Facilitating HIV Pre-Exposure Prophylaxis (PrEP) Familiarity Among Vermont Primary Care Providers

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Facilitating HIV Pre-Exposure Prophylaxis (PrEP) Familiarity and Prescribing Among Vermont Primary Care Providers

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The Background

- Nationally, over 1.2 million Americans currently living with HIV
  - Nearly 1 in 8 (12.8%) are unaware of their status
- New infections consistently around 50,000 / yr
  - Men who have Sex with Men (MSM) carry largest burden
  - 25% of new infections are among youth (13-24yo), many whom are unaware of HIV status and can pass virus on to others
    - Family medicine is perfectly poised to intervene
- In Vermont:
  - Average 11-19 new Dx over past 10 years
  - Total of 670 HIV positive Vermonters (more accurately, closer to 800 considering those unaware of status)
  - 56% of newly Dx’ed are in MSM population
- 2016 US Federal Budget Request = $31.7 Billion for domestic and int’l HIV efforts
  - $18.5 billion = healthcare services / treatment for HIV+ individuals
  - Only $940 million for domestic HIV prevention
    - Unchanged for the past 6 years
The Arrival of PrEP

- 2012: FDA approval of Truvada (Emtricitabine-Tenofovir 200mg-300mg) for Pre-Exposure Prophylaxis (“PrEP”)
  - Drug had long history already for post-exposure treatment of HIV
- Clinical Practice Guidelines were immediately in place in cities with high LGBT populations (San Francisco City Clinic, Group Health Cooperative Seattle, Fenway Health Boston, Callen-Lorde / GMHC in NYC)
- Uptake / awareness elsewhere remains slow (especially in VT)
In Vermont

Provider comfort / familiarity remains limited

Latest estimate per Vermont Cares, excluding Planned Parenthood, UVM Student Health, or UVM Infectious Disease, is approximately [how many?] who have actively prescribed PrEP
In Vermont

Provider comfort / familiarity remains limited

Latest estimate per Vermont Cares, excluding Planned Parenthood, UVM Student Health, or UVM Infectious Disease, is approximately 9 providers who have actively prescribed PrEP

“Doctors and policy makers need to admit that 30 years of the ABC mantra – abstinence, be faithful, and use condoms – has failed. Men generally hate condoms, their lovers usually give in, almost no one abstains, precious few stay faithful” –

- Donald G McNeil, Jr is a New York Times science and health reporter who covers diseases of the world’s poor, including AIDS.
Table 2: Evidence Summary—Overall Evidence Quality (per GRADE Criteria)*

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Participants</th>
<th>Control</th>
<th>Limitations</th>
<th>Quality of Evidence (See Table 14, Appendix 2)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Agent</td>
<td>Control</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>TDF/FTC (n = 1251)</td>
<td>Placebo (n = 1248)</td>
<td>Adherence</td>
<td>High</td>
</tr>
<tr>
<td>iPrEx Trial</td>
<td>Phase 3</td>
<td>TDF (n = 201)</td>
<td>Placebo (n = 199)</td>
<td>Minimal</td>
<td>High</td>
</tr>
<tr>
<td>US MSM Safety Trial</td>
<td>Phase 2</td>
<td>TDF/FTC (n = 1589)</td>
<td>Placebo (n = 1586)</td>
<td>Minimal</td>
<td>High</td>
</tr>
<tr>
<td>Partners PrEP</td>
<td>Phase 3</td>
<td>TDF/FTC (n = 1062)</td>
<td>Placebo (n = 1058)</td>
<td>Stopped at interim analysis, limited follow-up time, very low adherence to drug regimen</td>
<td>Low</td>
</tr>
<tr>
<td>TDF2</td>
<td>Phase 2</td>
<td>TDF/FTC (n = 1007)</td>
<td>Placebo (n = 1003)</td>
<td>Stopped early for operational concerns, small sample size, limited follow-up time on assigned drug</td>
<td>Low</td>
</tr>
<tr>
<td>FEM-PrEP</td>
<td>Phase 3</td>
<td>TDF/FTC (n = 1004)</td>
<td>Placebo (n = 1007)</td>
<td>TDF arm stopped at interim analysis (fatality), very low adherence to drug regimen in both TDF and TDF/FTC arms</td>
<td>Low</td>
</tr>
<tr>
<td>West African Trial</td>
<td>Phase 2</td>
<td>TDF/FTC (n = 1004)</td>
<td>Placebo (n = 1007)</td>
<td>TDF arm stopped at interim analysis (fatality), very low adherence to drug regimen in both TDF and TDF/FTC arms</td>
<td>Low</td>
</tr>
<tr>
<td>VOICE</td>
<td>Phase 2B</td>
<td>TDF/FTC (n = 1004)</td>
<td>Placebo (n = 1007)</td>
<td>TDF arm stopped at interim analysis (fatality), very low adherence to drug regimen in both TDF and TDF/FTC arms</td>
<td>Low</td>
</tr>
</tbody>
</table>

Among Men Who have Sex with Men

Among Heterosexual Men and Women

Among Heterosexual Women

Among Injection Drug Users

Note: GRADE quality ratings:
- high = further research is very unlikely to change our confidence in the estimate of effect;
- moderate = further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate;
- low = further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate;
- very low = any estimate of effect is very uncertain.

* All trials in this table were randomized, double-blind, prospective clinical trials.

<table>
<thead>
<tr>
<th>Study</th>
<th>Outcome Analyses — HIV incidence [mITT]</th>
<th>Effect — HR [Efficacy Estimate] (95% CI)</th>
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<tbody>
<tr>
<td></td>
<td>Agent</td>
<td>Control</td>
</tr>
<tr>
<td>iPrEx (MSM)</td>
<td>36 infections among 1224 persons</td>
<td>64 infections among 1217 persons</td>
</tr>
<tr>
<td>US MSM Safety Trial</td>
<td>3 infections among 201 persons (all 3 in delayed arm, not on TDF)</td>
<td>4 infections among 199 persons (1 acute infection at enrollment)</td>
</tr>
<tr>
<td>Partners PrEP (heterosexual men and women)</td>
<td>TDF, 17 infections among 1572 persons</td>
<td>52 infections among 1568 persons</td>
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<tr>
<td></td>
<td>TDF/FTC, 13 infections among 1568 persons</td>
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<tr>
<td>TDF2 (heterosexual men and women)</td>
<td>9 infections among 601 persons 1.2 infections/100 person-years</td>
<td>24 infections among 599 persons 3.1 infections per 100 person-years</td>
</tr>
<tr>
<td>FEM-PrEP (heterosexual women)</td>
<td>33 infections among 1024 persons 4.7 infections per 100 person-years</td>
<td>35 infections among 1032 persons 5.0 infections per 100 person-years</td>
</tr>
<tr>
<td>West African Trial (heterosexual women)</td>
<td>2 infections among 427 persons 0.86 infections per 100 person-years</td>
<td>6 infections among 432 persons 2.48 infections per 100 person-years</td>
</tr>
<tr>
<td>VOICE (heterosexual women)</td>
<td>TDF, 52 infections among 933 persons 6.3 infections per 100 person-years TDF/FTC, 61 infections among 985 persons 4.7 infections per 100 person-years</td>
<td>35 infections among 999 persons 4.2 infections per 100 person-years</td>
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<tr>
<td>BTS (injection drug users)</td>
<td>17 infections among 1204 persons 0.35 infections per 100 person-years</td>
<td>33 infections among 1207 persons 0.68 infections per 100 person-years</td>
</tr>
</tbody>
</table>

mITT: modified intent to treat analysis; HR: hazard ratio.

* Not statistically significant.
UVM COM PHP Project: Lack of Provider Training was the #1 Identified Barrier

Facilitators and Barriers to Prescribing Pre Exposure Prophylaxis (PrEP) for the Prevention of HIV

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University of Vermont College of Medicine¹, Burlington VT; Vermont CARES², Burlington VT

Background
What is PrEP and who gets it?
- PrEP is the use of medication by individuals to prevent HIV infection. It is approved by the FDA for individuals who are not infected with HIV and it is intended to complement other prevention strategies such as condoms.
- HIV infection risk is 92% lower in patients using PrEP.
- Primaquine, a combination of benidrox and mefloquin, taken orally, is the only approved PrEP regimen and is intended to complement other prevention strategies such as condoms.
- HIV-negative individuals at risk for exposure to HIV have been identified as a group who have sex with men (MSM), IV drug users, and people who have not participated in safer sex with partners of unknown HIV status, and those in person-to-person relationships. Barriers to PrEP Implementation
- PrEP is effective when patients adhere; however, both the medical community and some high-risk populations have been slow to adopt it as an HIV prevention strategy.
- Many have shown clinicians perceived barriers to PrEP such as adverse side effects, viral drug resistance, increased HIV-related treatment, and cost.

HIV in Vermont
- New diagnoses of HIV among Vermont residents have remained relatively stable over the last twenty years.
- Vermont CARES, a non-profit, offers free and anonymous HIV testing and in-person risk-reduction counseling. Clients are increasingly talking about PrEP as a prevention strategy, but the responses from the medical community is difficult to ascertain.

Objective
- To increase Vermont providers’ attitudes towards PrEP and to identify barriers to wider implementation of PrEP as a prevention strategy.
- To assess Vermont providers’ attitudes towards PrEP and to identify barriers to wider implementation of PrEP as a prevention strategy.

Methodology
Participants
- 143 MD, DO, NP, and PA affiliated with St. Barnabas Primary Care Associates, NAMHC, UVMMC, CFMC, SVMH, VA, etc. returned completed surveys.

Survey
- Barriers associated with PrEP prescription were identified.
- 33 questions were generated based on previous studies to assess knowledge about and barriers to prescription of PrEP among Vermont primary care practitioners.

Results
- Training is the most prevalent concern among all providers surveyed. Newer doctors show greater concern about lack of training than more experienced doctors.
- Cost to Patient is the second most prevalent concern.
- Providers care to HIV (+) patients expressed more concern with long-term safety and drug resistance.
- Providers who have not provided care to HIV (+) patients in the last year were more concerned with this.

PrEP Barriers (willing to prescribe PrEP expressed greater concern about the characteristics of HIV interventions with increased prescription of PrEP).
- About 40% of providers consider themselves “not confident at all” when asked to assess their confidence level around having an informed discussion with patients regarding PrEP.
- Of the providers surveyed, 55% were “very likely” or “very willing” to prescribe PrEP, though only 8% had prescribed PrEP in the last 12 months.

Recommendations
- Vermont providers experience many barriers to prescribing PrEP. Sharing this data with advocates and other PrEP barriers.
- Vermont providers experience many barriers to prescribing PrEP. Sharing this data with advocates and other PrEP barriers.
- Continued education regarding PrEP could decrease concerns about PrEP prescription and increase provider confidence about discussing PrEP with patients.
- Awareness of costs to patients and insurance coverage of PrEP may alleviate concerns about the cost of PrEP.

References
- [2] Vermont CARES. Vermont CARES is a non-profit organization dedicated to providing a safe and healthy environment for people living with HIV, their partners, and those affected by HIV. (2018). Available at: https://vermontcares.org/

Figure 1. PrEP Barriers (willing to prescribe PrEP expressed greater concern about the characteristics of HIV interventions with increased prescription of PrEP).
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Figure 2. Vermont regions surveyed. Distribution of births by region.
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Figure 3. PrEP Barriers (willing to prescribe PrEP expressed greater concern about the characteristics of HIV interventions with increased prescription of PrEP).
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Figure 4. PrEP Barriers (willing to prescribe PrEP expressed greater concern about the characteristics of HIV interventions with increased prescription of PrEP).
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Figure 5. PrEP Barriers (willing to prescribe PrEP expressed greater concern about the characteristics of HIV interventions with increased prescription of PrEP).
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**Objective**

To assess Vermont providers’ attitudes towards PrEP and to identify barriers to wider implementation of PrEP as a prevention strategy.

**Methodology**

Participants:
- 143 MD, DO, NP and PA, affiliated with Bi-state Primary Care Association, UVMHC, CVMC, SVMC, VA, etc. returned completed surveys.
- Survey: Barriers associated with PrEP prescription were identified.
- 23 question survey was generated based on previous studies to assess knowledge about and barriers to prescription of PrEP among Vermont primary care practitioners.

**Recommendations**

- Vermont providers experience modifiable barriers to prescribing PrEP. Sharing this data with advocates and could prompt the development of targeted interventions to reduce these barriers.
- Continuing education regarding PrEP could decrease concerns about proper training and increase provider confidence about discussing PrEP with patients.
- Awareness of costs to patients and insurance coverage of PrEP may alleviate concerns about the cost of PrEP.

**Discussion**

- Training is the most prevalent concern amongst all providers surveyed. **Newer doctors show greater concern** about lack of training than more experienced doctors.
- Cost to Patient is the second most prevalent concern.
- Providers of care to HIV (+) patients expressed more concern with **long-term safety and drug resistance**.
- Providers who have not provided care to HIV (+) patients in the last year were more concerned with time.
- Providers “unwilling” to prescribe PrEP expressed greater concern about the de-emphasis of alternative HIV interventions with increased prescription of PrEP.
- Nearly 47% of providers consider themselves “not confident at all” when asked to assess their confidence level around having an informed discussion with patients regarding PrEP.
- Of the providers surveyed, 55% were “willing” or “very willing” to prescribe PrEP, though only 6% had prescribed PrEP in the last 12 months.
How to get the word out about PrEP?

- **PCP and community awareness & education**
  - The ID community is well aware of PrEP
  - 2013 national survey of ID physicians demonstrated that 74% supported the use of PrEP, yet only 9% had actually prescribed it.

- HIV-negative, or assumed to be, gay men have no reason to see an ID specialist. If they’re seeing anyone for healthcare, it’s their PCP.
  - Within marginalized communities, word spreads quickly about which providers are open and “safe” to talk to.
Having The Talk: Approach to Clinical Assessment of the Patient – Sexual HIV Acquisition Risk

Sexual history taking:
- 76% of MSM surveyed in 2008 in 21 US cities reported a health care visit in the past year
  - However, many providers don’t ask about (and pts don’t disclose) same-sex behaviors

- CDC suggested questions for risk assessment
- Language unique to MSM: “bottoming” vs. “topping”

**Box A2: Risk Behavior Assessment for Heterosexual Men and Women**

**In the past 6 months:**
- Have you had sex with men, women, or both?
- *If opposite sex or both sexes* How many men/women have you had sex with?
- How many times did you have vaginal or anal sex when neither you nor your partner wore a condom?
- How many of your sex partners were HIV-positive?
- *If any positive* With these HIV-positive partners, how many times did you have vaginal or anal sex without a condom?

**Box A1: Risk Behavior Assessment for MSM**

**In the past 6 months:**
- Have you had sex with men, women, or both?
- *If men or both sexes* How many men have you had sex with?
- How many times did you have receptive anal sex (you were the bottom) with a man who was not wearing a condom?
- How many of your male sex partners were HIV-positive?
- *If any positive* With these HIV-positive male partners, how many times did you have insertive anal sex (you were the top) without you wearing a condom?
- Have you used methamphetamines (such as crystal or speed)?

***“Are you and your partner exclusive or open?”***

- San Francisco State Univ “Gay Couples Study”: found 47% of gay relationships are open, 45% monogamous, and 8% disagreed about their categorization
  - focused on HIV infections rising even among primary male couples
For all sexually active pts:
- Consider dx of bacterial STIs in past 6 months as evidence of potential HIV-exposure sexual activity, therefore, risk

Alcohol use / abuse screening (especially before sexual activity)

Screening for use of non-injection drug use in conjunction with sexual encounters:
- Amyl nitrite ("poppers") – assoc’d w/ sexual encounter enhancement
  - Smooth muscle (anal sphincter) relaxation, general vasodilation, and reflexive tachycardia (sensation of “excitement”)
- Stimulants: often popular in the circuit-party scene
**CDC Clinical Provider’s Supplement**

<table>
<thead>
<tr>
<th>MSM Risk Index[^25]</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1. How old are you today?</td>
<td>If &lt;18 years, score 0</td>
<td>If 18-28 years, score 8</td>
</tr>
<tr>
<td></td>
<td>If 29-40 years, score 5</td>
<td>If 41-48 years, score 2</td>
</tr>
<tr>
<td></td>
<td>If 49 years or more, score 0</td>
<td></td>
</tr>
<tr>
<td>2. In the last 6 months, how many men have you had sex with?</td>
<td>If ≥10 male partners, score 7</td>
<td></td>
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<tr>
<td></td>
<td>If 6-10 male partners, score 4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>If 0-5 male partners, score 0</td>
<td></td>
</tr>
<tr>
<td>3. In the last 6 months, how many times did you have receptive anal sex (you were the bottom) with a man without a condom?</td>
<td>If 1 or more times, score 10</td>
<td></td>
</tr>
<tr>
<td></td>
<td>If 0 times, score 0</td>
<td></td>
</tr>
<tr>
<td>4. In the last 6 months, how many of your male sex partners were HIV-positive?</td>
<td>If &gt;1 positive partner, score 8</td>
<td></td>
</tr>
<tr>
<td></td>
<td>If 1 positive partner, score 4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>If &lt;1 positive partner, score 0</td>
<td></td>
</tr>
<tr>
<td>5. In the last 6 months, how many times did you have insertive anal sex (you were the top) without a condom with a man who was HIV-positive?</td>
<td>If 5 or more times, score 6</td>
<td></td>
</tr>
<tr>
<td></td>
<td>If 0 times, score 0</td>
<td></td>
</tr>
<tr>
<td>6. In the last 6 months, have you used methamphetamine such as crystal or speed?</td>
<td>If yes, score 6</td>
<td></td>
</tr>
<tr>
<td></td>
<td>If no, score 0</td>
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</tbody>
</table>

**Note:**
- Age 18-28
- Receptive anal sex without condom x1
- Either of the above alone is nearly/already at threshold to consider Rx of PrEP

[^25]: Add down entries in right column to calculate total score

*If score is 10 or greater, evaluate for intensive HIV prevention services including PrEP.*
*If score is below 10, provide indicated standard HIV prevention services.*
Considering the IV drug use epidemic in the state, PrEP should also be first and foremost in prevention of HIV infection in these high-risk individuals.
1) HIV antibody test

- Confirm HIV (-) status before initiating, and every 3 months (ideally within the week before refilling Rx)
- Accomplish via serum HIV ELISA or rapid POC FDA approved fingerstick blood test
  - Do NOT use oral rapid tests in PrEP monitoring due to less sensitivity
  - Do NOT accept self-reported results or documented anonymous results
- If positive HIV antibody: follow normal procedure for confirmatory testing
- If acute infection suspected within “window period” before antibody test would become positive, must defer to HIV RNA test for acute exposure
Lab Tests and Evaluation

2) Renal Function
   - Obtain serum Cr and eCrCl
     - Minimum eCrCl of 60ml/min
   - Among HIV-infected persons prescribed Truvada-containing regimens, decreases in renal function (eCrCl) have been documented
   - Occasional cases of acute renal failure

3) Test for active HVB/HCV infection
   - MSM and IVDU at increased risk
   - Tenofovir has activity against HBV, thus if pt stops med, reactivation of HBV $\rightarrow$ hepatic damage
Lab Tests and Evaluation

- Conduct STI testing at least every 6 months
- Importance of site-specific testing (2010 CDC STD guidelines for MSM screening)
  - Urethral G/C if insertive intercourse in past year
  - Rectal G/C if receptive intercourse in past year
  - Pharyngeal G/C if receptive oral sex in past year
- Studies have not consistently borne out the idea of "risk-compensation" for individuals on PrEP (i.e. "PrEP instead of condoms"). Some studies have actually showed condom use increased long-term for individuals on PrEP
  - Perhaps due to more frequent/regular STI and HIV screening for individuals on PrEP
- Anal Paps?
  - NY State Dept. of Health recommends for HIV+ patients
  - CDC/USPSTF/ACS do not recommend
  - Recommendations? HIV- patients = baseline, q2-3 years
Road to Zero

- Campaign whose goal is to achieve zero new HIV infections in Vermont by 2020
  - Average of 20 new diagnoses per year (over the past 5 years)
  - “Vermont is in striking distance of becoming the first state ever to achieve this goal” – VT Cares

- PrEP is front and center

- Major limitation?
  - Currently only 9 providers actively prescribing PrEP
  - “Insufficient to fully demonstrate the public health impact PrEP can have”
    - Peter Jacobsen, Executive Director of VT Cares
Cost Concerns

- Truvada is covered by:
  - VT Medicaid
  - VT Blue Cross – Blue Shield
- Gilead “Advancing Access” Copay Card
  - [https://www.gileadadvancingaccess.com/copay-coupon-card](https://www.gileadadvancingaccess.com/copay-coupon-card)
  - Covers drug cost
    - U.S. residents
    - Available for each valid prescription, no other purchase necessary
    - Pt cannot be currently receiving other free drug assistance through Gilead patient assistance programs
HIV risk is not static throughout lifetime – “seasonality” of risk

Identification of high-risk people might be less helpful than identification of high-risk moments and the situations that cause them, for example:
- Leaving home
- Becoming an adult
- Coming out as a MSM
- Immigrating to a new city
- Ending a relationship

** Family Medicine again is perfectly poised to intervene **

PROUD study reported that unexpectedly high HIV incidence (9 infections per 100 person-years) in men who asked for PrEP and who were asked by clinician to defer starting the medication:
- HIV incidence was 3x expected based on epidemiologic trends
- People at higher risk of HIV infection were more likely to seek PrEP services, stay in care, and be adherent = the motivation is already there

iPrEx study: Evidence that PrEP is a strong attractor for those entering into a “season of high exposure to HIV”
- Temporal variation in risk behavior
Provider Handout

- Quick consult
- To be formalized into the UVM Academic Detailing program

Future Goals:
- Academic Detailing
- Family Medicine Grand Rounds
- eLearning module on LGBT health (to include PrEP) in Frymoyer project for current and future UVM COM students
References

- Flanagan et al. Facilitators and barriers to prescribing Pre Exposure Prophylaxis (PrEP) for the prevention of HIV. UVM College of Medicine.
- Velk et al. No New HIV Infection With Increasing Use of HIV Preexposure Prophylaxis in a Clinical Practice Setting, Clinical Infectious Disease, 2015: 61(10): 1601-3
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- CDC MSM health fact sheets: https://www.cdc.gov/msmhealth/resources/fact-sheets.htm