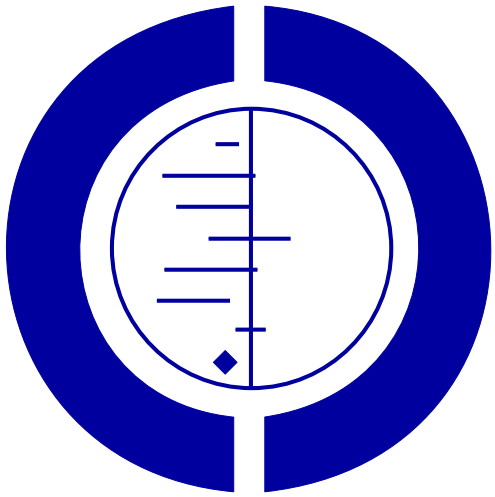
Interventions for reducing the risk of mother-to-child transmission of HIV infection (Review)

Brocklehurst P



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ABSTRACT

Background
At the end of 1998 over 33 million people were infected with the human immunodeficiency virus (HIV) and over one million children had been infected from their mothers.

Objectives
The objective of this review was to assess what interventions may be effective in decreasing the risk of mother-to-child transmission of HIV infection as well as their effect on neonatal and maternal mortality and morbidity.

Search strategy
The Cochrane Pregnancy and Childbirth Group trials register and the Cochrane Controlled Trials Register were searched.

Selection criteria
Randomised trials comparing any intervention aimed at decreasing the risk of mother-to-child transmission of HIV infection compared with placebo or no treatment, or any two or more interventions aimed at decreasing the risk of mother-to-child transmission of HIV infection.

Data collection and analysis
Trial quality assessments and data extraction were undertaken by the reviewer.

Main results
Zidovudine
Four trials comparing zidovudine with placebo involving 1585 participants were included. Compared with placebo, there was a significant reduction in the risk of mother-to-child transmission with any zidovudine (relative risk (RR) 0.54, 95% confidence interval (CI) 0.42-0.69). There is no evidence that 'long course therapy' is superior to 'short course therapy'.

Nevirapine
One trial compared intrapartum and postnatal nevirapine with intrapartum and postnatal zidovudine in 626 women, the majority of whom breast fed their infants. Compared with zidovudine, there was a significant reduction in the risk of mother-to-child transmission of HIV with nevirapine (RR 0.58, 95% CI 0.40-0.83). No trials are available comparing nevirapine with placebo.

Caesarean section
One trial comparing elective caesarean section with anticipation of vaginal delivery involving 436 participants was included. Compared with vaginal delivery, there was a significant reduction in the risk of mother-to-child transmission of HIV infection with caesarean section (RR 0.17, 95% CI 0.05-0.55).

Immunoglobulin
One trial comparing hyperimmune immunoglobulin plus zidovudine with non-specific immunoglobulin plus zidovudine involving 501 participants was included. The addition of hyperimmune immunoglobulin to zidovudine does not appear to have any additional effect on the risk of mother-to-child transmission (RR 0.67, 95% CI 0.29-1.55).

Authors' conclusions
Zidovudine, nevirapine and delivery by elective caesarean section appear to be very effective in decreasing the risk of mother-to-child transmission of HIV infection.

BACKGROUND

At the end of 1998 over 33 million people were infected with the human immunodeficiency virus (HIV) and over one million children had been infected from their mothers (UNAIDS 1998). The majority of these children will have acquired their infection as a result of mother-to-child transmission. The risk of mother-to-child transmission appears to be 15-20% in Europe, 15-30% in USA and 25-35% in Africa (Working Group on MTCT of HIV). Interventions aimed at reducing this risk are a priority if childhood mortality for this group is to be reduced. The greatest burden of disease due to HIV infection in pregnancy is in those parts of the world least able to afford expensive and complex interventions; therefore, simple and affordable interventions are essential if a global impact is to be made on childhood HIV disease.

Antiretroviral therapy
A. Single agent regimens:
Zidovudine
Zidovudine is an antiretroviral drug which has been used to treat HIV infected patients since its approval by the US Food and Drug Administration (FDA) in March 1987. It is a nucleoside analogue and inhibits HIV replication. Although initial studies with zidovudine demonstrated a delayed onset of AIDS in patients with moderately advanced immunosuppression (Fischl 1987), early treatment in patients with a relatively intact immune system demonstrated little benefit (Concorde 1994). Zidovudine was shown to be relatively safe when used in pregnant women with profound immunosuppression but its effect on the risk of mother-to-child transmission was not assessed (Sperling 1992). This review includes the randomized trials to date which have assessed the effect of zidovudine on mother-to-child transmission of HIV.

Nevirapine
Nevirapine is a non-nucleoside reverse-transcriptase inhibitor. It is rapidly absorbed when given orally and has potent antiretroviral activity. In addition it has a very long half life in pregnant women and neonates (Mirochnick 1998, Musoke 1999). These properties make nevirapine ideally suited to using in labour where it may be possible to provide effective antiretroviral activity during labour and delivery with a single oral dose.

Prolonged use of nevirapine as monotherapy leads to rapid development of resistant virus which limits it's usefulness when treating chronic infection.

B. Combination antiretroviral therapy
Recent trials in adults using combination antiretroviral therapy have suggested that combination therapy is associated with a prolonged suppression of viral replication with marked reductions in viral load as well as a delay in the emergence of viral resistance. These effects seem to be translated into clinical benefit (Hammer 1997). As the risk of mother-to-child transmission of HIV infection is associated with high maternal viral load, any intervention which substantially reduces viral load may be associated with benefit. Trials in pregnancy are necessary to balance these potential benefits with the potential risks of exposing large numbers of uninfected fetuses to drugs of unknown toxicity or teratogenicity.

Intrapartum interventions
C. Caesarean section
There is evidence from observational studies to suggest that elective caesarean section may decrease the risk of mother-to-child transmission of HIV infection by 50% (Dunn 1994; HIV Group 1999). There is anecdotal evidence that delivery by elective caesarean section for HIV infected women is being encouraged in many European countries. As it is possible that operative morbidity may be higher in HIV infected women when compared with immunocompetent women, it is essential that caesarean section is demonstrated to be effective in preventing mother-to-child transmission in the context of randomized controlled trials (RCT) before its use becomes more widespread.

D. Vaginal lavage
As a large proportion of mother-to-child transmission is thought to occur at the time of delivery, it has been suggested that a low cost and 'low tech' approach, which could be adopted in many developing countries, would be to disinfect the vagina prior to and/or during labour (Dabis 1995). Several agents have been suggested as potential candidates because of their in-vitro activity against HIV. Rigorous evaluation of this intervention is essential in settings where it might subsequently be used.

E. Artificial rupture of the membranes
Duration of membrane rupture has been identified as an independent risk factor for mother-to-child transmission of HIV infection (Landesman 1996). Avoidance of artificial rupture of the membranes (ARM) may, thus, be an effective and simple way of reducing the risk of transmission in those settings where other interventions are not feasible or too expensive. Avoiding ARM may, however, result in other difficulties such as prolonged labour which may increase the risk of transmission occurring. Only an appropriately sized RCT will be able to determine whether any potential advantage of delay in rupturing the membranes will result in a net benefit to the infant and mother.

Post-partum interventions
F. Avoidance of breast feeding

Breast feeding has been associated, in observational studies, with a doubling of the risk of mother-to-child transmission of HIV infection (Dunn 1992). The World Health Organisation (WHO) has recommended that HIV infected women who have access to safe artificial feeding methods should avoid breast feeding while those living in areas where artificial feeding may be unsafe because of unclean water supplies should breast feed their infants. This advice is based on relatively few studies of poor quality. The net effect of encouraging breast feeding in terms of infant mortality and morbidity in developing countries needs to be evaluated in RCTs.

Other interventions:
G. Immunotherapy
Passive and active immunotherapy have both been suggested as potential interventions to decrease mother-to-child transmission of HIV infection.

H. Vitamin A
Studies in developing countries have suggested that the risk of mother-to-child transmission of HIV infection is correlated with maternal vitamin A deficiency (Semba 1994). It is postulated that vitamin A supplementation will decrease this risk. This hypothesis requires further evaluation before it can be accepted.

OBJECTIVES

To determine whether, and to what extent, antenatal, intrapartum and post-partum interventions aimed at decreasing the risk of mother-to-child transmission of HIV infection achieve a clinically useful decrease in transmission risk, and what effect these interventions have on maternal and infant mortality and morbidity.

As mother-to-child transmission of HIV infection results in a substantial mortality in those infants affected, there is an understandable urgency to develop and evaluate potential interventions rapidly. Consequently, there is unlikely to be much repetition of trials in the search for the most effective interventions. This review will, therefore, contain all such trials within a single review so that the interventions can be viewed together.

CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW

Types of studies

All randomized controlled trials of any intervention aimed at decreasing the risk of mother-to-child transmission of HIV infection compared with placebo or no treatment.

All randomized controlled trials comparing any two or more interventions aimed at decreasing the risk of mother-to-child transmission of HIV infection.

Types of participants

HIV infected pregnant women: any age, any stage of pregnancy, any clinical stage of HIV disease, any background antiretroviral therapy.

Types of intervention

Any intervention whose specified aim is to decrease the risk of mother-to-child transmission of HIV infection.

Types of outcome measures

The outcome measures included will depend to an extent on the nature of the intervention under study. Outcomes will be listed as those relating to neonatal HIV infection status and survival (which will be common to all comparisons) and those which are specific for each intervention.

Common outcome measures:

(1) HIV infection status of the child;
(2) stillbirth;
(3) neonatal mortality;
(4) deaths after neonatal period (at end of initial follow-up to determine HIV status);
(5) late deaths (at longer term follow-up);
(6) maternal death.

Other outcomes specific to the intervention. This list is not intended to be exhaustive but suggests the major outcomes of interest for the child and the mother:

Antiretroviral therapy
A. Single agent regimens (zidovudine, nevirapine):
Child
(7) Premature delivery (if treatment started before labour)
(8) Low birth weight (if treatment started before labour)
(9) Haematological toxicity
(10) Mitochondrial myopathy
(11) Long term effects in survivors eg cancer
Mother
(12) Haematological toxicity

B. Combination antiretroviral therapy:
Child
(7) Premature delivery (if started before labour)
(8) Low birth weight (if started before labour)
(9) Haematological toxicity
(10) Mitochondrial myopathy
(11) Long term effects in survivors eg cancer
Mother
(12) Haematological toxicity

Intrapartum interventions:
C. Caesarean section:
Child
(7) Severe acute morbidity (including respiratory distress syndrome, major intracerebral bleeds, sepsis)

(8) Admission to neonatal unit
Mother
(9) Maternal post-operative complications

D. Vaginal lavage:
Child
(7) Neonatal sepsis (however defined)
Mother
(8) Post-partum fever

E. Artificial rupture of the membranes
Child
(7) Neonatal sepsis
Mother
(8) Caesarean section
(9) Instrumental delivery
(10) Post-partum fever

Post-partum interventions:
F. Avoidance of breast feeding
Child
(7) Episodes of diarrhoea
(8) Episodes of respiratory tract infection
(9) Growth
Mother
(10) Pregnancy interval

Other interventions:
G. Immunotherapy:
Child
(7) Neonatal sepsis (however defined)
Mother
(8) Anaphylaxis

H. Vitamin A supplementation:
Child
(7) Neonatal sepsis (however defined)
Mother
(8) Maternal post-partum fever

SEARCH METHODS FOR IDENTIFICATION OF STUDIES

See: HIV/AIDS Group methods used in reviews.

This review has drawn on the search strategy developed for the Pregnancy and Childbirth Group as a whole. Relevant trials are identified in the Group's Specialised Register of Controlled Trials. See Review Group's details for more information.

In addition the Cochrane Controlled Trials Register is searched with each new edition of the Cochrane Library.

METHODS OF THE REVIEW

All included trials have been selected for eligibility according to the criteria specified in this review. The information necessary for the review was abstracted from the trial reports. If additional information was required from the authors, this was requested.

All trials were assessed for methodological quality using standard Cochrane criteria. Summary ratio measures (relative risks and odds ratios) have been calculated if appropriate using the Cochrane statistical software package, Review Manager (RevMan).

DESCRIPTION OF STUDIES

Studies which have evaluated drug therapy have been classified according to the principal author and the drug regimen used. 'Short course' therapy is loosely defined as any course which is shorter in duration than the first trial of zidovudine by Connor et al published in 1994 which evaluated the use of zidovudine in the antenatal, intrapartum and post-natal (given to the baby) periods. 'Short courses' which have subsequently been evaluated in trials, however, have varied considerably in the timing of the intervention. The convention for 'naming' each study adopted in this review describes whether the drug(s) was given in the antenatal period (AN), intrapartum period (IP) or postnatal period to the mother (PNm) or baby (PNb) or both (PNmb). For example a trial by Smith et al which evaluates antenatal and intrapartum zidovudine will be labelled as 'Smith AN, IP'.

See table of 'Characteristics of Included Studies' for more details of each trial.

METHODOLOGICAL QUALITY

Connor AN, IP, PNb
There was adequate allocation concealment. Placebo was used for comparison with all three preparations of zidovudine; tablet, intravenous infusion and suspension. An intention-to-treat analysis was reported.

Dabis AN, IP, PNm
There appears to be adequate allocation concealment from the trial report. Placebo was used for the antenatal, intrapartum and postnatal treatment. There were exclusions from the analysis (10 women before delivery and six twins) in addition to losses to follow-up (14 children). Therefore not an intention-to-treat analysis.

Guay IP, PNb
There was adequate allocation concealment, however, there was no subsequent blinding as the treatment regimens were different. Although there were very few post-randomisation exclusions from the analysis, this trial does not strictly report an intention-to-treat analysis.

MOD
There was good allocation concealment. Open study. Exclusions from the analysis include 20 mother-infant pairs recruited from South Africa (excluded because the women breastfed) and a further 15 women were withdrawn before delivery. Not an intention-to-treat analysis.

Shaffer AN, IP
There was adequate allocation concealment and placebo was used throughout the antenatal and intrapartum period. An intention-to-treat analysis was reported.

Stiehm AN, IP, PNb
The quality of allocation concealment could not be assessed from the trial report. The intervention was placebo controlled. There were no post-randomisation exclusions therefore an intention-to-treat analysis was presented (although 8% of the women were undelivered at the time of analysis and could not be included).

Wiktor AN, IP
There was adequate allocation concealment. Placebo was used during the antenatal and intrapartum periods. There were no post-randomisation exclusions and therefore an intention-to-treat analysis was reported.

RESULTS

Zidovudine
There is a significant reduction in the risk of mother-to-child transmission with any zidovudine (relative risk (RR) 0.54, 95% confidence interval (CI) 0.42 - 0.69). There is no evidence of significant heterogeneity between the trials and there have been no direct randomized comparisons between short course and long course therapy. It is therefore not possible to state whether long course therapy is superior to short course therapy in reducing the risk to mother-to-infant transmission. In addition it can be seen that the size of risk reduction is similar in populations where the majority of women breast feed (RR 0.62, 95% CI 0.46 - 0.85) and in populations where women do not breast feed (RR 0.50, 95% CI 0.30 - 0.85). The incidence of transmission in both the treatment and placebo groups is higher in breast feeding than non-breast feeding populations but the relative risk reduction in transmission is similar in both populations. Zidovudine also appears to decrease the risk of still birth (RR 0.31, 95% CI 0.11 - 0.90) and deaths after the neonatal period (RR 0.46, 95% CI 0.24 - 0.90). Zidovudine appears to have no effect on the incidence of premature delivery, birth weight or maternal deaths.

Nevirapine
One large well conducted randomised controlled trial of nevirapine demonstrates clear evidence of effectiveness in preventing mother-to-child HIV transmission when compared with an intrapartum and post-partum regimen of zidovudine (RR 0.58, 95% CI 0.40-0.83). Toxicity of both interventions appear to be similar and infrequent.

Caesarean Section
Only one randomized controlled trial has compared elective caesarean section with anticipation of vaginal delivery and this demonstrates a marked decrease in the risk of transmission with elective caesarean section (RR 0.17, 95% CI 0.05 - 0.55). There was no evidence of significant post-partum complications for either group in this trial.

Immunoglobulin
The addition of HIV hyperimmune immunoglobulin to zidovudine appears to offer no advantage when compared with zidovudine and non-specific immunoglobulin. The mother-to-child HIV transmission risk was similar in each group (RR 0.67, 95% CI 0.29 - 1.55).

Combination Therapy (data not presented in meta-analysis)
Only one trial has so far presented preliminary findings of the effect of combination therapy on HIV mother-to-child transmission risk by six weeks of age (PETRA). Follow-up of the completed trial population for early outcomes, including mother-to-child transmission risk is on-going and longer term follow-up is planned. Preliminary findings suggest a decrease in the risk of transmission when a combination of zidovudine and lamivudine (3TC) is given during the antenatal and intrapartum period (RR 0.52, 95% CI 0.35 - 0.76) or during the intrapartum and postpartum period (RR 0.66, 95% CI 0.46 - 0.94). There was no evidence that intrapartum zidovudine and lamivudine (3TC) alone was sufficient to decrease the risk of transmission (RR 1.01, 95% CI 0.74 - 1.38).

DISCUSSION

To date four randomized controlled trials have compared the effect of zidovudine monotherapy with placebo on the risk of mother-to-child transmission of HIV. All demonstrate a marked reduction in the risk of transmission. The confidence intervals for this effect from all four trials overlap so there is no suggestion from this review that any one regimen is superior to any other. In addition there have been no direct randomized comparisons between two or more different zidovudine regimens.

The regimen of zidovudine adopted in the trial by Connor 1994 has been used extensively in the developed world since this first trial was reported. Numerous observational studies have confirmed that the incidence of transmission is low if this regimen is used (Wade 1998). In addition, long term follow-up of the children included in this trial has been undertaken. Unfortunately follow-up has been reported only for babies who were uninfected. This report (Culnane 1999), however, provides reassurance that there are no major adverse effects of zidovudine up to the age of four years.

In developed countries clinical practice is already changing in response to the dramatic improvements in patient's clinical condition when treated with combination therapy. Combination therapy often involves three or more drugs, one of which is usually a protease inhibitor. The advantage of combination therapy appears to be that prolonged inhibition of viral replication is possible because of the delayed emergence of drug resistance. As a consequence, monotherapy is now considered substandard treatment because it is likely to lead to the development of resistant virus which becomes more difficult to treat. Many women are now conceiving on combination therapy and in those women who have their infection diagnosed in pregnancy combination therapy is often commenced for maternal indications.

No protease inhibitors have been tested in randomised trials in pregnancy to assess the effect on mother-to-child transmission. The only randomised trial of combination therapy in pregnancy used a fixed combination of two agents (zidovudine and lamivudine). The PETRA trial appears to demonstrate that a fixed combination of zidovudine and lamivudine (3TC) given from 36 weeks until delivery or from the start of labour until one week after delivery to the mother and child was effective at reducing transmission risk. This combination was not, however, compared with zidovudine alone and therefore the addition of lamivudine (3TC) to zidovudine in further decreasing transmission risk cannot reliably be assessed.

A non-randomized study in France using a combination of long course zidovudine plus lamivudine (3TC) from 34 weeks gestation until delivery has been reported in abstract (Blanche 1999). The transmission risk in this group of 200 women was compared with a historical cohort of 899 women receiving zidovudine alone. There was evidence that the transmission risk was decreased with combination therapy (2.6% compared with 6.5%). There may, however, be other explanations for this apparent decrease in transmission and until the relevant randomized trials are undertaken the relative effectiveness of combination therapy on the risk of transmission remains unknown. In addition, two uninfected babies who had received zidovudine and lamivudine (3TC) in-utero died from a neurological disorder due to a mitochondrial myopathy. This uncommon event occurring in two babies suggests that nucleoside analogue drugs may be responsible for these deaths. A further report from the French group (Blanche 1999), has looked for evidence of mitochondrial toxicity in other study populations and found evidence of further cases, some of whom were exposed to zidovudine alone.

Observational studies had suggested a halving in the risk of HIV transmission associated with elective caesarean section. This has now been confirmed in a randomized controlled trial in which approximately 65% of the women recruited also received zidovudine. The size of the decrease in risk associated with elective caesarean section appeared similar in women receiving and not receiving zidovudine. In addition no serious postpartum complications occurred. Anecdotal evidence suggests that in women receiving combination antiretroviral therapy and who are also delivered by elective caesarean section the risk of mother-to-child transmission of HIV infection is negligible.

In developing countries the situation is very different. Combination antiretroviral therapy is expensive, and cheaper and simpler interventions are needed which can be used in the existing health services. Short course monotherapy with zidovudine has been shown to be effective, however, nevirapine appears to be particularly suitable for these countries. When nevirapine is used in the context of a population where breastfeeding is almost universal, it appears to result in a substantial reduction in the risk of mother-to-child transmission of HIV when compared with an intrapartum and postpartum regimen of zidovudine. This regimen of zidovudine has not been used in any previous trials and it's effectiveness against other regimens is unknown. It is possible the zidovudine regimen used has little effect on the risk of mother-to-child transmission and is therefore little better than placebo. This is supported by the finding of a 26% risk of transmission in the zidovudine arm of the trial which is similar in size to the placebo arms of other trials in breastfeeding populations. However, the absolute effectiveness of nevirapine cannot be extrapolated from this trial, and may be greater than the relative effectiveness compared with the ziduvodine regimen used. The economic evaluation which accompanied the trial report (Marseille 1999) demonstrates that nevirapine is substantially cheaper than short course zidovudine and could lead to affordable and substantial health gains in resource poor settings.

The role of caesarean section in middle income and resource poor settings is still uncertain. In developed countries the morbidity associated with elective caesarean section is very low and women's subsequent pregnancies will be cared for by adequately trained health professionals. As a consequence, the use of elective caesarean section has become widespread. This situation is not the same in many other countries. In areas of high HIV seroprevelance, such as South Africa, the use of elective caesarean section for HIV infection is increasing the number of caesarean sections performed several fold. In the presence of effective short course zidovudine or nevirapine therapy, the additional benefit of delivery by elective caesarean section may be small and offset by an increase in the risk of the procedure for the mother.

AUTHORS' CONCLUSIONS

Implications for practice

How the existing randomized trials evidence is used to inform practice will depend to a great extent on the setting in which HIV infected women are cared for. In developed countries practice has already moved on from the current evidence and combination antiretroviral therapy appears to be the standard of care. In addition many centres appear to be offering delivery by elective caesarean

section in the hope that this will reduce the risk of transmission further.

In developing countries the use of short course zidovudine and single-dose nevirapine appear to be effective therapies. The challenge now will be to institute this therapy in practice. The widespread use of elective caesarean section is unlikely in those areas of the world where the burden of disease is greatest but may be possible in those countries with adequate resources.

Implications for research

In developed countries the scientific communities must decide how to rigorously evaluate the use of combination antiretroviral therapy in pregnancy. In particular, attempts should be made to limit the exposure of the fetus in utero, either in duration or dose, to drugs of unknown teratogenicity. Ideally all children born to women receiving combination antiretroviral therapy in pregnancy should be followed up so that evidence of long term toxicity, if it occurs, can be recognised early.

In developing countries ongoing randomized trials evaluating the use of vaginal cleansing, vitamin and nutritional supplementation and breast versus artificial feeding will inform future practice. If alternatives to antiretroviral therapy are shown to be effective then there will be an urgent need for trials to compare these interventions with antiretroviral therapy. If alternative interventions are as effective as zidovudine or nevirapine it will then become important to demonstrate that these can work in practice and that the results from trials can be translated into real health benefits. The effectiveness of elective caesarean section in women receiving optimal antiretroviral therapy needs further evaluation.

In addition the potential value of nevirapine used for longer durations in breastfeeding populations should be considered as it may further reduce the risk of mother-to-child transmission, particularly if combined with early weaning. This would have to be balanced against the potential for harm with the development of viral resistance.

In populations where the majority of women deliver at home with traditional birth attendants, ensuring that intrapartum interventions are effectively delivered will be challenging. In addition, in order to introduce an intervention which is aimed specifically at HIV infected women, as opposed to interventions (such as vaginal cleansing) which can be used for all pregnant women, it will be necessary to identify those women who are HIV infected before the intervention can be given. If this cannot be achieved, for whatever reason, then even the most effective intervention will not reduce the burden of disease in these populations.

POTENTIAL CONFLICT OF INTEREST

None known.

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Internal sources of support

- No sources of support supplied

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** Indicates the major publication for the study*

TABLES

Characteristics of included studies

Study	Connor AN, IP, PNb
Methods	Central randomization. Double blind.
Participants	477 women enrolled. Confirmed HIV infection. Estimated gestational age over 14 weeks and less than 34 weeks. No previous antiretroviral therapy. Excluded: CD4 count <200 cells/mm3. Setting: 60 centre trial in USA and France. Reported 1994.
Interventions	Zidovudine from time of presentation in pregnancy if >14 weeks and <34 weeks, 100mg orally x 5 per day until labour. In labour: intravenous zidovudine 2mg/kg loading dose over one hour followed by 1 mg/kg/h until delivery. Zidovudine syrup 2mg/kg six hourly to infant for six weeks

	or matching placebo throughout pregnancy, labour and to infant.
Outcomes	HIV infection in the infant - analysis is based on Kaplen-Meier survival curves for time to positive viral culture with estimates taken at 18 months to produce differences in effect. This was used because full follow-up had not been acheived at the time of the analysis and some babies had only had one viral culture taken. Maternal haematological toxicity. Neonatal haematological toxicity.
Notes	NO INFANT BREASTFED Trial stopped at first interim analysis. 32 women (6.7%) lost to follow-up.
Allocation concealment	A

Study	**Dabis AN, IP, PNm**
Methods	Sequentially numbered sealed treatment packs prepared by central pharmacy - random order in blocks of 10 stratified by centre. Double blind.
Participants	431 women enrolled. Confirmed HIV-1 infection. Less than 36 weeks gestational age. Excluded: sickle cell markers, anaemia, low absolute neutropil count, high serum liver enzymes. Setting: Cote d'Ivoire and Burkina Faso. Reported 1999.
Interventions	Oral zidovudine - twice daily from 36-38 weeks followed by a single loading dose at onset of labour and then a 7 day course of twice daily postpartum treatment for mother. For early stage of trial dose was 500mg per day and then changed to 600mg per day (available drug fomulation changed during course of trial). No treatment to newborn.
Outcomes	HIV infection in infant Infant mortality Preterm delivery Birthweight Intrauterine growth restriction Neonatal toxicity Maternal toxicity Compliance.
Notes	>75% INFANTS BREASTFED at six months Exclusions from analysis - 10 women before delivery (5 in each arm). - 6 twins (2 ZDV, 4 placebo). 14 lost to follow-up (8 ZDV, 6 placebo).
Allocation concealment	A

Study	**Guay IP, PNb**
Methods	Randomised prepacked sequentially numbered drug packs. Not blind once packs opened.
Participants	626 women enrolled. Confirmed HIV-1 infection. Estimated gestational age over 32 weeks.

	Excluded: under 18 years, current antiretroviral or immunotherapy, uncontrolled hypertension, anaemia, high blood creatinine or alanine transaminase concentration, chronic alcohol or drug use, benzodiazepine use, anticoagulant therapy, magnesium sulphate within 2 weeks. Setting: Uganda. Reported 1999.
Interventions	Oral nevirapine 200mg single dose at onset of labour + single dose nevirapine suspension 2mg/kg to neonate at 72 hours or hospital discharge (whichever was soonest) or oral zidovudine 600mg at onset of labour plus 200mg 3 hourly during labour + zidovudine syrup, 4mg/kg to neonate twice daily for 7 days after birth.
Outcomes	HIV infection in infant Neonatal mortality Neonatal toxicity Maternal toxicity
Notes	98.8% INFANTS BREASTFED Excluded from analysis - 13 second and third borns (9 nevirapine, 4 ZDV). 10 lost to follow-up (4 nevirapine, 6 ZDV).
Allocation concealment	A

Study	**MOD**
Methods	Central telephone randomization.
Participants	436 women enrolled. Confirmed HIV-1 infection. Gestational age between 34 and 36 weeks. Excluded: clinical indication for either caesarean section or vaginal delivery. Setting: 19 centres in Europe. Reported 1999.
Interventions	Elective caesarean section at 38 weeks or vaginal delivery 63% of women received zidovudine during pregnancy.
Outcomes	HIV infection in the infant Actual mode of delivery Maternal postpartum complications.
Notes	NO BREASTFEEDING 20 mother-infant pairs randomized in South Africa excluded because of breastfeeding. Initial centres in Italy randomized 2 vaginal deliveries to 1 caesarean section and later changed to 1:1 randomization. 15 women withdrawn from trial before delivery (5 CS, 10 V Del). 13 delivery information not available (8 CS, 5 V Del). 28 babies lost to follow-up (12 CS, 16 V Del). 12 babies infection status intermediate (7 CS, 5 V Del). Of randomized women only 85% of each group included in analysis.
Allocation concealment	A

Characteristics of included studies (*Continued*)

Study	**PETRA**
Methods	'Randomized'
Participants	1792 HIV infected pregnant women in Africa. Breast feeding population. Preliminary report 1999.
Interventions	Arm A. Zidovudine 300mg bd plus lamivudine 150mg bd from 36 weeks, during labour and for 1 week to mother and child (zidovudine 4mg/kg bd plus lamivudine 2mg/kg bd). Arm B. Zidovudine 300mg bd plus lamivudine 150mg bd during labour and for 1 week to mother and child (zidovudine 4mg/kg bd plus lamivudine 2mg/kg bd). Arm C. Zidovudine 300mg bd plus lamivudine 150mg bd during labour. Arm D. Placebo.
Outcomes	HIV infection in child Mortality in mother and child.
Notes	Preliminary findings presented in abstract only.
Allocation concealment	B

Study	**Shaffer AN, IP**
Methods	Randomization list prepared centrally and woman assigned by sequential number to blinded drug packs. Double blind.
Participants	397 women enrolled. Confirmed HIV-1 infection. 34 weeks gestation or less. Excluded: history of intolerance to zidovudine, fetal abnormality, use of antiretroviral therapy during current pregnancy, amniocentesis during current pregnancy, anaemia, low absolute neutrophil count, low platelet count, high serum liver enzymes, high creatinine or high urinary protein levels. Setting: 2 hospitals in Thailand. Reported 1999.
Interventions	Oral zidovudine 300mg twice daily from 36 weeks until onset of labour and then 300mg every 3 hours until delivery or matching placebo.
Outcomes	HIV infection in infant Birthweight Maternal CD4 count.
Notes	NO INFANT BREASTFED <1% loss to follow-up.
Allocation concealment	A

Study	**Stiehm AN, IP, PNb**
Methods	Not specified.
Participants	501 women enrolled. Confirmed HIV infection, current zidovudine use, CD4 count 500 or less, gestational age 20 - 30 weeks. Excluded: pre-existing fetal anomalis, chorionic villous sampling or percutaneous umbilical blood sampling during current pregnancy, illness associated with extensive protein loss, indications for IVIG therapy, receipt of HIV vaccine or passive immunotherapy during current pregnancy, severe pre-eclampsia, anaemia, high serum creatinine, high urinary protein.

Characteristics of included studies (*Continued*)

	Setting: 53 centres in USA and Puerto Rico. Reported 1999.
Interventions	HIVIG 200mg/kg IV infusion every 4 weeks beginning between 20 - 30 weeks gestation and during delivery plus 200mg/kg IV infusion to baby within 12 hours of birth or standard polyvalent HIV antibody-negative IVIG to mother and baby as above All women and babies recieved standard course of zidovudine.
Outcomes	HIV infection in infant Premature delivery Birthweight Neonatal deaths Side effects.
Notes	NO INFANT BREASTFED <1% loss to follow-up. 8% still pregnant at time of analysis.
Allocation concealment	A

Study	**Wiktor AN, IP**
Methods	Random list prepared before trial commenced and allocation carried out by study pharmacist. Double blind.
Participants	280 women enrolled. Confirmed HIV-1 infection. Less than 36 weeks gestation. Excluded: HIV-2 positivity, previous antiretroviral therapy, medical or obstetric complications not related to HIV-1 infection, anaemia, low absolute neutrophil count, low platelets, abnormal serum liver enzymes, high serum creatinine. Setting: 1 hospital Cote d'Ivoire. Reported 1999.
Interventions	Oral zidovudine 300mg twice daily from 36 weeks gestation until onset of labour, then 300mg every 3 hours until delivery or matching placebo.
Outcomes	HIV infection in the infant Birthweight Stillbirth Death after birth Congenital anomalies Obstetric complications Compliance.
Notes	>95% BREASTFED 4% of each group lost to follow up or not delivered.
Allocation concealment	A

bd = twice daily; HIV = human immunodeficiency virus; HIVIG = hyperimmune anti-human immunodeficiency virus immunoglobulin; IV = intravenous; IVIG = intravenous immunoglobulin;
mg = milligram; CS = caesarean section; V Del = vaginal delivery; ZDV = zidovudine

Characteristics of included studies (*Continued*)

Characteristics of excluded studies

Biggar 1996	Not randomized - women enrolled in blocks of time - first two months: no intervention, next three months: intervention, final month: no intervention. No account taken of clustering of women within blocks. 41% loss to follow-up for determing HIV status of children.
Coutsoudis 1997	Letter of preliminary trial analysis giving data on effect of vitamin A supplementation on maternal HIV-1 viral load only.
Fawzi 1998	No pre-specified outcomes included in report. This is a preliminary report and provides no data about the mothers or children after birth. The trial suggested that multivitamins, given to HIV infected women during pregnancy in Tanzania, did decrease the risk of fetal death (miscarriage and stillbirth). Vitamin A alone did not appear to have any effect. Follow-up continues to ascertain the HIV infection status of surviving children.

HIV = human immunodeficiency virus

Characteristics of ongoing studies

Study	**Lallemant**
Trial name or title	The North Thailand perinatal HIV prevention trial (NT-PHPT) study update.
Participants	
Interventions	
Outcomes	
Starting date	
Contact information	
Notes	

ANALYSES

Comparison 01. Any zidovudine vs placebo/no treatment

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 HIV infection status in the child	4	1250	Relative Risk (Fixed) 95% CI	0.54 [0.42, 0.69]
02 Stillbirth	3	1096	Relative Risk (Fixed) 95% CI	0.31 [0.11, 0.90]
03 Neonatal mortality	3	1204	Relative Risk (Fixed) 95% CI	1.62 [0.61, 4.25]
04 Deaths after neonatal period	2	809	Relative Risk (Fixed) 95% CI	0.46 [0.24, 0.90]
05 Late deaths	1	400	Relative Risk (Fixed) 95% CI	0.41 [0.19, 0.87]
06 Maternal deaths	2	816	Relative Risk (Fixed) 95% CI	0.68 [0.12, 4.05]
07 Premature delivery	2	757	Relative Risk (Fixed) 95% CI	0.84 [0.49, 1.43]
08 Low birth weight	3	1063	Relative Risk (Fixed) 95% CI	0.93 [0.69, 1.24]
09 Neonatal haematological toxicity	4	1483	Relative Risk (Fixed) 95% CI	1.29 [0.91, 1.83]
10 Maternal haematological toxicity	2	884	Relative Risk (Fixed) 95% CI	1.17 [0.70, 1.96]

Comparison 02. Short course zidovudine versus placebo/no treatment (all trials)

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 HIV infection status in the child	3	1002	Relative Risk (Fixed) 95% CI	0.60 [0.46, 0.79]
02 Stillbirth	2	687	Relative Risk (Fixed) 95% CI	0.22 [0.06, 0.75]
03 Neonatal mortality	2	795	Relative Risk (Fixed) 95% CI	2.12 [0.70, 6.41]
04 Deaths after neonatal period	1	400	Relative Risk (Fixed) 95% CI	0.41 [0.19, 0.87]
05 Late deaths	1	400	Relative Risk (Fixed) 95% CI	0.41 [0.19, 0.87]
06 Maternal deaths	1	407	Relative Risk (Fixed) 95% CI	0.68 [0.12, 4.05]
07 Premature delivery	1	342	Relative Risk (Fixed) 95% CI	0.48 [0.20, 1.16]
08 Low birth weight	2	648	Relative Risk (Fixed) 95% CI	1.06 [0.72, 1.57]
09 Neonatal haematological toxicity	3	1068	Relative Risk (Fixed) 95% CI	0.77 [0.44, 1.35]
10 Maternal haematological toxicity	1	407	Relative Risk (Fixed) 95% CI	1.41 [0.58, 3.43]

Comparison 04. Short course zidovudine versus placebo/no treatment (breast feeding)

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 HIV infection status in the child	2	619	Relative Risk (Fixed) 95% CI	0.64 [0.47, 0.88]
02 Stillbirth	2	687	Relative Risk (Fixed) 95% CI	0.22 [0.06, 0.75]
03 Neonatal mortality	1	400	Relative Risk (Fixed) 95% CI	2.00 [0.61, 6.54]
04 Deaths after neonatal period	1	400	Relative Risk (Fixed) 95% CI	0.41 [0.19, 0.87]
05 Late deaths	1	400	Relative Risk (Fixed) 95% CI	0.41 [0.19, 0.87]
06 Maternal deaths	1	407	Relative Risk (Fixed) 95% CI	0.68 [0.12, 4.05]
07 Premature delivery	1	342	Relative Risk (Fixed) 95% CI	0.48 [0.20, 1.16]
08 Low birth weight	2	648	Relative Risk (Fixed) 95% CI	1.06 [0.72, 1.57]
09 Neonatal haematological toxicity	2	673	Relative Risk (Fixed) 95% CI	0.75 [0.41, 1.35]
10 Maternal haematological toxicity	1	407	Relative Risk (Fixed) 95% CI	1.41 [0.58, 3.43]

Comparison 05. Caesarean section versus vaginal delivery

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 HIV infection status in the child	1	370	Relative Risk (Fixed) 95% CI	0.17 [0.05, 0.55]
02 Stillbirth	0	0	Relative Risk (Fixed) 95% CI	Not estimable
03 Neonatal mortality	1	370	Relative Risk (Fixed) 95% CI	Not estimable
04 Deaths after neonatal period	1	370	Relative Risk (Fixed) 95% CI	3.53 [0.37, 33.62]
05 Late deaths	0	0	Relative Risk (Fixed) 95% CI	Not estimable
06 Maternal deaths	1	370	Relative Risk (Fixed) 95% CI	2.35 [0.22, 25.72]
07 Maternal postpartum complications	1	410	Relative Risk (Fixed) 95% CI	Not estimable

Comparison 06. HIVIG plus zidovudine versus IVIG plus zidovudine

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 HIV infection status in the child	1	454	Relative Risk (Fixed) 95% CI	0.67 [0.29, 1.55]
02 Stillbirth	1	459	Relative Risk (Fixed) 95% CI	0.33 [0.01, 8.03]
03 Neonatal mortality	1	506	Relative Risk (Fixed) 95% CI	1.91 [0.17, 20.90]
04 Deaths after neonatal period	1	506	Relative Risk (Fixed) 95% CI	0.48 [0.04, 5.23]
05 Late deaths	0	0	Relative Risk (Fixed) 95% CI	Not estimable
06 Maternal deaths	1	459	Relative Risk (Fixed) 95% CI	1.97 [0.37, 10.67]
07 Premature delivery	1	458	Relative Risk (Fixed) 95% CI	1.14 [0.77, 1.69]
08 Low birth weight	1	458	Relative Risk (Fixed) 95% CI	1.14 [0.73, 1.76]
09 Neonatal haematological toxicity	1	506	Relative Risk (Fixed) 95% CI	1.15 [0.65, 2.07]

Comparison 07. Nevirapine versus zidovudine

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 HIV infection status in the child	1	496	Relative Risk (Fixed) 95% CI	0.58 [0.40, 0.83]
02 Neonatal mortality	1	559	Relative Risk (Fixed) 95% CI	0.72 [0.39, 1.34]
03 Deaths after neonatal period	0	0	Relative Risk (Fixed) 95% CI	Not estimable
04 Late deaths	0	0	Relative Risk (Fixed) 95% CI	Not estimable
05 Maternal deaths	1	618	Relative Risk (Fixed) 95% CI	0.33 [0.01, 8.10]
06 Neonatal haematological toxicity	1	572	Relative Risk (Fixed) 95% CI	1.44 [0.63, 3.33]
07 Maternal haematological toxicity	1	626	Relative Risk (Fixed) 95% CI	1.24 [0.81, 1.91]

INDEX TERMS

Medical Subject Headings (MeSH)

Anti-HIV Agents [therapeutic use]; Cesarean Section; Disease Transmission, Vertical [*prevention & control]; HIV Infections [*prevention & control; *transmission]; Immunoglobulins, Intravenous [therapeutic use]; Infant, Newborn; *Pregnancy Complications, Infectious; Vitamin A [therapeutic use]

MeSH check words

Female; Humans; Pregnancy

COVER SHEET

Title	Interventions for reducing the risk of mother-to-child transmission of HIV infection
Authors	Brocklehurst P
Contribution of author(s)	Information not supplied by author
Issue protocol first published	/
Review first published	1995/2
Date of most recent amendment	23 February 2002

Date of most recent SUBSTANTIVE amendment	28 November 2001
What's New	This review will be replaced by a series of reviews addressing the issue of mother-to-child HIV transmission. Once all reviews are completed this review will be withdrawn from the Cochrane Library. The reviews include: - antiretroviral interventions (Brocklehurst P. complete review Cochrane Library 2001, Issue 4). - Cesarean sections (Read J., in progress) - Breastfeeding (Dabis, in progress) - Vaginal lavage (Wiysonge C., in progress) Vitamin A (Wiysonge, C, in progress)
Date new studies sought but none found	Information not supplied by author
Date new studies found but not yet included/excluded	Information not supplied by author
Date new studies found and included/excluded	Information not supplied by author
Date authors' conclusions section amended	Information not supplied by author
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DOI	10.1002/14651858.CD000102
Cochrane Library number	CD000102
Editorial group	Cochrane HIV/AIDS Group
Editorial group code	HM-HIV

GRAPHS AND OTHER TABLES

Analysis 01.01. Comparison 01 Any zidovudine vs placebo/no treatment, Outcome 01 HIV infection status in the child

Review: Interventions for reducing the risk of mother-to-child transmission of HIV infection

Comparison: 01 Any zidovudine vs placebo/no treatment

Outcome: 01 HIV infection status in the child

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Connor AN, IP, PNb	9/121	31/127		20.5	0.30 [0.15, 0.61]
Dabis AN, IP, PNm	33/192	52/197		34.7	0.65 [0.44, 0.96]
Shaffer AN, IP	18/188	37/195		24.6	0.50 [0.30, 0.85]
Wiktor AN, IP	19/115	30/115		20.3	0.63 [0.38, 1.06]
Total (95% CI)	616	634		100.0	0.54 [0.42, 0.69]

Total events: 79 (Treatment), 150 (Control)

Test for heterogeneity chi-square=3.90 df=3 p=0.27 I^2 =23.0%

Test for overall effect z=4.85 p<0.00001

Analysis 01.02. Comparison 01 Any zidovudine vs placebo/no treatment, Outcome 02 Stillbirth

Review: Interventions for reducing the risk of mother-to-child transmission of HIV infection

Comparison: 01 Any zidovudine vs placebo/no treatment

Outcome: 02 Stillbirth

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Connor AN, IP, PNb	1/205	0/204		3.5	2.99 [0.12, 72.86]
Dabis AN, IP, PNm	1/203	7/211		47.7	0.15 [0.02, 1.20]
Wiktor AN, IP	2/137	7/136		48.8	0.28 [0.06, 1.34]
Total (95% CI)	545	551		100.0	0.31 [0.11, 0.90]

Total events: 4 (Treatment), 14 (Control)

Test for heterogeneity chi-square=2.42 df=2 p=0.30 I^2 =17.4%

Test for overall effect z=2.16 p=0.03

Analysis 01.03. Comparison 01 Any zidovudine vs placebo/no treatment, Outcome 03 Neonatal mortality

Review: Interventions for reducing the risk of mother-to-child transmission of HIV infection

Comparison: 01 Any zidovudine vs placebo/no treatment

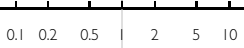
Outcome: 03 Neonatal mortality

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Connor AN, IP, PNb	1/205	2/204		30.8	0.50 [0.05, 5.44]
Dabis AN, IP, PNm	8/200	4/200		61.5	2.00 [0.61, 6.54]
Shaffer AN, IP	1/196	0/199		7.6	3.05 [0.12, 74.31]
Total (95% CI)	601	603		100.0	1.62 [0.61, 4.25]

Total events: 10 (Treatment), 6 (Control)

Test for heterogeneity chi-square=1.21 df=2 p=0.55 I^2 =0.0%

Test for overall effect z=0.97 p=0.3



Analysis 01.04. Comparison 01 Any zidovudine vs placebo/no treatment, Outcome 04 Deaths after neonatal period

Review: Interventions for reducing the risk of mother-to-child transmission of HIV infection

Comparison: 01 Any zidovudine vs placebo/no treatment

Outcome: 04 Deaths after neonatal period

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Connor AN, IP, PNb	3/205	4/204		15.4	0.75 [0.17, 3.29]
Dabis AN, IP, PNm	9/200	22/200		84.6	0.41 [0.19, 0.87]
Total (95% CI)	405	404		100.0	0.46 [0.24, 0.90]

Total events: 12 (Treatment), 26 (Control)

Test for heterogeneity chi-square=0.50 df=1 p=0.48 I^2 =0.0%

Test for overall effect z=2.28 p=0.02

Analysis 01.05. Comparison 01 Any zidovudine vs placebo/no treatment, Outcome 05 Late deaths

Review: Interventions for reducing the risk of mother-to-child transmission of HIV infection

Comparison: 01 Any zidovudine vs placebo/no treatment

Outcome: 05 Late deaths

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Dabis AN, IP, PNm	9/200	22/200		100.0	0.41 [0.19, 0.87]
Total (95% CI)	200	200		100.0	0.41 [0.19, 0.87]
Total events: 9 (Treatment), 22 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=2.33 p=0.02					

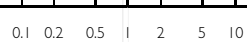
Analysis 01.06. Comparison 01 Any zidovudine vs placebo/no treatment, Outcome 06 Maternal deaths

Review: Interventions for reducing the risk of mother-to-child transmission of HIV infection

Comparison: 01 Any zidovudine vs placebo/no treatment

Outcome: 06 Maternal deaths

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
× Connor AN, IP, PNb	0/205	0/204		0.0	Not estimable
Dabis AN, IP, PNm	2/201	3/206		100.0	0.68 [0.12, 4.05]
Total (95% CI)	406	410		100.0	0.68 [0.12, 4.05]
Total events: 2 (Treatment), 3 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.42 p=0.7					

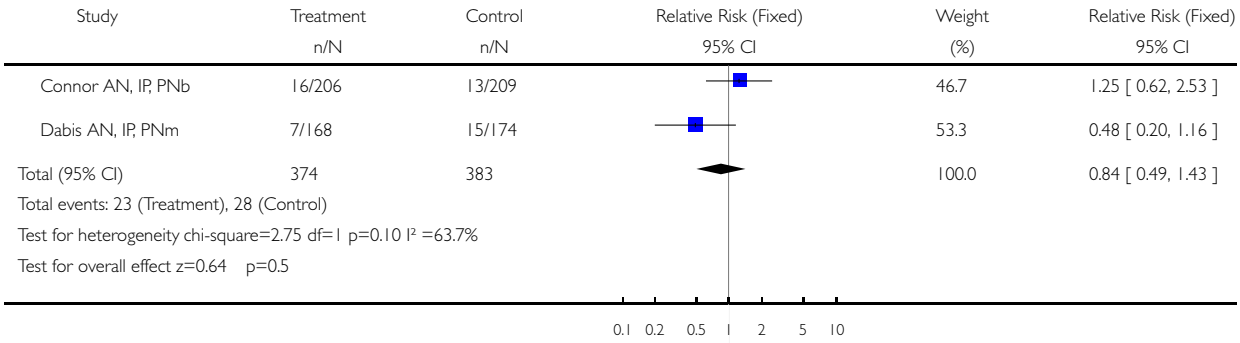


Analysis 01.07. Comparison 01 Any zidovudine vs placebo/no treatment, Outcome 07 Premature delivery

Review: Interventions for reducing the risk of mother-to-child transmission of HIV infection

Comparison: 01 Any zidovudine vs placebo/no treatment

Outcome: 07 Premature delivery

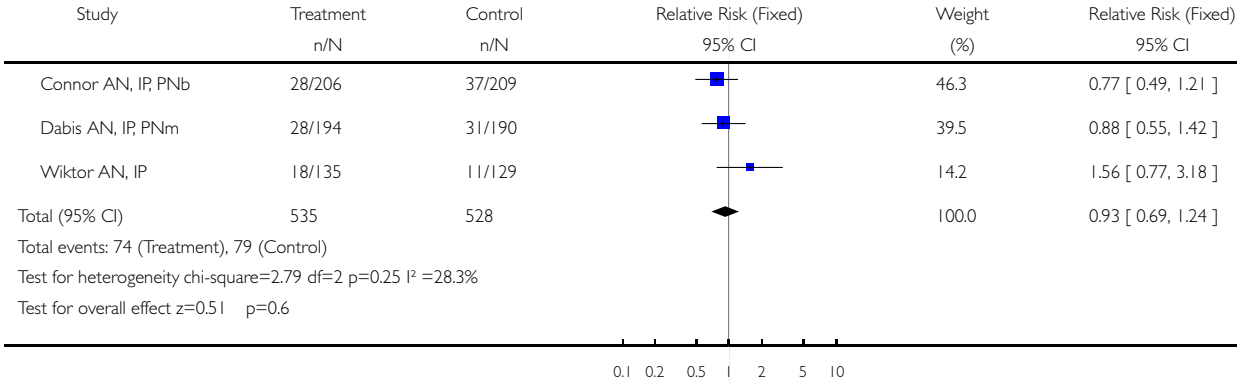


Analysis 01.08. Comparison 01 Any zidovudine vs placebo/no treatment, Outcome 08 Low birth weight

Review: Interventions for reducing the risk of mother-to-child transmission of HIV infection

Comparison: 01 Any zidovudine vs placebo/no treatment

Outcome: 08 Low birth weight



Analysis 01.09. Comparison 01 Any zidovudine vs placebo/no treatment, Outcome 09 Neonatal haematological toxicity

Review: Interventions for reducing the risk of mother-to-child transmission of HIV infection

Comparison: 01 Any zidovudine vs placebo/no treatment

Outcome: 09 Neonatal haematological toxicity

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Connor AN, IP, PNb	44/206	24/209		47.8	1.86 [1.18, 2.94]
Dabis AN, IP, PNm	10/200	12/200		24.1	0.83 [0.37, 1.88]
Shaffer AN, IP	2/196	2/199		4.0	1.02 [0.14, 7.14]
Wiktor AN, IP	8/137	12/136		24.2	0.66 [0.28, 1.57]
Total (95% CI)	739	744		100.0	1.29 [0.91, 1.83]

Total events: 64 (Treatment), 50 (Control)

Test for heterogeneity chi-square=5.91 df=3 p=0.12 I^2 =49.2%

Test for overall effect z=1.43 p=0.2

Analysis 01.10. Comparison 01 Any zidovudine vs placebo/no treatment, Outcome 10 Maternal haematological toxicity

Review: Interventions for reducing the risk of mother-to-child transmission of HIV infection

Comparison: 01 Any zidovudine vs placebo/no treatment

Outcome: 10 Maternal haematological toxicity

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Connor AN, IP, PNb	18/239	17/238		68.3	1.05 [0.56, 2.00]
Dabis AN, IP, PNm	11/201	8/206		31.7	1.41 [0.58, 3.43]
Total (95% CI)	440	444		100.0	1.17 [0.70, 1.96]

Total events: 29 (Treatment), 25 (Control)

Test for heterogeneity chi-square=0.27 df=1 p=0.60 I^2 =0.0%

Test for overall effect z=0.58 p=0.6

Analysis 02.01. Comparison 02 Short course zidovudine versus placebo/no treatment (all trials), Outcome 01 HIV infection status in the child

Review: Interventions for reducing the risk of mother-to-child transmission of HIV infection

Comparison: 02 Short course zidovudine versus placebo/no treatment (all trials)

Outcome: 01 HIV infection status in the child

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Dabis AN, IP, PNm	33/192	52/197		43.6	0.65 [0.44, 0.96]
Shaffer AN, IP	18/188	37/195		30.9	0.50 [0.30, 0.85]
Wiktor AN, IP	19/115	30/115		25.5	0.63 [0.38, 1.06]
Total (95% CI)	495	507		100.0	0.60 [0.46, 0.79]

Total events: 70 (Treatment), 119 (Control)

Test for heterogeneity chi-square=0.63 df=2 p=0.73 I^2 =0.0%

Test for overall effect z=3.73 p=0.0002

Analysis 02.02. Comparison 02 Short course zidovudine versus placebo/no treatment (all trials), Outcome 02 Stillbirth

Review: Interventions for reducing the risk of mother-to-child transmission of HIV infection

Comparison: 02 Short course zidovudine versus placebo/no treatment (all trials)

Outcome: 02 Stillbirth

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Dabis AN, IP, PNm	1/203	7/211		49.4	0.15 [0.02, 1.20]
Wiktor AN, IP	2/137	7/136		50.6	0.28 [0.06, 1.34]
Total (95% CI)	340	347		100.0	0.22 [0.06, 0.75]

Total events: 3 (Treatment), 14 (Control)

Test for heterogeneity chi-square=0.24 df=1 p=0.62 I^2 =0.0%

Test for overall effect z=2.42 p=0.02

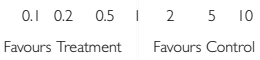
Analysis 02.03. Comparison 02 Short course zidovudine versus placebo/no treatment (all trials), Outcome 03 Neonatal mortality

Review: Interventions for reducing the risk of mother-to-child transmission of HIV infection

Comparison: 02 Short course zidovudine versus placebo/no treatment (all trials)

Outcome: 03 Neonatal mortality

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Dabis AN, IP, PNm	8/200	4/200		89.0	2.00 [0.61, 6.54]
Shaffer AN, IP	1/196	0/199		11.0	3.05 [0.12, 74.31]
Total (95% CI)	396	399		100.0	2.12 [0.70, 6.41]
Total events: 9 (Treatment), 4 (Control)					
Test for heterogeneity chi-square=0.06 df=1 p=0.81 I^2 =0.0%					
Test for overall effect z=1.33 p=0.2					



Analysis 02.04. Comparison 02 Short course zidovudine versus placebo/no treatment (all trials), Outcome 04 Deaths after neonatal period

Review: Interventions for reducing the risk of mother-to-child transmission of HIV infection

Comparison: 02 Short course zidovudine versus placebo/no treatment (all trials)

Outcome: 04 Deaths after neonatal period

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Dabis AN, IP, PNm	9/200	22/200		100.0	0.41 [0.19, 0.87]
Total (95% CI)	200	200		100.0	0.41 [0.19, 0.87]
Total events: 9 (Treatment), 22 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=2.33 p=0.02					

Analysis 02.05. Comparison 02 Short course zidovudine versus placebo/no treatment (all trials), Outcome 05 Late deaths

Review: Interventions for reducing the risk of mother-to-child transmission of HIV infection

Comparison: 02 Short course zidovudine versus placebo/no treatment (all trials)

Outcome: 05 Late deaths

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Dabis AN, IP, PNm	9/200	22/200		100.0	0.41 [0.19, 0.87]
Total (95% CI)	200	200		100.0	0.41 [0.19, 0.87]
Total events: 9 (Treatment), 22 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=2.33 p=0.02					

Analysis 02.06. Comparison 02 Short course zidovudine versus placebo/no treatment (all trials), Outcome 06 Maternal deaths

Review: Interventions for reducing the risk of mother-to-child transmission of HIV infection

Comparison: 02 Short course zidovudine versus placebo/no treatment (all trials)

Outcome: 06 Maternal deaths

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Dabis AN, IP, PNm	2/201	3/206		100.0	0.68 [0.12, 4.05]
Total (95% CI)	201	206		100.0	0.68 [0.12, 4.05]
Total events: 2 (Treatment), 3 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.42 p=0.7					

Analysis 02.07. Comparison 02 Short course zidovudine versus placebo/no treatment (all trials), Outcome 07 Premature delivery

Review: Interventions for reducing the risk of mother-to-child transmission of HIV infection

Comparison: 02 Short course zidovudine versus placebo/no treatment (all trials)

Outcome: 07 Premature delivery

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Dabis AN, IP, PNm	7/168	15/174		100.0	0.48 [0.20, 1.16]
Total (95% CI)	168	174		100.0	0.48 [0.20, 1.16]
Total events: 7 (Treatment), 15 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.63 p=0.1					

Analysis 02.08. Comparison 02 Short course zidovudine versus placebo/no treatment (all trials), Outcome 08 Low birth weight

Review: Interventions for reducing the risk of mother-to-child transmission of HIV infection

Comparison: 02 Short course zidovudine versus placebo/no treatment (all trials)

Outcome: 08 Low birth weight

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Dabis AN, IP, PNm	28/194	31/190		73.6	0.88 [0.55, 1.42]
Wiktor AN, IP	18/135	11/129		26.4	1.56 [0.77, 3.18]
Total (95% CI)	329	319		100.0	1.06 [0.72, 1.57]
Total events: 46 (Treatment), 42 (Control)					
Test for heterogeneity chi-square=1.72 df=1 p=0.19 I^2 =41.9%					
Test for overall effect z=0.31 p=0.8					

Analysis 02.09. Comparison 02 Short course zidovudine versus placebo/no treatment (all trials), Outcome 09 Neonatal haematological toxicity

Review: Interventions for reducing the risk of mother-to-child transmission of HIV infection

Comparison: 02 Short course zidovudine versus placebo/no treatment (all trials)

Outcome: 09 Neonatal haematological toxicity

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Dabis AN, IP, PNm	10/200	12/200		46.1	0.83 [0.37, 1.88]
Shaffer AN, IP	2/196	2/199		7.6	1.02 [0.14, 7.14]
Wiktor AN, IP	8/137	12/136		46.3	0.66 [0.28, 1.57]
Total (95% CI)	533	535		100.0	0.77 [0.44, 1.35]

Total events: 20 (Treatment), 26 (Control)

Test for heterogeneity chi-square=0.23 df=2 p=0.89 I^2 =0.0%

Test for overall effect z=0.92 p=0.4

Analysis 02.10. Comparison 02 Short course zidovudine versus placebo/no treatment (all trials), Outcome 10 Maternal haematological toxicity

Review: Interventions for reducing the risk of mother-to-child transmission of HIV infection

Comparison: 02 Short course zidovudine versus placebo/no treatment (all trials)

Outcome: 10 Maternal haematological toxicity

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Dabis AN, IP, PNm	11/201	8/206		100.0	1.41 [0.58, 3.43]
Total (95% CI)	201	206		100.0	1.41 [0.58, 3.43]

Total events: 11 (Treatment), 8 (Control)

Test for heterogeneity: not applicable

Test for overall effect z=0.76 p=0.4

Analysis 04.01. Comparison 04 Short course zidovudine versus placebo/no treatment (breast feeding), Outcome 01 HIV infection status in the child

Review: Interventions for reducing the risk of mother-to-child transmission of HIV infection

Comparison: 04 Short course zidovudine versus placebo/no treatment (breast feeding)

Outcome: 01 HIV infection status in the child

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Dabis AN, IP, PNm	33/192	52/197		63.1	0.65 [0.44, 0.96]
Wiktor AN, IP	19/115	30/115		36.9	0.63 [0.38, 1.06]
Total (95% CI)	307	312		100.0	0.64 [0.47, 0.88]

Total events: 52 (Treatment), 82 (Control)

Test for heterogeneity chi-square=0.01 df=1 p=0.93 I^2 =0.0%

Test for overall effect z=2.78 p=0.005

Analysis 04.02. Comparison 04 Short course zidovudine versus placebo/no treatment (breast feeding), Outcome 02 Stillbirth

Review: Interventions for reducing the risk of mother-to-child transmission of HIV infection

Comparison: 04 Short course zidovudine versus placebo/no treatment (breast feeding)

Outcome: 02 Stillbirth

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Dabis AN, IP, PNm	1/203	7/211		49.4	0.15 [0.02, 1.20]
Wiktor AN, IP	2/137	7/136		50.6	0.28 [0.06, 1.34]
Total (95% CI)	340	347		100.0	0.22 [0.06, 0.75]

Total events: 3 (Treatment), 14 (Control)

Test for heterogeneity chi-square=0.24 df=1 p=0.62 I^2 =0.0%

Test for overall effect z=2.42 p=0.02

Analysis 04.03. Comparison 04 Short course zidovudine versus placebo/no treatment (breast feeding), Outcome 03 Neonatal mortality

Review: Interventions for reducing the risk of mother-to-child transmission of HIV infection

Comparison: 04 Short course zidovudine versus placebo/no treatment (breast feeding)

Outcome: 03 Neonatal mortality

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Dabis AN, IP, PNm	8/200	4/200		100.0	2.00 [0.61, 6.54]
Total (95% CI)	200	200		100.0	2.00 [0.61, 6.54]
Total events: 8 (Treatment), 4 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.15 p=0.3					

Analysis 04.04. Comparison 04 Short course zidovudine versus placebo/no treatment (breast feeding), Outcome 04 Deaths after neonatal period

Review: Interventions for reducing the risk of mother-to-child transmission of HIV infection

Comparison: 04 Short course zidovudine versus placebo/no treatment (breast feeding)

Outcome: 04 Deaths after neonatal period

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Dabis AN, IP, PNm	9/200	22/200		100.0	0.41 [0.19, 0.87]
Total (95% CI)	200	200		100.0	0.41 [0.19, 0.87]
Total events: 9 (Treatment), 22 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=2.33 p=0.02					

Analysis 04.05. Comparison 04 Short course zidovudine versus placebo/no treatment (breast feeding), Outcome 05 Late deaths

Review: Interventions for reducing the risk of mother-to-child transmission of HIV infection

Comparison: 04 Short course zidovudine versus placebo/no treatment (breast feeding)

Outcome: 05 Late deaths

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Dabis AN, IP, PNm	9/200	22/200		100.0	0.41 [0.19, 0.87]
Total (95% CI)	200	200		100.0	0.41 [0.19, 0.87]
Total events: 9 (Treatment), 22 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=2.33 p=0.02					

Analysis 04.06. Comparison 04 Short course zidovudine versus placebo/no treatment (breast feeding), Outcome 06 Maternal deaths

Review: Interventions for reducing the risk of mother-to-child transmission of HIV infection

Comparison: 04 Short course zidovudine versus placebo/no treatment (breast feeding)

Outcome: 06 Maternal deaths

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Dabis AN, IP, PNm	2/201	3/206		100.0	0.68 [0.12, 4.05]
Total (95% CI)	201	206		100.0	0.68 [0.12, 4.05]
Total events: 2 (Treatment), 3 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.42 p=0.7					

Analysis 04.07. Comparison 04 Short course zidovudine versus placebo/no treatment (breast feeding), Outcome 07 Premature delivery

Review: Interventions for reducing the risk of mother-to-child transmission of HIV infection

Comparison: 04 Short course zidovudine versus placebo/no treatment (breast feeding)

Outcome: 07 Premature delivery

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Dabis AN, IP, PNm	7/168	15/174		100.0	0.48 [0.20, 1.16]
Total (95% CI)	168	174		100.0	0.48 [0.20, 1.16]
Total events: 7 (Treatment), 15 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.63 p=0.1					

Analysis 04.08. Comparison 04 Short course zidovudine versus placebo/no treatment (breast feeding), Outcome 08 Low birth weight

Review: Interventions for reducing the risk of mother-to-child transmission of HIV infection

Comparison: 04 Short course zidovudine versus placebo/no treatment (breast feeding)

Outcome: 08 Low birth weight

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Dabis AN, IP, PNm	28/194	31/190		73.6	0.88 [0.55, 1.42]
Wiktor AN, IP	18/135	11/129		26.4	1.56 [0.77, 3.18]
Total (95% CI)	329	319		100.0	1.06 [0.72, 1.57]
Total events: 46 (Treatment), 42 (Control)					
Test for heterogeneity chi-square=1.72 df=1 p=0.19 I^2 =41.9%					
Test for overall effect z=0.31 p=0.8					

Analysis 04.09. Comparison 04 Short course zidovudine versus placebo/no treatment (breast feeding), Outcome 09 Neonatal haematological toxicity

Review: Interventions for reducing the risk of mother-to-child transmission of HIV infection

Comparison: 04 Short course zidovudine versus placebo/no treatment (breast feeding)

Outcome: 09 Neonatal haematological toxicity

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Dabis AN, IP, PNm	10/200	12/200		49.9	0.83 [0.37, 1.88]
Wiktor AN, IP	8/137	12/136		50.1	0.66 [0.28, 1.57]
Total (95% CI)	337	336		100.0	0.75 [0.41, 1.35]

Total events: 18 (Treatment), 24 (Control)

Test for heterogeneity chi-square=0.14 df=1 p=0.70 I^2 =0.0%

Test for overall effect z=0.96 p=0.3

Analysis 04.10. Comparison 04 Short course zidovudine versus placebo/no treatment (breast feeding), Outcome 10 Maternal haematological toxicity

Review: Interventions for reducing the risk of mother-to-child transmission of HIV infection

Comparison: 04 Short course zidovudine versus placebo/no treatment (breast feeding)

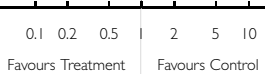
Outcome: 10 Maternal haematological toxicity

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Dabis AN, IP, PNm	11/201	8/206		100.0	1.41 [0.58, 3.43]
Total (95% CI)	201	206		100.0	1.41 [0.58, 3.43]

Total events: 11 (Treatment), 8 (Control)

Test for heterogeneity: not applicable

Test for overall effect z=0.76 p=0.4



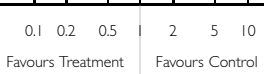
Analysis 05.01. Comparison 05 Caesarean section versus vaginal delivery, Outcome 01 HIV infection status in the child

Review: Interventions for reducing the risk of mother-to-child transmission of HIV infection

Comparison: 05 Caesarean section versus vaginal delivery

Outcome: 01 HIV infection status in the child

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
MOD	3/170	21/200		100.0	0.17 [0.05, 0.55]
Total (95% CI)	170	200		100.0	0.17 [0.05, 0.55]
Total events: 3 (Treatment), 21 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=2.93 p=0.003					



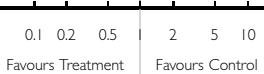
Analysis 05.02. Comparison 05 Caesarean section versus vaginal delivery, Outcome 02 Stillbirth

Review: Interventions for reducing the risk of mother-to-child transmission of HIV infection

Comparison: 05 Caesarean section versus vaginal delivery

Outcome: 02 Stillbirth

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Total (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Treatment), 0 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					



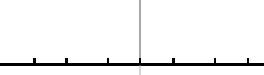
Analysis 05.03. Comparison 05 Caesarean section versus vaginal delivery, Outcome 03 Neonatal mortality

Review: Interventions for reducing the risk of mother-to-child transmission of HIV infection

Comparison: 05 Caesarean section versus vaginal delivery

Outcome: 03 Neonatal mortality

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
× MOD	0/170	0/200		0.0	Not estimable
Total (95% CI)	170	200		0.0	Not estimable
Total events: 0 (Treatment), 0 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					



Analysis 05.04. Comparison 05 Caesarean section versus vaginal delivery, Outcome 04 Deaths after neonatal period

Review: Interventions for reducing the risk of mother-to-child transmission of HIV infection

Comparison: 05 Caesarean section versus vaginal delivery

Outcome: 04 Deaths after neonatal period

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
MOD	3/170	1/200		100.0	3.53 [0.37, 33.62]
Total (95% CI)	170	200		100.0	3.53 [0.37, 33.62]
Total events: 3 (Treatment), 1 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.10 p=0.3					

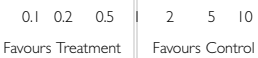
Analysis 05.05. Comparison 05 Caesarean section versus vaginal delivery, Outcome 05 Late deaths

Review: Interventions for reducing the risk of mother-to-child transmission of HIV infection

Comparison: 05 Caesarean section versus vaginal delivery

Outcome: 05 Late deaths

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Total (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Treatment), 0 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					



Analysis 05.06. Comparison 05 Caesarean section versus vaginal delivery, Outcome 06 Maternal deaths

Review: Interventions for reducing the risk of mother-to-child transmission of HIV infection

Comparison: 05 Caesarean section versus vaginal delivery

Outcome: 06 Maternal deaths

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
MOD	2/170	1/200		100.0	2.35 [0.22, 25.72]
Total (95% CI)	170	200		100.0	2.35 [0.22, 25.72]
Total events: 2 (Treatment), 1 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.70 p=0.5					

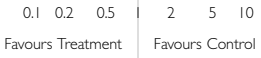
Analysis 05.07. Comparison 05 Caesarean section versus vaginal delivery, Outcome 07 Maternal postpartum complications

Review: Interventions for reducing the risk of mother-to-child transmission of HIV infection

Comparison: 05 Caesarean section versus vaginal delivery

Outcome: 07 Maternal postpartum complications

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
× MOD	0/189	0/221		0.0	Not estimable
Total (95% CI)	189	221		0.0	Not estimable
Total events: 0 (Treatment), 0 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					



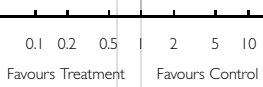
Analysis 06.01. Comparison 06 HIVIG plus zidovudine versus IVIG plus zidovudine, Outcome 01 HIV infection status in the child

Review: Interventions for reducing the risk of mother-to-child transmission of HIV infection

Comparison: 06 HIVIG plus zidovudine versus IVIG plus zidovudine

Outcome: 01 HIV infection status in the child

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Stiehm AN, IP, PNb	9/230	13/224		100.0	0.67 [0.29, 1.55]
Total (95% CI)	230	224		100.0	0.67 [0.29, 1.55]
Total events: 9 (Treatment), 13 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.93 p=0.4					



Analysis 06.02. Comparison 06 HIVIG plus zidovudine versus IVIG plus zidovudine, Outcome 02 Stillbirth

Review: Interventions for reducing the risk of mother-to-child transmission of HIV infection

Comparison: 06 HIVIG plus zidovudine versus IVIG plus zidovudine

Outcome: 02 Stillbirth

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Stiehm AN, IP, PNb	0/231	1/228		100.0	0.33 [0.01, 8.03]
Total (95% CI)	231	228		100.0	0.33 [0.01, 8.03]
Total events: 0 (Treatment), 1 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.68 p=0.5					

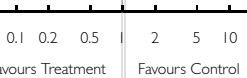
Analysis 06.03. Comparison 06 HIVIG plus zidovudine versus IVIG plus zidovudine, Outcome 03 Neonatal mortality

Review: Interventions for reducing the risk of mother-to-child transmission of HIV infection

Comparison: 06 HIVIG plus zidovudine versus IVIG plus zidovudine

Outcome: 03 Neonatal mortality

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Stiehm AN, IP, PNb	2/259	1/247		100.0	1.91 [0.17, 20.90]
Total (95% CI)	259	247		100.0	1.91 [0.17, 20.90]
Total events: 2 (Treatment), 1 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.53 p=0.6					



Analysis 06.04. Comparison 06 HIVIG plus zidovudine versus IVIG plus zidovudine, Outcome 04 Deaths after neonatal period

Review: Interventions for reducing the risk of mother-to-child transmission of HIV infection

Comparison: 06 HIVIG plus zidovudine versus IVIG plus zidovudine

Outcome: 04 Deaths after neonatal period

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Stiehm AN, IP, PNb	1/259	2/247		100.0	0.48 [0.04, 5.23]
Total (95% CI)	259	247		100.0	0.48 [0.04, 5.23]
Total events: 1 (Treatment), 2 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.61 p=0.5					

Analysis 06.05. Comparison 06 HIVIG plus zidovudine versus IVIG plus zidovudine, Outcome 05 Late deaths

Review: Interventions for reducing the risk of mother-to-child transmission of HIV infection

Comparison: 06 HIVIG plus zidovudine versus IVIG plus zidovudine

Outcome: 05 Late deaths

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Total (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Treatment), 0 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					

Analysis 06.06. Comparison 06 HIVIG plus zidovudine versus IVIG plus zidovudine, Outcome 06 Maternal deaths

Review: Interventions for reducing the risk of mother-to-child transmission of HIV infection

Comparison: 06 HIVIG plus zidovudine versus IVIG plus zidovudine

Outcome: 06 Maternal deaths

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Stiehm AN, IP, PNb	4/231	2/228		100.0	1.97 [0.37, 10.67]
Total (95% CI)	231	228		100.0	1.97 [0.37, 10.67]
Total events: 4 (Treatment), 2 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.79 p=0.4					

Analysis 06.07. Comparison 06 HIVIG plus zidovudine versus IVIG plus zidovudine, Outcome 07 Premature delivery

Review: Interventions for reducing the risk of mother-to-child transmission of HIV infection

Comparison: 06 HIVIG plus zidovudine versus IVIG plus zidovudine

Outcome: 07 Premature delivery

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Stiehm AN, IP, PNb	44/231	38/227		100.0	1.14 [0.77, 1.69]
Total (95% CI)	231	227		100.0	1.14 [0.77, 1.69]
Total events: 44 (Treatment), 38 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.64 p=0.5					

Analysis 06.08. Comparison 06 HIVIG plus zidovudine versus IVIG plus zidovudine, Outcome 08 Low birth weight

Review: Interventions for reducing the risk of mother-to-child transmission of HIV infection

Comparison: 06 HIVIG plus zidovudine versus IVIG plus zidovudine

Outcome: 08 Low birth weight

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Stiehm AN, IP, PNb	37/231	32/227		100.0	1.14 [0.73, 1.76]
Total (95% CI)	231	227		100.0	1.14 [0.73, 1.76]
Total events: 37 (Treatment), 32 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.57 p=0.6					

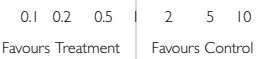
Analysis 06.09. Comparison 06 HIVIG plus zidovudine versus IVIG plus zidovudine, Outcome 09 Neonatal haematological toxicity

Review: Interventions for reducing the risk of mother-to-child transmission of HIV infection

Comparison: 06 HIVIG plus zidovudine versus IVIG plus zidovudine

Outcome: 09 Neonatal haematological toxicity

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Stiehm AN, IP, PNb	23/259	19/247		100.0	1.15 [0.65, 2.07]
Total (95% CI)	259	247		100.0	1.15 [0.65, 2.07]
Total events: 23 (Treatment), 19 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.48 p=0.6					



Analysis 07.01. Comparison 07 Nevirapine versus zidovudine, Outcome 01 HIV infection status in the child

Review: Interventions for reducing the risk of mother-to-child transmission of HIV infection

Comparison: 07 Nevirapine versus zidovudine

Outcome: 01 HIV infection status in the child

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Guay IP, PNb	37/246	65/250		100.0	0.58 [0.40, 0.83]
Total (95% CI)	246	250		100.0	0.58 [0.40, 0.83]
Total events: 37 (Treatment), 65 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=2.95 p=0.003					

Analysis 07.02. Comparison 07 Nevirapine versus zidovudine, Outcome 02 Neonatal mortality

Review: Interventions for reducing the risk of mother-to-child transmission of HIV infection

Comparison: 07 Nevirapine versus zidovudine

Outcome: 02 Neonatal mortality

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Guay IP, PNb	16/281	22/278		100.0	0.72 [0.39, 1.34]
Total (95% CI)	281	278		100.0	0.72 [0.39, 1.34]
Total events: 16 (Treatment), 22 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.04 p=0.3					

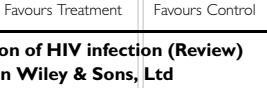
Analysis 07.03. Comparison 07 Nevirapine versus zidovudine, Outcome 03 Deaths after neonatal period

Review: Interventions for reducing the risk of mother-to-child transmission of HIV infection

Comparison: 07 Nevirapine versus zidovudine

Outcome: 03 Deaths after neonatal period

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Total (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Treatment), 0 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					



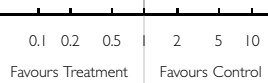
Analysis 07.04. Comparison 07 Nevirapine versus zidovudine, Outcome 04 Late deaths

Review: Interventions for reducing the risk of mother-to-child transmission of HIV infection

Comparison: 07 Nevirapine versus zidovudine

Outcome: 04 Late deaths

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Total (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Treatment), 0 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					



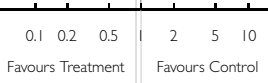
Analysis 07.05. Comparison 07 Nevirapine versus zidovudine, Outcome 05 Maternal deaths

Review: Interventions for reducing the risk of mother-to-child transmission of HIV infection

Comparison: 07 Nevirapine versus zidovudine

Outcome: 05 Maternal deaths

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Guay IP, PNb	0/310	1/308		100.0	0.33 [0.01, 8.10]
Total (95% CI)	310	308		100.0	0.33 [0.01, 8.10]
Total events: 0 (Treatment), 1 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.68 p=0.5					



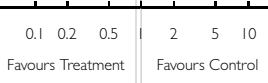
Analysis 07.06. Comparison 07 Nevirapine versus zidovudine, Outcome 06 Neonatal haematological toxicity

Review: Interventions for reducing the risk of mother-to-child transmission of HIV infection

Comparison: 07 Nevirapine versus zidovudine

Outcome: 06 Neonatal haematological toxicity

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Guay IP, PNb	13/286	9/286		100.0	1.44 [0.63, 3.33]
Total (95% CI)	286	286		100.0	1.44 [0.63, 3.33]
Total events: 13 (Treatment), 9 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.86 p=0.4					



Analysis 07.07. Comparison 07 Nevirapine versus zidovudine, Outcome 07 Maternal haematological toxicity

Review: Interventions for reducing the risk of mother-to-child transmission of HIV infection

Comparison: 07 Nevirapine versus zidovudine

Outcome: 07 Maternal haematological toxicity

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Guay IP, PNb	41/313	33/313		100.0	1.24 [0.81, 1.91]
Total (95% CI)	313	313		100.0	1.24 [0.81, 1.91]
Total events: 41 (Treatment), 33 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.99 p=0.3