

#Adherence2014



9th International Conference on **HIV TREATMENT AND PREVENTION ADHERENCE**

jointly sponsored by



Postgraduate Institute
for Medicine



PrEP: State of the ART

Kenneth H. Mayer, M.D.

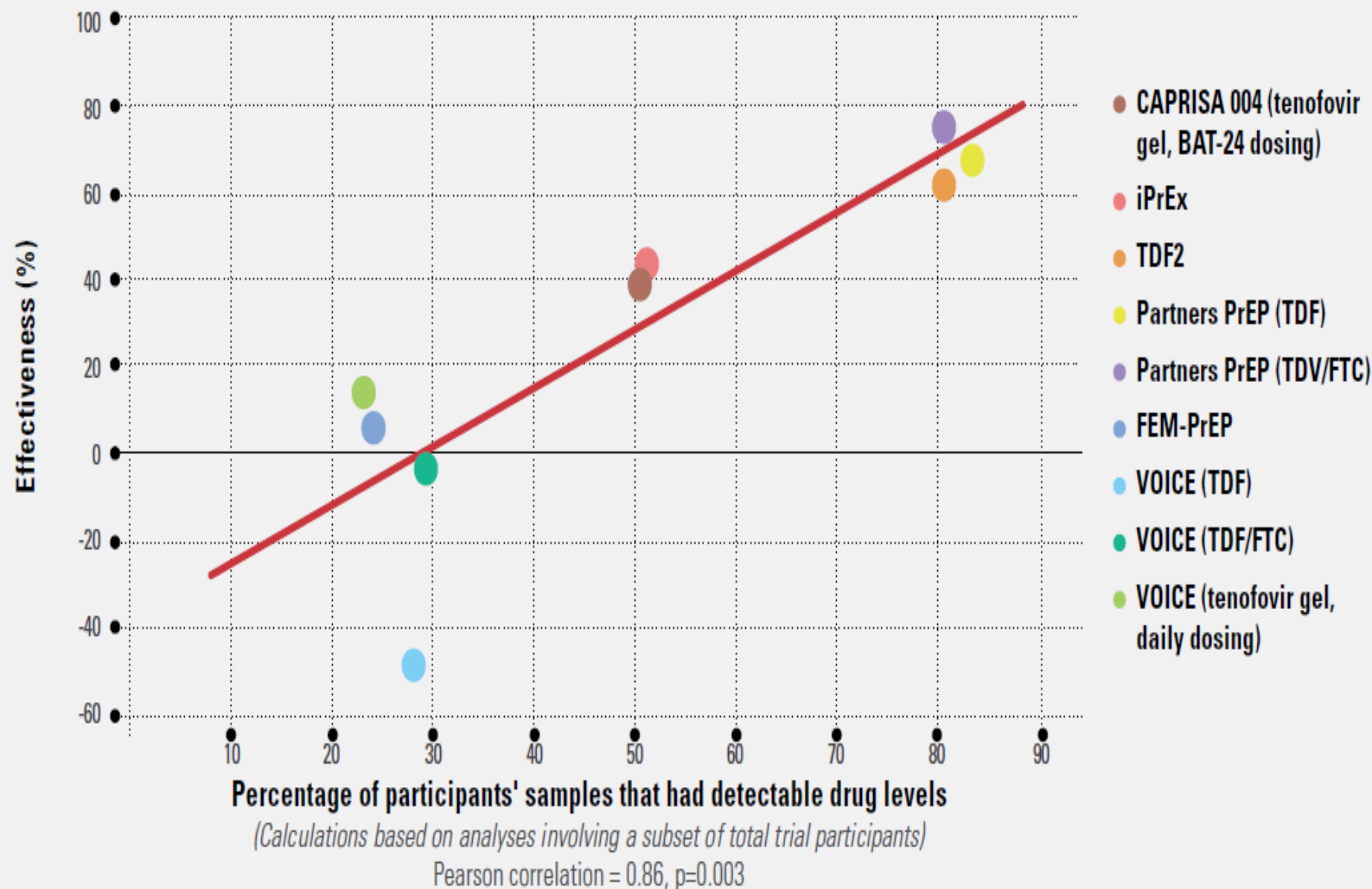
Fenway Health

Beth Israel Deaconess Medical Center

Harvard Medical School & School of Public Health

Disclosure: Unrestricted research/educational grants
from Gilead, BMS, and Merck

→ Effectiveness and Adherence in Trials of Oral and Topical Tenofovir-Based Prevention



Residual PrEP Concerns

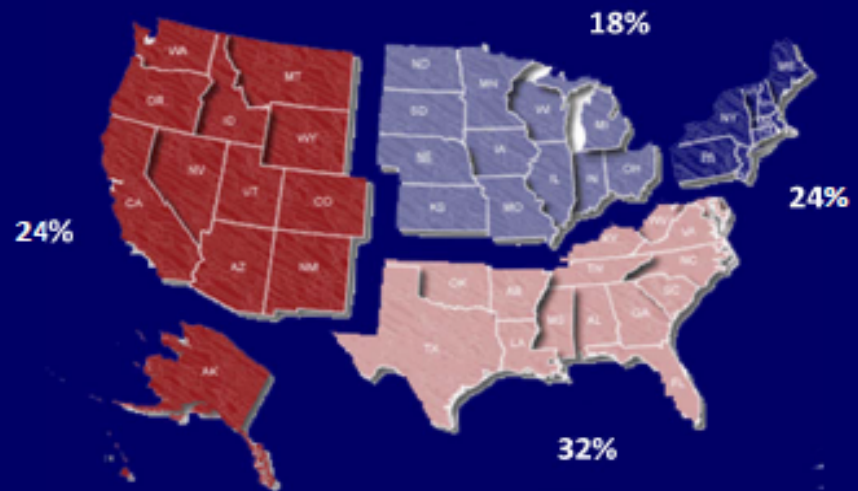
- **Risk Compensation:** not seen in trials
- **Renal insufficiency:** rare, reversible
 - but pts had to have normal function for trials
- **Bone demineralization:** statistically significant, not clinically significant at 18 months, **needs f/u**
- **Transmission of resistance**
 - Primarily in pts started on PrEP with acute HIV
 - Most were 184V (3TC/FTC^R, less fit virus)

Role of Genital Tract Inflammation and PK need f/u

(Naranbhai, JID, 2012; Hendrix, CROI, 2014)

Assessment of Truvada for PrEP Utilization in the US

- Geographically prescribers of TVD for PrEP are located in 49 states and distributed across approximately 700 cities
- Only 37% also prescribed Truvada for HIV treatment
- Overall 6 specialties initiated 75.6% of PrEP prescriptions
 - Family Practice 16%
 - Internal Medicine 15%
 - Emergency Medicine 14%
 - Infectious Diseases 12%
 - Nurse Practitioners 9%
 - Physician Assistants 8%
- When compared to HIV positive patients ^a, uninfected individuals receiving TVD for PrEP were:
 - 1.4 times more likely to be from the South (95% CI 1.3 – 1.6)^b
 - 1.8 times more likely to be female (95% CI 1.7 – 2.0)^b
 - 1.4 times more likely to be younger than 25 years old (95% CI 1.2 – 1.6)^b
 - 3.8 times more likely to be treated by a non-ID physician (95% CI 3.3 – 4.2)^b



Ongoing and Planned Phase 3/4 Research, Including Demonstration Projects

- ◆ Phase 3 studies are continuing to evaluate PrEP in various demographic groups
- ◆ Gilead is committed to post-marketing demonstration studies in the U.S. and globally
- ◆ Collaborators: ANRS, CDC, FHI, MRC, NIAID (DAIDS), NICHD (ATN), SFPDPH, U. Washington, and Gilead Sciences

Population	Studies	Participants
MSM	17	14,100
Heterosexual Men & Women Serodiscordant Couples	8	10,201
Total	25	24,301

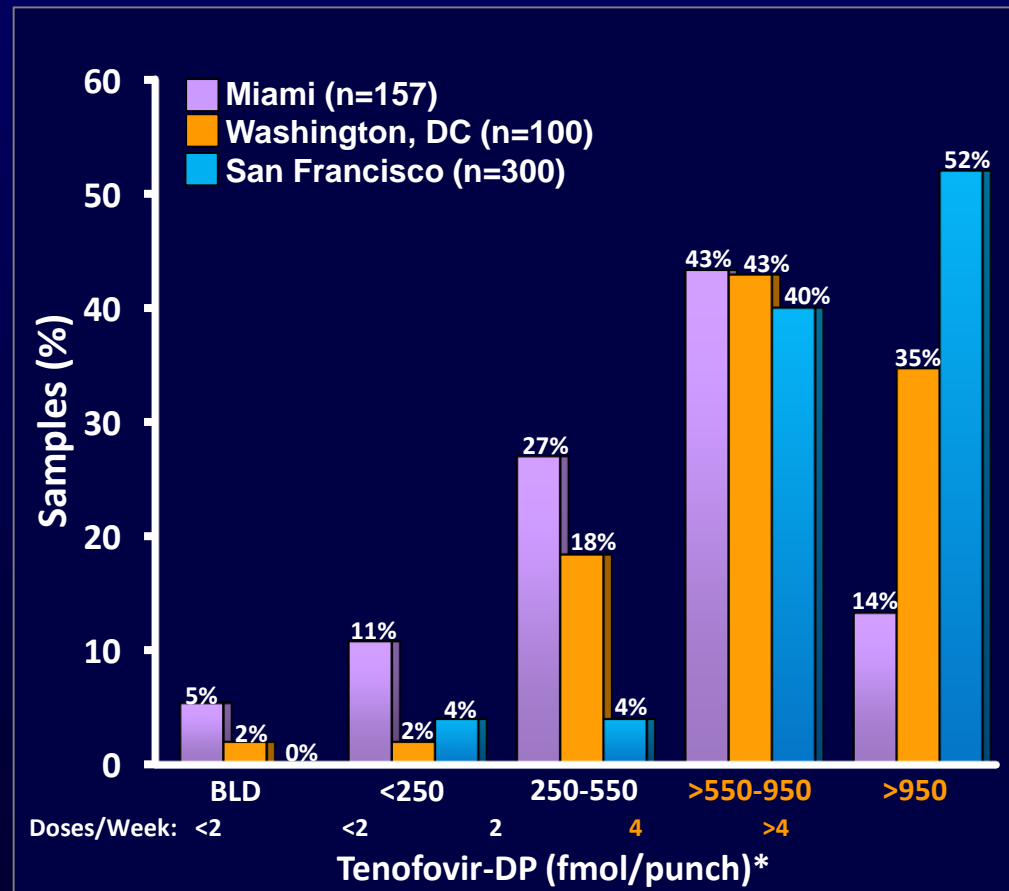
US PrEP Demonstration Project: Implementation of PrEP (2012-2014)

- STD clinics in San Francisco, Miami, Washington, DC (n=831)
 - MSM, transgender women (1.4%)
 - Clinic referrals (63%)
 - Self-referrals (37%): more likely to be white, higher education level, higher sexual risk behaviors and risk perception versus clinic referrals
- Offered up to 48 weeks of open-label emtricitabine/tenofovir DF
 - Accepted PrEP: 60.4%
 - 77% had TDF-DP levels consistent with taking ≥ 4 doses/week
- PrEP uptake associated with
 - Self-referral, prior PrEP awareness, higher-risk sexual behaviors

BLD: below limit of detection.

Cohen SE, et al. 21st CROI. Boston, 2014. Abstract 954.

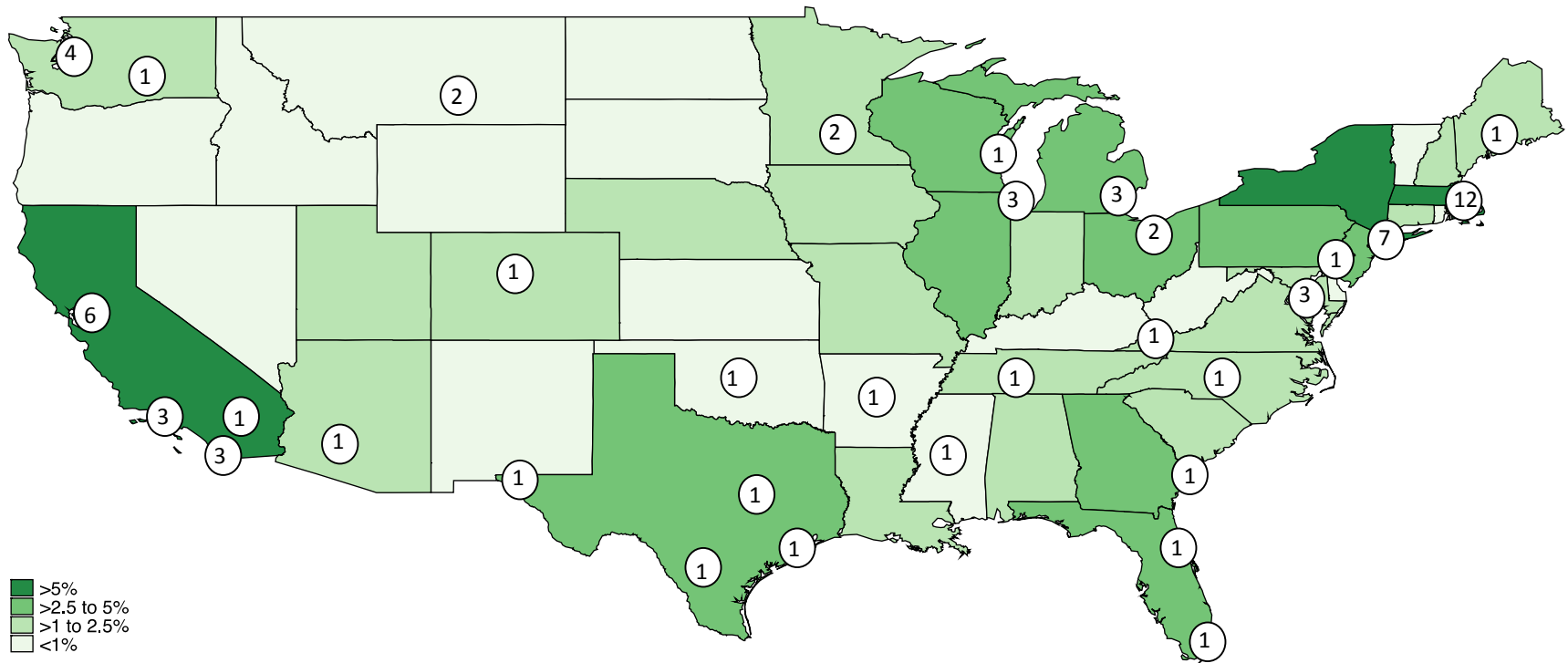
Tenofovir-DP Levels (Week 4)



*femtomole/punch: measure of flux density.

Proportion of PrEP Users by State of Residence

(MH PrEP Survey, Mayer et al, CROI 2014)



Proportion of responders; darker shades of green indicate a higher proportion of participants.
Not pictured: Alaska (0.2%) and Hawaii (0.6%)

N=9,179 1.2% had used PrEP

Circles indicate locations where PrEP use was reported and number of participants reporting PrEP use in that location

Factors Associated with PrEP Use among US MSM

Multivariable Model, Manhunt Survey, CROI, 2014

Characteristic	Multivariable OR (95% CI)
College graduate or above (vs. less than college education)	5.33 (1.25 to 22.7)
Ever diagnosed with an STI	2.74 (1.36 to 5.52)
Used PEP	16.0 (8.24 to 31.2)
Comfortable talking with provider about MSM sex	4.19 (1.51 to 11.6)

PrEP Culture Wars?

WE INTERRUPT THE STIGMATIZING AND SEX-SHAMING TO BRING YOU THIS IMPORTANT MESSAGE FROM THE AIDS HEALTHCARE FOUNDATION.

"IF A PERSON TAKES TRUVADA [AS PrEP] WHEN THEY ARE SUPPOSED TO, AND THEY TAKE IT EVERY DAY, THEN THEIR **CHANCE OF BECOMING INFECTED WITH HIV IS CLOSE TO ZERO.**"

- MICHAEL WEINSTEIN
NOVEMBER 9, 2013

LEARN THE FACTS FROM A RELIABLE SOURCE. MORE INFO AT PREPFACTS.ORG

THE **S+IGMA** PROJECT

A black and white photograph of Michael Weinstein, a man with short dark hair, wearing a striped shirt and tie. He is smiling and holding a small blue pill between his fingers.

Reality: Lively Discussion in the E-Universe

Project Inform launches new educational video series on PrEP!



Making decisions to take PrEP with your doctor.



Using PrEP in relationships with HIV-positive men.

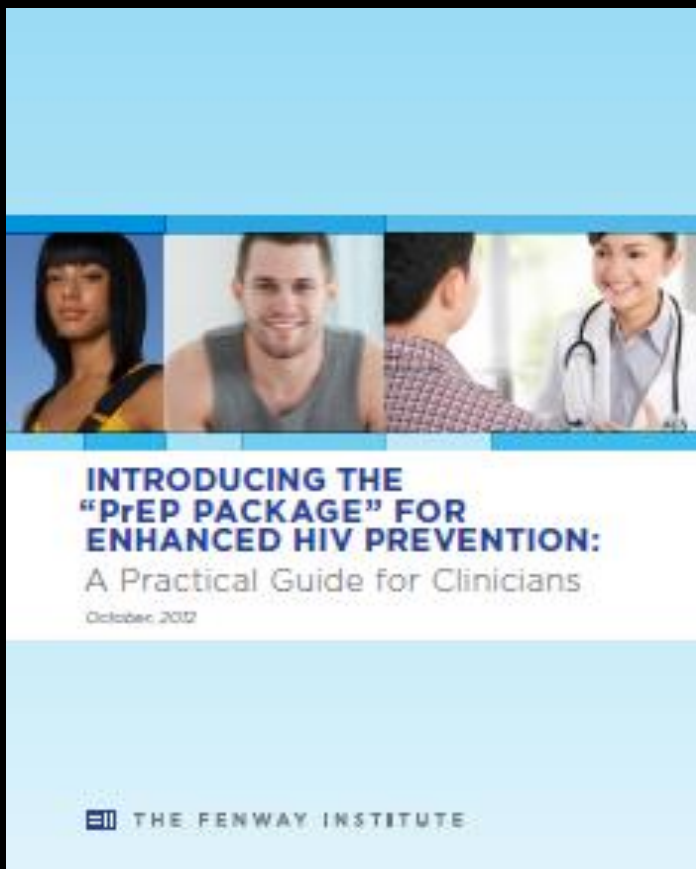


Figuring out how PrEP fits into your life.

- Brief video testimonials developed regarding PrEP users' decisions and motivations to take PrEP and experiences taking PrEP
- Also: www.myprepxperience.blogspot.com AIDS Foundation of Chicago
- <https://www.facebook.com/groups/PrEPFacts>



**My PrEP
experience**



- www.thefenwayinstitute.org



Preexposure Prophylaxis for the Prevention of HIV Infection in the United States – 2014 Clinical Practice Guideline

- PrEP is recommended as one prevention option for sexually-active adult MSM (men who have sex with men) at substantial risk of HIV acquisition **(IA)**¹
- PrEP is recommended as one prevention option for adult heterosexually active men and women who are at substantial risk of HIV acquisition. **(IA)**
- PrEP is recommended as one prevention option for adult injection drug users (IDU) at substantial risk of HIV acquisition. **(IA)**
- PrEP should be discussed with heterosexually-active women and men whose partners are known to have HIV infection (i.e., HIV-discordant couples) as one of several options to protect the uninfected partner during conception and pregnancy so that an informed decision can be made in awareness of what is known and unknown about benefits and risks of PrEP for mother and fetus **(IIB)**

Strategies to improve PrEP delivery and adherence

New PrEP drugs and dosing strategies



Novel adherence strategies



Alternative delivery systems and formulations



**Vaginal & Rectal
Microbicides:
MTN-017 (TFV
rectal gel)**



**Intra-vaginal rings:
ASPIRE (Dapivirine)**

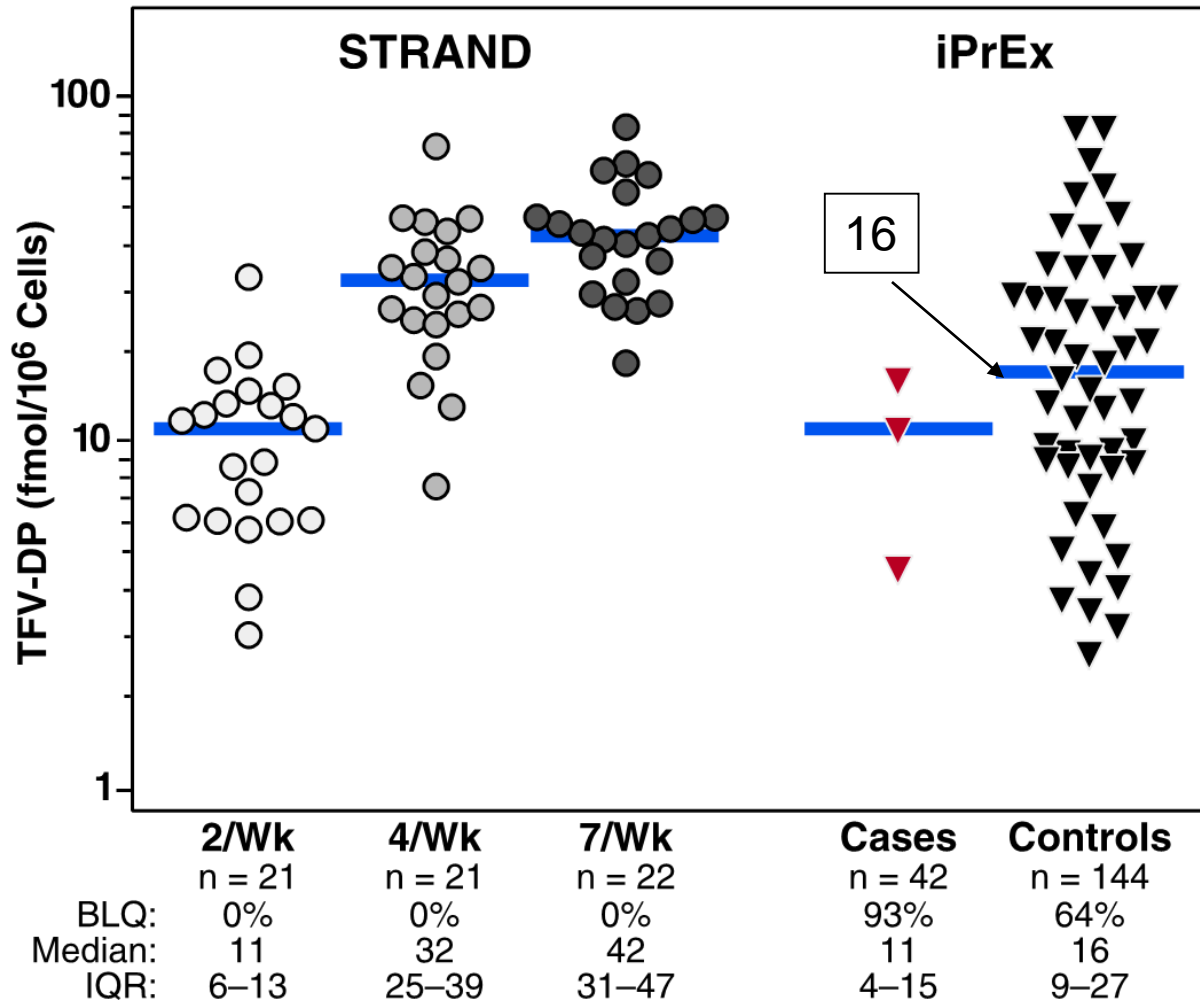


**Injectables:
Rilpivirine-LA
GSK744**

Oral Contraceptives Vs. PrEP

Issue	The Pill (Envoid)	TDF/FTC (PrEP)
1 st year on market	1957 (infertility)	2004 (treatment)
Year of FDA approval for prevention	1960	2012
N pts included in FDA filing	897 women	76919 men & women
Median time on med for pts included in FDA filing	<1 yr	1-2 years
Monthly cost	\$77	\$1425 in US \$6 in LMIC

TFV-DP Concentrations in IPrEx and STRAND



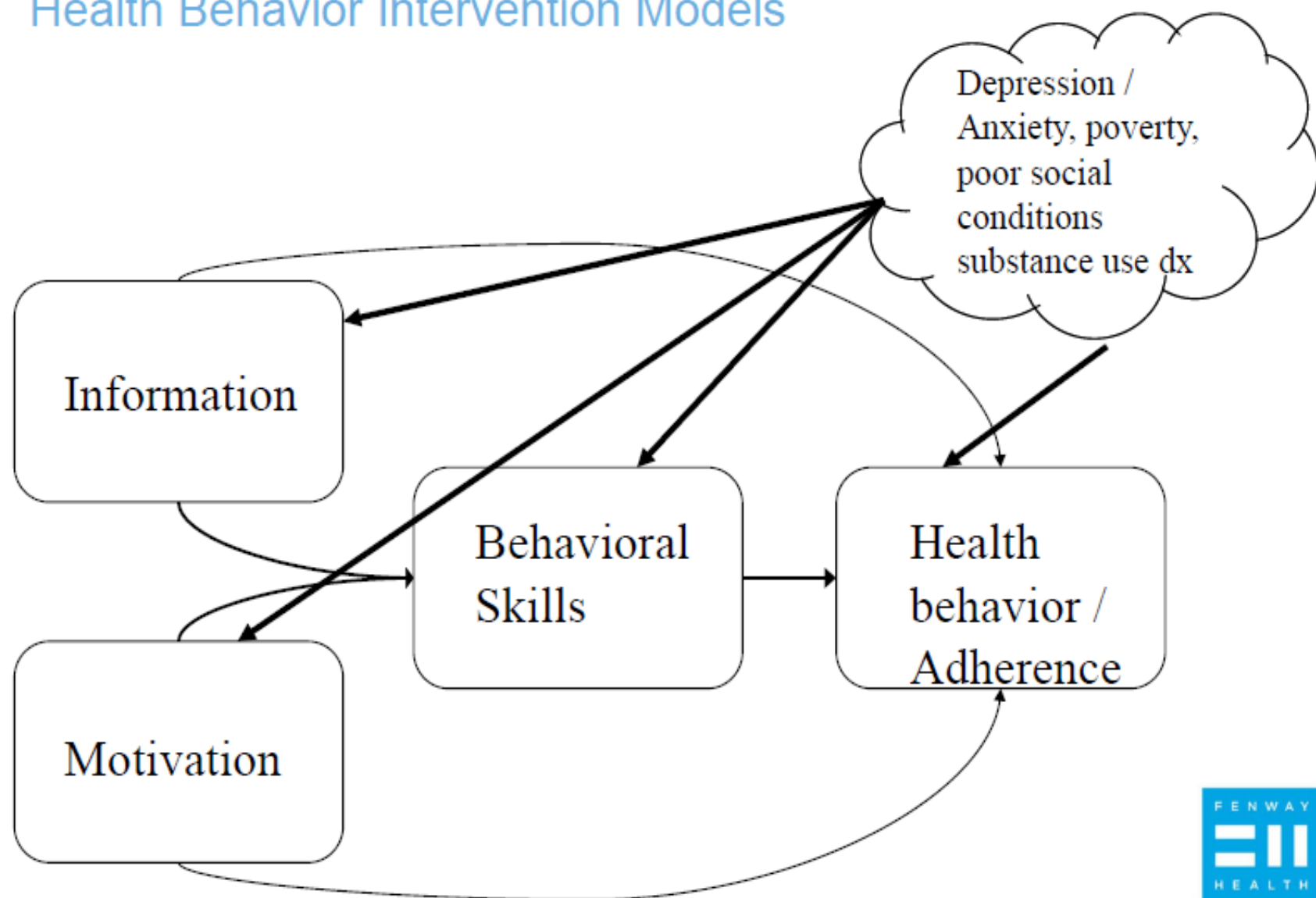
Regression analysis in
iPrEx: 90% reduction in
HIV acquisition when
TFV-DP > 16 fmol/10⁶ cells

Predicted risk reduction:
76% with 2 pills / week
96% with 4 pills / week
99% with 7 pills / week

Less than daily TDF/FTC for PrEP?

- HPTN 066: assessed dose proportionality: takes time to accumulate and lose intracellular drug
- HPTN 067: MSM in NYC and Bangkok, women in Cape Town: assessing fixed interval vs. pericoital PrEP acceptability, not efficacy
- iPREGAY: Placebo controlled trial of pericoital TDF/FTC in French, German, Quebecois MSM
- No efficacy data yet, but drug level determinations in demonstration projects will be informative, full scale RCT will require resources
- Data suggest “forgiveness” but threshold not established

Mental Health / Substance Use Can Interfere with Health Behavior Intervention Models

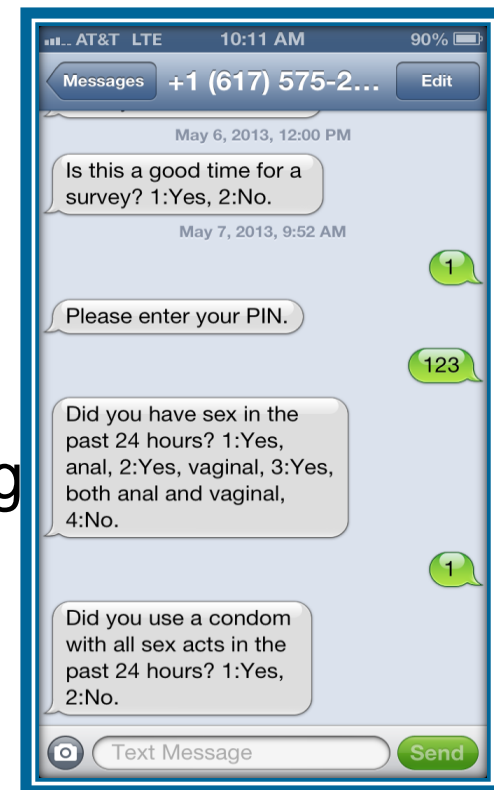


Project PrEPare (NIMH R34, Fenway)

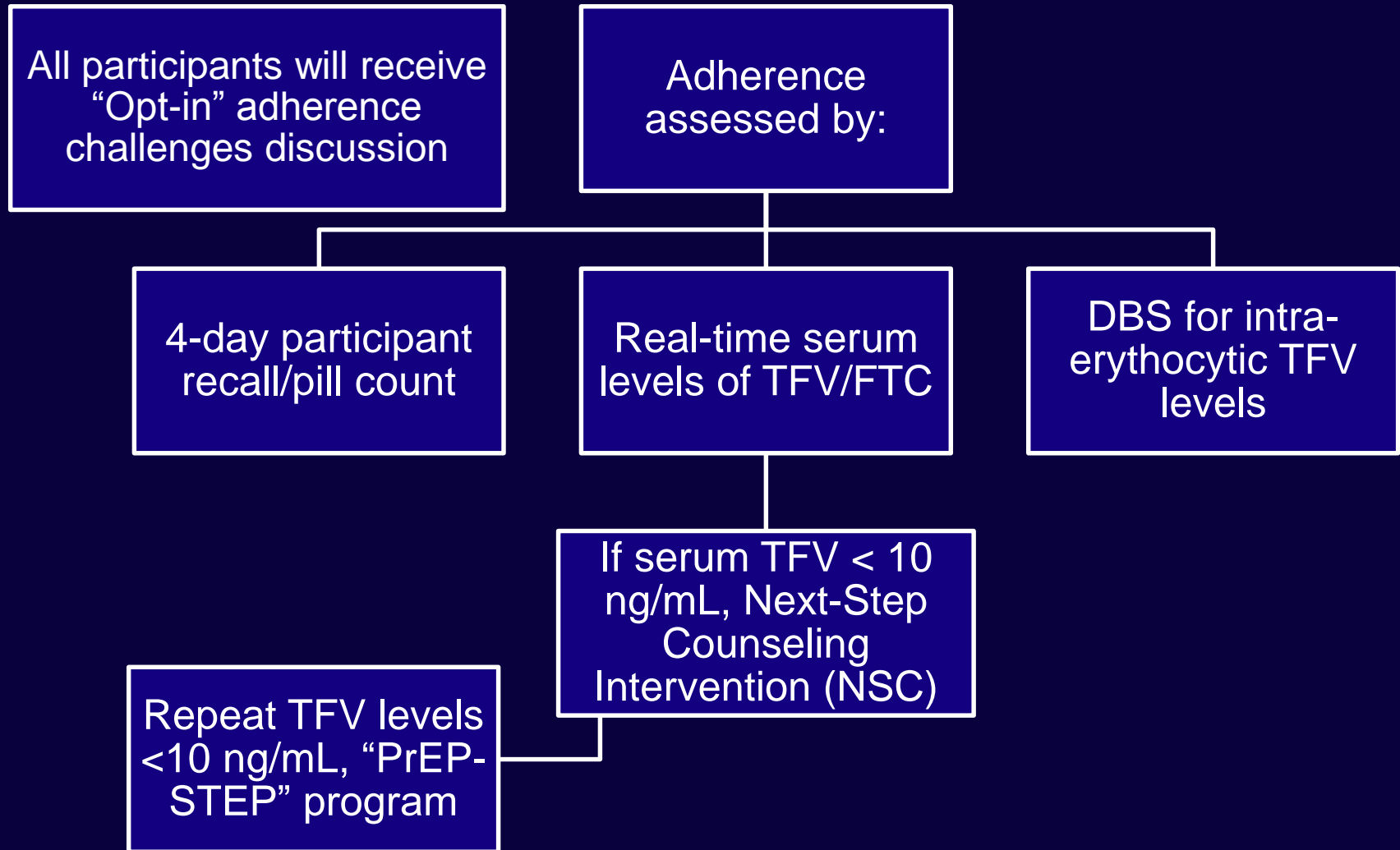
- Modeled after “Life-Steps,” (Safren et al) ART adherence intervention
- Modular intervention: 4 weekly visits and 2 booster sessions. Nurse-delivered
- Intervention content:
 - CBT-oriented adherence problem-solving
 - Brief motivational interviewing
 - Identification of barriers and solutions
 - Sexual risk-reduction strategies

Optional modules:

- Mental health and substance use concerns
- Adherence to PrEP measured daily via Wisepill
- Sexual risk taking was assessed by text messages (Lester, 2010)



Southern California: Path-PrEP: Staged Adherence (R Landovitz; see Kofron, Session 12)



PrEP and Black MSM (Lessons from HPTN 061)

Annual HIV incidence 3%; for 18-29 y.o. 5.9%

-Koblin B et al PLoS ONE, 2013

High rates of STIs, associated with HIV


-Mayer KH et al PLoS ONE, 2014

Many men with advanced HIV were identified

-Mannheimer S et al, AIDS 2012, MS under review

Many unmet social needs, poverty, incarceration

-Brewer, R et al, AJPH, 2013; JAIDS, 2013



*We've launched a new PrEP demonstration project
for Black men who have sex with men.*

Participate in the live Twitter chat on

#HPTN073 **Wednesday, August 14** **#PrEPChat**
at 10 am PT / 1 pm ET

With our guests: @JonPaulLucas and @cchauncey
Be sure to follow @HIVptn

Join the HPTN 073 Webinar:

"Introducing HPTN 073: A BMSM PrEP Demonstration Study"
at 11 am PT / 2 pm ET

by registering at
<http://bit.ly/073Webinar>

Find out more about HPTN 073 at
www.HPTN.org and at Facebook/HIVptn

Top 4 1 Medication Adherence 2 ARTAS 3 Diffusion of Effective Behavioral Interventions (DEBI) 4 Condom Distribution

Biomedical Interventions

Public Health Strategies

Behavioral Interventions

Structural Interventions

Social Marketing

CLEAR
(Cuide!e!
Connect
d-up: Defend Yourself!
FOF: Focus on the Future
FIO: The Future is Ours
Focus on Youth + IMPACT
Healthy Love
Healthy Relationships
Holistic Health Recovery Program
Many Men, Many Voices
MIP
Monument

HIV prevention
that works

to support
intervention
to reduce ne
the HIV epic



THE FENWAY INSTITUTE

YOLO

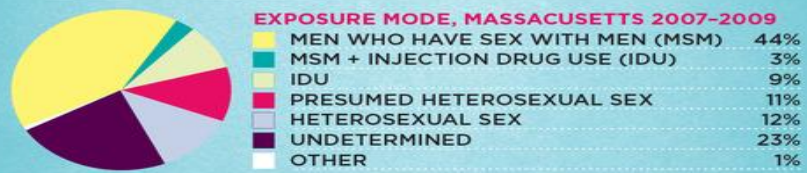
PROTECT YOURSELF

25,000-27,000
People in MA are living with HIV/AIDS.

almost 30%
live in Boston

Approximately 374
of people living with HIV/AIDS in Boston are between the ages of 13-24.

87 young people in MA were diagnosed with HIV or AIDS in 2010.



IT'S A FACT

ONE PILL A DAY CAN HELP PREVENT HIV
Fenway Health is looking for young men who have sex with men (MSM), ages 18-22, who would be willing to take one pill a day as part of a research study to prevent HIV. We'd love to tell you more!

Give us a call at: 617.927.6450. Eligible participants will be compensated for their time.



To implement PrEP successfully, it will be essential to engage practicing clinicians



REVIEW

Annals of Internal Medicine

What Primary Care Providers Need to Know About Preexposure Prophylaxis for HIV Prevention

A Narrative Review

Douglas Krakower, MD, and Kenneth H. Mayer, MD

As HIV prevalence climbs globally, including more than 50 000 new infections per year in the United States, we need more effective HIV prevention strategies. The use of antiretrovirals for preexposure prophylaxis (PrEP) among high-risk persons without HIV is emerging as one such strategy. Randomized, controlled trials have demonstrated that once-daily oral PrEP decreased HIV incidence among at-risk men who have sex with men and African heterosexuals, including serodiscordant couples. An additional randomized, controlled trial of a topical pericoital antiretroviral microbicide gel decreased HIV incidence among at-risk heterosexual South African women. Two other studies in African women did not demonstrate the efficacy of oral or topical PrEP, raising concerns about adherence patterns and efficacy in this population.

The U.S. Food and Drug Administration (FDA) Antiviral Drugs Advisory Committee reviewed these studies and additional data in May 2012 and voted to advise the approval of oral tenofovir-emtricitabine for PrEP in high-risk populations. On 16 July 2012,

the FDA recommended that this combination medication be approved for use as PrEP in high-risk persons without HIV. Patients may seek PrEP from their primary care providers, and those receiving PrEP require monitoring. Thus, primary care providers should become familiar with PrEP. This review outlines current knowledge about PrEP as it pertains to primary care, including identifying persons likely to benefit from PrEP; counseling to maximize adherence and reduce potential increases in risky behavior; and monitoring for potential drug toxicities, HIV acquisition, and antiretroviral drug resistance. Issues related to cost and insurance coverage are also discussed. Recent data suggest that PrEP, combined with other prevention strategies, holds promise in helping to curtail the HIV epidemic.

Ann Intern Med. 2012;157:490-497.

For author affiliations, see end of text.

This article was published on www.annals.org on 22 July 2012.

www.annals.org

Purview paradox: contradictory beliefs about which providers will prescribe PrEP

(see Krakower and Flash in Session 16 today)

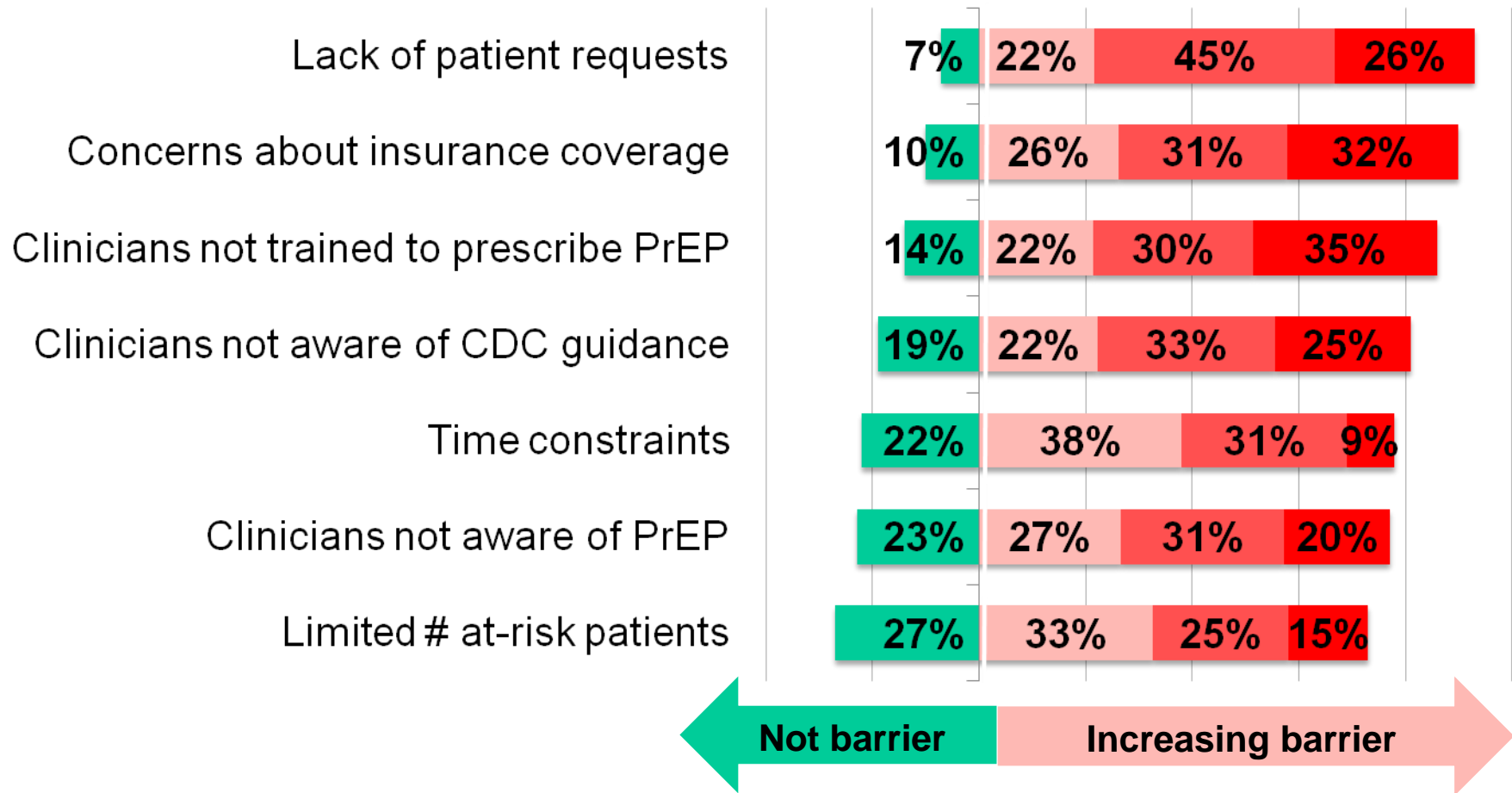
HIV providers

Primary care providers
are in the best position
to prescribe PrEP

Primary care providers

It would not be feasible
to prescribe PrEP

New England providers perceived numerous barriers to prescribing PrEP (Krakower, Adherence 2014)



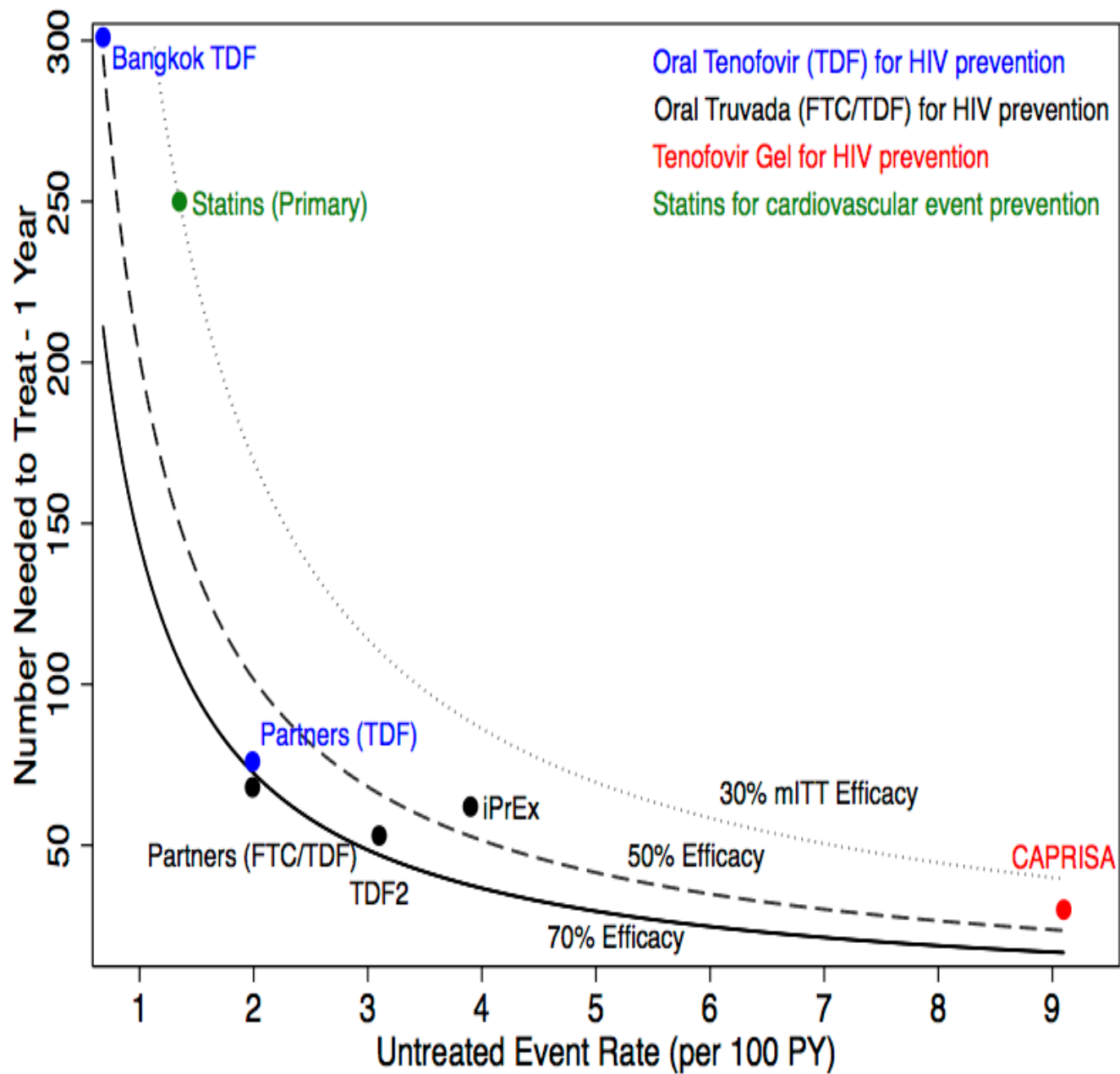
Beth Israel Deaconess
Medical Center



A teaching hospital of
Harvard Medical School



Numbers represent percentage for each response category: not a barrier, minor barrier, moderate barrier, major barrier. Bars total to 100%



A tool for risk-stratifying MSM: CDC risk index ("HIRI-MSM")

"In the past
(year) have
you had
sex?"



"With men,
women, or
both?"



Score < 9: standard prevention
Score ≥ 10: consider PrEP

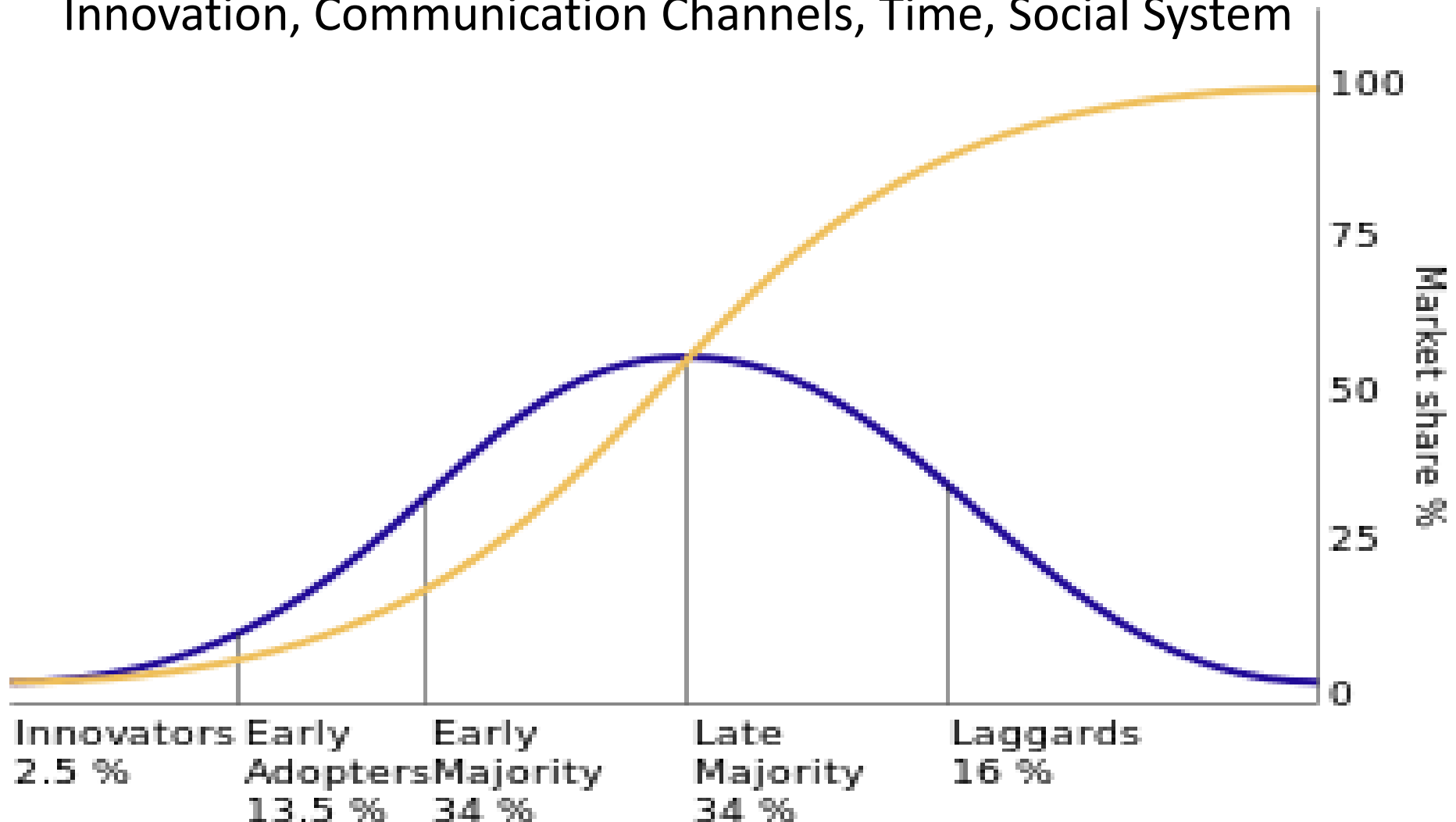


HIRI-MSM Risk Index*			
1	How old are you today (yrs)?	<18 years	score 0
		18–28 years	score 8
		29–40 years	score 5
		41–48 years	score 2
		≥49 years	score 0
2	How many men have you had sex with in the last 6 months?	>10 male partners	score 7
		6–10 male partners	score 4
		0–5 male partners	score 0
3	In the last 6 months, how many times did you have receptive anal sex (you were the bottom) with a man?	1 or more times	score 10
		0 times	score 0
4	How many of your male sex partners were HIV positive?	>1 positive partner	score 8
		1 positive partner	score 4
		<1 positive partner	score 0
5	In the last 6 months, how many times did you have insertive anal sex (you were the top) with a man who was HIV positive?	5 or more times	score 6
		0 times	score 0
6	In the last 6 months, have you used methamphetamines such as crystal or speed?	Yes	score 5
		No	score 0
7	In the last 6 months, have you used poppers (amyl nitrate)?	Yes	score 3
		No	score 0
Add down entries in right column to calculate total score			Total score†

Diffusion of Innovations

(Everett Rogers, 1962)

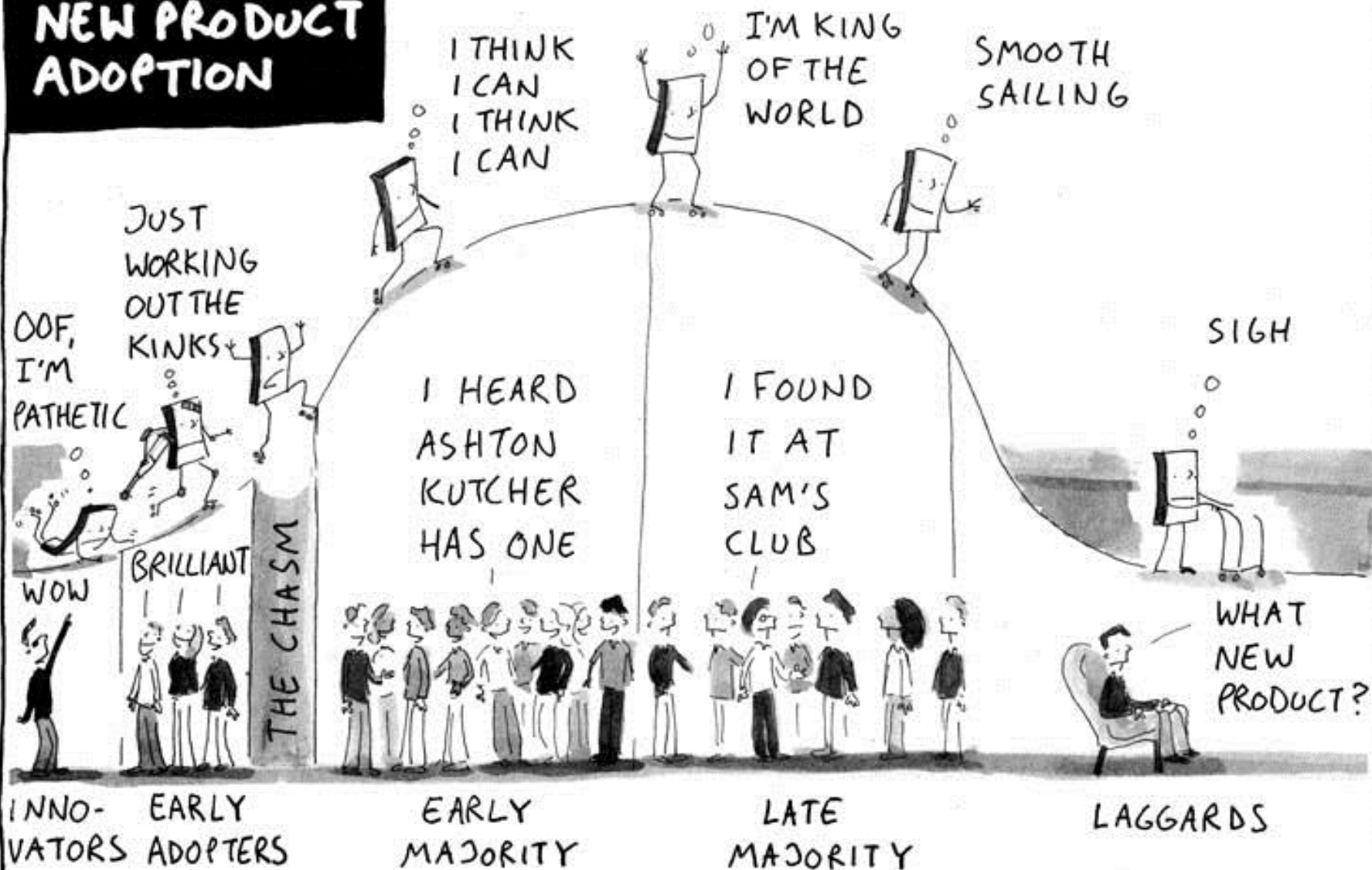
Innovation, Communication Channels, Time, Social System



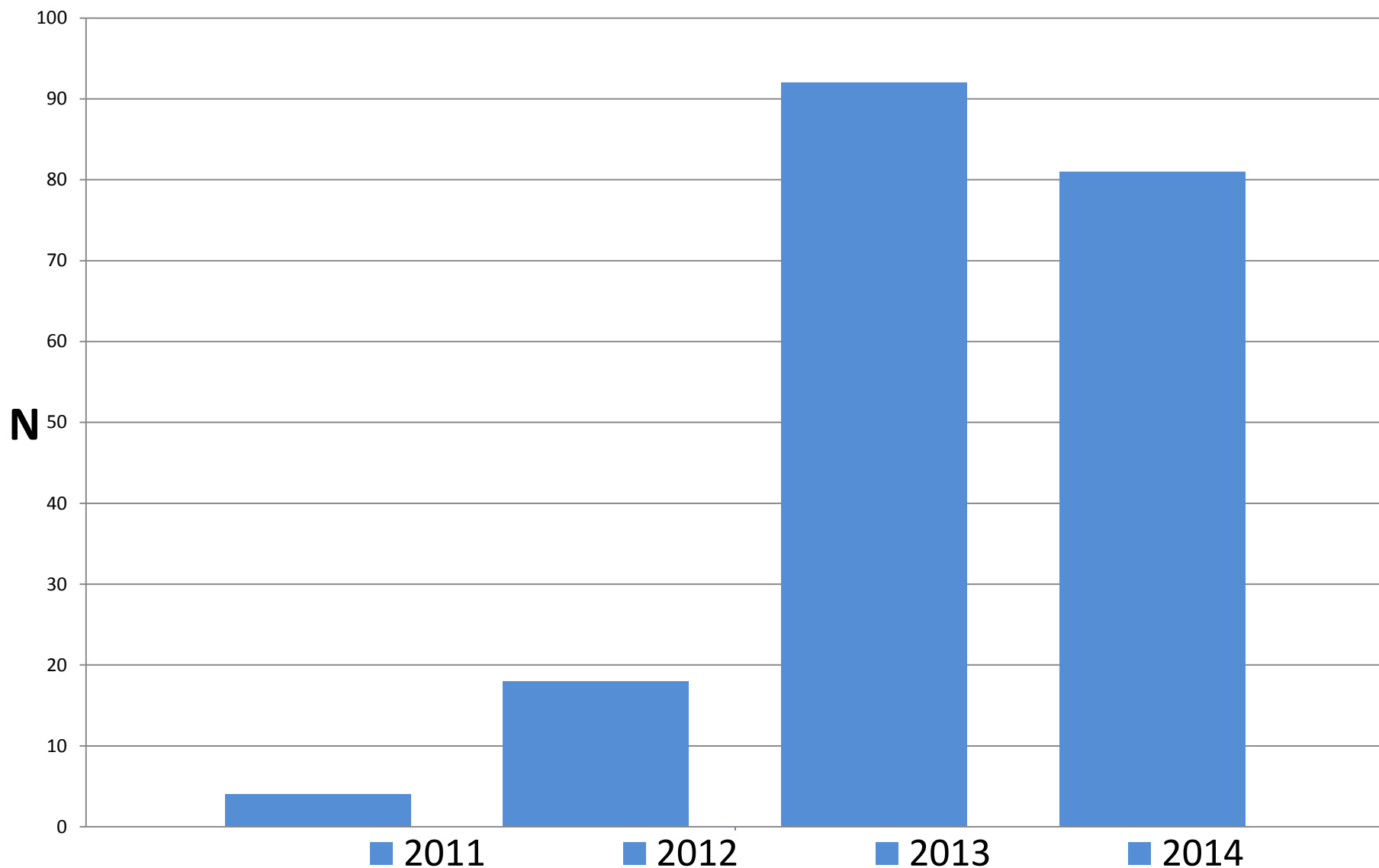
BRAND CAMP

by Tom Fishburne

NEW PRODUCT ADOPTION



Non-Trial PrEP Uptake at Fenway Health

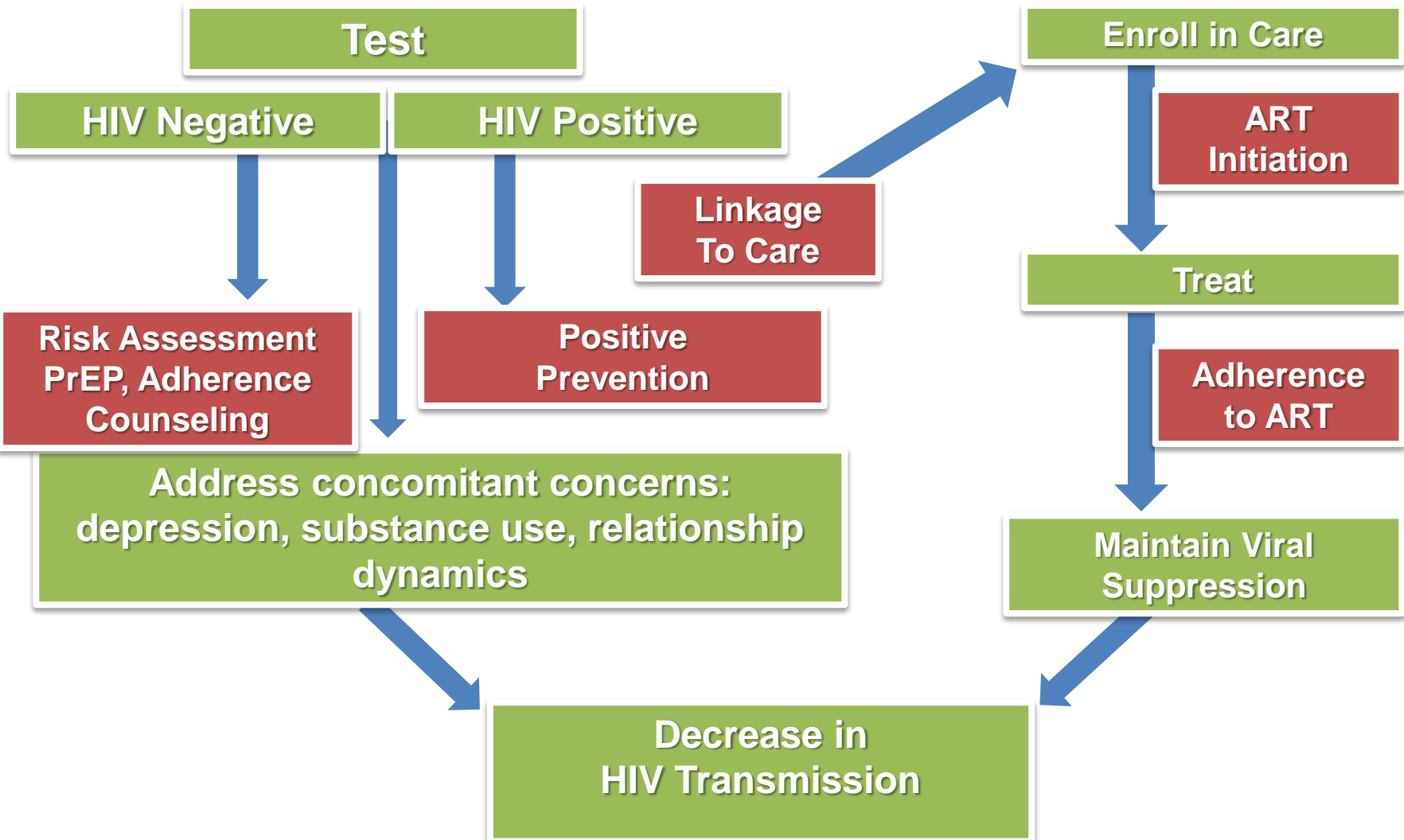


Sociodemographics of Fenway Health PrEP Patients

- MSM except for 2 transgender women
- Only Whites initiated in 2011
by 2013, 24.4% non-White,
with ~8% each among Black, Latino, multiracial MSM
- 3% <20 y.o.; 38% 20-29 y.o. ; 28% 30-40 y.o.
- 90% commercially insured; 4% Medicaid; 2% self-pay

Combination Antiretroviral Prevention

Interventions to Increase Testing



Thank You

Fenway Clinical, Epidemiological and
Behavioral Research Teams
Fenway Medical Department

Salim Abdool Karim

Rivet Amico

Susan Buchbinder

Charlene Flash

David Glidden

Chris Grasso

Sybil Hosek

Robert Grant

Doug Krakower

Raphy Landovitz

Albert Liu

Beryl Koblin

Matthew Mimiaga

Jim Pickett

David Novak

Jim Rooney

Steve Safren

Dawn Smith

Darrell Wheeler

NIAID, NIMH, NIDA, NICHD, CDC, HRSA,
Mass DPH, Gilead

www.thefenwayinstitute.org

