

Early-Stage Investigator Lecture

Scaling up Pre-Exposure Prophylaxis to End the HIV Epidemic



Presented by:

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Mentors

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NIMHD Loan Repayment Award (2015-2018)



K01 AI122853 (**Marcus**): “Optimizing Care for HIV/HCV-Coinfected Patients in the New HCV Treatment Era” (2016-2021)



R21 AI143386 (**Marcus/Young**): “Population-Level Effects of Increasing PrEP Uptake on HIV and Bacterial STIs” (2019-2021)



P30 AI060354 (**Marcus/Krakower**): “Harvard University Center for AIDS Research: EHRs to Scale Up PrEP in the South” (2019-2020)



R34 MH122291 (**Marcus/Krakower**): “EHR-Based Prediction Models to Improve PrEP Uptake in Community Health Centers” (2019-2022)



R01 MD013565-02S1 (**Dehlendorf**): “Offering Women PrEP with Education, Shared Decision-Making, and Trauma-Informed Care: The OPENS Trial” (2019-2020)



P30 AI060354 (**Marcus/Krakower**): “Harvard University Center for AIDS Research: Clinical Decision Support for PrEP” (2020-2022)



P50 CA244433 (**Emmons/Taveras**): “Implementation Science Center in Cancer Control Equity: Accelerating COVID Testing in Vulnerable Communities” (2022-2022)

Overview

- 1) PrEP for HIV prevention and sexual health
- 2) Mitigating barriers to PrEP implementation

THE NEW YORK TIMES,

FRIDAY, JULY 3, 1981

A20

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RARE CANCER SEEN IN 41 HOMOSEXUALS

Outbreak Occurs Among Men
in New York and California
—8 Died Inside 2 Years

By LAWRENCE K. ALTMAN

Doctors in New York and California have diagnosed among homosexual men 41 cases of a rare and often rapidly fatal form of cancer. Eight of the victims died less than 24 months after the diagnosis was made.

The cause of the outbreak is unknown.

A BAD REPUTATION ISN'T ALL YOU CAN GET FROM SLEEPING AROUND.



Think about it. When you sleep with someone, you're sleeping with everyone he or she has slept with for the past eight years. And if someone along the line had the AIDS virus, you would have been exposed.

Unfortunately, there is no known cure for AIDS. Everyone who gets it dies. But AIDS can be prevented. By saying

no to sex. And by saying no to needle drugs.

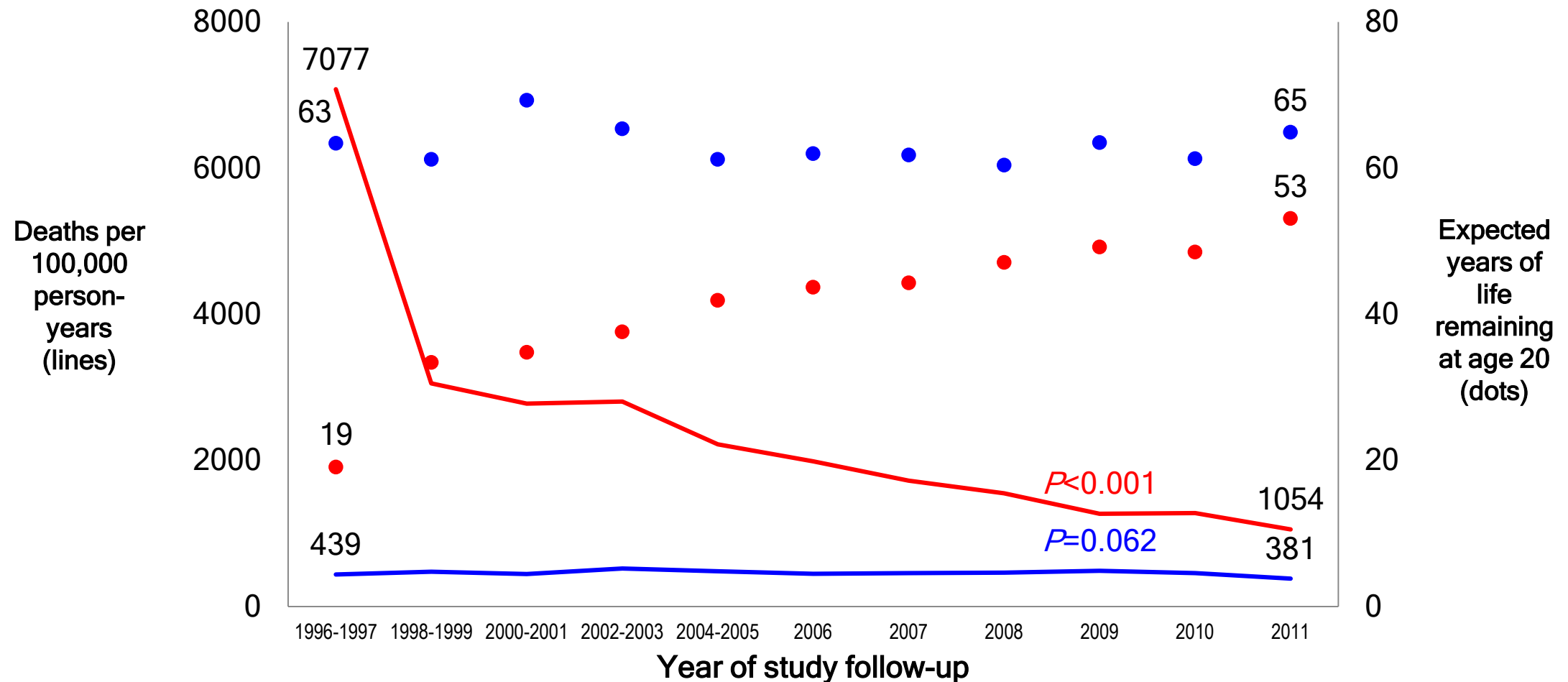
Don't let it embarrass you to death. Get all the facts about AIDS, and talk about them with your girlfriend or boyfriend. Then if you choose to have sex, stick to one partner. And use a condom, properly, every time. It's one of the best defenses against AIDS. The point is, if you're going to have sex,

you should do it responsibly.

Don't fool around with your life. Find out more about how AIDS is transmitted, and how you can protect yourself. Call the Dallas County Health Department, (214) 251-4333. All calls are strictly confidential.

AIDS CLIMATE OF FEAR
IT'S ONE OF THE MOST PREVENTABLE

A revolution in HIV treatment

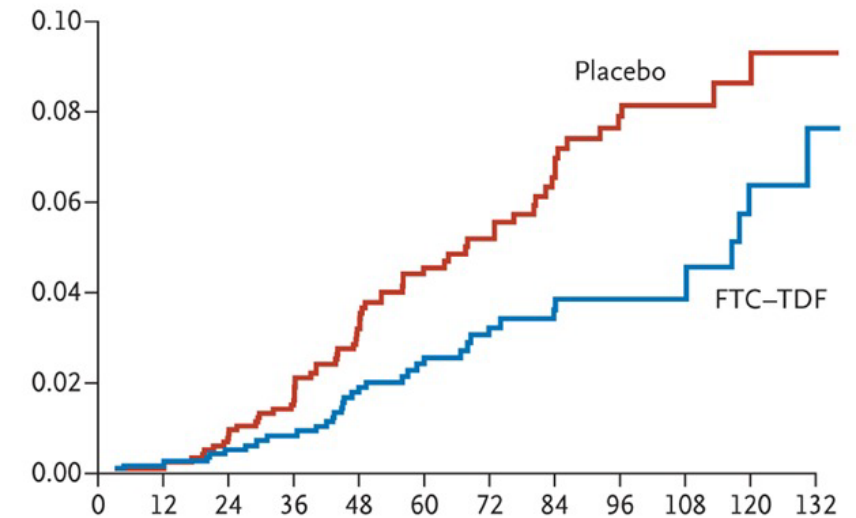


A revolution in HIV prevention



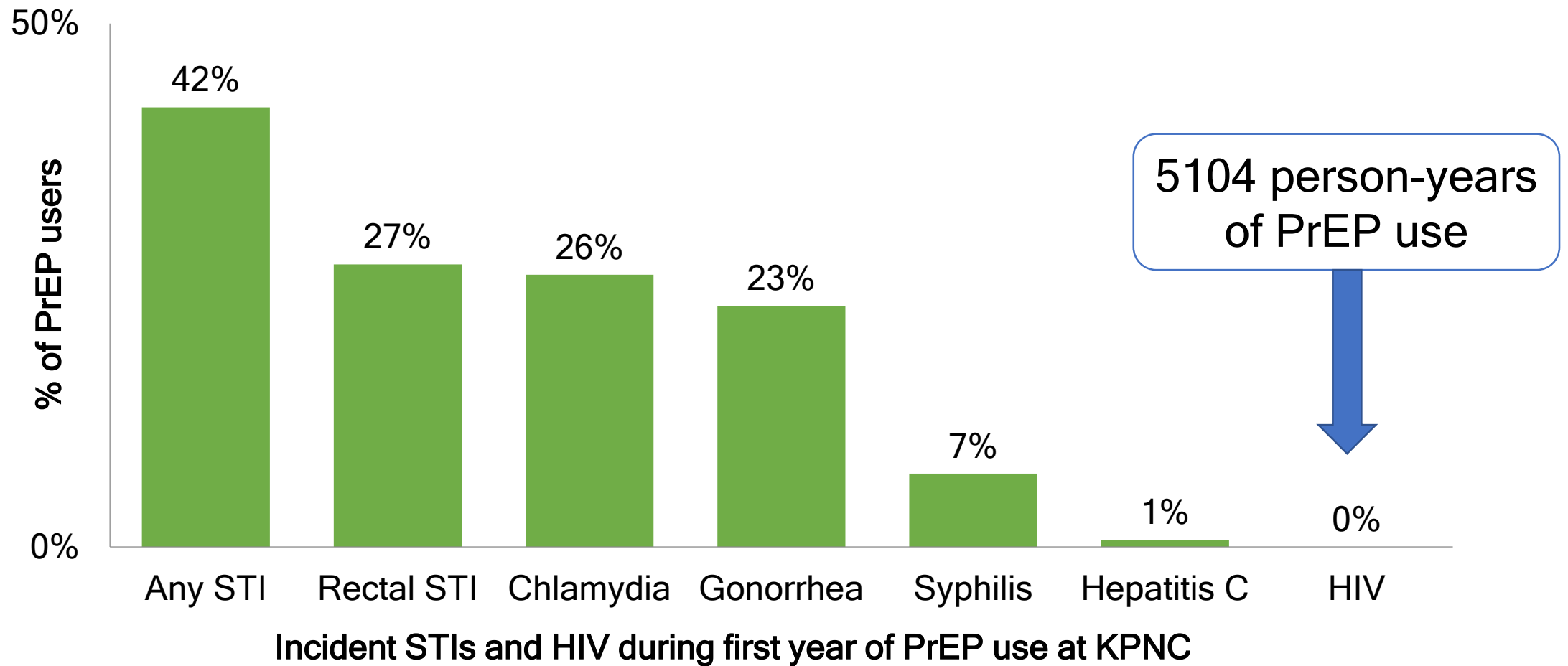
Preexposure Chemoprophylaxis for HIV Prevention in Men Who Have Sex with Men

Robert M. Grant, M.D., M.P.H., Javier R. Lama, M.D., M.P.H., Peter L. Anderson, Pharm.D., Vanessa McMahan, B.S., Albert Y. Liu, M.D., M.P.H., Lorena Vargas, Pedro Goicochea, M.Sc., Martín Casapía, M.D., M.P.H., Juan Vicente Guanira-Carranza, M.D., M.P.H., Maria E. Ramirez-Cardich, M.D., Orlando Montoya-Herrera, M.Sc., Telmo Fernández, M.D., Valdilea G. Veloso, M.D., Ph.D., Susan P. Buchbinder, M.D., Suwat Chariyalertsak, M.D., Dr.P.H., Mauro Schechter, M.D., Ph.D., Linda-Gail Bekker, M.B., Ch.B., Ph.D., Kenneth H. Mayer, M.D., Esper Georges Kallás, M.D., Ph.D., K. Rivet Amico, Ph.D., Kathleen Mulligan, Ph.D., Lane R. Bushman, B.Chem., Robert J. Hance, A.A., Carmela Ganoza, M.D., Patricia Defechereux, Ph.D., Brian Postle, B.S., Furong Wang, M.D., J. Jeff McConnell, M.A., Jia-Hua Zheng, Ph.D., Jeanny Lee, B.S., James F. Rooney, M.D., Howard S. Jaffe, M.D., Ana I. Martinez, R.Ph., David N. Burns, M.D., M.P.H., and David V. Glidden, Ph.D., for the iPrEx Study Team*



**44% risk reduction for
TDF/FTC PrEP vs.
placebo**

Even more effective in clinical practice



Insurer Says Clients on Daily Pill Have Stayed H.I.V.-Free



“This shows that the effectiveness of PrEP is really strikingly high,” Dr. Fauci said. “And this study takes it out of the realm of clinical trials and into the real world.”

A Truvada PrEP prescription, filled in July in New York City. New data points to the efficacy of this daily preventive pill. Nicole Bengiveno/The New York Times

PrEP effectiveness with optimal use

Population	Effectiveness	Source
Men who have sex with men	~99%	Grant, 2014 Liu, 2015 McCormack, 2015 Volk, 2015 Marcus, 2017
Heterosexual men and women	~99%	Baeten, 2012
People who inject drugs	74-84%	Choopanya, 2013 Martin, 2015

Has Pre-exposure Prophylaxis Made a Difference at a Population Level? Jury Is Still Out

Julia L. Marcus,^{1,✉} A. David Paltiel,² and Rochelle P. Walensky³

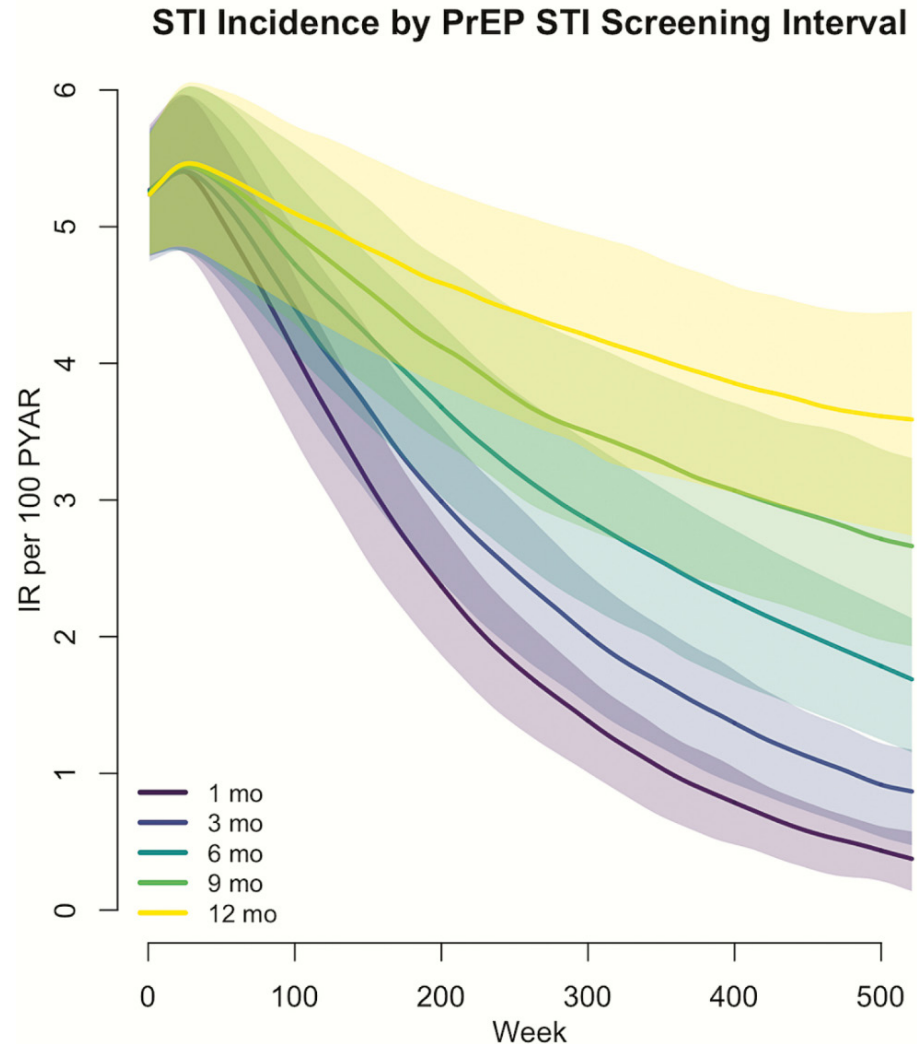
- Plateau in new HIV infections at ~38,000 per year
- Declining HIV incidence in white MSM but not others
- Limited evidence that states with more PrEP use have less HIV

R21 AI143386 (Marcus/Young): “Population-Level Effects of Increasing PrEP Uptake on HIV and Bacterial STIs” (2019-2021)

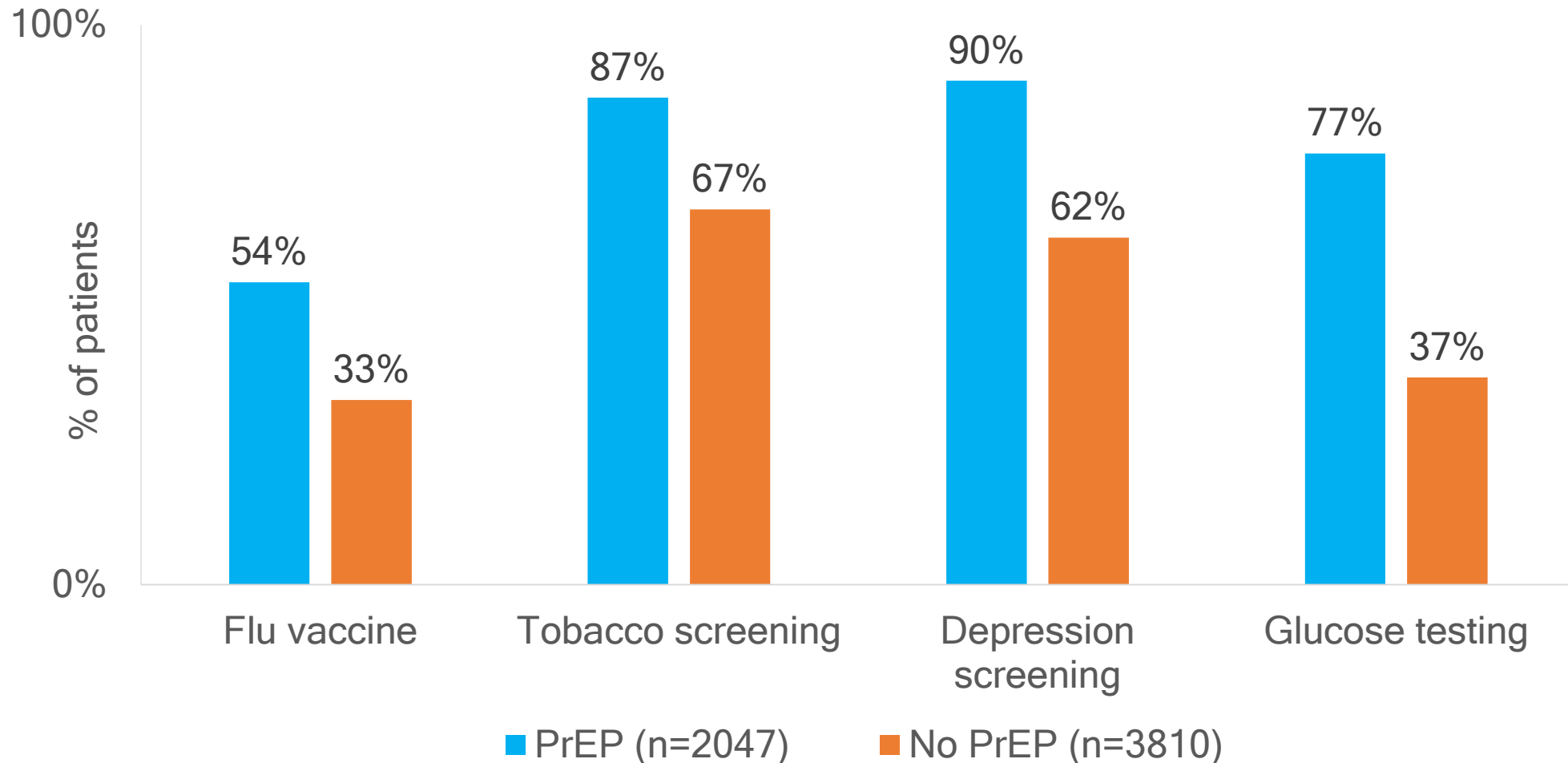
PrEP is an opportunity to intervene on STIs

- PrEP users screened every 3-6 months for STIs
- Frequent STI screening and treatment during PrEP use could **decrease** STI incidence among MSM

R01 submitted to NIMH (Jenness): “STIRRUP: STI Responses and Recommendations Under PrEP”



Benefits extend beyond HIV and sexual health



Overview

- 1) PrEP for HIV prevention and sexual health
- 2) Mitigating barriers to PrEP implementation**

THE NEW YORKER

NEWS

CULTURE

BOOKS

SCIENCE & TECH

BUSINESS

HUMOR

CARTOONS

MAGAZINE

AUDIO

SEPTEMBER 30, 2013

WHY IS NO ONE ON THE FIRST TREATMENT TO PREVENT H.I.V.?

BY CHRISTOPHER GLAZEK



Of the estimated 1.2 million Americans with indications for PrEP, only **18%** used it in 2018

PrEP used least by people who need it most

Lifetime Risk of HIV Diagnosis among MSM by Race/Ethnicity



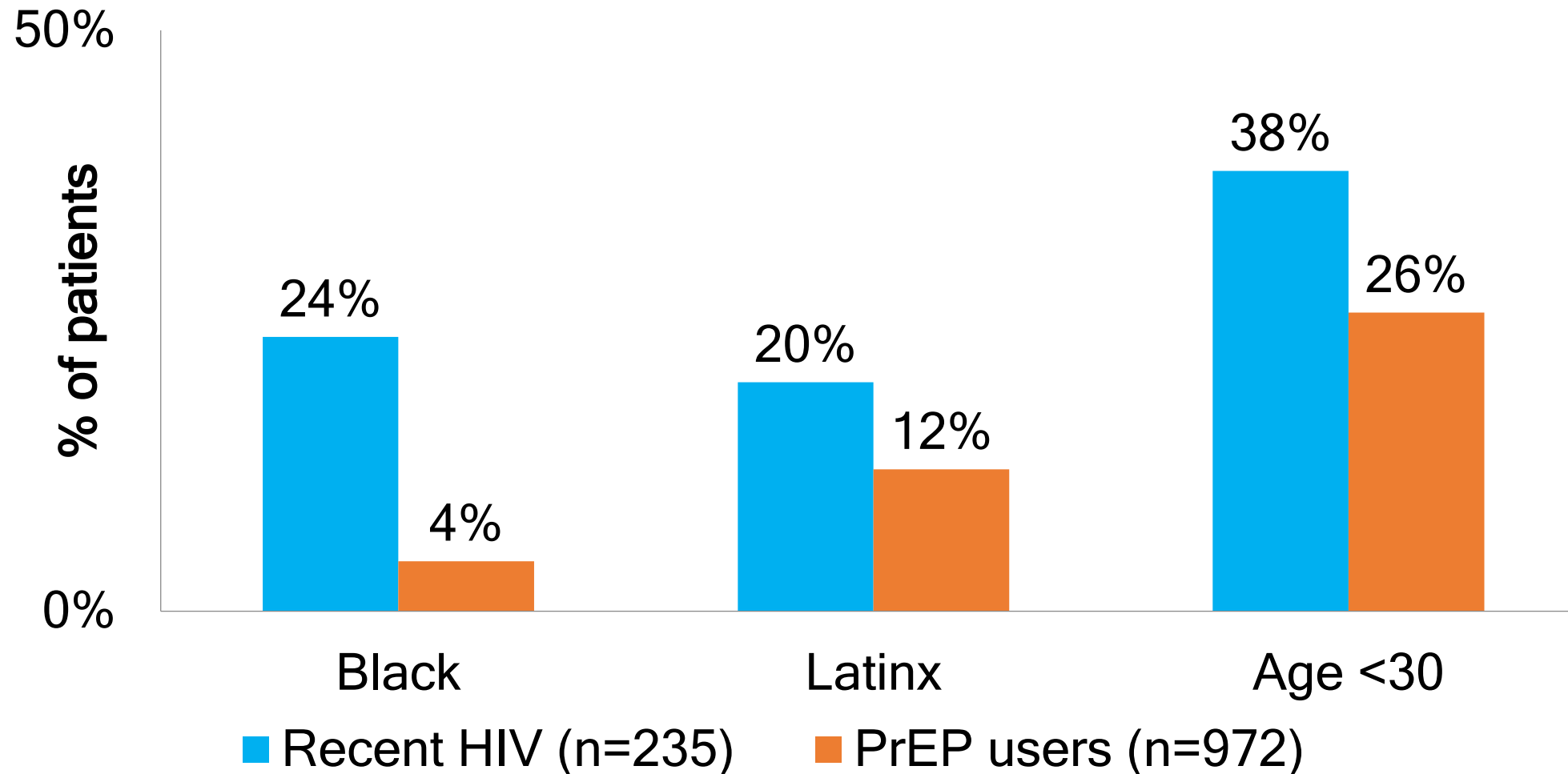
PrEP coverage

Black: 6%

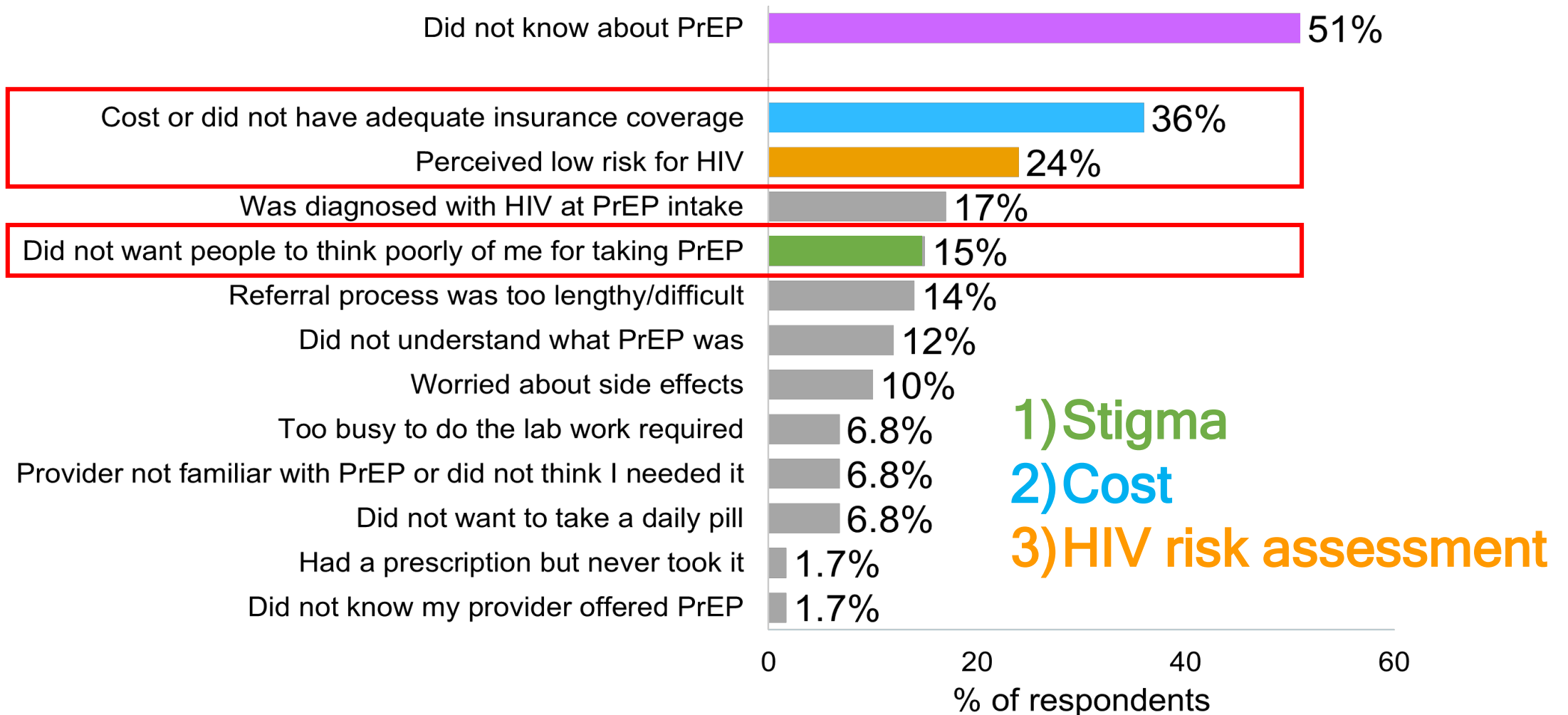
Hispanic: 11%

White: 42%

Disparities in PrEP use even among insured



Barriers to PrEP use before HIV diagnosis



Overview

- 1) PrEP for HIV prevention and sexual health
- 2) Mitigating barriers to PrEP implementation**
 - a. Stigma**



FDA Panel Recommends Anti-HIV Drug for Prevention

SILVER SPRING, MARYLAND—On 10 May, the Antiviral Drugs Advisory Committee of the U.S. Food and Drug Administration (FDA) held a marathon debate about whether an anti-HIV drug on the market as a treatment should receive approval as a preventive for uninfected people. For more than 12 hours, the committee heard scientific evidence and impassioned arguments for and against, ultimately recommending that FDA approve the use of the drug Truvada for what's called pre-exposure prophylaxis (PrEP). The decision was not unanimous, and there was a protracted back and forth about how to reduce the possibility that PrEP might cause more harm than good. By the time the committee chair asked whether the 22 members were ready to vote—which took place after the scheduled 6:30 p.m. adjournment—one person in the audience said, “Amen!”

There's little question that Truvada, made by Gilead Sciences Inc. in Foster City, California, can prevent sexual transmission of HIV: Large, controlled studies in both uninfected men who have sex with men (MSM) and uninfected heterosexuals who have long-term partners known to be infected have proved that the drug reduces risk by more than 90% when taken daily. But adherence is the rub. Many of the participants in clinical tri-

A central concern about PrEP, shared by advocates and opponents alike, is that it will lead to “risk compensation”—in other words, people will assume the pill protects them and abandon other proven prevention strategies like condom use. A small PrEP study Buchbinder participated in extensively evaluated risk compensation and found that none occurred. Similarly, none of the large-scale

by itself to prevent an HIV infection, as a treatment, it must be used with other drugs to avoid the emergence of resistant strains. The challenge with PrEP, then, is making sure that people use Truvada as a solo drug only if they are not infected—otherwise, resistant strains could run rampant and render the drug useless as both a treatment and a preventive.

If FDA approves the label change, Gilead explained in a “risk mitigation” plan how it would educate providers about the importance of prescribing PrEP only to patients who test HIV negative. But making sure only uninfected people use PrEP is easier said than done.

In clinical trials of PrEP, few cases of drug resistance were seen in the thousands of study participants. But researchers checked for infection each month and also ran sensitive PCR assays that can detect HIV in the first few weeks after infection, which is missed on standard antibody tests. In the real world, who would oversee repeated tests of people prescribed PrEP? Would retesting be required for refills? It is possible to restrict access to drugs—women receiving the acne medication Accutane must receive pregnancy tests before each prescription is filled—but as several committee mem-

Minor discord. Michael Weinstein of the AIDS Healthcare Foundation led a small but vocal campaign against the approval of Truvada as a preventive.



“If something comes along that’s better than condoms, I’m all for it, but Truvada is not that. Let’s be honest: It’s a party drug.”

– Michael Weinstein, AIDS Healthcare Foundation



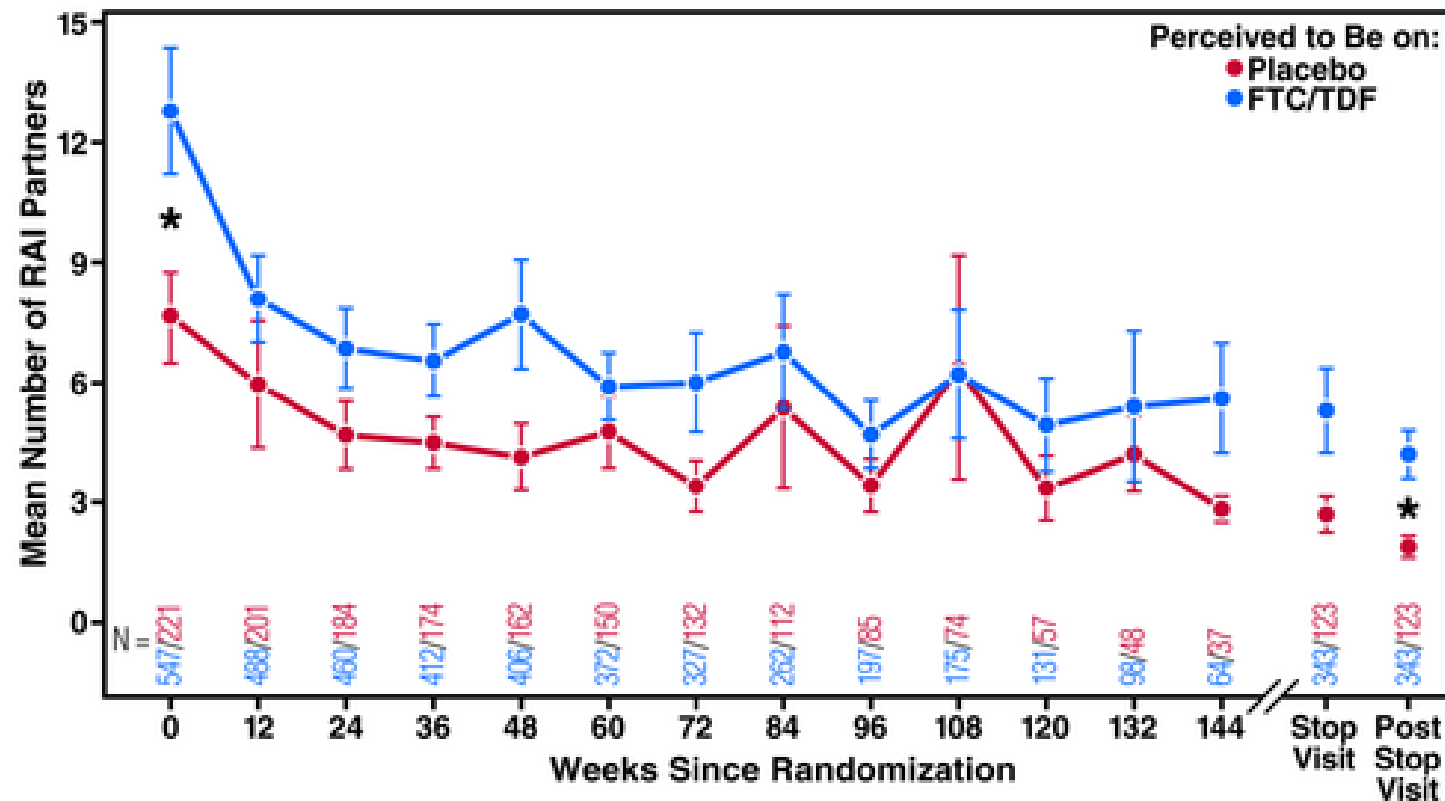
David Duran, Contributor
Journalist

Truvada Whores?

11/12/2012 07:59 pm ET | Updated Feb 02, 2016

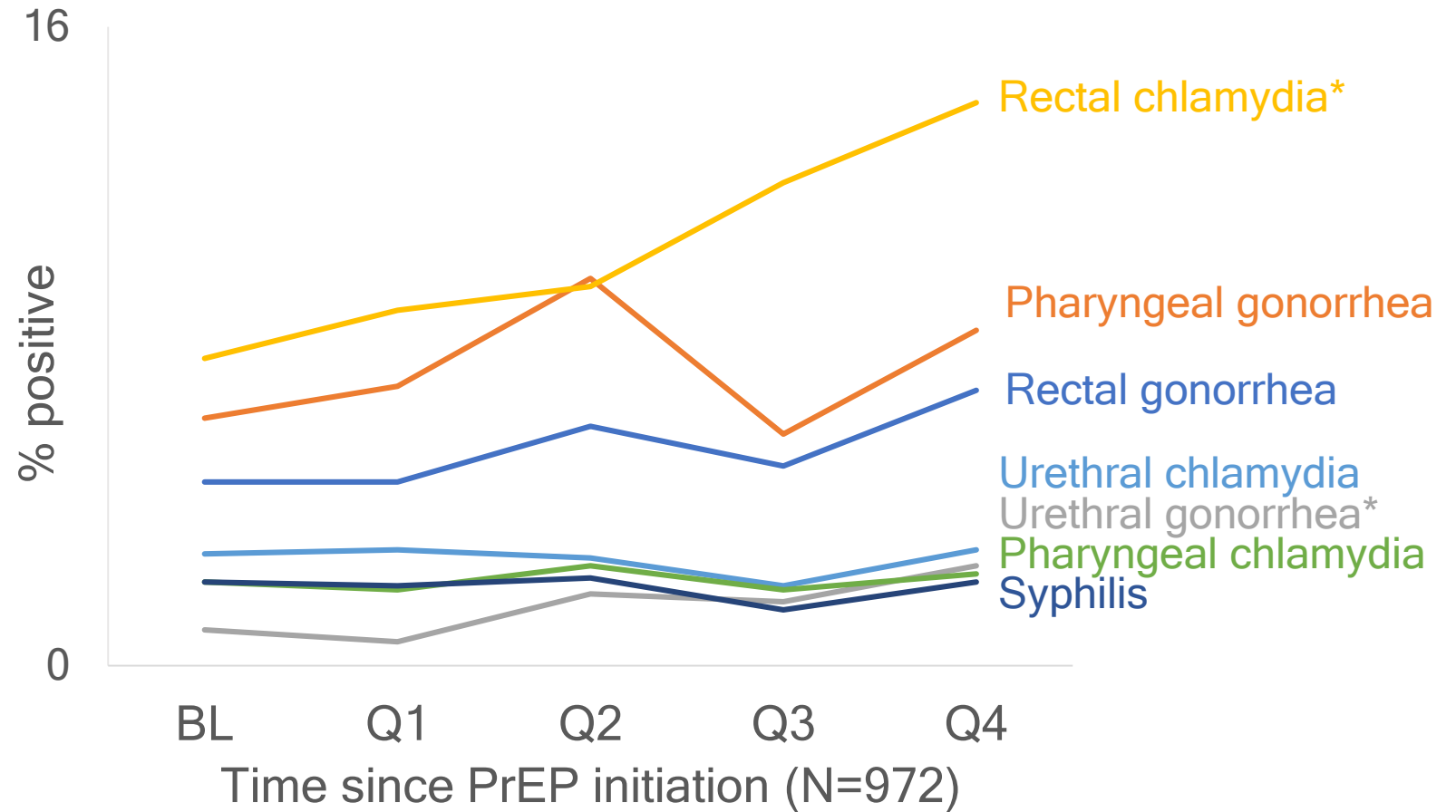
No Evidence of Sexual Risk Compensation in the iPrEx Trial of Daily Oral HIV Preexposure Prophylaxis

Julia L. Marcus^{1,2}, David V. Glidden³, Kenneth H. Mayer^{4,5}, Albert Y. Liu^{3,6}, Susan P. Buchbinder^{3,6}, K. Rivet Amico⁷, Vanessa McMahan¹, Esper Georges Kallas⁸, Orlando Montoya-Herrera⁹, Jose Pilotto¹⁰, Robert M. Grant^{1,3*}



STIs during PrEP use in clinical practice

- Increasing STIs may reflect:
 - Decreasing condom use in PrEP users
 - Decreasing condom use in the community
 - Appropriate PrEP prescribing





* Indicates $P < 0.05$

Concerns are not just about STIs

RESEARCH ARTICLE

Prevention paradox: Medical students are less inclined to prescribe HIV pre-exposure prophylaxis for patients in highest need

Sarah K Calabrese^{1,2§} , Valerie A Earnshaw³, Kristen Underhill^{4,5}, Douglas S Krakower^{6,7,8}, Manya Magnus⁹, Nathan B Hansen¹⁰, Kenneth H Mayer^{6,7,11} , Joseph R Betancourt¹², Trace S Kershaw² and John F Dovidio^{2,13}

Reason for discontinuing condoms	Acceptability
Conception	68.5%
Intimacy	23.4%
Pleasure	14.4%
Sexual functioning	12.6%



Risk Compensation and Clinical Decision Making — The Case of HIV Preexposure Prophylaxis

Julia L. Marcus, Ph.D., M.P.H., Kenneth A. Katz, M.D., M.S.C.E., Douglas S. Krakower, M.D.,
and Sarah K. Calabrese, Ph.D.

“Patient-centered care requires recognizing that disease prevention may not be the most important health outcome to patients.”

R34 in preparation for submission to NIMH (Marcus/Krakower): Intervention to Reduce Stigma and Increase PrEP Prescribing Among Resident Physicians in the South

Overview

- 1) PrEP for HIV prevention and sexual health
- 2) Mitigating barriers to PrEP implementation
 - a. Stigma
 - b. Cost

Will the newest pill for HIV prevention fuel progress — or profits?

By DOUGLAS KRAKOWER, KENNETH KATZ, and JULIA L. MARCUS / FEBRUARY 26, 2020

[Reprints](#)



Descovy and Truvada are only two FDA-approved pills for PrEP.

RICH PEDRONCELL/AP

Table. Effectiveness, Safety, and Cost of TDF-FTC and TAF-FTC for HIV PrEP

Variable	TDF-FTC	TAF-FTC
Effectiveness, %*		
MSM and transgender women	~99	~99
Heterosexual women and men	~99	Unknown
Persons who inject drugs	74 to 84	Unknown
Changes in safety parameters at 48 wk (4, 9)		
Mean estimated glomerular filtration rate, mL/min/1.73 m ²	-2.0	+2.0
Mean hip bone mineral density, %	-1.0	+0.2
Median fasting low-density lipoprotein cholesterol level mmol/L	-0.17	+0.03
mg/dL	-6.5	+1.0
Mean body weight, kg	0	+1.1
Cost		
Average wholesale price per month, \$	2110	2110
Year in which generic version will be available	2020	2022 to 2025

Overview

- 1) PrEP for HIV prevention and sexual health
- 2) Mitigating barriers to PrEP implementation
 - a. Stigma
 - b. Cost
 - c. HIV risk assessment

Need effective tools to assess HIV risk

Recommendation Summary		
Population	Recommendation	Grade (What's This?)
Persons at high risk of HIV acquisition	The USPSTF recommends that clinicians offer preexposure prophylaxis (PrEP) with effective antiretroviral therapy to persons who are at high risk of HIV acquisition.	A

“Research is needed to **develop and validate tools** that are highly accurate for identifying persons at high risk of HIV acquisition who would benefit from PrEP.”

Limitations of HIV risk prediction tools

MSM Risk Index

1. How old are you today?	If <18 years, score 0. If 18-28 years, score 8. If 29-40 years, score 5. If 41-48 years, score 2. If 49 years or more, score 0.	_____
2. In the last 6 months, how many men have you had sex with?	If >10 male partners, score 7. If 6-10 male partners, score 4. If 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 without a condom?	If 1 or more times, score 10. If 0 times, score 0.	_____
4. In the last 6 months, how many of your male sex partners were HIV-positive?	If >1 positive partner, score 8. If 1 positive partner, score 4. If <1 positive partner, score 0.	_____
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?	If 5 or more times, score 6. If 0 times, score 0.	_____
6. In the last 6 months, have you used methamphetamines such as crystal or speed?	If yes, score 6. If no, score 0.	_____
Add down entries in right column to calculate total score.		_____ 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.

Preexposure Prophylaxis for the Prevention of HIV Infection in the United States – 2014 Clinical Providers' Supplement Page 21 of 43






- Require providers to know patient is in a risk group
- Difficult to use during busy clinical visits
- Only moderately predictive
- Underestimate HIV risk in Black MSM

EHRs are an untapped opportunity

PROMPT

Go To Patient PROMPT →

Catastrophic Hold 🔒

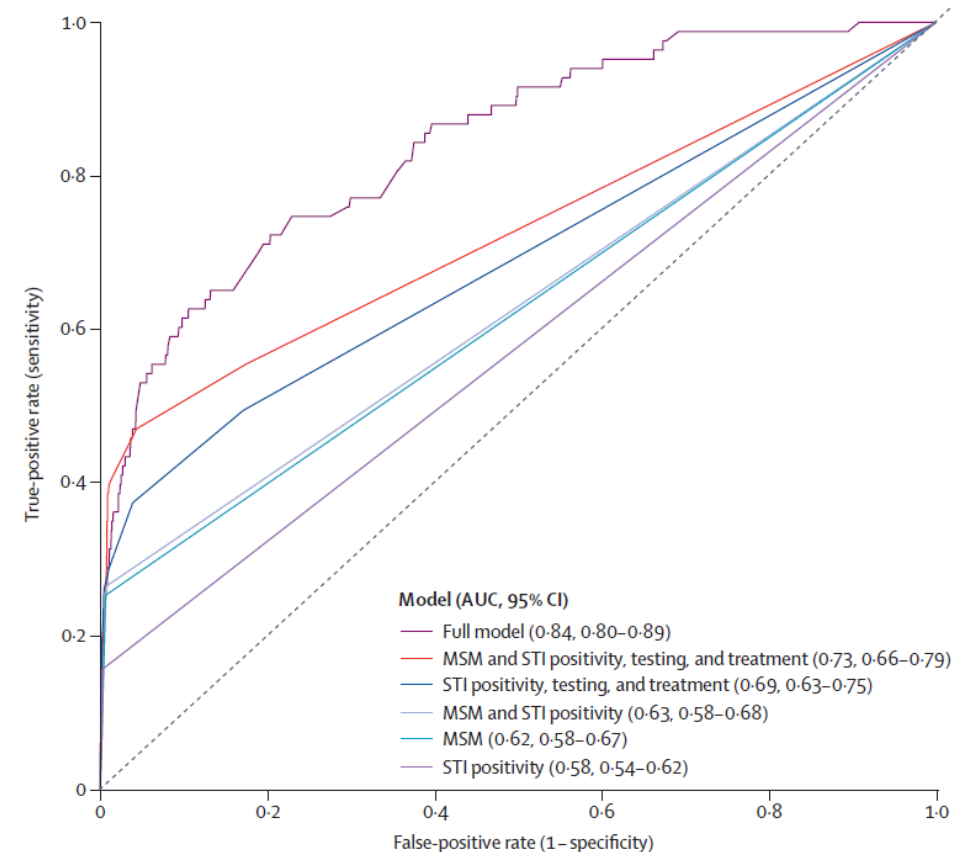
APM	Value		Actions
+ ASA		needs discussion - 15.9%, 60-69 Last: Due:	CV Calc Discuss Rx
+ CRC		up to date - followed by GI Last: 01/23/2015 Due: 01/27/2020	Done Outside Colectomy Holds ▼
+ D/T/Td		up to date Last: 10/02/2014 Due: 10/02/2024	
+ Flu		up to date Last: 10/18/2017 Due: 10/01/2018	
+ Pneum		up to date Last: 02/29/2016 Due:	

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request timestamp: 09/21/2018 08:28:50
request url: prompt.kp.org
program version: 2.34.1

Identification of potential PrEP candidates

- 3.7 million members of Kaiser Permanente Northern CA
- Machine learning model to predict incident HIV
- Outperformed simpler models, especially for Black patients



R01 MD013565-02S1 (Dehlendorf): “Offering Women PrEP with Education, Shared Decision-Making, and Trauma-Informed Care: The OPENS Trial” (2019-2020)

Would You Want a Computer to Judge Your Risk of H.I.V. Infection?

A new software algorithm decides which patients are most likely to become infected with the virus. But this is not like other risk calculators, some experts say.

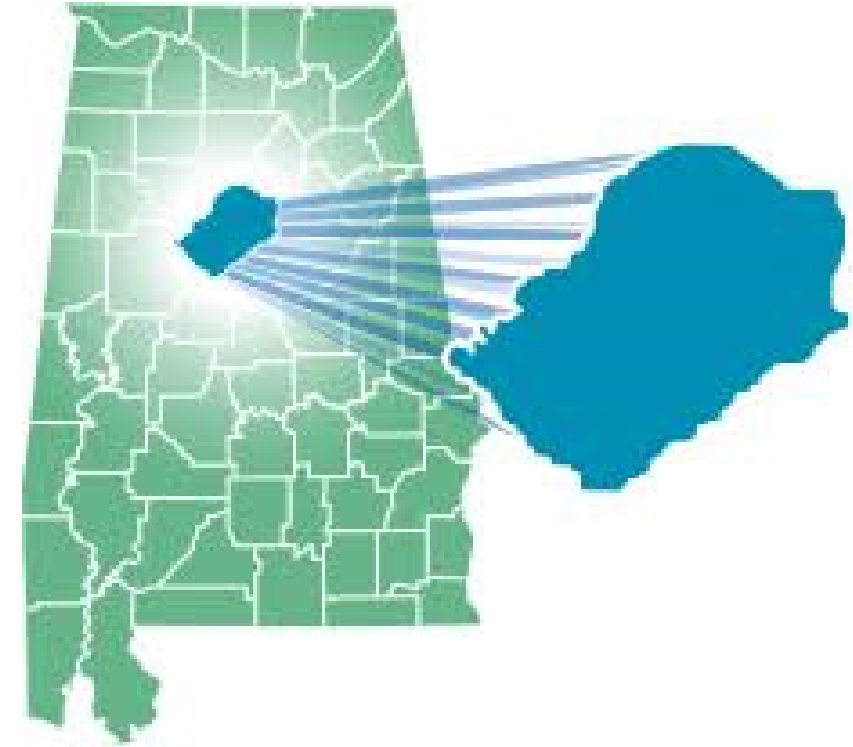


By Gina Kolata

July 30, 2019

Implementation in public health clinics

- 1 of 7 hotspot states in Ending the Epidemic initiative
- Jefferson County diagnoses the most HIV cases in the state
- 3 primary care clinics and 1 STI clinic, with 17 years of EHR data

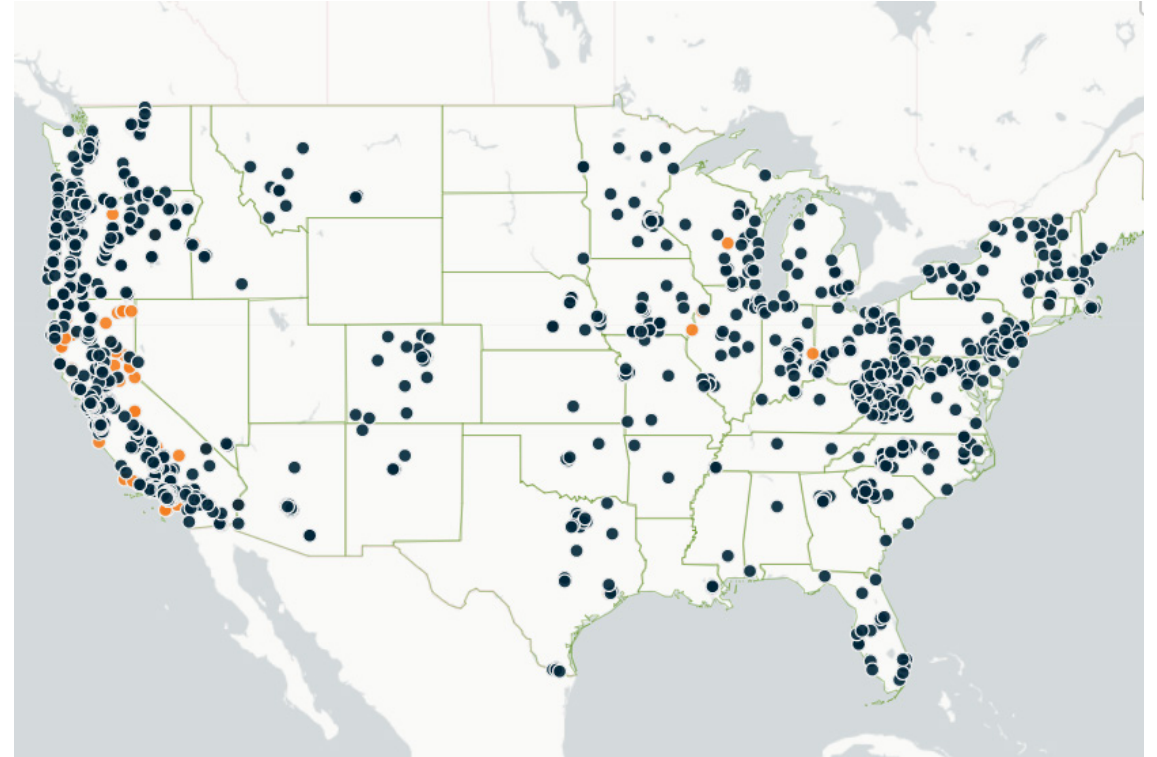


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Pilot trial in community health centers

- 2.8 million patients
- 19% Black, 35% Latinx, 65% below poverty line
- 155 clinics in HIV hotspot counties



OCHIN

R34 MH122291 (Marcus/Krakower): “EHR-Based Prediction Models to Improve PrEP Uptake in Community Health Centers” (2019-2022)

Key points

- PrEP prevents HIV, promotes sexual health, and connects people to primary care
- Uptake has been limited because of cost, stigma, structural racism, and challenges with HIV risk assessment
- Need to mitigate these barriers to achieve population impact and equity
- **We have the tools to end the HIV epidemic, we just need to deliver them better**

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 - Miguel Marino
 - Sam Jenness





Thank you!

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