

PrEP Update and Interactive Cases

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Learning Objectives

After attending this presentation, learners will be able to:

- Review the latest data on PrEP
- Learn about new candidate PrEP drugs
- Understand how to manage complicated PrEP cases

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Question #1

- Have you prescribed HIV PrEP?

1. Yes

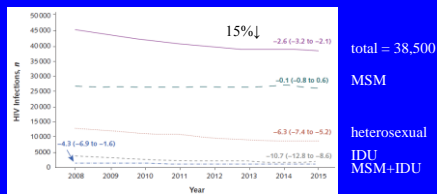
2. No

Question #2

• How do you most commonly prescribe HIV PrEP?

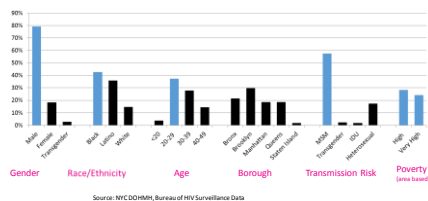
1. TDF/FTC once daily
2. TDF/FTC on demand
3. TAF/FTC once daily
4. TAF/FTC on demand
5. Something else

U.S. HIV Incidence – 2008-2015



Singh Ann Intern Med 2018;168:685

New HIV Diagnoses, NYC, 2017



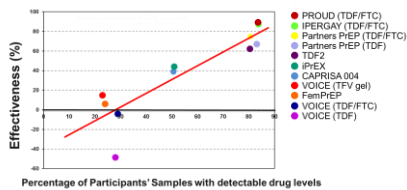
PrEP Approval

Slide #8

- In July 2012, U.S. FDA approves TDF/FTC for pre-exposure prophylaxis (PrEP) in combination with safer sex practices to reduce the risk of sexually acquired HIV-infection in adults at high risk.



Effectiveness of Daily TDF/FTC in Clinical Trials



SS Abouk Karim, personal communication

U.S. Preventive Services Task Force (USPSTF)

Slide #10

Draft: Recommendation Summary (12/18)

Population	Recommendation	Grade
Persons at high risk of HIV acquisition	The USPSTF recommends that clinicians offer PrEP with effective ART to persons who are at high risk of HIV acquisition.	A

Federal Rule: Private Insurance and Medicare must offer A or B services without a co-pay.

Intermittent PrEP (I-PrEP)

Slide #11

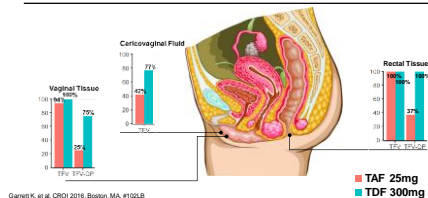
IPREX F/U: Modeling PK in MSM

Using data from a separate PK study:

- 2 doses/week: 76% risk reduction
- 4 doses/week: 97% risk reduction
- 7 doses/week: 99% risk reduction

Anderson Sci Transl Med 2012;4:151ra125.

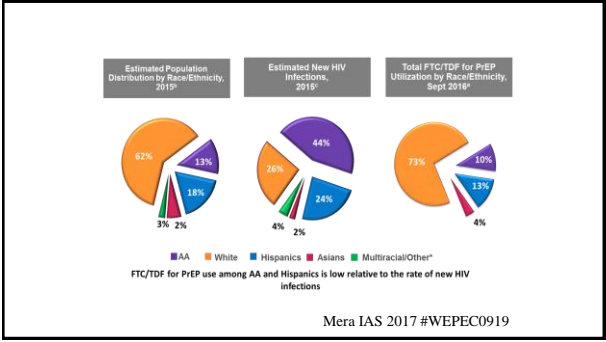
Rates of Detectable TFV/TFV-metabolite detection in Female mucosal tissues – single dose



There were over **77,000 PrEP users** in 2016.



In 2017 → 120,000 PrEP users
In 2019 → 270,000 PrEP users



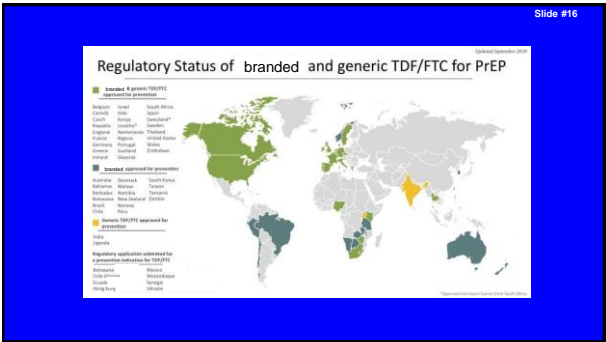
ESTIMATED NUMBER OF ADULTS WHO COULD POTENTIALLY BENEFIT FROM PREP, UNITED STATES, 2015

	Gay, bisexual, or other men who have sex with men	Men who inject drugs	Persons who inject drugs	Total by race/ethnicity
Black/African American, non-Hispanic	309,190	164,660	26,490	500,340
Hispanic/Latino	220,760	46,580	14,920	282,260
White, non-Hispanic	238,670	36,540	28,000	303,230
Total who could potentially benefit from PrEP	813,970	258,080	72,510	1,144,550

Notes: PrEP-eligible population data for "other race/ethnicity" are not shown.

Source: CDC, Behavioral Risk Factor Surveillance System, 2015

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Governor Cuomo's Plan to End AIDS in New York

Slide #17

1. Diagnose HIV and link to care
2. Link, retain and treat to achieve virologic suppression
3. Provide **PrEP** for high-risk people to keep them HIV negative



<http://www.governor.ny.gov/news> October 2014

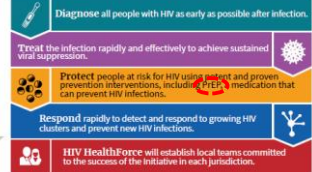
Trump Administration's Plan to End AIDS by 2030

GOAL:

75% reduction in new HIV infections in 5 years and at least 90% reduction in 10 years.



Our goal is ambitious and the pathway is clear – employ strategic practices in the places focused on the right people to:



February 2019

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IS **PrEP** Right FOR ME?




THIS SATURDAY

GMHC

Join Gay Men's Health Crisis (GMHC) for
PrEP Rally
A celebration of
**SEX, HIV PREVENTION,
PRE-EXPOSURE
PROPHYLAXIS (PrEP)
& POST-EXPOSURE
PROPHYLAXIS (PEP)**

Saturday, August 30

Slide #20



PrEP YOURSELF AGAINST HIV.

PrEP YOURSELF AGAINST HIV
A Daily Pill Can Prevent HIV Infection

PrEP is an HIV medicine that is used to prevent yourself from HIV.
 PrEP gives you protection against HIV by blocking the virus.
 PrEP is not a cure for HIV.
 PrEP is not a vaccine.
 PrEP is not a condom.
 PrEP is not a needle.
 PrEP is not a syringe.
 PrEP is not a condom.
 PrEP is not a needle.
 PrEP is not a syringe.

Take an important step to reduce your worry about HIV.
 Ask your doctor about PrEP. For additional information, visit www.cdc.gov/prEP.
 PrEP is available at www.cdc.gov/prEP.
 Call 1-800-458-5231 for more information.
 Or visit www.health.ny.gov/prEP.



Slide #21

CDC HIV PrEP Guidelines (2017)

“Recommended for substantial risk of HIV Infection”

Table 1: Summary of Guidance for PrEP Use

	Men Who Have Sex with Men	Heterosexual Women and Men	Persons Who Inject Drugs
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 HIV prevalence area or network	HIV-positive injecting partner Sharing injection equipment
Clinically eligible	Documented negative HIV test result before prescribing PrEP No signs/symptoms of acute HIV infection Normal renal function; no contraindicated medications Documented hepatitis B virus infection and vaccination status		
Prescription	Daily, continuing, oral doses of TDF/FTC (Truvada), ≥90-day supply		






Slide #22

CDC HIV PrEP Guidelines II (2017)

Table 1: Summary of Guidance for PrEP Use

	Men Who Have Sex with Men	Heterosexual Women and Men	Persons Who Inject Drugs
Other services	Follow-up visits at least every 3 months to provide the following: HIV test, medication adherence counseling, behavioral risk reduction support, side effect assessment, STI symptom assessment. At 3 months and every 6 months thereafter, assess renal function. Every 3-6 months, test for bacterial STIs.		
	Do oral/rectal STI testing	For women, assess pregnancy intent Pregnancy test every 3 months	Access to clean needles/syringes and drug treatment services

WHO Evaluation of PrEP Data

Slide #23

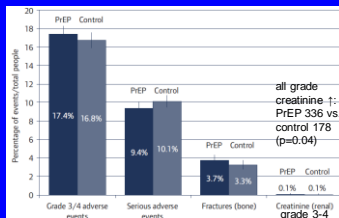
- Efficacy: Effective across groups, genders
- Adherence: Heterogeneous
- Side effects: no more common than placebo (subclinical renal/bone issues)
- Drug resistance: low (0.1%) risk
- Risk compensation: did not increase
- Cost: could be cost-effective/cost-saving
- Logistics: significant concerns

<http://www.who.int/hiv/pub/guidelines/en/irrelease-arc-en>

PrEP Safety: Meta Analysis

Slide #24

13 randomized trials of PrEP vs. placebo (or no rx)
N=15,678



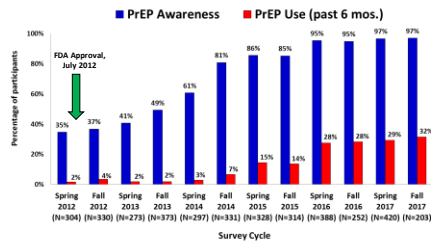
Pilkington J Virus Erad 2018;4:215-224

Case Reports: HIV Infection with High Adherence to PrEP

Slide #25

Patient	PrEP Adherence	Seroconversion	Likely Cause of PrEP Failure
43-yr-old MSM (Knox NEJM 2017)	2 years, supported by hx/ pharmacy records, blood drug concentrations	Acquired MDR-HIV infection	exposure to MDR-HIV strain
MSM in his 20s (Markowitz JAIDS 2017)	excellent (self report), supported by blood/hair drug concentrations	Acquired MDR-HIV infection	exposure to MDR-HIV strain
50-yr-old MSM (Hoarensborg Lancet HIV 2017)	excellent (self report), supported by blood drug concentrations	Acquired wild-type HIV infection; 2-5 condomless anal sex partners/day	chronic rectal inflammation +/- trauma

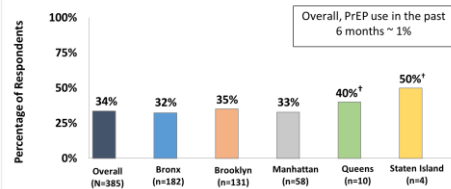
**PrEP Awareness and Use among MSM*, Sexual Health Survey,
Online Sample, NYC, 2012-2017**



*Sample includes sexually active MSM aged 18-40 years and who do not report HIV positive status
Scanlon et al. Unpublished data, 2018



**PrEP Awareness among Black and Latina Women*, Sexual Health Survey,
In-person Sample, NYC, Fall 2017, By Borough of Residence**



*Sample includes sexually active women aged 18-64 years who self-identify as Black and/or Latina and who do not report HIV-positive status; women are recruited in neighborhoods with high HIV diagnosis rates
† Percentage based on very small number of participants; interpret with caution



PrEP in San Francisco: Data

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- Kaiser Permanente Health Care System takes care of >170,000 in San Francisco
- From July 2012-February 2015
 - 1045 referrals for PrEP
 - 835 evaluated for PrEP
 - 657 started PrEP (mean age 37, 99% MSM)
- After 12 months, 50% diagnosed with a sexually transmitted infection
- NO NEW HIV DIAGNOSES!

Volk Clin Infect Dis 2015;61:1601-3



Interim Analysis (1)

- Open-label, prospective cohort study of PrEP in Paris region
- Goal: demonstrate $\geq 15\%$ in HIV in MSM
- Planned study population: N=3000, HIV-neg, high-risk adults (85% MSM), inconsistent condom use, CrCl ≥ 50 , HBsAg (-)
- Choose between TDF/FTC daily or on-demand (and can change)
- f/u every 3 months

Molina IAS 2018 #WEAE0406LB



Interim Analysis (2)

- Results:
 - Study population: N=1628 enrolled, 99% MSM, avg age 36, 85% white, 57% prior PrEP
 - 45% chose daily, 55% chose on-demand, 15% switched at each visit
 - Avg f/u 7 months; >900 pt-yrs of follow-up
 - # sex partners: 15 (daily) vs. 10 (on demand)
 - PrEP use: 98% (daily) vs. 81% (on demand) (89% total)
 - Correct PrEP use: 96% in both groups
 - Condom use: 19% (daily) vs. 22% (on demand)
 - No drug discontinuations for adverse events

Molina IAS 2018 #WEAE0406LB



HIV Incidence (mITT Analysis)

Treatment	Follow-Up Pts-years	HIV Incidence per 100 Pts-years (95% CI)
TDF/FTC (Daily)	443	
TDF/FTC (On Demand)	506	

Mean Follow-up in this Open-Label Cohort: 7 months (SD: 4)

Incidence of study discontinuation:
3.3/100 PY including 1.5/100 PY who discontinued PrEP

85 HIV-infections averted*

* assuming an incidence of 9.1/100 PY as observed in the ANRS Sperm study in Paris

- STI and HIV population effects: pending

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PrEP in NSW, Australia

Slide #32

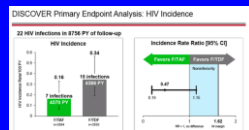
- Expanded PrEP Implementation in Communities in New South Wales (EPIC-NSW)
- Goal: recruit 3700 MSM at high risk of HIV in NSW from 3/16-10/16 in >20 clinics and follow for new HIV infections
- Results:
 - 499 MSM/month recruited
 - Of the first 3700, 97% had f/u HIV test
 - 2 new HIV seroconversions documented
 - both were **OFF** PrEP; rate 0.05/100 (vs. 2/100 expected)
 - 25% ↓ in new HIV in NSW vs. prior year
 - recruitment continues Gardlich Lancet HIV 2018;5:e629-e637

Newer PrEP Agents

study drug	mechanism	dosing route	dosing	PrEP stage
TAF	NRTI	oral	daily	phase 3
maraviroc	CCR5 antagonist	oral	daily	HPTN 069 phase 2
rilpivirine-LA	NNRTI	injectable, SC	once monthly	HPTN 076 phase 2 pilot
cabotegravir	integrase inhibitor	injectable, SC	once every other month	phase 2b/3 studies
monoclonal antibodies	CD4 or gp120 attachment inhibitors	injectable, SC		pilot studies; phase 2b/3 AMP studies

DISCOVER: TDF vs. TAF for PrEP

- Double-blind, non-inferiority PrEP study
- Study population: MSM and TGW (N=5387)
 - median 34 yo, 84% W, 24% L, 16% non-white, 74 TGW
- Study rx: daily oral TDF vs. **TAF**
- Results:
 - 22 incident infections
 - 5 at first visit
 - 15 with ↓ drug levels
 - 2 with adeq. drug levels
 - >57% with STI
 - Improved bone, renal markers with TAF
- Conclusion: TAF non-inferior to TDF for PrEP



Here CROI 2019 #104

Question #3

- With these new data, how will you most commonly prescribe HIV PrEP?
1. TDF/FTC once daily
 2. TDF/FTC on demand
 3. TAF/FTC once daily
 4. TAF/FTC on demand
 5. Something else

HPTN 083: PrEP with TDF/FTC oral vs CAB IM

- Study population: Adult MSM and TGW, at high-risk for HIV acquisition (N=4500)
 - High risk
 - any non-condom receptive anal intercourse (RAI)
 - >5 partners
 - stimulant drug use
 - rectal or urethral STI in past 6 months
- Study regimen: TDF/FTC daily oral vs. CAB q2 month injections
 - double-blind, double-dummy design
- Design: non-inferiority, efficacy study
- U.S. enrollment completed! >3500 enrolled in total globally

PrEP: Pros and Cons

PROS

- Proven efficacy
- CDC + WHO recommended
- Can be highly effective
- Generally well-tolerated
- Drug resistance rare
- Population effects





CONS

- Short-term data
- Daily adherence required
- Side effects
- Drug resistance
- Risk compensation leading to ↓ condoms; ↑ STIs
- Cost and logistics

Acknowledgments

Slide #38

- Cornell HIV Clinical Trials Unit (CCTU)
- Division of Infectious Diseases
- Weill Cornell Medicine
- AIDS Clinical Trials Group (ACTG)
- Division of AIDS, NIAID, NIH
- The patient volunteers!
- Demetre Daskalakis, Raphy Landovitz, Ken Mayer



PrEP Cases

Slide #39

Panelists

Gerald Friedland
Rajesh Gandhi
Sharon Nachman
Michael Saag
Magdalena Sobieszczuk

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Slide #41

Case 1: FC

- 34 yo gay man
- HIV-negative
- 10-year partner is HIV+ on ART with VL <20 consistently
- Requests HIV PrEP
- Physical examination: normal
- Baseline creatinine 0.8, urinalysis negative

Slide #42

Question

What do you recommend?

1. Take more history
2. No PrEP
3. Daily TDF/FTC
4. On-demand TDF/FTC
5. Daily TAF/FTC
6. On-demand TAF/FTC

Slide #43

FC

- Further history reveals that the couple is monogamous and have not used condoms “in years”.

Question

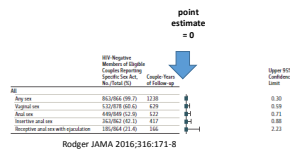
Slide #44

Now, what do you recommend?

1. No PrEP
2. Daily TDF/FTC
3. On-demand TDF/FTC
4. Daily TAF/FTC
5. On-demand TAF/FTC

PARTNER Study: Prospective Cohort Study

- 1166 serodifferent couples from 14 European countries
 - 62% heterosexual, 38% homosexual
 - Median f/u 1.3 years
 - ~58,000 condomless sex acts
 - No PrEP or PEP use in HIV- partners
 - Result: NO linked infections



Opposites Attract Study: Observational Cohort

- 343 serodiscordant MSM couples in Australia, Brazil, Thailand
 - No exclusion for ART use, VL <200, or PrEP use
- Median f/u 1.7 years
- ~16,800 condomless sex acts
- Result: NO new linked infections

Bavinton Lancet HIV 2018;5:438-47

So, does U=U?



People who take ART daily as prescribed and achieve and maintain an undetectable viral load have effectively no risk of sexually transmitting the virus to an HIV-negative partner.

September, 2017



Science Validates Undetectable =
Untransmittable HIV Prevention Message

[NIAID Now](#) | July 22, 2018

People living with HIV whose virus is completely, durably suppressed by treatment will not sexually transmit the virus to an HIV-negative partner, according to NIAID Director Anthony S. Fauci, M.D.



Question

Slide #49

Routine rectal Chlamydia NAT test+

Besides STD treatment with ceftriaxone and azithro, what do you recommend?

1. Start PrEP – he's having unsafe sex
2. Start PrEP – his partner is having unsafe sex
3. Start PrEP and consider couples counseling
4. No PrEP

Slide #50

Case 2: RP

- 47 yo woman
- HIV-negative
- No prior history of kidney disease
- HIV+ male partner, not on ART
- Requests HIV PrEP
- Physical examination: normal
- Baseline creatinine 1.0, urinalysis negative

Slide #51

Question

What do you recommend?

1. Daily TDF/FTC
2. On-demand TDF/FTC
3. Daily TAF/FTC
4. On-demand TAF/FTC
5. Continue condoms -- no PrEP

Slide #52

RP

- Prescribed TDF/FTC daily
- Routine follow-up at 3 months
 - HIV Ag/Ab (4th generation) negative
 - creatinine 1.2 mg/dl
 - Calculated creatinine clearance 56 cc/min
 - Urinalysis negative
 - Urine culture negative

Question

Slide #53

What do you recommend?

1. Continue daily TDF/FTC
2. Change TDF/FTC to every other day
3. Change TDF/FTC to “on-demand” dosing
4. Change to daily TAF/FTC
5. Discontinue PrEP

RP

Slide #54

One month later...

- Feels “dehydrated”
- Taking NSAIDs for knee pain
- Creatinine ↑ 1.4
- Calculated creatinine clearance ↓ 45
- BP normal
- Urinalysis negative
- Renal USG negative

Question

Slide #55

In addition to encouraging hydration and holding NSAIDs, what do you recommend?

1. Continue daily TDF/FTC
2. Change TDF/FTC to every other day
3. Change TDF/FTC to “on-demand” dosing
4. Change to daily TAF/FTC
5. Discontinue PrEP

RP

Slide #56

- Changed to every other day TDF/FTC
- Repeat labs
 - Creatinine 1.03 mg/dl
 - Calculated creatinine clearance >60 cc/min
 - Serum phosphate normal
 - Urinalysis negative
- Changed back to daily TDF/FTC

RP

Slide #57

- 4 months later....
 - HIV Ag/Ab (4th generation) negative
 - Creatinine 1.08 mg/dl
 - Calculated creatinine clearance >60 cc/min
 - Urinalysis negative

Case 3: AC

Slide #58

- 27 yo gay man
- Baseline HIV Ag/Ab test negative
- Starts PrEP with daily TDF/FTC
- Reports excellent adherence
- Intermittently uses condoms
- Week 4: HIV Ag/Ab test negative
- Week 12: HIV Ag/Ab test negative
- Week 24: HIV Ag/Ab test positive, Immunoblot for HIV-1 and HIV-2 negative, HIV RNA <20 copies/ml

Question

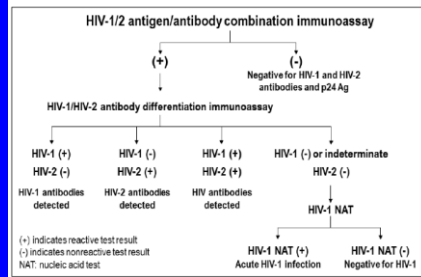
Slide #59

What is your interpretation?

1. He's not infected -- this is a false positive Ag/Ab test.
2. He is infected -- this is a false negative Immunoblot test.
3. He is infected -- PrEP has decreased the HIV RNA level.
4. I need more information.

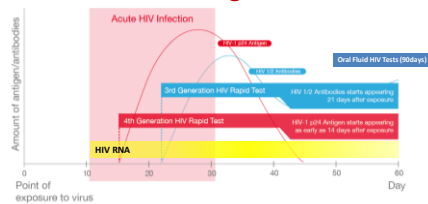
Recommended Laboratory HIV Testing Algorithm for Serum or Plasma Specimens

Slide #60



CDC 6/14

Timeline Following HIV Infection



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AC

Slide #62

Repeat testing 1 week later shows:

- HIV Ag/Ab test positive
- Immunoblot for HIV-1 and HIV-2 negative
- HIV RNA <20 copies/ml

Question

Slide #63

Now what?

1. Continue PrEP and retest
2. Add a PI to his PrEP and retest
3. Add an II to his PrEP and retest
4. Stop PrEP and retest

Managing Ambiguous HIV Tests in PrEP

Slide #64

Possible Strategy	Pros	Cons
Continue PrEP	If adherent, low pre-test probability of HIV; ↓ risk of HIV infection	If infected, may select drug mutations
Start ART (PrEP + PI or II)	If infected, prevent drug resistance and ↓ seeding of reservoirs	If uninfected, unnecessary ART exposure; diagnosis and insurance issues
Discontinue PrEP	May facilitate diagnosis quickly by allowing HIV replication	If uninfected, ↑ risk of HIV infection

Smith OFID; 2018;5:ofy180

Case #3 Follow-up

Slide #65

- Off PrEP, repeat testing shows:
- HIV Ag/Ab test negative
- HIV Ag/Ab DIFFERENT test negative
- Immunoblot for HIV-1 and HIV-2 negative
- HIV RNA <20 copies/ml
- HIV DNA negative

Question-and-Answer

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