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Oral abstract session

HIV prevention: Novel approaches and promising findings

Association of HIV pre-exposure prophylaxis (PrEP) use and bacterial sexually transmitted infections (bSTI) among men who have sex with men (MSM) and transgender women (TGW) in HVTN 704/HPTN 085



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Summary

What is your main question?

- Bacterial STIs (chlamydia, gonorrhea, and syphilis) are increasing among MSM and TGW worldwide.
- PrEP use has sometimes been associated with risk compensation
- Increased bacterial STIs among PrEP users in Americas/Europe AMP trial?

What did you find?

- High burden of bacterial STIs among Americas/Europe AMP trial participants.
- Regional differences in bacterial STI burden
- Increased bacterial STIs while being on PrEP (risk compensation)

Why is it important?

- HVTN is engaging communities who are highly vulnerable to HIV and STIs
- We need to start thinking about STI prevention: Think on DoxyPEP!



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Could PrEP use be associated with increased bSTI?

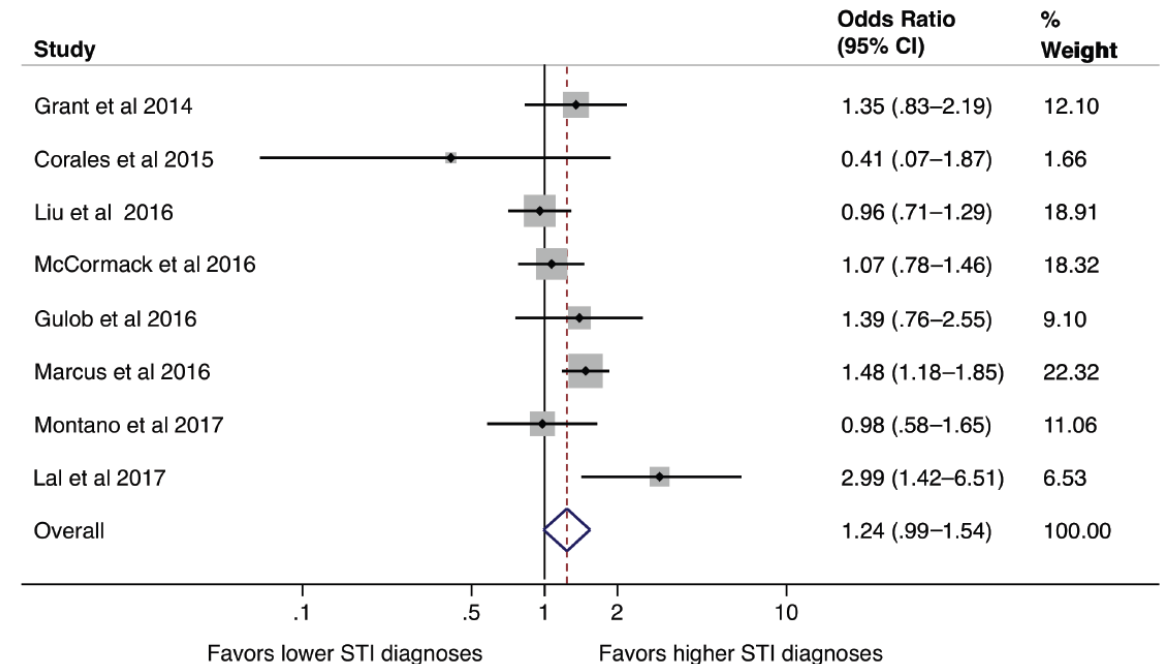
- Risk compensation

- Increase in risk-related behaviors when an intervention reduces perceptions of risk among individuals or a population



Increased STI diagnosis among PrEP users?

- 2018 meta-analysis: open-label PrEP use
 - Non-significant increase in STI diagnosis:
 - OR 1.24 (95%CI 0.99-1.54)
 - Significant increases in
 - Follow-up after 2016: OR 1.47 (95%CI 1.05–2.05)
 - Rectal infections: OR 1.39 (95%CI 1.03–1.87)





HVTN 704/HPTN 085: The Americas/Europe AMP trial

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- Phase 2b RCT to evaluate VRC01 for HIV prevention
- Enrolled MSM and TGW in 4 countries
 - Brazil, Peru, US, and Switzerland
- Access to an enhanced HIV prevention package
 - Periodic STI testing (every 6 months)
 - PCR for Chlamydia/Gonorrhea – Syphilis serology
 - Education on PrEP → could opt to use it
- Post-enrollment PrEP initiations:
 - US/Switzerland: 66.8%
 - Brazil: 83.3%
 - Peru: 5.8%
- **Association of PrEP use with bSTI incidence?**





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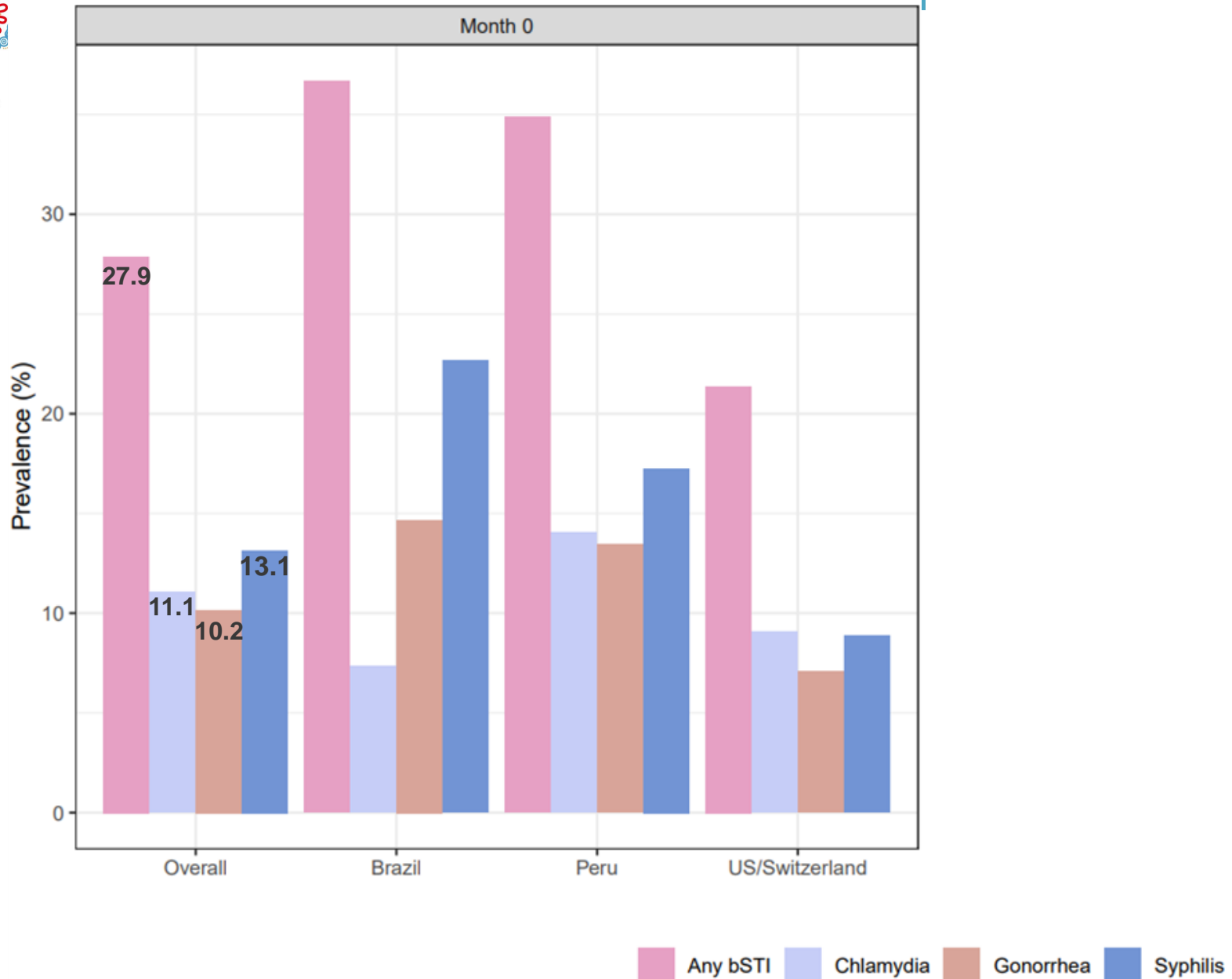
Methods

- Study Design:
 - Post hoc analysis of HVTN 704/HPTN 085 data (N=2687)
 - Participants who received at least one infusion AND had bSTI results available from at least one study visit
- Statistical analysis:
 - Descriptive statistics for bSTI prevalence and incidence rates within each bSTI category
 - Incidence rates: First occurrence of bSTI among those negative at baseline
 - Categorized bSTI prevalence by subgroups:
 - Scheduled STI visit, sociodemographics (race, ethnicity, gender identity), geographic region (Brazil, Peru, US/Switzerland), HIV Behavioral Risk Score (BRS)
 - *BRS: A risk model based on SuperLearner (ensemble of several machine learning algorithms) - Tertiles*
 - Categorized bSTI incidence rates by PrEP use
 - Time-varying PrEP use covariate: bSTI diagnosis while time on PrEP/off PrEP
 - Pairwise associations between covariates: age, BRS, and post-enrollment PrEP use
 - Effect of PrEP use on bSTI incidence using Cox proportional hazards models
 - Additionally adjusted for age, region, race, ethnicity, and treatment arm



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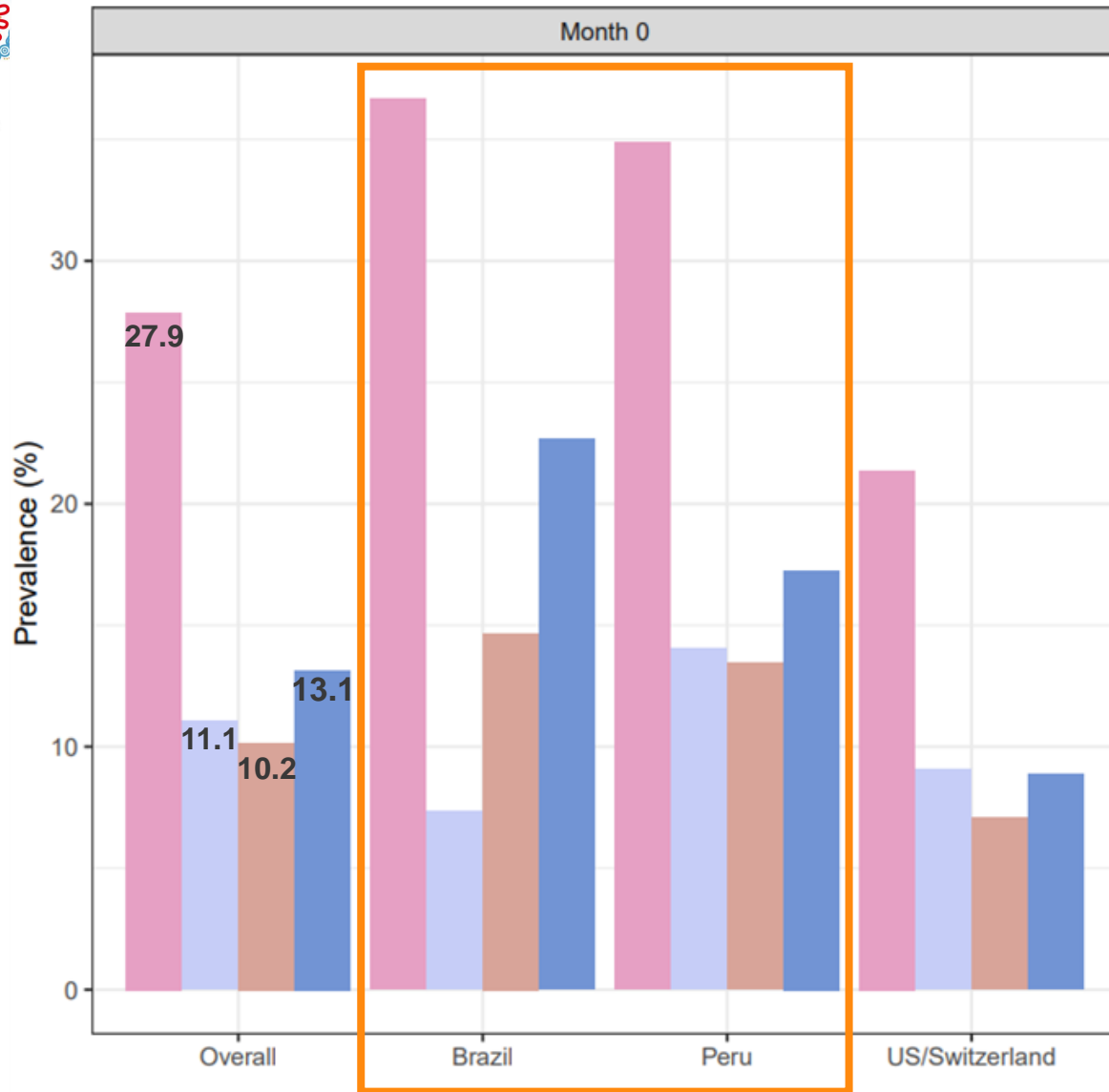
HVTN 704/HPTN 085: Prevalence by bSTI and region





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HVTN 704/HPTN 085: Prevalence by bSTI and region



Regional differences:

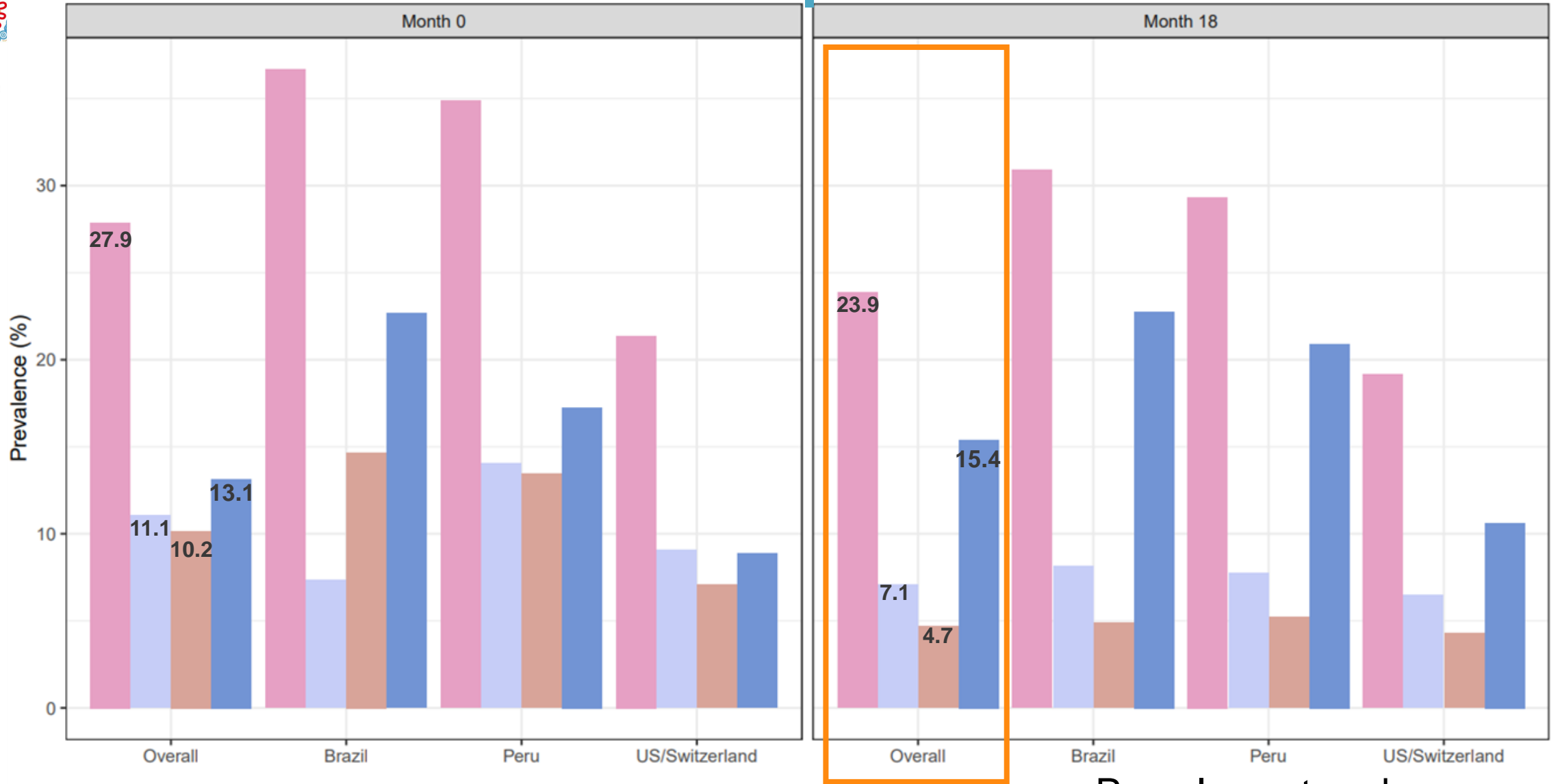
Highest prevalence: Latin America

Any bSTI Chlamydia Gonorrhea Syphilis



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HVTN 704/HPTN 085: Prevalence by bSTI and region



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Highest prevalence: Latin America

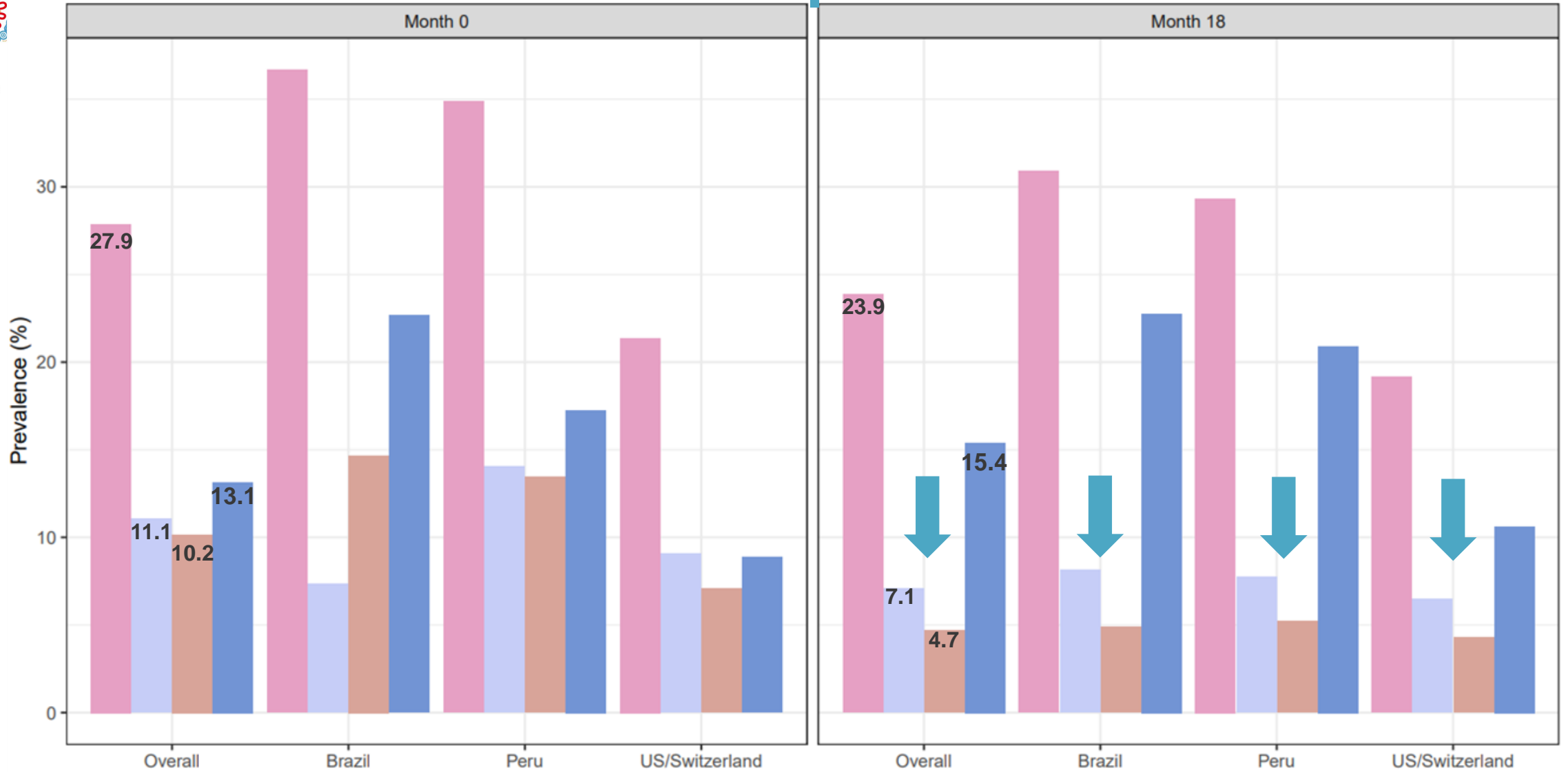
Any bSTI Chlamydia Gonorrhea Syphilis

Prevalence trends:
Decrease in chlamydia and gonorrhea
Increase in syphilis seropositivity



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HVTN 704/HPTN 085: Prevalence by bSTI and region



Regional differences:

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HVTN 704/HPTN 085: bSTI baseline by subgroups

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- Highest baseline prevalence:
 - <20 years old (35.7%)
 - High BRS (40.2%)
 - Hispanic/Latinx (32.4%)
 - Non-Black/non-White (32.1%)
 - TGW (35.3%)
 - MSM (28.9%)



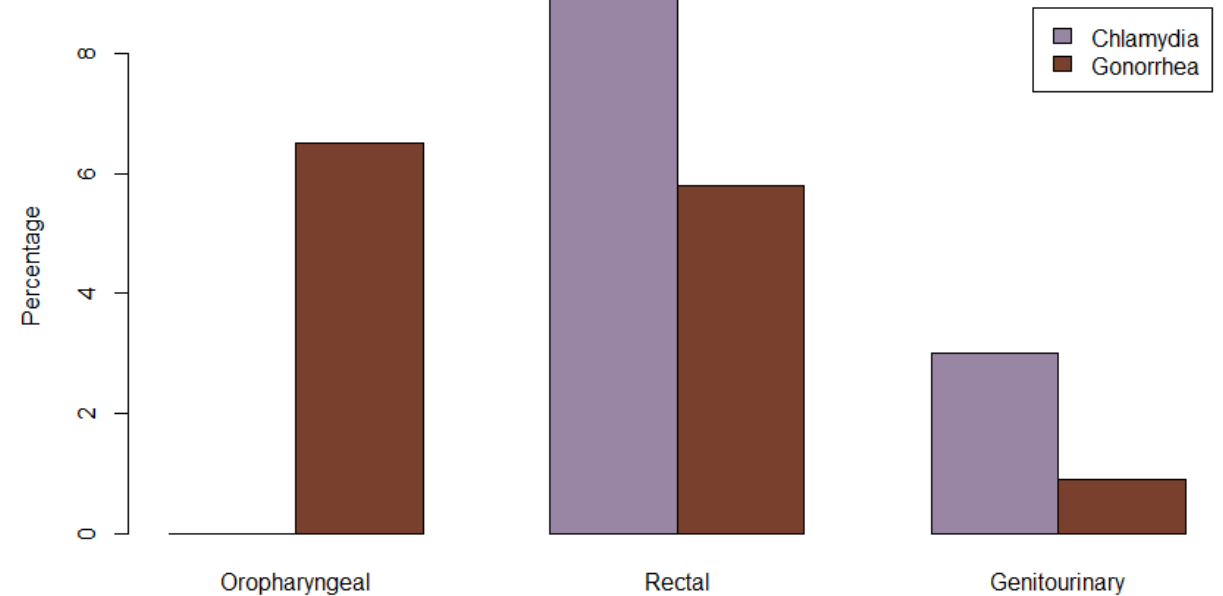
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HVTN 704/HPTN 085: bSTI baseline by subgroups

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- Differences by anatomical site
 - Rectal & OP > genitourinary

Baseline prevalence of chlamydia and gonorrhea by anatomical site





HVTN 704/HPTN 085: Effect of PrEP use on bSTI incidence

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bSTI incidence rates

| bSTI | No. Events | Person-Years at Risk | Incidence Rate (95% CI) |
|-----------|------------|----------------------|-------------------------|
| Any STI | 617 | 2154.7 | 28.6 (26.4-31.0) |
| Chlamydia | 375 | 2335.4 | 16.1 (14.5-17.8) |
| Gonorrhea | 290 | 2373.0 | 12.2 (10.9-13.7) |
| Syphilis | 165 | 2459.7 | 6.7 (5.7-7.8) |

Incidence is summarized for 100 person-years.

bSTI incidence rates by PrEP use

| STI Category | While on PrEP | No. Events | Person-Years at Risk | Incidence Rate (95% CI) |
|--------------|---------------|------------|----------------------|-------------------------|
| Any bSTI | Yes | 283 | 760.2 | 37.2 (33.0-41.8) |
| | No | 334 | 1,394.5 | 24.0 (21.5-26.7) |
| Chlamydia | Yes | 175 | 856.6 | 20.4 (17.5-23.7) |
| | No | 200 | 1,478.8 | 13.5 (11.7-15.5) |
| Gonorrhea | Yes | 141 | 869.2 | 16.2 (13.7-19.1) |
| | No | 149 | 1,503.8 | 9.9 (8.4-11.6) |
| Syphilis | Yes | 80 | 907.9 | 8.8 (7.0-11.0) |
| | No | 85 | 1,551.8 | 5.5 (4.4-6.8) |

Incidence is summarized for 100 person-years at risk

Higher incident bSTI while participants were on PrEP



Being on PrEP was significantly associated with increased hazard of bSTI

- Any STI (HR 1.7, 95% CI 1.4-2.1)
- Chlamydia (HR 1.7, 95% CI 1.3-2.2)
- Gonorrhea (HR 1.8, 95% CI 1.4-2.5)
- Syphilis (HR 1.9, 95% CI 1.3-2.8)



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Conclusions

- **High burden of bSTI** in HVTN 704/HPTN 085 participants
- **Regional differences** in the burden of bSTI among trial participants
 - Likely reflect the existence of distinct epidemics in participating countries.
 - Reduced access to bSTI etiologic diagnostic methods in Latin America
- **PrEP initiators in AMP:**
 - Had somehow lower predicted behavioral vulnerability to HIV at baseline
 - Had lower HIV incidence (stay tuned for Dr. Cantos presentation)
 - **Had higher rates of bSTI while being on PrEP**
 - **All this may suggest risk compensation**
- **Implications for HIV vaccine research**
 - HVTN 704/HPTN 085 engaged communities with significant vulnerability to HIV and STIs
 - Need for tailored strategies to increase PrEP uptake among those with higher vulnerability
 - We need to advance STI prevention in HIV vaccine research: DoxyPEP



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Next steps

- Sensitivity analysis on the effect of individual risk behaviors on the association between PrEP use and bSTI incidence
 - Understand drivers of bSTI incidence among diverse communities
- Evaluate the association of incident bSTIs and HIV acquisition among participants who acquired HIV during HVTN 704/HPTN 085

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