Infant Feeding in the context of HIV: Revised WHO Principles and Recommendations 2010

Investing in maternal and child survival

Nigel Rollins
Department of Child and Adolescent Health and Development
WHO

World Health Organization
UNICEF/WHO/UNAIDS recommendations (2007) on HIV and infant feeding

- Exclusive breastfeeding is recommended for HIV-infected mothers for the first 6 months of life unless replacement feeding is acceptable, feasible, affordable, sustainable and safe for them and their infants before that time.
- At six months, if replacement feeding is still not acceptable, feasible, affordable, sustainable and safe, continuation of breastfeeding with additional complementary foods is recommended, while the mother and baby continue to be regularly assessed.

- Rapid cessation of breastfeeding and modified cows milk as a replacement feed dropped as recommendations.
If prevention of mother-to-child transmission of HIV were the only priority then ... 

- Give all HIV-infected mothers antiretroviral drugs, and,
- Stop all breastfeeding
Geographical distribution of HIV burden, 2007

- 19 of 20 countries with highest PMTCT burden are in sub-Saharan Africa
- 68 countries share 97% of global maternal and child deaths
- 12 reported an increase in child mortality rates between 1990 and 2006
  - All 12 in Africa
  - 8 high HIV prevalence countries
  - All have high or very high maternal mortality

Source: UNAIDS 2008
Changes in World Poverty 1981-2001
73.7 million more people in SSA in poverty since 1987

-600  -400  -200  0  200
Millions living on <$1 per day, PPP

Sub-Saharan Africa
South Asia
Middle-East/North Africa
Latin America
E. Europe and Central Asia
East Asia

Chen and Ravallion 2004
UNDP. Human Development Report. 2006

- More than 1.1 billion people worldwide do not have access to clean water,
- 2.6 billion do not have adequate sanitation and
- Diarrhoea due to a lack of clean water kills five times more children than HIV/AIDS.
- the “..roots of the crisis in water can be traced to poverty, inequality, and unequal power relationships, as well as flawed water management policies ...”.
MTCT in 100 HIV+ mothers by timing of transmission

- 63 uninfected
- 15 infected during BF for 2 yrs
- 15 infected during delivery
- 7 infants infected during pregnancy
HIV free survival

• To have children of mothers known to be HIV-infected survive while remaining HIV uninfected is the top priority.

• The success of PMTCT activities, including cost-effectiveness, needs to be measured in terms of HIV-free survival and not just transmissions averted.
HIV transmission through breastfeeding

- Maternal health
- Duration of breastfeeding (vs. early cessation)
- Type of breastfeeding
- Breast health
  - Mastitis and subclinical mastitis
  - Cracked and/or bleeding nipples
Maternal health and child outcomes

- Strong relationship between maternal health and both HIV transmission risk and also child survival
- ~40% HIV-infected mothers have CD4 counts <350 but account for 80% transmissions (26/36) and 80% HIV-associated 'maternal mortality'

Maternal ART improves child survival independent of the effect on transmission

- In the absence of any interventions about 36% infants will become infected.
- 26 of the infants will be born to mothers with CD4 counts <350

- 60%

- 40%

- 10%

- 26

Mothers with CD4>350
Mothers with CD4<350

HIV-infected mothers
Infected infants
The risk of HIV transmission through breastmilk over 24 months

Cumulative rates of late postnatal HIV infection (> 4 wks)

Transmission risk persists and is equivalent throughout exposure period. Approx. 0.7% per month of BF
## Infant infections by feeding mode – VTS study

<table>
<thead>
<tr>
<th>Feeding Mode</th>
<th>HR</th>
<th>p</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>EBF</td>
<td>1.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BM + fluid/food</td>
<td>1.56</td>
<td>0.308</td>
<td>0.66-3.69</td>
</tr>
<tr>
<td>BM + solids</td>
<td>10.87</td>
<td>0.018</td>
<td>1.51-78.00</td>
</tr>
<tr>
<td>BM+FF (@12wks)</td>
<td>1.82</td>
<td>0.057</td>
<td>0.98-3.36</td>
</tr>
</tbody>
</table>

Coovadia H. Lancet 2007
Infant infections by feeding mode – Zvitambo

**Zvitambo Vitamin A trial**

4495 HIV-infected mothers + 2870 infants uninfected at 6 wks
(feeding data on 2060 infants)

*Postnatal transmission*

<table>
<thead>
<tr>
<th>Exclusive BF</th>
<th>Predominant BF</th>
<th>Mixed BF</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.1</td>
<td>6.7</td>
<td>10.5</td>
</tr>
<tr>
<td>100 child yrs</td>
<td>100 child yrs</td>
<td>100 child yrs</td>
</tr>
</tbody>
</table>
WHO recommendations

• Last revised 2006/2007
  – 'HIV and Infant Feeding Update' - ISBN 978 92 4 159596 4

• 2009/2010 revisions considered ...
  – New research evidence
  – Accumulated programmatic experience
  – Public health implications

• Overall aim – to improve HIV free survival of infants born to mothers known to be HIV-infected
Strength of recommendations

**Strong recommendations can be interpreted as:**

- Most individuals should receive the intervention;
- Most well informed individuals would want the recommended course of action and only a small proportion would not;
- Could unequivocally be used for policy making.

**Weak recommendations can be interpreted as:**

- The majority of well informed individuals would want the suggested course of action, but an appreciable proportion who would not;
- Widely varying values and preferences;
- Policy making will require extensive debates and involvement of many stakeholders.
Revised WHO Recommendations on the use of antiretroviral drugs for treating pregnant women and preventing HIV infection in infants (2009)

- Eligibility criteria for ART
  - CD4 count <350, irrespective of clinical stage
  - Clinical stage 3 or 4, irrespective of CD4 count

- The 2009 recommendations ... provide two alternative options for women who are not on ART and breastfeeding:
  - 1) If a woman received AZT during pregnancy, daily NVP is recommended for her child from birth until the end of the breastfeeding period.
  - 2) If a woman received a three-drug regimen during pregnancy, a continued regimen of triple therapy is recommended through the end of the breastfeeding period.

- ARV prophylaxis .... should continue until one week after all exposure to breast milk has ended.
Principles and Recommendations

- Principles define the values and context within which recommendations are implemented
- Recommendations reflect the best available evidence base

- 9 principles and 7 recommendations
  - Generally reinforced former principles and recommendations including:
    - Optimal feeding practices of infants of HIV uninfected mother or mothers of unknown HIV status
    - Feeding of infants already known to be HIV-infected
    - Protecting and promoting optimal infant feeding practices in general population
  - 2 significant changes from 2007
    - Effective ARV interventions have transformed the 'landscape' for decisions re. infant feeding in HIV settings
2010 WHO Principles on HIV and infant feeding

1. Balancing HIV prevention with protection from other causes of child mortality;
2. Integrating HIV interventions into maternal and child health services;
3. Setting national recommendations for infant feeding in the context of HIV;
4. When antiretroviral drugs are not (immediately) available;
5. Informing mothers known to be HIV-infected about infant feeding alternatives;
6. Providing services to specifically support mothers to appropriately feed their infants;
7. Avoiding harm to infant feeding practices in the general population;
8. Advising mothers who are HIV uninfected or whose HIV status is unknown;
9. Investing in improvements in infant feeding practices in the context of HIV.
2010 WHO Recommendations on HIV and infant feeding

1. Ensuring mothers receive the care they need;
2. Which breastfeeding practices and for how long;
3. When mothers decide to stop breastfeeding;
4. What to feed infants when mothers stop breastfeeding;
5. Conditions needed to safely formula feed;
6. Heat-treated, expressed breast milk;
7. (Feeding) When the infant is HIV-infected.
Setting national recommendations for infant feeding in the context of HIV

National (or sub-national) health authorities should decide whether health services will principally counsel and support mothers known to be HIV-infected to:

- breastfeed and receive ARV interventions, or,
- avoid all breastfeeding,

as the strategy that will most likely give infants the greatest chance of HIV-free survival.

This decision should be based on international recommendations and consideration of the socio-economic and cultural contexts of the populations served by Maternal and Child Health services, the availability and quality of health services, the local epidemiology including HIV prevalence among pregnant women and main causes of infant and child mortality and maternal and child under-nutrition.
Which breastfeeding practices and for how long?

**Mothers known to be HIV-infected (and whose infants are HIV uninfected or of unknown HIV status)** should exclusively breastfeed their infants for the first 6 months of life, introducing appropriate complementary foods thereafter, and continue breastfeeding for the first 12 months of life.

Breastfeeding should then only stop once a nutritionally adequate and safe diet without breast milk can be provided.

When HIV-infected mothers decide to stop breastfeeding (at any time) they should do so gradually within one month

- 12 months represents the duration for most HIV-infected mothers that capitalizes on the maximum benefit of breastfeeding in terms of survival (excluding any consideration of HIV transmission). In the presence of ARV intervention to reduce risk of transmission, this combination may give best balance of protection vs. risk
• What is the evidence base in support of the main revisions?
  – Efficacy and safety of ARVs to prevent HIV transmission through BF
  – The risks associated with not BF
  – The optimal duration of BF by HIV-infected mothers
  – Maternal health considerations

• Why WHO recommends that national authorities promote a single infant feeding strategy for all HIV-infected mothers and their infants?
  – Programmatic experiences of implementing previous recommendations
    • Counselling and outcomes
  – Financial considerations

• What are the 'opportunities' and 'challenges' of adopting and implementing the revised recommendations?
  – Programmatic requirements of implementing revised recommendations
    • Communication and commitment
    • Integrated approaches and scaling up
  – Rights considerations
  – MDGs 4 and 5
Maternal ARV prophylaxis studies antepartum and postpartum (Dual or triple ARVs/ART)

Between age 4-6 weeks and 6-7 months HIV transmission rates

4 non-randomized-controlled studies show reduced HIV breastfeeding transmission

- DREAM (CROI 2008) 6 mo EBF: 0.6%
- Mitra Plus (IAS 2007) 6 mo EBF: 0.9%
- Amata (IAS2007) 6 mo EBF: 0.6%
- KIBS (CROI 2008) 6 mo EBF: 1.1%

Courtesy: Lynne Mofenson
**Kesho Bora:**
*All infants: HIV infections*

RCT in Kenya, Burk. Faso and SA
2 arms - AZT + 3TC + LPV/r until
• Delivery only (Short) then nil  Or
• End of BF ~6mths (Triple)

Log rank test $p = 0.039$
(stratified on centre and intention to BF)

<table>
<thead>
<tr>
<th>Age at risk</th>
<th>Triple Events (cum) / at risk</th>
<th>Rate (95% CI)</th>
<th>Short Events (cum) / at risk</th>
<th>Rate (95% CI)</th>
<th>Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth</td>
<td>7/395</td>
<td>1.8 (0.8, 3.7)</td>
<td>9/401</td>
<td>2.2 (1.2, 4.3)</td>
<td>18%</td>
</tr>
<tr>
<td>6 weeks</td>
<td>13/376</td>
<td>3.3 (1.9, 5.6)</td>
<td>19/373</td>
<td>4.8 (3.1, 7.4)</td>
<td>31%</td>
</tr>
<tr>
<td>6 months</td>
<td>19/337</td>
<td>4.9 (3.1, 7.5)</td>
<td>33/329</td>
<td>8.5 (6.1, 11.8)</td>
<td>42%</td>
</tr>
<tr>
<td>12 months</td>
<td>21/275</td>
<td>5.5 (3.6, 8.4)</td>
<td>36/249</td>
<td>9.5 (6.9, 13.0)</td>
<td>42%</td>
</tr>
</tbody>
</table>
**Kesho Bora:**

**All infants:**

HIV-free survival

RCT in Kenya, Burk. Faso and SA

2 arms - AZT + 3TC + LPV/r until

- Delivery only (Short) then nil  **Or**
- End of BF ~6mths (Triple)

Log rank test \( p = 0.022 \)

(stratified on centre and intention to BF)

<table>
<thead>
<tr>
<th>Age (in months)</th>
<th>Triple Events (cum) / at risk</th>
<th>Rate (95% CI)</th>
<th>Short Events (cum) / at risk</th>
<th>Rate (95% CI)</th>
<th>Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth</td>
<td>11/400</td>
<td>2.7 (1.5, 4.9)</td>
<td>11/403</td>
<td>2.7 (1.5, 4.9)</td>
<td>0 %</td>
</tr>
<tr>
<td>6 weeks</td>
<td>19/377</td>
<td>4.8 (3.1, 7.4)</td>
<td>24/376</td>
<td>6.0 (4.1, 8.8)</td>
<td>20 %</td>
</tr>
<tr>
<td>6 months</td>
<td>33/347</td>
<td>8.3 (6.0, 11.5)</td>
<td>50/334</td>
<td>12.6 (9.7, 16.3)</td>
<td>34 %</td>
</tr>
<tr>
<td>12 months</td>
<td>40/278</td>
<td>10.4 (7.7, 13.9)</td>
<td>62/252</td>
<td>16.3 (12.9, 20.5)</td>
<td>36 %</td>
</tr>
</tbody>
</table>
Mma bana study

2 randomised arms and one observational
Mothers not eligible for ART received either:
lopinavir/ritonavir and combivir } for 6m
or  abacavir/AZT/3TC     } while BF
Mothers eligible for ART – outcomes observed
Breastfeeding infants received either sdNVP only (n=986) or daily NVP for 6 weeks (n=901)

Modified ITT analysis (excluded infants HIV infected on D1 sample)

Infant HIV transmission rates %

- 5.5% for sdNVP at 6 weeks (RR=0.54, p=0.009)
- 8.8% for sdNVP at 6 months
- 2.8% for Inf NVP for 6 weeks
- 6.9% for Inf NVP for 6 months (RR=0.8, p=0.16)

AEs
- sdNVP: 393
- Inf NVP: 346
- p=0.54
Probability of HIV-1 Infection in Infants Uninfected at Birth by Treatment Arm: PEPI-Malawi

3 arms:
- Control
- NVP to infants for 14 wks
- NVP and AZT to infants for 14 wks

<table>
<thead>
<tr>
<th>Infant Age</th>
<th>Control</th>
<th>Extended NVP</th>
<th>Extended NVP+ZDV</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 wk</td>
<td>0.3</td>
<td>0.1</td>
<td>0.2</td>
</tr>
<tr>
<td>6 wks</td>
<td>5.1</td>
<td>1.7</td>
<td>1.6</td>
</tr>
<tr>
<td>9 wks</td>
<td>7.4</td>
<td>2.6</td>
<td>2.4</td>
</tr>
<tr>
<td>14 wks</td>
<td>8.4</td>
<td>2.8</td>
<td>2.8</td>
</tr>
<tr>
<td>6 mos</td>
<td>10.1</td>
<td>4.0</td>
<td>5.2</td>
</tr>
<tr>
<td>9 mos</td>
<td>10.6</td>
<td>5.2</td>
<td>6.4</td>
</tr>
<tr>
<td>12 mos</td>
<td>11.5</td>
<td>7.0</td>
<td>8.1</td>
</tr>
<tr>
<td>15 mos</td>
<td>12.4</td>
<td>7.8</td>
<td>8.7</td>
</tr>
<tr>
<td>18 mos</td>
<td>13.9</td>
<td>10.1</td>
<td>10.2</td>
</tr>
<tr>
<td>24 mos</td>
<td>14.5</td>
<td>11.2</td>
<td>12.3</td>
</tr>
</tbody>
</table>
MASHI study

Factorial design testing whether AZT to infants reduces HIV transmission through breastfeeding
Breastfeeding, Antiretroviral and Nutrition (BAN) study

3 Arms:  Control
Mothers receive lopinavir/ritonavir for 28 wks throughout BF period
Breastfeeding infants received daily NVP for 6 mths

![Graph showing transmission and mortality rates](image)

Transmission at 6 mo
- Control: 6.4% (p=0.003)
- Maternal LPV/r: 3% (p=0.001)
- Inf NVP: 1.8%

Death at 6 mo
- Control: 7.6%
- Maternal LPV/r: 4.7%
- Inf NVP: 2.9% (p=0.001)
• **Strong evidence that**

  – ARV interventions to infants or mothers significantly reduce HIV transmission through breastfeeding
    • No evidence of diminished protection over time
  – No evidence of significant drug-related adverse events
    • No increased adverse events with prolonged ARV intervention.
    • NVP adverse events occur within first few weeks and do not accumulate with longer exposure
    • Dose of NVP given to infants as prophylaxis is less than that routinely given as ART for infected infants
Risks associated with not breastfeeding

- Non breastfeeding from birth
- Early cessation of BF

- While the risks of not breastfeeding by HIV uninfected mothers in resource-limited settings were recognised in 2000, there was hope that HIV-infected mothers
  - with additional counselling and support, and,
  - the added motivation of preventing all HIV transmission

... would somehow be different
Effect of breastfeeding on infant and child mortality due to infectious diseases in less developed countries: A pooled analysis – WHO, Lancet 2000

Protection provided by breastmilk

<table>
<thead>
<tr>
<th></th>
<th>&lt; 2 mths</th>
<th>2-3 mths</th>
<th>4-5 mths</th>
<th>6-8 mths</th>
<th>9-11 mths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Odd ratio</td>
<td>5.8</td>
<td>4.1</td>
<td>2.6</td>
<td>1.8</td>
<td>1.4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Condition</th>
<th>&lt; 6 mths</th>
<th>6-11mths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhoea</td>
<td>6.1</td>
<td>2.4</td>
</tr>
<tr>
<td>ARI</td>
<td>1.9</td>
<td>2.5</td>
</tr>
</tbody>
</table>
Breastfeeding recognised as the single most important intervention to prevent child deaths

How many child deaths can we prevent this year?

Gareth Jones, Richard W Steketee, Robert E Black, Zulfiqar A Bhutta, Saul S Morris, and the Bellagio Child Survival Group*

This is the second of five papers in the child survival series. The first focused on continuing childhood mortality (over 10 million each year) from preventable causes: diarrhoea, pneumonia, measles, malnutrition, and a small group of causes leading to neonatal deaths. We reclassified interventions feasible for delivery at high coverage in low-income settings, and classified these as level 1 (evidence of effect), level 2 (limited evidence), or level 3 (inadequate evidence). Our results showed:

- Level 1 intervention is available for preventing or treating each main cause of death among children younger than 5 years, apart from birth asphyxia, for which a level-2 intervention is available. There is also level-1 intervention for several other interventions. However, global coverage for most interventions is below 50%. If level-1 interventions were universally available, 63% of child deaths could be prevented. These findings show that the international community needs to achieve the millennium development goal of reducing child mortality by two-thirds by 2015 and that many children are not being delivered to the mothers and children who need them.
Early Mortality in Formula-Fed Infants in Nairobi FF vs. BF trial

*Nduati R, et al. JAMA 2000;283:1167-74*

![Bar chart showing early excess mortality with formula](chart.png)
Early Mortality (Through Age 7 Months) is Higher in Formula-Fed than Breastfed + AZT Infants

Thior I et al. JAMA 2006;296:794-805

Predominant causes infant death: Diarrhoeal diseases and pneumonia
Survival in the first 6 months of life
– VTS S. Africa

Coovadia H. Lancet 2007

- 94 deaths amongst 1034 infants started on EBF
- 73 of these children were HIV-infected
- Overall HIV-free survival was 75.41% at 6 months (i.e. 223 deaths or infections amongst 1037 infants)

- 8 deaths amongst 101 infants on RF from birth
- Deaths occurred in first 3 months of life

<table>
<thead>
<tr>
<th>Cumulative mortality according to initial infant feeding type</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Feeding type</strong></td>
</tr>
<tr>
<td>------------------</td>
</tr>
<tr>
<td>EBF</td>
</tr>
<tr>
<td>RF</td>
</tr>
</tbody>
</table>
Jan-Mar 2006

- x3 increase diarrhoea cases and x25 increase in deaths
- 35% of all infants are born to HIV-infected mothers and do not BF
- Of infants admitted to 2nd largest hospital in Botswana
  - 97% less than 2 yrs
  - 88% were not BF
  - 87% households used piped water
  - Severe acute malnutrition developed in 25% patients and 22% died
  - Only one BF infant died
  - Mothers commonly reported inconsistent supply of FF
  - Cryptosporidium and enteropathogenic E.coli were common
Decreased survival among infants who stopped BF early or who were never BF.

AHR = 6.19; (95% CI 1.41–27.0, P = 0.015)

97% infants were tested at 6 wks – none infected.

Difference was independent of maternal health or if receiving ART
Mortality in FF vs. BF infants (excl. infants weaned before 12m) HR 6.3 (95%CI = 1.4-28.0, p=0.02)

In the absence of ARVs interventions, HIV free survival of uninfected infants who were BF or FF @12 m was equivalent.
A. In the absence of ARV interventions, HIV free survival of uninfected infants who were BF for 16m equal to HIV FS of infant who stopped BF @ 4m. Additional mortality in early cessation group = additional transmissions in continued BF group.

B. Infants already HIV-infected by 4 m, early cessation of BF resulted in significantly worse HIV free survival compared to those who continued to BF. For infants that are HIV-infected, continued BF prolongs survival.
Growth faltering due to breastfeeding cessation in uninfected children born to HIV-infected mothers in Zambia

Stephen Arpadi, Ashraf Fawzy, Grace M Aldrovandi, Chipepo Kankasa, Moses Sinkala, Mwiya Mwiya, Donald M Thea, and Louise Kuhn

ABSTRACT
Background: The effect of breastfeeding on growth in HIV-exposed infants is not well described.
Objective: The objective was to evaluate the effect of early breastfeeding cessation on growth.

In addition to minimizing postnatal transmission of HIV,

Significant weight loss between 4 and 16 months in infants who stop BF early at 4 months and given replacement feeds

<table>
<thead>
<tr>
<th>Month</th>
<th>Still BF (N)</th>
<th>Stopped BF (N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>564</td>
<td>-</td>
</tr>
<tr>
<td>1</td>
<td>554</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>550</td>
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<td>18</td>
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<td>21</td>
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<td>24</td>
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<td>0</td>
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<tr>
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<td>4</td>
<td>347</td>
<td>403</td>
</tr>
<tr>
<td>5</td>
<td>442</td>
<td></td>
</tr>
</tbody>
</table>
## Frequency of Gastroenteritis and Gastroenteritis-Associated Mortality with Early Weaning in HIV-1–Uninfected Children Born to HIV-Infected Women in Malawi

George Kafutuliza, MBBS, MMed, * Donald R. Hoover, MPH, PhD, † Taha E. Taha, MD, PhD, ‡ Michael Thigpen, MD, § Qing Li, MSc, † Mary Glenn Fowler, MD, MPH, ¶ Newton I. Kumwenda, PhD, ‡ Kondwani Nkanaunena, MSc, ‖ Linda Mipando, RN, MN, ‖‖ and Lynne M. Mofenson, MD§

### Outcome

<table>
<thead>
<tr>
<th>Outcome</th>
<th>PEPI (early BF cessation)</th>
<th>NVAZ (prolonged BF)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>GE Hospitalisation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-6m</td>
<td>0.06-0.9%</td>
<td>0-0.32%</td>
<td></td>
</tr>
<tr>
<td>7-9m</td>
<td>2.9%</td>
<td>0.1%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>10-12m</td>
<td>1.6%</td>
<td>0.2%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>GE mortality</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-6m</td>
<td>5/1000</td>
<td>3/1000</td>
<td></td>
</tr>
<tr>
<td>0-9m</td>
<td>19/1000</td>
<td>7/1000</td>
<td></td>
</tr>
<tr>
<td>0-12m</td>
<td>24/1000</td>
<td>12/1000</td>
<td>0.0002</td>
</tr>
<tr>
<td>All mortality</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-6m</td>
<td>35/1000</td>
<td>40/1000</td>
<td></td>
</tr>
<tr>
<td>0-9m</td>
<td>62/1000</td>
<td>54/1000</td>
<td></td>
</tr>
<tr>
<td>0-12m</td>
<td>79/1000</td>
<td>66/1000</td>
<td>0.03</td>
</tr>
</tbody>
</table>

Non-BF after 6 mo associated with increased:
- hospitalisations
- GE-related mortality
- all-cause mortality
• What is the evidence base in support of the main revisions of the 2000 and 2007 recommendations?
  – Efficacy and safety of ARVs to prevent HIV transmission through BF
  – The risks associated with not BF
  – The optimal duration of BF by HIV-infected mothers
  – Maternal health considerations

• Why WHO recommends that national authorities promote a single infant feeding strategy for all HIV-infected mothers and their infants?
  – Programmatic experiences of implementing previous recommendations
    • Counselling and outcomes
  – Financial considerations
Replacement feeding in PMTCT sites

- Sample of milk collected from bottles (n=94) being offered to infants brought by mothers to PMTCT clinic follow-up visits
  - 63% heavily contaminated with E.coli
  - 28% diluted (based on protein concentration)

In spite of
- All mothers having completed 12 years of education
- 72% having fridges
- All received good counselling on IFP

- 15-20% mothers reported free FF being used for something other than index child
  - Sold
  - Exchanged

- 50-75% reported running out
  - Mainly because of clinic supply

Knowledge of nurses and counsellors about risk of BF transmission

Response to question: If 100 HIV-infected women breastfeed until their children are two years old how many children will be infected at 2 years of age? (mother and child do not receive any antiretroviral medicines)

Feeding at some PMTCT sites

The quality of infant feeding counselling translated into HIV free survival of infants

Woldenbeset. IAS 2009
Balancing cost and outcomes

- While financial costs need to be considered, these must be placed against the health impact of each scenario in terms of infant HIV-free survival
## Cost of scenarios - 10,000 HIV mothers (US$)

**Assume eligibility criteria for ART <350**

<table>
<thead>
<tr>
<th>Health system provides commodities for ....</th>
<th>6 months</th>
<th>12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Scenario A</strong></td>
<td>&lt;350</td>
<td>1,212,542</td>
</tr>
<tr>
<td></td>
<td>&gt;350</td>
<td>BF+NVP for 12m</td>
</tr>
<tr>
<td><strong>Scenario B</strong></td>
<td>&lt;350</td>
<td>1,212,542</td>
</tr>
<tr>
<td></td>
<td>&gt;350</td>
<td>BF+NVP 6m, then FF</td>
</tr>
<tr>
<td><strong>Scenario C</strong></td>
<td>&lt;350</td>
<td>2,063,100</td>
</tr>
<tr>
<td></td>
<td>&gt;350</td>
<td>FF</td>
</tr>
<tr>
<td><strong>Scenario D</strong></td>
<td>&lt;350</td>
<td>522,542</td>
</tr>
<tr>
<td></td>
<td>&gt;350</td>
<td>BF+NVP for 12m</td>
</tr>
<tr>
<td><strong>Scenario E</strong></td>
<td>&lt;350</td>
<td>522,542</td>
</tr>
<tr>
<td></td>
<td>&gt;350</td>
<td>BF+NVP 6m then FF</td>
</tr>
<tr>
<td><strong>Scenario F</strong></td>
<td>No CD4 and no ART</td>
<td>All BF+NVP for 12m</td>
</tr>
<tr>
<td><strong>Scenario G</strong></td>
<td>No CD4 and no ART</td>
<td>All FF</td>
</tr>
</tbody>
</table>
Balancing cost and outcomes

• While financial costs need to be considered, these must be placed against the health impact of each scenario in terms of infant HIV free survival

• If equivalent health impacts, then what is the best investment and how could savings be reinvested?
  – Improved quality of adherence counselling
  – Better drug regimens
  – More extensive ART services
... in settings where national authorities decide to promote and support BF and ARVs to improve HIV FS in exposed infants ...

Which breastfeeding practices and for how long?

** Mothers known to be HIV-infected (and whose infants are HIV uninfected or of unknown HIV status) ** should exclusively breastfeed their infants for the first 6 months of life, introducing appropriate complementary foods thereafter, and continue breastfeeding for the first 12 months of life.

Breastfeeding should then only stop once a nutritionally adequate and safe diet without breast milk can be provided.

When HIV-infected mothers decide to stop breastfeeding (at any time) they should do so gradually within one month

- 12 months represents the duration for most HIV-infected mothers that capitalizes on the maximum benefit of breastfeeding in terms of survival (excluding any consideration of HIV transmission). In the presence of ARV intervention to reduce risk of transmission, this combination may give best balance of protection vs. risk.
Quality of evidence

• The quality of evidence describes the extent to which one can be confident that an estimate of effect or association is correct,
• For the purposes of the GRADE process, evidence is categorized as high, moderate, low or very low.
• Low, or very low 'quality of evidence' does not necessarily imply that the studies were conducted poorly but that the data were not perhaps optimal for developing this recommendation.
• Quality of evidence downgraded if:
  – Not a RCT
  – Not designed for outcome of interest (indirectness)
  – Small sample sizes (e.g. feeding of HIV infected infants)
  – Publication bias – few authors on a given subject (e.g. expressed HTBM)
  – Inconsistency between studies
• Evidence from other sources e.g. non-HIV populations can offer strong support
'12 months' or more?

- In the presence of ARV interventions, being able to breastfeed to 12 months avoids many of the complexities associated with stopping breastfeeding and providing a safe and adequate diet without breast-milk to infants 6-12 months of age.
- No evidence of harm to the mother if she continues breastfeeding.
- WHO not confident to recommend, *without any qualification*, for all HIV-infected mothers to breastfeed indefinitely, or beyond 12 months to 24 months, unless there were no other options.
Preparation of mothers to stop BF

✓ Counsellors gave limited practical advice to guide mothers to successfully stop BF early and rapidly

“I usually tell them, if it is cold, rainy or sunny, the day you have chosen to stop BF, it is **THE day when you stop BF once and for all.**” (PMTCT counsellor, 23 years)

“We just tell them that when the baby is crying you have to try by all means to give formula or just anything to him/her.” (PMTCT counsellor, 22 years)
Ad hoc feeding plans

“I will stop BF tomorrow afternoon. But, I do not know what to feed the twins. I am not sure how to go about it. I will take a chance and ask my sister to give ‘something’. I have not disclosed to her, but I had told her that I was only going to BF for 6 months and then I would get free milk from the clinic. My sister has a job, and I do not think that she will refuse me money as there is no milk at the clinic.

I will not ask the father of the babies. We are not on good terms since I disclosed my HIV-status to him. When I ask him for money he gets upset.”

(Mother, 23 years)
Probability of HIV infection or death by maternal status, ART/ARV intervention and infant feeding practice among infants who are HIV uninfected at birth

<table>
<thead>
<tr>
<th>Infant Feeding scenario #</th>
<th>Mothers fulfil eligibility criteria and on ART</th>
<th>Mothers do not fulfil criteria for ART. Infant NVP prophx. or maternal triple ARV prophx.</th>
<th>Probability of infant HIV infection or death if maternal ART criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Feeding practice</td>
<td>Feeding practice</td>
<td>CD4 &lt;200</td>
</tr>
<tr>
<td></td>
<td>0-6m</td>
<td>6-12m</td>
<td>12-18m</td>
</tr>
<tr>
<td>1</td>
<td>RF</td>
<td>RF</td>
<td>RF</td>
</tr>
<tr>
<td>2</td>
<td>RF</td>
<td>RF</td>
<td>RF</td>
</tr>
<tr>
<td>3</td>
<td>RF</td>
<td>RF</td>
<td>RF</td>
</tr>
<tr>
<td>4</td>
<td>RF</td>
<td>RF</td>
<td>RF</td>
</tr>
<tr>
<td>5</td>
<td>EBF</td>
<td>CBF</td>
<td>CBF</td>
</tr>
<tr>
<td>6</td>
<td>EBF</td>
<td>CBF</td>
<td>RF</td>
</tr>
<tr>
<td>7</td>
<td>EBF</td>
<td>RF</td>
<td>RF</td>
</tr>
<tr>
<td>8</td>
<td>EBF</td>
<td>CBF</td>
<td>RF</td>
</tr>
</tbody>
</table>

Where CD4 count is unknown

<table>
<thead>
<tr>
<th></th>
<th>Feeding practice</th>
<th>Feeding practice</th>
<th>CD4 &lt;200</th>
<th>CD4 &lt;350</th>
</tr>
</thead>
<tbody>
<tr>
<td>9</td>
<td>RF</td>
<td>RF</td>
<td>RF</td>
<td>RF</td>
</tr>
<tr>
<td>10</td>
<td>EBF</td>
<td>CBF</td>
<td>CBF</td>
<td>EBF</td>
</tr>
</tbody>
</table>
Relative risk of death from formula feeding (without HIV)

Childs infected with HIV at 12 months (%) vs. Mortality/1000 at 12 months.

- Formula feed
- Breastfeed

Formula feed is associated with higher mortality rates compared to breastfeed.
Convergence of recommendations and benefits

- Major opportunity to improve maternal and child HIV-free survival
- 'Cost' of implementing all three guidelines outweighs the 'cost' of not introducing the revisions
  - Cost of infections averted vs. lifetime gains
- Effective PMTCT enables care and treatment to be delivered to children who still become infected
- Simplified messages provides the best opportunity in 20 years to promote the best infant feeding practices for both HIV-infected and uninfected mothers and their infants without compromising safety
Guidance to countries

• Review position/policies
  – Review the evidence
  – Assess type of epidemic
  – Assess contribution of infectious diseases and malnutrition to infant mortality and potential impact of safer BF on HIV-free survival
  – Assess quality and coverage of PMTCT/ART services
  – Consider financial and human resource costs of options
  – Formulate national infant feeding and HIV strategy
Guidance to countries

• Review position/policies
  – Review the evidence
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  – Assess quality and coverage of PMTCT/ART services
  – Consider financial and human resource costs of options
  – Formulate national infant feeding and HIV strategy

• Plan implementation
  – Advocacy to health care workers, health professionals and communities to gain confidence for support in implementation
  – Training, commodities,
  – Local prototypes and plan for scale-up
  – Identify what national materials need to be revised
  – Funding applications e.g. Global fund
Programmatic/Protocol questions

- What is the rationale for extending ARV prophylaxis to 12 months when the research data only provides evidence up to 6 months?
- How would mothers respond to recommendations other than default formula feeds?
- Are there consequences of breastfeeding for maternal health?
- How would a breastfeeding/ARV approach relate to the national policy on IYCF?
- How would a decision to support BF and ARVs translate into approaches in clinics and hospitals – initial messages / support provided?
- What support is needed beyond clinics to improve infant feeding practices?
- How should 'success' of HIV/PMTCT interventions be defined?
What is the rationale for extending ARV prophylaxis to 12 m when the research data only provides evidence up to 6 months?

• Linear relationship between exposure to ARV interventions (0-6m) and protection
  – Once interventions stopped, the risk of transmission reverted to higher rate
  – No indication of reduced protection over time
• No increase with AEs with longer ARV exposure
  – NVP SEs occur early
  – Kesho Bora and observational studies report very low AEs
• NVP – dose used as prophylaxis to infants is lower than the dose used as ART to infants already infected
• Potential gains significantly outweigh any likely adverse outcome
• Quality of drugs (efficacy and AE profiles) and cost will improve over time
How would mothers respond to recommendations other than default formula feeds?
• The effectiveness of ARVs to reduce HIV transmission transforms the landscape in which decision can/should be made;
• In conjunction with the known benefits of breastfeeding to reduce mortality from other causes, an approach that strongly recommends a single option as the standard of care can be justified:
  – Information about options should be made available but services would principally support one approach.

• **Consider: "What does the 'reasonable patient' want to hear?"**
  – If there is a medical consensus in favour of a particular option, the reasonable patient would prefer a recommendation.
A continuum of options

Confidence in intervention
- Balance of risks between options not clear (equipoise)
- Effective interventions supported by high quality evidence and cost-benefit
- Danger to others if intervention not adhered to

'Counselling' approach
- Non-directive counseling (e.g., genetic testing; medical research)
- Disclosure of all options combined with professional recommendation (e.g., most major medical treatment)
- Disclosure of single option as standard, with notification of right to refuse (e.g., HIV testing)
- Disclosure of single option as standard; right to refuse may be recognized, but patients are not notified of this right (e.g., TB treatment)
- Nonconsensual interventions (e.g., psychotropic medications to stabilize dangerous patients)
Mma bana study

2 randomised arms and one observational
Mothers not eligible for ART received either:
lopinavir/ritonavir and combivir } for 6m
or abacavir/AZT/3TC } while BF
Mothers eligible for ART – outcomes observed

1248 pregnant women referred to study sites. After counselling about study interventions, 110 (8.8%) declined enrolment as preferred to give formula feeds.
Health and survival of HIV-infected breastfeeding mother

- Data has not demonstrated any increased mortality
- Data reported has been in the context of no ARV interventions – ART or extended ARV prophylaxis
- Kesho Bora – extended triple ARVs through BF period. At 18m, in women who received ARVs
  - Reduced rate of CD4 decline
  - Reduced number of women with clinical progression
  - But, if analyses according to time from stopping ARVs e.g. 12 m after stopping, then no difference in outcomes
HIV infected breastfeeding mothers lost more weight and fat mass than HIV uninfected breastfeeding mothers

<table>
<thead>
<tr>
<th></th>
<th>HIV positive</th>
<th>HIV negative</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Change between 8 and 24 weeks postpartum</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight Kg (SD)</td>
<td>-1.4 (3.1)</td>
<td>0.4 (3.3)</td>
<td>0.004</td>
</tr>
<tr>
<td>BMI Kg/m²(SD)</td>
<td>-0.54 (2.0)</td>
<td>0.15 (1.3)</td>
<td>0.005</td>
</tr>
</tbody>
</table>

Papathakis P. JAIDS 2006. 33(4)
Two prior analyses of HIV-1–infected mothers’ mortality according to their children’s feeding modality had produced conflicting results.

No difference in mortality in this individual patient meta analysis of 4237 HIV-infected mothers

<table>
<thead>
<tr>
<th>Months After Delivery</th>
<th>Overall (n = 4237)</th>
<th>Never Breast-Fed† (n = 520)</th>
<th>Ever Breast-Fed (n = 3717)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>0.6 (0.4–0.8)</td>
<td>0.8 (0.02–1.5)</td>
<td>0.5 (0.3–0.8)</td>
</tr>
<tr>
<td>6</td>
<td>1.3 (0.9–1.7)</td>
<td>0.8 (0.02–1.5)</td>
<td>1.4 (1.0–1.8)</td>
</tr>
<tr>
<td>9</td>
<td>2.0 (1.5–2.4)</td>
<td>1.7 (0.5–2.9)</td>
<td>2.0 (1.5–2.5)</td>
</tr>
<tr>
<td>12</td>
<td>2.9 (2.3–3.4)</td>
<td>2.2 (0.8–3.5)</td>
<td>3.0 (2.4–3.5)</td>
</tr>
<tr>
<td>15</td>
<td>3.9 (3.3–4.6)</td>
<td>2.8 (1.2–4.4)</td>
<td>4.2 (3.4–4.9)</td>
</tr>
<tr>
<td>18</td>
<td>4.8 (4.1–5.6)</td>
<td>3.3 (1.4–5.1)</td>
<td>5.0 (4.2–5.8)</td>
</tr>
</tbody>
</table>

*Kaplan-Meier method.
†P = 0.16 for comparison of the 2 children’s feeding modalities.
How would a breastfeeding/ARV approach relate to the national policy on IYCF?

- **Simplified messages.**
  - All infants can now gain the protection and benefits of breastfeeding
  - If mothers have HIV-infection, then clinics will provide ARV interventions (ART or prophylaxis) that significantly reduce the risk of transmission
  - Mothers who are HIV-infected should breastfeed for 12 m while HIV uninfected mothers should breastfeed for 24m
How would a decision to support BF and ARVs translate into approaches in clinics and hospitals – initial messages / support provided?
Key principle 4.
Informing mothers known to be HIV-infected about infant feeding alternatives
Pregnant women and mothers known to be HIV-infected should be informed of the infant feeding strategy recommended by the national or sub-national authority to improve HIV-free survival of HIV-exposed infants and the health of HIV-infected mothers, and informed that there are alternatives that mothers might wish to adopt;

- This principle is included to affirm that individual rights should not be forfeited in the course of public health approaches.
Key principle 5. Providing services to specifically support mothers to appropriately feed their infants

Skilled counselling and support in appropriate infant feeding practices and ARV interventions to promote HIV-free survival of infants should be available to all pregnant women and mothers;

- Recommending a single option within a national health framework does not remove the need for skilled counselling and support to be available to pregnant women and mothers.
- The nature and content of counselling and support that are required will be specified in implementation guides and training courses.
Key principle 6. Avoiding harm to infant feeding practices in the general population
Counselling and support to mothers known to be HIV-infected, and health messaging to the general population, should be carefully delivered so as not to undermine optimal breastfeeding practices among the general population;

- Included to reinforce the protection and promotion of breastfeeding in the general population especially for mothers who are known to be HIV uninfected.
- The application of the International Code of Marketing of Breast-milk Substitutes has particular importance.
Questions raised at recent workshops

• How would mothers and communities respond to an approach that promotes breastfeeding and ARVs?
• How to give health workers confidence in an approach that promotes breastfeeding and ARVs?
• How can an approach that promotes breastfeeding be promoted when EBF rates are already low?
• How can the impact of PMTCT interventions best be estimated?
• Maternal health and breastfeeding
• Option A vs. option B
What to do when ARVs are not available

• When antiretroviral drugs are not (immediately) available, breastfeeding may still provide infants born to HIV-infected mothers with the greatest chance of HIV-free survival
  – Exclusive breastfeeding in the first 6 months of life and continued breastfeeding thereafter remain, even in the absence of ARVs, key infant feeding practices to increase survival among infants born to mothers known to be HIV-infected. While ARV interventions are being scaled up or in exceptional situations such as emergencies, national authorities should not be deterred from recommending HIV-infected mothers to breastfeed as the most appropriate infant feeding practice.
  – Need to avoid the misconception that mothers can only breastfeed if they have ARVs
  – Every effort should be made to accelerate access to ARVs for both maternal health and also prevention of HIV transmission to infants.
Myth: Exclusive breastfeeding for 6 months is impossible

Median duration of exclusive breastfeeding = 159 days

Coovadia et al., *Lancet* 2007