Progress & challenges in PMTCT: The unfinished agenda

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Acknowledgements

• Priscilla Idele UNICEF
• Tyler Porth UNICEF
• Sostena Romano UNICEF
• Charles Kiyaga MOH UGANDA
• Lynn Mofensen EGPAF
Estimated number of pregnant women living with HIV, globally and sub-Saharan Africa, 1990–2013

Global: 1.5 million pregnant women living with HIV (2013)

Sub-Saharan Africa: 1.3 million pregnant women living with HIV (2013)
Risk of mother to child transmission of HIV

- Overall cumulative risk MTCT (without antiretroviral drugs): is 40-45%
- Distribution of this risk across pregnancy, labour and breastfeeding:

Modified from Kevin De Cock et al 2000
Body of scientific evidence on use of ARVs to reduce MTCT

1994 U.S. AZT Trial ACTG 076 Non-breasfeeding

1998 Thai Bangkok short AP/IP AZT trial - Non-breasfeeding

1998 Cote d’Ivoire short AP/IP AZT trials (breastfeeding)

1999 PETRA AZT+3TC trial (partly breastfeeding)

1999 Uganda 2-dose IP/PP NVP trial (HIVNET 012)

2000 Thailand PHPT-1 Long vs short AZT regimens

2002 Cote d’Ivoire DITRAME Plus 1201.0 AZT & IP/PP NVP

2003 DITRAME Plus 1201.1 AZT+3TC & IP/PP NVP

2004 Thailand PHPT-2 AZT & IP/PP NVP

2008 PEPI NVP + short vs long AZT for infant (breastfeeding)

2009 Mma Bana comparative trial for CD4<200 (breastfeeding)
The AZT Regimen PACTG 076 demonstrates a 67% reduction in mother to child transmission of HIV in formula fed infants in women with CD4 >200.

Placebo: 25.5%
Zidovudine: 8.3%

1999: Modified shorter course AZT demonstrates reduction in MTCT in formula fed infants in Thailand and BF infants in Africa

Shaffer et al. Lancet 1999; Witkor et al. 1999 – Benefit reduced with BF

Other short course efficacy studies in Africa – PETRA, DITRAMME
50% reduction with single dose delivery of nevirapine to mother and baby at the time of delivery in breastfeeding infants.

Benefit reduced 48% at 6-8 weeks to 41% at 18 months due to BF transmission.

Jackson B. Lancet 2003
<table>
<thead>
<tr>
<th>Study</th>
<th>Intervention arms</th>
<th>Postpartum MTCT</th>
<th>% reduction (efficacy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SWEN, Ethiopia, India, Uganda. Lancet: Study team 2008</td>
<td>sdNVP vs 6 wks NVP</td>
<td>5.3% vs 2.5%</td>
<td>53% efficacy</td>
</tr>
<tr>
<td>PEPI, Malawi. NEMJ: Kumwenda N et al. 2008</td>
<td>sdNVP/1 wk AZT vs 14 wks NVP</td>
<td>8.4% vs 2.8%</td>
<td>67% efficacy</td>
</tr>
<tr>
<td>BAN, Malawi. NEMJ: Chasela C et al. 2010</td>
<td>sdNV 6 mos NVP P/1 wk AZT-3TC vs</td>
<td>5.7% vs 1.7%</td>
<td>70% efficacy</td>
</tr>
<tr>
<td>Study</td>
<td>Intervention arms</td>
<td>Postpartum MTCT</td>
<td>% Reduction (Efficacy)</td>
</tr>
<tr>
<td>-------------------------------------------</td>
<td>------------------------------------------</td>
<td>----------------------</td>
<td>------------------------</td>
</tr>
<tr>
<td>BAN Malawi. Chasela C et al. NEMJ: 2010</td>
<td>sdNVP/1 wk AZT-3TC vs 6 mos maternal ART</td>
<td>5.7% vs 2.9%</td>
<td>49% efficacy</td>
</tr>
<tr>
<td>WHO Keshobora Study. Keshobora Study Group. Lancet Inf Disease. 2011</td>
<td>AP AZT/sdNVP+tail vs 6 mos maternal ART</td>
<td>5.9% vs 3.1%</td>
<td>41% efficacy</td>
</tr>
<tr>
<td>Kisumu Breastfeeding Study (KIBS). Thomas T. PLoS Med. 2010</td>
<td>6 mos maternal ART</td>
<td>2.5%</td>
<td></td>
</tr>
<tr>
<td>Mma Bana, Botswana. Shapiro R et al. NEMJ: 2010</td>
<td>6 mos maternal ART</td>
<td>0.5%</td>
<td></td>
</tr>
</tbody>
</table>
From Evidence to Policy: Evolution of WHO PMTCT ARV Recommendations

<table>
<thead>
<tr>
<th>Year</th>
<th>PMTCT Recommendations</th>
<th>ART Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>2001</td>
<td>4 weeks AZT; AZT+ 3TC, or SD NVP</td>
<td>No recommendation</td>
</tr>
<tr>
<td>2004</td>
<td>AZT from 28 wks + SD NVP</td>
<td>CD4 &lt;200</td>
</tr>
<tr>
<td>2006</td>
<td>AZT from 28 wks + sdNVP +AZT/3TC 7days</td>
<td>CD4 &lt;200</td>
</tr>
<tr>
<td>2010</td>
<td>Option B (triple ARVs)</td>
<td>CD4 ≤350</td>
</tr>
<tr>
<td>2013</td>
<td>Option B or B+ ART for all PW/BF women regardless of CD4</td>
<td>For B - CD4 ≤500</td>
</tr>
</tbody>
</table>

Move towards: more effective ARV drugs, extending coverage throughout MTCT risk period, and ART for the mother’s health
Superiority AP Triple ARV > AZT/sdNVP

Fowler MG et al. CROI 2015. Seattle, WA. Abs. 31LB


Sites in:
- India* (1)
- Malawi (2)
- S.Africa* (5)
- Tanzania (1)
- Uganda (1)
- Zambia (1)
- Zimbabwe (3)

ENROLLED 3,529 WOMEN

- Higher rates moderate but not severe maternal adverse events
- Higher rates LBW and preterm delivery

Courtesy Lynn Mofensen
Available Resources and Strategies

Global Plan Goal and Targets UNAIDS, 2011

Reduce HIV-related maternal deaths by 50%
Reduce number of new HIV infections among children by 90%
Reduce HIV-related infant deaths by >50%

For Childbearing Women
Reduce new infections in women by 50%

For Women Living with HIV
Reduce unmet need for family planning by 100%

For Pregnant Women Living with HIV
Provide ARVs to 90% of pregnant women to reduce MTCT to < 5%

Provide ART 90% to pregnant women in need of and HIV infected children
Implementation progress
Annual maternal ARV coverage in Sub-Saharan Africa 2009-2013

Eastern and Southern Africa
0,1 0,2 0,3 0,4 0,5 0,6 0,7 0,8 0,9 1

West and Central Africa
0,1 0,2 0,3 0,4 0,5 0,6 0,7 0,8 0,9 1

21 African Global Plan countries
0,1 0,2 0,3 0,4 0,5 0,6 0,7 0,8 0,9 1


*Note: Data from 2009 include single-dose nevirapine, a regimen no longer recommended by WHO; therefore values from 2009 are not comparable to those from 2010-2013.

Note: Countries in ESA and WCA include all countries in sub-Saharan Africa and are based on UNICEF regional designations.
HIV testing: Percent pregnant women who knew own HIV status, 22 Global Plan Plan Countries, 2013

- Zimbabwe
- Zambia
- Uganda
- Mozambique
- Botswana
- South Africa
- Kenya
- Swaziland
- Malawi
- Cote d'Ivoire
- Burundi
- Tanzania
- Ghana
- Lesotho
- Cameroon
- Ethiopia
- India
- Chad
- Angola
- Nigeria
- DRC

In 10 Global Plan countries, >=30% of pregnant women did not know their HIV status

Average: 45%

Source: WHO Health Sector Report, 2014
68% of women in the 21 Global Plan countries receiving antiretroviral drugs to prevent MTCT

2015 target: 4 countries have reached the 90% coverage

In 4 countries, <50% of pregnant WLHIV receiving ARV drugs

Source: UNAIDS 2013 estimates
More progress in PMTCT since 2009: 40% reduction compared to 30% in 9 prior years

Estimated number of new HIV infections in children (aged 0–14): global trend, percent decline and projection, 2001–2015

- 30% decline over 8 years (average 21,000 per year) 2001–2009
- 40% decline over 4 years (average 41,000 per year) 2001–2009
- 83% decline needed over 3 years (average 100,000 per year) 2009–2013
- Global Plan target: 90% reduction by 2015
- 240,000 globally; 200,000 Global Plan countries

Simplification of ART delivery in PMTCT services: Adoption of option B/B+ in the 22 priority countries

PMTCT national regimens adopted following WHO 2010 ARV guidelines

PMTCT regimen policy in the 22 Global Plan Priority Countries as of July 31, 2014

2011

2014
Botswana: Decline MTCT with Option B
Powis K et al.  CROI 2015. Seattle, WA. Abs. 870

HIV Transmission Significantly Lower in Option B Era

<table>
<thead>
<tr>
<th></th>
<th>PRE-Option B (born 5/11-12/12) N=1,376</th>
<th>POST-Option B (born 1/13-6/14) N=1,151</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV infection</td>
<td>22 (1.6%)</td>
<td>8 (0.7%)</td>
<td>0.04</td>
</tr>
</tbody>
</table>

PROMISE results very similar: ZDV 1.8%, Triple 0.6%

Multivariate Analysis: Risk Factors for MTCT in Women Taking Triple ART during Pregnancy with Known Delivery Viral Load

<table>
<thead>
<tr>
<th>Independent MTCT Risk Factors</th>
<th>Transmitting Women (N=16)</th>
<th>Non-Transmitting Women (N=731)</th>
<th>Adjusted OR</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;4 wks triple ARV before delivery</td>
<td>4 (25%)</td>
<td>27 (3.8%)</td>
<td>3.7 (1-13)</td>
<td>0.04</td>
</tr>
<tr>
<td>Non-suppressed at delivery</td>
<td>12 (75%)</td>
<td>194 (26.5%)</td>
<td>6.7 (2-22)</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Courtesy Lynn Mofensen
But what do we need to do?
Understanding country progress in reducing new HIV infections among children aged 0–14 in 21 Global Plan priority countries in sub-Saharan Africa, 2009–2013

<table>
<thead>
<tr>
<th>Country</th>
<th>Progress (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malawi</td>
<td>67%</td>
</tr>
<tr>
<td>Ethiopia</td>
<td>57%</td>
</tr>
<tr>
<td>Zimbabwe</td>
<td>57%</td>
</tr>
<tr>
<td>Botswana</td>
<td>57%</td>
</tr>
<tr>
<td>Namibia</td>
<td>57%</td>
</tr>
<tr>
<td>Mozambique</td>
<td>57%</td>
</tr>
<tr>
<td>South Africa</td>
<td>52%</td>
</tr>
<tr>
<td>Ghana</td>
<td>50%</td>
</tr>
<tr>
<td>Burundi</td>
<td>49%</td>
</tr>
<tr>
<td>United Rep. of Tanzania</td>
<td>49%</td>
</tr>
<tr>
<td>Uganda</td>
<td>47%</td>
</tr>
<tr>
<td>Swaziland</td>
<td>46%</td>
</tr>
<tr>
<td>Côte d'Ivoire</td>
<td>40%</td>
</tr>
<tr>
<td>Kenya</td>
<td>38%</td>
</tr>
<tr>
<td>Zambia</td>
<td>37%</td>
</tr>
<tr>
<td>Cameroon</td>
<td>32%</td>
</tr>
<tr>
<td>Dem. Rep. of the Congo</td>
<td>27%</td>
</tr>
<tr>
<td>Chad</td>
<td>25%</td>
</tr>
<tr>
<td>Lesotho</td>
<td>23%</td>
</tr>
<tr>
<td>Nigeria</td>
<td>19%</td>
</tr>
<tr>
<td>Angola</td>
<td>10%</td>
</tr>
</tbody>
</table>
Understanding trends in new HIV infections among children aged 0-14 in 12 selected high burden countries and the rest of the world, 2009 and 2013

**2009**

400,000 new infections, global

- **Nigeria**: 63,000 (16%)
- **South Africa**: 33,000 (8%)
- **Uganda**: 30,000 (7%)
- **Mozambique**: 27,000 (7%)
- **Malawi**: 23,000 (6%)
- **Kenya**: 21,000 (5%)
- **Zimbabwe**: 21,000 (5%)
- **Cameroon**: 14,000 (3%)
- **Dem. Rep. of the Congo**: 10,000 (2%)
- **Zambia**: 19,000 (5%)
- **Ethiopia**: 20,000 (5%)

**Rest of the World**: 93,000 (23%)

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**2013**

240,000 new infections, global

- **Nigeria**: 51,000 (21%)
- **United Republic of Tanzania**: 16,000 (7%)
- **South Africa**: 16,000 (7%)
- **Uganda**: 16,000 (6%)
- **Kenya**: 13,000 (5%)
- **Mozambique**: 12,000 (5%)
- **Zambia**: 12,000 (5%)
- **Cameroon**: 9,500 (4%)
- **Malawi**: 7,400 (3%)
- **Dem. Rep. of the Congo**: 7,400 (3%)
- **Ethiopia**: 8,300 (3%)
- **Zimbabwe**: 9,000 (4%)

**Rest of the World**: 65,000 (27%)
What does the data tell us in 8 countries contributing to up to 68% of new infections in 2013:

<table>
<thead>
<tr>
<th>Country</th>
<th>No. HIV+ pregnant women delivering (% of total Global Plan pop), 2013</th>
<th>Mother to child transmission (MTCT) rate overall, 2013</th>
<th>MTCT rate at 6 weeks, 2013</th>
<th>Number of new infections (% Global Plan burden), 2013</th>
<th>ARVs for PMTCT coverage , 2013</th>
<th>PMTCT regimen policy as of July</th>
</tr>
</thead>
<tbody>
<tr>
<td>South Africa</td>
<td>260,000 (20%)</td>
<td>6%</td>
<td>3%</td>
<td>16,000 (8%)</td>
<td>90%</td>
<td>B+ (early)</td>
</tr>
<tr>
<td>Nigeria</td>
<td>190,000 (15%)</td>
<td>26%</td>
<td>14%</td>
<td>51,000 (26%)</td>
<td>27%</td>
<td>B</td>
</tr>
<tr>
<td>Kenya</td>
<td>79,000 (6%)</td>
<td>16%</td>
<td>7%</td>
<td>13,000 (6%)</td>
<td>63%</td>
<td>B+ (early)</td>
</tr>
<tr>
<td>Mozambique</td>
<td>100,000 (8%)</td>
<td>12%</td>
<td>5%</td>
<td>12,000 (6%)</td>
<td>84%</td>
<td>B+ (scale up)</td>
</tr>
<tr>
<td>Uganda</td>
<td>120,000 (9%)</td>
<td>13%</td>
<td>6%</td>
<td>16,000 (8%)</td>
<td>75%</td>
<td>B+ (national)</td>
</tr>
<tr>
<td>Tanzania</td>
<td>100,000 (8%)</td>
<td>16%</td>
<td>7%</td>
<td>16,000 (8%)</td>
<td>73%</td>
<td>B+ (scale up)</td>
</tr>
<tr>
<td>Zambia</td>
<td>78,000 (6%)</td>
<td>15%</td>
<td>4%</td>
<td>12,000 (6%)</td>
<td>76%</td>
<td>B+ (early)</td>
</tr>
<tr>
<td>Cameroon</td>
<td>38,000 (3%)</td>
<td>25%</td>
<td>10%</td>
<td>9,500 (4%)</td>
<td>61%</td>
<td>B+ (early)</td>
</tr>
</tbody>
</table>

Understanding incident infections: HIV Prevalence in BF Women with Prior Negative HIV Test and HIV incidence in Women Overall by Country

Maman D et al. CROI 2015. Seattle, WA. Abs.32

HIV prevalence in breastfeeding women reporting negative HIV test at ANC

<table>
<thead>
<tr>
<th>Country</th>
<th>Kenya (N=925)</th>
<th>Malawi (N=1,054)</th>
<th>South Africa (N=264)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>7.4%</td>
<td>2.1%</td>
<td>4.9%</td>
</tr>
</tbody>
</table>

HIV incidence in women overall using incidence assays

<table>
<thead>
<tr>
<th>Country</th>
<th>Incidence in Women 15-29 Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kenya</td>
<td>3.8/100 PY (95% CI 2.1-5.5)</td>
</tr>
<tr>
<td>Malawi</td>
<td>0.9/100 PY (95% CI 0.1-1.7)</td>
</tr>
<tr>
<td>South Africa</td>
<td>3.2/100 PY (95% CI 1.4-4.9)</td>
</tr>
</tbody>
</table>

- Population RNA suppression in pregnant/BF women ranged from 27-72%.
- Proportion undiagnosed pregnant/BF women higher where incidence high, suggesting importance of HIV acute infection during pregnancy/BF.
- Majority of pregnant/BF women with RNA >1,000 c/mL were undiagnosed.

Courtesy Lynn Mofensen
Greater emphasis on understanding the PMTCT Cascade/ loss to follow up/retention monitoring

Pregnant women tested

Testing HIV+

On ART during pregnancy

Testing HIV−

HIV− on EID test

Infant ARV prophylaxis and CTX

EID test at <2 months

HIV+ on EID test

HIV− on EID test

Started on ART

Continuum of prevention, care and treatment

New ART patients

Testing HIV+ throughout breastfeeding

Retained on ART for life

Exit & child welfare follow up

Virally suppressed

EID = early infant diagnosis, CTX = cotrimoxazole
Uganda – 3-month Retention

3-month retention comparison
(All ages)

- At least one visit since baseline: 85.7%, 82.9%
- Within (±) 30 days of 3-month visit: 81.7%, 77.1%
- Completing a visit in month 3: 71.0%, 68.6%
- Completing 3/3 visits: 64.9%, 62.9%

4 definitions of measuring 3-month retention

3-month retention comparison (Adolescents 10-19yrs only)

- At least one visit since baseline: 82.9%
- Within (±) 30 days of 3-month visit: 77.1%
- Completing a visit in month 3: 68.6%
- Completing 3/3 visits: 62.9%

OHTA Project, UNICEF/ICAP 2014
<table>
<thead>
<tr>
<th>Domains</th>
<th>Promising Practices</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>EMPOWER CLIENTS</strong></td>
<td>• Individual client support</td>
<td>Increased service uptake, adherence and retention in PMTCT and ART</td>
</tr>
<tr>
<td></td>
<td>• Participatory women’s groups</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Targeted food assistance</td>
<td></td>
</tr>
<tr>
<td><strong>PROVIDE LONGITUDINAL FOLLOW UP</strong></td>
<td>• Community case management</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• mHealth for client communication</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Active outreach for return to care</td>
<td></td>
</tr>
<tr>
<td><strong>IMPROVE THE CARE-SEEKING ENVIRONMENT</strong></td>
<td>• Male partner involvement</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Community leader engagement</td>
<td></td>
</tr>
<tr>
<td><strong>FACILITATE ACCESS</strong></td>
<td>• Engagement of local organizations</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Community-based HCT</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Community ART distribution</td>
<td></td>
</tr>
</tbody>
</table>
We are not meeting the demand of children living with HIV. Access to ART in children is very low.

Source: UNAIDS 2013 estimates
Children not benefiting from ART as much as adults

Percentage of adults (aged 15+) and children (aged 0–14) living with HIV receiving ART, 22 Global Plan priority countries, 2013

Note: The coverage estimate is based on the estimated unrounded number of children living with HIV receiving ART. This has changed from previous years, where coverage was defined as the percentage of children living with HIV and eligible for ART based on WHO eligibility treatment criteria who were receiving ART.

In 16 of 21 countries, <50% of HEI receive virological test for HIV within two months of birth in 21 Global Plan countries, 2013

Source: Number of infants receiving a virological test for HIV within two months of births reported by countries: Global AIDS Response Progress Reporting (WHO/UNICEF/UNAIDS); number of pregnant women living with HIV as a proxy for HIV-exposed infants: UNAIDS 2013 estimates
30% of HIV infected children will die by age 1 year.

HIV related mortality peaks at around 2-3 months of age in infancy.
Birth HIV PCR Testing in South Africa: Risk Factor Analysis
Technau K-G et al. CROI 2015. Seattle, WA. Abs. 910

- **Sept 2013-May 2014 (Era A):** Birth HIV PCR testing provided for low birth weight or preterm neonates in accordance with national guidelines.

- **June 2014-on (Era B):** All HIV-exposed neonates were tested (weekend cover commencing Aug 2014).

- The Roche COBAS® TaqMan® HIV-1 Qual Test (Versions 1 and 2 in Era A and B respectively) was used.

- Results returned ~1 week from birth and all neonates with positive or indeterminate results are followed.

- PCR negative neonates are referred for routine testing at 6 weeks. Describe coverage, transmission rates and risk factors for transmission.
Birth HIV PCR Testing in South Africa: Risk Factor Analysis  
Technau K-G et al. CROI 2015. Seattle, WA. Abs. 910

- **Era A (9 months) (LBW or PT infants only)**
  - 16% (193/1240) of all HIV-exposed neonates (66% [193/261] of targeted neonates) were offered testing with 100% uptake.
  - 6.7% (13/193) (95% CI: 3.2-10.3) of infants tested PCR positive (n=9) or indeterminate (n=4) with 38% (5/13) female
  - Median HIV RNA 5.7 log (IQR 4.0-6.0)

- **Era B (4 months) (all HIV-exposed newborns)**
  - 90% (675/750) of all HIV-exposed neonates were offered testing with 99% uptake.
  - 2.1% (14/663) (95% CI: 1.0-3.2) tested positive (n=10) or indeterminate (n=4) and 86% (12/14) were female (p=0.018).
  - Median HIV RNA 3.2 log (IQR 2.2-4.5) (p=0.009 vs Era A).
ART initiation: Only 5% ART Clients are children referred from PMTCT programs – Zimbabwe 2012

EID is not enough to increase pediatric ART numbers

Source of EID/DBS Samples
- pmtct/mnch: 75%
- no entry point recorded: 5%
- EPI: 5%
- inpatient: 3%
- OI/ART: 4%
- OPD: 4%
- other: 2%
- outreach: 2%

Referral Source to ART
- Hospital: 52%
- HTC/VCT: 30%
- PMTCT: 5%
- Others: 7%

Maternal, Child Survival and HIV

The Double Dividend is a concept that moves us toward better alignment of the MNCH and paediatric HIV platforms.

THE DOUBLE DIVIDEND

Action to improve survival of HIV-exposed children in the era of eMTCT and renewed child survival campaigns.