Ending the STI Epidemic Through Prevention

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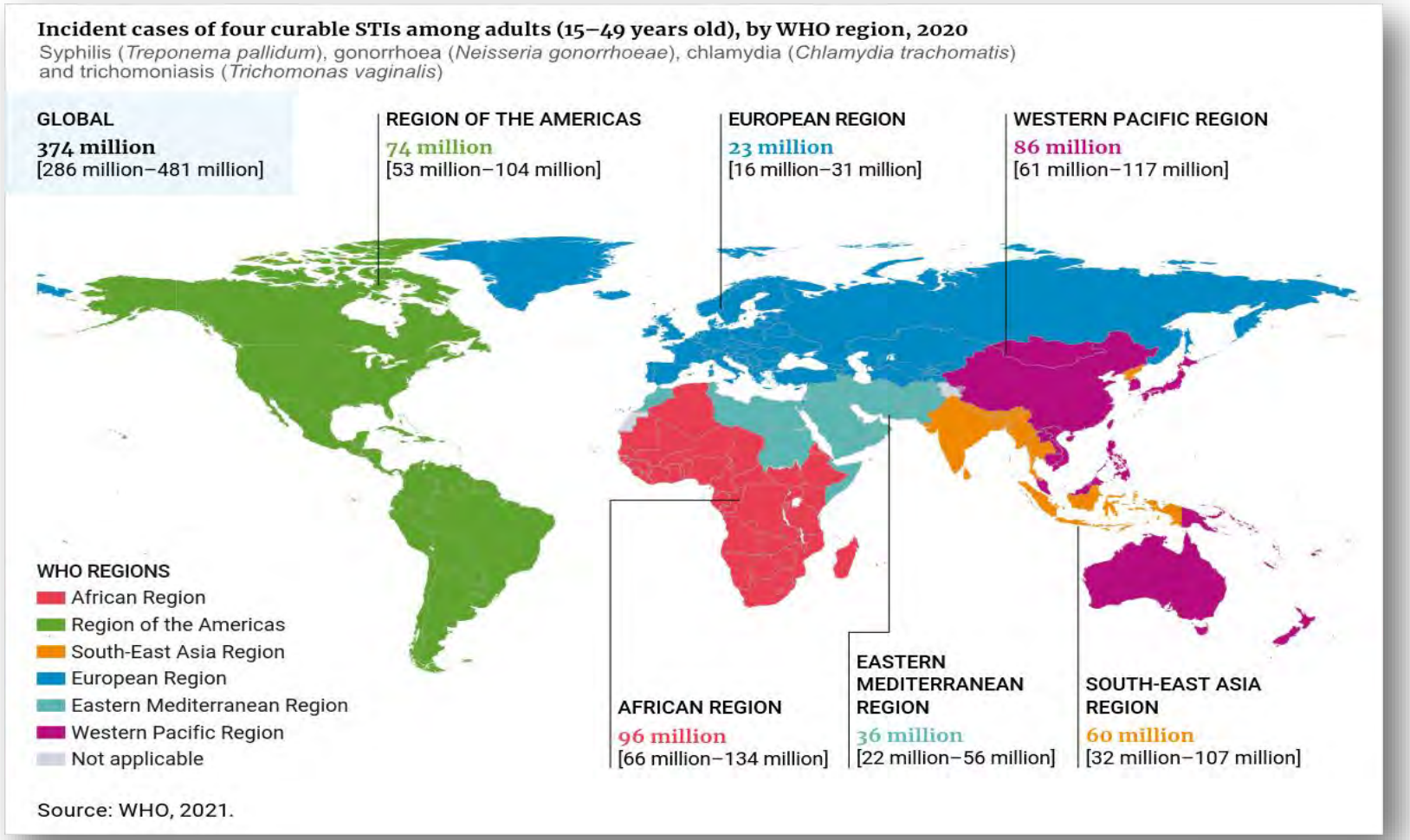
Objectives

1. Review the state of the STI Epidemic
2. Summarize the current landscape of STI prevention options
3. Appraise new methods for STI prevention like Doxy-PEP
4. Discuss implementation of Doxy-PEP

STIs Represent A Worsening Epidemic – Worldwide



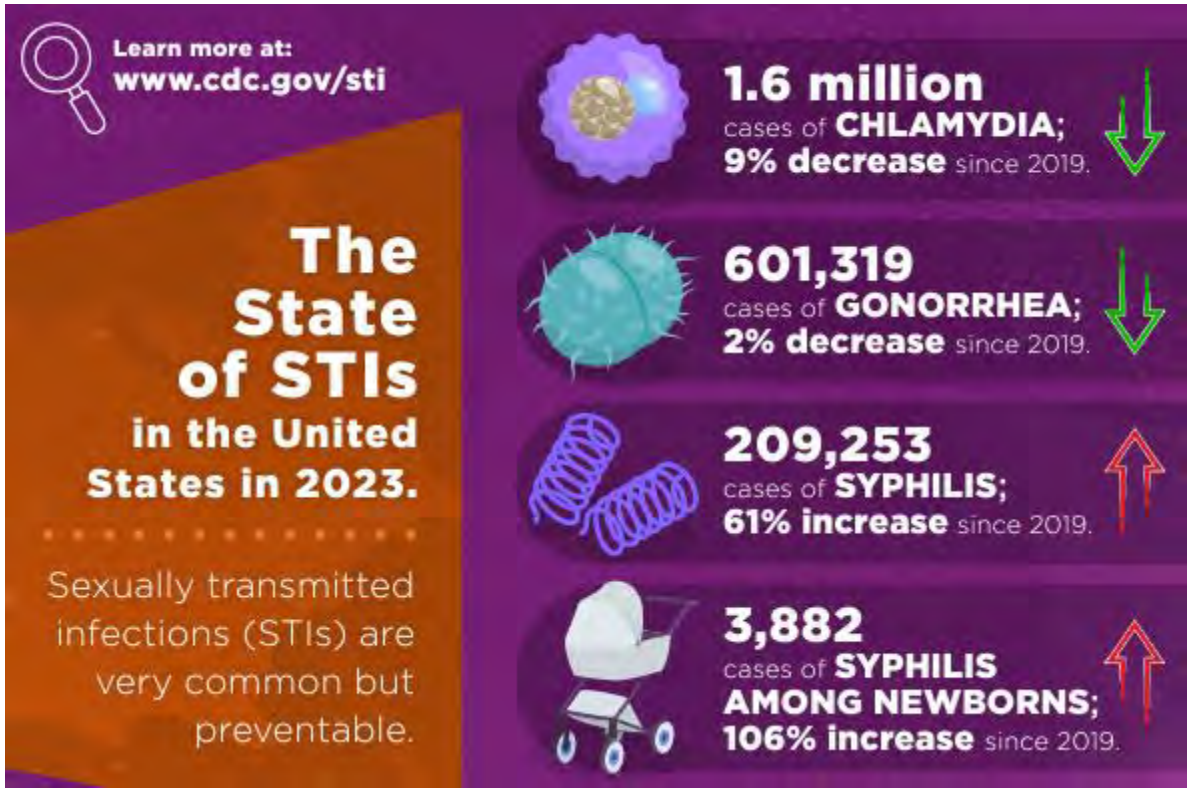
- 1 million STIs are acquired every day

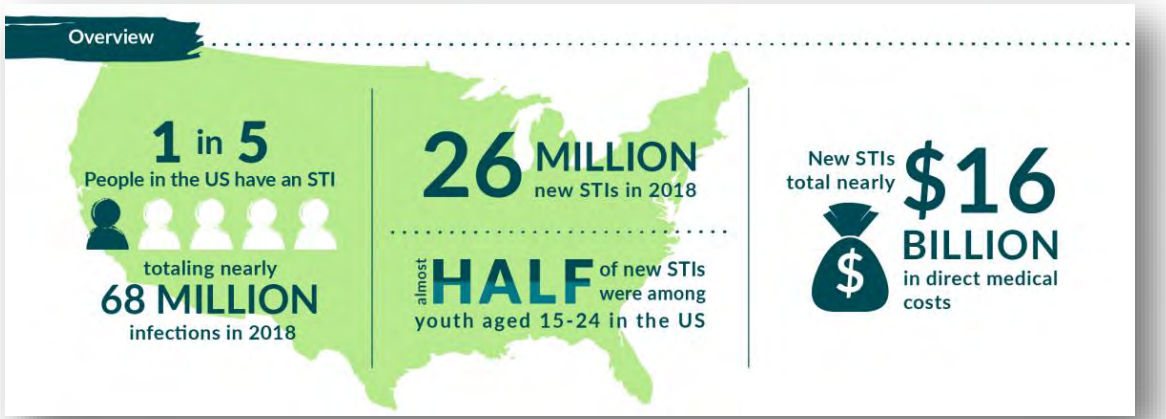
Annual new infections:

- Chlamydia 129 million
- Gonorrhea 82 million
- Syphilis 7.1 million

https://www.who.int/teams/global-hiv-hepatitis-and-stis-programmes/stis/strategic-information
https://www.who.int/news-room/fact-sheets/detail/sexually-transmitted-infections-(stis)

STIs Represent A Worsening Epidemic – In US

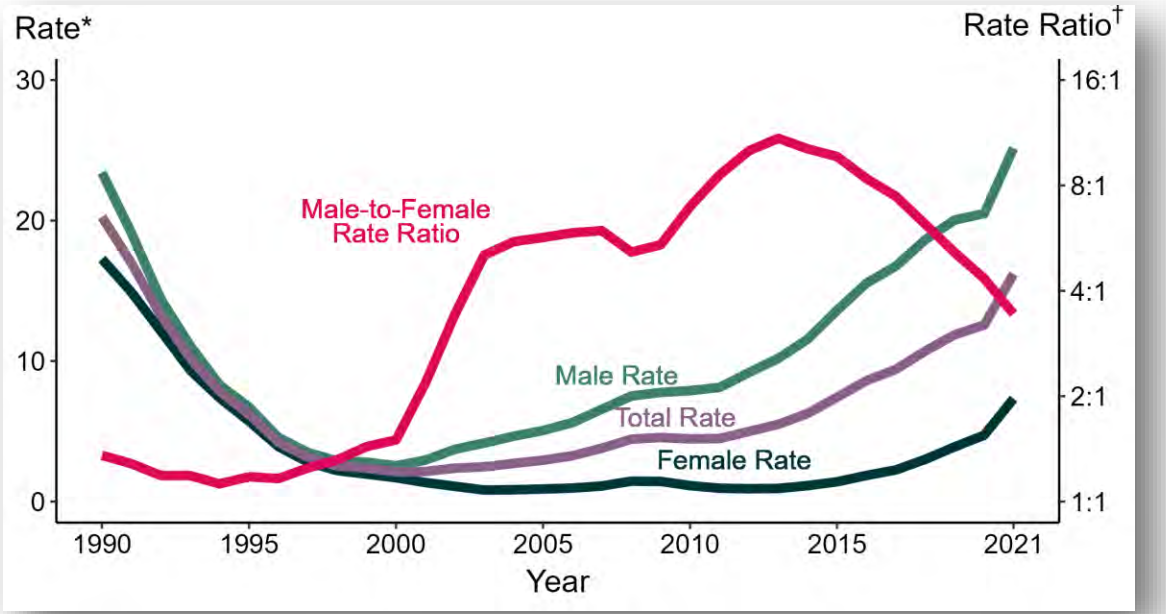




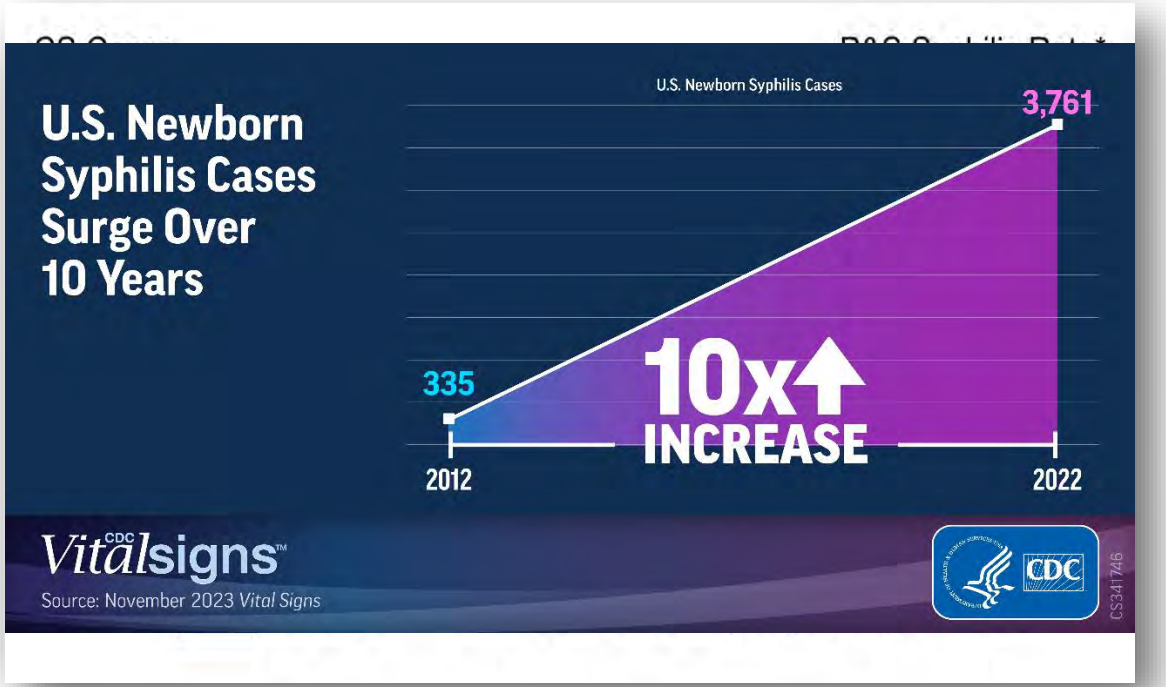
- https://www.cdc.gov/std/statistics/infographic.htm
- https://www.cdc.gov/std/statistics/2023/figures.htm

Why Do We Need to Prevent STIs?

Males to Female Ratio - Syphilis



Congenital Syphilis



- https://www.cdc. /std/statistics/2021/default.htm

Why Do We Need to Prevent STIs?

Rising Gonorrhea Resistance

The Commonwealth of Massachusetts
Executive Office of Health and Human Services
Department of Public Health
Bureau of Infectious Disease and Laboratory Sciences
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CLINICAL ALERT
January 19, 2023

MULTI-DRUG NON-SUSCEPTIBLE GONORRHEA IN MASSACHUSETTS

- A novel strain of multidrug-non-susceptible *Neisseria gonorrhoeae* with reduced susceptibility to ceftriaxone, cefixime, and azithromycin, and resistance to ciprofloxacin, penicillin, and tetracycline, has been identified in a Massachusetts resident. Although ceftriaxone 500 mg IM was effective at clearing infection for this case, this is the first isolate identified in the United States to demonstrate resistance or reduced susceptibility to all drugs that are recommended for treatment.
- Enhanced surveillance has identified a second isolate that, based on its genome, likely has similarly reduced susceptibility to ceftriaxone and cefixime.

STIs Are Not Benign

- Pelvic inflammatory disease
- Chronic pelvic pain
- Infertility
- Adverse pregnancy outcomes
  - Prematurity
  - Stillbirth
- Urethral strictures
- Gastrointestinal fistulas
- Peri-rectal abscesses
- Severe complications of syphilis
  - Permanent hearing or vision impairment

STI Prevention Landscape

- Illustrated by Barolini, Nicoletta. 2024.

CDC Routine Screening Recommendations

Population	Recommendations
Men who have sex with men	At least annually, test at each site of exposure (urethra, rectum) for sexually active MSM regardless of condom use or every 3-6 months **if at increased risk**.
Patients taking PrEP	All patients starting and taking oral PrEP should have genitourinary and extra-genital testing performed at baseline and every 3 months.
Persons living with HIV	For sexually active individuals, screen at first HIV evaluation and at least annually thereafter. More frequent screening might be appropriate depending **on individual risk behaviors** and local epidemiology
Non-pregnant Women	Test at least annually for sexually active women under 25 years of age and those aged 25 years and older **if at increased risk** Rectal chlamydial testing can be considered in females **based on sexual behaviors and exposure** through shared clinical decision making.
Men who have sex with women***	Consider screening young men in high prevalence clinical settings (adolescent and STI clinics and correctional facilities)
Pregnant Women	All pregnant women under 25 years of age and those aged 25 years and older **if at increased risk**. Retest during 3rd trimester if under 25 years of age or at risk.

Workowski KA, Bachmann LH, Chan PA, et al. Sexually Transmitted Infections Treatment Guidelines, 2021. MMWR Recomm Rep. 2021;70(4):1-187. Published 2021 Jul 23. doi:10.15585/mmwr.rr7004a1
https://www.who.int/publications/i/item/9789240052390

Syndromic Testing, Treatment, and Presumptive Treatment

- Urethritis
- Cervicitis
- Dysuria
- Proctitis
- Pharyngitis

Ceftriaxone 500 mg IM x 1
for persons weighing <150kg*

*For persons weighing ≥ 150kg, 1 g of IM ceftriaxone should be administered

If chlamydia has **not** been excluded, treat for chlamydia with:

Doxycycline 100 mg PO twice daily x 7 days

*For pregnancy, allergy, or concern for non-adherence 1g PO Azithromycin can be used

- Exposure

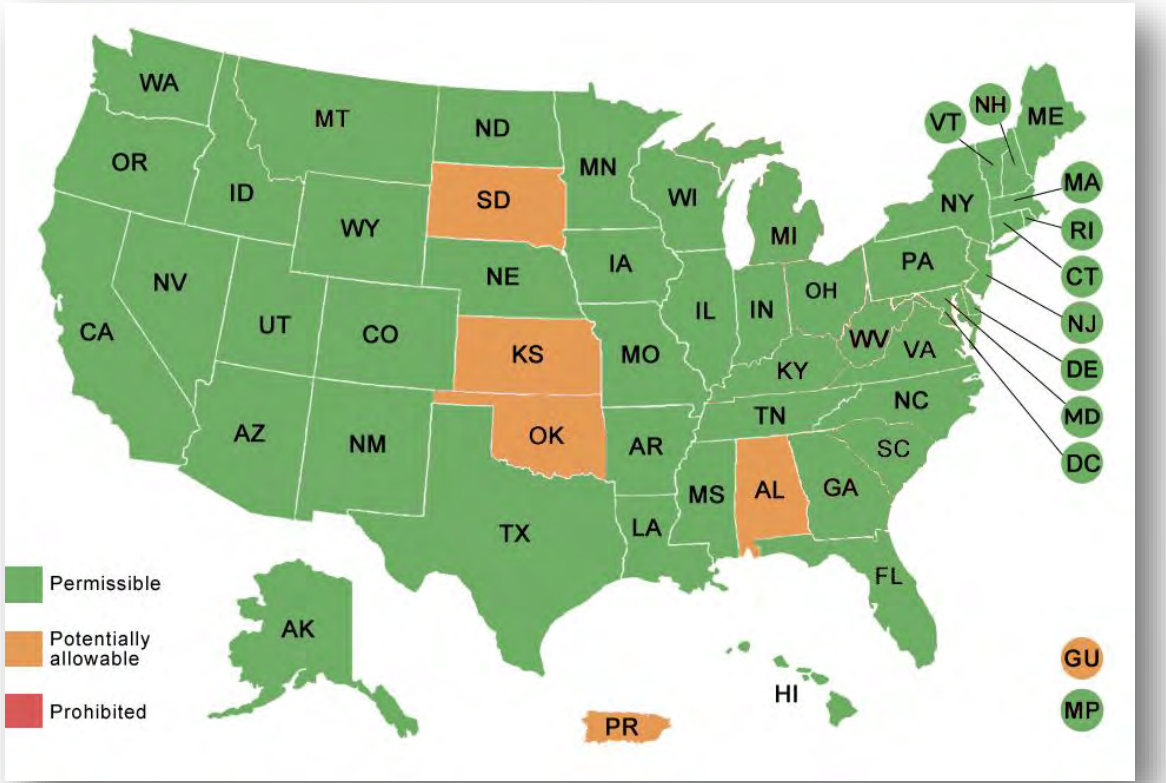
Workowski KA, Bachmann LH, Chan PA, et al. Sexually Transmitted Infections Treatment Guidelines, 2021. MMWR Recomm Rep. 2021;70(4):1-187. Published 2021 Jul 23. doi:10.15585/mmwr.rr7004a1

Partner Services

Providing Partner Services

1. Evaluate all sex partners in person if possible
   - Empirically treat all partners <60 days
   - Most recent partner if last contact >60 days

2. Expedited Partner Therapy
   - Heterosexual men and women
   - **Men Who Have Sex With Men – Shared Decision Making**



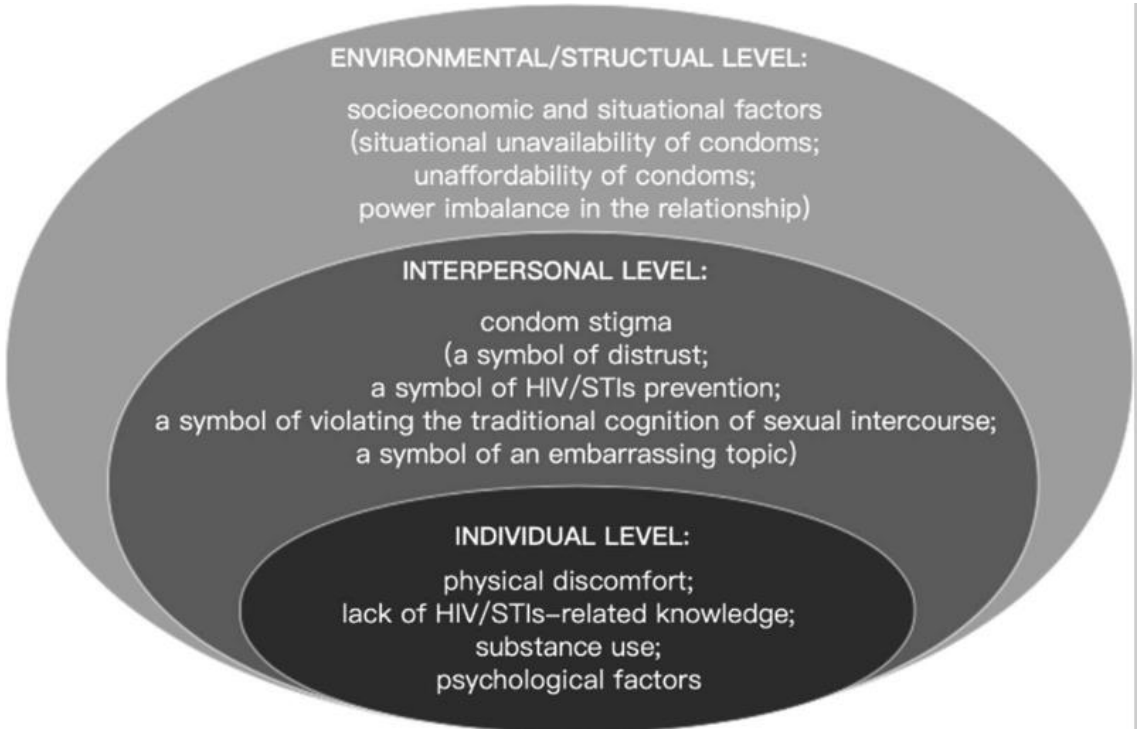
- https://www.cdc.gov/std/ept/legal/default.htm

Barrier Protection

Condoms

- When used correctly prevent multiple sexually transmitted infections
- Not as effective as HIV-PrEP
- Not used consistently for all sexual activities (i.e. oral sex)

Why Don't People Use Condoms?



- Smith DK, Herbst JH, Zhang X, Rose CE. Condom effectiveness for HIV prevention by consistency of use among men who have sex with men in the United States. *J Acquir Immune Defic Syndr*. 2015;68(3):337-344. doi:10.1097/QAI.0000000000000461
- Shen Y, Zhang C, Valimaki MA, Qian H, Mohammadi L, Chi Y, Li X. Why do men who have sex with men practice condomless sex? A systematic review and meta-synthesis. BMC Infect Dis. 2022 Nov 14;22(1):850. doi: 10.1186/s12879-022-07843-z. PMID: 36376835; PMCID:

Behavioral Counseling

The USPSTF recommends behavioral counseling for all sexually active adolescents and for adults at increased risk for sexually transmitted infections (STIs).	B

- "Behavioral counseling for persons at increased risk for STIs can reduce the likelihood of acquiring STIs (OR, 0.66 [95% CI, 0.54-0.81]) and also increase condom use or decrease the occurrence of unprotected intercourse"
- "Interventions with the largest effects for STI prevention tended to involve **more than 120 min** of total contact time and group counseling, often delivered over multiple sessions for up to 1 year"

- US Preventive Services Task Force, Krist AH, Davidson KW, et al. Behavioral Counseling Interventions to Prevent Sexually Transmitted Infections: US Preventive Services Task Force Recommendation Statement. *JAMA*. 2020;324(7):674-681. doi:10.1001/jama.2020.13095

Vaccination

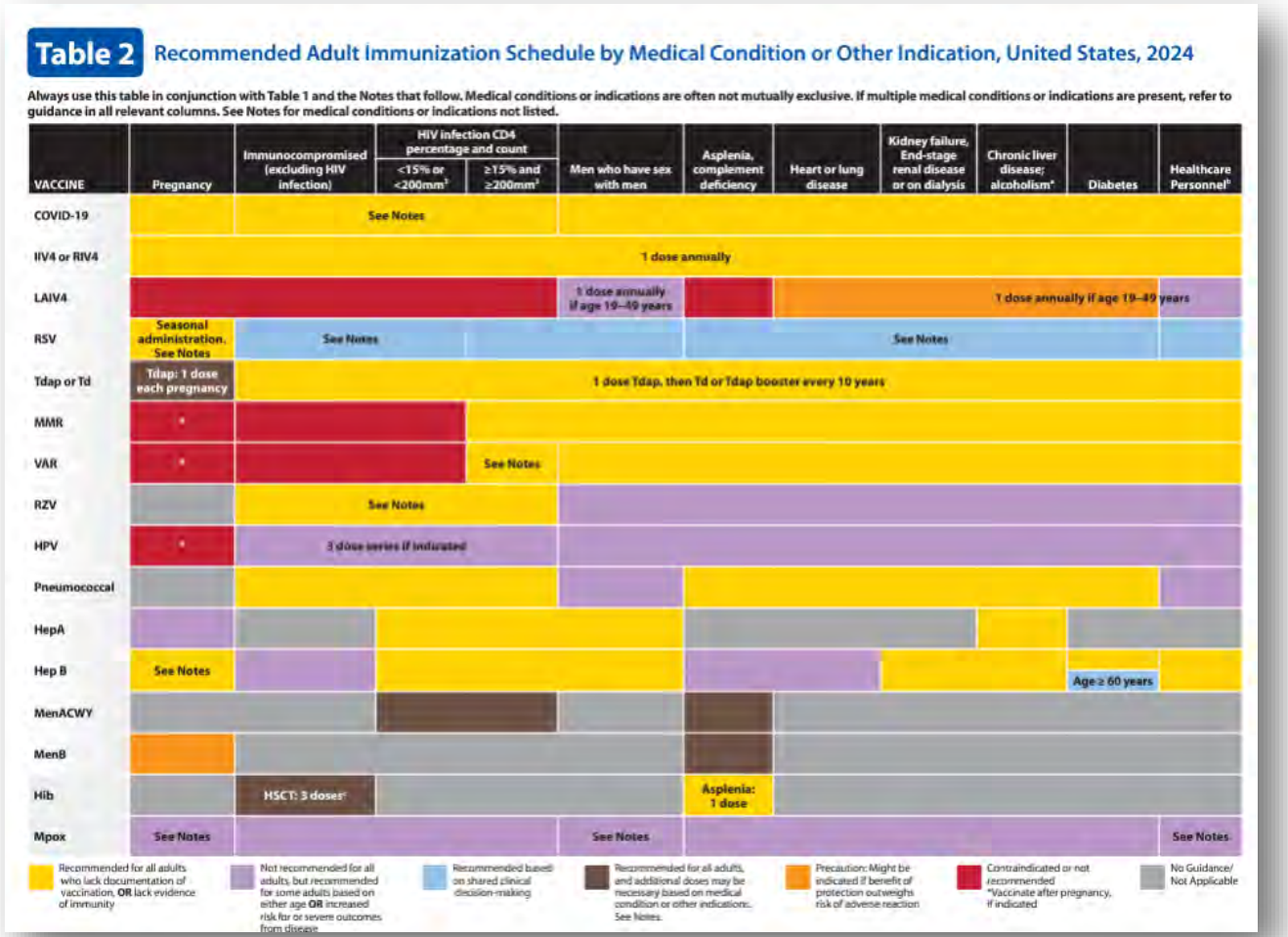


Table 2 Recommended Adult Immunization Schedule by Medical Condition or Other Indication, United States, 2024

Always use this table in conjunction with Table 1 and the Notes that follow. Medical conditions or indications are often not mutually exclusive. If multiple medical conditions or indications are present, refer to guidance in all relevant columns. See Notes for medical conditions or indications not listed.

VACCINE	Pregnancy	Immunocompromised (excluding HIV infection)	HIV infection CD4 percentage and count: <15% or <200mm³	HIV infection CD4 percentage and count: ≥15% and ≥200mm³	Men who have sex with men	Asplenia, complement deficiency	Heart or lung disease	Kidney failure, End-stage renal disease or on dialysis	Chronic liver disease; alcoholism[4]	Diabetes	Healthcare Personnel[5]
COVID-19		See Notes									
IIV4 or RIV4	1 dose annually										
LAIV4					1 dose annually if age 19–49 years					1 dose annually if age 19–49 years	
RSV	Seasonal administration. See Notes	See Notes				See Notes					
Tdap or Td	Tdap: 1 dose each pregnancy	1 dose Tdap, then Td or Tdap booster every 10 years									
MMR	•										
VAR	•			See Notes							
RZV		See Notes									
HPV	•	3 dose series if indicated									
Pneumococcal											
HepA											
Hep B	See Notes									Age ≥ 60 years	
MenACWY											
MenB											
Hib		HSCT: 3 doses[7]				Asplenia: 1 dose					
Mpox	See Notes				See Notes						See Notes

Recommended for all adults who lack documentation of vaccination, OR lack evidence of immunity

Not recommended for all adults, but recommended for some adults based on either age OR increased risk for or severe outcomes from disease

Recommended based on shared clinical decision-making

Recommended for all adults, and additional doses may be necessary based on medical condition or other indications. See Notes.

Precaution: Might be indicated if benefit of protection outweighs risk of adverse reaction

Contraindicated or not recommended *Vaccinate after pregnancy, if indicated

No Guidance/ Not Applicable

Specific Recommendations

- Hepatitis A/B
- HPV
- Men ACYW
- Mpox

- https://www.cdc.gov/vaccines/schedules/downloads/adult/adult-combined-schedule.pdf

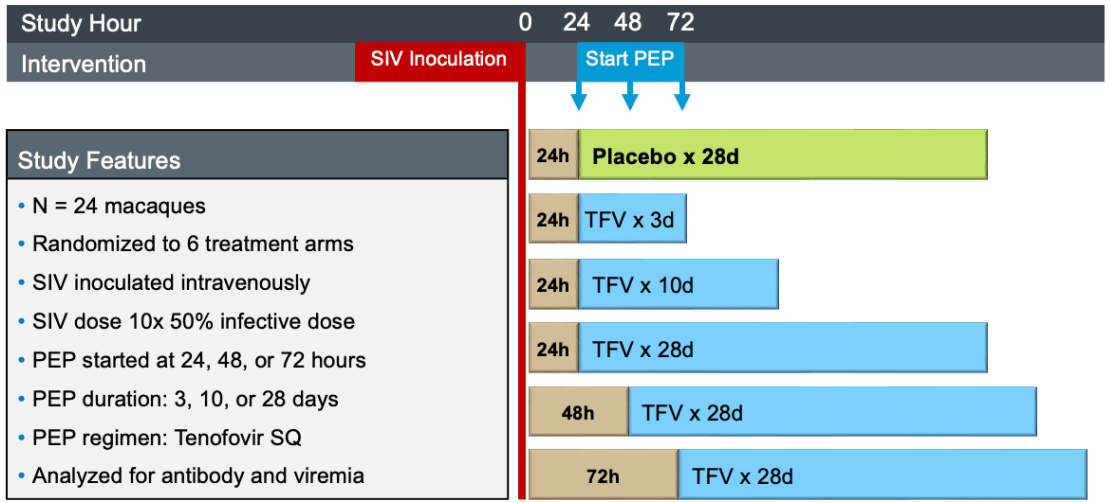
Medication Prophylaxis

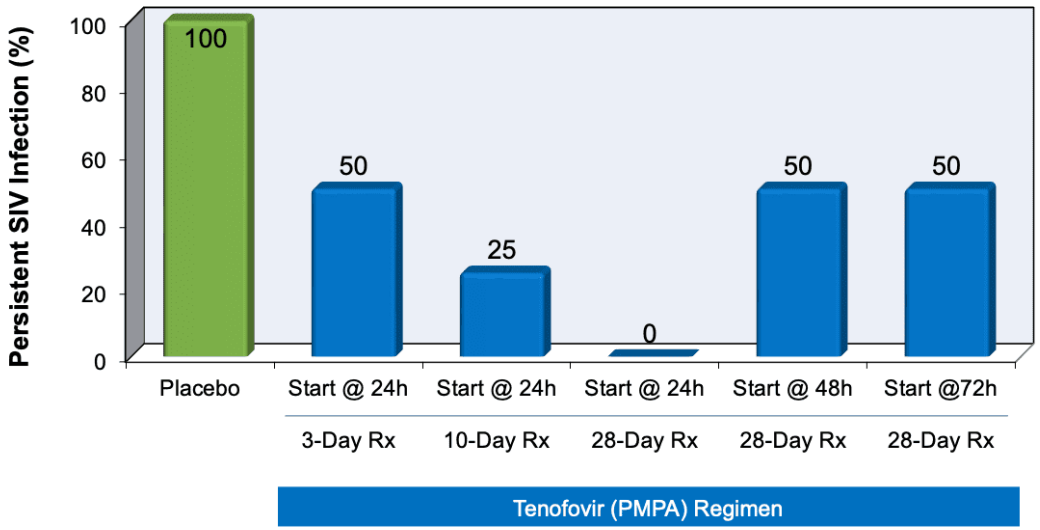
Medication Prophylaxis

1. **HIV post-exposure prophylaxis (PEP)**
2. HIV pre-exposure prophylaxis (PrEP)

PEP Is a Medical Emergency

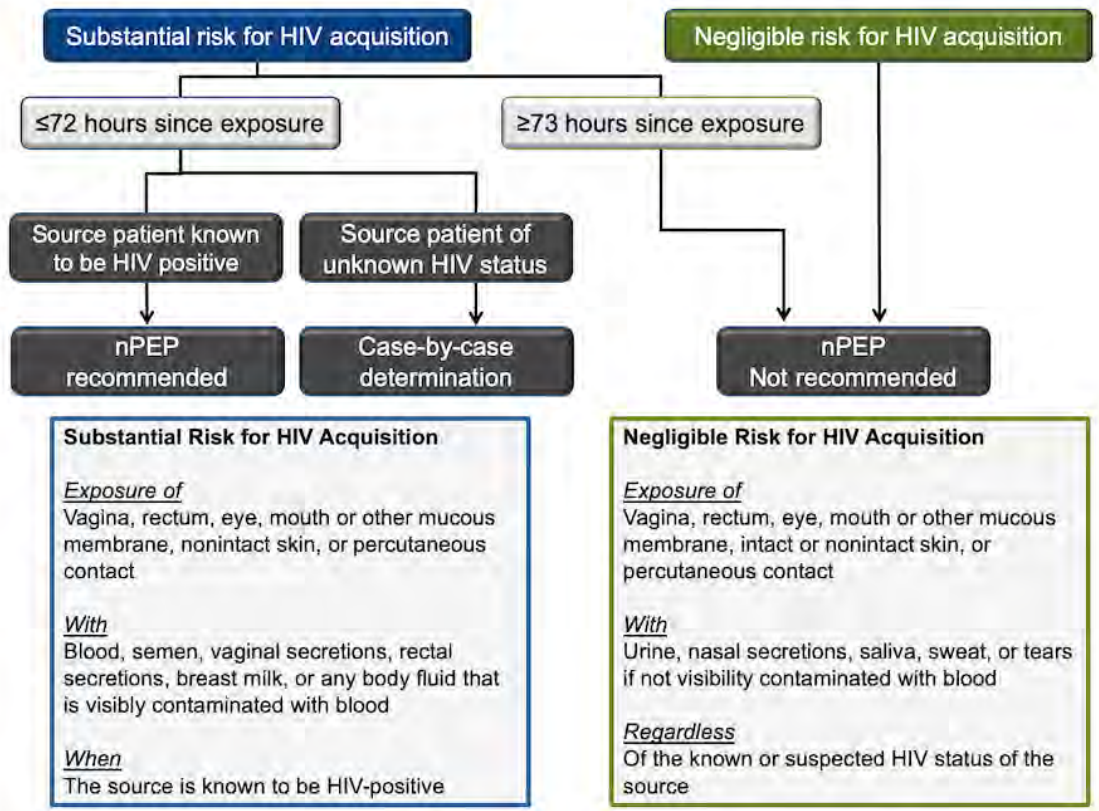
HIV Post-Exposure Prophylaxis Time Matters





- https://www.hiv.uw.edu/go/prevention/nonoccupational-postexposure-prophylaxis/core-concept/
- Tsai CC, Emau P, Follis KE, et al. Effectiveness of postinoculation (R)-9-(2-phosphonylmethoxypropyl) adenine treatment for prevention of persistent simian immunodeficiency virus SIVmne infection depends critically on timing of initiation and duration of treatment. J Virol. 1998;72:4265-73.

Evaluating Patients for HIV PrEP



Information You Need to Assess

1. Information on Exposed Persons HIV Status
2. Information Related to Source Person's HIV Status
3. Risk Related to the Exposure Type

PEP Indications By Exposure Type

Consider

- Condomless vaginal or anal intercourse during sexual abuse
- Oral sex with ejaculation or blood exposure during sexual abuse
- Injuries with exposure to blood from a source known to have HIV
- Injuries with exposure to blood from a source of unknown HIV status (including needlesticks and human bites)

Not Needed

- Kissing, spitting
- Oral-to-oral contact in the absence of mucosal damage (e.g., mouth-to-mouth resuscitation)
- Human bites not involving blood
- Exposure to needles or sharps that have not been in contact with an individual with or at risk of HIV

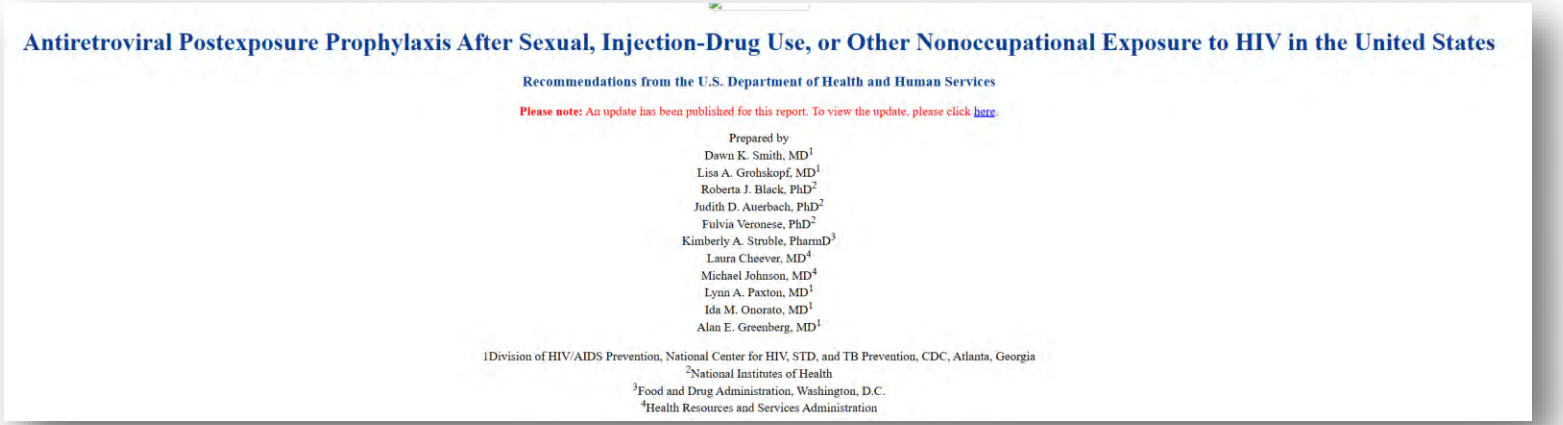
What Do I Need To Do For PEP?

Nonoccupational HIV PEP: Recommended Laboratory Monitoring of Source and Exposed Persons

Test	Source	Exposed			
	Baseline	Baseline	4-6 Weeks after exposure	3 Months after exposure	6-[illegible]
		For all persons considered for or prescribed nPEP for[illegible]			
HIV-1/2 Ag/Ab (or Ab testing if Ag/Ab test unavailable)[a]	√	√	√		
Hepatitis B serology, including: HBsAg anti-HBs anti-HBc	√	√			√[c]
Hepatitis C antibody test	√	√		—	√[d]
		For all p[illegible]		[illegible] sexual exposure	
Syphilis serology[e]	√			—	√
Gonorrhea[f]			√[g]	—	—
Chlamydia[f]			√[g]	—	—
Pregnancy[h]			√	—	—
		[illegible] persons prescribed: Tenofovir DF-emtricitabine + raltegravir Tenofovir DF-emtricitabine + dolutegravir			
[illegible] estimated		√	√	—	—
[illegible] ansferase, aspartate [illegible]sferase		√	√	—	—
	For all persons with HIV confirmed at any visit				
HIV RNA level	√			√[i]	
HIV genotypic drug resistance test	√			√[i]	

Assessment of exposure, HIV and other baseline testing, and other related activities can proceed after the first dose of PEP is administered.

CDC HIV PEP "Original" Guidelines (2005)



Antiretroviral Postexposure Prophylaxis After Sexual, Injection-Drug Use, or Other Nonoccupational Exposure to HIV in the United States

Recommendations from the U.S. Department of Health and Human Services

Please note: An update has been published for this report. To view the update, please click here.

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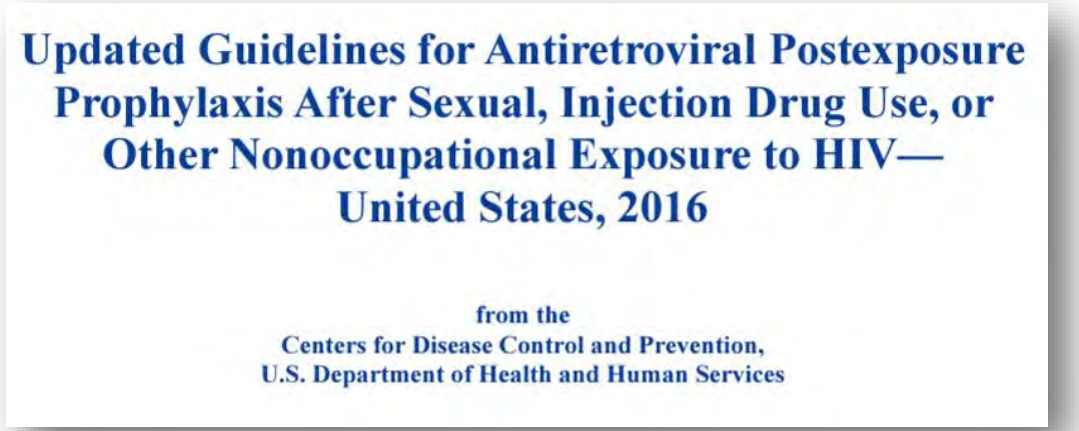
"DHHS recommends the prompt initiation of nPEP with HAART when persons seek care within 72 hours after exposure, the source is known to be HIV infected, and the exposure event presents a substantial risk for transmission. "

TABLE 2. Antiretroviral regimens for nonoccupational postexposure prophylaxis of HIV infection

Preferred regimens	
NNRTI*-based	Efavirenz† plus (lamivudine or emtricitabine) plus (zidovudine or tenofovir)
Protease inhibitor (PI)-based	Lopinavir/ritonavir (co-formulated as Kaletra) plus (lamivudine or emtricitabine) plus zidovudine
Alternative regimens	
NNRTI-based	Efavirenz plus (lamivudine or emtricitabine) plus abacavir or didanosine or stavudine§
PI-based	Atazanavir plus (lamivudine or emtricitabine) plus (zidovudine or stavudine or abacavir or didanosine) or (tenofovir plus ritonavir [100 mg/day])
	Fosamprenavir plus (lamivudine or emtricitabine) plus (zidovudine or stavudine) or (abacavir or tenofovir or didanosine)
	Fosamprenavir/ritonavir¶ plus (lamivudine or emtricitabine) plus (zidovudine or stavudine or abacavir or tenofovir or didanosine)
	Indinavir/ritonavir¶** plus (lamivudine or emtricitabine) plus (zidovudine or stavudine or abacavir or tenofovir or didanosine)
	Lopinavir/ritonavir (co-formulated as Kaletra) plus (lamivudine or emtricitabine) plus (stavudine or abacavir or tenofovir or idanosine)
	Nelfinavir plus (lamivudine or emtricitabine) plus (zidovudine or stavudine or abacavir or tenofovir or didanosine)
	Saquinavir (hgc* or sgc*)/ritonavir† plus (lamivudine or emtricitabine) plus (zidovudine or stavudine or abacavir or tenofovir or didanosine)
Triple NRTI*	Abacavir plus lamivudine plus zidovudine (only when an NONRTI- or PI-based regimen cannot or should not be used)

- Smith DK, Grohskopf LA, Black RJ, et al. Antiretroviral postexposure prophylaxis after sexual, injection-drug use, or other nonoccupational exposure to HIV in the United States: recommendations from the U.S. Department of Health and Human Services. MMWR Recomm Rep. 2005;54(No. RR-2):1-20.

CDC HIV PEP "Updated" Guidelines (2016)



Updated Guidelines for Antiretroviral Postexposure Prophylaxis After Sexual, Injection Drug Use, or Other Nonoccupational Exposure to HIV—United States, 2016

from the
Centers for Disease Control and Prevention,
U.S. Department of Health and Human Services

"A 3-drug nPEP regimen is recommended for all persons for whom nPEP is indicated."

Table 5. Preferred and alternative antiretroviral medication 28-day regimens for nPEP[a,b]

Age group	Preferred/ alternative	Medication
Adults and adolescents aged ≥ 13 years, including pregnant women, with normal renal function (creatinine clearance ≥60 mL/min)	Preferred	A 3-drug regimen consisting of tenofovir DF 300 mg ***and*** fixed dose combination emtricitabine 200 mg (Truvada[c]) once daily ***with*** raltegravir 400 mg twice daily ***or*** dolutegravir 50 mg once daily
	Alternative	A 3-drug regimen consisting of tenofovir DF 300 mg ***and*** fixed dose combination emtricitabine 200 mg (Truvada) once daily ***with*** darunavir 800 mg (as 2, 400-mg tablets) once daily ***and*** ritonavir[c] 100 mg once daily
Adults and adolescents aged ≥ 13 years with renal dysfunction (creatinine clearance ≤59 mL/min)	Preferred	A 3-drug regimen consisting of zidovudine ***and*** lamivudine, with both doses adjusted to degree of renal function ***with*** raltegravir 400 mg twice daily ***or*** dolutegravir 50 mg once daily
	Alternative	A 3-drug regimen consisting of zidovudine ***and*** lamivudine, with both doses adjusted to degree of renal function ***with*** darunavir 800 mg (as 2, 400-mg tablets) once daily ***and*** ritonavir[c] 100 mg once daily
Children aged 2–12 years	Preferred	A 3-drug regimen consisting of tenofovir DF, emtricitabine, and raltegravir, with each drug dosed to age and weight[d]
	Alternative	A 3-drug regimen consisting of zidovudine ***and*** lamivudine ***with*** raltegravir ***or*** lopinavir/ritonavir[c], with raltegravir and lopinavir/ritonavir dosed to age and weight[d]
	Alternative	A 3-drug regimen consisting of tenofovir DF ***and*** emtricitabine ***and*** lopinavir/ritonavir[c], with each drug dosed to age and weight[d]

- Announcement: Updated Guidelines for Antiretroviral Postexposure Prophylaxis after Sexual, Injection-Drug Use, or Other Nonoccupational Exposure to HIV - United States, 2016. *MMWR Morb Mortal Wkly Rep*. 2016;65(17):458. Published 2016 May 6. doi:10.15585/mmwr.mm6517a5

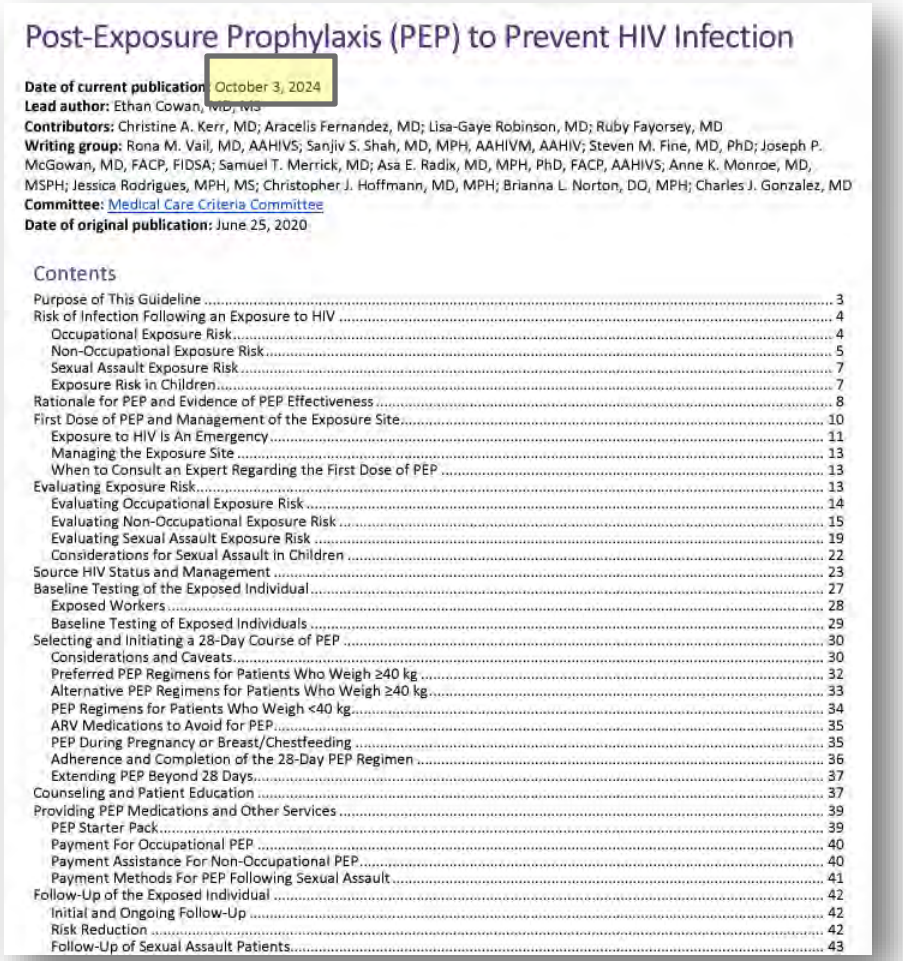
Alternative Regiments That Have Been Explored

- Fenway Health
  - Elvitegravir-Cobicistat-Tenofovir DF-Emtricitabine
  - Raltegravir plus Tenofovir DF-Emtricitabine
  - **Bictegravir-tenofovir alafenamide-emtricitabine**

- Sydney Study
  - Dolutegravir plus Tenofovir DF-Emtricitabine (Sydney Study)
  - Raltegravir plus Tenofovir DF-Emtricitabine
  - Rilpivirine-Tenofovir DF-Emtricitabine (Sydney Study)

- https://www.hiv.uw.edu/go/prevention/nonoccupational-postexposure-prophylaxis/core-concept/all#introduction-background

New NYS AIDS Institute Guidelines



Post-Exposure Prophylaxis (PEP) to Prevent HIV Infection

Date of current publication: October 3, 2024
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Committee: Medical Care Criteria Committee
Date of original publication: June 25, 2020

Contents

Selecting and Initiating a 28-Day Course of PEP

☑ RECOMMENDATIONS

Preferred Regimens

- Clinicians should administer a preferred or alternative PEP regimen (the following recommended regimens also have activity in the rare possibility of an exposure to known HIV-2 or a source patient at risk of HIV-2 infection). (A2)
  - Preferred single-tablet regimen: BIC/TAF/FTC by mouth once daily (preferred because of the lower discontinuation rates and minimal adverse effects).
  - Preferred multi-tablet regimen [a,b]: TDF/FTC plus either RAL *or* DTG; 3TC may be substituted for FTC in either regimen.
  - For alternative regimens, see Table 3: Alternative PEP Regimens for Patients Who Weigh ≥40 kg.

- Cowan E, Kerr CA, Fernandez A, et al. *PEP to Prevent HIV Infection*. Baltimore (MD): Johns Hopkins University; October 2024.

Efficacy of HIV PEP

Efficacy of HIV Postexposure Prophylaxis: Systematic Review and Meta-analysis of Nonhuman Primate Studies

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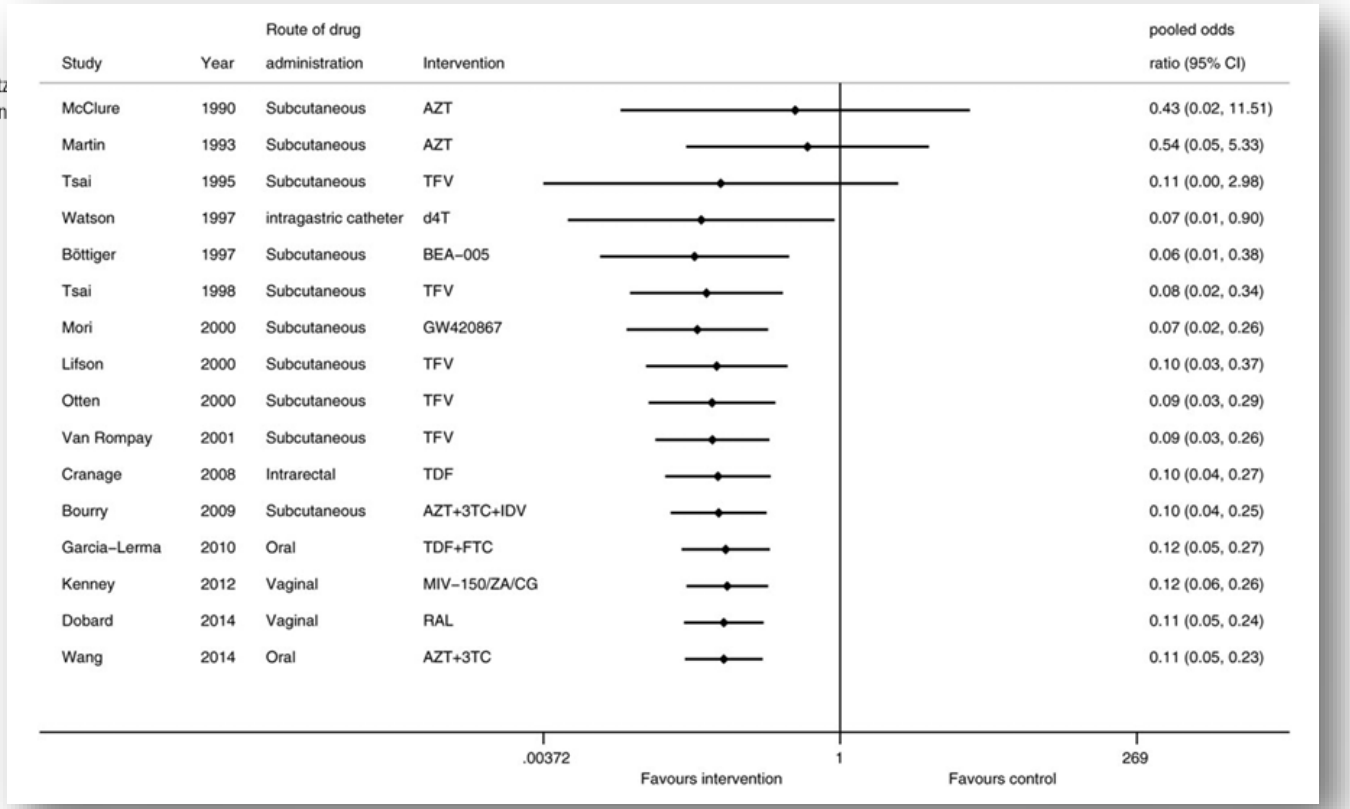


Study	Year	Route of drug administration	Intervention	pooled odds ratio (95% CI)
McClure	1990	Subcutaneous	AZT	0.43 (0.02, 11.51)
Martin	1993	Subcutaneous	AZT	0.54 (0.05, 5.33)
Tsai	1995	Subcutaneous	TFV	0.11 (0.00, 2.98)
Watson	1997	intragastric catheter	d4T	0.07 (0.01, 0.90)
Böttiger	1997	Subcutaneous	BEA–005	0.06 (0.01, 0.38)
Tsai	1998	Subcutaneous	TFV	0.08 (0.02, 0.34)
Mori	2000	Subcutaneous	GW420867	0.07 (0.02, 0.26)
Lifson	2000	Subcutaneous	TFV	0.10 (0.03, 0.37)
Otten	2000	Subcutaneous	TFV	0.09 (0.03, 0.29)
Van Rompay	2001	Subcutaneous	TFV	0.09 (0.03, 0.26)
Cranage	2008	Intrarectal	TDF	0.10 (0.04, 0.27)
Bourry	2009	Subcutaneous	AZT+3TC+IDV	0.10 (0.04, 0.25)
Garcia–Lerma	2010	Oral	TDF+FTC	0.12 (0.05, 0.27)
Kenney	2012	Vaginal	MIV–150/ZA/CG	0.12 (0.06, 0.26)
Dobard	2014	Vaginal	RAL	0.11 (0.05, 0.24)
Wang	2014	Oral	AZT+3TC	0.11 (0.05, 0.23)

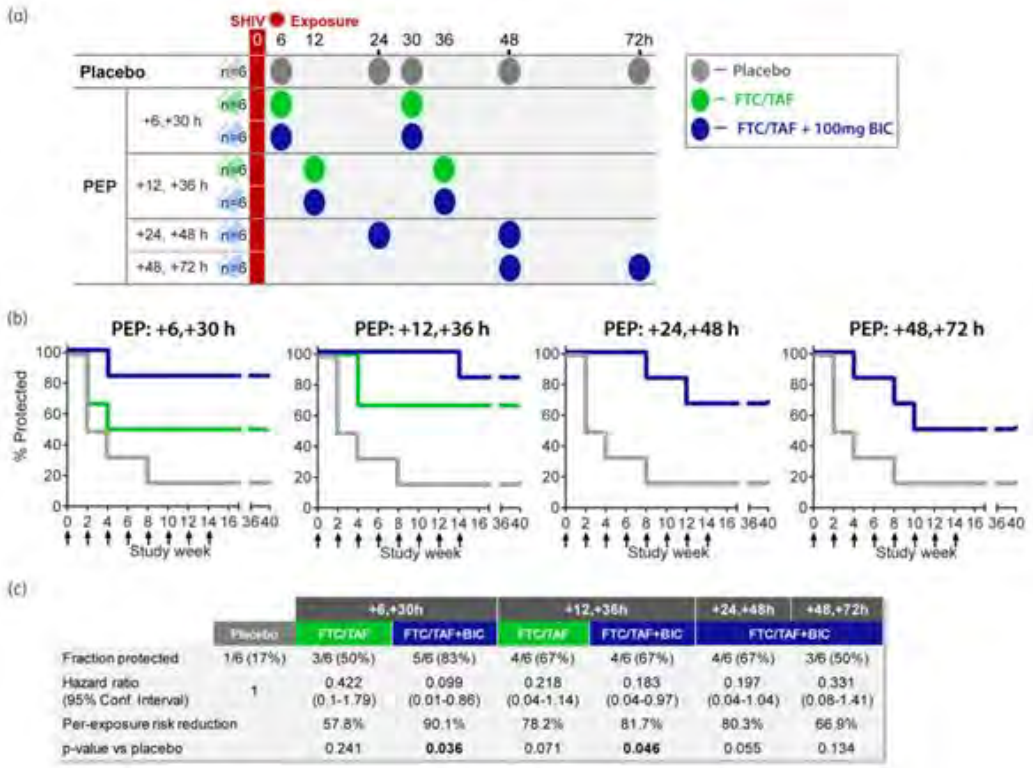
- Irvine C, Egan KJ, Shubber Z, Van Rompay KK, Beanland RL, Ford N. Efficacy of HIV Postexposure Prophylaxis: Systematic Review and Meta-analysis of Nonhuman Primate Studies. *Clin Infect Dis*. 2015;60 Suppl 3:S165-S169. doi:10.1093/cid/civ069

Efficacy of HIV PEP With BIC/FTC/TAF

Two-dose emtricitabine/tenofovir alafenamide plus bictegravir prophylaxis protects macaques against SHIV infection

Elena Bekerman[1]*, Stephanie Cox[1], Darius Babusis[1], Federico Campigotto[1], Moupali Das[1], Dan H. Barouch[2], Tomas Cihlar[1] and Christian Callebaut[1]

[1]Gilead Sciences, Foster City, CA, USA; [2]Center for Virology and Vaccine Research, Beth Israel Deaconess Medical Center, Bosta MA, USA



	Placebo	+6,+30h FTC/TAF	+6,+30h FTC/TAF+BIC	+12,+36h FTC/TAF	+12,+36h FTC/TAF+BIC	+24,+48h FTC/TAF+BIC	+48,+72h FTC/TAF+BIC
Fraction protected	1/6 (17%)	3/6 (50%)	5/6 (83%)	4/6 (67%)	4/6 (67%)	4/6 (67%)	3/6 (50%)
Hazard ratio (95% Conf. Interval)	1	0.422 (0.1-1.79)	0.099 (0.01-0.86)	0.218 (0.04-1.14)	0.183 (0.04-0.97)	0.197 (0.04-1.04)	0.331 (0.08-1.41)
Per-exposure risk reduction		57.8%	90.1%	78.2%	81.7%	80.3%	66.9%
p-value vs placebo		0.241	**0.036**	0.071	**0.046**	0.055	0.134

- Bekerman E, Cox S, Babusis D, et al. Two-dose emtricitabine/tenofovir alafenamide plus bictegravir prophylaxis protects macaques against SHIV infection. *J Antimicrob Chemother*. 2021;76(3):692-698. doi:10.1093/jac/dkaa476

Real-World Data on BIC/FTC/TAF for HIV-PEP

PREVENTION RESEARCH

Safety and Tolerability of Once Daily Coformulated Bictegravir, Emtricitabine, and Tenofovir Alafenamide for Postexposure Prophylaxis After Sexual Exposure

Kenneth H. Mayer, MD,[a,b,c] Marcy Gelman, NP,[a] Johnathon Holmes, NP,[a] Jessica Kraft, NP,[a] Kathleen Melbourne, PharmD,[d] and Matthew J. Mimiaga, ScD, MPH[a,e]

TABLE 1. Demographic and Behavioral Risk Profile of Participants Who Used BIC/FTC/TAF for Postexposure Prophylaxis (N = 52)

	Mean (Range)
Age, yrs	37.2 (21–71)
Race	% (n)
White	76.9 (40)
Black/African American	5.8 (3)
Asian/Pacific Islander	5.8 (3)
Multiracial	11.5 (6)
Ethnicity	% (n)
Lantinx/Hispanic	9.6 (5)
Sexual orientation/gender identity	% (n)
Gay/cisgender man	67.3 (35)
Bisexual/cisgender man	11.5 (6)
Heterosexual/cisgender man	7.7 (4)
Heterosexual/cisgender woman	3.8 (2)
"Heteroflexible"/cisgender man	1.9 (1)
Pansexual/cisgender man	1.9 (1)
Queer/transgender man	1.9 (1)
Declined/cisgender man	1.9 (1)
Sexual behavior (yes/no)	% yes (n)
Receptive anal sex	51.9 (27)
Insertive anal sex	42.3 (22)
Receptive vaginal sex	5.8 (3)
Insertive vaginal sex	5.8 (3)
Receptive or insertive oral sex	57.7 (30)
Condomless anal or vaginal sex with a known HIV-Positive partner	15.4 (8)

- Mayer KH, Gelman M, Holmes J, Kraft J, Melbourne K, Mimiaga MJ. Safety and Tolerability of Once Daily Coformulated Bictegravir, Emtricitabine, and Tenofovir Alafenamide for Postexposure Prophylaxis After Sexual Exposure. *J Acquir Immune Defic Syndr*. 2022;90(1):27-32. doi:10.1097/QAI.0000000000002912

BIC/FTC/TAF Had Lower Rates of Side Effects

TABLE 2. Commonly Reported Adverse Events Among BIC/FTC/TAF PEP Users Compared With Those Using Other PEP Regimens, Fenway Health, Boston, 2000–2020

	AZT/3TC/PI (N = 119) %	TDF/FTC/RAL (N = 100) %	EVG/COB/FTC/TDF (N = 100) %	BIC/FTC/TAF (N = 52) %
	Dates Recruited			
	January 2000–May 2004	March 2008–March 2010	May 2013–November 2015	August 2018–March 2020
Diarrhea/loose stool	58.8*	21.0†	38.0*	7.7
Fatigue	48.5*	14.0	28.0‡	9.6
Nausea/vomiting	58.8*	27.0	28.0	15.4
Headache	11.8†	15.0‡	14.0‡	1.9
Dizziness/lightheadedness	8.4†	10.0‡	6.0	0.0
Myalgia/arthralgia	10.9†	8.0	2.0	1.9

- Mayer KH, Gelman M, Holmes J, Kraft J, Melbourne K, Mimiaga MJ. Safety and Tolerability of Once Daily Coformulated Bictegravir, Emtricitabine, and Tenofovir Alafenamide for Postexposure Prophylaxis After Sexual Exposure. *J Acquir Immune Defic Syndr.* 2022;90(1):27-32. doi:10.1097/QAI.0000000000002912

BIC/FTC/TAF Had Higher Completion Rates

TABLE 3. Regimen Completion Rates Among TAF/FTC/BIC Users Compared With Those Using Other Postexposure Prophylaxis Regimens, Fenway Health, Boston, 2000–2020

	AZT/3TC/PI (N = 119) %	TDF/FTC/RAL (N = 100) %	EVG/COB/FTC/TDF (N = 100) %	BIC/FTC/TAF (N = 52) %
	Dates Recruited			
	January 2000–May 2004	March 2008–March 2010	May 2013–November 2015	August 2018–March 2020
Completed as prescribed	38.8*	57.0†	71.0‡	90.4
Stopped or modified	14.0†	28.0*	15.0†	0
Lost to follow-up	47.3*	15.0	14.0	9.6

- Mayer KH, Gelman M, Holmes J, Kraft J, Melbourne K, Mimiaga MJ. Safety and Tolerability of Once Daily Coformulated Bictegravir, Emtricitabine, and Tenofovir Alafenamide for Postexposure Prophylaxis After Sexual Exposure. *J Acquir Immune Defic Syndr.* 2022;90(1):27-32. doi:10.1097/QAI.0000000000002912

Replicated In This Study

Original Article — Chinese Medical Journal

An open-label evaluation of safety and tolerability of coformulated bictegravir/emtricitabine/tenofovir alafenamide for post-exposure prophylaxis following potential exposure to human immunodeficiency virus-1

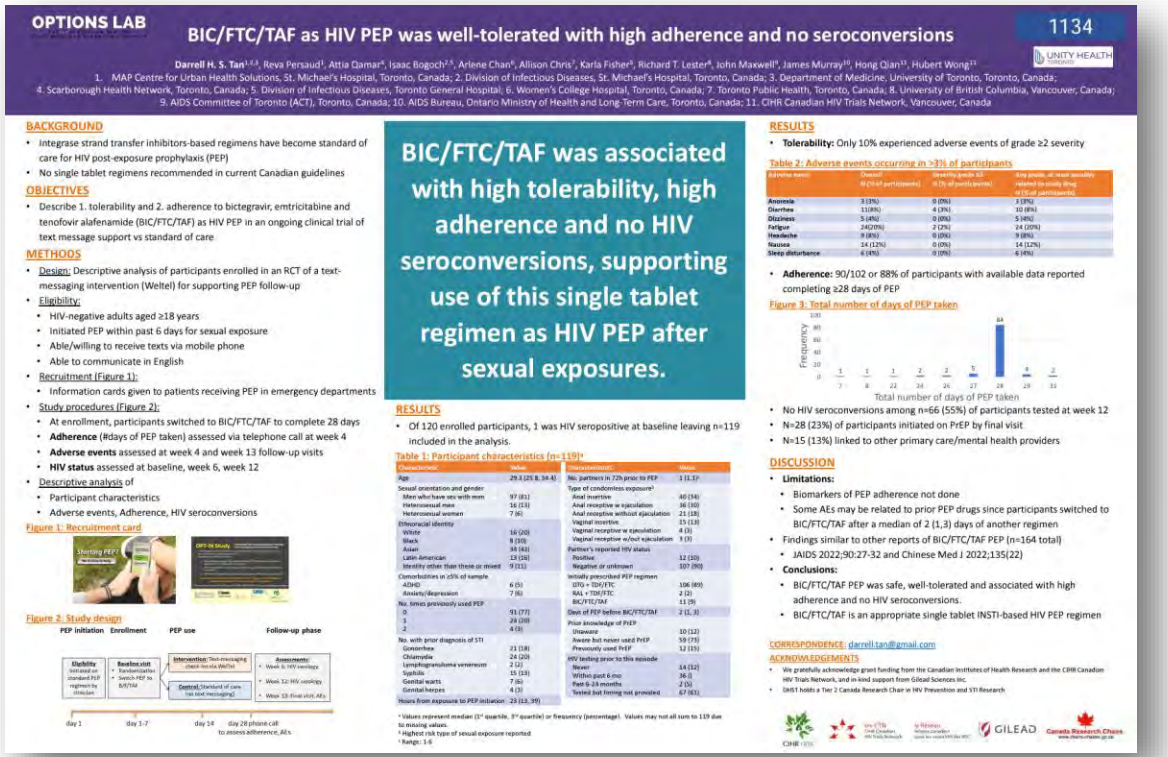
An Liu[1], Ruolei Xin[2], Hongwei Zhang[1], Lili Dai[1], Ruojun (Esther) Wu[3], Xi Wang[1], Aixin Li[1], Wei Hua[1], Jianwei Li[1], Ying Shao[1], Yue Gao[1], Zhangli Wang[1], Jiangzhu Ye[1], Gulimila A bu dou re xi ti[4], Zaicun Li[1], Lijun Sun[1]

[1]Clinic of Center for Infection, Beijing Youan Hospital, Capital Medical University, Beijing 100069, China;
[2]Institute of STD/AIDS Prevention and Control, Beijing Center for Disease Prevention and Control, Beijing 100013, China;
[3]Department of Chemistry, Colgate University, Hamilton NY, USA;
[4]Care Center, The Eighth Affiliated Hospital of Xinjiang Medical University, Urumchi, Xinjiang 830054, China.

- 112 participants
  - PEP completion was 96.4%
  - PEP adherence was high (98.9%)
  - 4 side effects (2 headache, 2 diarrhea, 1 nausea)
  - 4 had a mild increase in Cr that resolved at the end of therapy
  - No HIV seroconversions
- "In conclusion, a once-daily, STR of BIC/FTC/TAF used as PEP for 28 days was well tolerated, with high levels of adherence and high completion rates. Using BIC/FTC/TAF as PEP may be a good option."

- Liu A, Xin R, Zhang H, Dai L, Wu RE, Wang X, Li A, Hua W, Li J, Shao Y, Gao Y, Wang Z, Ye J, Bu Dou Re Xi Ti GA, Li Z, Sun L. An open-label evaluation of safety and tolerability of coformulated bictegravir/emtricitabine/tenofovir alafenamide for post-exposure prophylaxis following potential exposure to human immunodeficiency virus-1. Chin Med J (Engl). 2022 Nov 20;135(22):2725-2729. doi: 10.1097/CM9.0000000000002494. PMID: 36719359; PMCID: PMC9944392.

Confirmed in This Randomized Study



OPTIONS LAB

BIC/FTC/TAF as HIV PEP was well-tolerated with high adherence and no seroconversions

1134

Darrell H. S. Tan[1,2,3], Reva Persaud[1], Attia Qamar[4], Isaac Bogoch[2,5], Arlene Chan[6], Allison Chris[7], Karla Fisher[8], Richard T. Lester[4], John Maxwell[9], James Murray[10], Hong Qian[11], Hubert Wong[11]

1. MAP Centre for Urban Health Solutions, St. Michael's Hospital, Toronto, Canada; 2. Division of Infectious Diseases, St. Michael's Hospital, Toronto, Canada; 3. Department of Medicine, University of Toronto, Toronto, Canada; 4. Scarborough Health Network, Toronto, Canada; 5. Division of Infectious Diseases, Toronto General Hospital; 6. Women's College Hospital, Toronto, Canada; 7. Toronto Public Health, Toronto, Canada; 8. University of British Columbia, Vancouver, Canada; 9. AIDS Committee of Toronto (ACT), Toronto, Canada; 10. AIDS Bureau, Ontario Ministry of Health and Long-Term Care, Toronto, Canada; 11. CIHR Canadian HIV Trials Network, Vancouver, Canada

BACKGROUND

- Integrase strand transfer inhibitors-based regimens have become standard of care for HIV post-exposure prophylaxis (PEP)
- No single tablet regimens recommended in current Canadian guidelines

OBJECTIVES

- Describe 1. tolerability and 2. adherence to bictegravir, emtricitabine and tenofovir alafenamide (BIC/FTC/TAF) as HIV PEP in an ongoing clinical trial of text message support vs standard of care

METHODS

- Design: Descriptive analysis of participants enrolled in an RCT of a text-messaging intervention (Weltel) for supporting PEP follow-up
- Eligibility:
  - HIV-negative adults aged ≥18 years
  - Initiated PEP within past 6 days for sexual exposure
  - Able/willing to receive texts via mobile phone
  - Able to communicate in English
- Recruitment (Figure 1):
  - Information cards given to patients receiving PEP in emergency departments
- Study procedures (Figure 2):
  - At enrollment, participants switched to BIC/FTC/TAF to complete 28 days
  - **Adherence** (#days of PEP taken) assessed via telephone call at week 4
  - **Adverse events** assessed at week 4 and week 13 follow-up visits
  - **HIV status** assessed at baseline, week 6, week 12
- Descriptive analysis of
  - Participant characteristics
  - Adverse events, Adherence, HIV seroconversions

Figure 1: Recruitment card

Figure 2: Study design

PEP initiation Enrollment PEP use Follow-up phase

BIC/FTC/TAF was associated with high tolerability, high adherence and no HIV seroconversions, supporting use of this single tablet regimen as HIV PEP after sexual exposures.

RESULTS

- Of 120 enrolled participants, 1 was HIV seropositive at baseline leaving n=119 included in the analysis.

Table 1: Participant characteristics (n=119)*

RESULTS

- **Tolerability:** Only 10% experienced adverse events of grade ≥2 severity

Table 2: Adverse events occurring in >3% of participants

- **Adherence:** 90/102 or 88% of participants with available data reported completing ≥28 days of PEP

Figure 3: Total number of days of PEP taken

- No HIV seroconversions among n=66 (55%) of participants tested at week 12
- N=28 (23%) of participants initiated on PrEP by final visit
- N=15 (13%) linked to other primary care/mental health providers

DISCUSSION

- **Limitations:**
  - Biomarkers of PEP adherence not done
  - Some AEs may be related to prior PEP drugs since participants switched to BIC/FTC/TAF after a median of 2 (1,3) days of another regimen
- Findings similar to other reports of BIC/FTC/TAF PEP (n=164 total)
  - JAIDS 2022;90:27-32 and Chinese Med J 2022;135(22)
- **Conclusions:**
  - BIC/FTC/TAF PEP was safe, well-tolerated and associated with high adherence and no HIV seroconversions.
  - BIC/FTC/TAF is an appropriate single tablet INSTI-based HIV PEP regimen

CORRESPONDENCE: darrell.tan@gmail.com

ACKNOWLEDGEMENTS

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- DHST holds a Tier 2 Canada Research Chair in HIV Prevention and STI Research

- **Tolerability:** Only 10% experienced adverse events of grade ≥2 severity

Table 2: Adverse events occurring in >3% of participants

Adverse event	Overall N (% of participants)	Severity grade ≥2 N (% of participants)	Any grade, at least possibly related to study drug N (% of participants)
Anorexia	3 (3%)	0 (0%)	3 (3%)
Diarrhea	11(8%)	4 (3%)	10 (8%)
Dizziness	5 (4%)	0 (0%)	5 (4%)
Fatigue	24(20%)	2 (2%)	24 (20%)
Headache	9 (8%)	0 (0%)	9 (8%)
Nausea	14 (12%)	0 (0%)	14 (12%)
Sleep disturbance	6 (4%)	0 (0%)	6 (4%)

- **Adherence:** 90/102 or 88% of participants with available data reported completing ≥28 days of PEP

Figure 3: Total number of days of PEP taken

- Tan DHS, Persaud R, Qamar A, et al. BIC/FTC/TAF as HIV PEP Was Well -Tolerated With High Adherence and No Seroconversions. [Poster 1134]. Paper presented at: Conference on Retroviruses and Opportunistic Infections (CROI); March 3-6, 2024; Denver, Colorado.

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Consider BIC/TAF/FTC?

- Efficacy
  - Animal studies demonstrated up to 91% protection with early initiation.
  - Animal studies suggest improved efficacy with late initation
  - No HIV seroconversions reported in multiple human studies.
- Tolerability
  - Significantly fewer side effects (e.g., diarrhea, fatigue) compared to older PEP regimens.
  - Well-tolerated in both real-world and clinical trial settings.
- Completion Rates:
  - Over 90% regimen completion in multiple studies.
  - Single-tablet regimen enhances adherence.
- Accessibility
  - On most formularies
  - Single manufacturer for patient assistance programs
- Recommended in the NYS AIDS Institute Guidelines and **gaining traction in other jurisdictions**
- Consistent findings across animal, observational, and randomized studies highlight its safety and effectiveness.