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# Simplified antiviral prophylaxis with or and without artificial feeding to reduce mother-to-child transmission of HIV in low and middle income countries: modelling positive and negative impact on child survival

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## SUMMARY

***Background:*** *Antiviral prophylaxis is recommended for HIV positive mothers to prevent mother-to-child transmission of HIV. To date UNAIDS and WHO policy has been based on a study in Thailand which showed a reduction in transmission by half with short course AZT (Zidovudine) treatment together with artificial feeding. We modelled the possible positive and negative effects on child deaths in low and middle resource developing country settings of two interventions to reduce mother to child transmission (MTCT) of HIV: antenatal testing, short-course antivirals (zidovudine or nevirapine), firstly with and then without artificial feeding.*

***Material and methods:*** *Estimates are made of child lives likely to be saved by the programme by age ten years, balanced against increases in deaths due to more uninfected mothers choosing to use artificial feeds where these are part of the intervention. Mid-point values for variables affecting the balance of mortality gains and losses are taken from recent published data for low and middle income developing countries and a sensitivity analysis is undertaken.*

***Results:*** *In low income settings the use of antivirals alone would result in an estimated gain in child survival of around 0.36%, representing 360 deaths avoided from a birth cohort of 100,000 by age 10 years. Adding artificial feeding could reduce the gain to 0.03% (30 deaths avoided). In middle income settings the gain from antivirals alone would be 0.26% but as 'spill-over' of artificial feeding to uninfected women was more likely it could result in a net increase of child deaths of up to 1.08% (1,080 additional deaths). A sensitivity analysis emphasised this potential for regimens using artificial feeding if progamme participation was low, and under most circumstances in middle income settings.*

***Conclusions:*** *HIV testing and use of antivirals by infected mothers, if well implemented, will be effective at a population level in reducing MTCT. However the addition of artificial feeding is potentially be a high risk strategy, especially in middle income countries.*

## BACKGROUND

At the end of 1999, more than 33 million people were estimated to be living with HIV/AIDS [1], almost half of whom were women in their reproductive years. Transmission from these women to their children is the predominant source of HIV infection for children, with higher transmission rates reported of up to 30% for African developing countries - where breast feeding is the norm [2]. In 1999 alone, more than 400,000 children were estimated to have been infected globally. Over 90% of these were born in sub-Saharan Africa, though the number of cases in India and Southeast Asia

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are rising rapidly [1]. In countries such as Zimbabwe Under 5 mortality is thought to have more than doubled because of HIV [3]. There has therefore been an urgent hunt for methods to reduce mother-to-child transmission of HIV (MTCT).

In 1994 a course of an antiretroviral drug, Zidovudine (ZDV), given during pregnancy, labour and postnatally to the infant, accompanied by artificial feeds to replace breastfeeding, was found to reduce MTCT by around two-thirds [4]. Given the cost and logistical problems of implementing this programme in developing countries, a short course version was tested in a trial in Thailand. This consisted of a package of antenatal maternal voluntary counselling and testing (VCT), administering ZDV twice daily during the last 4 weeks of pregnancy and during labour, and replacing breastfeeding with free or subsidised artificial feeds, the 'Thailand' regime. This trial found the intervention reduced MTCT by about half [5]. A simplified varient without the artificial feeding and tested in African settings, the 'African regime' still reduced MTCT by nearly 40% [6, 7]. In another African setting, single dose nevirapine (NVP) given once during labour and once in the first 3 days of life to the newborn infants who continued to breast feed has been recently reported to be effective in Uganda, with a rate of transmission of 13% as compared to 25% in short course ZDV at 15 weeks follow-up in Uganda [8].

The Thailand package is now being promoted by UNAIDS, WHO and UNICEF as a successful HIV/AIDS prevention strategy [9]. Some guidance lists considerable minimum requirements for the intervention, including the availability of safe and affordable alternatives to breastfeeding [10], but another gives an optimistic perspective on the potential benefits and indicates that the intervention should be implemented [9].

Using published data, this paper explores the possible consequences on child mortality of implementing these interventions (voluntary testing and anti-virals with and without artificial feeding) in middle and low income developing countries. It also examines the possibility that in a context where most women do not know their HIV status, one of the effects of promoting the Thai package may be a reduction of breastfeeding among both HIV positive and negative women.

## MATERIAL AND METHODS

### Methods

By constructing two hypothetical (middle and low-income) scenarios using published data, we examined what the net gains of the programme are likely to in low and middle income developing countries (where most vertical transmission takes place). [1]

The outcome measure used is the effect on in infant and child deaths, which is appropriate both for reduced MTCT and the decision whether or not to breastfeed. Estimates are made to determine what percentage of a birth cohort the intervention would save from dying by their tenth birthday, that is, a 1% gain would represent prevention of 1,000 deaths before age 10 if in a birth cohort of 100,000 competing cause effects are ignored. Breastfeeding has been associated with other benefits, both for the child, such as decreased morbidity and higher scores on intelligence tests, and for the mother, such as reduced risks of breast and ovarian cancer. However, for this study we focus on the decreased risk of mortality in the child as the main benefit [11].

### Data

*1. Positive impact: reduced child deaths*

The main benefits of the intervention on child mortality will depend on a number of factors, principally:

- degree of HIV seroprevalence among pregnant women
- their willingness to present for VCT and to return for the results
- reliability of HIV testing
- compliance with interventions (all stages)
- initial estimates of MTCT
- reduced transmission as a result of the interventions
- case fatality rate (CFR) for HIV positive infants
- life expectancy of survivors, given that they have an increased risk of being ophaned.

**HIV prevalence amongst pregnant women** in developing countries varies greatly [1]. High risk (usually urban) areas in countries where the programme is likely to be promoted can have a prevalences around 30% and some recent figures include 43% antenatal HIV prevalence in Francistown, Botswa-

na; 32% in Harare, Zimbabwe; and 28% in Kwazulu, South Africa [3]. We have assumed a mid-point of 25% and we test the range 5–40% for prevalence.

**Numbers of HIV-infected women presenting for HIV testing.** Published data, based on experience from UNAIDS and other trials, have indicated that around 60% of eligible women present for VCT [12,13]. The split between HIV-infected and un-infected women is uncertain. If they are genuinely unaware of their status, a 50–50 split is a reasonable assumption. Our estimate of the proportion of HIV-infected women presenting for testing ranges from 20 to 80%.

**Numbers of HIV infected returning for test results** is also an important factor, particularly where there is a delay in results availability. A study in the Cote d'Ivoire found that a substantial proportion of women who had been tested did not return for their results and that this was more likely where the woman were infected [14]. A range of 40–90% is examined.

**Accuracy of tests.** HIV testing is very accurate in ideal conditions, but in the field there is often no quality control such as repeat or confirmatory testing. Labelling and transcription errors will occasionally occur. There will therefore be a certain degree of inaccuracy. We have made the assumption of 95% accuracy.

**Numbers complying with treatment.** This is a complex area. Some mothers may not comply from the start; others may end the treatment early; others again may share their medication or omit some doses even in well managed trials [6]. Much will depend on the organisation of services, their cost, the convenience of the package and the degree of stigmatisation which may be incurred by practices which reveal a woman's status. Currently only about half of women in developing countries deliver with the aid of a skilled attendant [15]. It may therefore be realistic to assume a relatively low level of compliance with the package. We assume 60% compliance and test a range of 40% to 80%.

**Overall MTCT in the absence of treatment** varies with a number of viral, immunological and other factors such as the mode of delivery, length of rupture of membranes and infant feeding practices [16]. Estimates from different regions vary from 14–40%, with the lowest rates occurring in European countries [16]. For low income scenarios, with populations almost entirely breastfeeding, we assume an MTCT of 30%. For middle income countries, we assume that the 80% of women who commence breast-feeding will have rates of MTCT of 30%, while non-breastfeeders (20%) will have 15% [2,16,17]. This allows for HIV infected women who intend to formula feed in developing countries but find difficulties in doing so and end up breastfeeding [18].

In terms of **reduction of transmission,** for the full package (short-course ZDV with artificial feeding) we use the results of the Thailand trial which, with good compliance and total non-breastfeeding, resulted in a 50% reduction in MTCT (It should be noted that the women in this study were not severely immunosuppressed) [7]. We also consider the African trial [5,6] option, of providing short-course ZDV or nevirapine with continued breastfeeding, in which case a 40% reduction in MTCT is anticipated [8].

**Case fatality rate** amongst HIV-infected infants will be higher in low income than in middle income settings. We assume a probability of death of 0.7 by the age of 5 and 0.9 by the age of 10 in low income countries; in middle income countries, the equivalent figures are 0.35 and 0.60 [19].

**Life expectancy of uninfected children with HIV infected parents.** Children who escaped infection through the intervention still face an increased likelihood of death compared to their peers living in families free of HIV, for example because of the adverse effects of orphanhood [20]. Using data from a cohort study in Kampala, Uganda, and excluding the higher mortality attributable to the transmission of HIV to the infants themselves, we reduce the estimate of beneficiaries by between 1 and 3 times the prevailing CMR in those regions [21].

*2. Potential Negative impact: increased child deaths*

There are also a number of potential negative consequences of these interventions, which need to be considered. Probably the most important is a potential reduction in breastfeeding by HIV uninfected mothers (either false positives, or women who have attended VCT and not returned for their results, or amongst the general population of antenatal women who have not attended VCT but have heard about the intervention) [10]. This has been referred to as 'spill-over' of the artificial feeding intervention. The impact of this will depend on:

- the proportion of HIV uninfected women in the population who decide not to breastfeed as a result of the intervention programme
- the increased risk of infant morbidity and mortality through loss of the benefits of breast feeding, such as inadequate nutrition, lack of immunological benefits of breast milk, loss of child-spacing, diarrhoeal disease etc. These in turn will depend on factors such as the availability and affordability of breast-milk substitutes and access to clean water [17]. For example in a randomised trial of breast versus artificial feeding in Nairobi, Kenya, though artificial feeding reduced MTCT of HIV there was no difference in child mortality by two years of age, presumably because of increased mortality in formula fed children [18].

**Proportion of HIV uninfected women who cease breastfeeding as a result of the a package including artificial feeding.** This is currently unknown. Much will depend on how the programme message is presented and disseminated and local cultural factors. Least effect might be expected if the intervention was low-key and all antenatal women present for VCT and return for their results and in settings when breast feeding was already universal. Here even women known to be HIV infected may be reluctant to use artificial feeding [18]. At the other end of the scale, the worst result could be where there was already significant use of artificial feeding; where the programme is well-publicised; where involvement by antenatal women is low; where a large proportion came for testing and counselling but failed to receive their results; and if antenatal HIV testing had a low positive predictive value. Much will also depend on the pre-existing prevalence of breastfeeding and the availability and affordability of artificial feeds [10].

The **child mortality rate** in the country or region will strongly influence the extent to which infants are put at risk by non-breastfeeding. We have used the under five mortality rate estimates for Central and Eastern Africa of 140/1,000 for low income settings and 70/1,000 from Brazil, Thailand, India and South Africa for middle income. These do not take into account the effects of HIV/AIDS and competing risk effects are ignored [3].

In low income settings it is assumed that close to 100% of women will breastfeed their babies in the absence of the intervention [17]. The concern is that HIV negative women may be influenced by promotion of artificial feeding for HIV-infected women, or by seeing other women feeding babies artificially. Set against that is the fear of stigmatisation if artificial feeding becomes a marker for HIV infection in a woman, and the expense which switching to artificial feeds might involve [18]. We test a range of percentages of women switching away from breastfeeding, from 1 to 5% of HIV-negative women.

In middle income countries, artificial feeding is already more common (we assume a base level average prevalence at birth of 20% [17]). The stigma will therefore be less significant, and artificial feeds more affordable, and so a more substantial swing towards artificial feeding might be expected. We assume 20% of women shift away from breastfeeding in this population, if the full Thailand package is implemented, and test a range of 10–30%.

It is also likely that some mothers will breastfeed initially and then stop early or mix feed [17]. However, for simplicity in this analysis we have assumed that mothers either breastfeed optimally or avoid it altogether.

**Increased risk of mortality for non-breastfed infants.** This is in comparison with optimal breast-feeding infants (exclusive breastfeeding up to at least 4 and if possible 6 months, followed by continued breastfeeding supplemented by solids up to 12 months). This is the subject of some continued controversy and a paucity of information. There are few recent published data, especially from African settings, though results of the Kenya breastfeeding verses artificial feeding trial implied an increased risk of dying among HIV uninfected infant receiving formula feeds [18]. Victora et al. [22,23] found an increased risk in Brazil of dying of diarrhoeal disease of 14.2 and of respiratory disease of 3.6 for infants who do not receive any breastmilk. Kuhn and Stein [24] quote a relative risk from all causes of mortality in developing countries of 2.5. A combination of other studies quote a relative risk of non-HIV mortality in the first year of life of formula-fed infants compared with breastfed of 3 or 4 [25].

Most of these studies were carried out in middle income countries with IMRs in the range of 40–50/1,000 births. These probably underestimate the potential dangers in low income countries with higher rates of infectious diseases. Golding et al. recently reviewed breast feeding related mortality, noting many methodological problems in direct studies of deaths and retrospective studies [25],

**Table 1.** Benefits (Reduction in child deaths) from short course ZDV, plus abstinence from breastfeeding. (Thailand regime)

| Midpoint figures for variables | low income | cumulative %[1] | middle income | cumulative % |
|---|---|---|---|---|
| Seroprevalence among pregnant women | 25 | 25 | 25 | 25 |
| Proportion of HIV+ presenting for VCT | 50 | 12.5 | 50 | 12.5 |
| Proportion completing VCT | 65 | 8.1 | 65 | 8.1 |
| Accuracy of testing | 95 | 7.7 | 95 | 7.7 |
| Compliance rate | 60 | 4.6 | 60 | 4.6 |
| MTCT before treatment | 30 | 1.4 | 27 | 1.25 |
| Reduction in transmission | 50 | 0.70 | 50 | 0.63 |
| CFR for infected children | 90 | 0.63 | 60 | 0.38 |
| Adjustment for higher child mortality rate | 72 | 0.45 | 86 | 0.32 |
| Percentage reduction in child deaths | | 0.45% | | 0.32% |

[1] Rounded up to two significant figures

**Table 2.** Benefits from short course ZDV or nevirapine with breastfeeding (midpoint figures for variables). (African regime)

| Midpoint figures for variables | low income | cumulative % | middle income | cumulative % |
|---|---|---|---|---|
| Seroprevalence among pregnant women | 25 | 25 | 25 | 25 |
| Proportion of HIV+ presenting for VCT | 50 | 12.5 | 50 | 12.5 |
| Proportion completing VCT | 65 | 8.1 | 65 | 8.1 |
| Accuracy of testing | 95 | 7.7 | 95 | 7.7 |
| Compliance rate | 60 | 4.6 | 60 | 4.6 |
| MTCT before treatment | 30 | 1.4 | 27 | 1.3 |
| Reduction in transmission | 40 | 0.56 | 40 | 0.50 |
| CFR for infected children | 90 | 0.50 | 60 | 0.30 |
| Adjustment for higher child mortality rate | 72 | 0.36 | 86 | 0.26 |
| Percentage reduction in child deaths | | 0.36% | | 0.26% |

and identified only two reliable prospective population studies. Allowing for social factors a study in Malaysia found a relative risk for post-neonatal infant mortality of non breast feeding of 2 [26]. In urban Guinea-Bissau children 12–36 months of age who were no longer having breast milk had an increased risk (odds ratio) of 2.6, rising to 3.5 (95% CI, 1.4–8.3) [27].

We assume a conservative value of 2 for the relative risk of mortality and test a range from 1 (no change) to 3 for non-breastfed infants in developing countries. This means an attributable risk of between 0 and 2. Any protective effect of breast-feeding beyond the first year of life is ignored.

## RESULTS

The effects of all of the variables analysed are potentially significant – their values will affect the final balance of benefits and disbenefits of the intervention. Moreover, to illustrate all permutations would be impossible here and we therefore initially focus on assumed values at or near the mid-point in the range for uncertain parameters and then undertake a sensitivity analysis across the range. Results are presented for low and medium income settings (or regions).

Data are shown for estimated benefits in terms of the proportion of child deaths reduced by the use of the Thailand (Table 1) and African regimes (Table 2). The potential estimated disbenefits of increased child mortality due to reduced breastfeeding are then shown in Table 3. All three tables contain results for low-income and middle income settings. The net results are presented at the end of Table 3.

These results indicate that the benefits would be greater in low income countries (0.49%) than in middle income countries (0.34%) (Table 1 and 2). This is primarily attributable to higher MTCT before the treatment and higher case fatality rates for HIV-positive children. In contrast, the potential for increased child deaths is higher in middle income countries, despite lower child mortality rates in general, because of the increased vulnerability to a spill-over of non-breastfeeding into the HIV-negative population (Table 3).

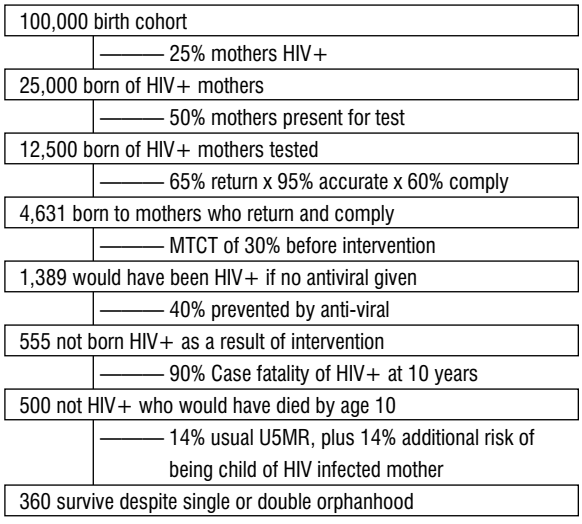
Looked at in terms of net benefits using the Thailand regime, low income settings could realize a small gain in child survival of 0.03%, as against a potential net loss (increased deaths) for middle income settings of –1.08%. Considering the African regime alone although the gains are smaller (0.36% for low income; 0.26% for middle income) (Table 2), they would not be offset by the estimated losses due to non-breastfeeding, so that the net gain would be larger (Table 3).

The expected effects remaining through each stage of intervention for the African regime (from Table 2) on a birth cohort of 100,000 in a low income setting is illustrated in figure 1.

**Table 3.** Disbenefits (increased child deaths) as a result of non-breastfeeding by HIV-negative mothers.

| Midpoint figures | low income | middle income |
|---|---|---|
| % women (HIV-) ceasing breast-feeding as a result of intervention A | 3 | 20 |
| Attributable risk of dying for non-bf children | 1 | 1 |
| Child mortality rate | 14 | 7 |
| % increase in child deaths | 0.42 | 1.4 |
| **Net effects: % reduction in child mortality** | | |
| Short course ZDV plus artificial feeding (Thailand regime) | 0.03% decrease in deaths | -1.08% increase in deaths |
| Short course ZDV alone (African regime) | 0.36% decrease in deaths | 0.26% decrease in deaths |

**Figure 1.**




The numbers of pregnant women needed to test to save one child's life is 35 (12,500 / 360) while the number needed to treat is 13 (4,631/ 360). While these changes on child mortality appear small, they become more significant when applied to populations. For example for a low income setting country such as Zimbabwe with an estimated annual births of 346,000 [3] the net effect of 0.36% would, ignoring competing causes of mortality, avoid approximately 1,250 deaths for the country's annual birth cohort by its tenth year.

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**Table 4.** Sensitivity analysis on net effect results – a negative value indicates increased child mortality overall. (keeping other variables at midpoint values and changing one variable at a time)

| Short course ZDV plus artificial feeding (Thailand regime) | low income | | middle income | |
|---|---|---|---|---|
| Baseline result | 0.03% | | -1.08% | |
| | variable | net result | variable | net result |
| Seroprevalence % | 5.00 | -0.33 | 5.00 | -1.33 |
| | 40 | 0.3 | 40 | -0.88 |
| Proportion presenting for VCT | 20 | -0.24 | 20 | -1.27 |
| | 80 | 0.3 | 80 | -0.88 |
| Proportion completing VCT | 40 | -0.14 | 40 | -1.2 |
| | 90 | 0.2 | 90 | -0.95 |
| Compliance rate | 40 | -0.12 | 40 | -1.18 |
| | 80 | 0.18 | 80 | -0.97 |
| Adjustment for higher CMR | | | | |
| 1 x CMR | 86 | 0.12 | 93 | -1.05 |
| 3 x CMR | 58 | -0.06 | 79 | -1.1 |
| Spillover' of non breastfeeding | 1 | 0.31 | 10 | -0.38 |
| | 5 | -0.25 | 30 | -1.78 |
| Attributable risk of death for non-bf | 0 | 0.45 | 0 | 0.32 |
| child | 2 | -0.39 | 2 | -2.48 |
| **Short course ZDV or nevirapine only (African regime)** | | | | |
| Baseline result | 0.26% | | 0.36% | |
| Seroprevalence % | 5.00 | 0.07 | 5.00 | 0.05 |
| | 40 | 0.58 | 40 | 0.41 |
| Proportion presenting for VCT | 20 | 0.14 | 20 | 0.1 |
| | 80 | 0.58 | 80 | 0.41 |
| Proportion completing VCT | 40 | 0.22 | 40 | 0.16 |
| | 90 | 0.5 | 90 | 0.36 |
| Compliance rate | 40 | 0.24 | 40 | 0.17 |
| | 80 | 0.48 | 80 | 0.34 |
| Adjustment for higher CMR | | | | |
| 1 x CMR | 86 | 0.43 | 93 | 0.28 |
| 3 x CMR | 58 | 0.29 | 79 | 0.24 |

This analysis undertaken for the zidovudine plus artificial feeding (Thailand) regime (Table 4) shows that the net outcome of the interventions are highly sensitive to their success of application. With this model in both low and middle income setting, if all other variables remain unchanged, a failure of women to present for HIV testing, to complete testing or to comply with treatment – as for example happened in the Nairobi trial for artificial feeding [18] – would result in more child deaths than lives saved (Table 4). If mortality rates are higher than we have assumed among HIV negative children born to HIV infected mothers then the positive effects of the intervention will be undone in both the low income and high income setting. Predictably, if the spill-over of the artificial feeding

regime is greater than anticipated then the negative effect is greater, while in middle income settings the only time that the intervention shows a positive effect is if artificial feeding has no negative effect compared to breastfeeding (Table 4). For the African regime (anti-virals plus breastfeeding) heightened compliance will substantially increase the improvement in child survival while the only negative effect comes if the mortality among HIV negative children born to HIV infected mothers is higher than anticipated. Even if that mortality rate is three times that seen in children born to uninfected mothers there will still be a net benefit.

## DISCUSSION

The magnitude of the these different variables will have to be assessed for any given context in which implementation of the package is being considered. HIV prevalence, for example, varies widely, and both numbers presenting and compliance with treatment are likely to be quite context-specific. On the negative side, the relative risk faced by non-breastfed infants will depend on local conditions, and the manner of implementation of the package is likely to affect the 'spill-over' of the message.

However, the above estimates suggest that in some quite plausible circumstances the disbenefits of implementing the Thailand regime (antivirals plus artificial feeding), considered solely in terms of child deaths, could be greater than the benefits. This conclusion is made all the stronger by the fact that costs have been entirely omitted at this stage, as have other considerations, such as operational constraints, drug resistance and other factors mentioned below [9,28].

This conclusion is reinforced if the deaths are discounted. As the increased deaths from non-breastfeeding occur within the first two years, they would have a higher present value in relation to deaths avoided from HIV/AIDS, which occur over 1–12 years [17].

However, it also has to be acknowledged that there are areas of uncertainty relating to some of the variables considered in this model. In particular, there is little evidence about the likely 'spillover' of non-breastfeeding in different contexts, and how this could be minimised. There appears also to be little consensus about the increased risks faced by non-breastfed infants and children, and how these vary in different socio-economic settings. (We have applied the same rate of additional risk to low and middle income settings, but this could be challenged on the basis that the risk is likely to be higher in poorer environments). These are areas which would benefit from further research and are being addressed in pilot sites looking at the feasibility of either treatment regime [29].

Countries which face difficulties financing the Thailand regime may promote alternatives to breastfeeding without being able to provide access to reliable VCT, short course ZDV or subsidised breastmilk substitutes. Abstinence from breastfeeding may be promoted without assistance for families with the considerable financial burden and cost in time and resources that it would bring [30]. Equally there may be a failure to make available family planning services to offset the loss of child spacing due to breastfeeding [27]. These would be likely to worsen outcomes. On the other hand, the option of sustaining initial breastfeeding, but introducing early weaning, might usefully be tested.

These packages also raises other issues, such as:

- whether the intervention will increase the spread of drug resistance, particularly if antiviral drugs escape from the antenatal system and are used in an uncontrolled way (for example, if nevirapine was given to all pregnant women, irrespective of their HIV status, as has been suggested) [8].

- the personal and social costs of VCT, especially if a woman's status HIV becomes public through the advertisement of artificial feeding in predominately breastfeeding populations. Isolation, fear, guilt and loss of self-esteem have been reported in some cases, and abuse from partners, poverty, abandonment and even violence have sometimes followed [32].

- the economic implications for governments and families (see below). Where artificial feeding is advocated, there is also a considerable time loss to the mother or other carer, as well as the cost of providing health care for the child who is likely to suffer more frequently from infectious diseases. This is likely to affect the nutritional status of other family members.

- the ethical difficulties of preventing MTCT while leaving infected mothers untreated.
- the opportunity costs of imposing this intervention on antenatal/MCH services, which are already under strain in many resource poor coun-

tries, and possibly diverting resources from other AIDS prevention work.

- there are also possible positive effects, for example from VCT, such as the opportunity to provide health education on avoiding infection and to reduce transmission to sexual partners. These however depend on effective counselling and behavioural change, which cannot be assumed [10].

The financial costs of the intervention may be considerable. On the government side, these could include providing reliable and confidential voluntary testing and counselling; the antiretroviral drugs and their administration; basic equipment for safe deliveries; counselling and support for infant feeding for the first two years; and (in some cases) contributions towards the cost of breastmilk substitutes for the first six months, and other milk products up to at least one year. Health workers would also have to be trained to teach mothers to prepare feeds as safely as possible. Costs have been estimated at $11 per person for VCT; $50 for short-course ZDV; $100–200 for breastmilk substitutes plus the costs of nutrition counselling and support and food supplements beyond 6 months. This compares with annual per capita health budgets of less than $20 in many low income countries [29]. Equally however use of nevirapine in the African regime represents a more cost-effective package since the cost of the drug alone is only around $4. 00 [8,28].

These requirements may considerably reduce both feasibility and compliance with the Thailand regime and increase the attractiveness of the simpler African regime. The costs of preventing a child being HIV infected are estimated to be $1,109 with the Thailand regime and $298 with voluntary testing and counselling and nevirapine in the African regime, equivalent to $41.8 and $11.3 per disability adjusted life-year (DALY) gained [28]. The attractiveness of the African regime could be increased by use of exclusive breastfeeding which may reduce the risk of HIV transmission [35]. However this also needs piloting since exclusive breastfeeding is in fact uncommon, even in developing countries [17].

## CONCLUSION

This article has considered two options for reducing MTCT of HIV/AIDS in low and middle income settings: a short-course of antiviral drugs, with artificial feeding (the Thailand regime), and antiviral regimes alone (the African regime: either short course zidovudine or using a single dose of nivirapine given to the mother and newborn, with continued breastfeeding). It has tried to model the net benefits of these approaches, taking into account the possibility of a 'spillover' of non-breastfeeding into the HIV-negative population of women under the Thailand regime.

Using reasonable assumptions about the key variables, this study found that the disbenefits of the Thailand regime could outweigh its benefits in some contexts. Benefits increase with the increase in rates of seropositivity, of HIV-positive women presenting for VCT, of completion of VCT, of compliance with treatment, of vertical transmission prior to the intervention, and of case fatality for HIV-infected children. Disbenefits increase as the 'spill-over' of the non-breastfeeding message increases, as the relative risk of dying for non-breastfed children increases, and as child mortality rates themselves increase [34].

Ironically, we found that middle income countries, which are most likely to be able to afford to implement the package, may suffer most from a drop in breastfeeding. This is partly because there may be less stigma attached to non-breastfeeding in contexts where it is less universal, and also because of the increased affordability of artificial feeds. The package may accelerate existing trends away from breastfeeding in those relatively more affluent settings.

Although the African regime with continued breastfeeding is less effective in reducing MTCT, it offers considerable advantages in terms of reduced likelihood of 'spill-over' (which could outweigh the gains in many contexts), reduced programme costs (especially with nevirapine), increased simplicity of implementation, and greater convenience for affected families. Although there is considerable uncertainty about some of the variables in this model, sensitivity analysis reinforces this conclusion. However that does not outweigh the need for careful piloting before widespread implementation [29].

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