Patterns and Correlates of PrEP Drug Detection among MSM and Transgender Women in the Global iPrEx Study

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Disclosures

- Gilead Sciences donated study drug for this study.

Background

- Adherence to pre-exposure prophylaxis (PrEP) is critical for efficacy[1-6]
- Antiretroviral drug concentrations are an objective measure of PrEP use and correlate with efficacy[1-4]
- Understanding patterns and correlates of drug detection can identify populations at risk for non-adherence and inform design of PrEP adherence interventions
- We evaluated rates and correlates of PrEP drug detection in the Global iPrEx study[1]

[1]Grant NEJM 2010; [2]Anderson Sci Transl Med 2012; [3]Baeten NEJM 2012; [4]Thigpen NEJM 2012; [5] Hendrix Cell 2013; [6]Koenig American Journal of Preventive Medicine 2013;

iPrEx: Phase 3 PrEP efficacy trial among MSM and transgender women in 6 countries

Sites	11
Participants	2499

New England Journal of Medicine, online Nov 23, 2010

Goals of analysis

- Perform a cross-sectional analysis of prevalence and correlates of drug detection at week 8 *(drug initiation and early adherence)*

- Conduct a longitudinal analysis of patterns of drug detection across multiple time-points through 72 weeks of participation *(persistence, consistency of use)*

Methods: sample selection (active-arm only)

Cross-sectional analysis

- Random sample of serum specimens at week 8, stratified by site
- 25% of active arm samples or at least 40 specimens selected per site (whichever was larger)

Longitudinal analysis

- All available plasma (every 12 weeks) and peripheral blood mononuclear cells (PBMCs) (every 24 weeks) tested
  - DEXA substudy evaluating impact of FTC/TDF on bone (7 sites)
  - Matched active-arm controls in case-control study of seroconverters (9 sites)

Methods (cont'd)

Drug concentrations determined using LC-MS/MS

- Serum/plasma: lower limit of quantification (LLQ) for TFV and FTC: 10 ng/ml
- Lysed PBMCs: LLQ 2.5 fmol/sample for TFV-DP and 0.1 picomole/sample for FTC-TP

Correlates of drug detection variables

- Sociodemographics at screening (CASI)
- Sexual behaviors (interview) and drug use (CASI) at screening
- HIV risk perception at screening, perceived treatment assignment and PrEP efficacy at week 12 (CASI)
- Clinical symptoms at weeks 4 and 8 (symptom checklist)

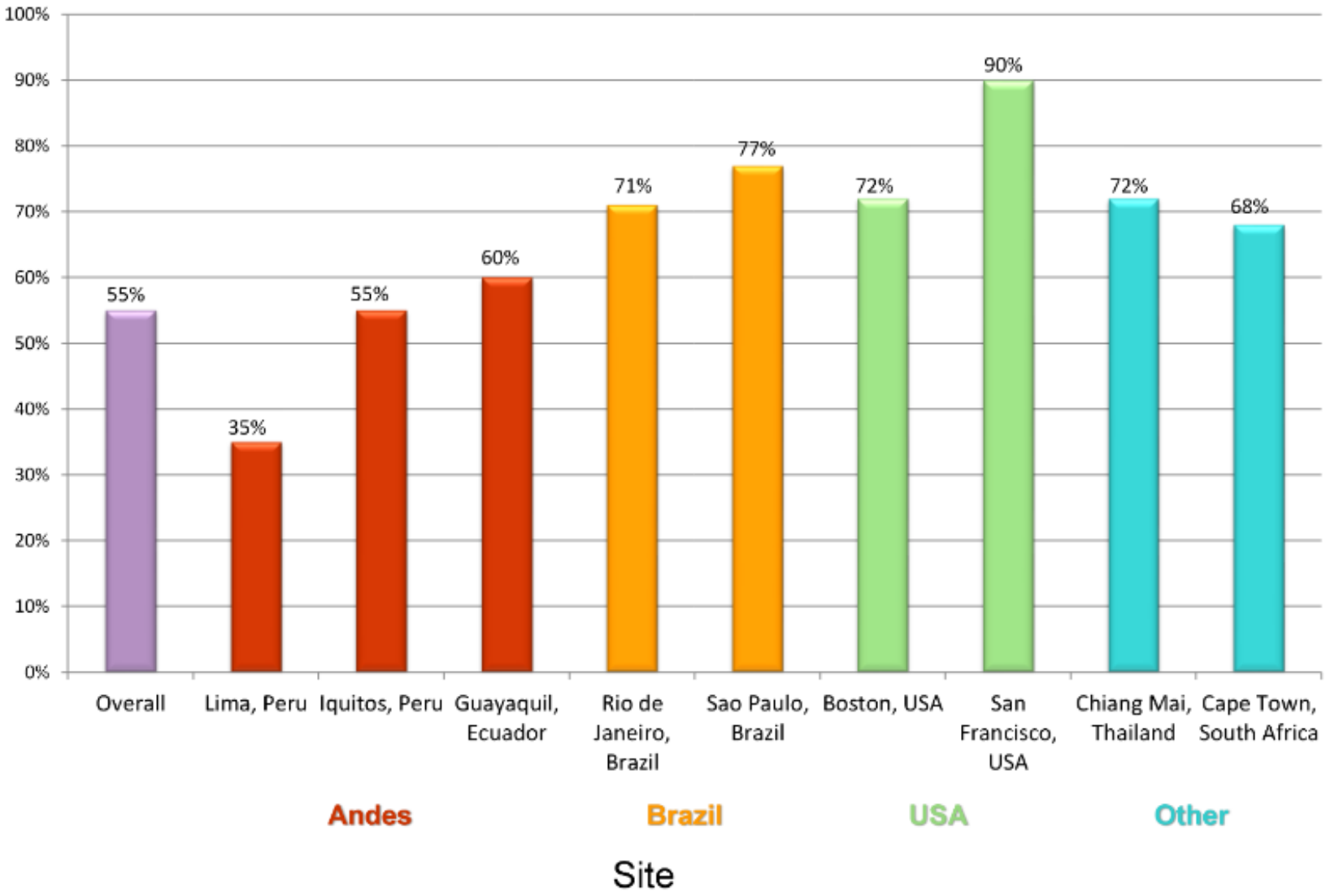
Statistical analysis

- Cross-sectional: any drug detection in serum (either TFV or FTC)
  - Logistic regression with site as fixed effect to assess correlates of detection
- Longitudinal: % drug detected in plasma or PBMCs at none, some, or all visits
  - Multinomial logistic regression to assess correlates of patterns of drug detection

Baseline characteristics of iPrEx participants with drug levels tested at week 8 or in longitudinal cohort

Characteristic (n %)	Active Arm (N=1,251)	Week 8 cohort (N=470)	Longitudinal cohort (N=303)
Age ≤25	51%	50%	52%
Some College or more education	23%	31%	18%
<u>Site Region</u> Andes (Peru, Ecaudor) Brazil US Thailand South Africa	 68% 15% 9% 5% 4%	 44% 24% 17% 9% 8%	 56% 10% 11% 15% 9%
Transgender	13%	13%	13%
Condomless receptive anal sex at baseline	58%	57%	60%
# drinks per day when drinking (prior mo.)	53%	51%	45%
Meth or cocaine use, at baseline (past mo)	7%	12%	8%
Sexually transmitted infection at baseline	27%	23%	28%
<u>Perceived likelihood of HIV at baseline</u> Probably/almost certain will happen	 17%	 11%	 17%
<u>Competing priorities</u> Concern about a place to live Concern about having a job	 47% 68%	 49% 67%	 44% 71%

Week 8 Drug Detection, by site



Results: correlates of drug detection (week 8)

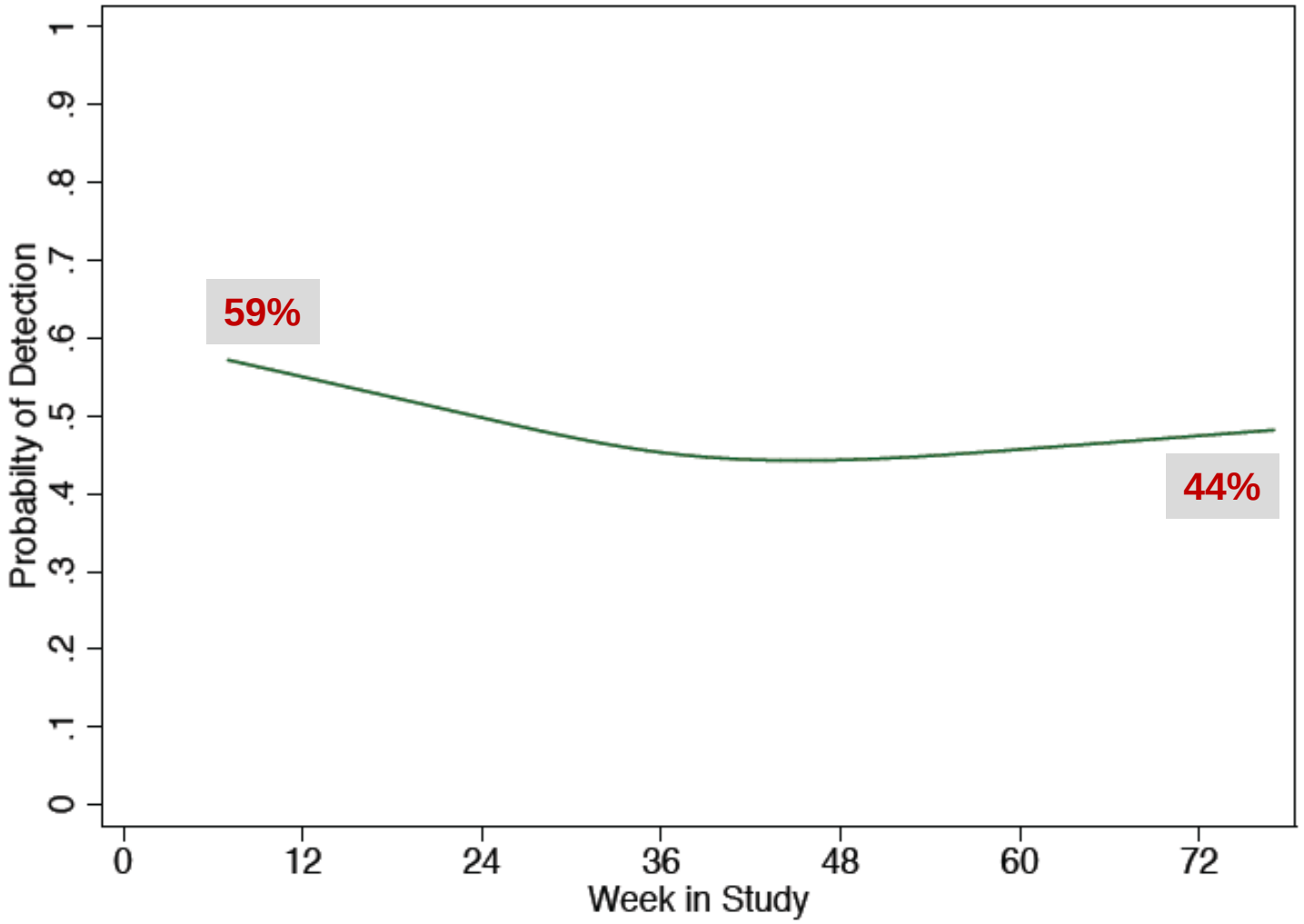
- Older age associated with drug detection (OR 2.86 for age>30 vs. age≤ 20)

- Level of education, number of sex partners, ncRAI*, substance use, creatinine clearance, being transgender, living situation, and concern about having a job or place to live were *not associated* with drug detection

- Reporting GI symptoms (nausea, vomiting, diarrhea, flatulence, or abdominal pain) or headache at week 4 or 8 was *not associated* with drug detection at week 8 or 24

***ncRAI=non-condom (condomless) receptive anal sex**

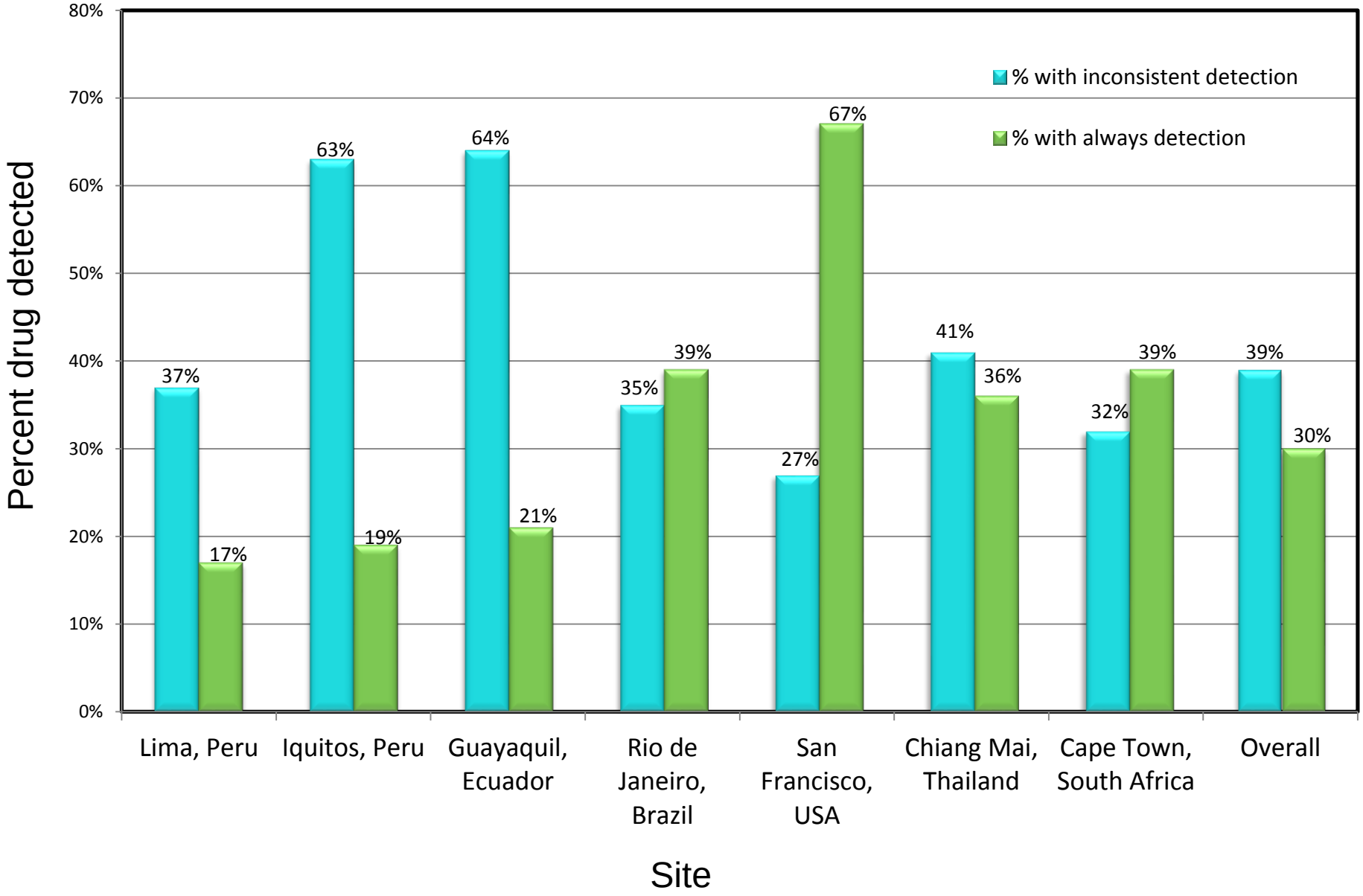
Longitudinal cohort: Drug detection over time



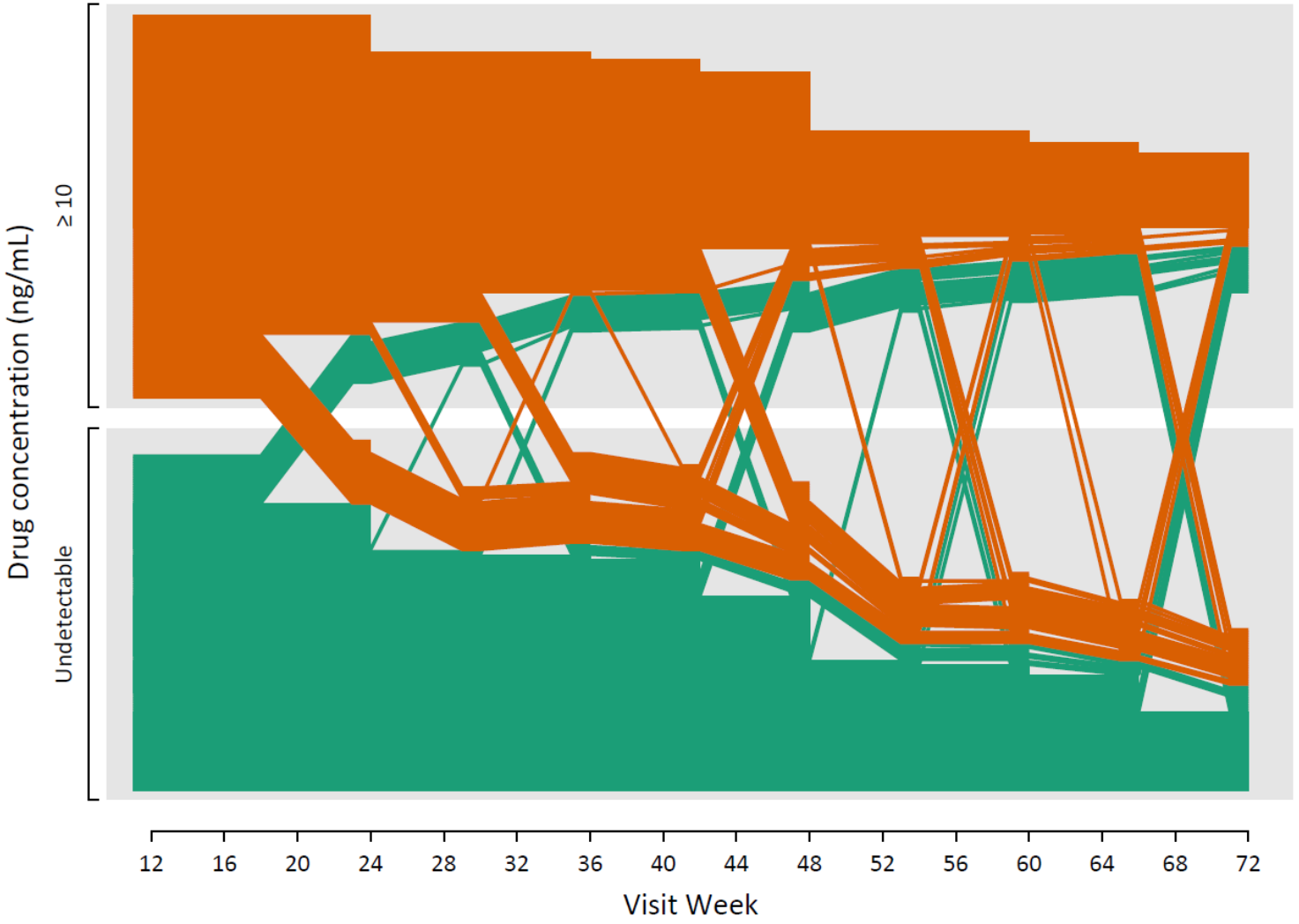
Longitudinal cohort: patterns of detection

- Mean # samples tested: 3.8 (range 2-6)
- 31% did not have drug detected in any sample
- 30% had drug detected in all samples
- 39% had inconsistent drug detection pattern
- Among 163 ppts who had drug detected at the first visit:
  - 68% had drug detection at some or all follow-up visits
  - 32% “discontinued” drug: median stop time 24 weeks
- Among 139 ppts who had no drug detected at first visit:
  - 68% did not have drug detected at subsequent time points

Longitudinal drug detection at some or all visits, by site



Different patterns of drug detection: Always, sometimes, and never users



Factors associated with sometimes and always (vs. never) drug detection over time

Characteristic	OR (some vs. never)	P Value	OR (always vs. never 95% CI)	P Value
Age				
≤20	Ref		Ref	
21-25	**4.04**	**0.002**	**6.32**	**0.001**
26-30	**3.42**	**0.02**	**4.74**	**0.021**
>30	**5.13**	**0.001**	**33.24**	**<0.001**
# sex partners at baseline (prior 3 mo)				
≤1 male partner	Ref	Ref	Ref	Ref
>1-5 partners	1.54	0.462	**3.41**	**0.05**
>5-10 partners	1.08	0.908	2.16	0.259
>10 partners	1.54	0.508	2.70	0.155
Non-condom RAI	**4.29**	**<0.001**	**3.25**	**0.002**
Perception of PrEP Efficacy (week 12)				
<50% effective	Ref		Ref	
50-99% effective	1.44	0.489	3.17	0.068
100 effective	1.12	0.855	2.49	0.197
Don't know	**2.51**	**0.058**	**4.40**	**0.014**
Perceived likelihood of HIV infection (lifetime)				
Not likely	Ref		Ref	
Could happen	1.21	0.688	**2.45**	**0.07**
Probably/almost certain will happen	1.60	0.417	**3.01**	**0.093**

Limitations

- Serum and plasma TFV/FTC represent relatively short windows of drug exposure (dosing over last 2-3 days)
  - But high concordance between plasma and PBMC drug detection
  - Future studies needed to validate quantitative biomarkers reflecting longer periods of PrEP use (dried blood spots, hair)

- Drug levels only available in a random sample at week 8 and among DEXA and case-control longitudinal cohorts
  - May not be fully representative of overall iPrEx cohort

- Drug detection in a placebo-controlled trial may not reflect PrEP use in open-label contexts

Conclusions

- Drug detection seen in approximately half of iPrEx ppts at week 8
  - Higher with older age, varied by site
  - High adherence achievable in PrEP clinical trials (90% in SF)

- Distinct patterns of study product use identified
  - ~1/3 had no evidence of starting study product (or early discontinuation)
  - ~1/3 consistently used study product

- Drug use, being transgender, and having housing/employment concerns were not associated with lower drug detection – should not exclude these potential PrEP users

- Research literacy may explain greater drug detection among populations with greater research experience (older MSM in the US, those reporting “don’t know” to efficacy of a drug under study)

- Greater drug detection among those reporting highest risk sexual practices is expected to increase the impact and cost-effectiveness of PrEP

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GLOBAL iPrEX

The iPrEx Study: **Safety, Efficacy, Behavior, and Biology**