A Cluster-Randomized Controlled Trial of Antenatal Care and HIV Treatment Integration in Rural Kenya

Principal Investigator: Craig R. Cohen
Co-Investigators: Janet M. Turan, Sierra Washington, Starley Shade, Marta Ackers, Dorothy Mbori-Ngacha and Elizabeth A. Bukusi
Study Background and Rationale

• In 2005, most antenatal care (ANC) services & HIV treatment services were offered in separate clinics
• We recognized missed opportunities and inefficiencies in referral-based systems

• **Hypothesis:** Integrating ANC and HIV treatment services for pregnant women in a single clinic may result in improved maternal outcomes and decreased mother-to-child transmission (MTCT).
SHAIP Study Design

| Study Design          | An operational study  
                          | Prospective cluster randomized controlled trial |
|-----------------------|------------------------------------------------|
| Intervention          | Full integration of HIV care including highly active antiretroviral therapy (HAART) into antenatal care clinics (intervention), compared to referral for HIV care and treatment (control) |
| Major outcomes        | • Vertical transmission of HIV  
                          | • Uptake of infant HIV testing  
                          | • Linkage and retention in care for mother-infant pairs  
                          | • Maternal health outcomes (WHO stages, CD4 counts) |
| Study sites           | 12 facilities in 3 districts |
| Health facilities     | District hospitals, sub-district hospitals, health centers, and dispensaries |
| Participants          | 1172 HIV-positive pregnant women (not yet enrolled in HIV care) and their exposed infants |
| Data sources          | Electronic medical records and registers |
| Study Period          | Women enrolled in pregnancy and mother-infant pairs followed for one year. |
Separate Clinics at the Facility

ANC / MNCH Clinic

Patient Support Center = HIV Clinic
The Control Clinics N=6

ANC / MNCH Clinic

FANC = Focused Antenatal Care

FANC & WHO OPTION A PMTCT

HIV Care and HAART

Patient Support Center = HIV Clinic
The Intervention Clinics N=6

FANC &
WHO OPTION A
PMTCT &
HIV Care and
HAART*

ANC / MNCH Clinic

Patient Support Center = HIV Clinic

*Women transferred to PSC 18 months postpartum
Patient Characteristics at Enrollment  
(N=1172 pregnant women)

<table>
<thead>
<tr>
<th></th>
<th>Intervention (n=569)</th>
<th>Control (n=603)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age in years (SE)</td>
<td>25.0 (0.19)</td>
<td>24.8 (0.18)</td>
<td>0.58</td>
</tr>
<tr>
<td>Education, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None or Some Primary</td>
<td>481 (85%)</td>
<td>533 (89%)</td>
<td>0.37</td>
</tr>
<tr>
<td>Some Secondary or more</td>
<td>84 (15%)</td>
<td>68 (11%)</td>
<td></td>
</tr>
<tr>
<td>Marital status, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>472 (84%)</td>
<td>500 (84%)</td>
<td>0.99</td>
</tr>
<tr>
<td>Single/Separated/Divorced</td>
<td>49 (8%)</td>
<td>50 (8%)</td>
<td></td>
</tr>
<tr>
<td>Widowed</td>
<td>43 (8%)</td>
<td>48 (8%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Intervention (n=569)</td>
<td>Control (n=603)</td>
<td>P value</td>
</tr>
<tr>
<td>------------------------------------</td>
<td>----------------------</td>
<td>-----------------</td>
<td>---------</td>
</tr>
<tr>
<td>Median Gravidae (IQR)</td>
<td>3 (2-4)</td>
<td>3 (2-4)</td>
<td>0.94</td>
</tr>
<tr>
<td>Median Parity (IQR)</td>
<td>2 (1-3)</td>
<td>2 (1-3)</td>
<td>0.92</td>
</tr>
<tr>
<td>Mean Gestational Age in weeks (SE)</td>
<td>26 (0.3)</td>
<td>25.2 (0.3)</td>
<td>0.10</td>
</tr>
<tr>
<td>WHO HIV stage n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WHO Stage 1</td>
<td>339 (63%)</td>
<td>455 (80%)</td>
<td>0.40</td>
</tr>
<tr>
<td>WHO Stage 2</td>
<td>79 (15%)</td>
<td>42 (7%)</td>
<td></td>
</tr>
<tr>
<td>WHO Stage 3 or 4</td>
<td>31 (6%)</td>
<td>8 (1%)</td>
<td></td>
</tr>
<tr>
<td>Not Staged</td>
<td>85 (15%)</td>
<td>67 (12%)</td>
<td></td>
</tr>
<tr>
<td>Mean Baseline CD4 (SE)</td>
<td>495 (19.87)</td>
<td>523 (19.18)</td>
<td>0.34</td>
</tr>
<tr>
<td>Eligible for HAART</td>
<td>127 (22%)</td>
<td>87 (14%)</td>
<td>0.28</td>
</tr>
</tbody>
</table>
The PMTCT CASCADE

All Pregnant women

Attend ANC clinic

Be offered and accept HIV testing

Get CD4 assessment

Be given ARVs

Enroll in HIV care and treatment

Adhere to ARVs during pregnancy

Deliver with skilled attendant & take ARVs

Follow safe infant feeding practices

Bring infant for HIV testing

Adhere to maternal/infant ARVs after birth

Use postpartum family planning

HIV-positive Pregnant women

Department of Obstetrics, Gynecology & Reproductive Sciences
School of Medicine
Department of Obstetrics, Gynecology & Reproductive Sciences
School of Medicine

- Get baseline CD4
- Be given ARVs
- Enroll in HIV care and treatment
- Adhere to ARVs during pregnancy
- Deliver with skilled attendant and take ARVs
- Bring infant for HIV testing

Intervention (n=569)
Control (n=603)

OR=1.19 (0.41 - 3.46)
- Get baseline CD4
- Be given ARVs
- Enroll in HIV care and treatment
- Adhere to ARVs during pregnancy
- Deliver with skilled attendant and take ARVs
- Bring infant for HIV testing

**Intervention (n=569)**

- 93%

**Control (n=603)**

- 96%

**OR = 0.49 (0.23 - 1.02)**
Department of Obstetrics, Gynecology & Reproductive Sciences

- Get baseline CD4
- Be given ARVs
- Enroll in HIV care and treatment
- Adhere to ARVs during pregnancy
- Deliver with skilled attendant and take ARVs
- Bring infant for HIV testing

Median time to enrollment in HIV care:
- Intervention sites: 0 days
- Control sites: 8 days
  - HR = 2.2 (1.62-3.01)

OR=3.94 (1.14 - 13.63)
Retention in Care among Enrolled Women

At least 2 HIV care follow-up visits in the 6 months following enrollment in HIV care

- Intervention (n=393)
- Control (n=219)

OR=0.73 (0.47 - 1.14)
Get baseline CD4

Be given ARVs

Enroll in HIV care and treatment

Adhere to ARVs during pregnancy^*

Deliver with skilled attendant and take ARVs

Bring infant for HIV testing

OR=4.05 (2.00 - 8.00)

^Self report from women with postpartum forms (n=325)

Intervention (n=173)

Control (n=152)
Get baseline CD4

Be given ARVs

Enroll in HIV care and treatment

Adhere to ARVs during pregnancy^*

Delivery in a health facility^*

Bring infant for HIV testing

OR = 1.31 (0.54 - 3.19)

Intervention (n=149)

Control (n=148)

^Self report from women with postpartum forms (n=325)
Get baseline CD4

Be given ARVs

Enroll in HIV care and treatment

Adhere to ARVs during pregnancy

Delivery in a health facility

Infant HIV testing

By close of study (around 9 months of age):
- Intervention: 67%
- Control: 56%
OR = 1.60 (0.75-3.39)
Time to HAART Initiation Among Eligible Women

Median days to initiation of HAART (IQR):
- Intervention: 125 days (35-273)
- Control: 185 days (83-316)

HR=2.74 (1.56-4.80)

Log rank test P <0.001
## Maternal Outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Intervention N (%)</th>
<th>Control N (%)</th>
<th>Adjusted OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Composite clinical or immunologic progression to AIDS</td>
<td>10 (4.9)</td>
<td>7 (5.1)</td>
<td>0.83</td>
<td>0.41-1.68</td>
</tr>
<tr>
<td>Lost to Follow up (LTFU)</td>
<td>147 (25.8)</td>
<td>200 (33.2)</td>
<td>0.74</td>
<td>0.37-1.51</td>
</tr>
<tr>
<td>Maternal Death – N (%)</td>
<td>9 (1.6)</td>
<td>8 (1.5)</td>
<td>1.19</td>
<td>0.43-3.29</td>
</tr>
<tr>
<td>Composite LTFU or Death</td>
<td>156 (27.4)</td>
<td>208 (34.5)</td>
<td>0.76</td>
<td>0.40-1.44</td>
</tr>
</tbody>
</table>
Randomized
N = 1172

Pregnant women enrolled in intervention clinics
N = 569

Miscarriage/pregnancy loss
N = 1

Live births
N = 568

Alive at 12 weeks
N = 539

6 weeks infant PCR data available
N = 143

Alive at study close
N = 535

Tested by study close
N = 382

Pregnant women enrolled in control clinics
N = 603

Live births
N = 594

Alive at 12 weeks
N = 562

6 weeks infant PCR data available
N = 106

Alive at study close
N = 555

Tested by study close
N = 338

Infants followed to 9 months in both arms
# Infant Outcomes

<table>
<thead>
<tr>
<th></th>
<th>Intervention N (%)</th>
<th>Control N (%)</th>
<th>Adjusted OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total exposed infants (All live births)</td>
<td>568 (99.8)</td>
<td>594 (98.5)</td>
<td>10.76</td>
<td>(1.14-101.85)</td>
</tr>
<tr>
<td>Infant Exclusively breastfed(^)</td>
<td>70 (58)</td>
<td>69 (58)</td>
<td>1.10</td>
<td>(0.61-2.01)</td>
</tr>
<tr>
<td>HIV infected at 6 weeks PCR test</td>
<td>6 (4.2)</td>
<td>7 (6.6)</td>
<td>0.62</td>
<td>(0.20-1.90)</td>
</tr>
<tr>
<td>HIV infected by end study period (by 9 months)</td>
<td>28 (7.3)</td>
<td>27 (8.0)</td>
<td>0.89</td>
<td>(0.56-1.43)</td>
</tr>
</tbody>
</table>

\(^){Self report from women with postpartum forms (n=325)}
HIV Free Survival Among Exposed Infants

Kaplan-Meier HIV Free Survival Estimates

Log Rank P value = 0.882
Conclusions

• Results indicate strong positive effects of integration on:
  • Women’s timely enrollment in HIV care
  • Use of ARVs during pregnancy
  • Early infant diagnosis remained a challenge in both study arms
Conclusions: Outcomes

• Integration was not associated with a reduced risk of MTCT
• In the short term, there was no difference in maternal health outcomes
• Integration of HIV services into the ANC clinic resulted in earlier initiation of HAART in eligible patients
• Important lessons for roll-out of WHO Option B+
  – Systems strengthening
    • Enrollment
    • Follow-up to support adherence and retention
    • Tracing and community linkages
  – Move towards immediate initiation of HAART models
  – Stigma reduction
Acknowledgments

• UCSF
  – Rachel Steinfeld
  – Starley Shade
• UAB
  – Janet Turan
• Albert Einstein
  – Sierra Washington
• U.S. CDC
  – Marta Ackers
  – Dorothy Mbori-Ngacha
• KEMRI
  – Director, KEMRI
    Elizabeth Bukusi
  – Maricianah Onono
  – Kevin Owour
• FACES
  – Patrick Oyaro
  – Jeremy Penner
  – Reson Marima
  – FACES team
• Kenya Ministry of Health

This research has been supported by the President’s Emergency Plan for AIDS Relief (PEPFAR) through the U.S Centers for Disease Control and Prevention under the terms of Cooperative Agreement #5U2GPS001913-02. The findings and conclusions in this presentation are those of the authors and do not necessarily represent the official position of the U.S. Centers for Disease Control and Prevention.