Jorge A. Gallardo-Cartagena, MD
Centro de Investigaciones Tecnológicas, Biomédicas y Medioambientales – Lima, Peru

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
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!
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)

<table>
<thead>
<tr>
<th>Study</th>
<th>Odds Ratio (95% CI)</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grant et al 2014</td>
<td>1.35 (.83–2.19)</td>
<td>12.10</td>
</tr>
<tr>
<td>Corales et al 2015</td>
<td>0.41 (.07–1.87)</td>
<td>1.66</td>
</tr>
<tr>
<td>Liu et al 2018</td>
<td>0.96 (.71–1.29)</td>
<td>18.91</td>
</tr>
<tr>
<td>McCormack et al 2016</td>
<td>1.07 (.78–1.46)</td>
<td>18.32</td>
</tr>
<tr>
<td>Gulob et al 2016</td>
<td>1.39 (.76–2.55)</td>
<td>9.10</td>
</tr>
<tr>
<td>Marcus et al 2016</td>
<td>1.48 (1.18–1.85)</td>
<td>22.32</td>
</tr>
<tr>
<td>Montano et al 2017</td>
<td>0.98 (.58–1.65)</td>
<td>11.06</td>
</tr>
<tr>
<td>Lai et al 2017</td>
<td>2.99 (1.42–6.51)</td>
<td>6.53</td>
</tr>
<tr>
<td>Overall</td>
<td>1.24 (.99–1.54)</td>
<td>100.00</td>
</tr>
</tbody>
</table>
HVTN 704/HPTN 085: The Americas/Europe AMP trial

- 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?
• 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
HVTN 704/HPTN 085: Prevalence by bSTI and region
Regional differences:
Highest prevalence: Latin America
Regional differences:
Highest prevalence: Latin America

Prevalence trends:
Decrease in chlamydia and gonorrhea
Increase in syphilis seropositivity
Regional differences:
Highest prevalence: Latin America

Prevalence trends:
Decrease in chlamydia and gonorrhea
Increase in syphilis seropositivity
HVTN 704/HPTN 085: bSTI baseline by subgroups

- 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%)
HVTN 704/HPTN 085: bSTI baseline by subgroups

- Differences by anatomical site
  - Rectal & OP > genitourinary

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

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)

Higher incident bSTI while participants were on PrEP

### bSTI incidence rates

<table>
<thead>
<tr>
<th>bSTI</th>
<th>No. Events</th>
<th>Person-Years</th>
<th>Incidence Rate (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any STI</td>
<td>617</td>
<td>2154.7</td>
<td><strong>28.6</strong> (26.4-31.0)</td>
</tr>
<tr>
<td>Chlamydia</td>
<td>375</td>
<td>2335.4</td>
<td><strong>16.1</strong> (14.5-17.8)</td>
</tr>
<tr>
<td>Gonorrhea</td>
<td>290</td>
<td>2373.0</td>
<td><strong>12.2</strong> (10.9-13.7)</td>
</tr>
<tr>
<td>Syphilis</td>
<td>165</td>
<td>2459.7</td>
<td><strong>6.7</strong> (5.7-7.8)</td>
</tr>
</tbody>
</table>

Incidence is summarized for 100 person-years.

### bSTI incidence rates by PrEP use

<table>
<thead>
<tr>
<th>STI Category</th>
<th>While on PrEP</th>
<th>No. Events</th>
<th>Person-Years</th>
<th>Incidence Rate (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any bSTI</td>
<td>Yes</td>
<td>283</td>
<td>760.2</td>
<td><strong>37.2</strong> (33.0-41.8)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>334</td>
<td>1,394.5</td>
<td><strong>24.0</strong> (21.5-26.7)</td>
</tr>
<tr>
<td>Chlamydia</td>
<td>Yes</td>
<td>175</td>
<td>856.6</td>
<td><strong>20.4</strong> (17.5-23.7)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>200</td>
<td>1,478.8</td>
<td><strong>13.5</strong> (11.7-15.5)</td>
</tr>
<tr>
<td>Gonorrhea</td>
<td>Yes</td>
<td>141</td>
<td>869.2</td>
<td><strong>16.2</strong> (13.7-19.1)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>149</td>
<td>1,503.8</td>
<td><strong>9.9</strong> (6.4-11.6)</td>
</tr>
<tr>
<td>Syphilis</td>
<td>Yes</td>
<td>80</td>
<td>907.9</td>
<td><strong>8.8</strong> (7.0-11.0)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>85</td>
<td>1,551.8</td>
<td><strong>5.5</strong> (4.4-6.8)</td>
</tr>
</tbody>
</table>

Incidence is summarized for 100 person-years at risk.
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
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
AMP Studies Protocol Team Acknowledgements

Chairs
• Larry Corey
• Mike Cohen

Co-chairs
• Srilatha Edupuganti
• Nyaradzo Mgodi

Protocol Team Leader
• Shelly Karuna

Statisticians
• Allan DeCamp
• Peter Gilbert
• Michal Juraska
• Deborah Donnell
• Abby Isaacs
• Nidhi Kochar
• Jing Wang

DAIDS Medical Officers
• Margarita Gomez Lorenzo
• David Burns

Laboratory Lead
• John Hural

Bioethics Consultant
• Mark Barnes

CAB Members
• Jim Wick
• Likhapha Faku
• Mark Hubbard

Community Educators
• DaShawn Usher
• Luciana Kamel

Community Program Representatives
• Gail Broder
• Jonathan Lucas
• Jontraye Davis

Clinic Coordinators
• Ana Patricia Rimachi Zuiroz
• Christie Heiberg
• Debora Dunbar

Consultative Investigators
• Ken Mayer
• LaRon Nelson
• Erica Lazarus
• Sinead Delany-MoretIwe

Clinical Safety Specialist
• Maija Anderson

Clinical Trial/Research Mgr
• Carissa Karg
• Elizabeth Greene
• Philip Andrew

Data Management
• Gina Escamilla
• Lynda Emel
• Alison Ayres

Developer Representatives
• Barney Graham, VRC
• John Mascola, VRC
• Julie Ledgerwood, VRC

Technical Editor
• Erik Schwab

Lab Representatives
• David Montefiori
• Estelle Piwowar-Manning
• On Ho
• Robert Coombs
• Susan Eshleman
• Vanessa Cummings

HPTN LOC Director
• Nirupama Sista

Protocol Development Mgr
• Carter Bentley

Pharmacist
• Katherine Shin

Regional Medical Liaisons
• Robert De La Grecca
• Simba Takuva

Regulatory Affairs
• Megan Brandon

Social Behavioral Scientist
• Michele Andrasik
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- April Ross, CER
- Chloe Jordan, CER
- Javani Williams, CER
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- Shashi Nagar, Lead CRS Coordinator
- Srilatha Edupuganti, IoR

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- Carlos del Rio, IoR
- Edwin Worthington-Blount, CER
- John Gharbin, Research Assistant
- Philip Powers, Pharmacist
- Rotrease Regan, Clinical Nurse Coordinator

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- Catrena Johnson, Clinic Coord.
- Deon Powell, Pharmacist
- Heather Logan, Clinic Coordinator
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- Lindsey Baden, PI
- Rachel Filter, Clinic Coordinator
- Elvin Fontana-Martinez, Clinic Coordinator
- Jon Gothing, Study Nurse
- Jane Higley, Research Assistant
- Jennifer Johnson, Co-Investigator
- Jane Kleinjan, Study Nurse
- Maureen Macgowan, Study PA
- Karen Magsipoc, Study Nurse
- Xhoi Mitre, Research Assistant
- Alisha Pandit, Clinic Coordinator
- Alka Patel, Pharmacist
- Naina Rao, Research Assistant
- Stephen Walsh, Co-Investigator
- Behnaz Yousefzadeh, Research Assistant
- Kenneth Mayer, IoR
- Marcy Gelman, Sub-Investigator
- Douglas Krakower, Sub-Investigator
- Ryan Tappin, Sub-Investigator
- Christopher Chianese, Clinic Coordinator
- Rossi Fish, Clinic Coordinator
- Johnathon Holmes, Study Nurse
- Janey Scuzzarella, Study Nurse
- Christopher Mistretta, Study Nurse
- Catherine Adams, Study Nurse
- Mark Estano, Study Nurse
- Rob Moyers, Research Assistant
- Sehar Khalid, Research Assistant
- Janet Dargon, Research Assistant
- Kathleen Bailey, CER
- Alka Patel, Pharmacist
- Jessica Kraft, Research Clinician

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- Cindy Gay, IoR
- Gabrielle Evans, CER
- Linda Manor, Pharmacist
- Susan Henderson, Research Coordinator
- Maureen Furlong, Research Coordinator
- Betelehem Shenbulo, Research Assistant
- Tracy Eldred, Clinical Research Assistant
- Brittney Soderman, Research Assistant
- Catherine Kronk, Quality Assurance and Data Manager
- Nazneen Howerton, Regulatory Specialist
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- Cheryl Smith, Regulatory Coordinator
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- Kim Fussell, Pharmacy Technician
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- Michael Morgan, CER
- Robert Bucklew, CER
- Theresa Jones, Lab Technician
- Todd Bonin, Data Coordinator
- Ann Conrad, Nurse Practitioner
- Benigno Rodriguez, IoR
- Jane Baum, Clinic Coordinator
- Julie Pasternak, Research Nurse
- Michael Banchy, Pharmacist

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- Fabio Candotti – Co-investigator
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- Carlos Antón, Data Manager
- Consuelo Tristan, Clinic Coordinator
- Jose Luis Castro, CER
- Robinson Cabello, IoR
- Rocio Pérez, Pharmacist

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- Christina Shin, Pharmacist
- Christopher Blades, CER
- Jesse Clark, IoR
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- Arielle Gronberg, Data Manager
- Christie Lyn Costanza, CER
- Eric Ascencio, Research Associate
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- Ellen Morrison, Sub Investigator
- Rita Sondengam, Site Manager
- Ann Kahn, Site Clinician
- Martha Cavallo, Site Clinician
- Ana Victoria Cruz, Lab Manager
- Jawindy Swengbe, Community Outreach Assistant
- Kevin Mines, Community Outreach Assistant
- Marbella Silverio, Project Assistant
- Maria Rivas Alvarado, Lab/Data Manager

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- Jaron Cook, CER
- Jessica Justman, IoR
- Joshua Hinkson, Lab Manager
- Jun Loquere, Clinic Coordinator
- Kinara Young, Pharmacist
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- Hong Van Tieu, IoR
- Tarashon Broomes, Research Clinician
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- Kinara Yang, Pharmacist

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- Deborah Dunbar, Clinician Coordinator
- Ann Davison, Research Nurse
- Dana Brown, Research Coordinator
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- Dan Mangini, Recruiter

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- Jeanne Jordan, Laboratory Director
- Irene Kuo, Associate CRS Leader
- Arley Hunter, Pharmacist
- Mayna Magnus, CRS and Study Leader, IoR
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