Infant feeding and HIV – Policy, Evidence and Hospital Challenges

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MMH/SCAH
MY BRIEF

• Overview of infant feeding within the PMTCT program including national policy, feeding choices & research evidence

• Perinatal perspective / hospital challenges & problems (including preterm babies)
Talk Outline

• Burden of HIV
• Burden of Infant Mortality
• Breastfeeding – a powerful public health intervention
• Global Policy
• National Policy
• Challenges in Hospital
• Conclusions
Timing of Mother-to-Child Transmission

**Timing of Mother-to-Child Transmission**

Early Antenatal (<36 wks)  
Early Postpartum (0-6 months)  
Late Postpartum (6-24 months)

- Pregnancy: 5-10%  
- Labor and Delivery: 10-20%  
- Breastfeeding: 10-20%

**MTCT in 100 HIV+ Mothers by Timing of Transmission**

- Uninfected: 63  
- Breastfeeding: 15  
- Delivery: 15  
- Pregnancy: 7

Adapted from N. Shaffer, CDC

From the presentation given by Jay Ross during the first plenary session
Risk factors for postnatal transmission: Maternal immune status

Hazard ratio for postnatal HIV transmission

BHITS meta-analysis, Read et al (CROI 2003)
Burden of HIV
ADULTS AND CHILDREN ESTIMATED TO BE LIVING WITH HIV IN 2005

- North America: 1.2 million (650,000 - 1.8 million)
- Caribbean: 300,000 (200,000 - 510,000)
- Latin America: 1.8 million (1.4 - 2.4 million)
- Western and Central Europe: 720,000 (570,000 - 890,000)
- North Africa and Middle East: 510,000 (230,000 - 1.4 million)
- Sub-Saharan Africa: 25.8 million (23.8 - 28.9 million)
- South and South-East Asia: 7.4 million (4.5 - 11.0 million)
- Eastern Europe and Central Asia: 1.6 million (990,000 - 2.3 million)
- East Asia: 870,000 (440,000 - 1.4 million)
- Oceania: 45,000 - 120,000

Total: 40.3 (36.7 - 45.3) million
Figure 7c: HIV distribution by district among 15-49 year old pregnant women in South Africa, 2008
Table: Mid-year population estimates by year and province. (Numbers)

© Statistics Denmark
Figure 10: HIV prevalence distribution among antenatal women in KwaZulu-Natal by district, 2008.
Figure 33: HIV prevalence trends among antenatal women by district, Western Cape, 2006 to 2008.

Figure 34: HIV prevalence distribution among antenatal women by district, Western Cape, 2008.
Prevalence: National vs WC

National 29.1%: Western Cape 15.1%
An in-depth analysis of the 2008 data for the Western Cape confirms the differential in HIV prevalence by race.

The overall HIV prevalence in this province is 16.1% with the distribution of participants as follow: 50.8% (1896) Africans; 48.6% (1817) Coloureds; 0.6 (21) Whites and one Asian.

The HIV results in this province show that 29.4% of Africans and only 3.0% of Coloureds were infected.

> 90% of participants in other provinces were African!
## AREA LEVEL HIV SURVEY

### TABLE 1. Area Level Surveys: HIV Prevalence for the Western Cape by Area 2004-2006

<table>
<thead>
<tr>
<th>AREA</th>
<th>HIV PREVALENCE (95% CI)</th>
<th>2004</th>
<th>2005</th>
<th>2006</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Blaauwberg</strong></td>
<td></td>
<td>1.2±1.0</td>
<td>7.3±3.6</td>
<td>5.8±3.5</td>
</tr>
<tr>
<td><strong>Cape Town Central</strong></td>
<td></td>
<td>13.7±4.7</td>
<td>11.5±3.3</td>
<td>11.1±3.1</td>
</tr>
<tr>
<td><strong>Greater Athlone</strong></td>
<td></td>
<td>16.4±3.6</td>
<td>17.7±3.5</td>
<td>12.9±3.1</td>
</tr>
<tr>
<td><strong>Helderberg</strong></td>
<td></td>
<td>18.8±3.3</td>
<td>12.8±3.0</td>
<td>17.3±3.6</td>
</tr>
<tr>
<td><strong>Khayelitsha</strong></td>
<td></td>
<td>33.0±3.5</td>
<td>32.6±3.2</td>
<td>32.7±3.2</td>
</tr>
<tr>
<td><strong>Mitchells Plain</strong></td>
<td></td>
<td>12.9±3.5</td>
<td>5.1±2.0</td>
<td>11.3±2.8</td>
</tr>
<tr>
<td><strong>Gugulethu/Nyanga</strong></td>
<td></td>
<td>29.1±2.8</td>
<td>29.1±3.9</td>
<td>28.8±3.8</td>
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<tr>
<td><strong>Oosenberg</strong></td>
<td></td>
<td>14.8±3.3</td>
<td>16.2±3.5</td>
<td>18.8±4.4*</td>
</tr>
<tr>
<td><strong>South Peninsula</strong></td>
<td></td>
<td>10.8±3.2</td>
<td>12.4±3.2</td>
<td>11.5±3.1</td>
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<tr>
<td><strong>Tygerberg Eastern</strong></td>
<td></td>
<td>12.7±3.6</td>
<td>15.2±3.5</td>
<td>15.6±2.8</td>
</tr>
<tr>
<td><strong>Tygerberg Western</strong></td>
<td></td>
<td>15.1±4.0</td>
<td>15.0±3.1</td>
<td>16.0±3.0</td>
</tr>
<tr>
<td><strong>Metropole Total</strong></td>
<td></td>
<td>17.8±1.1²</td>
<td>17.0±1.1²</td>
<td>18.2±1.8³</td>
</tr>
</tbody>
</table>
HIV in communities

- Prevalence variation within sub-districts and areas is poorly shown by the survey.

- E.g. Metropole’s Southern sub-district average prevalence is 11.5% but in Imizamo Yethu (Hout Bay) and Masiphumelele (Noordhoek) prevalence is close to that in Khayelitsha.
Burden of Infant Mortality
### Infant Mortality Rates for World and UN Regions, 1960–2005 (per 1,000 live births)

<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td>World</td>
<td>119</td>
<td>93</td>
<td>78</td>
<td>66</td>
<td>57</td>
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<td>Sub-Saharan Africa</td>
<td>149</td>
<td>130</td>
<td>115</td>
<td>107</td>
<td>101</td>
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<tr>
<td>Asia</td>
<td>3</td>
<td>12</td>
<td>96</td>
<td>77</td>
<td>63</td>
</tr>
<tr>
<td>Latin America and Caribbean</td>
<td>96</td>
<td>75</td>
<td>52</td>
<td>35</td>
<td>26</td>
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<tr>
<td>Europe</td>
<td>33</td>
<td>23</td>
<td>17</td>
<td>11</td>
<td>9</td>
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</table>

## South Africa

<table>
<thead>
<tr>
<th>Year</th>
<th>Infant mortality rate</th>
<th>Rank</th>
<th>Percent Change</th>
<th>Date of Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>2003</td>
<td>60.84</td>
<td>57</td>
<td></td>
<td>2003 est.</td>
</tr>
<tr>
<td>2004</td>
<td>61.81</td>
<td>52</td>
<td>1.59 %</td>
<td>2004 est.</td>
</tr>
<tr>
<td>2005</td>
<td>61.81</td>
<td>50</td>
<td>0.00 %</td>
<td>2005 est.</td>
</tr>
<tr>
<td>2006</td>
<td>60.66</td>
<td>49</td>
<td>-1.86 %</td>
<td>2006 est.</td>
</tr>
<tr>
<td>2007</td>
<td>59.44</td>
<td>43</td>
<td>-2.01 %</td>
<td>2007 est.</td>
</tr>
<tr>
<td>2008</td>
<td>45.11</td>
<td>59</td>
<td>-24.11 %</td>
<td>2008 est.</td>
</tr>
<tr>
<td>2009</td>
<td>44.42</td>
<td>59</td>
<td>-1.53 %</td>
<td>2009 est.</td>
</tr>
<tr>
<td>2010</td>
<td>43.78</td>
<td>60</td>
<td>-1.44 %</td>
<td>2010 est.</td>
</tr>
<tr>
<td>2011</td>
<td>43.2</td>
<td>57</td>
<td>-1.32 %</td>
<td>2011 est.</td>
</tr>
</tbody>
</table>

[http://www.indexmundi.com/south_africa/infant_mortality_rate.html](http://www.indexmundi.com/south_africa/infant_mortality_rate.html)
Cape Town: IMR 2003-2009
Deaths in children < 1 year of age

AIDS
- 2001: 50
- 2002: 49
- 2003: 39
- 2004: 37
- 2005: 32
- 2006: 15
- 2007: 27
- 2008: 34
- 2009: 32

Gastro
- 2001: 52
- 2002: 48
- 2003: 34
- 2004: 34
- 2005: 32
- 2006: 49
Khayelitsha: IMR
Breastfeeding – a powerful public health intervention
Breastfeeding Saves Lives

Relative risk of infectious disease mortality from never breastfeeding

Source: WHO, 2000
BF Survival Benefit

WHO 2000: odds of infant death due to not breast-feeding rapidly declines with age (pooled data from 6 developing countries):

- < 2 mnths: 5.8 [95% CI: 3.4–9.8]
- 4–5 mnths: 2.6 (95% CI: 1.6–3.9)
- 6–8 mnths: 1.8 (95% CI: 1.2–2.8)
- 9–11 mnths: 1.4 (95% CI: 0.8–2.6)
Timing the Introduction of Replacement Feeding

Additional Risk of Death

Breastfed

Not Breastfed

0

0

optimum

Age
Global Policy
Essential dilemma

- Much of the HIV burden is in the developing world with high background IMR

- Breastfeeding is the single most cost effective intervention to improve child health & nutrition and reduce child mortality in the developing world

- Avoiding breastfeeding prevents postnatal vertical transmission of HIV but incurs significant mortality and morbidity in the less developed world.

- Public health approach vs individual choice
WHO 2010 Policy

- Countries should choose default feeding option
- Formula feeding only if safe
- Maternal ARVs/infant dNVP for duration of BF
EVIDENCE
Exclusive Breast feeding 1999 (Coutsoudis et al)

- Breastfed vs never Breastfed in Vit A study
- At 3 months EBF decreases VT compared to Mixed BF
  - EBF 14.6% vs MBF 24.1% (p =0.03)
  - Hazard ratio 0.52 (0.28 – 0.98) for EBF vs MBF
  - Hazard ratio 0.85 (0.51 – 1.42) for EBF vs never BF
Feeding mode and Morbidity of children born to Women with HIV

Percent of children ill or hospitalized in the first two months

Coutsoudis et al, 2003
SWEN (6 weeks dNVP)

- Ethiopia, India, Uganda: 1887 HIV-exposed infants PCR negative at birth randomised to ...
  
- Maternal/infant sdNVP vs sdNVP + 6/52 dNVP
  
- Frequent mixed feeding and weaning between 14 wks and 6 mnths
  
- At 6 wks VT
  - sdNVP = 5,2%
  - dNVPp = 2,5% (p = 0,54, 0,34 – 0,85, p = 0,009)
  
- At 6 months significance lost
  - 9,0% vs 6,9% (RR 0,8; 0,58 – 1,10; p = 0,16)

Lancet July 26 2008
PEPI (Malawi)- 14 wks dNVP

- 3016 infants randomised to
  - sdNVP + 1 week AZT
    - VT = 10,6% (control)
  - 6/12 extended dNVP (14 weeks)
    - VT = 5,2% (p = 0,001)
  - 6/12 extended dNVP and AZT (14 weeks)
    - VT = 6,4% (p = 0,002)
- Increased neutropaenia with dual therapy

NEJM 10 July, 2008
Follow-up of PEPI subjects: 2188 Infants HIV-negative at 14 weeks

- VT in HAART-eligible (CD4<250) treated vs HAART-eligible untreated vs ART ineligible in cases per 100 person-years
  - ART-ineligible: VT = 3,66 (2,86 -4,81)
  - ART-eligible treated: VT = 1,79 (0,58-4,18)
  - ART-eligible untreated: VT = 10,56 (7,91 – 13,82)
  - Ratio of VT in ART-eligible treated vs untreated = 0,18 (0,07 – 0,44)
BAN (Malawi) – 28 wks dNVP

- Women with CD4 > 250 cells/ml; minimal antepartum ARVs
- Infants PCR negative after birth
- Std vs Infant dNVPp vs Maternal ART to reduce transmission during breastfeeding to 28 weeks
- Std: VT – 6.4%; VT or Death – 7.6%
- Maternal ART: VT – 3%; VT or Death - 4.7%
- dNVPp: VT – 1.8%; VT or Death – 2.9%

NEJM: 17 June 2010
BAN: Probability HIV positive by week 28 visit in infants uninfected at birth

Control vs Maternal HAART: $p = 0.0032$
Control vs Infant NVP: $p < 0.0001$
Maternal HAART vs Infant NVP: $p = 0.1203$
BAN: Probability HIV positive or death by week 28 visit in infants uninfected at birth

Control vs Maternal HAART: $p = 0.0310$
Control vs Infant NVP: $p < 0.0001$
Maternal HAART vs Infant NVP: $p = 0.0698$

Age (weeks)

Estimated probability HIV positive or death

Control
Maternal HAART
Infant NVP

7.6%
4.7%
2.9%
HPTN 046

- Breastfeeding transmission in PCR negative infants from 6 weeks through to 6 months
- Extended dNVPp vs placebo to 6 months in all
- 30% maternal ART - VT 0,2% at 6 months
- Overall VT @ 6/12: NVP = 1,2%; Pl = 2,4%; p=0,048 (Loses significance after 6 months)
- Maternal CD4 > 350: 6; 9/12: NVP = 0,7%; 0,9% and Pl = 2,8 and 3,3%. (p=0,014)
- Death rates similar between dNVPp and Pl
- 2/3 deaths after BF cessation (2nd 6 months)
HAART

- Mma Bana: ART from 26-34 wks gestation to weaning @ 6/12 - Postnatal VT= 0,4%; overall=1,3%

- Kesho Bora: 855 Women with CD4 = 200 - 500 c/ml randomised to receive ART or dual therapy during pregnancy. Standard infant prophylaxis with sdNVP and 1/52 AZT. ART continued during breastfeeding. Significant reduction in VT and VT or Death at 6 wks, 6 months and 12 months

- HPTN 046: Women on ART at randomisation (30%) had only 0,2% risk of vertical transmission at 6 months.
Duration of Prenatal ARVs is a Key Determinant of Vertical Transmission and Infant Health and Survival
HIV transmission and/or deaths between 1 to 6 months according to pre-delivery length of ART

n= 2,161 infants

<table>
<thead>
<tr>
<th>Pre-delivery Length of ART</th>
<th>HIV+</th>
<th>HIV+ &amp; Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-30 days</td>
<td>3.6</td>
<td>5.7</td>
</tr>
<tr>
<td>31-90</td>
<td>1</td>
<td>2.9</td>
</tr>
<tr>
<td>&gt;90</td>
<td>0.3</td>
<td>2</td>
</tr>
</tbody>
</table>

p = <0.001
p = 0.011
Potential Problems
Nevirapine Resistance

- NVP Tail cover reduces resistance to about 12%.
- Maternal sdNVP unnecessary if >1mnth antenatal AZT. (MASHI)
- Breastmilk may have NVP resistant virus.
- Infants on dNVPp !
- Maternal 1st line regimen still contains NVP
- Infant 1st line doesn’t contain NVP.
Multiclass Drug Resistance

- Breastfeeding infants whose mothers are on HAART may be infected with multiclass drug resistant virus.
- There may be fewer transmissions but case management may be more complicated.
Preterm dNVPp

- No evidence on pk or efficacy
- Study underway
- Interim guideline for PVT in preterms
National Policy
Aims of PMTCT 2010

- KEEP WOMEN AND CHILDREN HEALTHY
- IMPROVE THEIR QUALITY OF LIFE
- REDUCE MORTALITY.
Feeding Guidelines

• The South African national PMTCT programme adopts an approach to infant feeding that maximizes child survival, not only the avoidance of HIV transmission.

The South African Infant and Young Child Feeding Policy, its implementation guidelines, and the Baby Friendly Hospital Initiative (BFHI) – in particular, the ten steps to safe infant feeding outlined in the BFHI – should be followed to facilitate feeding support for HIV-positive and HIV-negative women.
Feeding Guidelines

- HCWs get standardized training on infant feeding, counselling, and HIV.
- Infant feeding should be discussed with women at every antenatal visit.
- Pregnant HIV-positive woman should receive at least four antenatal counselling sessions on infant feeding and ARV prophylaxis.
- HIV-positive pregnant women should be fast-tracked for lifelong ART or PMTCT regimens.
2010 National Guidelines

**Mother**

CD4 ≤ 350 or stage 3 and 4:
- HAART (now TDF, 3TC/FTC and NVP) within 2 weeks
- Nil extra intra-partum

CD4 > 350 or stage 1 and 2:
- AZT 12hrly from 14 wks
- Intrapartum sdNVP + TDF/FTC + 3hrly AZT.
Feeding Guidelines

- All mothers who are known to be HIV-infected either on lifelong ART or not, who exclusively breastfeed their infants should do so for 6 months, introduce appropriate complementary foods thereafter, and continue breastfeeding for the first 12 months of life.

- Mothers who are known to be HIV-infected, and not on lifelong ART, who decide to stop breastfeeding at any time should do so gradually during one month whilst the baby continues to receive daily NVP and should continue for one week after all breastfeeding has stopped.
2010 PMTCT Guidelines

INFANT:

- Daily NVP x 6 wk from soon after delivery for all.
- Continue daily NVP beyond 6 weeks for duration of BF if mum not on HAART.
- Stop dNVPp at 6 weeks if formula fed or mum on HAART.
- Emphasis on EBF but individual choice and free formula still available.
- 6 wk PCR – fast track to HAART if positive – encourage BF for at least 2 years (MASHI – Botswana)
Formula Feeding

• Free commercial infant formula will be provided to infants for at least 6 months.

• Discuss the dangers associated with bottle-feeding and how bottles should be cared for, if used. Discuss and demonstrate cup feeding as a recommended alternative to bottle-feeding.
Figure 3: Infants who are exclusively formula fed

- Identify HIV-exposed infant
- 6 weeks: EPI
  - Start CTX
  - Do PCR
  - Discontinue infant NVP
  - Safe infant feeding counseling and support
- PCR
- PCR negative
  - HIV Negative
  - Stop CTX
  - Rapid HIV at 18 months
- PCR positive
  - Prompt referral for ART
  - Continue infant CTX
- Confirm status with Viral Load
Figure 4: Infants who are exclusively breastfed whose mothers are on lifelong ART

- **IDENTIFY HIV-exposed infant**
- **6 weeks: EPI**
  - Start CTX
  - Do PCR
  - Discontinue infant NVP
  - Safe infant feeding counseling and support
- **PCR negative**
  - Continue EBF for 6 months
  - Continue infant CTX until BF stopped and infant negative
  - Repeat HIV test 6-weeks post-cessation of BF
  - Rapid HIV at 18 months
- **PCR positive**
  - Prompt referral for ART
  - Confirm status with viral load
  - Continue BF for 2 years
  - Continue infant infant CTX
Figure 5: Infants who are exclusively breastfed whose mothers are NOT on lifelong ART

- **IDENTIFY HIV-exposed infant**
  - Start CTX
  - Do PCR
  - Continue infant NVP

- **6 weeks: EPI**
  - PCR negative
    - Continue EBF for 6 months
    - Continue infant NVP until BF stopped
    - Continue infant CTX until BF stopped and infant negative
  - PCR positive
    - Prompt referral for ART
    - Confirm status with viral load
    - Continue BF for 2 years
    - Continue infant CTX
    - Stop infant NVP

- **PCR positive**
  - Repeat HIV test 6 weeks after cessation of BF

- **PCR negative**
  - **HIV negative**
    - Stop CTX
    - Rapid HIV test at 18 months

**NB:** All HIV-exposed infants not on ART should have a rapid test at 18 months of age to confirm HIV status conferred by the 6-week PCR test.
Discrepancy Between Feeding Policy and PMTCT Guidelines

Individual counselling and free formula still available!
Challenges in Hospital
Preterm Infants

- No specific guidelines in national or global guidelines for this group
- May be at increased risk of transmission due to immature gut
- Circular H20/2011 (WC DOH) could be first to be formally implemented anywhere in the world
- Pasteurised own mother’s milk is preferred
- Donor milk to complement this
- Revisit feeding choice close to discharge
- Formula milk as an option of last resort
- Weight based daily NVP dosing
Sick infants

- Avoid raw own mothers milk if gut may be compromised – flash-heat treat
Sick Mothers

- Donor milk an option
- Preserves option of exclusive breastfeeding in the long run
- Importance of fast-tracking eligible mothers to lifelong ART
Orphans and Abandoned HIV-exposed Infants

Ideally donor milk best option but stocks currently too limited
Conclusions
I think risk:benefit and cost:benefit of feeding strategy lies in promoting EBF on infant dNVPp or maternal HAART in WC because …

- Breastfeeding is much safer on ARV’s.
- HIV prevalence is particularly high in relatively deprived areas and groups in WC.

But there is an urgent need to monitor HIV-free survival in HIV exposed infants on formula feeding and breastfeeding in WC.
The Future

HAART for all pregnant women living with HIV and during breast feeding ????