

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

Number of people living with HIV/AIDS	Total	42 m
	Adults	38.6 m
	<i>Women</i>	<i>19.2 m</i>
	Children under 15 years	3.2 m
People newly infected	Total	5 m
	Adults	4.2 m
	<i>Women</i>	<i>2 m</i>
	Children under 15 years	800 000
Aids deaths in 2002	Total	3.1 m
	Adults	2.5 m
	<i>Women</i>	<i>1.2 m</i>
	Children under 15 years	610 000

Regional HIV/AIDS statistics and features, end of 2002

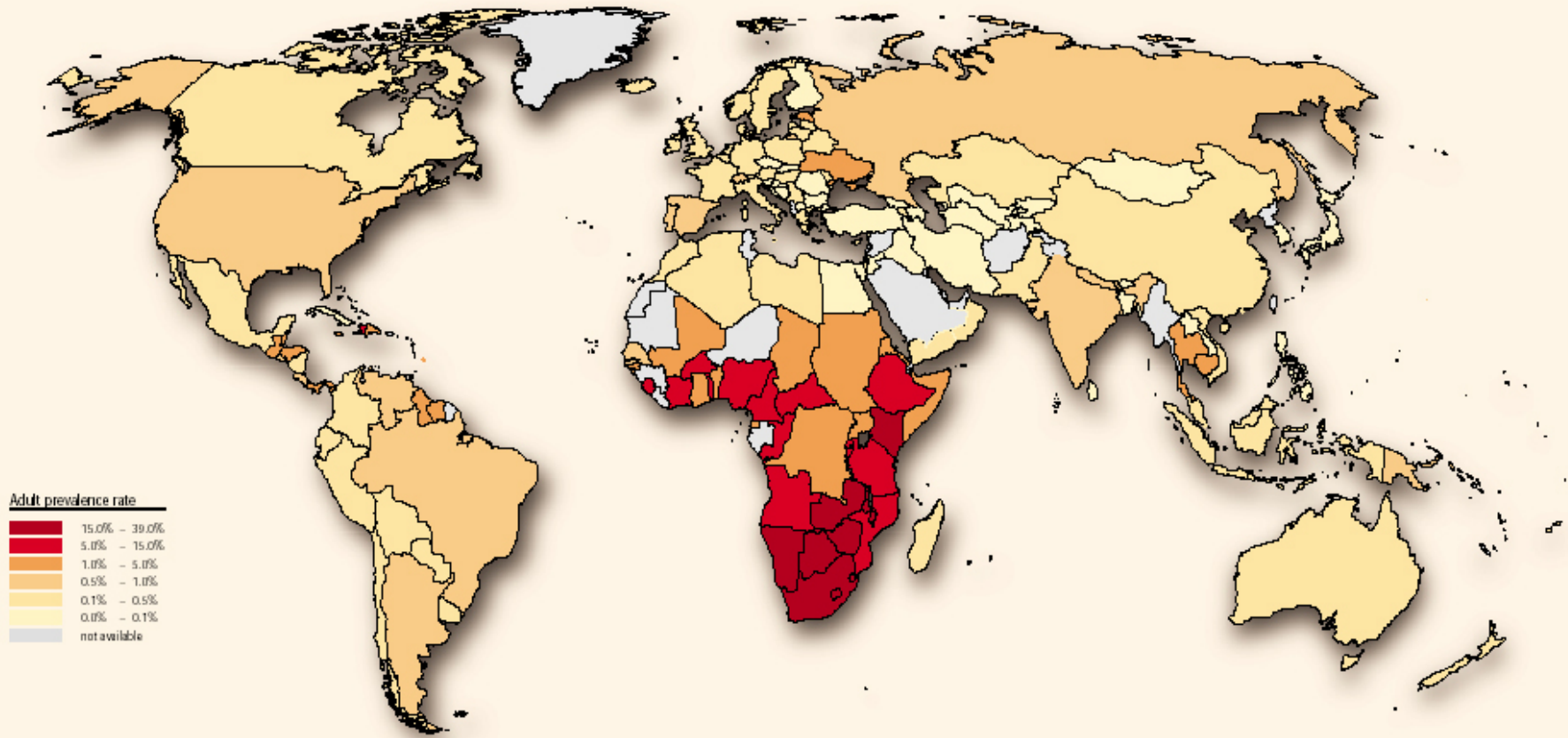
	Epidemic started	Adults & children Living with HIV	Adults and children newly infected with HIV	Adult prevalence rate*	% of HIV-positive adults who are women	Main mode(s) of transmission for those living with HIV/AIDS**
Sub-Saharan Africa	Late '70s Early '80s	29.4 m	3.5 m	8.8%	58%	Hetero
N Africa & Middle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



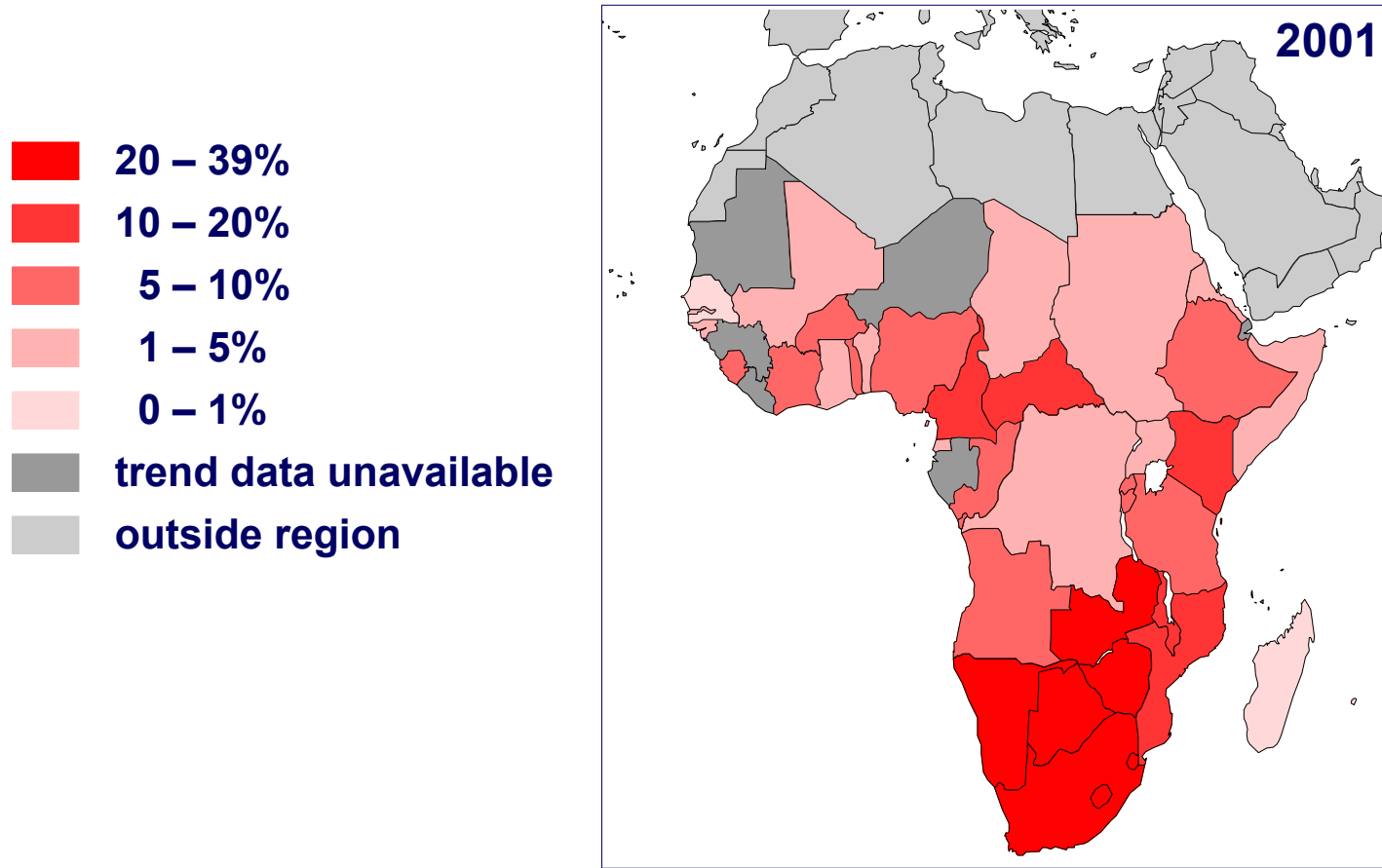
Joint United Nations Programme on HIV/AIDS
UNAIDS
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A global view of **HIV** infection

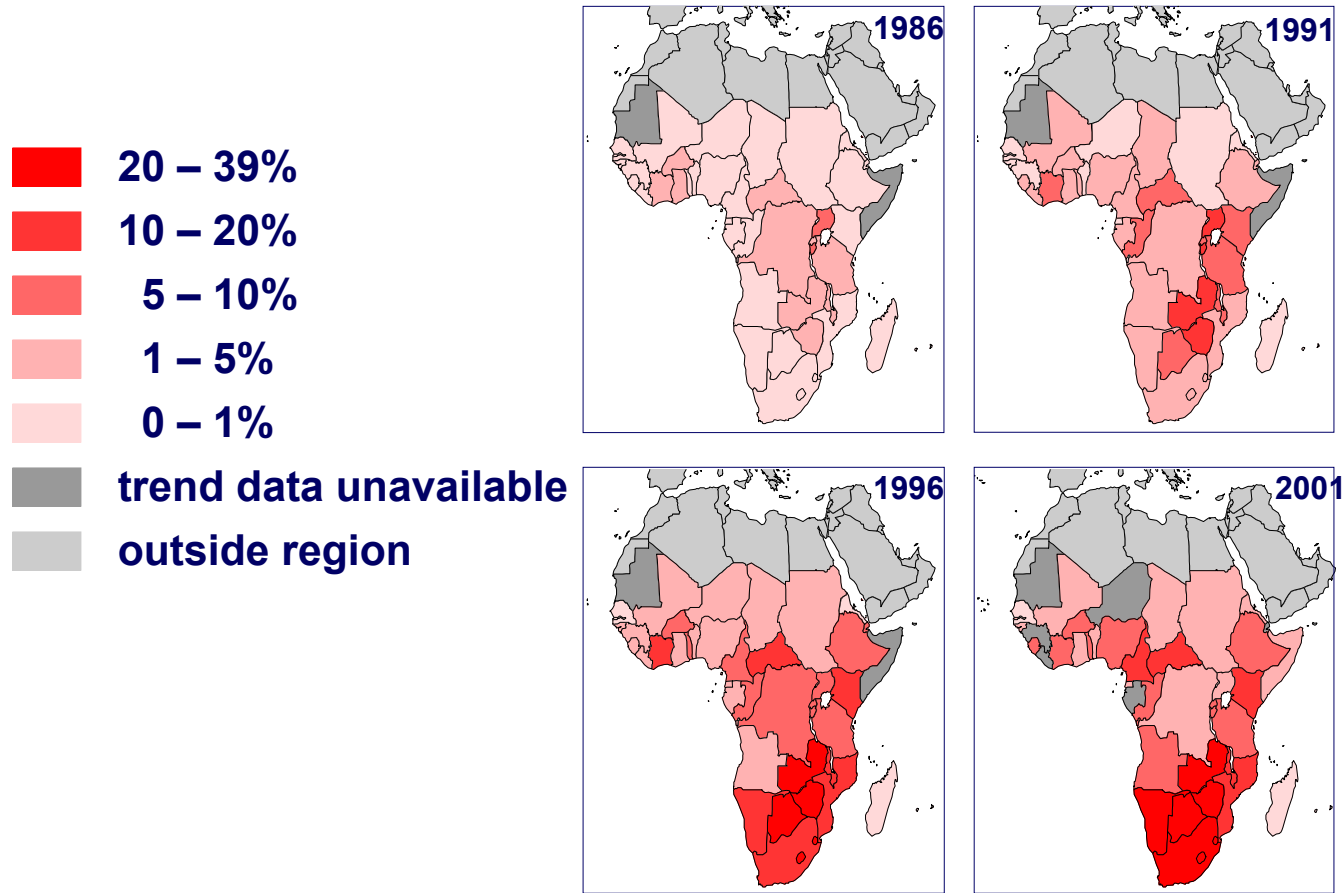
40 million adults living with HIV/AIDS as of end 2001



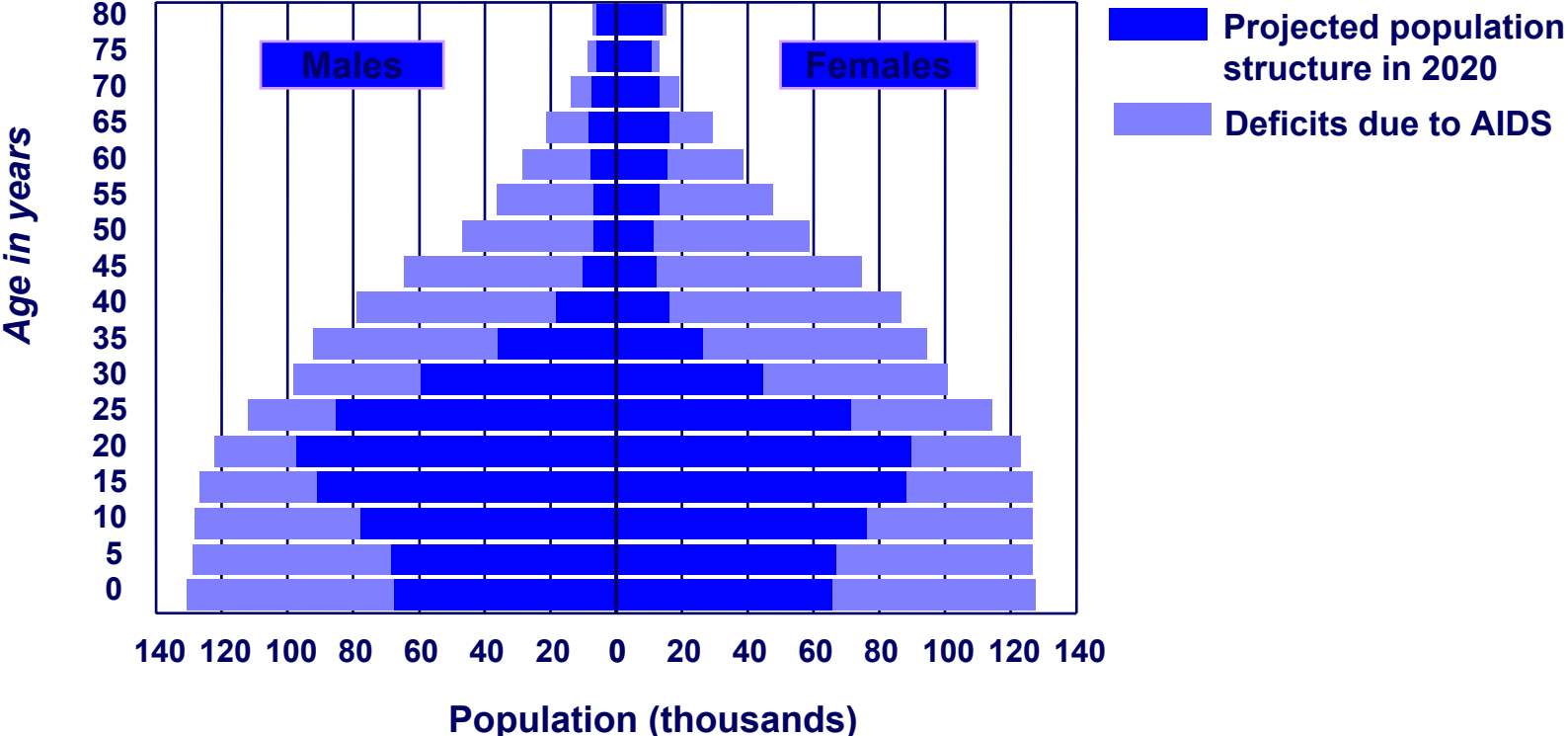
HIV prevalence in adults in sub-Saharan Africa, end 2001



HIV prevalence in adults in sub-Saharan Africa, 1986-2001

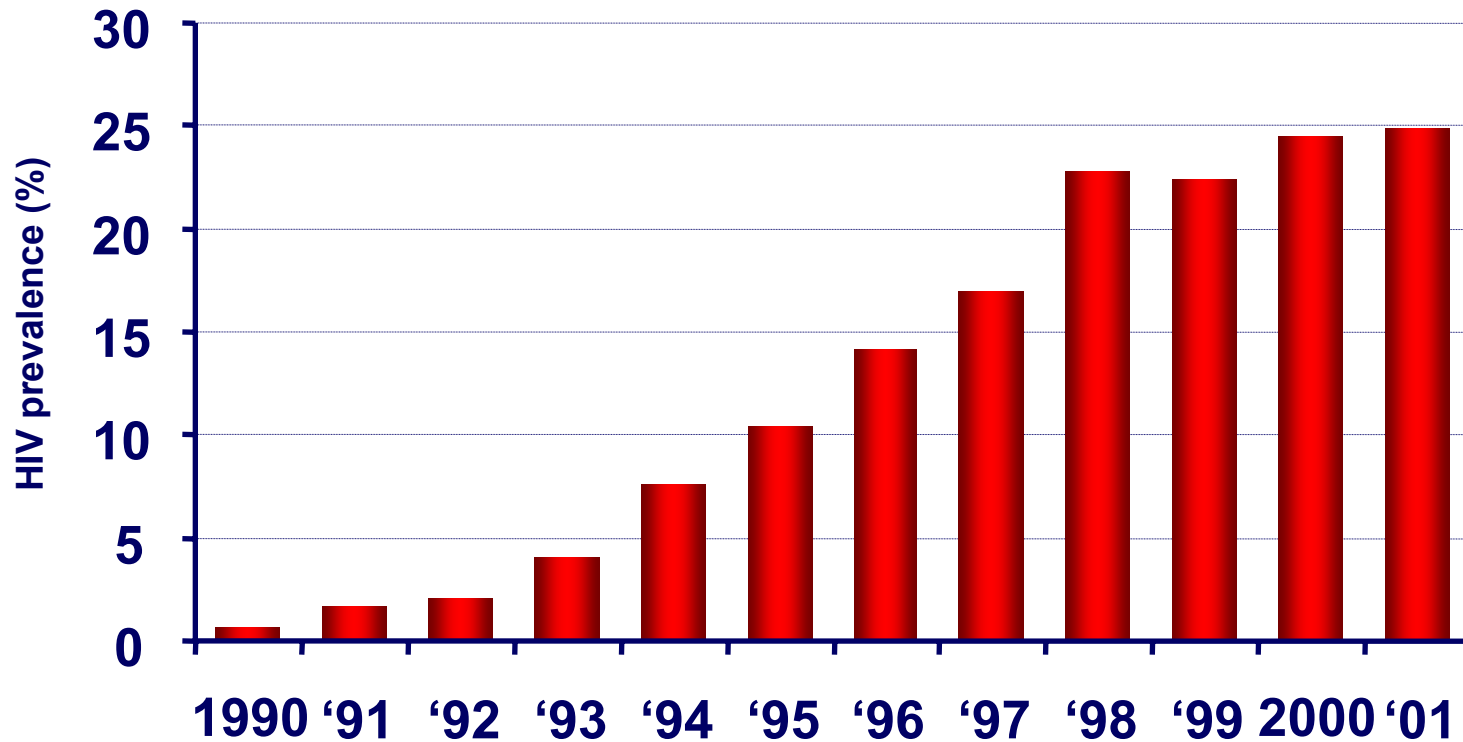


Projected population structure with and without the AIDS epidemic, Botswana, 2020



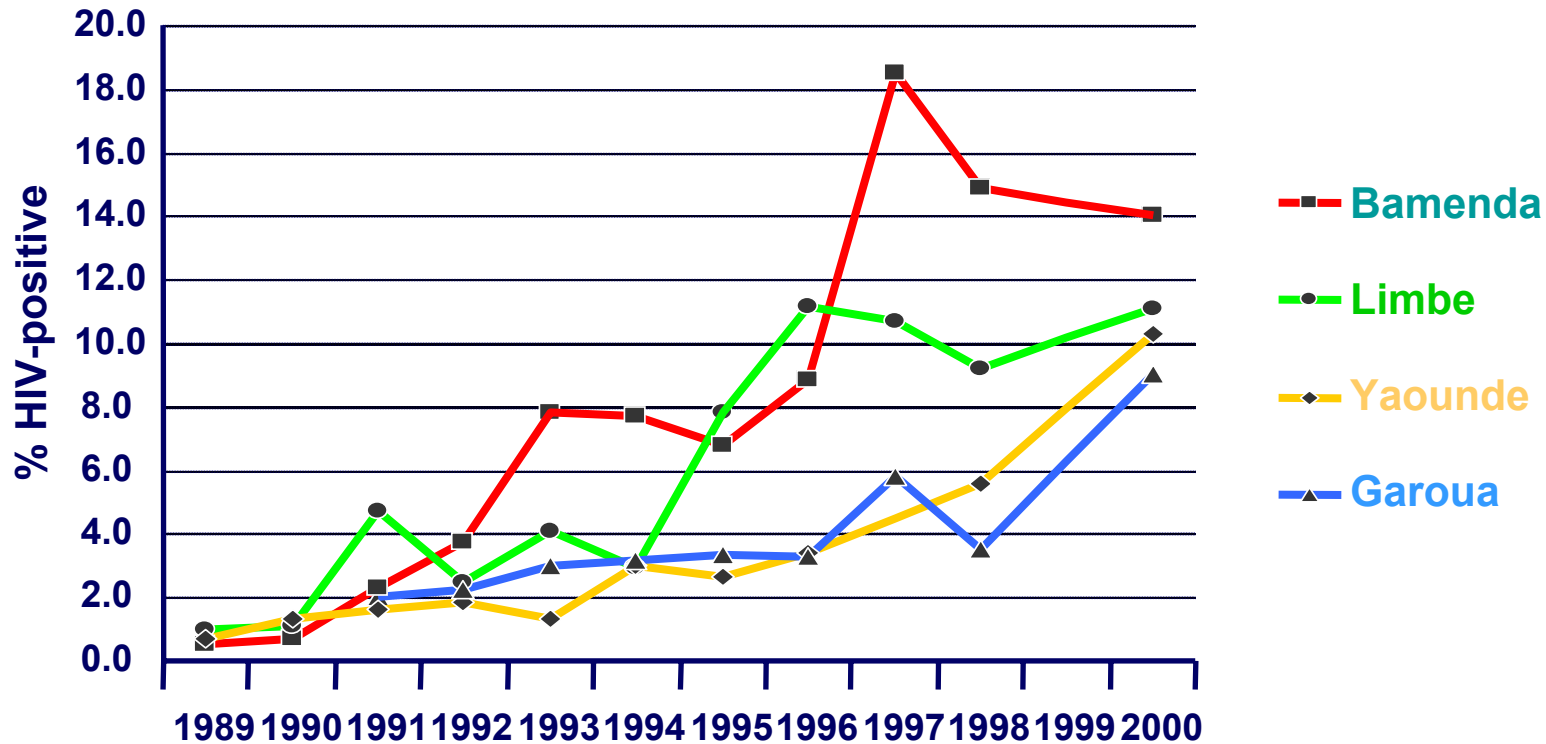
Source: US Census Bureau, World Population Profile 2000

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



Source: National AIDS Programme, Cameroon (1989-2000). Data compiled by the US Census Bureau

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



UNAIDS
UNITED NATIONS
PROGRAMME ON
HUMAN IMMUNODEFICIENCY
ACQUISITION (HIV/AIDS)

00000-8-7 - 1 December 2002



World Health
Organization

Estimated number of children (<15 years) newly infected with HIV during 2002



Total: 800 000

Estimated deaths in children (<15 years) from HIV/AIDS during 2002



Total: 610 000



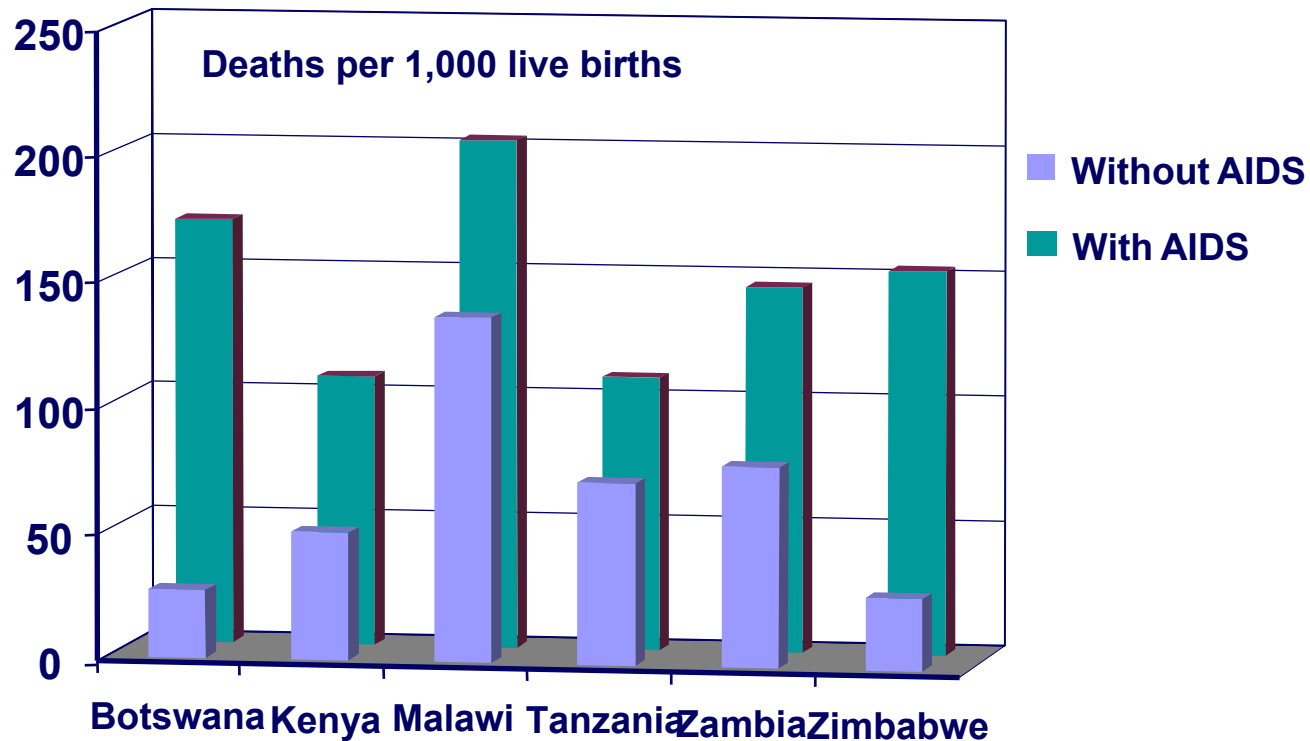
UNAIDS
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HIV/AIDS

00000-E-0 - 1 December 2002



World Health
Organization

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

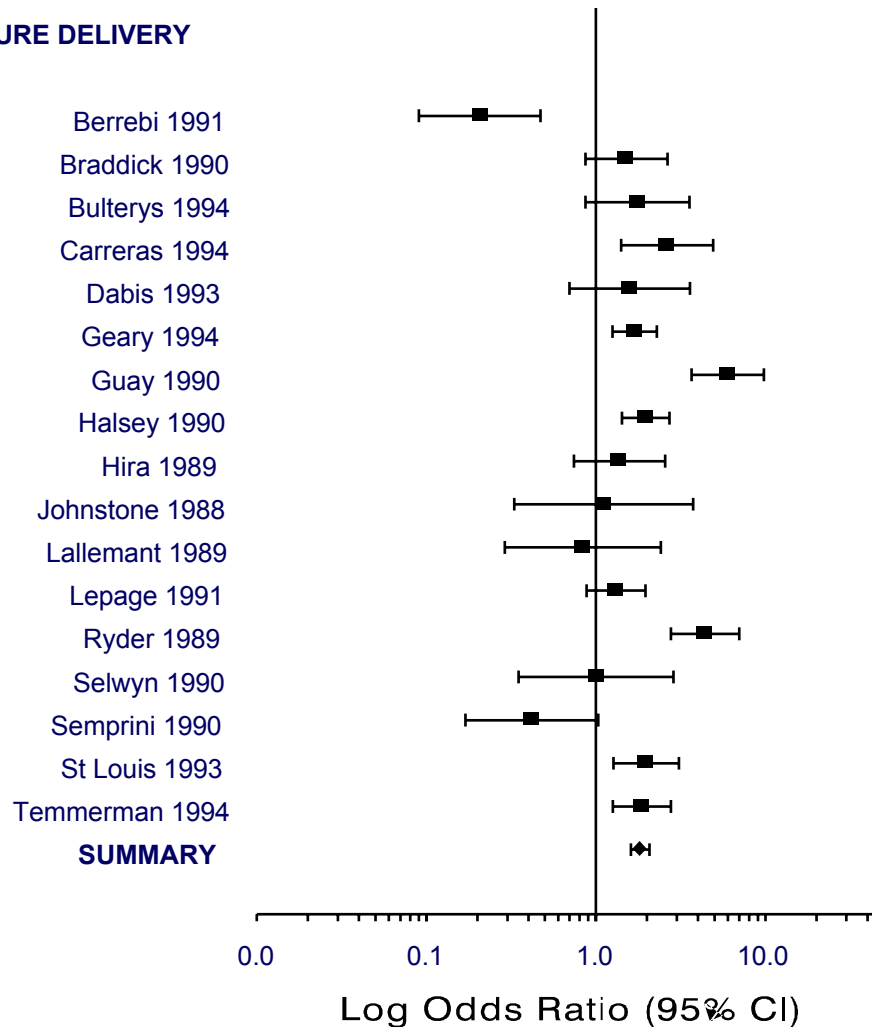
- Progression of HIV disease in mother in absence of treatment
- Progression of HIV disease in mother with treatment (antiretroviral therapy)
- Impact of maternal death on children under 1 year of age

Effect of HIV infection on pregnancy

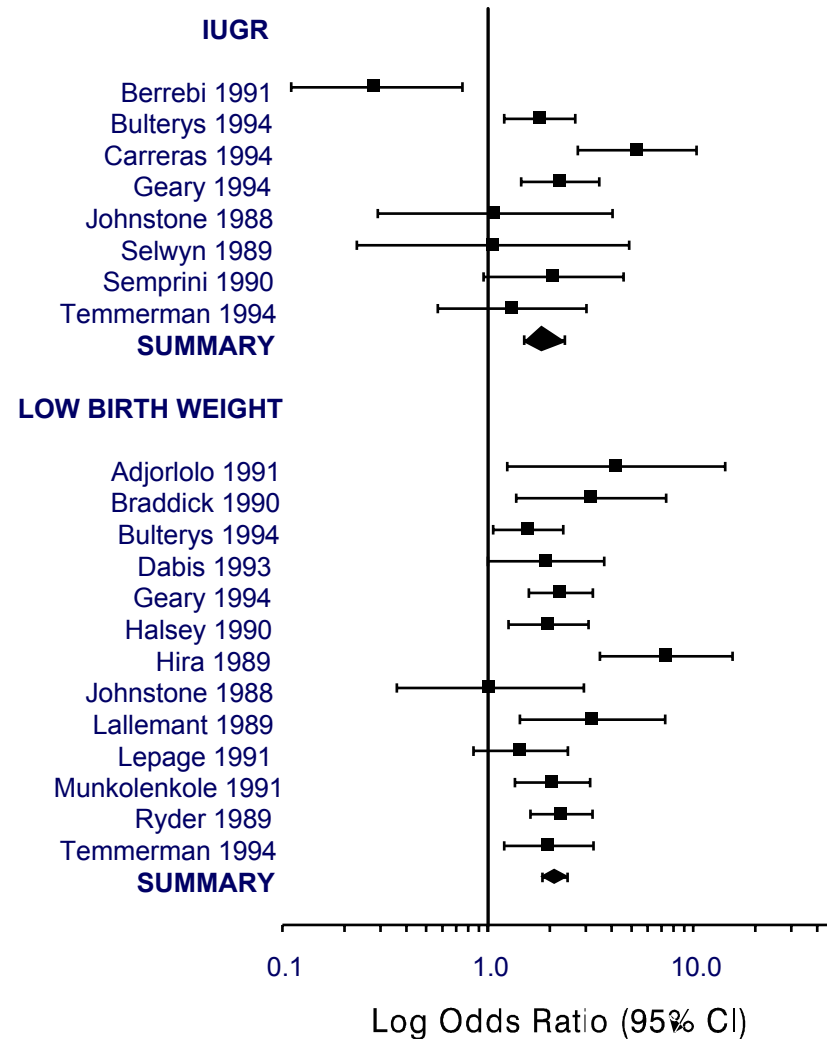
- Pregnancy outcome
 - preterm birth
 - IUGR/SGA and low birthweight
 - stillbirth
 - perinatal/neonatal/infant mortality

Effect on Perinatal Outcome

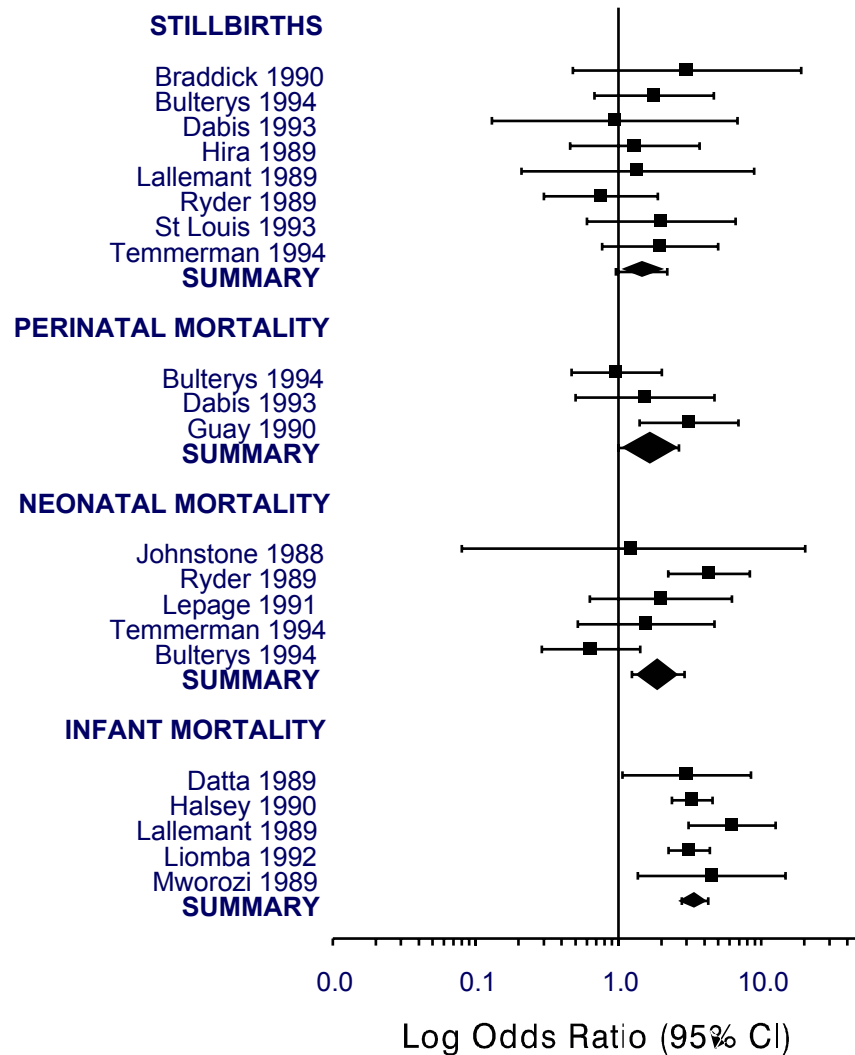
PREMATURE DELIVERY



Effect on Perinatal Outcome



Effect on Perinatal Outcome



Mother-to-child transmission

Mother-to-child transmission

- In resource poor countries
 - 25-45%
- In industrialised countries
 - 15-30%

Mother-to-child transmission

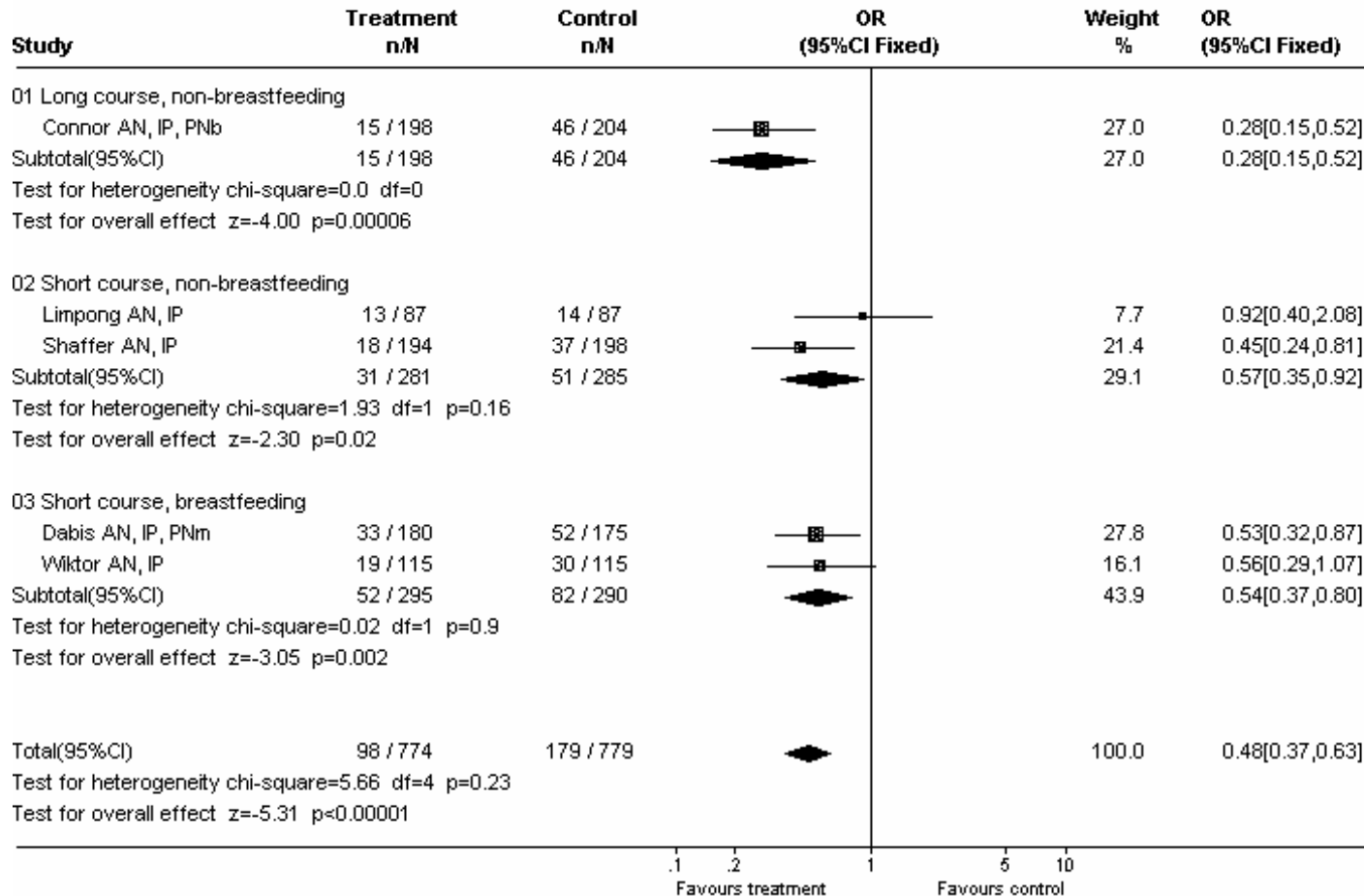
- Risk factors for transmission
 - prematurity
 - high viral load
 - symptomatic maternal disease
 - low CD4 cell count
 - breast feeding
 - mode of delivery
 - duration of membrane rupture
 - duration of second stage
 - sexually transmitted infections

Antiretroviral therapy

- Brocklehurst P, Volmink J. Antiretrovirals for reducing the risk of mother-to-child transmission of HIV infection (Cochrane Review). In: *The Cochrane Library*, Issue 1, 2003. Oxford: Update Software.
- Randomised controlled trials

Any ZDV versus placebo – HIV in child

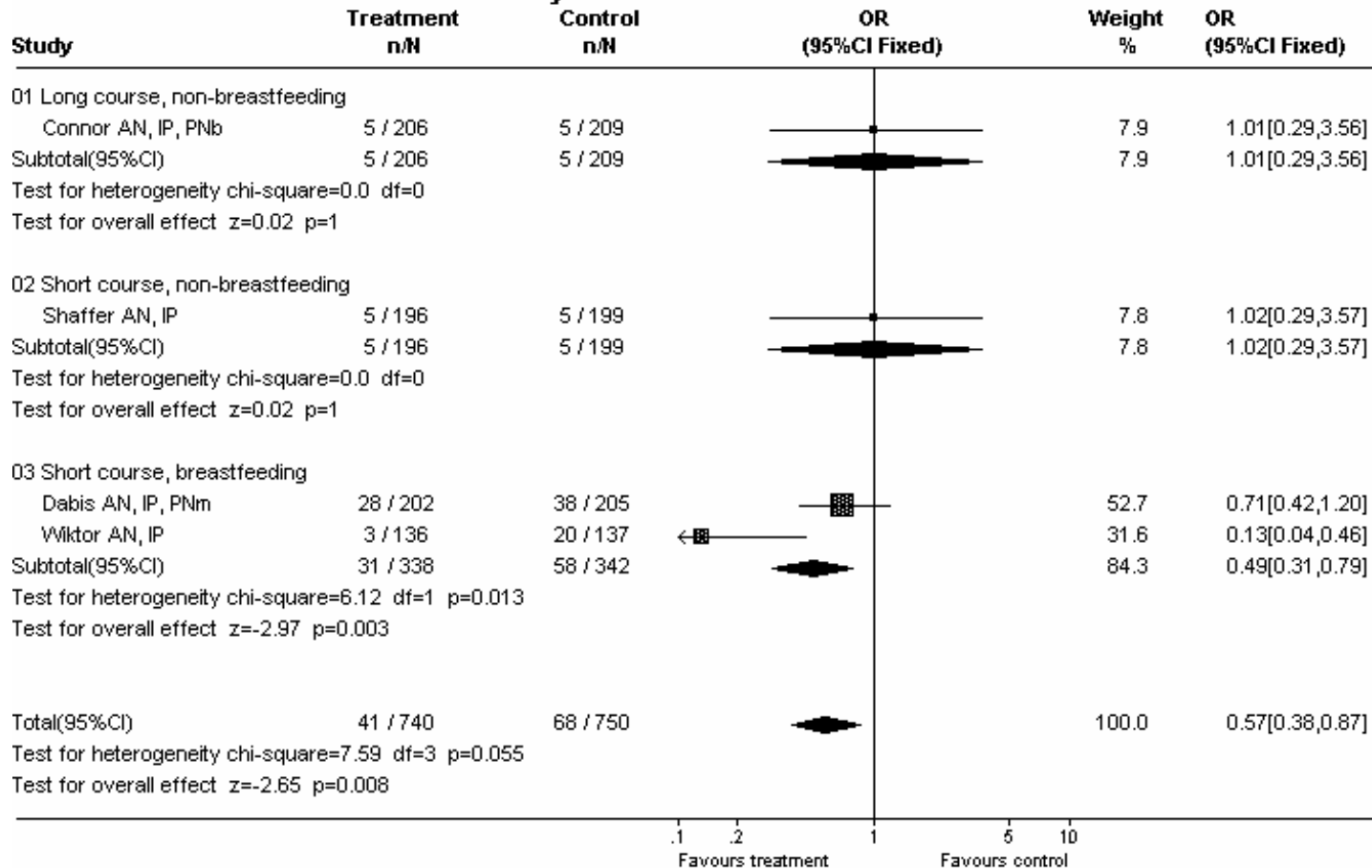
Comparison: 01 Zidovudine vs placebo
Outcome: 01 HIV infection of the child



Any ZDV versus placebo – death <1 year

Comparison: 01 Zidovudine vs placebo

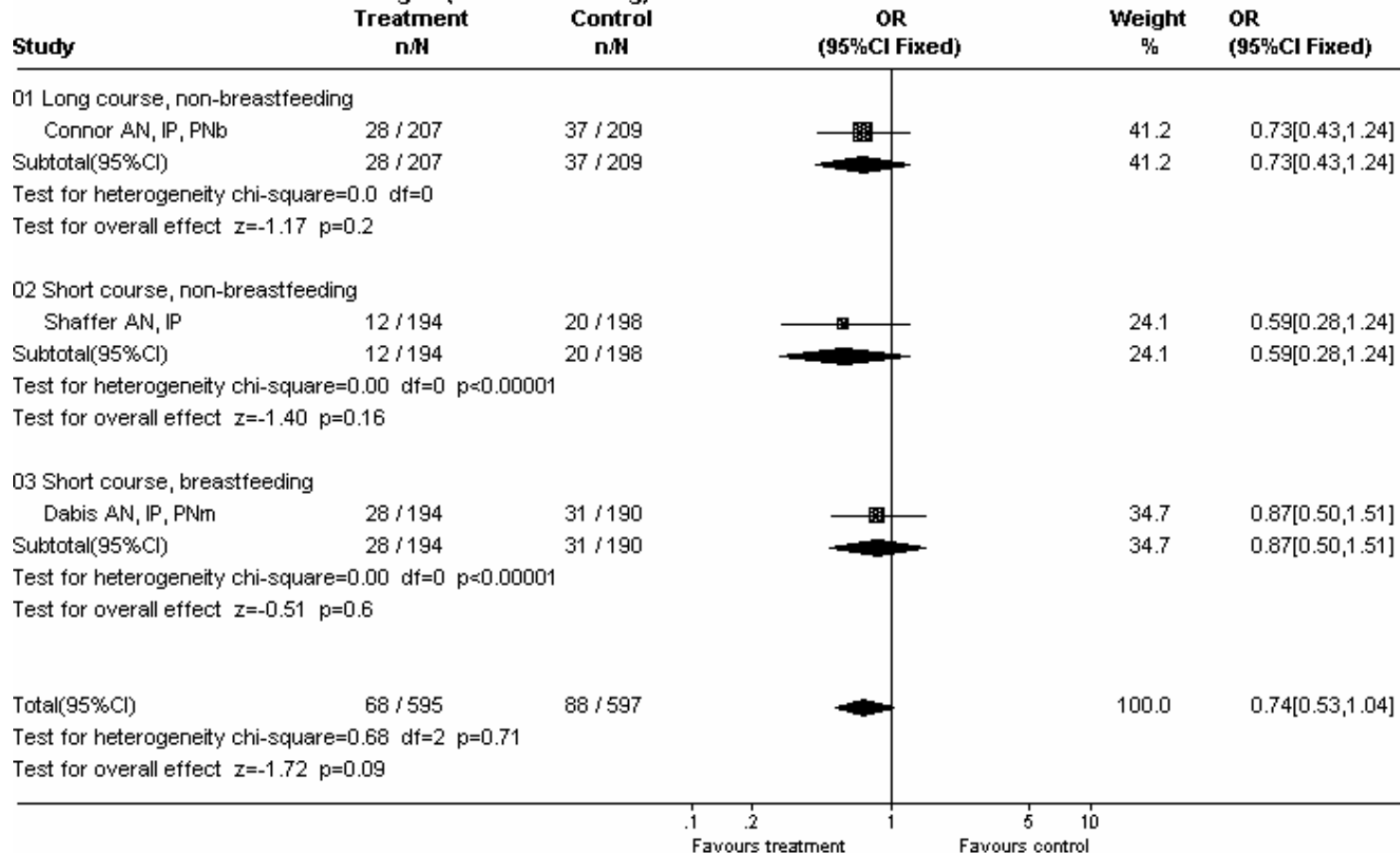
Outcome: 03 Death of the child within 1 year after birth



Any ZDV versus placebo – low birth weight

Comparison: 01 Zidovudine vs placebo

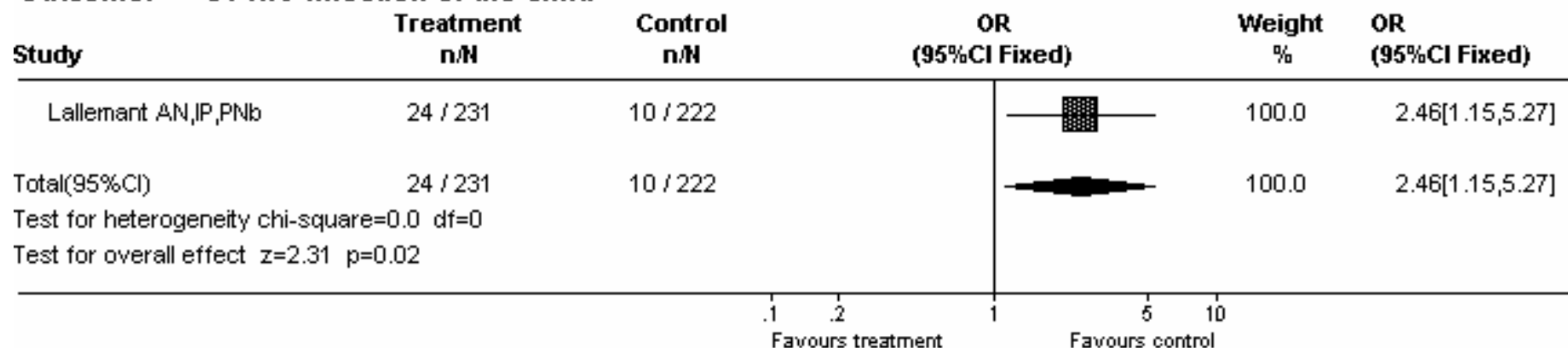
Outcome: 07 Low birth weight (less than 2500g)



Short course ZDV versus long course ZDV – HIV in child

Comparison: 02 Zidovudine (short-short) vs zidovudine (long-long)

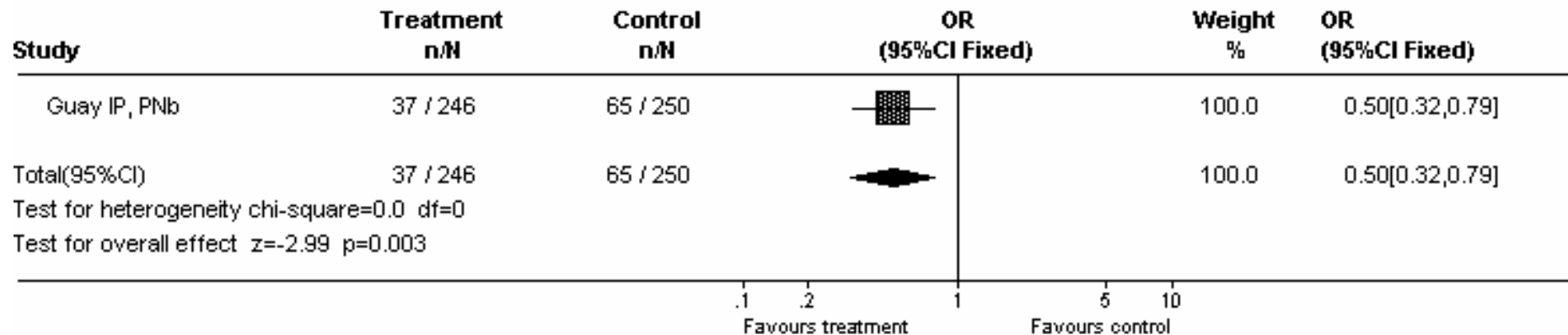
Outcome: 01 HIV infection of the child



NVP versus ZDV – HIV in child

Comparison: 05 Nevirapine vs zidovudine

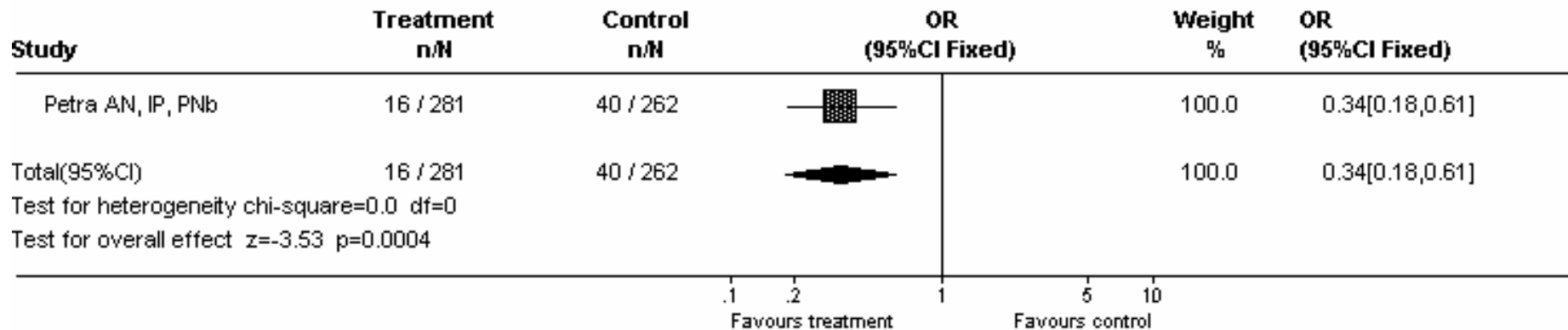
Outcome: 01 HIV infection of the child



ZDV plus 3TC versus placebo – HIV in child

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

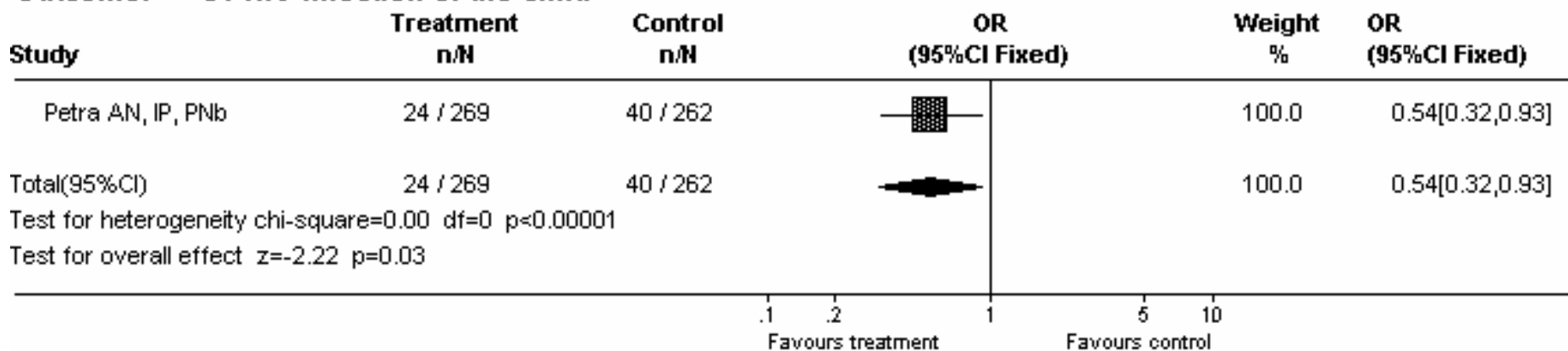
Outcome: 01 HIV infection of the child



ZDV plus 3TC versus placebo – HIV in child

Comparison: 07 Zidovudine + lamivudine (IP, PNmb) vs placebo

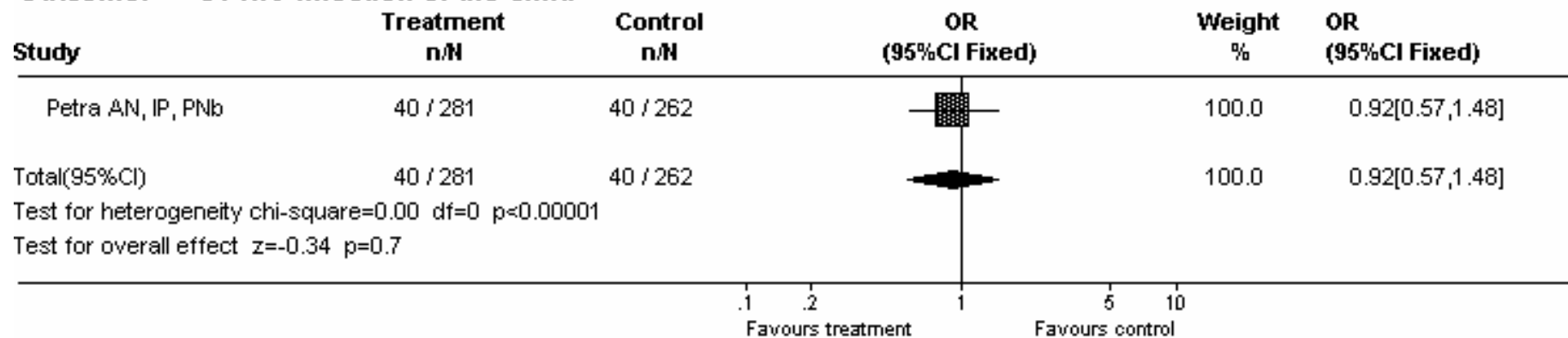
Outcome: 01 HIV infection of the child



ZDV plus 3TC versus placebo – HIV in child

Comparison: 08 Zidovudine + lamivudine (IP) vs placebo

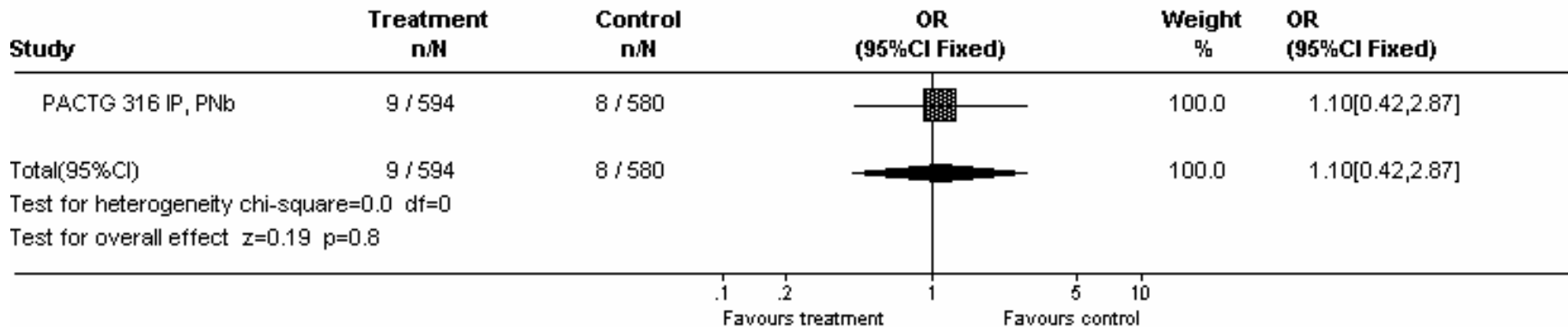
Outcome: 01 HIV infection of the child



NVP plus ART versus ART – HIV in child

Comparison: 13 Nevirapine + standard ART vs placebo + standard ART

Outcome: 01 HIV infection of the child



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.
- Prevention of mother-to-child transmission of HIV. Use of nevirapine among women of unknown serostatus. Report of a technical consultation, 5-6 December 2001, Geneva.

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
- Nduati R, John G, Mbori-Ngacha D, Richardson B, Overbaugh J, Mwatha A, Ndinya-Achola J, Bwayo J, Onyango F, Hughes J, Kreiss J. Effect of breastfeeding and formula feeding on transmission of HIV-1. A randomized clinical trial. JAMA 2000;283:1167-1174
- Four clinics in Nairobi
- Formula provided and safe preparation taught

Breastfeeding and HIV infection

	No. of infants with HIV-1 infection		Cumulative HIV-1 infection rates		
Infants age	Breastfeeders	Formula Feeders	Breastfeeders	Formula Feeders	p value
Birth	15	7	7.0	3.1	0.35
6 weeks	43	20	19.9	9.7	0.005
14 weeks	47	28	24.5	13.2	0.007
6 months	53	32	28.0	15.9	0.009
12 months	63	36	32.3	18.2	0.003
24 months	71	41	36.7	20.5	0.001

Breastfeeding and mortality

	No. of cumulative infant deaths		Cumulative mortality rates		
Infants age	Breastfeeders	Formula Feeders	Breastfeeders	Formula Feeders	p value
6 weeks	2	8	1.0	3.9	0.06
14 weeks	8	13	4.1	6.4	0.30
6 months	17	22	8.8	10.8	0.48
12 months	32	31	16.7	15.4	0.71
24 months	45	39	24.4	20.0	0.30

Caesarean section

The European Mode of delivery Collaboration. Elective caesarean-section versus vaginal delivery in prevention of vertical HIV-1 transmission: a randomised clinical trial. Lancet 1999;353:1035-9.

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

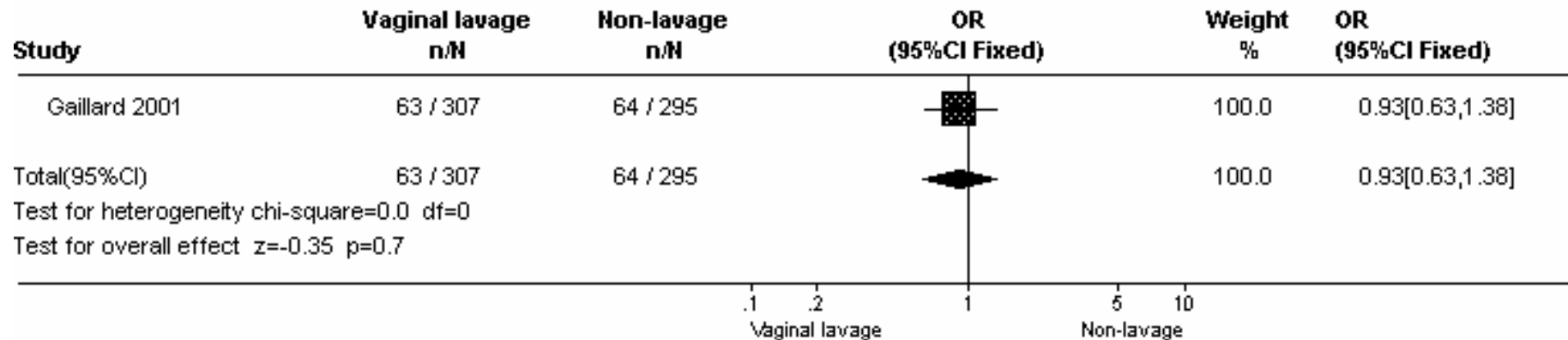
Vaginal lavage

- Shey Wiysonge CU, Brocklehurst P, Sterne JAC. Vaginal disinfection during labour for reducing the risk of mother-to-child transmission of HIV infection (Cochrane Review). In: *The Cochrane Library*, Issue 1, 2003. Oxford: Update Software.

Vaginal disinfection – HIV infection

Comparison: 01 Vaginal lavage compared with non-lavage

Outcome: 01 HIV infection status of the child



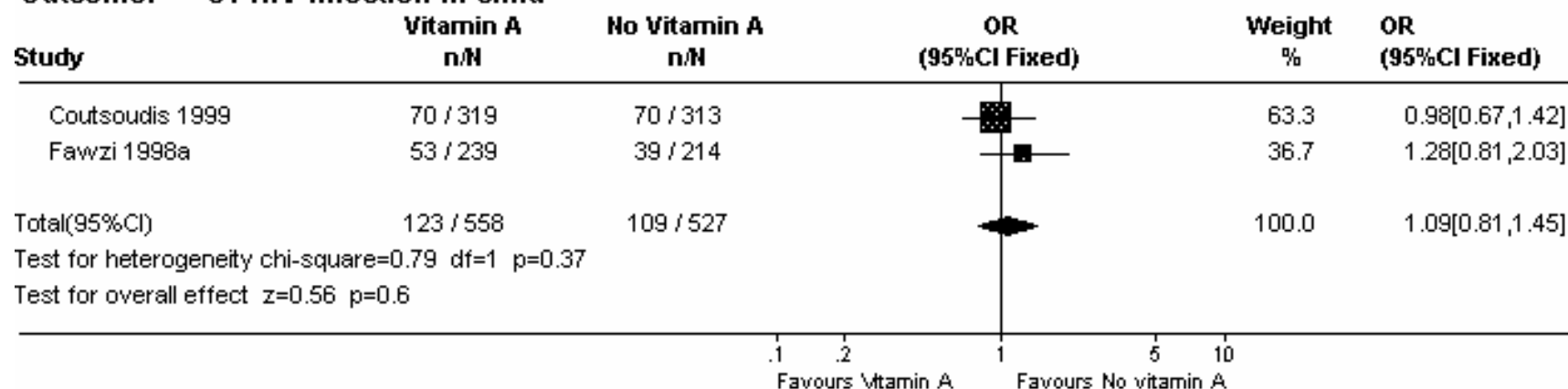
Vitamin A

- Shey Wiysonge CU, Brocklehurst P, Sterne JAC. Vitamin A supplementation for reducing the risk of mother-to-child transmission of HIV infection (Cochrane Review). In: *The Cochrane Library*, Issue 1, 2003. Oxford: Update Software.

Vitamin A – HIV infection

Comparison: 01 Vitamin A supplementation versus no vitamin A supplementation

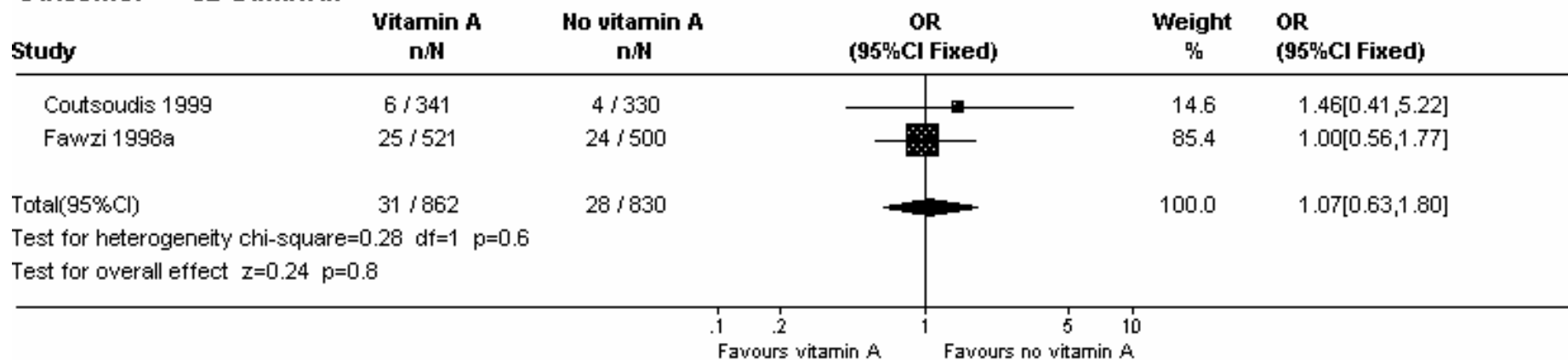
Outcome: 01 HIV infection in child



Vitamin A - stillbirth

Comparison: 01 Vitamin A supplementation versus no vitamin A supplementation

Outcome: 02 Stillbirth



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

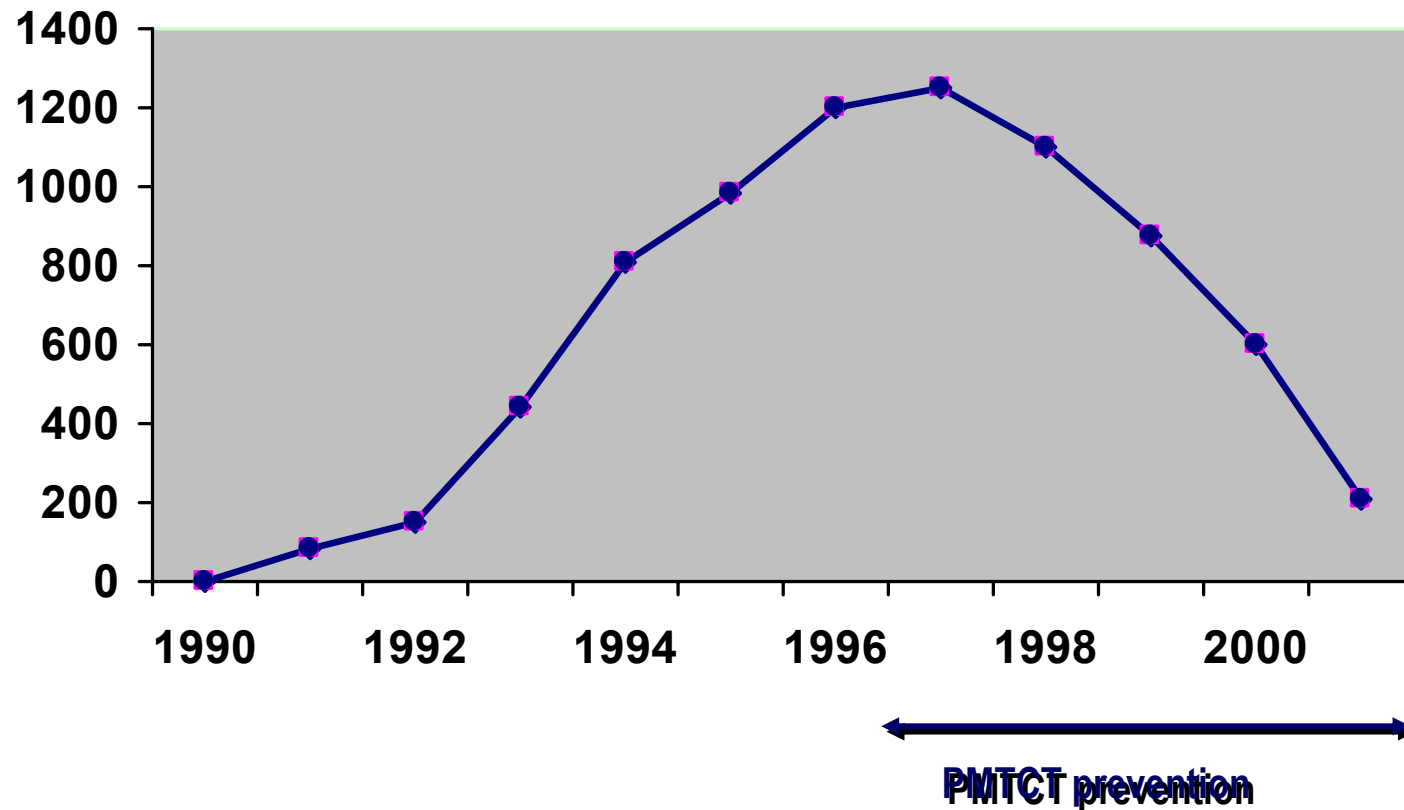
- voluntary HIV testing
- antiretroviral therapy during late pregnancy or in labour
- antiretroviral therapy to the newborn
- avoidance of episiotomy, ARM, invasive fetal monitoring

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



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
 - womens 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

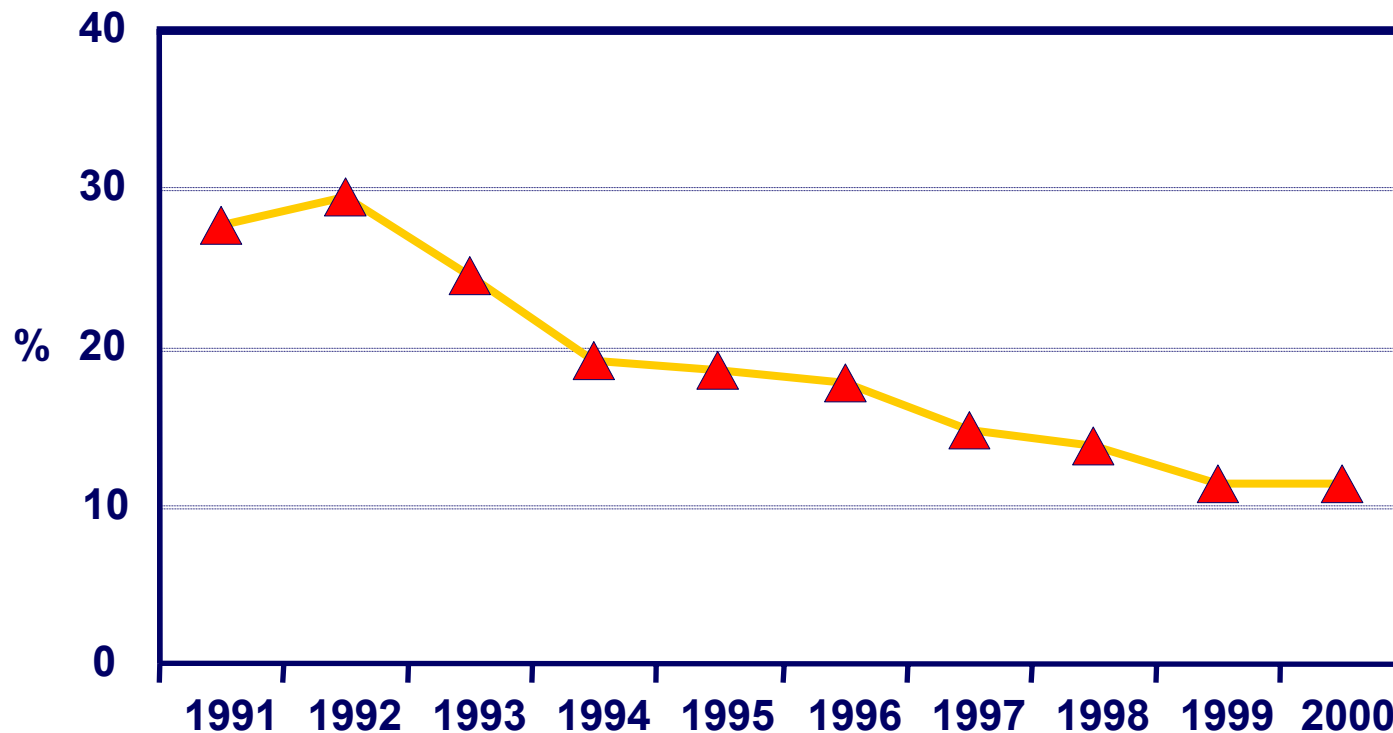
The future

- Primary prevention
- Delivery of effective interventions
- Improved prevention of MTCT (risk versus benefit)
- Maintenance of maternal health
- ?Status of chronic disease

- Equity of prognosis

Is primary prevention possible?

Trends in HIV prevalence among pregnant women in Kampala, Uganda: 1991-2000



Source: STD/AIDS Control Programme, Uganda (2001) HIV/AIDS Surveillance Report