Management options for HIV-1 infected pregnant women

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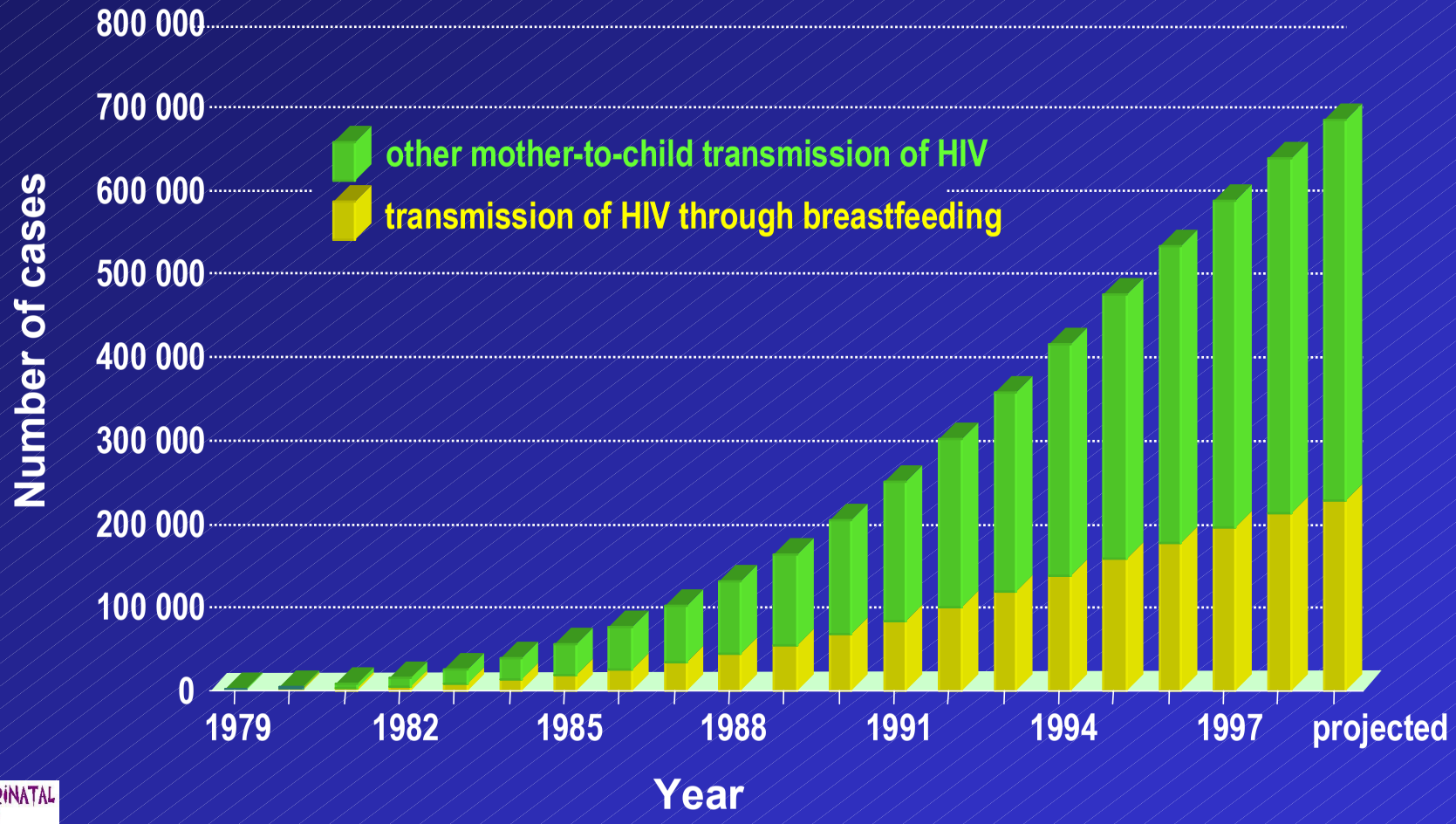
Mother-to-Child Transmission (MTCT) of HIV
Estimated Children Newly Infected in World



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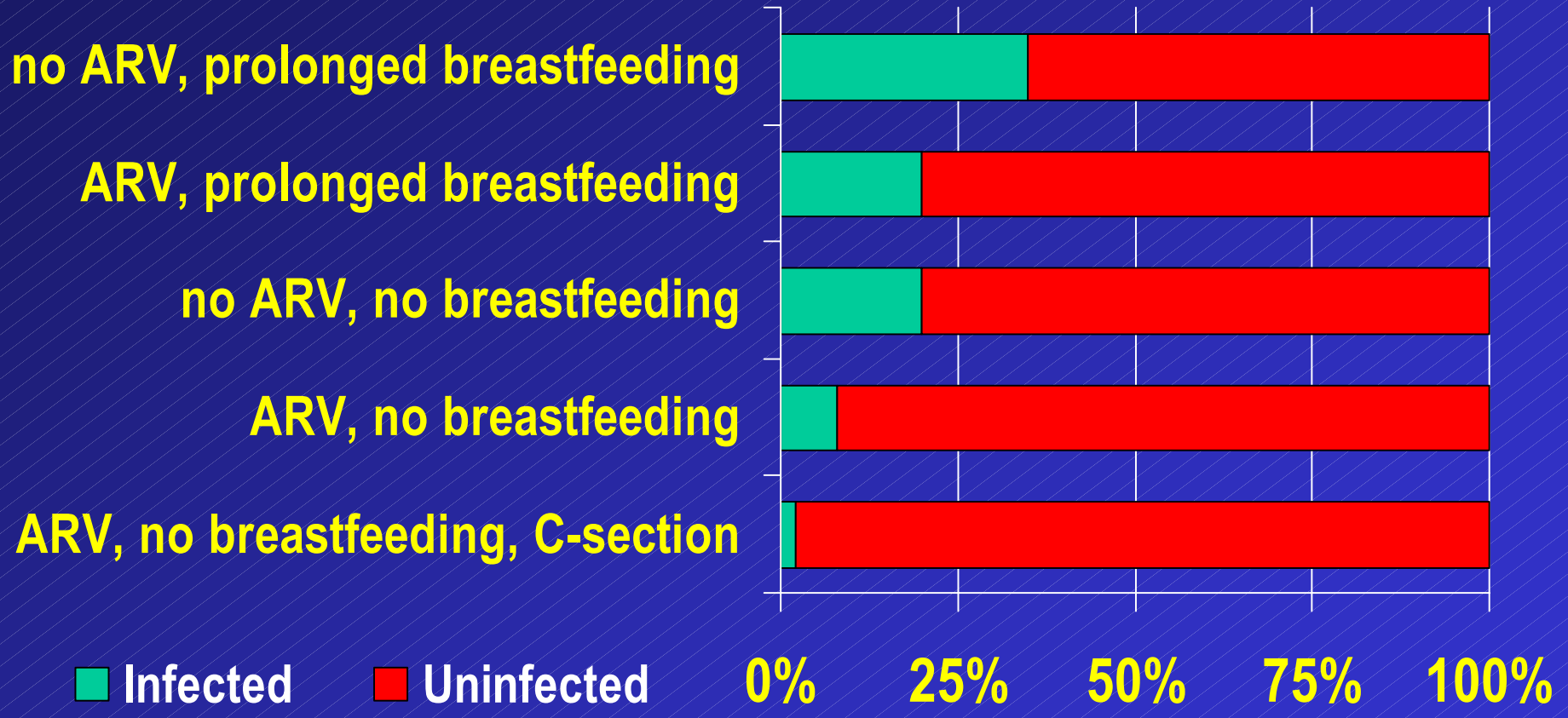
The variable risk of MTCT of HIV (with and without preventive interventions)



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HIV and pregnancy

- In high prevalence areas, HIV/AIDS has become a major cause of maternal mortality
- HIV/AIDS was the leading cause of maternal mortality in the South African Confidential Enquiry into Maternal deaths in 2000
- Accounts for 90% of deaths among child-bearing urban Rwandan women
- Some evidence for reduced fertility with disease progression

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Danger that HIV-positive women are seen "not as individuals, but merely as vectors of virus transmission"

The primary factor for deciding on treatment options should be the woman's clinical, immunological and virological status

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Management of an HIV-positive pregnant woman

- Screening for and treatment of concurrent STD
- Diagnosis and management of any opportunistic infections
- Cotrimoxazole prophylaxis if CD4 < 200/mm^3
- Malaria intermittent treatment in endemic areas
- Appropriate antiretroviral treatment
- Cervical smear
- Access to ongoing care postpartum
- Access to contraception

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TREATMENT DURING PREGNANCY

Pregnancy is not generally a contraindication for the most appropriate antiretroviral therapy for a woman or for most of the medical management of HIV-related conditions, but the risk to the fetus should always be considered, and treatment modified if necessary

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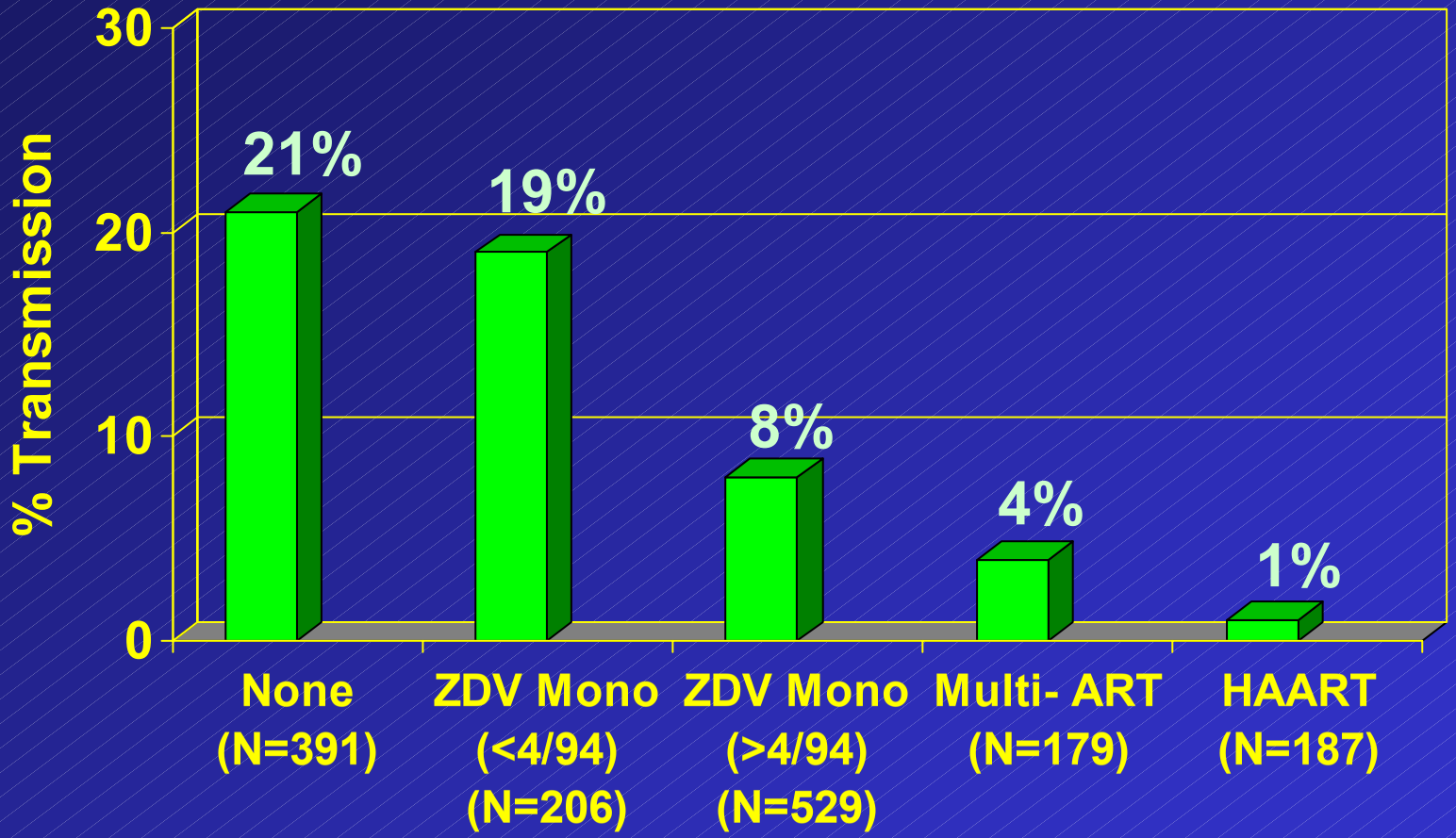
Antenatal Antiretroviral Treatment and Perinatal Transmission in WITS, 1990-1999

Blattner W. XIII AIDS Conf, July 2000, Durban S Africa (LBOr4)



Type ARV vs None				
p value:	0.76	<0.01	<0.01	<0.01

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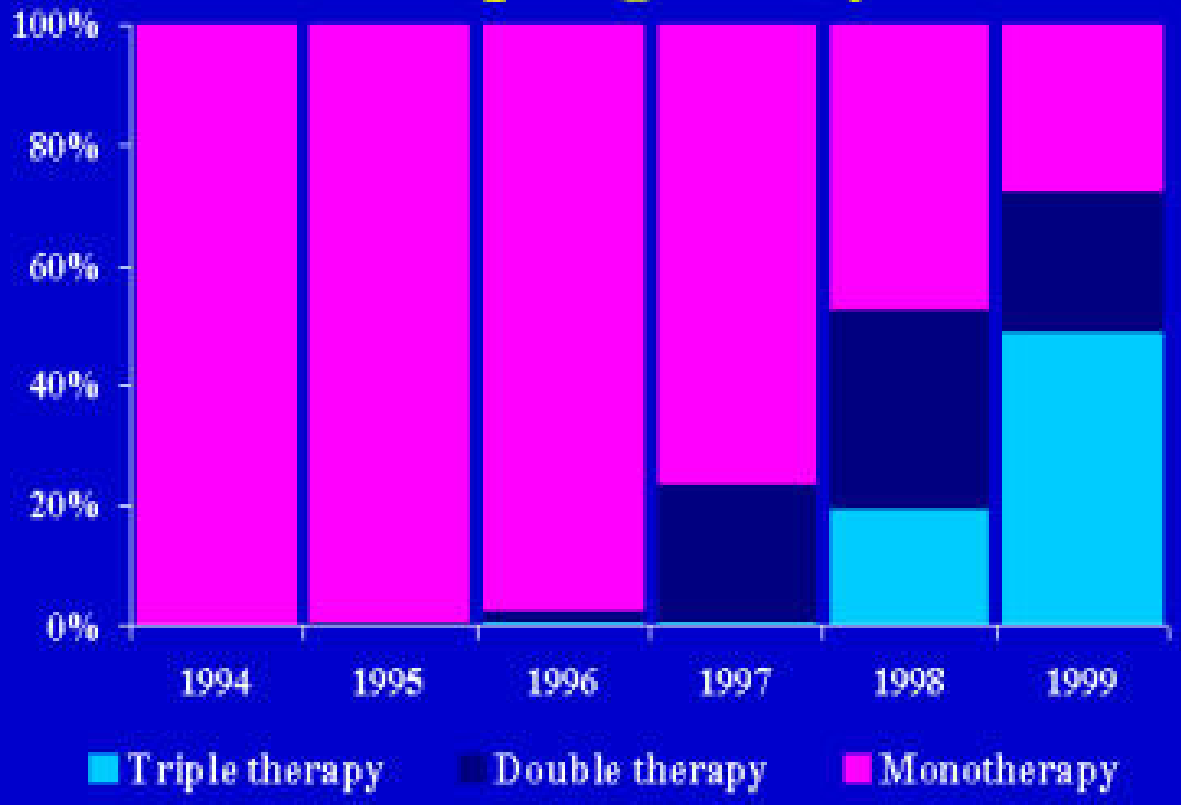
Changes over time in type of ART started in pregnancy, ECS



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Approved Anti-HIV Drugs

Drug	Approval Date	Annual Cost*
Retrovir (zidovudine, AZT)†	March 1987	$ 3,822
Videx (didanosine, ddI)†	October 1991	$ 2,729
Hivid (zalcitabine, ddC)	June 1992	$ 3,000
Zerit (stavudine, d4T)†	June 1994	$ 3,589
Epivir (lamivudine, 3TC)†	November 1995	$ 3,271
Invirase (saquinavir–HGC)	December 1995	$ 7,465
Norvir (ritonavir)†	March 1996	$ 8,618
Crixivan (indinavir)	March 1996	$ 6,016
Viramune (nevirapine)†	June 1996	$ 3,508
Viracept (nelfinavir)†	March 1997	$ 7,309
Rescriptor (delavirdine)	April 1997	$ 3,396
Combivir (AZT and 3TC)	September 1997	$ 7,093
Fortovase (saquinavir–SGC)	November 1997	$ 7,702
Sustiva (efavirenz)†	September 1998	$ 4,730
Ziagen (abacavir)†	December 1998	$ 4,396
Agenerase (amprenavir)†	April 1999	$ 7,613
Kaletra (lopinavir and ritonavir)†	September 2000	$ 8,125
Trizivir (AZT + 3TC + abacavir)	November 2000	$11,967

*Average annual wholesale price for recommended adult dosages
† Pediatric approval
Sources: 2000 Red Book; HHS/Kaiser Family Foundation HIV Treatment Guidelines

ARV THERAPY IN PREGNANCY

	FDA PREGNANCY CATEGORY
ZIDOVUDINE	C
ZALCITABINE (ddC)	C
DIDANOSINE (ddI)	B
STAVUDINE (d4T)	C
LAMIVUDINE (3TC)	C
NEVIRAPINE	C
SAQUINIVIR	C
INDINAVIR	C
NELFINAVIR	B
RITONAVIR	B

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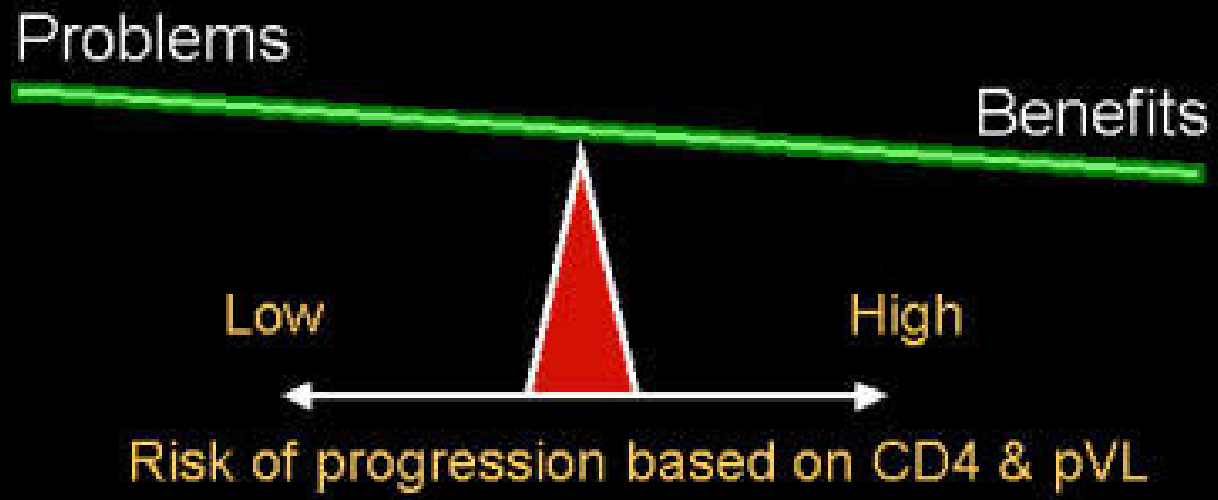
Initiation of Therapy



ARV THERAPY IN PREGNANCY

- Use optimal ARV as indicated by the specific circumstances in the woman
- Consider adding AZT to the regimen, even if not indicated in the patient

- "Pregnancy-friendly" regimens needed

- Avoid ddI and d4T
- Avoid efavirenz

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ARV THERAPY IN PREGNANCY

- Pregnancy has a range of metabolic changes and “side effects”
- May need to consider changes due to side effects of ARV:
  - ritonavir : GI side effects may be a problem in early pregnancy
  - indinavir has been associated with hyperbilirubinaemia: water & food restrictions may be more difficult
  - Antacids and absorption

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ARV THERAPY IN PREGNANCY

Consider 4 scenarios:

1] HIV-Infected Pregnant women who have not received prior ARV

2] HIV-infected women receiving ARV during the current pregnancy.

3] HIV-infected women in labour who have had no prior therapy.

4] Infants born to mothers who have received no antiretroviral therapy during pregnancy or in labour

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Scenario #1:

HIV-Infected Pregnant Women Who Have Not Received Prior Antiretroviral Therapy

- Standard clinical, immunologic, and virologic evaluation.
- Recommendations for initiation and choice of antiretroviral therapy should be based on the same parameters used for persons who are not pregnant
- The known and the unknown risks and benefits of such therapy during pregnancy must be considered and discussed

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Scenario #1:

HIV-Infected Pregnant Women Who Have Not Received Prior Antiretroviral Therapy

- Women who are in the first trimester of pregnancy may consider delaying initiation of therapy until after 10-12 weeks' gestation.
- The three-part ZDV chemoprophylaxis regimen, initiated after the first trimester, should be recommended for all pregnant women with HIV infection regardless of antenatal HIV RNA copy number to reduce the risk for perinatal transmission.

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Scenario #1: HIV-Infected Pregnant Women Who Have Not Received Prior Antiretroviral Therapy

- The combination of ZDV chemoprophylaxis with additional antiretroviral drugs for treatment of HIV infection is recommended for infected women whose clinical, immunologic or virologic status requires treatment or who have HIV RNA over 1,000 copies/mL regardless of clinical or immunologic status.

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Scenario #2

HIV-infected women receiving antiretroviral therapy during the current pregnancy.

- HIV-1 infected women receiving antiretroviral therapy in whom pregnancy is identified after the first trimester should continue therapy.
- ZDV should be a component of the antenatal antiretroviral treatment regimen after the first trimester whenever possible, although this may not always be feasible.

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Scenario #2

HIV-infected women receiving antiretroviral therapy during the current pregnancy

- Women on ARV in whom pregnancy is recognized during the first trimester, should be counselled regarding the benefits and potential risks of antiretroviral administration during this period, and continuation of therapy should be considered.
- If therapy is discontinued during the first trimester, all drugs should be stopped and reintroduced simultaneously to avoid the development of drug resistance.

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Scenario #2

HIV-infected women receiving antiretroviral therapy during the current pregnancy

- Regardless of the antepartum antiretroviral regimen, ZDV administration is recommended during the intrapartum period and for the newborn.
- Recommendations for resistance testing in HIV-infected pregnant women are the same as for non-pregnant patients: acute HIV infection and virologic failure or suboptimal viral suppression after initiation of antiretroviral therapy.

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Scenario #3

HIV-infected women in labour who have had no prior therapy.

Several effective regimens are available. These include:

1) single dose nevirapine at the onset of labour followed by a single dose of nevirapine for the newborn
2) oral ZDV/ 3TC during labour, followed by one week of oral ZDV/3TC for the newborn
3) Intrapartum ZDV followed by six weeks of ZDV for the newborn

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Scenario #3

HIV-infected women in labour who have had no prior therapy.

- In the immediate postpartum period, the woman should have appropriate assessments (e.g., CD4+ count and HIV-1 RNA copy number) to determine whether antiretroviral therapy is recommended for her own health.

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Scenario #4

Infants born to mothers who have received no antiretroviral therapy during pregnancy or during labour

- The 6 week neonatal AZT component of the AZT regimen should be discussed with the mother and offered for the newborn.
- AZT should be initiated as soon as possible after delivery – preferably within 6-12 hours of birth.
- Some clinicians may choose to use AZT in combination with other antiretroviral drugs,

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Scenario #4

Infants born to mothers who have received no antiretroviral therapy during pregnancy or intrapartum.

- In the immediate postpartum period, the woman should undergo appropriate assessments (e.g., CD4+ count and HIV-1 RNA copy number) to determine if antiretroviral therapy is required for her own health.
- The infant should undergo early diagnostic testing so that if HIV-infected, treatment can be initiated as soon as possible.

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ARV THERAPY IN PREGNANCY

No prior use of ARV	On ARV when became pregnant	No prior Rx at the time of delivery
•Consider ARV > 14 weeks •Add AZT during pregnancy •Use appropriate combination for patient	•Counsel & discuss •Continue existing Rx, if effective, •Add AZT •If discontinuing Rx prior to 14 weeks, stop ALL & re-start ALL <14 weeks	•NVP or AZT/3TC •AZT during labour •AZT to neonate •Modify Rx regimen after delivery, as clinically indicated

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US PHS guidelines:

http://www.hivatis.org

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Elective Caesarean Section

- **Elective caesarean section reduces transmission**

- **Evidence from:**
- **European randomized controlled trial**
- **A meta-analysis of data from 15 prospective studies including 8533 mother-infant pairs:**
  - **Overall 50% reduction, 8.2% vs. 16.7%**
    - **NO ARV: 10.4% vs 19%**
    - **Long course ARV: 2% vs 7.3%**

The European Mode of Delivery Collaboration. *Lancet* 1999; **353:**1035–1039.
Ricci et al, Lancet 2000 355: 496;

The International Perinatal HIV Group. *N Eng J Med* 1999; **340:** 977–987.

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Questions remain about the additional benefits of elective caesarean section for women on HAART with undetectable viral loads

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INFANT FEEDING

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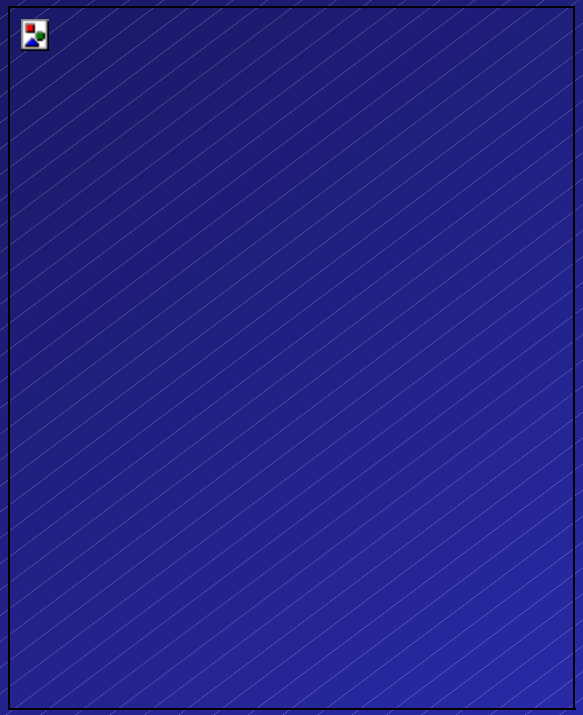
Infant Feeding Modifications



- Transmission through breast milk accounts for 1/3 to 1/2 of infections in children in developing countries
- An integrated package of ARV and breast milk substitutes is the most effective prevention strategy
- The risk of replacement feeding should be less than the risk of HIV infection

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Infant Feeding Modifications

- Prolonged breastfeeding dilutes or reverses the gains from short course antiretroviral strategies

- PETRA:
- 18 month: HIV infection

Arm A:	14.9%	(9.4 – 22.8)
Arm B:	18.1%	(12.1 – 26.2)
Arm C:	20.2%	(12.9 – 30.1)
Placebo:	22.2%	

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Infant Feeding Modifications

- Prolonged breastfeeding dilutes or reverses the gains from short course antiretroviral strategies

- HIVNET 012
- Additional 8% transmission at 18 months, but benefit remains compared to AZT arm

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ARV treatment and breastfeeding

- **Little information on ARV treatment in breastfeeding mothers and potential effects on child**

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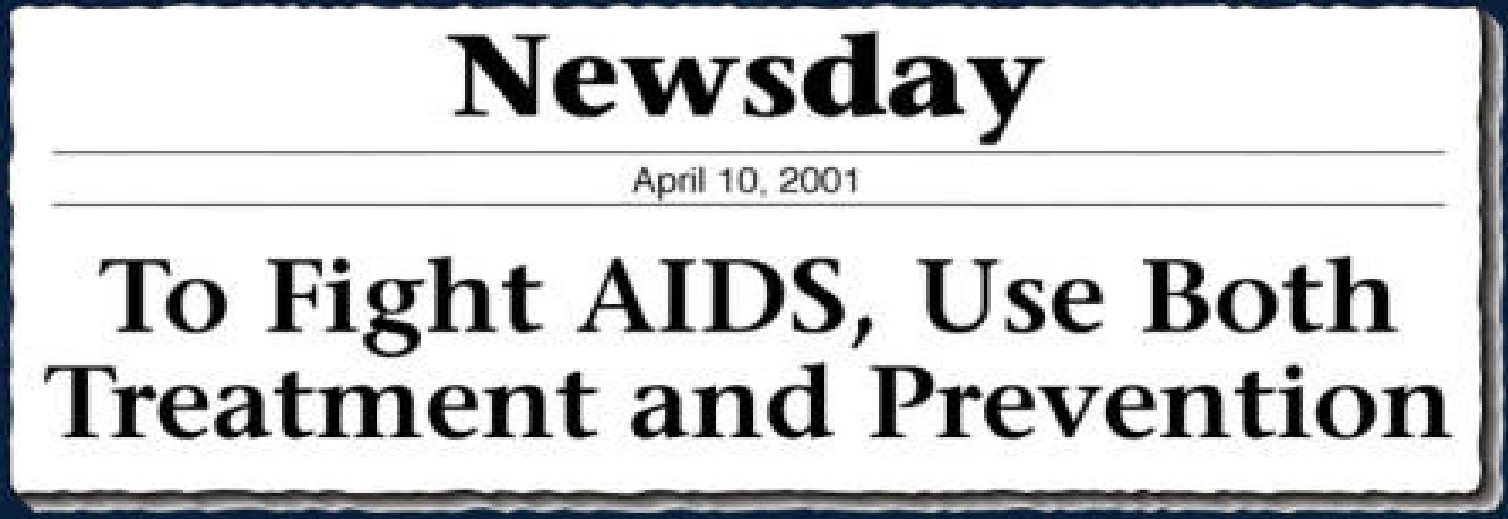

Newsday

April 10, 2001

To Fight AIDS, Use Both Treatment and Prevention

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