

CONTROLLING THE HIV EPIDEMIC WITH ANTIRETROVIRALS



Treatment as Prevention
and Pre-Exposure Prophylaxis

22-24 September 2013
Queen Elizabeth II Conference Centre, London

Adherence to PrEP Elements of Success

K Rivet Amico, PhD
University of Connecticut
Connecticut, USA



CONTROLLING THE HIV EPIDEMIC WITH ANTIRETROVIRALS
Treatment as Prevention and Pre-Exposure Prophylaxis

Major findings from the evidence base gathered to date and future directions

IN GENERAL (WITH CAVEATS) PREP IS EFFECTIVE

- **Studies completed to date generally support efficacy of PrEP, with exceptions**
- **Adherence relates to levels of protection**
- **Heterogeneity in product use is under study**

PREP ADHERENCE IS UNDER INVESTIGATION

- **Study product vs effective PrEP**
 - **Adherence may not resemble study product adherence**
- **Success relies on taking it...but many questions remain**

IN PROGRESS AND CRITICAL QUESTIONS



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IN PROGRESS AND CRITICAL QUESTIONS





IN GENERAL (WITH CAVEATS) PREP IS EFFECTIVE

Study	Efficacy	
PinP-TDF/FTC	75%*	<p>Other Countries are awaiting more evidence...</p> <p>Daily oral- PROUD</p> <p>Intermittent Oral- iPerGAY</p> <p>1% BAT₂₄ Gel- FACTS</p>
PinP- TDF	67%*	
TDF ₂ – TDF/FTC	62%*	
BKK- TDF	49%*	
iPrEX – TDF/FTC	44%*	
CAPRISA –Gel BAT ₂₄	39%*	
VOICE- Gel Daily	14.7%	
FemPrEP – TDF/FTC	6%	
VOICE- TDF/FTC	-4%	
VOICE- TDF	-49%	



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Adherence relates to levels of protection



IN GENERAL (WITH CAVEATS) PREP IS EFFECTIVE

Study	Efficacy	Estimated Adherence by Drug Concentration
PinP-TDF/FTC	75%*	75-80%
PinP- TDF	67%*	67-80%
TDF₂ – TDF/FTC	62%*	80%
BKK- TDF	49%*	67%
iPrEX – TDF/FTC	44%*	51%
CAPRISA –Gel BAT₂₄	39%*	38% - 98%
VOICE- Gel Daily	14.7%	22%
FemPrEP – TDF/FTC	6%	37%
VOICE- TDF/FTC	-4%	29%
VOICE- TDF	-49%	28%



IN GENERAL (WITH CAVEATS) PREP IS EFFECTIVE

Study

Efficacy

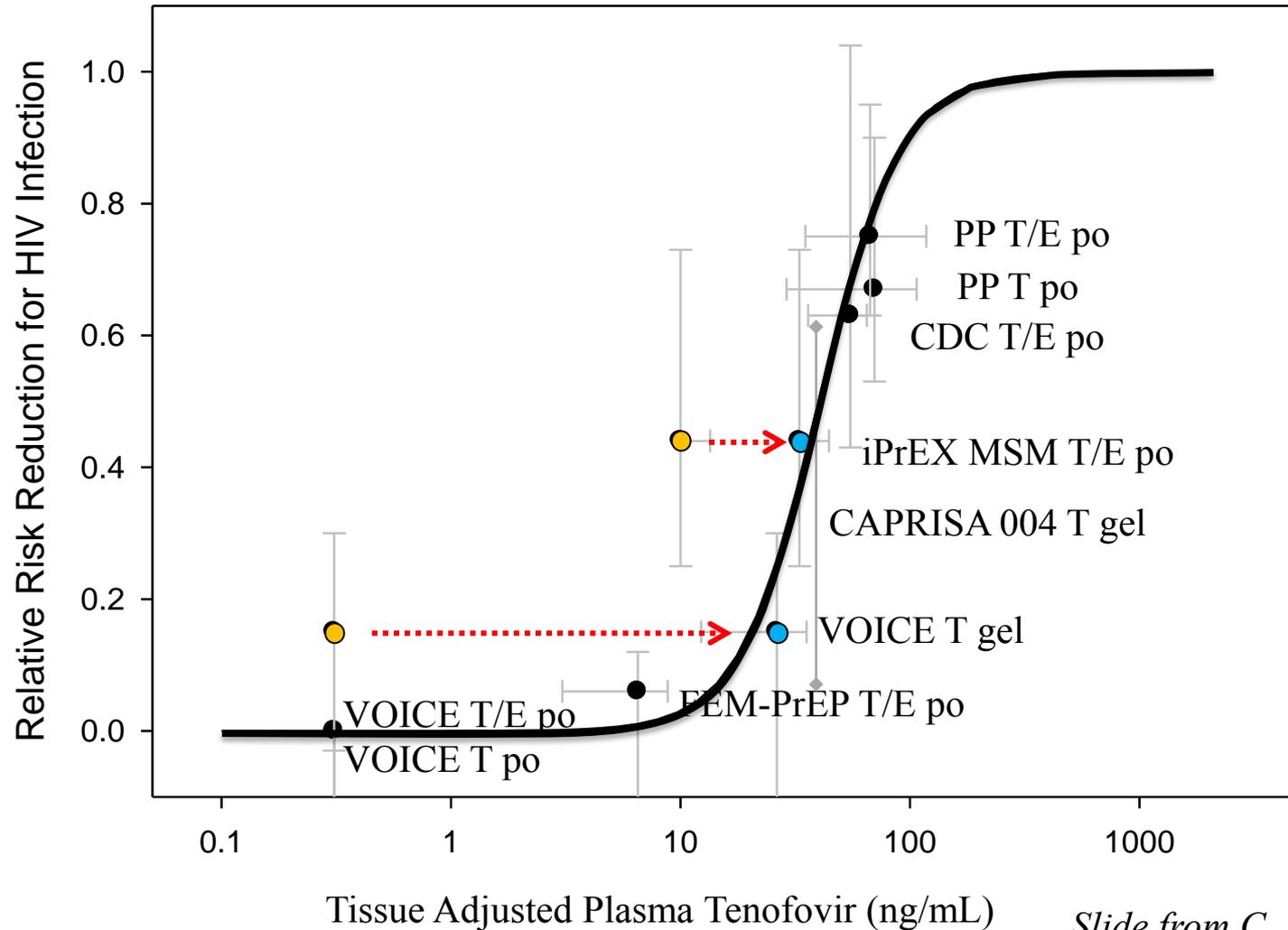
**Estimated Adherence
by Drug Concentration**

EFFICACY BY ADHERENCE



Drug Concentration Response

Adjusted for PK concentrations, differences in outcomes across trials largely driven by differences in adherence (once accounting for PK)



‘If you take it, it works’: The importance of adherence

The single biggest Achilles heel in all the PrEP studies

EDITORIAL

Pre-exposure prophylaxis for HIV prevention: Ready for prime time in South Africa?

Eakle, Venter, & Rees S Afr Med J 2013



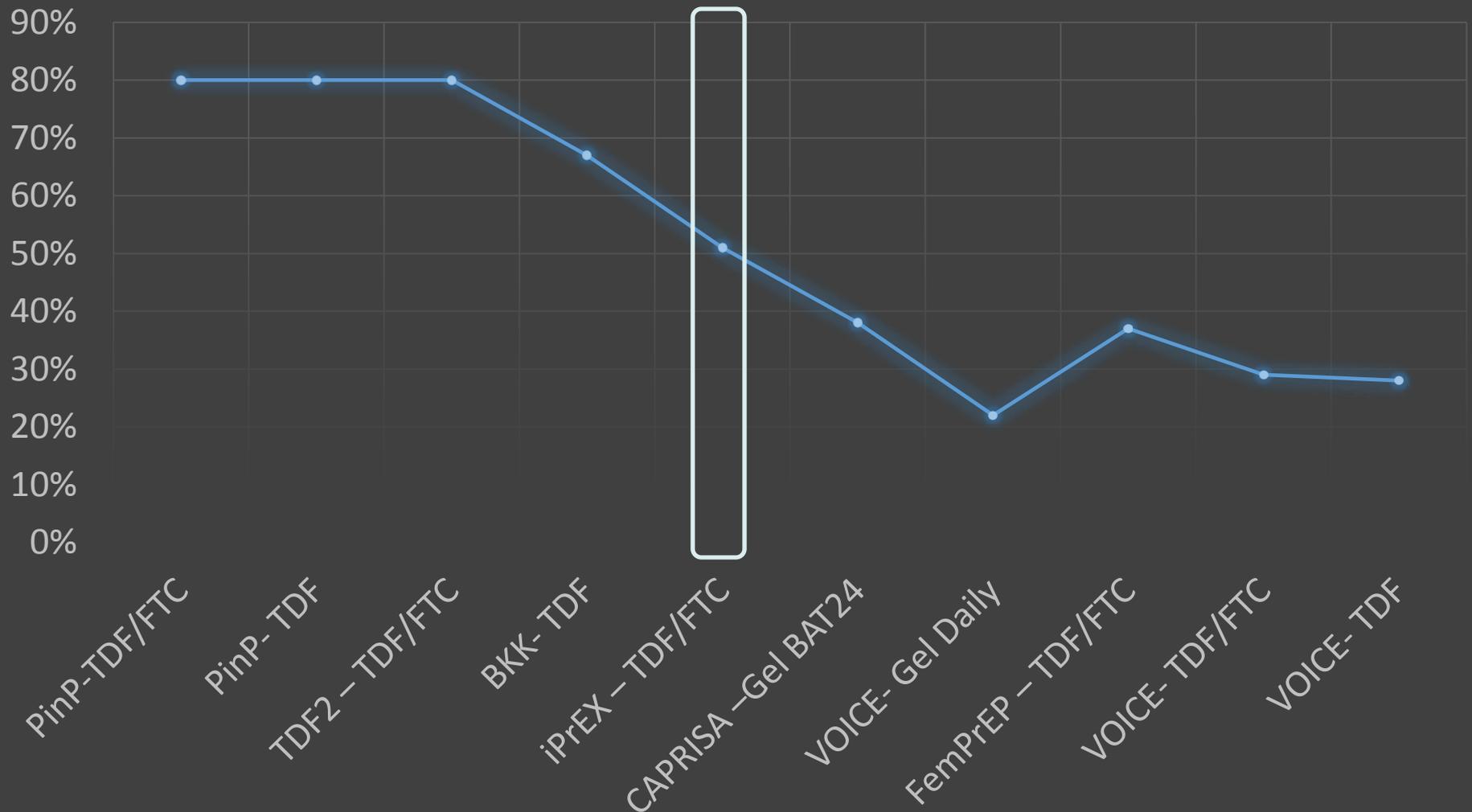
CONTROLLING THE HIV EPIDEMIC WITH ANTIRETROVIRALS
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Estimated Adherence by Drug Concentration



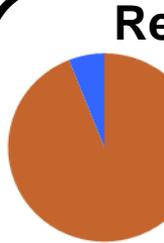
Sizable differences found in use of study product...between and within studies

Estimated Adherence by Drug Concentration



TFV-DP Detection

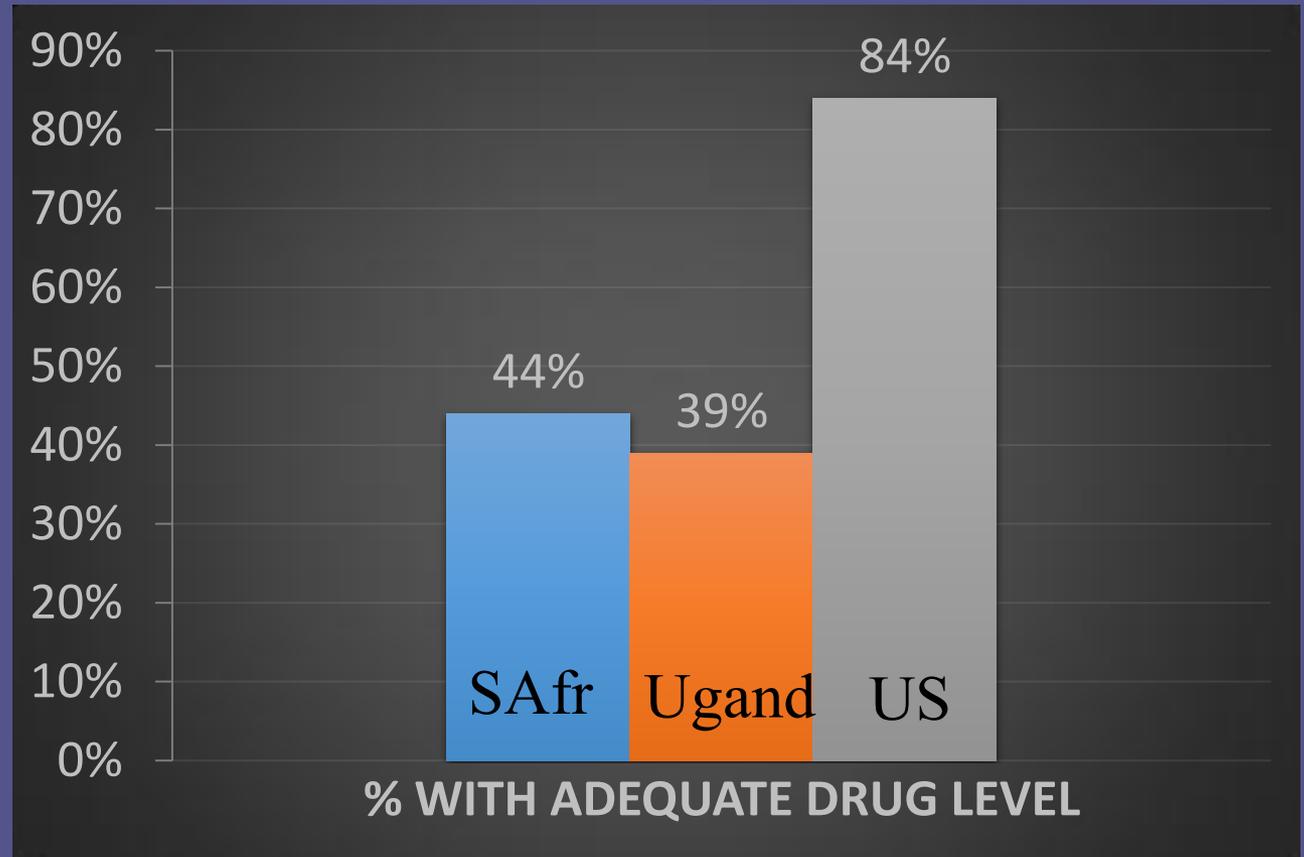
Drug Detection* (%)	94%
Time Points	53
Median TFV-DP Level	26



P <

USA

MTN-001 Crossover Study Minnis et al 2013



*Detection of TFV/FTC/TFV-DP or FTC-TP in plasma or PBMC [Anderson et al 2011]

- **Non-adherence may signal poor acceptability, but could also signal community/cultural conflicts with the research paradigm itself.**



- **Study drug adherence may be driven by social/political climate, research, community and participant(s).**
 - 401 interviews 179 female microbicide trial participants, 28 interviews with partners, 42 focus groups community members [2005-2009]

Medical Anthropology Quarterly

Eirik Saethre

Department of Anthropology
University of Hawai'i at Mānoa

Jonathan Stadler

Wits Reproductive Health and HIV Research Institute
University of the Witwatersrand

Malicious Whites, Greedy Women, and Virtuous Volunteers

Negotiating Social Relations through Clinical Trial Narratives in South Africa

As clinical trial research increasingly permeates sub-Saharan Africa, tales of purposeful HIV infection, blood theft, and other harmful outcomes are widely reported by

MEDICAL ANTHROPOLOGY QUARTERLY, Vol. 27, Issue 1, pp. 103–120, ISSN 0745-5194, online ISSN 1548-1387. © 2013 by the American Anthropological Association. All rights reserved. DOI: 10.1111/maq.12018

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Other factors influencing study drug NON-ADHERENCE:

- **Age (younger)**
- **Gender (Male)**
- **Lower SES**
- **Heavy or binge alcohol use**
- **Lower perceived risk for HIV**
- **No sex [PinP] or polygamous marriage**



PRODUCT NON- COMPLIANCE IN PREP TRIALS

- Interferes with sex
- Lack partner support
- Stigma as participant
- HIV stigma
- Demanding/difficult
- Poor match with culture

- Young
- Unmarried
- Low perc risk
- Low perc benefit
- Low intentions
- Low motivation

Person

Regimen

- Under study
- Placebo controlled
- No evidence
- Discomfort

Relationship
with care
team

- Distrust
- Intentional non-adherence
- Fearful

- Complex messages
- Unclear procedures
- Long visits



Hard to tell who will be non-adherent, but we may be able to tell who IS/IS NOT using product during a trial...

MONITORING/BEING MONITORED MAY NOT BE AN

STILL NEED TO WORK THROUGH HOW TO BEST

OPEN ACCESS Freely available online

PLOS MEDICINE

Adherence to Antiretroviral Prophylaxis for HIV Prevention: A Substudy Cohort within a Clinical Trial of Serodiscordant Couples in East Africa

Jessica E. Haberer^{1,2*}, Jared M. Baeten^{3,4,5}, James Campbell⁶, Jonathan Wangisi⁶, Elly Katabira⁷, Allan Ronald⁸, Elioda Tumwesigye⁹, Christina Psaros^{10,11}, Steven A. Safren^{10,11}, Norma C. Ware¹², Katherine K. Thomas³, Deborah Donnell^{3,13}, Meighan Krows³, Lara Kidoguchi³, Connie Celum^{3,4,5}, David R. Bangsberg^{1,2,14}



CONTROLLING THE HIV EPIDEMIC WITH ANTIRETROVIRALS
Treatment as Prevention and Pre-Exposure Prophylaxis

Better Products May Promote Better Product Adherence in RCTs AND real-world open label

- **Long acting agents- less frequent dosing**
- **Slow release (Dapivirine Vaginal Ring- ASPIRE)**
- **Dual purpose- Birth control + ARV; Lube + ARV**
- **On Demand or Intermittent PrEP**

All other things being equal...

- ✓ **Simpler is better.**
- ✓ **Products matched to common practices is better.**
- ✓ **Products that address multiple needs is better.**

Does not eliminate adherence (acceptability, feasibility) from the picture but could minimize demands of it.



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IN PROGRESS AND CRITICAL QUESTIONS



NON-ADHERENCE

Study drug vs Effective PrEP

Real world PrEP

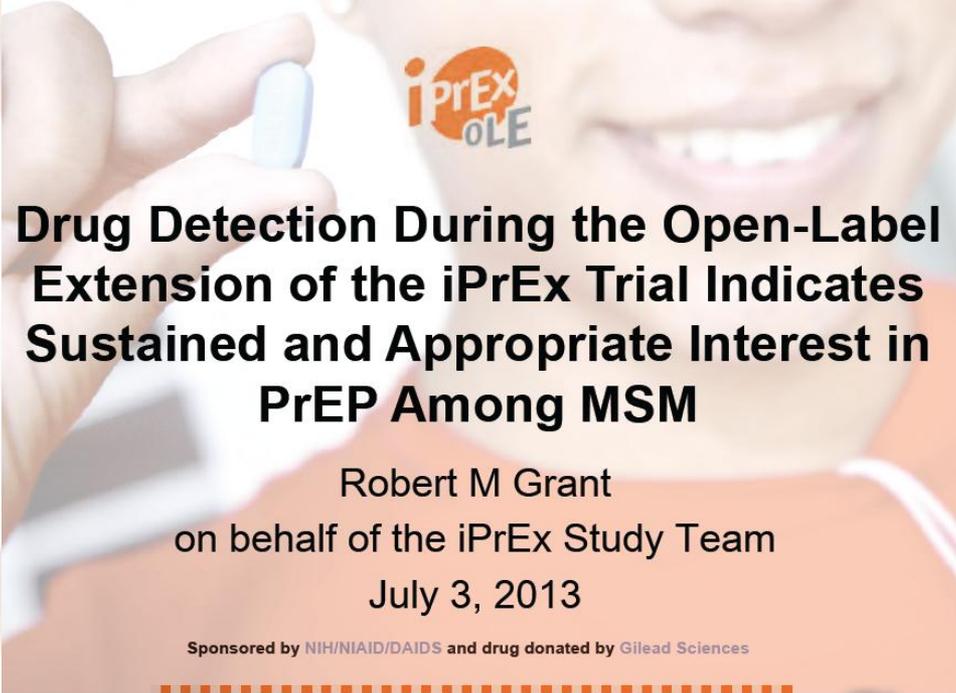
- **Interferes with sex**
- **Lack of *PrEP* partner support**
- **Stigma as “PrEP” user participant**

Some differences...	Placebo Controlled Drug	Effective PrEP
User	Participant/Volunteer	User
Motivation for Enrollment/Uptake	Medical care Testing Resources	Comprehensive prevention plan Access to PrEP
Drug	May/may not be active drug Under investigation for efficacy and/or safety	Effective and safe
Why take it?	To contribute to research and community	To protect self from HIV infection/Sexual health
Consequence of non-use?	Jeopardize research and finding community solutions	No PrEP protection benefits (may or may not mean increased risk)
Duration of use?	Continuous while on-study	As needed? Times of risk?



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Drug Detection During the Open-Label Extension of the iPrEx Trial Indicates Sustained and Appropriate Interest in PrEP Among MSM

Robert M Grant
on behalf of the iPrEx Study Team
July 3, 2013

Sponsored by NIH/NIAID/DAIDS and drug donated by Gilead Sciences

- **OLE enrolled from June 2011 to June 2012.**
- **OLE participation did not require PREP use.**
- **Of 1451 eligible for PrEP, 72% selected it (older, lower ed, recent nc-RAI)**
- **Of those on PrEP, 72% had detectable drug (older, higher ed)**



IAS 2013

7th IAS CONFERENCE ON HIV PATHOGENESIS,
TREATMENT AND PREVENTION

30 June - 03 July 2013 - Kuala Lumpur, Malaysia

ceria

**International
AIDS Society**
Stronger Together Against HIV



PREP ADHERENCE IS PRESENTLY UNKNOWN

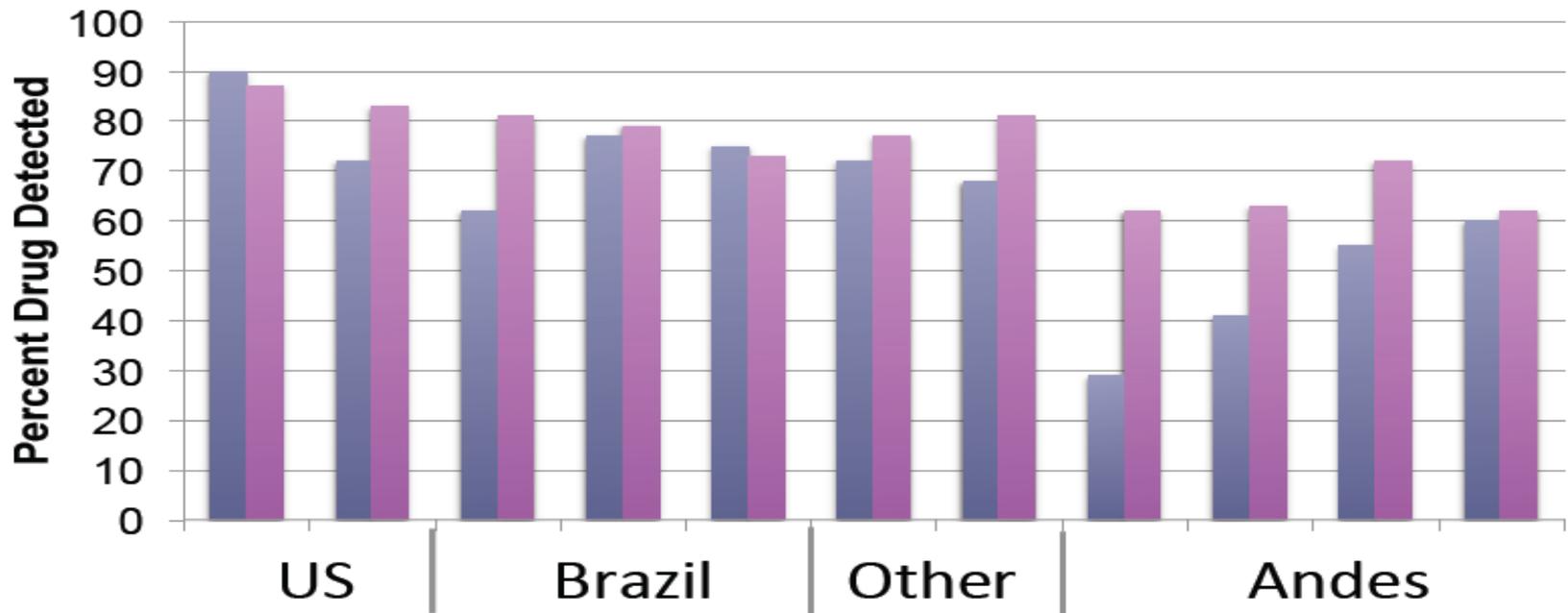
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Plasma Drug Detection by Region

iPrEx Randomized wk 8, OLE wks 4-12

■ Randomized ■ OLE





PREP ADHERENCE IS PRESENTLY UNKNOWN

- **Study product vs effective PrEP**
 - Adherence may not resemble study product adherence
 - Success relies on taking it; taking it may be higher among early adopters of an effective intervention (PrEP vs study product)...but many questions remain
- **What will rates of adherence be among those choosing to use PrEP- and will that differ dramatically by community or cohort or change over time?**
- **INTERVENTION DEVELOPMENT**
 - What are the cycles of PrEP use and how does that influence adherence? How to support transitions?
 - Should focus be on adherence interventions or prevention packages or menus? **PREVENTION SYNERGY?**
 - **MP3 Projects; Integrated Demonstration Projects**



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IN PROGRESS

Demonstration Projects in Progress

- **SMS text based reminders and motivators**
- **Text based outreach**
- **Targeted adherence support**
(increasing intensity with demonstrated non-adherence)
- **Drug level feedback**
- **Integrated Protection Menus**
- **Delivery locations**



IN PROGRESS

Other Projects in progress

- **Detailed PK DOT study**
- **Intermittent adherence**
- **Safety of alternative ARVs**
- **Framing messages**
- **Media to inform**
- **ATN 110/113**



CRITICAL QUESTIONS

How well will people adhere to PrEP in the real world?

- **We have reason to be concerned- plenty of warnings from other prevention/treatment fields.**
- **Maybe we can expect higher rates of effective PrEP adherence than study product from the RCTs.**
 - **Within many placebo controlled trials completed to date, participants with low/no intentions to use product OR disclose non-use have been identified.**
 - **Will this also occur in open-label PrEP programs?**



CRITICAL QUESTIONS

How well will people adhere to PrEP in the real world?

- **As an open question- we can help reduce confusion by adopting appropriate terms**
- **Reserve use of term 'PrEP adherence' for open label effective PrEP adherence.**



CRITICAL QUESTIONS

Will people want PrEP if it is available?

Drug utilization data from medical claims - starting TVD after Jan 1 2011

- **Individuals on PrEP- 1,774 mixed prescribers (37% experienced with HIV treatment)**
- **Mdn Age: 37**
- **Women: 47%**

Poster Number
H-663a

Scan this QR code to link to this poster and to download a PDF copy.

You will be prompted to enter the following password: H-663a

53rd International Conference on Antimicrobial Agents and Chemotherapy (ICAAC)
September 16-23, 2013
Denver, CO, USA

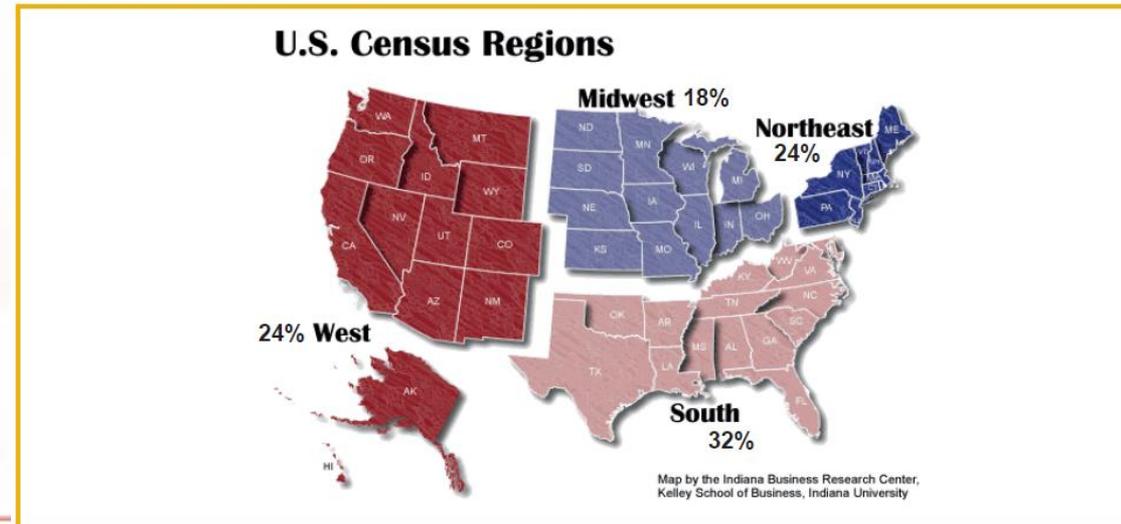
Status of Truvada (TVD) for HIV Pre-Exposure Prophylaxis (PrEP) in the United States: An Early Drug Utilization Analysis

RM Mera, MK Rawlings, A Pechonkina, JF Rooney, T Peschel, A Cheng

Gilead Sciences, Inc., Foster City, CA

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Figure 1. Geographic Distribution of PrEP Users



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CRITICAL QUESTIONS

Will stigma challenge PrEP uptake and adherence?

Friday, March 1, 2013

Interview Part 3: Toronto Health Promoter Chooses PrEP - "Maybe I should get a t-shirt made that says 'Truvada Whore' on it"

via Positive Lite (Canada)

Part 3 of an interview with Len Tooley, an HIV-negative gay guy who is taking pre-exposure prophylaxis. He works in Toronto as a gay men's health promoter, HIV educator, tester and counsellor.

Share
your
PrEP
story^{at}



My PrEP
experience



THE BLOG

Featuring fresh takes and real
HuffPost's signature lineup of



David Duran

Freelance journalist

GET UPDATES FROM DAVID DURAN



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Truvada Whores?

Posted: 11/12/2012 7:59 pm



Moving forward with both RCTs and roll out...

Develop social science agenda to understand and promote product use in RCTs

- Drivers of product use; strategies to promote product use (from recruitment to on-study); new designs (PrEP as an option); monitoring feedback strategies

Targeted research on PrEP adherence

- Potential success of PrEP will be characterized in demonstration studies – uptake, adherence, retention
- How common is poor adherence? Early? Late?
- How to best intervene to support? Integrated? Adherence?
- Monitoring and drug level feedback?

Continue to work collaboratively



Thank you

Special thanks for assistance, clarification or use of slides:

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Jessica Justman

Pete Anderson

Al Liu

Michael Stirratt

****THIS PRESENTATION DOES NOT REPRESENT THE VIEWS OF ANY
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