Prevention of HIV transmission from mother to child
Strategic options
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Prevention of HIV transmission from mother to child: Strategic options
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Prevention of HIV transmission from mother to child:

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1. Introduction

Mother-to-child transmission (M TCT) is by far the largest source of HIV infection in children below the age of 15 years. In countries where blood products are regularly screened and clean syringes and needles are widely available, it is virtually the only source in young children.

So far, the AIDS epidemic has claimed the lives of nearly 3 million children, and another 1 million are living with HIV today. Worldwide, one in ten of those who became newly infected in 1998 was a child. Though Africa accounts for only 10% of the world’s population, to date around nine out of ten of all HIV-infected babies have been born in that region, largely as a consequence of high fertility rates combined with very high infection rates. In urban centres in southern Africa, for example, rates of HIV infection of 20-30% among pregnant women tested anonymously at antenatal clinics are common. And rates of 59% and even 70% have been recorded in parts of Zimbabwe, and 43% in Botswana.

However there is no room for complacency elsewhere. African countries were among the earliest to be affected by HIV, and the epidemics on the sub-continent are therefore well advanced. But the virus is now spreading fast in other regions of the world, and everywhere the proportion of women among those infected is growing. Globally, there are around 12 million women of childbearing age who are HIV-positive. And the number of infants who acquire the virus from their mothers is rising rapidly in a number of places, notably India and South-East Asia.

The effects of the epidemic among young children are serious and far-reaching. AIDS threatens to reverse years of steady progress in child survival, and has already doubled infant mortality in the worst affected countries. In Zimbabwe, for instance, infant mortality increased from 30 to 60 per 1000 between 1990 and 1996. And deaths among one- to five-year-olds, the age group in which the bulk of child AIDS deaths are concentrated, rose even more sharply — from 8 to 20 per 1000 — in the same period.
1.1 The risk of MTCT

The virus may be transmitted during pregnancy (mainly late), childbirth, or breastfeeding. In the absence of preventive measures, the risk of a baby acquiring the virus from an infected mother ranges from 15% to 25% in industrialized countries, and 25% to 35% in developing countries. The difference is due largely to feeding practices: breastfeeding is more common and usually practised for a longer period in developing countries than in the industrialized world.

1.2 Prevention strategies

Until recently, countries had only two main strategies for limiting the numbers of HIV-infected infants:

- primary prevention of MTCT—taking steps to protect women of childbearing age from becoming infected with HIV in the first place;
- the provision of family planning services, and pregnancy termination where this is legal, to enable women to avoid unwanted births.

These remain the most important strategies for reducing HIV among young children and essential activities in all national AIDS campaigns. Today, however, there is a third option for HIV-positive women who want to give birth which consists of a course of antiretroviral drugs for the mother (and sometimes the child), and replacement feeding for the infant. A recent trial in Thailand using a short course of zidovudine has shown that this strategy is able to reduce the risk of MTCT to below 10% when breastfeeding is strictly avoided. Alternative regimens using short courses of other antiretroviral drugs, sometimes in combination, will soon be available. Furthermore, trials are being conducted to find out what happens if mothers do subsequently breastfeed their babies instead of giving replacement feeds. This is a critical issue since the majority of HIV-positive women who risk transmitting the virus to their infants come from cultures where breastfeeding is the norm, and where replacement feeding presents great difficulties for many women.

Introducing a strategy of antiretroviral drug use and replacement feeding is, however, a complex process. To take advantage of the intervention, mothers need to know that they are HIV-positive, and they must therefore have access to voluntary counselling and testing. Costs and benefits need to be carefully assessed. Policy-makers need to decide what kind of programme is feasible and most appropriate for their countries, and whether or not to test models of the strategy in pilot projects before introducing it more widely. Such a programme requires a commitment to ensuring there is an efficiently functioning primary health care system with certain key services as a basis for introducing the strategy. Where these conditions do not
already exist, decisions need to be made about how to strengthen the health infrastructure, what time-frame would be realistic, and what else is needed to create the conditions for safe and successful introduction of antiretroviral drugs and replacement feeding.

The purpose of this paper is to review the key issues for consideration in policy-making, and to propose ways in which the strategy might be tailored to suit local conditions. The paper is intended for all those with a part to play and a special interest in national policy making with respect to HIV prevention and care.

1.3 The cost of inaction

The cost of doing nothing to reduce MTCT will depend a great deal on the prevalence of HIV infection among parents-to-be. In areas where 20% or more of pregnant women are HIV-positive, the financial cost of caring for sick and dying HIV-infected children will be enormous, and there will be significant loss of the benefits from the huge commitment of time, energy and resources spent on reducing child morbidity and mortality over recent decades. Where HIV prevalence is low, health care costs will be relatively low too, and the waste of resources already spent on child survival not quite so dramatic. However, the costs for families and communities cannot be measured in financial terms alone, and many couples will bear responsibility for looking after their infected babies, often while struggling to cope with their own ill-health.

2. Major issues for decision-making

The following issues need consideration:

2.1 Counselling and voluntary testing

For women to take advantage of measures to reduce MTCT, they will need to know and accept their HIV status. Voluntary counselling and testing services therefore need to be widely available and acceptable. Ideally, everyone should have access to such services since there are clear advantages to knowing one’s serological status. People who know they are HIV-infected are likely to be motivated to look after their health, perhaps with behaviour and lifestyle changes, and to seek early medical attention for problems. They can make informed decisions about sexual practices, childbearing, and infant feeding, and take steps to protect partners who may still be uninfected. Those whose test results are negative can be counselled about how to protect themselves and their children from infection. Furthermore, voluntary counselling and testing has an important role to play in challenging denial of the epidemic: it helps societies which
are currently only aware of people who are ill with AIDS to recognize that there are many more people living with HIV and who show no outward signs. However, it must be emphasized that, unless people have real choices for action once they have their test results, there is no good reason to take a test.

However, providing voluntary counselling and testing for the whole population will not necessarily be justified in low HIV prevalence areas where resources are scarce. And even where justified on the basis of prevalence, it will not be a realistic option in some places because the health infrastructure is not sufficiently strong to support the service. For, besides the cost and practical requirements of providing counselling and testing itself, there must be an efficient referral system to a range of other basic services that people need once they have received their test results. These include family planning, prevention and treatment of sexually transmitted diseases (STDs), mother-and-child health services, and health care for infected people including prevention and treatment of opportunistic infections, counselling, and psychological support.

Taking local conditions into account, therefore, policy-makers need to decide what kind of counselling and testing services are most appropriate and feasible, and what action, if any, is required to strengthen the health system that supports them. In particular, decisions need to be made about whether to make counselling and testing available to the whole population (comprehensive VCT); or to target the service at women or couples making use of reproductive health services in areas where the HIV prevalence is especially high (targeted antenatal VCT); or to offer counselling and testing to all women attending antenatal services as part of a programme to reduce MTCT of HIV (routine antenatal VCT).

2.2 Stigma and discrimination

Measures to reduce MTCT of HIV, especially the administration of antiretroviral drugs and avoidance of breastfeeding, make it virtually impossible for HIV-positive women to keep their infection a secret from their families and people in the wider community. It is therefore essential to the safety and acceptability of MTCT interventions that effective steps be taken to combat rejection of people with HIV/AIDS. Where women fear discrimination, violence, and perhaps even murder if they are identified as HIV-infected, they will be reluctant or completely unable to take advantage of opportunities offered to protect their infants from infection. Special attention should be paid, in particular, to developing positive and non-judgmental attitudes towards HIV/AIDS in health staff so that they can serve their clients with empathy. In places where stigmatization of HIV-infected people is a serious problem, it would be advisable to
introduce the antiretroviral strategy for reducing MTCT in a pilot programme initially, so that the risks can be carefully monitored and ways of dealing with stigma and discrimination tested.

It is still common for women to be blamed for spreading STDs, including HIV, despite the fact that very often they are infected by the husband or partner to whom they are entirely faithful. To challenge this pervasive prejudice, as well as to encourage joint responsibility for childbearing and related decisions, it is a good idea to offer counselling and testing to pregnant women’s partners also, where this is feasible and desired.

2.3 Health care systems

A programme of voluntary counselling and testing, antiretroviral drugs and replacement feeding can only be set up where there is an efficiently functioning health system with certain key services. Mother-and-child health services, including widely available and acceptable antenatal, delivery and postnatal services, are essential. And counselling services, family planning services and medical care for HIV-positive women and their children should also be part of the basic health care provision. These services need to be carefully prepared for the integration of the new programme. In particular, steps are required to ensure:

a) easy access and privacy for clients attending services. This will require assessment of the physical environment of clinics, and perhaps rearrangement of activities;

b) continuity of care and a good flow of information between the various units involved in the management of HIV-positive clients;

c) technical supervision of services to enhance quality;

d) opportunities for clients to express their needs and their views.

Where the basic services are already in place and operating efficiently, the cost of providing counselling and testing, antiretroviral drugs and replacement feeding is likely to be well distributed across the health system and relatively easy to absorb. However, in places where the health infrastructure needs considerable strengthening and perhaps even building from scratch to support the new programme, the additional cost will assume greater significance. Since expansion and improvement of the health system benefit the whole of society, it is important that the MTCT programme is not expected to bear an undue and perhaps crippling proportion of the costs and responsibility. If the provision of antiretroviral drugs and replacement feeding is to be sustainable over the long term, the financial burden must be fairly distributed across the health services. Policy-makers should take account, also, of the fact that improvements in
access and quality of services have a tendency to increase public expectations of health and therefore the demands on the health services.

2.4 Replacement feeding

The issue of replacement feeding is a complex one. Promotion of breastfeeding as the best possible nutrition for infants has been the cornerstone of child health and survival strategies for the past two decades, and has played a major part in lowering infant mortality in many parts of the world. It remains the best option for the great majority of infants, and in providing for replacement feeding as part of the strategy to reduce MTCT of HIV, policy-makers need to take into account the risks of undermining breastfeeding generally, and of relaxing vital controls on the promotion of infant formula by the industry. They also need a sound assessment of how safe it is to recommend replacement feeding in their local setting. For example, is infant formula readily available; is the supply of formula assured over the long term; do people have access to clean water and fuel for boiling it; and are they sufficiently educated and informed to make up replacement feeds correctly? If used incorrectly — mixed with dirty, unboiled water, for example, or over-diluted — breastmilk substitutes can cause infection, malnutrition and death. Where the risks associated with replacement feeding are not clear, research will be necessary to establish the facts, and strategies should be tested in pilot projects. The fact that the fertility lowering effects of breastfeeding will be inactivated makes the availability of family planning services as part of postpartum care a necessity.

3. Pilot projects

In many places it will be a good idea to introduce prenatal voluntary counselling and testing and the use of antiretroviral drugs and replacement feeding in a limited way in pilot programmes initially, so that lessons can be learnt about how best to operate the new service before it is introduced more widely. Careful monitoring and evaluation of such an exercise are essential and must be planned for from the start. Pilot programmes are specially important in places where stigmatization of people with HIV/AIDS is common, and where there is uncertainty about the safety of replacement feeding, or the acceptability of voluntary counselling and testing. Pilot sites should be selected on the basis of having good basic health services (as described above) already in place and efficient referral systems. Only if the projects are successful under these carefully chosen pilot conditions will further testing be tried in more challenging environments.

Integration of services is a key requirement: measures to prevent MTCT of HIV are one part of the wider programme to cope with

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1 For a comprehensive discussion of the issue, see: HIV and infant feeding: guidelines for decision-makers UNAIDS/98.3
HIV/AIDS in a country, and should have strong links to all other aspects of the programme, such as primary prevention of infection, care of infected people, and the support of orphans.

4. The wider benefits of the package of interventions

Providing voluntary counselling and testing, antiretroviral drugs and replacement feeding for the reduction of MTCT has benefits that extend way beyond the direct benefits to the health and survival of infants. All pregnant women, mothers and infants will benefit from the expanded provision and improved quality of health care, especially mother-and-child health, antenatal, delivery and postnatal services. And the population as a whole will benefit from general strengthening of the health infrastructure, as well as from the increased understanding and acceptance of the HIV/AIDS epidemic and those affected that develop as a consequence of counselling and testing and measures to combat stigmatization. A decision to introduce the package of interventions can, in the first place, be a force for social change, providing the opportunity and impetus needed to tackle often long-standing problems of inadequate services and oppressive attitudes.

5. Questions of ethics

A guiding principle behind the introduction of any measure to reduce MTCT is that it is the pregnant woman’s absolute right to choose, on the basis of full information, whether or not to take advantage of the intervention. Coercion is not justified under any circumstances, even if it seems to be in the best interests of the woman or her child, and her choice should always be accepted and respected.

Introducing antiretroviral drug programmes for the prevention of mother-to-child transmission in countries where antiretrovirals are not available for the treatment of HIV-positive people more generally has raised sometimes heated debate about the ethical implications. The question is asked: If a mother’s access to antiretroviral drugs is limited to the period of pregnancy and labour, does this amount to treating the mother for the sake of her baby alone?

In fact, the question is based on an erroneous perception, for an antiretroviral drug used for the purpose of preventing MTCT of HIV is not really a treatment, but a “vaccine” for the infant. A useful analogy is the rubella vaccine given to pregnant women to protect their offspring from the ill-effects of maternal infection. Rubella vaccination does not meet with ethical objections, despite the fact
that it, too, could be seen as treating the mother for the sake of the baby.

The fact that antiretrovirals can serve two separate purposes — as vaccine for infants against MTCT of HIV, and as treatment for HIV-infected individuals — is, of course, very significant. But the issue of antiretroviral treatment for infected people must be considered separately from the issue of antiretroviral drugs used for the prevention of MTCT. It requires debate and policy decisions outside the scope of MTCT policy-making. However, it is a point of principle when adopting a strategy of antiretroviral drug use and replacement feeding that HIV-positive pregnant women must be assured of the best possible care available in their countries. In some places, antiretroviral drugs will be available for therapy, too; in others, such treatment will simply not be feasible.

It is important also to note that a short course of antiretrovirals during pregnancy, while increasing the chance that she will give birth to an uninfected baby, does no harm to the health of an HIV-positive woman. The only possible risk is anaemia. But anyone taking antiretrovirals for HIV should be screened for this condition in advance, and treated for it if necessary. Concern is sometimes expressed that the strategy might encourage the development of drug-resistant strains of HIV. However, the risk of resistance developing is minimal with such a short period of drug use.

Another concern is the idea that introducing this strategy for the prevention of MTCT might exacerbate the problem of orphaned children, increasing the burden of care on families and society. It is widely assumed that children born to HIV-infected mothers do not survive long enough to become orphans. But this is a misconception. In the absence of preventive measures for pregnant HIV-infected women, around 65% of the children born to them will escape infection but face orphanhood; of those who are infected (35%), many will likewise survive longer than their mother. With the prevention strategy, the percentage of uninfected children facing orphanhood will rise to almost 90% but in parallel there will be a significant decrease—two- to three-fold—in the number of infected orphans. Thus, with or without the intervention, the great majority of the babies born to HIV-infected mothers will be exposed to the risk of being orphaned. The intervention does not therefore affect in any significant way the need for societies to make provision for their orphaned children. However, from the point of view of planning for care and allocating resources, it is important to recognise that, with measures to reduce MTCT, many fewer orphaned children will be HIV-infected and in need of medical care and support, many of them long-term. It is also worth noting that improving perinatal care and diagnosing HIV infection to permit early access to
care may prolong the life of mothers. HIV-positive women may also live longer if they do not have to cope with sick children. Thus, their children will have the care of their mothers and be spared the misery and vulnerability of orphanhood for longer.

6. Affordability and cost-effectiveness of the strategy

The affordability of antiretroviral drugs and replacement feeding will depend a great deal on the condition of the health infrastructure within a country or district, and how much strengthening or expansion of services is needed before the strategy can be introduced.

Antiretroviral drugs for mothers known to be HIV-positive and replacement feeding for their infants are affordable in most countries, or districts within countries, where there are already well-functioning health care systems. For instance, countries that would be able to negotiate a price for the drugs of US$ 50 per woman, and infant formula at US$ 50 for six months, would need to spend US$ 130 per pregnant woman with HIV, including the costs of counselling and other inputs. In countries with a birth rate of 40 per thousand, and 15% HIV prevalence among pregnant women, and assuming that all women who know their status (estimated to be 10%) accept the intervention, the cost per capita of the specific inputs (i.e. drugs and replacement feeds) would amount to US$ 0.08. The much shorter antiretroviral regimens being tested in current trials (PETRA and nevirapine, in Uganda), are likely to be even cheaper than the currently recommended one-month course of ZDV. This calculation does not take into account savings of medical and other expenditures to care for HIV-positive infants — which, though admittedly very low in some countries, can be substantial in others. In fact, the savings may more than compensate for the cost of the intervention. Nor does it take into account the wider benefit of the intervention to the general population, which, as has been shown, is often considerable.

Voluntary counselling and testing also needs to be taken into consideration. If the cost of this service is to be borne exclusively by MTCT prevention programmes, the cost-effectiveness of the strategy will depend on the HIV prevalence in the area: the lower the prevalence, the more it will cost to identify each HIV-positive pregnant woman. Models show that cost-effectiveness remains fairly stable at HIV prevalence rates of 5–10% and over, but that where the prevalence rate is below this, the cost-effectiveness of the intervention rapidly decreases as the prevalence rate drops. In such situations, targeting HIV screening at women who are pregnant or who plan a pregnancy in specific population groups will lead to greater cost-effectiveness.

\[ \text{Cost per capita} = \text{cost per woman} \times \text{birth rate} \times \text{prevalence rate of HIV} \times \text{proportion of women knowing their status:} \]
\[ \text{US$ 130} \times 0.04 \times 0.15 \times 0.1 = \text{US$ 0.08 per capita.} \]
Where HIV prevalence is high, the cost of a programme of voluntary counselling and testing, antiretroviral drugs and replacement feeding compares well with the cost of interventions for other health problems. It is estimated, for example, that at HIV prevalence rates of more than 5%, this strategy costs around US$ 35 per Disability Adjusted Life Year (DALY), compared with US$ 20-40 per DALY for polio and diphtheria vaccination, and US$ 200-400 per DALY for river blindness prevention.

Definition

Disability-adjusted life-years (DALYs) are the number of years of life gained through a particular intervention, discounted slightly for each successive year gained to take account of the fact that the quality of life diminishes as time passes and the risk of dying of some other disease increases. Thus, the first year of life gained as the consequence of the intervention counts as a full year, whereas each successive year counts for a little less each time. The great strength of DALYs is that they reflect both quality of life and chances of survival, and allow for easy comparison between different kinds of intervention.
7. A decision tree

Clearly, national and local circumstances will have a major influence on decisions regarding the adoption of voluntary counselling and testing, antiretroviral drugs and replacement feeding. The following “decision tree” is proposed as a means of assisting those involved in national and local policy-making to decide on: a) the appropriate levels of provision, and b) the best model of operation of the strategy.

The influencing factors:

- Seroprevalence of HIV in the country or community will determine the costs of inaction and the relative cost-effectiveness of different screening strategies.

- Attitudes towards HIV in the country or community will determine the risk of discrimination against women found to have HIV, the likelihood of infringement of their rights, and the expected acceptability of the intervention.

- The risks associated with replacement feeding will determine whether or not the intervention can be introduced on a large scale immediately or whether pilot projects will be needed initially so that lessons can be learnt about how to make replacement feeding safer.

- The state of the existing health system and Mother-and-Child Health services (including family planning) will determine the expenditure of effort and resources required to strengthen them sufficiently to support the new programme.

- The maturity of the epidemic and level of social support that has developed to cope with it will determine how big a burden will be imposed upon the MTCT programmes by increased demand for health care and counselling.

- The wider benefits to society will have to be taken into account when balancing costs and benefits of the intervention.

- Available financing for MTCT interventions and associated services will be a major consideration in decision-making.

These factors will vary a great deal from one place to another. The following table proposes a decision-making process to assist policymakers who wish to consider adopting an antiretroviral drug and replacement feeding strategy that is suited to their situation, and that reflects the local HIV prevalence, available resources, health system performance and expected risks associated with replacement feeding.
Table 1: Combination of services appropriate to different circumstances

<table>
<thead>
<tr>
<th>Local health system</th>
<th>Local HIV prevalence</th>
<th>&lt;5%</th>
<th>&gt;5%</th>
</tr>
</thead>
<tbody>
<tr>
<td>M inimal resource constraints (e.g. in industrialized countries)</td>
<td></td>
<td>Routine antenatal VCT</td>
<td>Routine antenatal VCT</td>
</tr>
<tr>
<td>Resource constrained</td>
<td></td>
<td>Long ARV/RF</td>
<td>Long ARV/RF</td>
</tr>
<tr>
<td>Local health system meets requirements + Low risk associated with RF and VCT</td>
<td></td>
<td>Known HIV+/Targeted antenatal VCT</td>
<td>Routine antenatal VCT</td>
</tr>
<tr>
<td>Resource constrained</td>
<td></td>
<td>Short ARV/RF</td>
<td>Short ARV/RF</td>
</tr>
<tr>
<td>Local health system does not meet requirements and/or Unknown risks associated with RF</td>
<td></td>
<td>Known HIV+/Targeted antenatal VCT</td>
<td>Pilot introduction of routine antenatal VCT + short ARV/RF (ARV/RF to be offered also to known HIV+ women)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Short ARV/RF</td>
<td>Prepare health system</td>
</tr>
</tbody>
</table>

(Key: VCT = voluntary counselling and testing; ARV = antiretroviral drugs; RF = replacement feeding.)

Definitions

1. **Local health system meets requirements**
   Access to adequate Mother-and-Child Health services including antenatal, delivery, postnatal and family planning services and continuing medical and psychosocial support for mother and child

2. **Short ARV**
   Regimens as used in Thailand and Côte d’Ivoire studies
   300 mg ZDV twice-daily from 36 weeks
   300 mg ZDV 3-hourly during labour
   (Note: alternatives to the Thai regimen will soon be available for short ARV)

3. **Long ARV**
   Other regimens including ACTG 076 and regimens using a combination of antiretroviral drugs and antiretrovirals for the neonate as well as the mother.

4. **Known HIV-positive**
   Women who present for antenatal care having already been tested for HIV outside the maternal health services, and found to be infected.

5. **Targeted antenatal VCT**
   Voluntary counselling and testing offered to pregnant women and their partners in communities (geographical or social networks) where HIV prevalence is particularly high.

6. **Routine antenatal VCT**
   Voluntary counselling and testing offered to all women attending antenatal services and their partners as a matter of course

7. **Pilot introduction of VCT and ARV/RF**
   Introduction of the full strategy in a selected number of sites, and careful monitoring and evaluation of the processes and their impact, with particular attention to replacement feeding

8. **Prepare the health system**
   Where the health system does not meet the requirements for the successful introduction of the strategy, careful preparation is needed for voluntary counselling and testing, mother-and-child health services, and medical and support services for seropositive women and their children.
List of documents on MTCT available through UNAIDS Information Centre or through UNAIDS web site (www.unaids.org):

**General Information:**

UNAIDS Technical Update on HIV Transmission from Mother to Child (October 1998)


Prevention of HIV Transmission from Mother to Child: Strategic options (May 1999)

AIDS 5 years since ICPD: Emerging issues and challenges for women, young people and infants. (1998)

**HIV Counselling and Testing:**

Counselling and voluntary HIV testing for pregnant women in high HIV prevalence countries: Guidance for service providers (May 1999)

The importance of simple/rapid assays in HIV testing. WHO/UNAIDS recommendations (Weekly Epidemiological Record 1998, 73, 321-328)

**Antiretroviral treatments:**

WHO/UNAIDS recommendations on the safe and effective use of short-course ZDV for prevention of mother-to-child transmission of HIV. (Weekly Epidemiological Record 1998, 73, 313-320)

The use of antiretroviral drugs to reduce mother to child transmission of HIV (module 6). Nine guidance modules on antiretroviral treatments. (UNAIDS/98.7)

**HIV and Infant feeding:**

HIV and infant feeding: A review of HIV transmission through breastfeeding (UNAIDS/98.5)

HIV and infant feeding: Guidelines for decision-makers (UNAIDS/98.3)

HIV and infant feeding: A guide for health care managers and supervisors (UNAIDS/98.4)
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Planning, Implementation and Monitoring & Evaluation:


MTCT prevention in Asia:


MTCT prevention in Latin America:


MTCT prevention in Africa:

The Zimbabwe Mother-to-Child HIV Transmission Prevention Project: Situation Analysis.
Notes:
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UNAIDS both mobilizes the responses to the epidemic of its seven cosponsoring organizations and supplements these efforts with special initiatives. Its purpose is to lead and assist an expansion of the international response to HIV on all fronts: medical, public health, social, economic, cultural, political and human rights. UNAIDS works with a broad range of partners - governmental and NGO, business, scientific and lay - to share knowledge, skills and best practice across boundaries.