Rates of mother-to-child transmission and the impact of different PMTCT regimens

Report of a consultation organised by the UNAIDS Reference Group for Estimates, Modelling and Projections, February-March 2005

TECHNICAL REPORT AND RECOMMENDATIONS

UNAIDS

Rates of mother-to-child transmission and the impact of different PMTCT regimens

We are currently updating our methods, assumptions and tools that UNAIDS and WHO use to develop country, regional and global estimates of HIV prevalence, incidence and mortality.

Based on a consultation in February 2005, organised by the UNAIDS Reference Group on Estimates, Modelling and Projections, we have slightly modified the rates of Mother-to-Child transmission that are recommended for use in modelling work.

A recent review of PMTCT rates for various infant feeding options and PMTCT regimens has been summarised in the 2004 WHO document "Antiretroviral drugs for treating pregnant women and preventing HIV infections in infants". A table of the relevant findings from that review is overleaf, to which has been added summary information on pre-PMTCT transmission rates from De Cock et al, JAMA 2000.

In the past few years we have used a default rate of 32% for Mother-to-Child transmission, based on a 2001 recommendation of the UNAIDS Reference Group on Estimates, Modelling and Projections. The 32% default transmission rate can be lowered depending on coverage and effectiveness of PMTCT programmes and infant feeding options. In the past, for most countries with high HIV burden, the default rate has not been changed much since coverage of PMTCT was fairly low. However, many countries are now rapidly scaling up their PMTCT programs, and we would like to provide more flexibility in modelling MTCT by allowing several MTCT rates to be applied to subsections of the population of pregnant women.

Infant feeding patterns are a very important determinant of MTCT. For mothers using replacement feeding there is obviously no transmission through breastfeeding. De Cock et al suggest breastfeeding through 6 mos leads to about 10% extra transmission (from 20% to 30%), while breastfeeding through 18-24 mos leads to about 17.5% extra transmission (from 20% to 37.5%), compared to no breastfeeding. In PMTCT programmes, breastfeeding is proposed to be as short as possible, around 6 mos. Hence that will still lead to about 10% transmission.

In the new version of our tools we would like to distinguish baseline infant feeding patterns (long versus short versus none), and we would like to allow for implementation of different currently recommended PMTCT regimens. The proposed rates, based on the WHO review and the 2000 De Cock et al review, would be as listed below.

1. Infant feeding options:
- No intervention, long (18-24 mos) breastfeeding: 35% (De Cock, 2000)
- No intervention, short (6 mos) breastfeeding: 30% (De Cock, 2000, and DITRAME and RETRO-CI control arm, 2002)
- No intervention, replacement feeding: 20% (De Cock, 2000, and Bangkok CDC 1999 control arm)

2. PMTCT regimens:
- Single-dose NVP (mothers & infants), combined with short (6 months) breastfeeding: 16% (Based on HIVNET012, 2003).
- Single-dose NVP (mothers & infants), combined with replacement feeding: 11% (Based on SAINT NVP Bottle feeding arm, 2003).
- AZT long (from 28 weeks) and single-dose NVP (mothers & infants), combined with short (6 months) breastfeeding: 10% (Based on "DITRAME plus" with 6.5% through 6 weeks and assuming another 0.8% transmission per month for 5 months).
- AZT long (from 28 weeks) and single-dose NVP (mothers & infants), combined with replacement feeding: 2% (Based on Thai PHPT-2, 2004).

Other regimens to be considered *(for which data were not available at the time of the consultation)*
- AZT in third trimester plus 6 months of ZDV (or NVP) to infant during exclusive breastfeeding.
- HAART from 34 weeks thru 6 months post partum in exclusively breastfeeding and then weaned at 6 months.

Developing country studies on MTCT and PMTCT
Based on WHO 2004 "Antiretroviral drugs for treating pregnant women and preventing HIV infection in infants".
Transmission rates are at 18-24 mos for breastfeeding pops, at 6 months or later for non-breastfeeding pops.

Study	**Reference** (listed overleaf)	**Mother's treatment**				**Infant's treatment**		**Breastfeeding**	**Transmission rate**	**Comment** (see below)
		Long AZT mother (28wks)	**Short AZT mother (36wks)**	**Short 3TC mother (36wks)**	**NVP single intrapartum**	**NVP infant**	**Other infant**			
De Cock review	JAMA 2000	No No No	No No No	No No No	No No No	No No No	No No No	No 6 mos 18-24 mos	15-30 25-35 30-45	
Bangkok CDC 1999	Shaffer 1999	No No	No Yes	No No	No No	No No	No No	No No	18.9 9.4	
DITRAME and RETRO-CI 1999	Leroy 2002	No No	No Yes	No No	No No	No No	No No	Yes Yes	30.2 22.5	
PETRA S-A, Ug, Tanz 2002	Petra 2002	No No	No Yes	No Yes	No No	No No	No Yes (AZT+3TC)	Yes Yes	22.2 14.9	
HIVNET 012 Uganda	Jackson 2003	No No	No No	No No	No Yes	No Yes	Yes (AZT) No	Yes Yes	25.8 15.7	
Thai PHPT-1	Lallemant 2000	No Yes	Yes No	No No	No No	No No	Yes (AZT) Yes (AZT)	No No	10.5 5.6	 1
Thai PHPT-2	Lallemant 2004	Yes Yes Yes	No No No	No No No	No Yes Yes	No No Yes	Yes (AZT) No No	No No No	6.3 2.8 1.9	
SAINT NVP	Moodley 2003	No No	No No	No No	Yes Yes	Yes Yes	No No	No Yes	10.8 16	2 2
DITRAME plus	ANRS 2005	No No	Yes Yes (3)	No Yes (3)	Yes Yes	Yes Yes	Yes (AZT) Yes (AZT)	6 mos/No 6 mos/No	6.5 4.7	

Comments
1 Median transmission of 6 weeks post-partum and 3 days post-partum
2 Transmission rates at 8 weeks
3 Starting at 32 weeks

References

De Cock et al.
Prevention of mother-to-child HIV transmission in resource-poor countries: translating research into policy and practice. JAMA 2000, 283: 1175-1182

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Short-course zidovudine for perinatal HIV-1 transmission in Bangkok, Thailand: a randomised controlled trial. Lancet 1999, 353: 773-780

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Twenty-four month efficacy of a maternal short-course zidovudine regimen to prevent mother-to-child transmission of HIV-1 in West-Africa. AIDS 2002, 16: 631-641

Petra Study Team
Efficacy of three short-course regimens of zidovudine and lamivudine in preventing early and late transmission of HIV-1 from mother to child in Tanzania, South Africa, and Uganda (Petra study): a randomised, double-blind, placebo-controlled trial. Lancet 2002, 359: 1178-1186

Jackson JB et al
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Lallemant M et al.
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Lallemant M et al.
Single-dose perinatal nevirapine plus standard zidovudine to prevent mother-to-child transmission of HIV-1 in Thailand. NEJM 2004, 351: 217-228

Moodley D et al.
A multicenter randomized controlled trial of nevirapine versus a combination of zidovudine and lamivudine to reduce intrapartum and early postpartum mother-to-child transmission of HIV type 1. JID 2003, 187: 725-735

ANRS 1201/1202 DITRAME PLUS Study Group
Field efficacy of zidovudine, lamivudine and single-dose nevirapine to prevent peripartum HIV transmission. AIDS 2005, 19: 309-318