


**Antiretroviral Prophylaxis:
nPEP and PrEP**

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"The findings and conclusions in this presentation have not been formally dissemination by CDC and should not be construed to represent any agency determination or policy."



Disclosure

I have no real or perceived vested interests that relate to this presentation nor do I have any relationships with pharmaceutical companies, biomedical device manufacturers, and/or other corporations whose products or services are related to pertinent therapeutic areas.

Learning Objectives

- Identify when and how best to use nPEP in family planning settings
- Assess the potential for PrEP use in family planning settings to reduce HIV infection rates

Antiretroviral prophylaxis

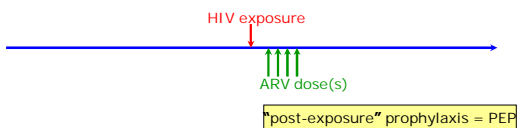
- Similar to prophylaxis for other infectious diseases
 - TB
 - Malaria
- Indicated only for those at high risk of HIV acquisition
 - nPEP – infrequent individual risk events
 - PrEP – ongoing risk events

Estimated Per-Act Risk for Acquisition of HIV by Exposure Route

Exposure Route	Risk per 10,000 exposures
Blood transfusion	9,000
Needle-sharing injection drug use	67
Receptive anal intercourse	50
Percutaneous needle stick	30
Insertive penile-vaginal intercourse	10
Receptive penile-vaginal intercourse	10
Insertive anal intercourse	6.5
Receptive oral intercourse	1
Insertive oral intercourse	0.5

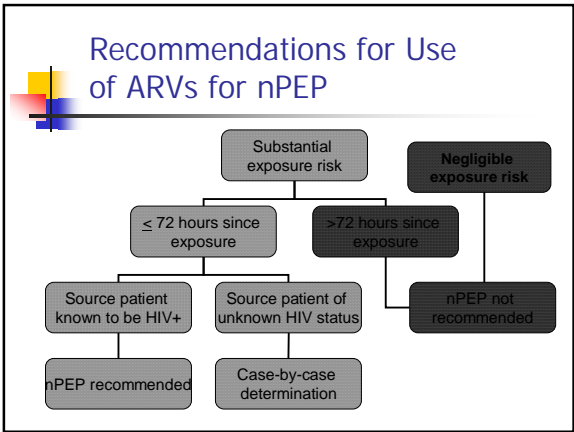
Centers for Disease Control and Prevention. Antiretroviral postexposure prophylaxis after sexual, injection-drug use, or other nonoccupational exposure to HIV in the United States: recommendations from the U.S. Department of Health and Human Services. MMWR. 2005;54(No. RR-2):1-22.

What is PEP?



Assessing Risk of HIV Exposure

<p>Substantial Risk of HIV Exposure</p> <p><u>Exposure of:</u></p> <ul style="list-style-type: none"> ■ vagina, rectum, eye, mouth or other mucous membrane, nonintact skin, or percutaneous contact <p><u>With:</u></p> <ul style="list-style-type: none"> ■ blood, semen, vaginal secretions, rectal secretions, breast milk, or any body fluid that is visibly contaminated with blood <p style="text-align: center; color: red;">When the source is known to be HIV infected</p>	<p>Negligible Risk of HIV Exposure</p> <p><u>Exposure of:</u></p> <ul style="list-style-type: none"> ■ vagina, rectum, eye, mouth or other mucous membrane, intact or nonintact skin, or percutaneous contact <p><u>With:</u></p> <ul style="list-style-type: none"> ■ urine, nasal secretions, saliva, sweat, or tears if not visibly contaminated with blood <p style="text-align: center; color: red;">Regardless of the known or suspected HIV status of the source</p>
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Barriers to effective nPEP use in family planning settings

- Limited awareness in potential user groups
- Recognizing eligible exposures within 72 hours
- Financing the medication
- Managing medication side effects and adherence
- Completion of 28d course*, especially in sexual assault survivors

* Bryant J, Baxter L, and Hird S. Non-occupational postexposure prophylaxis for HIV: a systematic review. Health Technol Assess. 2009;13(14). DOI:10.3310/hta13140

What is PrEP?

"pre-exposure prophylaxis" = PrEP

The diagram illustrates the concept of PrEP. A horizontal blue line represents time. Above the line, several red arrows point downwards, labeled "HIV exposures". Below the line, a series of green vertical bars represent "ARV dose(s)", showing a continuous regimen of antiretroviral therapy.

Why consider PrEP?

- Need more than condoms and counseling
- Effective microbicides and vaccines still years away
- Evidence of prophylaxis efficacy
 - In monkey studies
 - For PMTCT
 - Occupational PEP
- Antiretrovirals with desirable features available
 - Highly effective in blocking HIV replication
 - Daily dosing
 - Favorable toxicity/side effect profile
 - Favorable resistance profile

Infection per exposure: CDC Macaque studies

	Infections	Total exposures	Infection/exposure	Ratio to controls
Controls (n = 18)	17	83	0.21	1
TDF (n = 4)	3	35	0.09	2.3
Oral TDF/FTC (n = 6)	2	77	0.026	8.1

CDC, unpublished

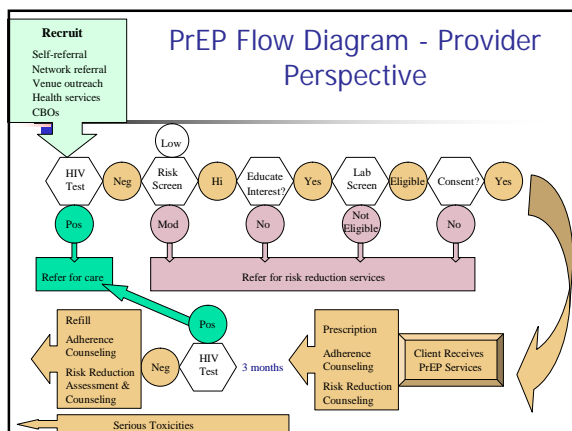
Why think about implementation now?

- Interim analyses in late 2009
- Final analyses 2010-2011
- Examples:
 - PMTCT - rapid implementation and roll-out
 - Male circumcision – unprepared
- Implementation will be complex and involve many sectors and partners

Who are most at risk?

	MSM	MSM/IDU	IDU	HET	Other	Total
AA	10,130 (19)	690 (1)	3,480 (6)	10,630 (20)	-	24,930 (46)
H	5,360 (10)	360 (1)	1,130 (2)	2,880 (5)	-	9,720 (18)
W	13,230 (24)	1,050 (2)	2000 (4)	3,300 (6)	-	19,580 (36)
Other	-	-	-	-	-	-
Total	28,720 (53)	2,100 (4)	6,610 (12)	16,800 (31)	-	54,230

Subpopulation Estimates from the HIV Incidence Surveillance System - United States, 2006. MMWR, September 12, 2008 / 57(36):985-989



In progress...

PrEP Implementation Planning

■ Goals

- To be prepared for
 - Rapid
 - Consensus-based
 - Effective and safe
 - Affordable and accessible
 - PrEP implementation in persons/populations most at risk for acquisition (MARA) of HIV
- In order to maximize reduction in new HIV infections

DHAP Planning activities

- PIP Working Group
 - Multiple DHAP branches and other CIOs
 - Frequent updates for Division and Center leadership
- Develop planning
 - Logic model
 - Task-specific subgroups and timelines
- External discussions (small meetings)
 - Guidelines development (Mar 08)
 - Funding reimbursement (Apr 08, Feb 09)
 - Ethics (Nov 08)
 - Network Models (Nov 08)
 - Evaluation framework (Nov 08)
 - Discordant couples and pregnancy (Feb 09)
- Outreach and community preparedness
- Begin development of toolkits
- Plan for implementation pilots
- Begin implementation research

Estimated Annual Drug Cost (US)

	Viread® TDF	Truvada® TDF+FTC
Pharmacy	\$7,200	\$10,800
Public Health Price	\$3,600	\$6,600



Financing

- Lower public health pricing of drug available
- Counseling/education often not reimbursable
- Ryan White and ADAP limited by law to HIV+ persons
- Medicaid of limited use (if at all)
- Employers/private insurers may be reluctant to cover cost for stigmatized behaviors
- Many PrEP eligible persons will be un/underinsured
- Economic disparity barrier to reducing existing racial/ethnic disparities in HIV infection



Points to Consider about Preventing Resistance

- Most on drug stay uninfected, no virus present
- Drugs chosen in part for lower resistance risk
 - Long plasma and intracellular half lives
 - Hi concentration at sites of exposure
 - TDF has high barrier to resistance
 - TDF + FTC complementary resistance profiles
- In minority who seroconvert on PrEP
 - Virus may respond to PREP drugs for treatment
 - May be less infectious



Potential nPEP and PrEP users

- HIV uninfected persons
 - With a sexual partner known to be HIV+
 - with frequent partner change or concurrency
 - with partner(s) at high risk of HIV infection (e.g. injection drug users, non-monogamous)
 - With other evidence of risk (e.g., frequent STD or unwanted pregnancies)
- Unable to (consistently) use other prevention modalities



Resources for more information

- nPEP
 - <http://aidsinfo.nih.gov/guidelines/>
 - National HIV Clinicians' Consultation Center
 - <http://www.nccc.ucsf.edu/>
 - National Clinician's Postexposure Hotline
 - 1-888-HIV-4911
- PrEP
 - <http://www.cdc.gov/hiv/resources/qa/prep.htm>
 - <http://www.prepwatch.org>



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