Pre-Exposure Prophylaxis: The New Frontier of Prophylaxis Against HIV Infection

William F. Ryan Community Health Network
PrEP Network Coordinator: Trevor Hedberg, MPH, CPH
Supervising Health Educator: Michael Slater

NYNJ AETC
AIDS EDUCATION & TRAINING CENTER

RYAN CENTER
William F. Ryan Community Health Center Network

HIV CEI
CLINICAL EDUCATION INITIATIVE
Learning Objectives

• To understand the rationale and indications pre-exposure prophylaxis (PrEP) against HIV infection
• To understand the clinical approach towards pre-exposure prophylaxis against HIV infection
• To understand and apply current guidelines for HIV pre-exposure prophylaxis in day-to-day clinical practice
• To understand effective PrEP in-reach and outreach strategies
Definitions

• Pre-exposure prophylaxis (PrEP): biomedical intervention which is taken prior to any potential exposure to HIV infection, to prevent HIV infection.

• Post-exposure prophylaxis (PEP): biomedical intervention which is taken after potential exposure to HIV infection, to abort infection before it becomes established in the host.

• The mechanism of actions of PEP and PrEP may or may not be the same, and may involve eradication of viral infection at the site of exposure, before infection disseminates and becomes permanently established.

• Although still evolving, PrEP is now a standard of care in the United States.
Rationale for Prophylaxis: Pathogenesis

• “Window of opportunity,” when PrEP may prevent HIV infection from becoming established:
  – **First 24 hours after initial exposure**: dendritic cells in the mucosa and at other sites of exposure are initial targets of HIV.
  – **24-48 hours after initial exposure**: migration of infected dendritic cells to regional lymph nodes, where viral replication begins.

• **3-5 days after initial exposure**: virus is detectable in peripheral blood, and infection is established permanently.
Exposure to HIV at mucosal surface or other exposure site

Virus collected by dendritic cells, carried to lymph node

HIV replicates in CD4 cells, released into blood

Virus spreads to other organs (brain, genital secretions)

Rationale of Prophylaxis

• The goals of PrEP:
  – To suppress viral replication that may occur at site of exposure
  – To shift the biologic advantage to the host cellular immune system, to prevent or abort early infection

• A small study of HCWs exposed percutaneously to HIV, but who did not seroconvert, suggested that limited viral replication can occur without establishment of infection.
  – HIV-specific T-cell proliferative responses were found in a majority exposed HCWs, suggesting that there was HIV replication in tissue macrophages.
  – That limited viral replication occurs early in infection is another justification for use of ARVs in PrEP regimens.
The Epidimiologic Urgency for PrEP

• The number of new HIV infections in the USA has remained at about 50,000 per year, an incidence that has not changed for the past 20 years.
  – 27% of new infections were in heterosexual men and women, 64% in MSM, including 3% in MSM who inject drugs.
  – 75% of new infections are in men.
  – MSM have a 19.3-fold higher odds of HIV infection on all continents.
  – HIV incidence in black men is 8 times higher than in whites.
  – HIV incidence in Hispanic men is 3 times higher than in whites.

• Unprotected anal sex in MSM (2% of the population over age 13) accounts for 56-61% of new HIV infections annually.

• New HIV infections in MSM 13-29 years of age increased 38% from 2006 to 2009, largely due to a 48% increase among young black MSM.

• The efficacy of early ART and PrEP is over 90% if these modalities are used consistently: adherence is key to efficacy.
Interventions to Prevent HIV Infection

- **Condoms**
  - Approximately 85% efficacy if used correctly and consistently; however, consistent condom use is unusual.
  - Intensive promotion of condoms is not associated with reductions in HIV risk.

- **Circumcision: 51-60% effective in heterosexual African men**
  - A single simple intervention that is the most cost-effective, evidence-based method of HIV prevention to date
  - Decreases susceptibility of the penis to HIV, but does not decrease infectiousness of HIV-infected men

- **Needle exchange**

- **HAART to prevent infectiousness of HIV-infected people:**
  - > 96% efficacy in HPTN 052 trial

- **ARVs to reduce susceptibility of uninfected people:** the current meaning of PrEP.
PrEP Clinical Trials
**PrEP Clinical Trials: Summary**

- Three randomized, placebo-controlled trials have found that PrEP with TDF/FTC (tenofovir/emtricitabine) can prevent HIV infection, with efficacy rates from 44-75%:
  - iPrEx trial of MSM
  - Partners PrEP of serodiscordant African couples
  - TDF2 trial of young adult men and women in Botswana
- Efficacy in the above three trials was strongly correlated with PrEP adherence, as measured by detectable drug concentrations.
  - In iPrEx and Partners PrEP, detectable drug levels were associated with a 90% reduction in risk of acquiring HIV.
  - Perfect adherence was not necessary to have detectable drug levels: 100% of subjects taking TDF/FTC twice a week had detectable levels.
<table>
<thead>
<tr>
<th>Study (location)</th>
<th>Population</th>
<th>Design</th>
<th>Relative RR</th>
<th>Efficacy relative to drug detection in plasma or PBMCs</th>
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<tbody>
<tr>
<td><strong>iPrEx (Ecuador, Peru, Brazil, South Africa, Thailand, the USA)</strong></td>
<td>2499 MSM or transgendered women</td>
<td>Randomized 1:1 to daily TDF–FTC or placebo</td>
<td>RR of 44% (95% CI: 14–63%; p = 0.005)</td>
<td>RR of 92% (95% CI: 40–99%)</td>
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<tr>
<td><strong>Partners PrEP (Kenya, Uganda)</strong></td>
<td>4747 heterosexual serodiscordant couples</td>
<td>Randomized 1:1:1 to daily TDF or TDF–FTC or placebo</td>
<td>TDF: RR of 67% (95% CI: 44–81%; p &lt; 0.001) TDF–FTC: RR of 75% (95% CI: 55–87%; p &lt; 0.001)</td>
<td>TDF: 86% (95% CI: 57–95%) TDF–FTC: 90% (95% CI: 56–98%)</td>
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<tr>
<td><strong>TDF2 (Botswana)</strong></td>
<td>1219 heterosexual men and women</td>
<td>Randomized 1:1 to daily TDF–FTC or placebo</td>
<td>RR of 62% (95% CI:22–83%; p = 0.03)</td>
<td>Risk reduction of 78% (95% CI: 41–94%) among participants in the 'as-treated' analysis</td>
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<tr>
<td><strong>FEM-PrEP (Kenya, Tanzania, South Africa)</strong></td>
<td>2120 heterosexual women</td>
<td>Randomized 1:1 to daily TDF–FTC or placebo</td>
<td>Study terminated early due to lack of effect</td>
<td>Less than 40% of participants had evidence of recent drug use</td>
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<tr>
<td><strong>VOICE (Uganda, South Africa, Zimbabwe)</strong></td>
<td>5029 heterosexual women</td>
<td>Randomized 1:1:1:1:1 to oral TDF, TDF–FTC, or placebo or daily vaginal tenofovir gel or placebo gel</td>
<td>Oral TDF and tenofovir gel arms terminated early due to lack of effect. TDF–FTC arm completed but showed no risk reduction</td>
<td>Drug was detected in only 28–29% of participants taking oral TDF or TDF–FTC</td>
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<tr>
<td><strong>Bangkok Tenofovir Study (Thailand)</strong></td>
<td>2413 males and females who inject drugs</td>
<td>Randomized 1:1 to TDF or placebo</td>
<td>RR of 48.9% (95% CI: 10–72%; p = 0.01)</td>
<td>RR of 70% (95% CI: 2–91%; p = 0.04)</td>
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Current CDC Guidelines for PrEP
Background: FDA Approval of TDF/FTC PrEP

- July 16, 2012: FDA panel recommended TDF/FTC for prevention of sexually acquired HIV infection, for the following people:
  - HIV-uninfected MSM (19-3 vote in favor)
  - HIV-uninfected partners in serodiscordant couples (19-2 in favor with 1 abstention)
  - Others, e.g., sex workers, who are at risk for HIV infection via sexual activity (12-8 in favor with 2 abstentions)
  - June 2013: The CDC added IDUs as a high-risk group for whom TDF/FTC PrEP should be considered.

- The panel favored monthly HIV testing and regular monitoring of renal function. Importance of strict daily adherence was stressed.
  - Gilead was asked to design a risk evaluation and mitigation strategy (REMS) to monitor side effects and risks of resistance if the patient becomes infected while on TDF/FTC.
Background: FDA Approval of TDF/FTC PrEP

• The FDA emphasized that TDF/FTC PrEP is approved for use as a part of a comprehensive HIV prevention strategy that includes other prevention methods, such as safe sex, risk reduction counseling, and regular HIV testing.

• The cost of TDF/FTC is $13,000 a year.
  – Annals of Internal Medicine: PrEP is cost-effective, but only if limited to high-risk MSM (≥ 5 male partners/year).

• Both the NY State AIDS Institute and the CDC have developed PrEP guidelines.

• Two interim guidelines were initially released by the CDC: 1) January 28, 2011: for MSM, and 2) August 10, 2012: for heterosexually active adults. Except for special discussion of pregnancy and PrEP in the latter release, these two guidelines are identical in both details and general policy.

• CDC Clinical Practice Guidelines were released in 2014.
• Daily oral PrEP with the fixed-dose combination of tenofovir disoproxil fumarate (TDF) 300 mg and emtricitabine (FTC) 200 mg has been shown to be safe and effective in reducing the risk of sexual HIV acquisition in adults.

• Currently the data on the efficacy and safety of PrEP for adolescents are insufficient. Therefore, the risks and benefits of PrEP for adolescents should be weighed carefully in the context of local laws and regulations about autonomy in health care decision-making by minors.

• Acute and chronic HIV infection must be excluded by symptom history and HIV testing immediately before PrEP is prescribed. HIV infection must be ruled out every 3 months while the patient is taking PrEP.

• Renal function should be assessed at baseline and monitored at least every 6 months while patients are taking PrEP.
2014 CDC Summary of Guidance for PrEP

• Effective risk-reduction services/counseling and adherence counseling should be provided at every visit.

• TDF alone has shown substantial efficacy and safety in trials with IDUs and heterosexually active adults and can be considered as an alternative regimen for these populations, but not for MSM, among whom its efficacy has not been studied.

• The use of other antiretroviral medications for PrEP, either in place of or in addition to TDF/FTC (or TDF) is not recommended.

• The prescription of oral PrEP for coitally-timed or other noncontinuous daily use is not recommended.
2014 CDC Indications for PrEP for MSM

- Adult man
- Without acute or established HIV infection
- Any male sex partners in past 6 months (if also has sex with women, see next slide)
- Not in a monogamous partnership with a recently tested, HIV negative man

AND at least one of the following:

- Any anal sex without condoms (receptive or insertive) in past 6 months
- Any STI diagnosed or reported in past 6 months
- Is in an ongoing sexual relationship with an HIV positive male partner
2014 CDC Indications for PrEP
By Heterosexually Active Men and Women

- Adult person
- Without acute or established HIV infection
- Any sex with opposite sex partners in past 6 months
- Not in a monogamous partnership with a recently tested HIV negative partner

AND at least one of the following:

- Is a man who has sex with both women and men (behaviorally bisexual) [also evaluate indications for PrEP use by MSM criteria, above]
- Infrequently uses condoms during sex with 1 or more partners of unknown HIV status who are known to be at substantial risk of HIV infection (IDU or bisexual male partner)
- Is in an ongoing sexual relationship with an HIV-positive partner
2014 CDC Indications for PrEP By IDUs

• Adult person
• Without acute or established HIV infection
• Any injection of drugs not prescribed by a clinician in past 6 months

AND at least one of the following:

• Any sharing of injection or drug preparation equipment in past 6 months
• Been in a methadone, buprenorphine, or suboxone treatment program in past 6 months
• Risk of sexual acquisition (also evaluate by above MSM and heterosexual criteria)
May 2014 Updated CDC Guidelines for PrEP

• Healthcare providers should consider advising the use of oral ARV therapy for HIV-uninfected patients who are at high risk for HIV infection.

• General principles:
  – PrEP must be targeted to persons at very high risk of HIV infection, e.g., partners of HIV-infected people.
  – The importance of adherence and its effect upon protection must be carefully discussed with the patient.
  – PrEP must not be started in anyone with symptoms of the acute retroviral syndrome, or in anyone known to be HIV-infected.
  – Although there have not been any known adverse effects upon infants exposed to TDF/FTC in utero and with breast feeding, data are incomplete for women in discordant couples who take TDF/FTC for PrEP.
May 2014 Updated CDC Guidelines for PrEP (2)

• General principles (continued):
  – To help protect the HIV-uninfected partner in discordant couples who are attempting to conceive, PrEP use may be one of several options.
  – PrEP must be part of a comprehensive set of prevention services, including risk reduction, adherence counseling, and ready access to condoms.
  – STI screening must be done every 6 months, with treatment provided as indicated.
  – At each 3 month visit, there must be monitoring of HIV status, pregnancy status, side effects, adherence, and risk behaviors.
May 2014 Updated CDC Guidelines for PrEP (3)

• Before initiating PrEP:
  – Confirm that patient is at substantial, ongoing, high risk for acquiring HIV infection.
  – Document negative HIV test immediately before starting PrEP.
  – Rule out acute HIV infection if patient has consistent symptoms or has had unprotected sex with an HIV-infected person in the prior month.
  – Determine if women are pregnant, plan to become pregnant, or are breastfeeding.
    • Do not prescribe PrEP to breastfeeding women.
    • Inform women that PrEP safety for infants exposed during pregnancy is not known, although no harm has been reported.
May 2014 Updated CDC Guidelines for PrEP (4)

• Before initiating PrEP (continued):
  – If any sexual partner is known to be HIV-infected, determine if he/she is in care, and if not, facilitate linkage to care.
  – Confirm that calculated $C_{\text{creat}}$ is $\geq 60\text{mL/minute}$ (Cockcroft Gault).
  – Screen for HBV infection and vaccinate if susceptible; if HBV-infected, consider treatment.
  – Screen and treat as needed for STIs.
  – Rule out medical comorbidities, e.g., renal or bone disease, which might contraindicate use of ARVs.
May 2014 Updated CDC Guidelines for PrEP (5)

- **Beginning PrEP medication regimen:**
  - Prescribe one tablet of Truvada (TDF/FTC) daily.
  - Prescribe no more than a 90 day supply, renewable only after HIV testing confirms that the patient remains HIV-uninfected.
  - For women, ensure that the pregnancy test is negative, or if pregnant, that the patient has been informed about current knowledge of risks/benefits.
  - Provide risk-reduction and PrEP medication adherence counseling and condoms.
  - Educate patient about symptoms of acute HIV infection, with instructions to return ASAP for evaluation if they occur.
May 2014 Updated CDC Guidelines for PrEP (6)

- Follow-up while on PrEP:
  - HIV test every 2-3 months.
  - For women, obtain pregnancy test; if pregnant, discuss continued use of PrEP with patient and prenatal care provider.
  - Evaluate and support PrEP medication adherence at every visit, more often if needed.
  - Monitor for TDF/FTC side effects (most common: GI symptoms, headache, weight loss)
  - Every 2-3 months, assess risk behaviors and provide risk reduction counseling and condoms.
  - Screen for symptoms of acute HIV infection.
  - Screen for STIs every 6 months, even if asymptomatic.
  - 3 months after PrEP initiation and then every 6 months while on PrEP: check creatinine and calculate creatinine clearance.
May 2014 Updated CDC Guidelines for PrEP (7)

• Other medications or other dosing schedules have not yet been shown to be safe and effective, and are not FDA-approved.

• What not to use for PrEP:
  – Do not use other ARVs, e.g. 3TC, in place of or in addition to TDF or TDF/FTC
  – Do not use dosing other than daily dosing, i.e., intermittent or on-demand PrEP
  – Do not use PrEP as expedited partner therapy, i.e., for an uninfected partner who is not in your care
May 2014 Updated CDC Guidelines for PrEP (8)

- Discontinuing PrEP (at patient request, for safety concerns, or if HIV infection is acquired):
  - HIV test to confirm whether HIV infection has occurred.
  - If HIV-infected, **obtain resistance assay** and establish linkage to HIV care.
  - If HIV-uninfected, establish linkage to risk-reduction support services as needed.
  - If HBV-infected, consider appropriate medication for continued treatment of HBV.
  - If pregnant, inform prenatal provider about PrEP use, and coordinate care to maintain HIV prevention during pregnancy and breastfeeding.
New York State PrEP Guidelines

PrEP: Unanswered Questions

• When to stop PrEP
• Who should provide PrEP
• How frequently HIV and renal function testing is necessary
• The frequency of dosing and whether dosing should be regular, e.g. daily, or timed with sexual activity
  – Pending ANRS IPERGAY and HPTN 067 trials will study nondaily use of PrEP.
• How best to ensure adequate adherence
• Who will pay for PrEP
• Whether PrEP should differ according to rectal, vaginal, and penile exposure
  – After oral TDF, rectal drug levels are higher than vaginal levels.
Summary

• Pending further data and direction, PrEP should be considered only for people at high risk of acquisition of HIV infection, e.g., high-risk MSM, uninfected partners of serodiscordant couples, IDUs, and certain bisexuals and heterosexuals, according to CDC criteria.

• PrEP involves much more than just risk assessment and provision of prophylactic medication:
  – The patient must understand the importance of adherence and close follow-up, including follow-up HIV testing and other laboratory tests, as indicated by the clinical situation.
  – Adherence education, review/management of side effects, risk reduction counseling, STI screening, consideration of acute HIV infection, and psycho-social support should be provided at every visit.
  – Patients who are HIV-infected must be linked to care ASAP.
PrEP Services in the William F. Ryan Community Health Network
PrEP Services

• The Ryan Network has been providing PrEP services since January 2014.
• It currently has three clinical sites that provide PrEP and PEP services
  – William F. Ryan Community Health Center (97th Street and Amsterdam Avenue)
  – Ryan-Chelsea-Clinton Community Health Center (46th Street and 10th Avenue)
  – Ryan-NENA Community Health Center (East 3rd Street between Avenues C and D)
PrEP Services

• Non-medical staff typically meet with a prospective PrEP client to provide an Intake and Eligibility Screening and rapid HIV test

• If the client is deemed an appropriate candidate they are scheduled with a provider for an initial medical visit

• Upon approval of baseline labs, the provider will initiate the client on PrEP and schedule them for their follow-up medical visit
Ryan-Chelsea-Clinton Community Health Center
medical staff
Patient Flow

Providing PrEP at Ryan
Patient Services Department Guide

Background
In 2014, the Ryan Network began providing Pre-Exposure Prophylaxis (PrEP) services across all clinics, with most of the services provided at 39th St, RCC, and NENA. PrEP is imperative to reduce the spread of HIV. Governor Andrew Cuomo included the provision of PrEP in the Ending the Epidemic Blueprint as key in helping New York State reduce the number of new HIV infections to 750 per year (see the WS BluePrint to end AIDS 2019 attachment).

In 2015, the Ryan Network developed a step-by-step procedure to streamline PrEP services (see Providing HIV Pre-Exposure Prophylaxis procedures 2015.07 and RCC PrEP procedures final July 2015). Below are steps for Patient Services Representative (PSR) staff to follow should a patient walk into the Center and request PrEP services or presents for a scheduled appointment for PrEP services.

Option 1: Patient arrives at a Ryan clinic for a scheduled PrEP Eligibility Screening visit (scheduled as a HIV testing visit) with designated point person at each site:
- WRIR-97th St = Gloria Santos or Trevor Hedberg if Gloria cannot be reached
- RCC = Victor Hogue
- NENA = Stephanie Suh (Please refer to Silvana Quintana while Stephanie Suh is on maternity leave)

Step 1: Registration
- If the patient is new to Ryan, Registration PSR must register patient and then direct the patient to the Cashiers.
- If the patient is a known Ryan patient, the patient proceeds directly to the Cashiers.

Step 2: Checking-in the patient
- Check patients in for their scheduled PrEP Eligibility Screening visit (scheduled as a HIV testing visit) and direct the patient to the Waiting Area.

*Please Note: As with all other HIV testing visits, the Care Technician conducting the HIV test will input the appropriate payment information for the visit*

Option 2: For patients seeking PrEP services on a walk-in basis:

Step 1: Registration
- If the patient is new to Ryan, Registration PSR must register patient and then direct the patient to the Cashiers.
- If the patient is a known Ryan patient, the patient proceeds directly to the Cashiers.

Step 2: Scheduling and Checking-in the patient
- Schedule an appointment for the patient on the eCW HIV Walk-In schedule.
- Check patients in for their visit and direct the patient to the Waiting Area.
- Contact the designated point person at each clinic and inform them of the visit:
  - WRIR-97th St = Gloria Santos
  - RCC = Victor Hogue
  - NENA = Stephanie Suh (Please refer to Silvana Quintana while Stephanie Suh is on maternity leave)

*Please Note: As with all other HIV testing visits, the Care Technician conducting the HIV test will input the appropriate payment information for the visit*
PrEP Education and Outreach

• The Ryan Network conducts both PrEP in-reach and outreach.
• In-reach consists of tabling in the various clinics and having trained staff provide basic PrEP education to clients in waiting areas.
• Ryan providers also refer patients to PrEP services.
• Non-medical and medical staff PrEP training is ongoing throughout the year.
PrEP Outreach

- Ryan Prevention staff conduct weekly bar outreach throughout Manhattan.
- Some of the bars include: Therapy, Castro, Boxers (Hell’s Kitchen), and Pieces.
- Additional sites include Sylvia’s Place and The Center.
Ryan Network Wrap N’ Go

• Through the year the Prevention, Education, and Outreach Department hosts “Wrap N’ Go” events for LGBT youth.
• Each event consists of sexual health and HIV education through the use of games, such as, the PrEP and PEP trivia wheel, STD Transmission module, and Dick-in-the-Box
• The events are emceed by community drag queens and include music and dancing.
Wrap N’ Go Events

IN VOGUE
HALLOWEEN SEXPOSÉ
A NIGHT OF PRIZES & SURPRISES
How to protect yourself from HIV/AIDS with PrEP & PEP without sacrificing fun & other sexual health
Oct 23rd, 2015
7:30-9:30PM
@LGBT Center
Bring a friend & your dancing shoes for a chance to win big!

FREE FOOD GAMES MUSIC & MORE

24yr and Under Event

MARTI GOULD CUMMINGS
MASTER OF CEREMONIES

The Center
208 W 13th Street
New York NY 10011

SPONSORED BY

America’s Next Top Bottom

Online
THERAPY
348 W 52nd St
February 10th
Event starts at 8:00PM
Showtime at 9:00PM
Looking for:
One night only

WANT TO BE ON BOTTOM?
Join emcee Kira Kennedy Chanel for a night of tawdry competition, sexy education and, most importantly, bottom pride!

• Learn more about our Mpowerment education groups for GBT youth
• Answer challenge questions on HIV prevention as well as PrEP and PEP services for your chance to win big!

Bottoms up!
Ryan Network Prevention and PrEP Staff
Generation PrEP

• The Network hosts PrEP education community forums through out a variety of venues in Manhattan.

• The forums include Ryan staff and PrEP providers, such as Dr. Demetre Daskalakis, who are able to address the issues surrounding PrEP.

• They provide opportunities for members of the communities to voice their concerns.
The Cost of PrEP
What will it mean for me... financially? socially? sexually?

The 3rd installment of the Ryan Network’s Generation PrEP Series
a FREE community forum, featuring 2 PrEP consumers, and:

Dr. Demetra Daskalakis
Assistant Commissioner, Bureau of HIV/AIDS Prevention and Control, New York City DOHMH

Carrie Davis
Chief Programs and Policy Officer, The Center

Victor Hogue
Care Technician, Ryan/Chelsea Clinton Community Health Center

Michael Slater
Moderator, supervising Health Educator, William F. Ryan Community Health Center

Thursday, November 19th 6:00-8:00pm at The Center (208 W. 13th St. NYC)
Refreshments will be provided

PREP + NYC = 

THE CENTER

FOR MORE INFORMATION, CALL WILLIAM ARBOLEDA @ 212-884-5807

Prepping for Sex: A Story Slam
Featuring
PrEP Expert
Dr. Michelle Cespedes

Join us for the Ryan Network’s 4th installment of the Generation PrEP Series, featuring stories from the community

THEME
PROTECT & CONNECT
Prepare a three minute story about a personal experience, sacrifice, or commitment surrounding PrEP and/or HIV prevention

TIME/DATE
April 21st 6:00-8:00 PM
Story telling sign up @ 5:45PM

LOCATION
Nuyorican Poets Café
236 East 3rd Street
(Between Avenues B&C)

RSVP
RSVP at eventbrite.com
Call/Text Sarah Kellman @ 646-584-4960
The New Wave of HIV Prevention

• In 2016, Ryan Network submitted a PrEP grant proposal to the AIDS Institute to expand Ryan Network PrEP services
• We submitted another proposal to Public Health Solutions on March 11\textsuperscript{th}
• Securing funding is essential to sustaining the PrEP Program
• PrEP is one of the key strategies to End the AIDS Epidemic
THANK YOU!