HIV infection in pregnancy

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What is the size of the problem?

- in the population as a whole?
- in women?
- in pregnant women?
- in children?
Global summary of the HIV/AIDS epidemic, December 2002

<table>
<thead>
<tr>
<th>Category</th>
<th>Total</th>
<th>Adults</th>
<th>Women</th>
<th>Children under 15 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of people living with HIV/AIDS</td>
<td>42 m</td>
<td>38.6 m</td>
<td>19.2 m</td>
<td>3.2 m</td>
</tr>
<tr>
<td>People newly infected</td>
<td>5 m</td>
<td>4.2 m</td>
<td>2 m</td>
<td>800 000</td>
</tr>
<tr>
<td>Aids deaths in 2002</td>
<td>3.1 m</td>
<td>2.5 m</td>
<td>1.2 m</td>
<td>610 000</td>
</tr>
</tbody>
</table>
## Regional HIV/AIDS statistics and features, end of 2002

<table>
<thead>
<tr>
<th>Region</th>
<th>Epidemic started</th>
<th>Adults &amp; children Living with HIV</th>
<th>Adults and children newly infected with HIV</th>
<th>Adult prevalence rate*</th>
<th>% of HIV-positive adults who are women</th>
<th>Main mode(s) of transmission for those living with HIV/AIDS**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sub-Saharan Africa</td>
<td>Late ’70s</td>
<td>29.4 m</td>
<td>3.5 m</td>
<td>8.8%</td>
<td>58%</td>
<td>Hetero</td>
</tr>
<tr>
<td></td>
<td>Early ’80s</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N Africa &amp; Middle East</td>
<td>Late ’80s</td>
<td>550 000</td>
<td>83 000</td>
<td>0.3%</td>
<td>55%</td>
<td>Hetero, IDU</td>
</tr>
<tr>
<td>South &amp; S-East Asia</td>
<td>Late ’80s</td>
<td>6.0 m</td>
<td>700 000</td>
<td>0.6%</td>
<td>36%</td>
<td>Hetero, IDU</td>
</tr>
<tr>
<td>East Asia &amp; Pacific</td>
<td>Late ’80s</td>
<td>1.2 m</td>
<td>270 000</td>
<td>0.1%</td>
<td>24%</td>
<td>IDU, Hetero, MSM</td>
</tr>
<tr>
<td>Latin America</td>
<td>Late ’70s</td>
<td>1.5 m</td>
<td>150 000</td>
<td>0.6%</td>
<td>30%</td>
<td>MSM, IDU, Hetero</td>
</tr>
<tr>
<td></td>
<td>Early ’80s</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caribbean</td>
<td>Late ’70s</td>
<td>440 000</td>
<td>60 000</td>
<td>2.4%</td>
<td>50%</td>
<td>Hetero, MSM</td>
</tr>
<tr>
<td></td>
<td>Early ’80s</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>E Europe &amp; Central Asia</td>
<td>Early ’90s</td>
<td>1.2 m</td>
<td>250 000</td>
<td>0.6%</td>
<td>27%</td>
<td>IDU</td>
</tr>
<tr>
<td>Western Europe</td>
<td>Late ’70s</td>
<td>570 000</td>
<td>30 000</td>
<td>0.3%</td>
<td>25%</td>
<td>MSM, IDU</td>
</tr>
<tr>
<td></td>
<td>Early ’80s</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>North America</td>
<td>Late ’70s</td>
<td>980 000</td>
<td>45 000</td>
<td>0.6%</td>
<td>20%</td>
<td>MSM, IDU, Hetero</td>
</tr>
<tr>
<td></td>
<td>Early ’80s</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Australia &amp; N Zealand</td>
<td>Late ’70s</td>
<td>15 000</td>
<td>500</td>
<td>0.1%</td>
<td>7%</td>
<td>MSM</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td></td>
<td>42 m</td>
<td>5 m</td>
<td>1.2%</td>
<td>50%</td>
<td></td>
</tr>
</tbody>
</table>
A global view of HIV infection

40 million adults living with HIV/AIDS as of end 2001
HIV prevalence in adults in sub-Saharan Africa, end 2001

- 20 – 39%
- 10 – 20%
- 5 – 10%
- 1 – 5%
- 0 – 1%
- Trend data unavailable
- Outside region
HIV prevalence in adults in sub-Saharan Africa, 1986-2001

- 20 – 39%
- 10 – 20%
- 5 – 10%
- 1 – 5%
- 0 – 1%
- Trend data unavailable outside region

Maps showing the prevalence of HIV in different years.
Projected population structure with and without the AIDS epidemic, Botswana, 2020

Source: US Census Bureau, World Population Profile 2000
HIV prevalence among pregnant women in South Africa, 1990 to 2001

Source: Department of Health, Republic of South Africa
HIV prevalence rates among pregnant women attending antenatal clinics in urban sites in Cameroon: 1989-2000

End-2002 global HIV/AIDS estimates
Children (<15 years)

- Children living with HIV/AIDS: 3.2 million
- New HIV infections in 2002: 800,000
- Deaths due to HIV/AIDS in 2002: 610,000
Children (<15 years) estimated to be living with HIV/AIDS as of end 2002

Total: 3.2 million
Estimated number of children (<15 years) newly infected with HIV during 2002

- North America: < 500
- Caribbean: 7,000
- Latin America: 10,000
- North Africa & Middle East: < 500
- Western Europe: < 500
- Eastern Europe & Central Asia: 1,000
- sub-Saharan Africa: 720,000
- East Asia & Pacific: 3,000
- South & South-East Asia: 60,000
- Australia & New Zealand: < 100

Total: 800,000
Estimated deaths in children (<15 years) from HIV/AIDS during 2002

Total: 610,000
Estimated impact of AIDS on under-5 child mortality rates, selected African countries, 2010

Source: US Census Bureau
About 14,000 new HIV infections a day in 2002

- More than 95% are in developing countries
- 2,000 are in children under 15 years of age
- About 12,000 are in persons aged 15 to 49 years, of whom:
  - almost 50% are women
  - about 50% are 15-24 year olds
HIV infection in pregnancy

• Effect of pregnancy on HIV infection
  – progression of HIV disease in mother
    • orphans
    • family structure
• Effect of HIV infection on pregnancy
  – pregnancy complications
  – mother-to-child transmission
Effect of pregnancy on HIV infection

- Progression of HIV disease in mother in absence of treatment

- Progression of HIV disease in mother with treatment (antiretroviral therapy)

- Impact of maternal death on children under 1 year of age
Effect of HIV infection on pregnancy

- Pregnancy outcome
  - preterm birth
  - IUGR/SGA and low birthweight
  - stillbirth
  - perinatal/neonatal/infant mortality
Effect on Perinatal Outcome

PREMATURE DELIVERY

- Berrebi 1991
- Braddick 1990
- Bulterys 1994
- Carreras 1994
- Dabis 1993
- Geary 1994
- Guay 1990
- Halsey 1990
- Hira 1989
- Johnstone 1988
- Lallemand 1989
- Lepage 1991
- Ryder 1989
- Selwyn 1990
- Semprini 1990
- St Louis 1993
- Temmerman 1994

SUMMARY
Effect on Perinatal Outcome

IUGR
- Berrebi 1991
- Bulterys 1994
- Carreras 1994
- Geary 1994
- Johnstone 1988
- Selwyn 1989
- Semprini 1990
- Temmerman 1994

SUMMARY

LOW BIRTH WEIGHT
- Adjorlolo 1991
- Braddick 1990
- Bulterys 1994
- Dabis 1993
- Geary 1994
- Halsey 1990
- Hira 1989
- Johnstone 1988
- Lallemant 1989
- Lepage 1991
- Munkolenkole 1991
- Ryder 1989
- Temmerman 1994

SUMMARY

Log Odds Ratio (95% CI)
Effect on Perinatal Outcome

Effect on Perinatal Outcome

STILLBIRTHS
- Braddick 1990
- Bulterys 1994
- Dabis 1993
- Hira 1989
- Lalleman 1989
- Ryder 1989
- St Louis 1993
- Temmerman 1994

SUMMARY

PERINATAL MORTALITY
- Bulterys 1994
- Dabis 1993
- Guay 1990

SUMMARY

NEONATAL MORTALITY
- Johnstone 1988
- Ryder 1989
- Lepage 1991
- Temmerman 1994
- Bulterys 1994

SUMMARY

INFANT MORTALITY
- Datta 1989
- Halsey 1990
- Lallemant 1989
- Lionba 1992
- Mworoz 1989

SUMMARY

Log Odds Ratio (95% CI)
Mother-to-child transmission
Mother-to-child transmission

• In resource poor countries
  – 25-45%

• In industrialised countries
  – 15-30%
Mother-to-child transmission

- Risk factors for transmission
  - prematurity
  - high viral load
    - symptomatic maternal disease
    - low CD4 cell count
  - breast feeding
  - mode of delivery
  - duration of membrane rupture
  - duration of second stage
  - sexually transmitted infections
Antiretroviral therapy


- Randomised controlled trials
### Any ZDV versus placebo – HIV in child

#### Comparison: 01 Zidovudine vs placebo

**Outcome:** 01 HIV infection of the child

<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment</th>
<th>Control</th>
<th>OR (95% CI Fixed)</th>
<th>Weight %</th>
<th>OR (95% CI Fixed)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>n/N</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>01 Long course, non-breastfeeding</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Connor AN, IP, PNb</td>
<td>15 / 198</td>
<td>46 / 204</td>
<td>0.29 (0.15, 0.52)</td>
<td>27.0</td>
<td></td>
</tr>
<tr>
<td>Subtotal(95% CI)</td>
<td>15 / 190</td>
<td>46 / 204</td>
<td>0.23 (0.15, 0.52)</td>
<td>27.0</td>
<td></td>
</tr>
<tr>
<td>Test for heterogeneity ch-square=0.0 df=0</td>
<td></td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>Test for overall effect z=4.00 p=0.00006</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>02 Short course, non-breastfeeding</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Limpong AN, IP</td>
<td>13 / 87</td>
<td>14 / 87</td>
<td>0.52 (0.40, 0.83)</td>
<td>7.7</td>
<td></td>
</tr>
<tr>
<td>Shaffer AN, IP</td>
<td>19 / 194</td>
<td>37 / 198</td>
<td>0.45 (0.24, 0.81)</td>
<td>21.4</td>
<td></td>
</tr>
<tr>
<td>Subtotal(95% CI)</td>
<td>31 / 201</td>
<td>51 / 285</td>
<td>0.57 (0.35, 0.92)</td>
<td>29.1</td>
<td></td>
</tr>
<tr>
<td>Test for heterogeneity ch-square=1.93 df=1 p=0.16</td>
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</tr>
<tr>
<td>Test for overall effect z=2.30 p=0.02</td>
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</tr>
<tr>
<td>03 Short course, breastfeeding</td>
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<td></td>
</tr>
<tr>
<td>Dabis AN, IP, PNb</td>
<td>33 / 180</td>
<td>52 / 175</td>
<td>0.53 (0.32, 0.87)</td>
<td>27.8</td>
<td></td>
</tr>
<tr>
<td>Wiktor AN, IP</td>
<td>19 / 115</td>
<td>30 / 115</td>
<td>0.65 (0.29, 1.07)</td>
<td>16.1</td>
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</tr>
<tr>
<td>Subtotal(95% CI)</td>
<td>52 / 295</td>
<td>82 / 290</td>
<td>0.54 (0.37, 0.80)</td>
<td>43.9</td>
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</tr>
<tr>
<td>Test for heterogeneity ch-square=0.02 df=1 p=0.9</td>
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</tr>
<tr>
<td>Test for overall effect z=3.05 p=0.002</td>
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<td></td>
</tr>
<tr>
<td>Total(95% CI)</td>
<td>93 / 774</td>
<td>179 / 779</td>
<td>0.43 (0.37, 0.63)</td>
<td>100.0</td>
<td></td>
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<tr>
<td>Test for heterogeneity ch-square=5.65 df=4 p=0.23</td>
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</tr>
<tr>
<td>Test for overall effect z=5.31 p=0.00001</td>
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<td></td>
</tr>
</tbody>
</table>
### Any ZDV versus placebo – death <1 year

#### Comparison: 01 Zidovudine vs placebo

#### Outcome: 03 Death of the child within 1 year after birth

<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment n/N</th>
<th>Control n/N</th>
<th>OR (95%CI Fixed)</th>
<th>Weight %</th>
<th>OR (95%CI Fixed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>31 Long course, non-breastfeeding</td>
<td>5 / 206</td>
<td>5 / 209</td>
<td></td>
<td>7.9</td>
<td>1.01[0.29,3.56]</td>
</tr>
<tr>
<td></td>
<td>Subtotal</td>
<td>5 / 206</td>
<td></td>
<td></td>
<td>7.9</td>
</tr>
<tr>
<td>Test for heterogeneity chi-square=0.0  df=0</td>
<td></td>
<td></td>
<td></td>
<td>0.02</td>
<td>p=1</td>
</tr>
<tr>
<td>Test for overall effect z=0.02  p=1</td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>32 Short course, non-breastfeeding</td>
<td>5 / 196</td>
<td>5 / 199</td>
<td></td>
<td>7.8</td>
<td>1.02[0.29,3.57]</td>
</tr>
<tr>
<td></td>
<td>Subtotal</td>
<td>5 / 196</td>
<td></td>
<td></td>
<td>7.8</td>
</tr>
<tr>
<td>Test for heterogeneity chi-square=0.0  df=0</td>
<td></td>
<td></td>
<td></td>
<td>0.02</td>
<td>p=1</td>
</tr>
<tr>
<td>Test for overall effect z=0.02  p=1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>33 Short course, breastfeeding</td>
<td>28 / 202</td>
<td>38 / 205</td>
<td></td>
<td>52.7</td>
<td>0.71[0.42,1.20]</td>
</tr>
<tr>
<td></td>
<td>Subtotal</td>
<td>31 / 338</td>
<td></td>
<td></td>
<td>64.3</td>
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<tr>
<td>Test for heterogeneity chi-square=6.12  df=1  p=0.013</td>
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<tr>
<td>Test for overall effect z=2.97  p=0.003</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>41 / 740</td>
<td>68 / 750</td>
<td></td>
<td>100.0</td>
<td>0.57[0.36,0.87]</td>
</tr>
<tr>
<td>Test for heterogeneity chi-square=7.59  df=3  p=0.055</td>
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<tr>
<td>Test for overall effect z=2.85  p=0.008</td>
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</tbody>
</table>
Any ZDV versus placebo – low birth weight

<table>
<thead>
<tr>
<th>Study Description</th>
<th>Treatment n/n</th>
<th>Control n/n</th>
<th>OR (95%CI Fixed)</th>
<th>Weight %</th>
<th>OR (95%CI Fixed)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>01 Long course, non-breastfeeding</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Connor AN, P, Pm</td>
<td>28 / 207</td>
<td>37 / 209</td>
<td>-</td>
<td>41.2</td>
<td>0.73[0.43,1.24]</td>
</tr>
<tr>
<td>Subtotal(95%CI)</td>
<td>28 / 207</td>
<td>37 / 209</td>
<td>-</td>
<td>41.2</td>
<td>0.73[0.43,1.24]</td>
</tr>
<tr>
<td>Test for heterogeneity chi-square=0.0 df=0</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Test for overall effect z=-1.17 p=0.2</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>02 Short course, non-breastfeeding</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shaffer AN, IP</td>
<td>12 / 194</td>
<td>20 / 198</td>
<td>-</td>
<td>24.1</td>
<td>0.59[0.28,1.24]</td>
</tr>
<tr>
<td>Subtotal(95%CI)</td>
<td>12 / 194</td>
<td>20 / 198</td>
<td>-</td>
<td>24.1</td>
<td>0.59[0.28,1.24]</td>
</tr>
<tr>
<td>Test for heterogeneity chi-square=0.00 df=0 p&lt;0.00001</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Test for overall effect z=-1.40 p=0.16</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>03 Short course, breastfeeding</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dabis AN, IP, Pm</td>
<td>28 / 194</td>
<td>31 / 190</td>
<td>-</td>
<td>34.7</td>
<td>0.87[0.50,1.51]</td>
</tr>
<tr>
<td>Subtotal(95%CI)</td>
<td>28 / 194</td>
<td>31 / 190</td>
<td>-</td>
<td>34.7</td>
<td>0.87[0.50,1.51]</td>
</tr>
<tr>
<td>Test for heterogeneity chi-square=0.00 df=0 p&lt;0.00001</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Test for overall effect z=-0.51 p=0.6</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Total(95%CI)</strong></td>
<td>68 / 595</td>
<td>88 / 597</td>
<td>-</td>
<td>100.0</td>
<td>0.74[0.53,1.04]</td>
</tr>
<tr>
<td>Test for heterogeneity chi-square=0.68 df=2 p=0.71</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Test for overall effect z=-1.72 p=0.09</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>
Short course ZDV versus long course ZDV – HIV in child

Comparison: 02 Zidovudine (short-short) vs zidovudine (long-long)
Outcome: 01 HIV infection of the child

<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment n/N</th>
<th>Control n/N</th>
<th>OR (95%CI Fixed)</th>
<th>Weight %</th>
<th>OR (95%CI Fixed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lallemand AN,IP,PNb</td>
<td>24 / 231</td>
<td>10 / 222</td>
<td></td>
<td>100.0</td>
<td>2.46[1.15,5.27]</td>
</tr>
<tr>
<td>Total(95%CI)</td>
<td>24 / 231</td>
<td>10 / 222</td>
<td></td>
<td>100.0</td>
<td>2.46[1.15,5.27]</td>
</tr>
</tbody>
</table>

Test for heterogeneity chi-square=0.0  df=0
Test for overall effect z=2.31  p=0.02
### Comparison: 05 Nevirapine vs zidovudine
#### Outcome: 01 HIV infection of the child

<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment n/N</th>
<th>Control n/N</th>
<th>OR (95%CI Fixed)</th>
<th>Weight %</th>
<th>OR (95%CI Fixed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guay IP, PNb</td>
<td>37 / 246</td>
<td>65 / 250</td>
<td></td>
<td>100.0</td>
<td>0.50[0.32,0.79]</td>
</tr>
<tr>
<td>Total(95%CI)</td>
<td>37 / 246</td>
<td>65 / 250</td>
<td></td>
<td>100.0</td>
<td>0.50[0.32,0.79]</td>
</tr>
</tbody>
</table>

Test for heterogeneity chi-square=0.0  df=0  
Test for overall effect z=-2.99  p=0.003
ZDV plus 3TC versus placebo – HIV in child

### Comparison: 06 Zidovudine + Lamivudine (AN, IP, PNmb) vs placebo

**Outcome:** 01 HIV infection of the child

<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment n/N</th>
<th>Control n/N</th>
<th>OR (95%CI Fixed)</th>
<th>Weight %</th>
<th>OR (95%CI Fixed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Petra AN, IP, PNmb</td>
<td>16 / 281</td>
<td>40 / 262</td>
<td></td>
<td>100.0</td>
<td>0.34[0.18,0.61]</td>
</tr>
<tr>
<td><strong>Total (95%CI)</strong></td>
<td><strong>16 / 281</strong></td>
<td><strong>40 / 262</strong></td>
<td></td>
<td><strong>100.0</strong></td>
<td><strong>0.34[0.18,0.61]</strong></td>
</tr>
</tbody>
</table>

Test for heterogeneity chi-square=0.0 df=0
Test for overall effect z=-3.53 p=0.0004
ZDV plus 3TC versus placebo – HIV in child

<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment n/N</th>
<th>Control n/N</th>
<th>OR (95%CI Fixed)</th>
<th>Weight</th>
<th>OR (95%CI Fixed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Petra AN, IP, PNmb</td>
<td>24 / 269</td>
<td>40 / 262</td>
<td></td>
<td>100.0</td>
<td>0.54[0.32,0.93]</td>
</tr>
<tr>
<td>Total(95%CI)</td>
<td>24 / 269</td>
<td>40 / 262</td>
<td></td>
<td>100.0</td>
<td>0.54[0.32,0.93]</td>
</tr>
</tbody>
</table>

Test for heterogeneity chi-square=0.00  df=0  p=0.00001
Test for overall effect  z=-2.22  p=0.03

Favours treatment   Favours control
ZDV plus 3TC versus placebo – HIV in child

Comparison: 08 Zidovudine + lamivudine (IP) vs placebo
Outcome: 01 HIV infection of the child

<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment n/N</th>
<th>Control n/N</th>
<th>OR (95%CI Fixed)</th>
<th>Weight %</th>
<th>OR (95%CI Fixed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Petra AN, IP, PNb</td>
<td>40 / 281</td>
<td>40 / 262</td>
<td></td>
<td>100.0</td>
<td>0.92[0.57,1.48]</td>
</tr>
</tbody>
</table>

Total(95%CI)
Test for heterogeneity chi-square=0.00  df=0  p<0.00001
Test for overall effect  z=-0.34  p=0.7

Favours treatment

Favours control
### Comparison: 13 Nevirapine + standard ART vs placebo + standard ART

#### Outcome: 01 HIV infection of the child

<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment n/N</th>
<th>Control n/N</th>
<th>OR (95%CI Fixed)</th>
<th>Weight %</th>
<th>OR (95%CI Fixed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PACTG 316 IP, PNb</td>
<td>9 / 594</td>
<td>8 / 580</td>
<td></td>
<td>100.0</td>
<td>1.10[0.42,2.87]</td>
</tr>
</tbody>
</table>

**Total (95%CI)**

9 / 594 | 8 / 580 | 100.0 | 1.10[0.42,2.87]

Test for heterogeneity chi-square=0.0  df=0
Test for overall effect z=0.19  p=0.8

![Diagram showing the comparison between treatment and control groups](image-url)
Side effects of ART

• Fatal lactic acidosis with stavudine plus didanosine
• Mitochondrial toxicity with ZDV and 3TC
• Long term effects on uninfected infants (>95%)
  – rare events may not be important when decreasing MTCT from 25% to 5% but may be important if decreasing MTCT from 1% to 0.5%
Nevirapine

• One dose of nevirapine in labour and one to baby. Low toxicity.

Nevirapine

- Offered to all HIV+ women
- Offered to all HIV+ women plus all women of unknown serostatus
- In areas of high prevalence without good VCT facilities – offered to all women
Breast feeding

- Randomised controlled trial


  - Four clinics in Nairobi
  - Formula provided and safe preparation taught
Breastfeeding and HIV infection

<table>
<thead>
<tr>
<th>Infants age</th>
<th>No. of infants with HIV-1 infection</th>
<th>Cumulative HIV-1 infection rates</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Breastfeeders</td>
<td>Formula Feeders</td>
</tr>
<tr>
<td>Birth</td>
<td>15</td>
<td>7</td>
</tr>
<tr>
<td>6 weeks</td>
<td>43</td>
<td>20</td>
</tr>
<tr>
<td>14 weeks</td>
<td>47</td>
<td>28</td>
</tr>
<tr>
<td>6 months</td>
<td>53</td>
<td>32</td>
</tr>
<tr>
<td>12 months</td>
<td>63</td>
<td>36</td>
</tr>
<tr>
<td>24 months</td>
<td>71</td>
<td>41</td>
</tr>
</tbody>
</table>
Breastfeeding and mortality

<table>
<thead>
<tr>
<th>Infants age</th>
<th>No. of cumulative infant deaths</th>
<th>Cumulative mortality rates</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Breastfeeders</td>
<td>Formula Feeders</td>
<td>Breastfeeders</td>
</tr>
<tr>
<td>6 weeks</td>
<td>2</td>
<td>8</td>
<td>1.0</td>
</tr>
<tr>
<td>14 weeks</td>
<td>8</td>
<td>13</td>
<td>4.1</td>
</tr>
<tr>
<td>6 months</td>
<td>17</td>
<td>22</td>
<td>8.8</td>
</tr>
<tr>
<td>12 months</td>
<td>32</td>
<td>31</td>
<td>16.7</td>
</tr>
<tr>
<td>24 months</td>
<td>45</td>
<td>39</td>
<td>24.4</td>
</tr>
</tbody>
</table>

HIV infection 3/170 versus 21/200 RR 0.17 (0.05-0.55)

Post-partum comps 0/189 versus 0/221

RR of CS on HIV infection the same for ART naïve and experienced
Caesarean section

- Caesarean section rate 5%
- HIV prevalence 25% in South Africa

- Increase Caesarean section rate to 30%
  - six-fold increase
  - who is going to do the caesarean sections?
  - what happens if the woman has another pregnancy?
If viral load is low can women deliver vaginally?

• 7 collaborative cohort studies
• 44 cases of MTCT from 1202 women with viral load <1000 copies/ml

• if on ART, MTCT risk ~1%
• if not on ART, MTCT ~10%
  – controlled for other factors including actual viral load

Ioannidis J et al. Perinatal transmission of human immunodeficiency virus type 1 by pregnant women with RNA viral loads <1000 copies/ml. J Inf Dis 2001;183:539-45
Vaginal lavage

### Comparison: 01 Vaginal lavage compared with non-lavage

**Outcome:** 01 HIV infection status of the child

<table>
<thead>
<tr>
<th>Study</th>
<th>Vaginal lavage n/N</th>
<th>Non-lavage n/N</th>
<th>OR (95%CI Fixed)</th>
<th>Weight %</th>
<th>OR (95%CI Fixed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gaillard 2001</td>
<td>63 / 307</td>
<td>64 / 295</td>
<td></td>
<td>100.0</td>
<td>0.93[0.63,1.38]</td>
</tr>
</tbody>
</table>

**Total (95%CI):** 63 / 307, 64 / 295

Test for heterogeneity chi-square=0.0 df=0

Test for overall effect z=-0.35 p=0.7

![Graph showing comparison between Vaginal lavage and Non-lavage]
Vitamin A

### Vitamin A – HIV infection

**Comparison: 01 Vitamin A supplementation versus no vitamin A supplementation**

**Outcome: 01 HIV infection in child**

<table>
<thead>
<tr>
<th>Study</th>
<th>Vitamin A n/N</th>
<th>No Vitamin A n/N</th>
<th>OR (95%CI Fixed)</th>
<th>Weight %</th>
<th>OR (95%CI Fixed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coutsoudis 1999</td>
<td>70 / 319</td>
<td>70 / 313</td>
<td></td>
<td>63.3</td>
<td>0.98[0.67,1.42]</td>
</tr>
<tr>
<td>Fawzi 1998a</td>
<td>53 / 239</td>
<td>39 / 214</td>
<td></td>
<td>36.7</td>
<td>1.28[0.81,2.03]</td>
</tr>
<tr>
<td><strong>Total(95%CI)</strong></td>
<td><strong>123 / 558</strong></td>
<td><strong>109 / 527</strong></td>
<td></td>
<td><strong>100.0</strong></td>
<td><strong>1.09[0.81,1.45]</strong></td>
</tr>
</tbody>
</table>

Test for heterogeneity chi-square=0.79, df=1, p=0.37
Test for overall effect z=0.56, p=0.6
### Comparison: Vitamin A supplementation versus no vitamin A supplementation

**Outcome:** Stillbirth

<table>
<thead>
<tr>
<th>Study</th>
<th>Vitamin A</th>
<th>No vitamin A</th>
<th>OR (95%CI Fixed)</th>
<th>Weight</th>
<th>OR (95%CI Fixed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coutsoudis 1999</td>
<td>6 / 341</td>
<td>4 / 330</td>
<td></td>
<td>14.6</td>
<td>1.46[0.41,5.22]</td>
</tr>
<tr>
<td>Fawzi 1998a</td>
<td>25 / 521</td>
<td>24 / 500</td>
<td></td>
<td>85.4</td>
<td>1.00[0.56,1.77]</td>
</tr>
<tr>
<td><strong>Total(95%CI)</strong></td>
<td><strong>31 / 862</strong></td>
<td><strong>28 / 830</strong></td>
<td></td>
<td>100.0</td>
<td>1.07[0.63,1.80]</td>
</tr>
</tbody>
</table>

Test for heterogeneity chi-square=0.28 df=1 p=0.6
Test for overall effect z=0.24 p=0.8
Prevention of MTCT

• With well funded healthcare services
  – antiretroviral therapy
  – elective caesarean section
  – avoidance of breast feeding
UK guidelines for management of HIV infection in pregnancy

Women who do not require treatment
  • zidovudine monotherapy from second trimester, in labour and to neonate for 6 weeks plus CS

Women who require treatment
  • triple therapy / HAART from second trimester, and to neonate for 6 weeks

Women who conceive on ART
  • consider suspending in first trimester
Prevention of MTCT

• With poorly funded health care services

  – short course zidovudine
  – nevirapine
  – ? combination antiretroviral therapy
  – ? avoidance of breast feeding
  – ? caesarean section
  – ? vaginal lavage
  – ? Vitamin A
  – others
    • episiotomy, instrumental delivery, early washing, nasopharyngeal aspiration
PMTCT programmes

• voluntary HIV testing
• antiretroviral therapy during late pregnancy or in labour
• antiretroviral therapy to the newborn
• avoidance of episiotomy, ARM, invasive fetal monitoring
But………

• Based on WHO estimates, in Africa:
  – antenatal care (at least one visit)
    • 20% to 99% (average 62%)
  – professional at delivery
    • 2% to 99% (average 36%)
Can PMTCT programmes work?
Paediatric AIDS cases in Thailand

![Line graph showing the number of paediatric AIDS cases in Thailand from 1990 to 2000.]
Enhanced PMTCT

• ART during pregnancy and after birth to mother
Voluntary HIV testing in pregnancy

- Necessary in order to offer effective interventions to prevent MTCT and perhaps prevent early maternal death

- Problems
  - quality control and availability of testing
  - women's attitudes to testing
  - clinicians' attitudes to testing
• “If we can get cold Coca Cola and beer to every remote corner of Africa, it should not be impossible to do the same with drugs.”

Joep Lange,
President, International AIDS Society, Barcelona, July 2002
The future

- Primary prevention
- Delivery of effective interventions
- Improved prevention of MTCT (risk versus benefit)
- Maintainance of maternal health
- Status of chronic disease
- Equity of prognosis
Is primary prevention possible?