

Efficacy of antiretroviral treatment in breastfed vs. formula-fed infants who were born to HIV-infected mothers in resources-limited countries

An evidence based review of literature



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**Question**

In resources-limited regions with high HIV prevalence, does the use of common antiretroviral treatment for HIV-infected mothers and their infants result in greater, equal, or lesser efficacy in the breastfeeding group compared to the formula-feeding group in terms of infant HIV infection and mortality rates?

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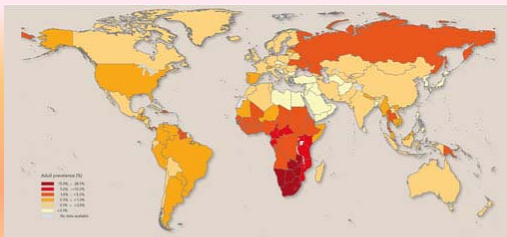
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**Background**



A global view of HIV infection in 2007:  
\_33 million people [range: 30-36 million] living with HIV

Adult prevalence (%)  
\_Dark red: 15 – 28%  
\_Red: 5 – 15%  
\_Orange red: 1 – 5%  
\_Orange: 0.5 – 1%

Source: WHO/UNAIDS, 2008 ([www.who.int/hiv/facts](http://www.who.int/hiv/facts))

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## Background

- In 2007, ~15.4 million women and 2.5 million children under the age of 15 years were living with HIV.
- Of these, about 330,000 children died of AIDS and 420,000 children were newly infected with the majority of infection coming from mother-to-child transmission (MTCT).

Source: UNAIDS. AIDS epidemic update 2007. Geneva: UNAIDS; 2007. ([http://data.unaids.org/pub/EPISlides/2007/2007\\_epiupdate\\_en.pdf](http://data.unaids.org/pub/EPISlides/2007/2007_epiupdate_en.pdf))

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## Background

- The MTCT of HIV can occur during the second and third trimester of pregnancy, during delivery, or at any point during breastfeeding.
- Of these MTCT routes, breastfeeding is the major concern since it may account for as many as 24-42% of the children newly infected with HIV.

Source: The Breastfeeding and HIV International Transmission Study Group. Late postnatal transmission of HIV-1 in breast-fed children: an individual patient data meta-analysis. *Journal of Infectious Diseases*. 2004; 189:2154-2166

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## Background

- In order to avoid MTCT of HIV, infants of HIV-infected mothers in Western and developed countries are fed with formula products and treated with the highly active antiretroviral therapy (HAART).
- The substitution of formula feeding was shown to prevent 44% of HIV infections in these infants (1,2) while the treatment of HAART was shown to reduce the vertical transmission rates to around 1-2% (3).

Sources: 1. Nduati R, John G, Mbori-Ngach Ed, et al. Effect of breastfeeding and formula feeding on transmission of HIV-1: a randomized clinical trial. *JAMA*. 2000; 283:1167-74.  
2. Nduati R, John G, Mbori-Ngach Ed, et al. Morbidity and mortality in breastfed and formula-fed infants of HIV-1-infected women: a randomized clinical trial. *JAMA*. 2001; 286:2413-2420.  
3. Suksomboon N, Poolsup N, and Ket-aim S. Systematic review of the efficacy of antiretroviral therapies for reducing the risk of mother-to-child transmission of HIV infection. *Journal of Clinical Pharmacy and Therapeutics*. 2007; 32:293-311.

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## Background

- Unfortunately, both formula feeding and HAART are not practical or feasible in resource-poor settings, especially in Africa or Southeast Asia.
- Contributing factors:
  - (1) unavailability of affordable formulas and HAART for poor mothers
  - (2) health hazards of formula feeding (e.g. using contaminated water for formula preparation)
  - (3) potential social stigma associated with avoiding breastfeeding .

Sources: Kuhn L and Stein Z. Infant survival, HIV infection, and feeding alternatives in less-developed countries. *Am J Public Health.* 1997; 96:203-211.  
Transmission of HIV-1 through breastfeeding among women in Dar es Salaam, Tanzania. *Journal of Acquired Immune Deficiency Syndromes.* 2002; 31:331-338.

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## Background

- While HIV transmission rate is increasing with breastfeeding in these underprivileged populations, infant morbidity and mortality rates are shown to be improved with the practice of exclusive breastfeeding.
- Morbidity and mortality improved because breast milk provides natural protection for infants against common childhood infections such as diarrhea, pneumonia, neonatal sepsis and acute otitis media.

Sources: Kuhn L and Stein Z. Infant survival, HIV infection, and feeding alternatives in less-developed countries. *Am J Public Health.* 1997; 96:203-211.  
<http://whqlibdoc.who.int/hq/2004/9241562714.pdf>

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## Background

- The dilemma arises when the public health and medical community try to reduce the risk of HIV transmission through breastfeeding while minimizing other infant health complications associated with formula feeding in resources-limited countries.

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## Background

- Several studies have looked into the use of short-courses of antiretroviral treatment for HIV-positive mothers and their infants to reduce the rate of HIV transmission from mother-to-child in these countries.
- However, how effective these regimens are in reducing the transmission rate and infant mortality rate in the breastfeeding group compared to formula feeding group is unknown.

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## Materials and Methods

- Computer-based search strategy
- Utilization of PubMed, Science Direct, and Cochrane Database
- Selection criteria:
  - Published between 1998 to 2008
  - Conducted in resources-poor countries
  - Reporting outcome measures have to be in terms of infant HIV infection rate , infant mortality rate, and HIV-free survival probability (the number of infants alive and HIV-free)
  - These outcome measures need to be the end point results of infants who are at least 6-month old

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## Studies

- Six randomized controlled studies reviewed
- Only one study , **Thior et al. (2006)** conducted in Bostwana, directly compares the efficacy of two infant feeding methods with antiretroviral prophylaxis (Zidovudine plus Nevirapine) given to both mothers and infants.

### **Nevirapine:**

\_200 mg single dose to mothers at labor onset and 6 mg single dose to infants within 72 hours of delivery.

### **Zidovudine:**

To all mothers: 300 mg twice daily at 34 weeks' gestation until labor onset and every 3 hours during labor

To BF infants: 4mg/kg/8hrs from 1-2 months of age and then 6 mg/kg/8 hrs from 2-6 months

To FF infants: 4mg/kg/12 hrs for 1 month

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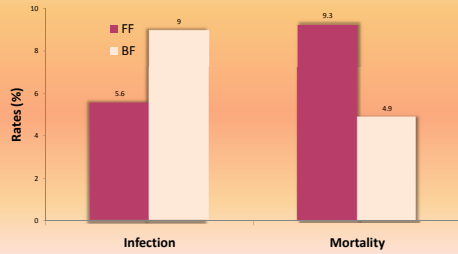
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## Results (From Thior et al. trial)

Figure 1: 7-months HIV infection and mortality rates in FF vs. BF



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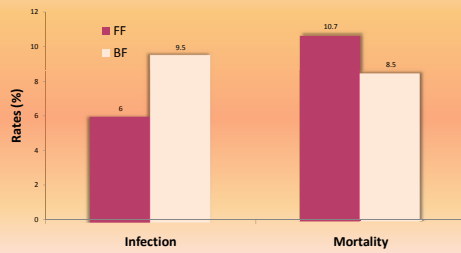
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## Results (From Thior et al. trial)

Figure 2: 18-months HIV infection and mortality rates in FF vs. BF



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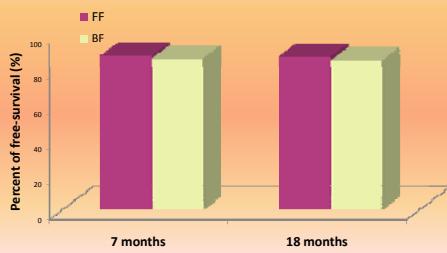
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## Results (From Thior et al. trial)

Figure 3: HIV-free survival probability in formula-fed versus breastfed infants



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**Result Summary  
(From Thior et al. trial)**

- **Lower HIV-infection rate** in formula-fed infants compared to breastfed infants at 7 months (5.6% vs. 9.0%) and 18 months (6.0% vs. 9.5%)
- **Higher infant mortality rate** in the formula-fed infants compared to breastfed infants at 7 months (9.3% vs. 4.9%) and 18 months (10.7% vs. 8.5% ).
- **Similar overall HIV-free survival probabilities** in both groups at 7 months and at 18 months.

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**Studies Cont.**

- Five other trials only focus on:
  - \_ Only one feeding strategy and compare the use of antiretroviral prophylaxis versus placebo
  - \_ Longer regimens versus shorter regimens using the same antiretroviral drugs
  - \_ Various antiretroviral regimens using different drugs and different durations of treatment.
- Two trials (breastfeeding group alone): conducted in Uganda and Cote d'Ivoire.
- Three trials (formula feeding group alone): conducted in Thailand

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**Result  
(From other 5 studies)**

Since these studies only focused on one feeding strategy, it is challenging to directly compare the efficacy of these various regimens in breastfed infants versus formula-fed infants.

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## Discussion

Our conclusion can only be drawn from the trial conducted by Thior et al. (2006) since it is the only study that directly compares the efficacy of antiretroviral treatment in breastfed infants vs. formula-fed infants.

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## Discussion

Thior et al. trial(2006) – in **Bostwana**

- A small country in South Africa with the second highest adult HIV prevalence rate (23.9%) in the world, after Swaziland.
- The first African country with a development of a comprehensive HIV/AIDS care and treatment program, aiming at providing anti-HIV drugs to all its needy citizens.
- This explains why this study could be accomplished with adequate data.
- \*Its antiretroviral regimen (Zidovudine and Nevirapine) is one of the best short-course regimens that provides optimal reduction rate in MTCT of HIV.

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## Discussion

- The results from Thior et al. trial indicates an equal efficacy for both formula-fed and breastfed infants being treated with this particular short course of antiretroviral regimen , when the risk of HIV-transmission is balanced with the risk of infant mortality rate.
  - Since this trial was only conducted in Bostwana, we cannot conclude that the above findings are also true for other impoverished countries.
- A need for future studies!!!

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### Clinical Pearls

- Breastfeeding has many well-established clinical advantages to both mother and child.
- But, breastfeeding contributes a significant risk of MTCT of HIV.
  - The longer the breastfeeding period, the more chance there is of MTCT.
- In most situations, formula feeding should be advised if the risk of HIV transmission from breastfeeding appears to be greater than the risk of formula feeding.
- However, in resources limited regions, encourage breastfeeding when in doubt!

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### Clinical Pearls

#### CDC recommendations

\_To prevent MCTC of HIV, CDC recommends this basic management for HIV-infected mothers and their infants:

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### CDC Recommendations

#### To prevent MTCT of HIV

- **HIV-infected mothers:**
  - 1) Should receive HAART including AZT (Retrovir or zidovudine) in their 1<sup>st</sup> trimester if symptomatic, or in 2<sup>nd</sup> or 3<sup>rd</sup> trimester if non-symptomatic
  - 2) Receive (IV) AZT during labor and delivery
  - 3) Exclusively avoid breastfeeding .

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## CDC Recommendations

### To prevent MTCT of HIV

- **Infants:**

1) To prevent *P. carinii/jiroveci* pneumonia, should receive:

- \*AZT (liquid form) q 6 hrs for 6 weeks after birth

- \*A combination of sulfamethoxazole & trimethoprim at 6 weeks old (when the course of AZT is completed)

2) They should have preliminary HIV tests at 3 time points:

- \*Birth to 14 days

- \*1-2 months of age

- \*3-6 months of age.

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## Questions



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