THE FINAL FRONTIER FOR eMTCT: ACUTE HIV INFECTION DURING AND AFTER PREGNANCY

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Disclosure

- I have nothing to disclose.
3. Preventing MTCT

1. Primary prevention in women

- Pre-exposure prophylaxis (PrEP)
  - Safety and efficacy
  - Eligibility
  - Screening tools
  - Innovative evaluations

2. Novel testing strategies
   - When to test
   - How to test

- Background on impact of acute maternal HIV on efforts to achieve eMTCT
Acute maternal infections contribute substantially to mother-to-child HIV transmission (MTCT)

50% ↓ MTCT  
2010-2015

MTCT 2-23%  
UNAIDS 2015

150,000  
New infections 2015

MTCT attributed to acute maternal HIV

30 - 46%  
46,000-69,000

UNAIDS Global Plan, 2016;  
Johnson LF, JAIDS 2012.
Temporal shift in MTCT: Increasingly attributed to acute maternal HIV

Figure 2: Johnson LF, JAIDS 2012.
Higher MTCT rates attributed to incident infection in era of ART

MTCT: 22.7%

OR = 0.5
95% CI = 0.05 - 2.1

OR = 2.2
95% CI = 1.6 - 3.1

OR = 2.3
95% CI = 1.2 - 4.4

OR = 9.1
95% CI = 4.9 - 16.0

OR = 15.1
95% CI = 6.9 - 33.1

Low rates in chronic infection

MTCT rates are underestimated due to acute maternal infections

Njuguna IN, AIDS Patient Care and STDs 2016.
Contributions to MTCT due to acute infections are high, but relatively small proportion of mothers have new infections.


South Africa 2011-2012
Long cumulative duration for maternal HIV risk

Average life expectancy (yrs) 63
Total fertility rate (per woman) 3.9
Years pregnant/lactating (per preg.) 1.75
Total years pregnant/lactating 6.8

= woman year
= pregnant/lactating
High maternal HIV incidence rates

<table>
<thead>
<tr>
<th>Author, year</th>
<th>Country</th>
<th>Pregnancy</th>
<th>Postpartum</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kinuthia &amp; Drake, 2015</td>
<td>Kenya</td>
<td>3.4</td>
<td>1.4</td>
<td>2.3</td>
</tr>
<tr>
<td>De Schacht, 2014</td>
<td>Mozambique</td>
<td>4.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dinh, 2015</td>
<td>S. Africa</td>
<td>3.3%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Kinuthia & Drake, 2015
De Schacht, 2014
Dinh, 2015

3. Preventing MTCT

- Background on impact of acute maternal HIV on efforts to achieve eMTCT

- **Novel testing strategies**
  - When to test
  - How to test

- **Pre-exposure prophylaxis** (PrEP)
  - Safety and efficacy
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  - Innovative evaluations
Guidance on timing of repeat testing lacks specificity

<table>
<thead>
<tr>
<th>Retesting criteria</th>
<th>Concentrated epidemic</th>
<th>Generalized epidemic</th>
</tr>
</thead>
<tbody>
<tr>
<td>3rd trimester, labor, or postpartum</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Serodiscordant couple</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Member of key population</td>
<td>✓</td>
<td></td>
</tr>
</tbody>
</table>

Diagram:

- Pregnancy
  - 3rd trimester
  - Labor
  - Postpartum
Country specific guidelines focus on retesting during late pregnancy and early postpartum.
No clear “best” time to test based on prospective research
Long potential duration of breastfeeding warrants guidance on postnatal testing.

Acute infection: postnatal transmission contributes disproportionately to MTCT.

Adapted from Figure 3b: Johnson LF, JAIDS 2012.
Timing of repeat testing will require balancing maternal and infant risks vs. benefits

**Early favors infant benefit**
- ↓ detection
- ↑ prevention

**Late favors maternal benefit**
- ↑ detection
- ↓ prevention

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Pregnancy

- 1st ANC
- 3rd trimester
- Delivery
- 2, 6, 10, 14 weeks

Postpartum

- 6 months
- 9 months
Implementation science approach to determining optimal timing of repeat testing

NIH/NIAID
K01 AI116298 (Drake, PI)

Retest 4650 women

Pregnancy
3rd trimester (n=930)  Delivery (n=930)  Postpartum
6 weeks (n=930)  6 months (n=930)  9 months (n=930)
Modeling impact and cost-effectiveness of repeat maternal testing for PMTCT

Model parameters

- Country scenarios: Kenya, South Africa, Belarus, Cuba
- HIV prevalence / incidence
- Repeat testing: timing, guidelines, practices
- Behaviors: breastfeeding, condom use, ART initiation/adherence
- Assays
- PrEP
3. Preventing MTCT

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  - Innovative evaluations
Barriers to repeat implementation of repeat testing

Implementation of repeat HIV testing during pregnancy in Kenya: a qualitative study

Anna Joy Rogers, Elly Weke, Zachary Kwena, Elizabeth A. Bukusi, Patrick Oyaro, Craig R. Cohen and Janet M. Turan

Individual

- Late ANC presentation
- Low ANC completion rates

Provider

- Heavy workload
- Time constraints
- Difficulty checking repeat test eligibility

Facility

- Inconsistent ANC volume
- Lack of private space for testing

Alternative delivery systems may expand coverage and reach

What approaches are acceptable and feasible for repeat maternal testing?

Choose:
Home, self test  
OR  
Clinic, blood test
Promoting male partner HIV testing and safer sexual decision making through secondary distribution of self-tests by HIV-negative female sex workers and women receiving antenatal and post-partum care in Kenya: a cohort study

Harsha Thirumurthy, Samuel H Masters, Sue Napierala Mavedzenge, Suzanne Maman, Eunice Omanga, Kawango Aaot

Peripartum women are willing to distribute self-tests to male partners

Half of women self-tested with their partner

Figure 2: Distribution to and use of self-tests with primary sexual partners
Among participants who have a primary sexual partner and completed a follow-up interview (58 in antenatal care, 106 in post-partum care, and 85 female sex workers).

Kenya first country to nationally roll-out self-testing

- **Resources to support roll-out**
  - Hotline
  - Website
WHO endorses self-testing

**Guidelines on**

HIV Self-Testing and Partner Notification

Supplement to Consolidated Guidelines on HIV Testing Services

December 2016

**Recommendation**

HIV self-testing should be offered as an additional approach to HIV testing services (*strong recommendation, moderate quality evidence*).
Service delivery approaches for self-testing

Delivery approaches in use for PMTCT

- Partner-delivered
- Community (door to door)
- Facility (pick-up/self-test)
- PrEP
- Integrated (reproductive health)
- Workplace
- Internet
- Pharmacy
- Vending machines / kiosks

Adapted from Figure 2.5, 2016 WHO self-testing guidelines
Outline

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Safety data on tenofovir suggest PrEP is safe during pregnancy and lactation

Tenofovir disoproxil fumarate safety for women and their infants during pregnancy and breastfeeding

Lynne M. Mofenson\textsuperscript{a}, Rachel C. Baggaley\textsuperscript{b} and Ioannis Mameletzis\textsuperscript{b}

Objectives: Pregnant/lactating women in some sub-Saharan Africa settings are at substantial risk of HIV acquisition and could benefit from preexposure prophylaxis (PrEP) with tenofovir disoproxil fumarate (TDF), but safety data in pregnancy/lactation are limited.

Design: Systematic data review through August 2016.

Methods: We reviewed research reports/conference abstracts with maternal/child adverse outcome data in HIV-infected and HIV-uninfected pregnant/lactating women receiving TDF alone or in combination with other drugs compared with non-TDF regimens.

Results: In total, 26 articles in HIV-infected and seven in HIV-uninfected women were identified. No statistically significant differences were observed between TDF and comparison non-TDF regimens in neonatal incidence: stillbirth/mortality loss.

Conclusion: Given available safety data, there does not appear to be a safety-related rationale for prohibiting PrEP during pregnancy/lactation or for discontinuing PrEP in HIV-uninfected women receiving PrEP who become pregnant and are at continuing risk of HIV acquisition.
**WHO technical brief on PrEP during pregnancy and breastfeeding**

**PrEP is safe and effective**

<table>
<thead>
<tr>
<th>Population</th>
<th>Additional considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-conception for women:</td>
<td>• &quot;Bridge to partner viral suppression&quot;</td>
</tr>
<tr>
<td>• Serodiscordant relationships</td>
<td></td>
</tr>
<tr>
<td>• Unknown partner status</td>
<td></td>
</tr>
<tr>
<td>• Partner unwilling to test</td>
<td></td>
</tr>
<tr>
<td><strong>✓</strong></td>
<td></td>
</tr>
<tr>
<td>Adolescents</td>
<td>• Requires additional support for information &amp; adherence</td>
</tr>
<tr>
<td><strong>✓</strong></td>
<td>• Consent may be barrier</td>
</tr>
<tr>
<td>Pregnant and postpartum women</td>
<td></td>
</tr>
<tr>
<td>with substantial HIV risk</td>
<td></td>
</tr>
<tr>
<td><strong>✓</strong></td>
<td></td>
</tr>
</tbody>
</table>
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PrEP implementation should maximize prevention while minimizing unnecessary exposure.
Potential strategies to identify PrEP eligibility during pregnancy and lactation

Universal HIV prevalence based Risk based

PrEP Coverage

Offered PrEP (All)
Offered PrEP (high-risk)
Unnecessary

Kenya well poised to evaluate PrEP during pregnancy and lactation

Kenyan government to roll out pre-exposure HIV drug

MONDAY MARCH 13 2017
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PrEP screening tools

Rapid Assessment Screening Tool (RAST)

- Partner
  - HIV status
  - Violence

- Sex
  - Unprotected
  - Forced
  - Trade

- STI

- Post-exposure prophylaxis

- Sharing needles

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A Risk Assessment Tool for Identifying Pregnant and Postpartum Women Who May Benefit From Preexposure Prophylaxis

Jillian Pintye,1,2 Alison L. Drake,1 John Kinuthia,3 Jennifer A. Unger,1,4 Daniel Matemo,3 Renee A. Heffron,1,6 Ruanne V. Barnabas,1,5,6 Pamela Kohler,1,7 R. Scott McClelland,1,5,8 and Grace John-Stewart1,5,9

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Value per factor</th>
<th>Complete score</th>
<th>Simplified score</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of lifetime sexual partners</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 point per sexual partner</td>
<td></td>
<td>Enter at least 1</td>
<td></td>
</tr>
<tr>
<td>Male partner HIV status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Known or no male partner</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Syphilis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RPR nonreactive</td>
<td>0</td>
<td></td>
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</tr>
<tr>
<td>RPR reactive</td>
<td>5</td>
<td></td>
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</tr>
<tr>
<td>Bacterial vaginosis</td>
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<td></td>
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<tr>
<td>Negative or not screened</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>2</td>
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<td>Candidiasis</td>
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<td>Negative or not screened</td>
<td>0</td>
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<td></td>
</tr>
<tr>
<td>Positive</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total risk score</td>
<td></td>
<td></td>
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Ongoing evaluations testing approaches to PrEP delivery in Kenya

PrEP counseling guided by risk score in high prevalence

Universally offer

Offer PrEP based on partner self-test + risk score

Offer PrEP based on partner self-test

Universally offer

(including age 15-17)
3. Preventing MTCT

- Acute maternal HIV contributes substantially to MTCT

- **Novel testing strategies can help, but need:**
  - Guidance on timing of retesting
  - Evaluations of new delivery systems
    - Oral self-, partner, and home-based testing

- **Increasing need to focus upstream on PrEP**
  - Safe and effective to use
  - Current projects will guide implementation
Future directions

3. Preventing MTCT

- Acute maternal HIV contributes substantially to MTCT and must be addressed to achieve eMTCT

- **Novel testing strategies**
  - Counseling messages & tools
  - Delivery systems & task-shifting
  - Economic evaluations

1. Primary prevention in women

- **Pre-exposure prophylaxis (PrEP)**
  - Counseling messages & tools
  - Maternal adherence support
  - Female controlled prevention

4. Preventing unintended pregnancies
2015
Cuba

2016
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Belarus
Thailand
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