National HIV Curriculum

HIV and STIs in 2023

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AETC AIDS Education & Training Center Program

Disclosures

None

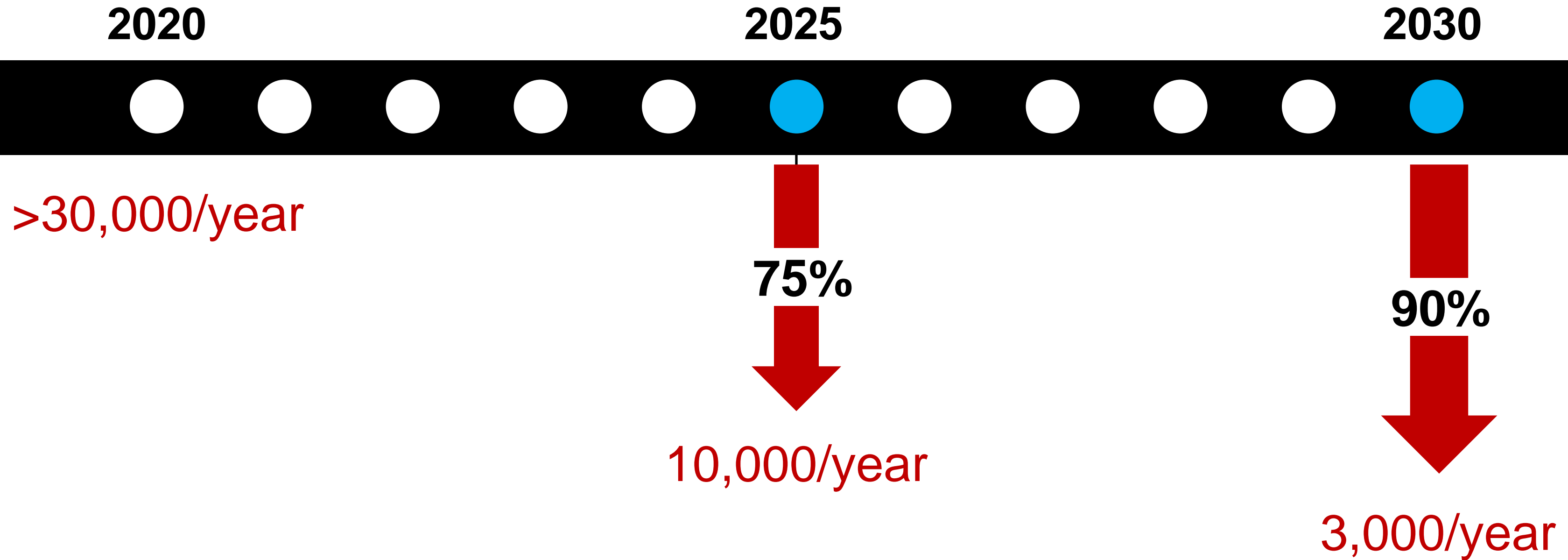
Objectives

- Review approach to HIV prevention with pre-exposure prophylaxis (PrEP)
- Review approaches to and updates in HIV treatment
- Rapid fire updates in STI

HIV: Prevention

Ending HIV Epidemic Initiative

Goals for Reducing Annual Number of New HIV Infection in U.S.



What is PrEP?

Preexposure prophylaxis (PrEP): a prevention strategy in which a person without HIV who is at risk for HIV exposures takes a medication regularly to prevent acquiring HIV.

Three Medications are FDA Approved for PrEP

1. Daily oral Tenofovir DF-emtricitabine (*Truvada*®) approved 7/2012
2. Daily oral Tenofovir alafenamide-emtricitabine (*Descovy*®) approved 10/2019 but NOT for persons having receptive vaginal intercourse
3. Injectable Cabotegravir (*Apretude*®) every 2 months approved 12/2021

Estimated Number of Persons with Need for HIV PrEP in United States

Need for PrEP

1,216,201

Source: CDC. HIV Surveillance Supplemental Report. 2021;26(No. 1). May 2021

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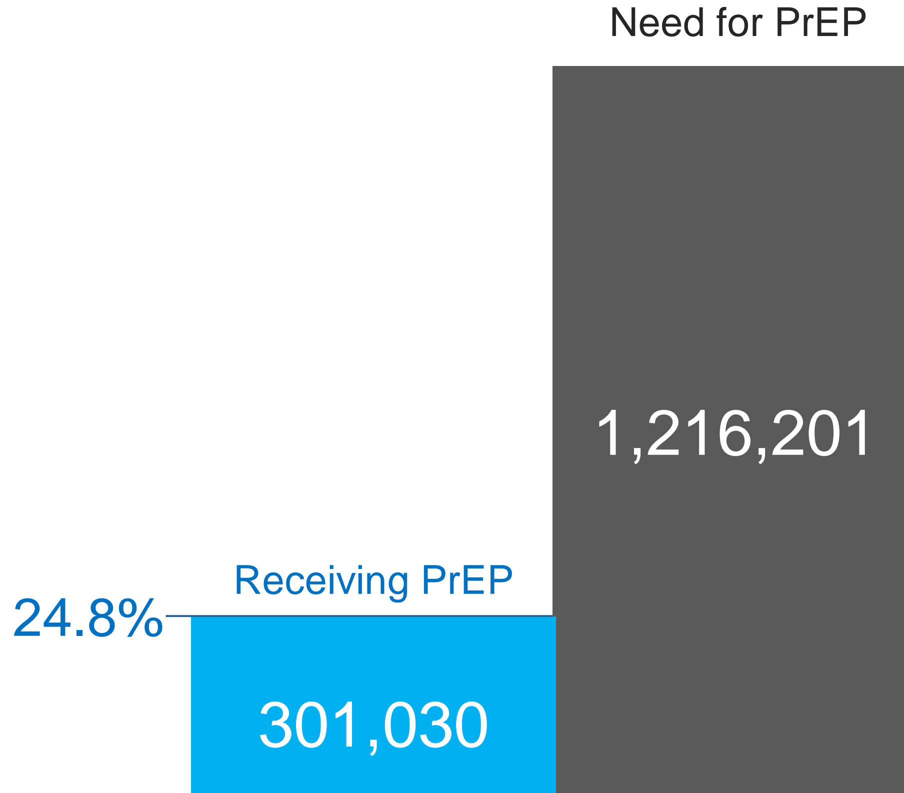
Proportion of Persons Receiving PrEP versus Need for PrEP



Inequities in Distribution:

- Race/Ethnicity
- Region
- Gender

Source: CDC. HIV Surveillance Supplemental Report. 2021;26(No. 1). May 2021

CDC Indications for PrEP

	HIV+ Partner	Recent Bacterial STI	Multiple Sex Partners	Sex Without Condoms	Exchange Sex	Sharing injection equipment
MSM	√	√	√	√	√	
Heterosexual M/W	√	√	√	√	√	
PWID*	√	√	√	√	√	√

*PWID = person with injection drug use

Anyone at risk for HIV

CDC 2017 Update Clinical Practice Guideline – PrEP for the Prevention of HIV in the US.

Counsel about PrEP

- Oral PrEP
  - Daily *Truvada*® (TDF/FTC 300mg/200mg) or *Descovy*® (TAF 25mg/FTC 200mg)
  - Side effects[1]
    - GI: Possible stomach upset initially, “start up syndrome”
    - Renal: CrCl can decrease slightly, by an average of 2.5% over 18 months[1]
    - Bone: Bone density can decrease by a small amount, but stabilizes and is reversible with discontinuation; no direct increased risk of fracture
- Injectable PrEP[2]
  - IM Cabotegravir (CAB 600mg IM q 2 months)
    - Optional 30mg oral cabotegravir lead-in prior to injection
  - Side effects
    - Injection site reactions common
      - Take OTC pain meds as needed for 1-2 days, apply warm compress to injection site for 15-20 minutes

1-Gandhi, CROI 2016 – Abstract 866. 2-CDC 2021 Update Clinical Practice Guideline – PrEP for the Prevention of HIV Infection in the US.

Comorbidities and PrEP

- Renal
  - TDF/FTC (*Truvada*®) is contraindicated with CrCl ≤ 60
  - TAF/FTC (*Descovy*®) is contraindicated with CrCl ≤ 30
  - Consider CAB for patients with significant renal disease in whom tenofovir-containing regimens are not recommended
- Bone
  - If high risk for osteoporosis, consider bone scan and consultation with bone health specialist prior to TDF or TAF use; TAF is more bone friendly than TDF
- If contraindications to TDF or TAF use, then use CAB
- If contraindications to CAB, do not prescribe PrEP

Krakower, OFID 2017

Indications and Recommended Use of HIV PrEP Medications

Indication	TDF-FTC	TAF-FTC	Cabotegravir
Cisgender men (who have sex with men)	✓	✓	✓
Transgender women (who have sex with men)	✓	✓	✓
Cisgender women (who have sex with men)	✓		✓
Cisgender men (who have sex with women)	✓	✓	✓
Persons who inject drugs	✓ (not FDA indicated)		
Persons who take "on demand" PrEP	✓ (not FDA indicated)		
Adolescents weighing ≥35 kg	✓	✓ (not cisgender women)	✓
Persons with CrCl 30-60 mL/min		✓	✓
Persons with CrCl 15-29 mL/min			✓ (increased monitoring)
ESRD with CrCl <15 mL/min (not on dialysis)			✓ (increased monitoring)
ESRD with CrCl <15 mL/min (on dialysis)		✓ (give after dialysis)	✓

Baseline Laboratory Studies in Persons Starting HIV PrEP

Recommended Routine Baseline Laboratory Studies Prior to Starting HIV PrEP			
Test	TDF-FTC	TAF-FTC	Cabotegravir
HIV-1/2 antigen-antibody immunoassay	✓	✓	✓
HIV-1 RNA assay			✓
Renal function (eCrCl)	✓	✓	
Lipid panel		✓	
Hepatitis B serology	✓	✓	
Hepatitis C serology	✓	✓	✓
STI Testing (syphilis, GC, CT)	✓	✓	✓

Source: CDC 2021 PrEP Clinical Practice Guideline. December 2021:1-108

Follow-Up Labs in Persons on Oral PrEP

- HIV testing (HIV Ag/Ab and HIV RNA[1]) every 3 months
- Serum creatinine q 12 months (every 6 months if age >50 or CrCL<90)
- HCV testing (if PWID, MSM, or TGW) every 12 months
- Lipid panel (if on TAF-FTC) every 12 months
- Screening for bacterial STIs (CT, GC, syphilis) every 3 months*

[1]Every 6 months if for all other sexually active persons

Follow-Up Labs in Persons on Cabotegravir

- HIV testing (HIV Ag/Ab and HIV RNA) every 2 months
- HCV testing (if PWID, MSM, or TGW) every 12 months
- Screening for bacterial STIs (CT, GC, syphilis) every 4 months

Undetectable = Untransmittable

- An individual with an undetectable HIV VL cannot transmit HIV to their sexual partners

STUDY	FINDINGS
HPTN-052	96% reduction in infections among heterosexual couples when the HIV+ partner started ART[1]
PARTNER-1	Of 58K condomless sex acts in 888 serodiscordant couples (40% gay M couples, HIV+ partner with UD VL), no new HIV infections phylogenetically linked[2]
PARTNER-2	972 serodiscordant gay M couples had 76K condomless sex acts, no HIV infections phylogenetically linked[3]

1-Cohen NEJM 2016, 2-Rodger JAMA 2016, 3-Rodger Lancet 2019

HIV Infection While Taking PreP

- Seroconversion in about 3% of persons taking PrEP
- Most PrEP “failures” attributed to poor adherence
- Some PrEP “failures” from undiagnosed HIV prior to starting PrEP
- Rare cases of transmitted resistant strain of HIV

Source: Ambrosioni J, et al. Lancet HIV 2021; 8:e166–e174

What to do if PrEP failure from any cause?

- Repeat HIV Ag/Ab, HIV RNA, and genotype
- **Contact the CCC PrEP line 855-448-7737**
- Start ART immediately if failure while on oral PrEP
- Access the PrEP guidelines as a resource

CDC 2021 Update Clinical Practice Guideline – PrEP for the Prevention of HIV Infection in the US.

What to Start: Recommended Initial Regimens

No Prior Cabotegravir

Order Standard Genotype

INSTI-Based Regimen

Prior Cabotegravir

Order Standard **and** Integrase Genotype

Pending genotype
Boosted-Darunavir + 2NRTIs (TDF/TAF + FTC/3TC)

After genotype if no integrase resistance
OK to Switch to INSTI-Based Regimen

Source: HHS Guidelines for Use of Antiretroviral Agents in Adults and Adolescents with HIV. Sept 21, 2022.

On-Demand (2-1-1) PrEP for Men at High Risk for HIV

Antiretroviral Medication

HIV Exposure Event

Time

24 hours

24 hours

2 tabs 2-24 hours before sex

1 tab 24 hours after pre-sex dose

1 tab 48 hours after pre-sex dose

On-Demand PrEP for Men at High Risk for HIV

Antiretroviral Medication

Initial
HIV Exposure

Ongoing
HIV Exposures

Time

2 tabs 2-24 hours before sex (or 1 pill if most recent dose taken <7 days prior)

1 tab 24 and 48 hours after the last pre-sex dose

If sexual activity continues, then PrEP continues daily until 48 hours after last sex
*Otherwise, same process repeated with next exposure event

Resources

- 2021 CDC PrEP Guidelines
- National Clinician Consultation Center PrEP Warmline 855-448-7737
- USPSTF PrEP Evidence Summary

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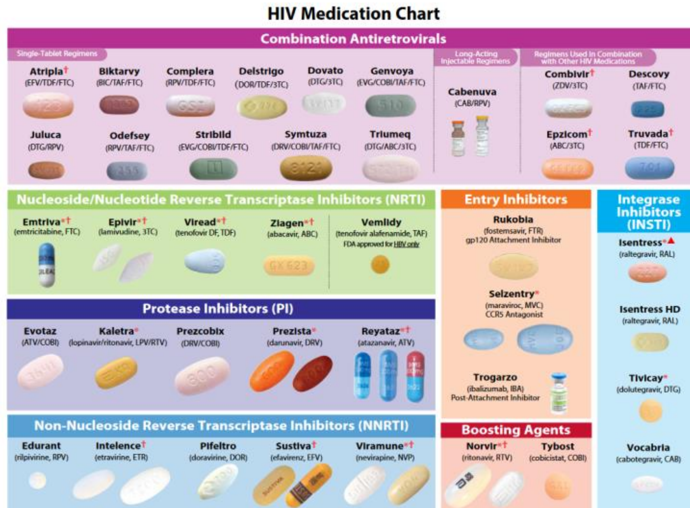
HIV: Treatment

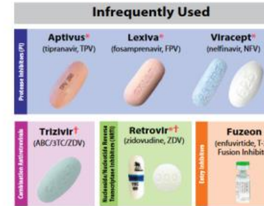
HIV treatment has come a long way!

ART Then…

ART Now…

HIV Treatment in 2023





Helpful Hints:

- Refill prescriptions before you run out. Call for refills when you have at least 3 or 4 days left.
- Use cues as a reminder to take your pills (after a meal or favorite TV show, or before bedtime).
- Use reminder aids such as phone alarms and pillboxes. Ask your pharmacist about these.
- Plan ahead (vacations, travel, count out weekly doses).
- Do not stop taking your medications until you have spoken with your health care provider or pharmacist.
- If you have a severe reaction or in case of emergency, contact your health care provider IMMEDIATELY.

Contact Information: Provider____________________

Clinic Phone____________ Pharmacy____________ Phone____________

Colorado AIDS Education & Training Center
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Reviewer: Jasjit Gill, PharmD, University of Colorado

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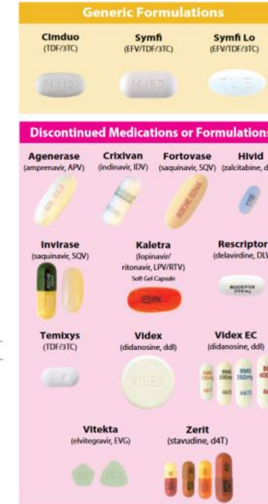

- Antiretroviral therapy (ART) is recommended for all persons with HIV to reduce morbidity and mortality **(AI)** and to prevent the transmission of HIV to others **(AI)**.

https://aidsetc.org/resource/hiv-medication-chart-pad
Source: HHS Antiretroviral Therapy Guidelines. AIDS Info. December 18, 2019

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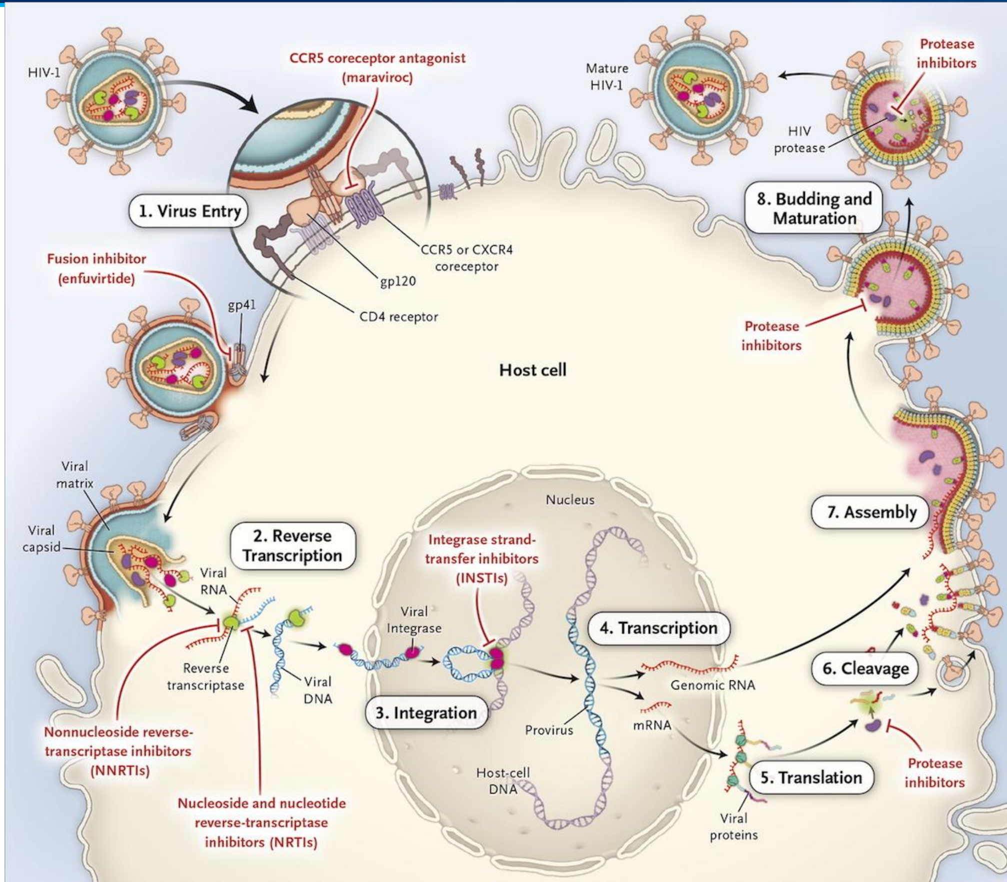
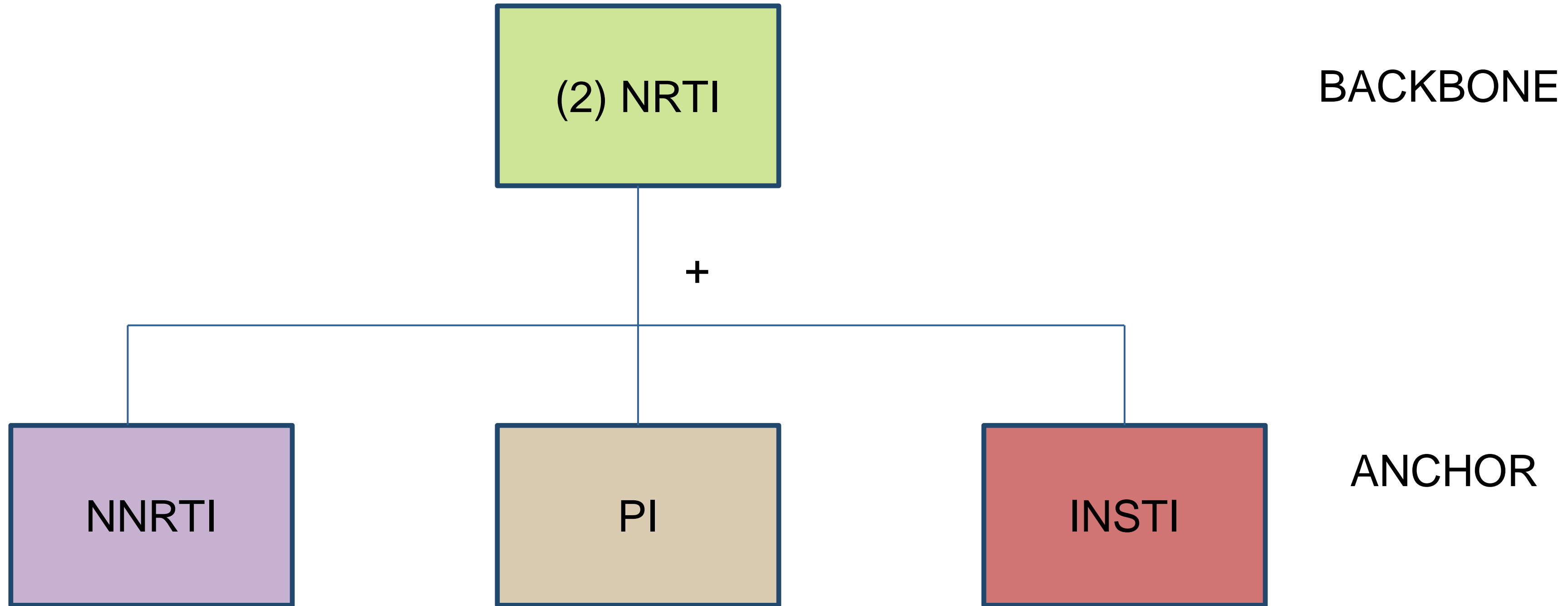
HIV Life Cycle and Drug Targets

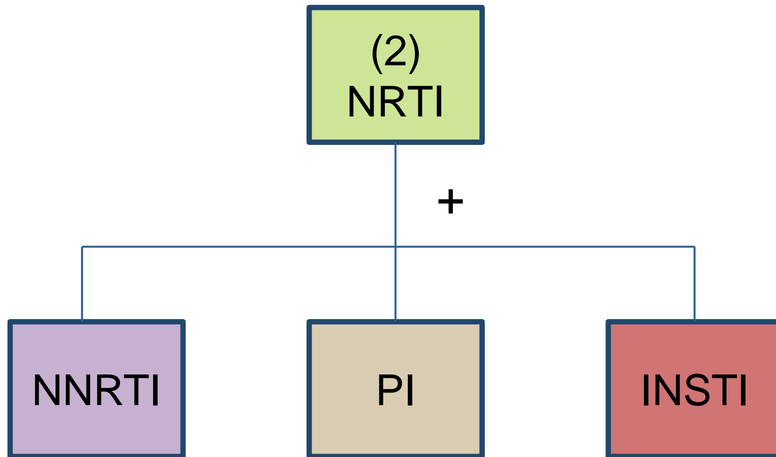


- *Entry/Attachment/Fusion Inhibitors*
- Reverse Transcriptase Inhibitors (RT)
  - NRTIs
  - NNRTIs
- Integrase Strand Nuclear Transfer Inhibitors (INSTI)
- Protease Inhibitors (PI)

Building a Regimen



Building a Regimen



Principles of Choice:

- Potency
- Barrier to Resistance
- Tolerability/side effects
- CD4/HIV RNA levels
- Formulation (STR, MTR, injectable)
- Dose Frequency
- Prior resistance/treatment experience
- Cost (unfortunately)

HHS Antiretroviral Therapy Guidelines: September 21, 2022
What to Start: Recommended Initial Regimens for Most People with HIV

No Prior Injectable Cabotegravir for HIV PrEP

Anchor Drug		Backbone
INSTI	+	2 NRTIs *OR* 1 NRTI

Source: HHS Guidelines for Use of Antiretroviral Agents in Adults and Adolescents with HIV. Sept 21, 2022.

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HHS Antiretroviral Therapy Guidelines: September 21, 2022
What to Start: Recommended Initial Regimens for Most People with HIV

No History of Taking Injectable Cabotegravir for HIV PrEP	
INSTI + 2NRTIs	**Abbreviation**
Bictegravir-tenofovir alafenamide-emtricitabine	BIC-TAF-FTC
Dolutegravir-abacavir-lamivudine (if HLA-B*5701 negative and no HBV)	DTG-ABC-3TC
Dolutegravir + Tenofovir alafenamide-emtricitabine	DTG + TAF-FTC
Dolutegravir + [Tenofovir DF-emtricitabine *or* Tenofovir DF-lamivudine]	DTG + [TDF-FTC *or* TDF-3TC]
INSTI + 1NRTI	**Abbreviation**
Dolutegravir-lamivudine (except: HIV >500,000 copies/mL, HBV, no genotype)	DTG-3TC

Source: HHS Guidelines for Use of Antiretroviral Agents in Adults and Adolescents with HIV. Sept 21, 2022.

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Two Drug Regimens (2DR)

- DTG/3TC- Dolutegravir + Lamivudine- (*Dovato*)
  - VL < 500k
  - No chronic HBV
  - Need RT/PI genotype

- DTG/RPV- Dolutegravir + Rilpivirine (*Juluca*)
  - Need to be virally suppressed
  - No chronic HBV
  - Need RT/PI genotype

- CAB/RPV- Cabotegravir + Rilpivirine (*Cabenuva*)
  - Need to be virally suppressed (for now)
  - No chronic HBV
  - Need RT and INSTI GT

Cabotegravir and Rilpivirine Indications

- First extended, injectable complete ART regimen in the US for HIV-1
- A “switch” regimen for adult PWH with HIV RNA <50 copies/mL for at least 3 months on a stable ARV regimen
  - Not yet recommended as an initial regimen
  - No history of treatment failure
  - No suspected or known resistance to cabotegravir or rilpivirine
- No active HBV infection (unless also on HBV treatment)
- Not pregnant or planning to become pregnant
- Not on medications with significant drug interactions with either agent

Source: Cabotegravir-Rilpivirine Prescribing Information

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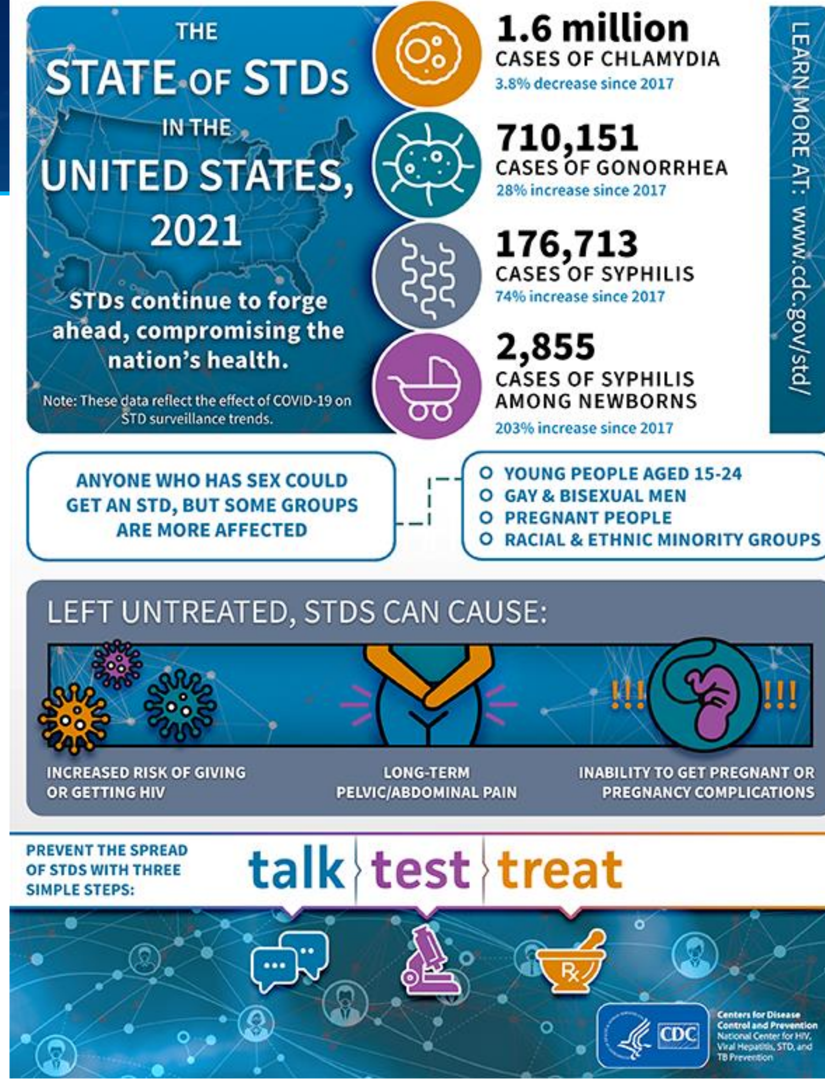
STI Updates

Epidemiology

- Chlamydia (CT), Gonorrhea (GC), and syphilis cases continue to increase
  - Disproportionate effect on: adolescents and young people; gay, bisexual, and other MSM; pregnant people; some racial/ethnic minority groups
- Concomitant substance use
  - Young adults using substances in the past year 3x more likely to get STI



CDC Sexually Transmitted Disease Surveillance 2021

Chlamydia

- Most common STI in US
- Impact: on women, untreated genital CT → PID, pelvic pain, infertility
- Syndromes: trachoma, anogenital infection, LGV, conjunctivitis
- Diagnosis: Nucleic Acid Amplification tests (NAAT)
- Screening: varies by group
- What's new?
  - Not much

Table 1. 2021 STI Treatment Guidelines: Chlamydial Infections

Treatment of Chlamydial Infections Among Adolescents and Adults

Recommended Regimen

Doxycycline
100 mg orally twice a day for 7 days

Alternative Regimens

Azithromycin
1 g orally in a single dose

or

Levofloxacin
500 mg orally once daily for 7 days

*LGV: doxycycline 100 mg BID x 21 days

National STD Curriculum; 2021 STI Guidelines

Gonorrhea

- Second most common STI in United States
- Syndromes: urogenital, pharyngeal, and rectal infections; conjunctivitis; PID and infertility; disseminated gonococcal infection (DGI)
- Diagnosis: Nucleic Acid Amplification tests (NAAT)
- Screening: varies by group
- What's new?
  - Concerns re: antimicrobial resistance
  - Rising MICs to azithromycin, cefixime, tetracyclines, even ceftriaxone

Gonorrhea

Table 1. 2021 STI Treatment Guidelines: Gonococcal Infections

Treatment of Uncomplicated Gonococcal Infection of the Cervix, Urethra, or Rectum

HIDE

Recommended Regimen if Chlamydial Infection Excluded

Ceftriaxone
500 mg* IM in a single dose for persons weighing <150 kg

Note: *For persons weighing ≥150 kg, ceftriaxone 1 g IM should be administered.

Recommended Regimen if Chlamydial Infection Has Not Been Excluded

Ceftriaxone
500 mg* IM in a single dose for persons weighing <150 kg

\+ **Doxycycline**
100 mg orally twice daily for 7 days

During pregnancy, oral azithromycin 1 gram in a single dose is recommended to treat chlamydia.

Note: *For persons weighing ≥150 kg, ceftriaxone 1 g IM should be administered.

Alternative Regimen if Ceftriaxone is Not Available

Gentamicin
240 mg IM in a single dose

\+ **Azithromycin**
2 g orally in a single dose

or

Cefixime
800 mg orally in a single dose

Note: If treating with cefixime, and chlamydial infection has not been excluded, providers should treat for chlamydia with doxycycline 100 mg orally twice daily for 7 days. During pregnancy, oral azithromycin 1 g in a single dose is recommended to treat chlamydia.

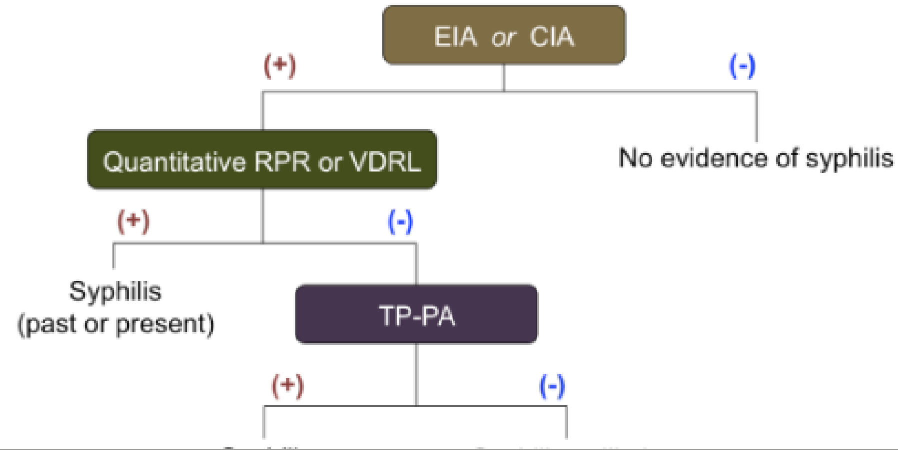
CHANGES in 2021 Guidelines:

- Uncomplicated GC infection of cervix, urethra or rectum: IM ceftriaxone 500 mg (previously 250 mg)
- No need for azithromycin dual therapy if CT has been excluded
- If CT has not been excluded: add doxycycline (not azithromycin)
- For pharyngeal gonorrhea: test of cure 1-2 weeks

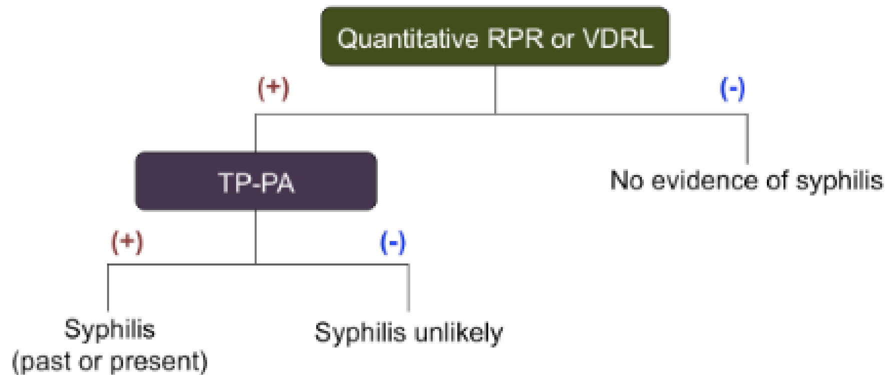
2021 CDC STI Treatment Guidelines

Syphilis

- Rising rates in recent years in the US
- Impact: chronic infection, congenital disease
- Syndromes: primary syphilis, secondary syphilis (rash, lymphadenopathy, systemic symptoms, condyloma lata, alopecia, visceral disease, early neurosyphilis), latent syphilis, tertiary syphilis (cardiovascular, late neurosyphilis such as general paresis, tabes dorsalis, psychiatric manifestations)
- Diagnosis: direct detection via microscopy, fluorescent Ab test; serologic testing with treponemal and non treponemal testing



Reverse Sequence Algorithm (top); Traditional Screening Algorithm (bottom)



Syphilis

Table 5. 2021 STI Treatment Guidelines: Syphilis

Treatment of Neurosyphilis, Ocular Syphilis, or Otosyphilis Among Adults

HIDE

Recommended Regimen

Aqueous crystalline penicillin G
18–24 million units per day, administered as 3–4 million units IV every 4 hours or continuous infusion, for 10–14 days

Alternative Regimen

Procaine penicillin G
2.4 million units IM once daily for 10-14 days

+

Probenecid
500 mg orally four times a day for 10–14 days

Note: If compliance with therapy can be ensured, this alternative regimen might be considered.

Table 2. 2021 STI Treatment Guidelines: Syphilis

Treatment of Primary and Secondary Syphilis Among Adults*

HIDE

*Recommendations for treating syphilis among persons with HIV infection and pregnant women are not addressed in this table.

Recommended Regimen

Benzathine penicillin G
2.4 million units IM in a single dose

Table 3. 2021 STI Treatment Guidelines: Syphilis

Treatment of Latent Syphilis Among Adults*

HIDE

*Recommendations for treating syphilis in persons with HIV and pregnant women are not addressed in this table.

Recommended Regimen for Early Latent Syphilis

Benzathine penicillin G
2.4 million units IM in a single dose

Note: Available data demonstrate that additional doses of benzathine penicillin G, amoxicillin, or other antibiotics in early latent syphilis do not enhance efficacy, regardless of HIV status.

Recommended Regimen for Late Latent Syphilis

Benzathine penicillin G
7.2 million units total, administered as 3 doses of 2.4 million units IM each at 1-week intervals

Syphilis: What's New

- Penicillin shortages: Bicillin (benzathine)
- Procaine penicillin no longer being manufactured as of mid 2023
- Now what?
  - Doxycycline:
    - 100 mg BID x 14 days for early syphilis
    - 100 mg BID x 28 days for latent syphilis
  - Preserve penicillin for those whom penicillin is the only option (pregnant people, allergies to doxycycline)

Congenital Syphilis

- *T. pallidum* transmission from pregnant person with syphilis to fetus
  - Risk highest with primary or secondary syphilis
- In 2021, cases of congenital **syphilis increased by 32%** and resulted in 220 stillbirths and infant deaths
- Early congenital syphilis: rhinitis/nasal discharge, hepatosplenomegaly, jaundice, bone involvement, rash, ophthalmic disorders, lymphadenopathy, hematologic abnormalities, neurologic
- Late congenital syphilis: facial changes (saddle deformity of nose), abnormal tooth development, bony abnormalities, ophthalmic disorders, deafness

****All pregnant persons diagnosed with syphilis should be treated with penicillin (formulation based on stage)- those with allergy need to be desensitized**

Questions?

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