Frontier AIDS Education and Training Center

Antiretroviral Therapy During Pregnancy and Delivery: 2015 Update

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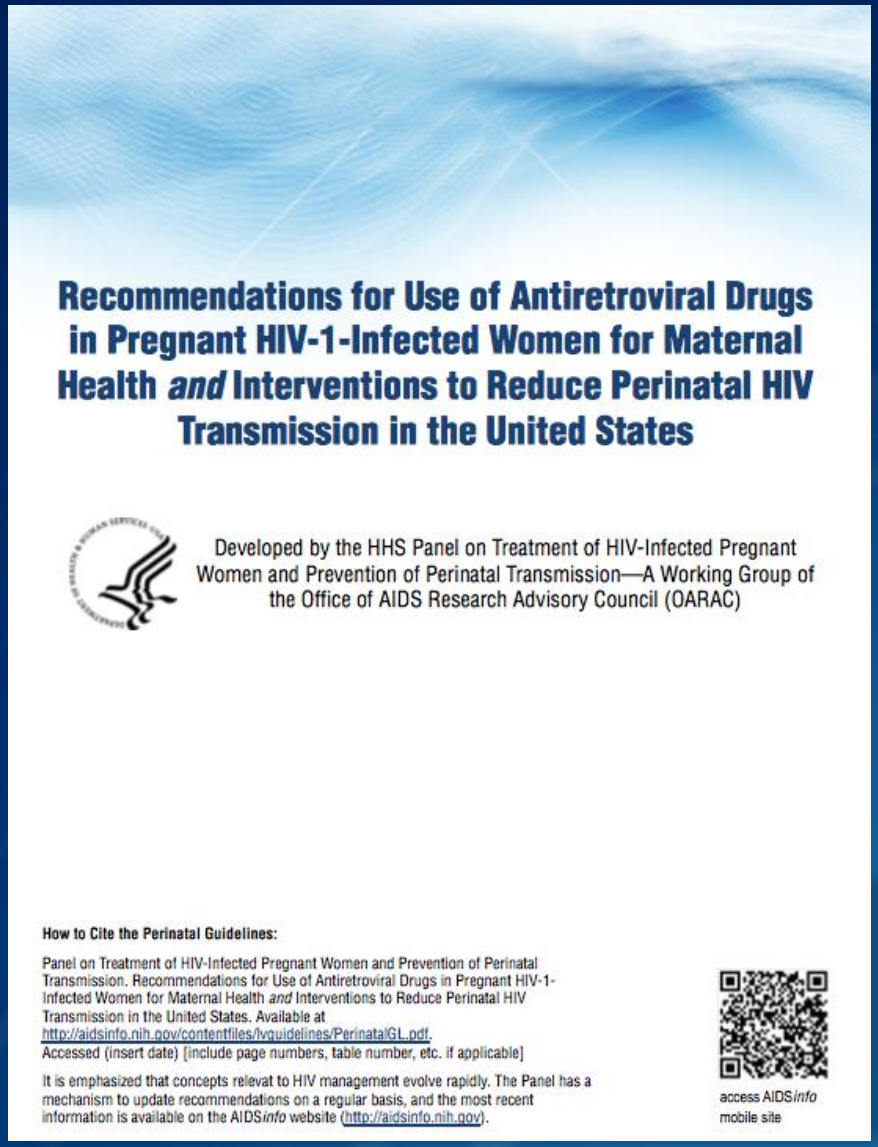
US Health and Human Services (HHS)
August 6, 2015 Perinatal Treatment Guidelines



Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health *and* Interventions to Reduce Perinatal HIV Transmission in the United States

Developed by the HHS Panel on Treatment of HIV-Infected Pregnant Women and Prevention of Perinatal Transmission—A Working Group of the Office of AIDS Research Advisory Council (OARAC)

How to Cite the Perinatal Guidelines:

Panel on Treatment of HIV-Infected Pregnant Women and Prevention of Perinatal Transmission. Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health *and* Interventions to Reduce Perinatal HIV Transmission in the United States. Available at http://aidsinfo.nih.gov/contentfiles/lvguidelines/PerinatalGL.pdf. Accessed (insert date) [include page numbers, table number, etc. if applicable]

It is emphasized that concepts relevat to HIV management evolve rapidly. The Panel has a mechanism to update recommendations on a regular basis, and the most recent information is available on the AIDS*info* website (http://aidsinfo.nih.gov).

access AIDS*info* mobile site

Source: 2015 HHS Perinatal Treatment Guidelines. AIDS Info (www.aidsinfo.nih.gov)

National Objectives

- Due to advances in screening and treatment, perinatal transmission of HIV has dramatically diminished to **2% or less** in the US and Europe
- The CDC has developed an objective of eliminating perinatal HIV transmission in the US
- The goal is to reduce perinatal transmission to an incidence **<1** infection per 100,000 live births and rate **<1%** among HIV-exposed infants

Source: 2015 HHS Perinatal Treatment Guidelines. AIDS Info (www.aidsinfo.nih.gov)

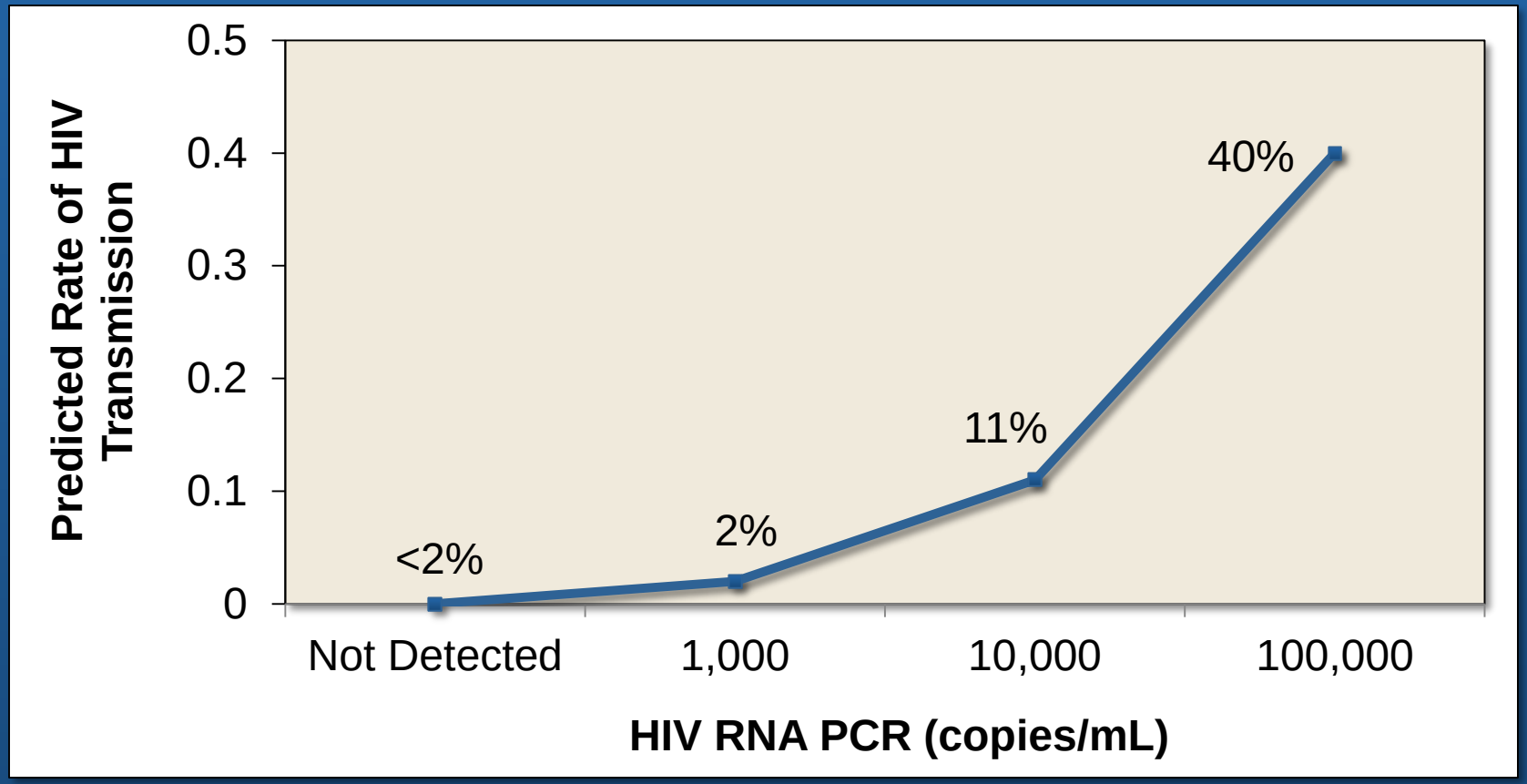
Overall Estimated Risk of Transmission in Non-Resource-Limited Settings

- **UK & Ireland** (N = 12,486 infants born to HIV-infected mothers)
  - Overall perinatal transmission rate: **0.46%** in 2010-2011
  - Rate **0.09%** if viral load <50 copies/mL; **1%** if 50-399 copies/mL
- **Canada** (N = 1,707 HIV-infected pregnant women, 1997 to 2010)
  - Perinatal transmission rate **1%** in all mothers receiving ART
  - Rate **0.4%** if more than 4 weeks of ART received

Sources:
Townsend CL et al. AIDS. 2014;28(7):1049-1057. Forbes JC et al. AIDS. 2012;26(6):757-763.

Probability of Perinatal HIV Transmission
By Maternal Viral Load Near Delivery

Predicted rate of HIV transmission based on a cohort of 94 live births



Source: O'Shea S et al. Journal of Medical Virology. 1998;54:113–117

Factors Associated with Lack of Viral Suppression at Delivery Among ART-Naïve Women with HIV: Study Features

Study Features

- N = 671 HIV-infected, ART-naïve pregnant women age 13 or older
- Setting: 67 sites in United States and Puerto Rico
- Timeline: enrolled participants between 2002 and 2011
- Primary outcome: detectable viral load (>400 copies/mL) at delivery, which was found in **13.1%** of participants
- Objective: assess socioeconomic, HIV-related, and pregnancy-related factors associated with detectable viral load at delivery

Source: Katz IT, et al. Ann Intern Med. 2015;162:90-9.

Factors Associated with Lack of Viral Suppression at Delivery Among ART-Naïve Women with HIV: Results

Percentage of women with viral load >400 copies/mL at delivery		
Factor (%)	**Comparison (%)**	**P Value**
Multiparous (16.4%)	Nulliparous (8.0%)	0.002
Black ethnicity (17.6%)	Hispanic (6.6%), white (6.6%)	<0.001
11th grade education or less (17.6%)	High school diploma (12.1%)	0.013
ART initiation in 3rd trimester	In 1st trimester (8.6%), in 2nd trimester (12.3%)	0.003
First prenatal visit during 3rd trimester (33.3%)	During 1st trimester (10.5%), during 2nd trimester (14.3%)	0.002
At least one treatment interruption (28.2%)	No treatment interruption (12.2%)	0.004
Reported nonadherence in previous 2 weeks (19.3%)	Reported nonadherence earlier (12.3%) or never (9.6%)	0.039

Source: Katz IT, et al. Ann Intern Med. 2015;162:90-9.

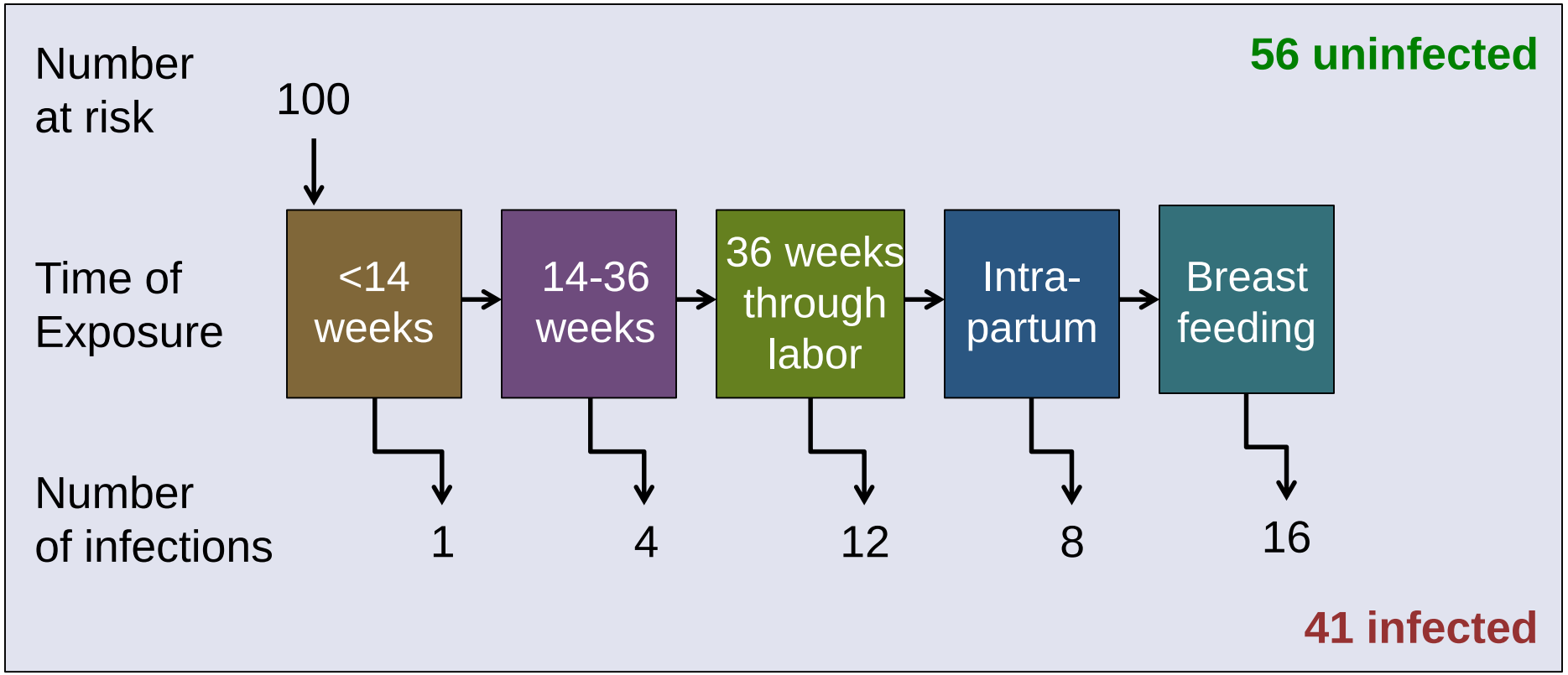
Factors Associated with Lack of HIV Suppression at Delivery
Conclusion

Conclusion: “A total of 13.1% of women who initiated HAART during pregnancy had detectable VL at delivery. The timing of HAART initiation and prenatal care, along with medication adherence during pregnancy, were associated with detectable VL at delivery. Social factors, including ethnicity and education, may help identify women who could benefit from focused efforts to promote early HAART initiation and adherence”

Source: Katz IT, et al. Ann Intern Med. 2015;162:90-9.

Probability of Perinatal HIV Transmission
By Stage of Pregnancy

Estimated number of HIV transmissions per pregnancy stage in the absence of intervention with breastfeeding



Source: Kourtis AP, et al. JAMA. 2001;285:709-12.

HHS Perinatal Treatment Guidelines: 2015
Preferred Agents

Class	Preferred Agents in Pregnancy
NRTI	Tenofovir with emtricitabine or lamivudine
	Abacavir* with lamuvidine**
	Zidovudine with lamivudine
NNRTI	Efavirenz***
INSTI	Raltegravir
PI	Darunavir + ritonavir
	Atazanavir + ritonavir

*Use only if HLA-B*5701 negative; **Abacavir with lamivudine not recommended in combination with efavirenz or boosted atazanavir if viral load >100,000 copies/mL; ***Start after the first 8 weeks of pregnancy

Source: 2015 HHS Perinatal Treatment Guidelines. AIDS Info (www.aidsinfo.nih.gov)

HHS Perinatal Treatment Guidelines: 2015
Alternative Agents and Agents with Insufficient Data

Class	Alternative Agents in Pregnancy	Insufficient Data for Use in Pregnancy
NNRTI	Rilpivirine*	
INSTI		Dolutegravir
		Elvitegravir
Entry inhibitor		Maraviroc
Fusion inhibitor		Enfuvirtide
Booster		Cobicistat

*Use only if CD4 count >200 cells/mL and HIV RNA <100,000 copies/mL and do not use with PPI's

Source: 2015 HHS Perinatal Treatment Guidelines. AIDS Info (www.aidsinfo.nih.gov)

What is the Optimal ART Regimen for an HIV-Infected Pregnant Woman?

Advantages and Disadvantages of Preferred ARV Backbone Agents in Pregnancy		
Agent	**Advantages**	**Disadvantages**
Tenofovir + lamivudine or emtricitabine	Daily dosing; overall well-tolerated	Caution if renal insufficiency; effects on fetal bone development unclear
Abacavir + lamivudine	Daily dosing; overall well-tolerated	Cannot use if HLA-B*5701 positive; data for CV risk with abacavir mixed
Zidovudine + lamivudine	Most clinical experience in pregnancy	BID dosing; relatively more side effects and more hematological toxicity

Source: 2015 HHS Perinatal Treatment Guidelines. AIDS Info (www.aidsinfo.nih.gov)

What is the Optimal ART Regimen for an HIV-Infected Pregnant Woman?

Advantages and Disadvantages of Preferred ARV Anchor Agents in Pregnancy		
Agent	**Advantages**	**Disadvantages**
Raltegravir	Well-tolerated; few drug interactions; rapid viral load decline	BID dosing; lower barrier to resistance as compared to boosted PI's
Efavirenz	Daily dosing	Questionable teratogenicity; mental health side effects
Atazanavir + ritonavir	Daily dosing; relatively high barrier to resistance; extensive experience in pregnancy	Risk of hyperbilirubinemia and kidney stones; interacts with antacids; optimal late pregnancy dose unclear
Darunavir + ritonavir	Relatively high barrier to resistance	BID dosing recommended in pregnancy

Source: 2015 HHS Perinatal Treatment Guidelines. AIDS Info (www.aidsinfo.nih.gov)

Intrapartum Antiretroviral Therapy

Continue antepartum ART on schedule as much as possible during labor or before scheduled cesarean section

Administer **IV AZT if maternal HIV RNA >1,000** copies/mL (or unknown) near delivery, or if no antenatal care and positive rapid HIV test

IV AZT not required if receiving ART with HIV RNA ≤1,000 during late pregnancy and near delivery and no concerns regarding adherence

Source: 2015 HHS Perinatal Treatment Guidelines. AIDS Info (www.aidsinfo.nih.gov)

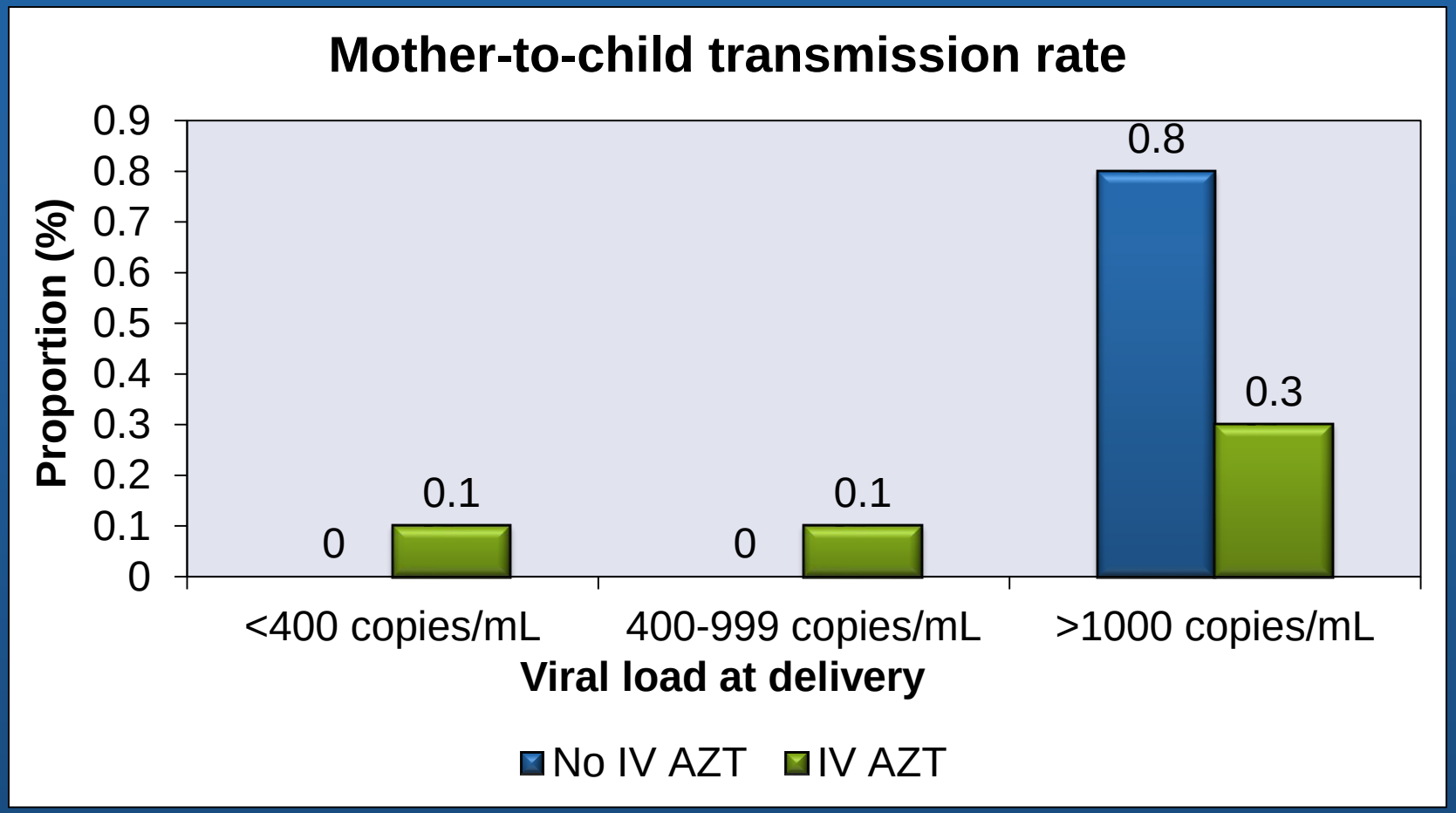
Intravenous Zidovudine (ZDV/AZT) in the French Perinatal Cohort: Study Features

Study Features

- Inclusion: all HIV-infected pregnant women delivering between 1997 and 2010 in the French Perinatal Cohort
- N = 11,538 total deliveries
- ART exposure during pregnancy: 10% received AZT alone, 18% dual ART, 72% triple ART, 95% received intrapartum IV AZT
- Objective: evaluate impact of IV AZT on perinatal transmission risk according to viral load at delivery and obstetrical conditions

Source: Briand N et al. Clin Infect Dis. 2013;57(6):903-14.

Intravenous Zidovudine (ZDV/AZT) in the French Perinatal Cohort: Results



Source: Briand N et al. Clin Infect Dis. 2013;57(6):903-14.

Antiretroviral Pregnancy Registry

- Report all ARV exposures during pregnancy to the Antiretroviral Pregnancy Registry; helps accumulate data on ARV's during pregnancy and determine safety

Antiretroviral Pregnancy Registry
Research Park, 1011 Ashes Drive, Wilmington, NC 28405

Telephone: 1–800–258–4263

Fax: 1–800–800–1052

http://www.APRegistry.com

Source: 2015 HHS Perinatal Treatment Guidelines. AIDS Info (www.aidsinfo.nih.gov)

What is the optimal ARV regimen during pregnancy?

A. Zidovudine-lamivudine + atazanavir + ritonavir

B. Tenofovir-emtricitabine + atazanavir + ritonavir

C. Tenofovir-emtricitabine + raltegravir

D. Tenofovir-emtricitabine + dolutegravir

E. Something else