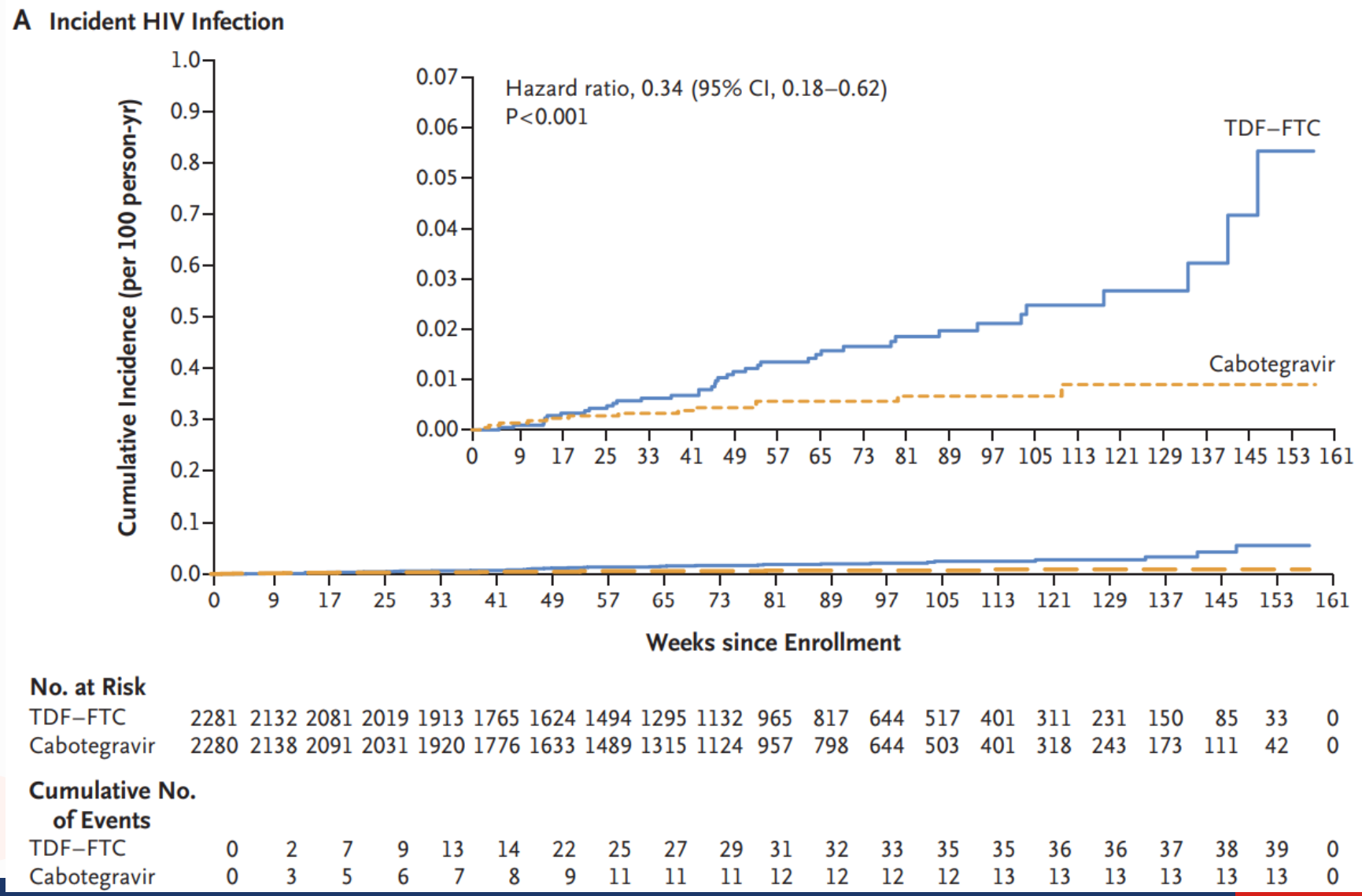
- Primary endpoints: incident HIV infections, grade ≥ 2 clinical and laboratory events
- Analysis of HIV infections in CAB arm: group A) HIV positive test at study enrollment; group B) no recent CAB exposure; group C) Infected during CAB oral lead-in period; group D) Infected in setting of on-time CAB injections

Marzinke. CROI 2021. Landovitz. AIDS 2020. Abstr OAXLB0101. Abstr 153. NCT02720094.

Slide credit: clinicaloptions.com

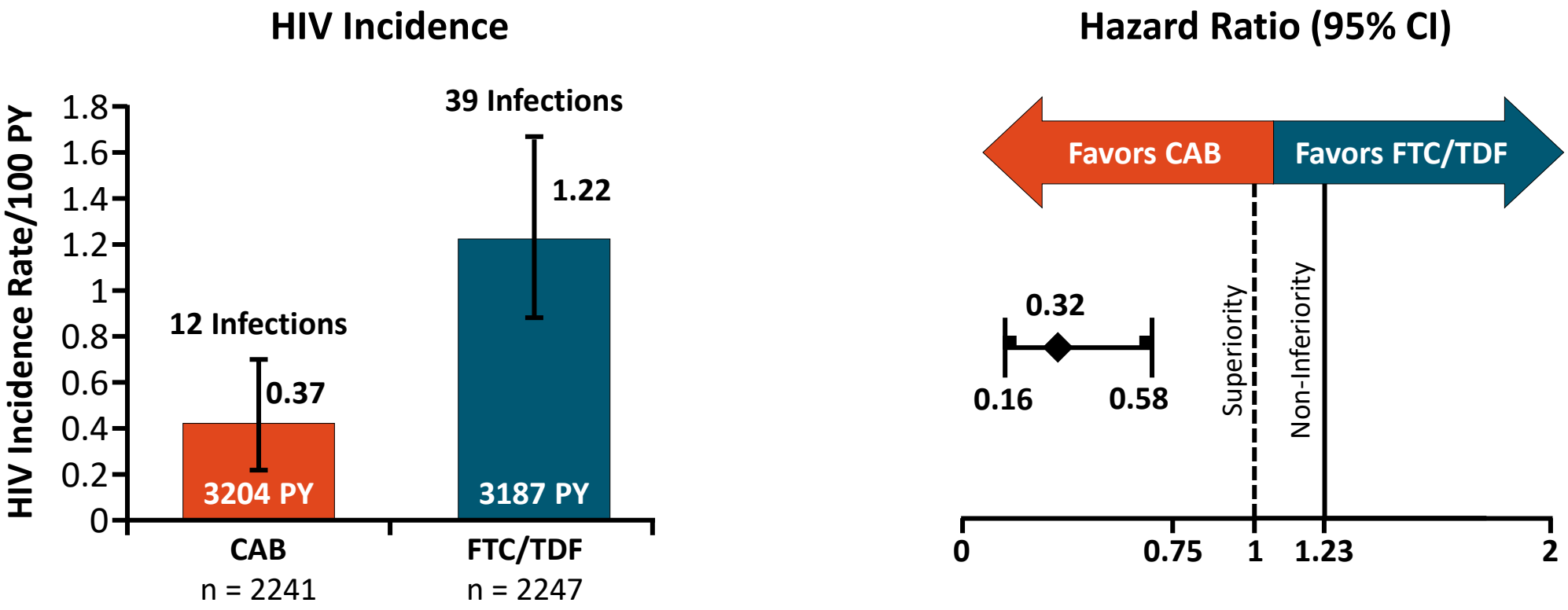
HPTN 083

- This trial showed that CAB-LA was superior to TDF–FTC in preventing HIV acquisition among MSM and transgender women who have sex with men
- 13 infections CAB
  - 1 of these re-adjudicated as a baseline infection
- 39 infections TDF/F



Landovitz et al. Cabotegravir for HIV Prevention in Cisgender Men and Transgender Women. N Engl J Med 2021;385:595-608. DOI: 10.1056/NEJMoa2101016

HPTN 083: HIV Incidence



Marzinke. CROI 2021. Abstr 153. Reproduced with permission.

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HPTN 083: Findings

- Of 12 incident HIV infections in CAB arm, 4 observed in participants with on-time injections and sufficient CAB concentrations
- Detection of HIV infection using standard testing algorithms delayed in patients receiving CAB LA
- INSTI resistance
  - Observed upon viremic “escape” at higher CAB concentrations
  - Not observed in 3 tail-phase infections or 1 tail “escape” case
- Therefore, prompt diagnosis and initiation of ART are important to avoid resistance with CAB LA
- Suboptimal adherence observed in 37/39 incident infections in FTC/TDF arm

Marzinke. CROI 2021. Abstr 153.

Slide credit: clinicaloptions.com

Press Release

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HIV Prevention Trials Network

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HPTN 084 Study Demonstrates Superiority of Injectable Cabotegravir to Oral FTC/TDF for the Prevention of HIV in Cisgender Women in Sub-Saharan Africa

Nov 9, 2020

Both cabotegravir and oral FTC/TDF have high efficacy for PrEP

Researchers from the HIV Prevention Trials Network (HPTN) announced today the HPTN 084 clinical trial data indicating that a pre-exposure prophylaxis (PrEP) regimen of long-acting cabotegravir (CAB LA) injections once every eight weeks was **safe and superior** to daily oral tenofovir/emtricitabine (TDF/FTC) for HIV prevention among cisgender women in sub-Saharan Africa. During a planned review of study data, an independent Data and Safety Monitoring Board (DSMB) recommended the study sponsor—the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health—stop the blinded phase of the trial and share the results. The study was originally designed to continue through 2022.

https://www.hptn.org/news-and-events/announcements/hptn-084-study-demonstrates-superiority-of-injectable-cabotegravir-to

PrEP Medications: What's in the pipeline?

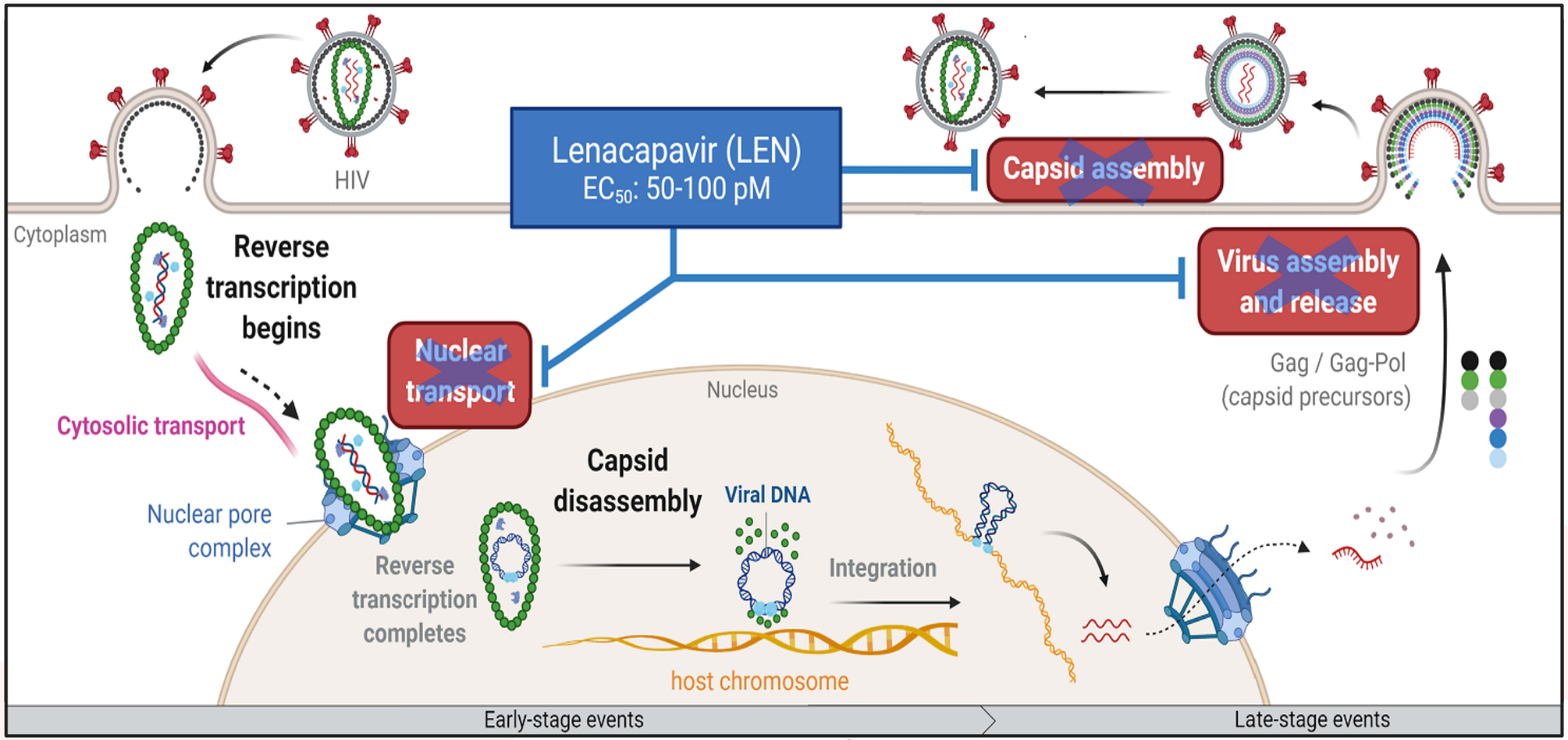
Lenacapavir

- Capsid inhibitor, unique mechanism of action
- Current investigations for use for PrEP are as a 6 month subcutaneous injection
- Also being studied for treatment for HIV as part of a combination regimen

Lenacapavir Targets Multiple Stages of the HIV Replication Cycle

LEN binding directly between capsid protein subunits and inhibits 3 essential steps of the viral lifecycle:

1. Capsid-mediated nuclear uptake of HIV proviral DNA
2. Virus assembly and release
3. Capsid core formation



Lenacapavir modulates the stability and/or transport of capsid complexes, leading to inhibition of multiple processes in the HIV lifecycle

Figure generated based on the following references: Link J, et al. Nature 2020;584:614-618; Bester SM, et al. Science 2020;370:360-364; Cihlar T. vCROI 2021. Oral #22; Muller B. vCROI 2021. Oral #19; Pathak VK. vCROI 2021. Oral #20; Ganser-Pornillos B. vCROI 2021. Oral #21

Islatravir

- Unique mechanism of action, Novel reverse transcriptase translocation inhibitor (NRTTI)
- Current investigations for use for PrEP as a once weekly oral dose OR yearly transdermal implant
  - Implant uses similar technology used for marketed implantable contraceptives, which is based on a drug-eluting polymeric matrix for potential once yearly implant

Martin Markowitz and Jay A Grobler. Curr Opin HIV AIDS. 2020 Jan;15(1):27-32. doi: 10.1097/COH.0000000000000599.

Summary

- There are currently two oral medications available for PrEP
  - TAF/FTC and TDF/FTC
- New injectable PrEP, such as CAB may be approved soon by the FDA and add an additional option
- PrEP is effective and a safe option for preventing HIV infections

References

- Centers for Disease Control and Prevention: US Public Health Service: Preexposure prophylaxis for the prevention of HIV infection in the United States—2017 Update: a clinical practice guideline. https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2017.pdf. Published March 2018.
- Mulligan K, Glidden DV, Anderson PL, et al. Effects of emtricitabine/tenofovir on bone mineral density in HIV-negative persons in a randomized, double-blind, placebo-controlled trial. Clin Infect Dis. 2015;61:572-580.
- Choopanya K, et al. Antiretroviral prophylaxis for HIV infection in injecting drug users in Bangkok, Thailand (the Bangkok Tenofovir Study): a randomised, double-blind, placebo-controlled phase 3 trial. Lancet. 2013;381:2083-2090
- Mayer KH, Chan PA, R Patel R, Flash CA , and Krakower DS. J Acquir Immune Defic Syndr. 2018 February 01; 77(2): 119–127. doi:10.1097/QAI.0000000000001579.
- Holec et al. Nucleotide Reverse Transcriptase Inhibitors: A Thorough Review, Present Status and Future Perspective as HIV Therapeutics. Curr HIV Res. 2017 ; 15(6): 411–421.
- Ogbuagu O, Ruane PJ, Podzamczer D, et al. Long-term safety and efficacy of emtricitabine and tenofovir alafenamide vs emtricitabine and tenofovir disoproxil fumarate for HIV-1 pre-exposure prophylaxis: week 96 results from a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet HIV 2021; 8: 397–407
- Pilkington et al. J Virus Erad. 2018 Oct; 4(4): 215–224.
- Martin Markowitz and Jay A Grobler. Curr Opin HIV AIDS. 2020 Jan;15(1):27-32. doi: 10.1097/COH.0000000000000599
- John Thornhill and Chloe Orkina. Curr Opin Infect Dis. 2021 Feb 1;34(1):8-15. doi: 10.1097/QCO.0000000000000701