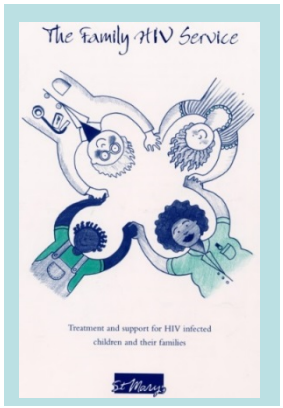


British HIV Association
BHIVA

National Study of HIV in Pregnancy and Childhood
NSHPC

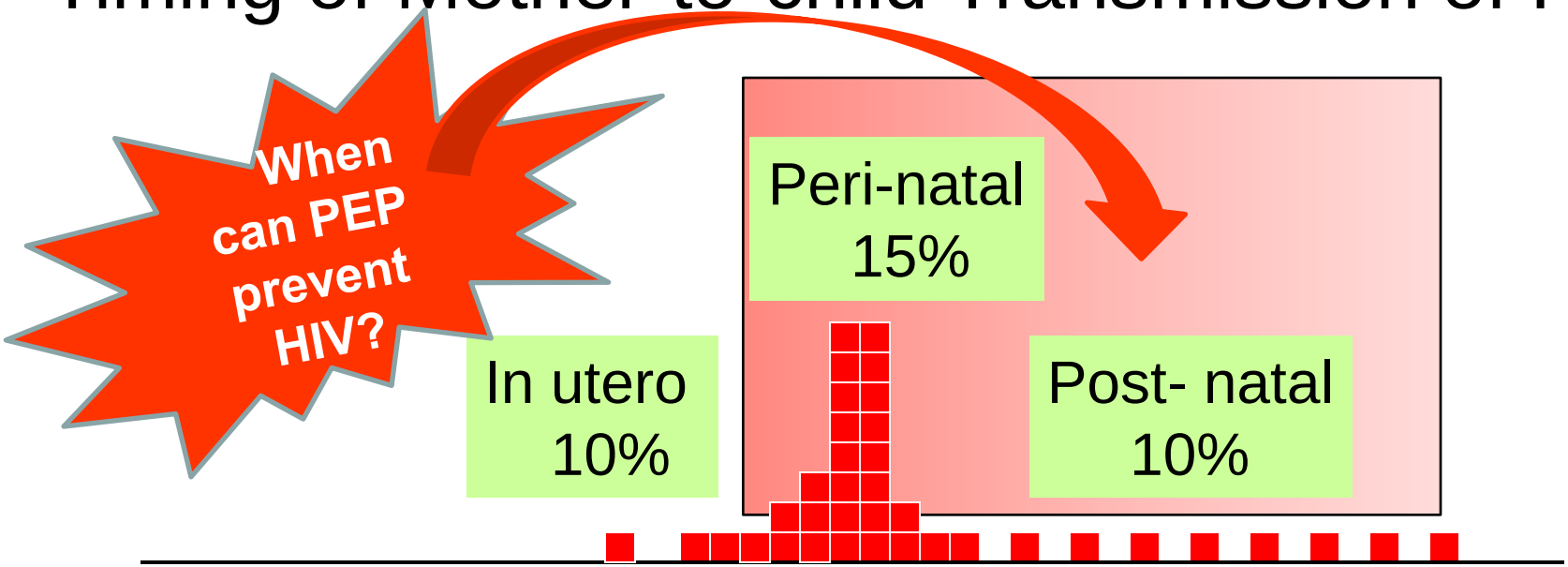
All HIV-exposed Infants Should Receive Triple Drug Antiretroviral Prophylaxis

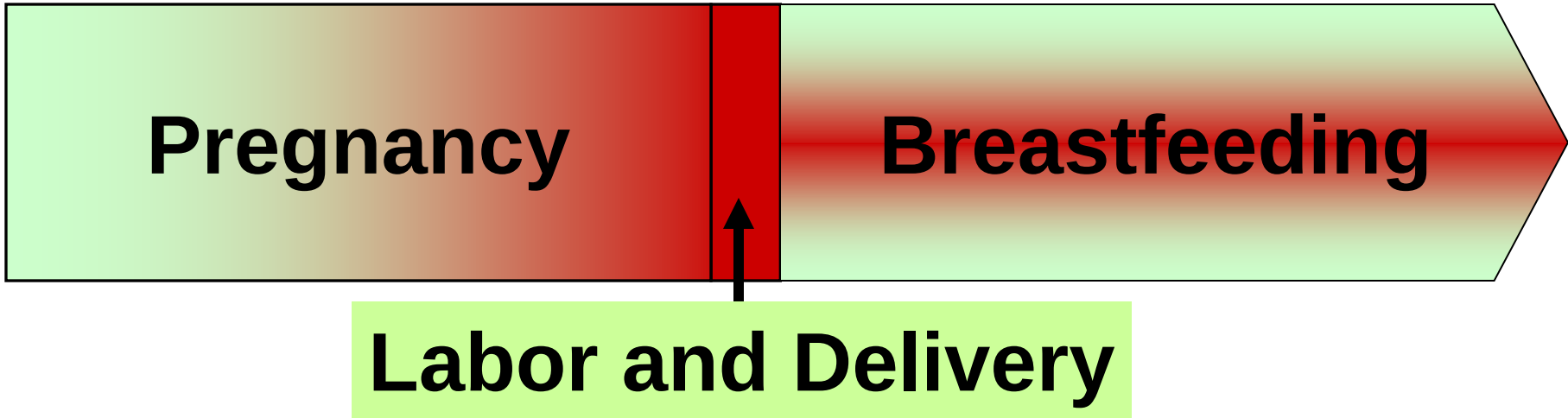
Against the motion

Hermione Lyall
Imperial Healthcare NHS Trust, London, UK

Acknowledgements:
Pat Tookey, Ali Judd, Claire Townsend, Claire Thorne, Jeannie Collins, Marc Lallemant Lynn Mofenson, Graham Taylor

Timing of Mother-to-child Transmission of HIV





UK → **Birth** PCR **6wk** PCR **12wk** PCR

To support optimal care we need timely & efficient EID

Infants most at risk of HIV Infection – need Triple PEP!

Detectable maternal HIV at delivery

Late presenters

Less than 14 days of maternal ART

Poor maternal adherence to treatment

Premature delivery

PROM with detectable HIV

Maternal diagnosis at or after delivery

Sero-conversion during pregnancy / lactation

First - get mother on to effective ART!

When to start ART in Pregnancy – BHIVA 2012

All should start ART by 24 weeks

VL > 100,000 c/ml → ASAP

VL > 30,000 c/ml → At 14 weeks

VL < 30,000 c/ml → By 24 weeks

British HIV Association
BHIVA

French Cohort — median duration of treatment

Transmitters	9.5 weeks
Non- transmitters	16 weeks ($p < 0.001$)

UK & Ireland(NSHPC) — gestation started treatment

Transmitters	30.1 weeks
Non- transmitters	25.9 weeks ($p < 0.001$)

Second - start Infant PEP ASAP

Cohort Study New York State	**Monotherapy ZDV**
Timing of ZDV dosing	**Transmission Rate**
n = 939	
ante-partum + intra-partum + post-partum	6.1%
intra-partum + post-partum	10.0 %
post-partum (within 48hrs)	9.3%
post-partum (72hrs or after)	18.4 %
No ZDV	26.6 %

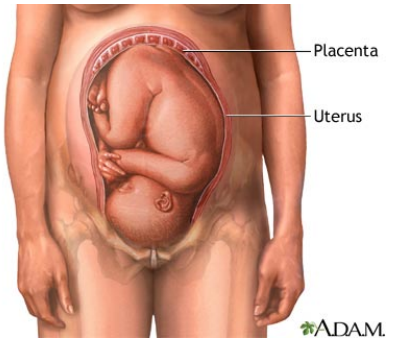
Wade et al NEJM 1998; 339: 1409-14.

What ever PEP you can give – give it as soon as you can!

Third - pre-load the foetus in Utero!

Maternal PRE- PEP

	Cord Blood : Maternal Plasma ratio
Zidovudine	***0.80***
Nevirapine	***0.90 (2hrs min)***
Lamivudine	***1.00***
Kaletra	0.20 (+/- 0.13)
Tenofovir	***0.6-0.99***
Raltegravir	***1.2 (0.09-2.25)***
Maraviroc	0.3
Enfurvitide (T20)	0.00



panna

http://www.pannastudy.com/

Maternal PRE-PEP –neonatal half-life?

ART transplacental transfer and T1/2 in neonate:

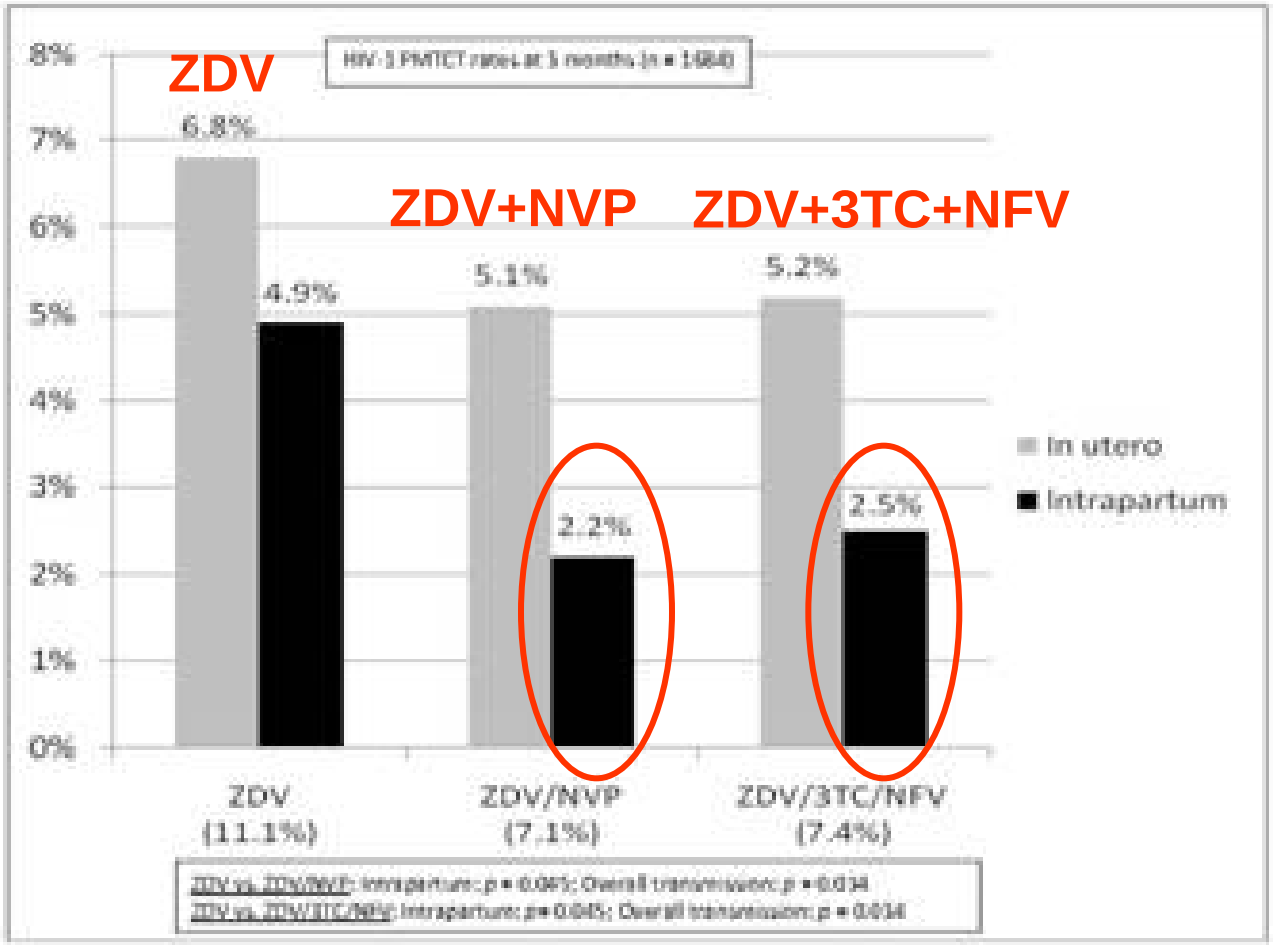
SD Nevirapine	→ 7 days
DD Tenofovir	→ 24-48 hours
Raltegravir	→ 24-48 hours (longer in prems)
Other NRTI's	→ < 24 hours
PI's	→ very poor transplacental Tx

*ART which crosses the placenta **"preloads"***
the infant for delivery & the 1st week of life
Reduces the need for oral infant PEP

Very important for the neonate who cannot feed

Efficacy of Triple PEP in neonates?

RCT - High Risk Women



Neonatal PEP with 2- or 3-ART is superior to ZDV mono in infants born to women who had **NO** ARV before delivery (Brazil, SA, Argentina, USA)

Nielsen-Saines K et al, N Engl J Med. 2012; 366 :2368-79.

BHIVA - Infant PEP – tailored to HIV risk

Low Risk PEP – monotherapy (Zidovudine)
maternal VL <50 HIV at 36 weeks

High Risk PEP – triple therapy (ZDV + 3TC + NVP)
Infants <72 hours old, maternal VL > 50
All circumstances where VL at 36 weeks / delivery is not <50

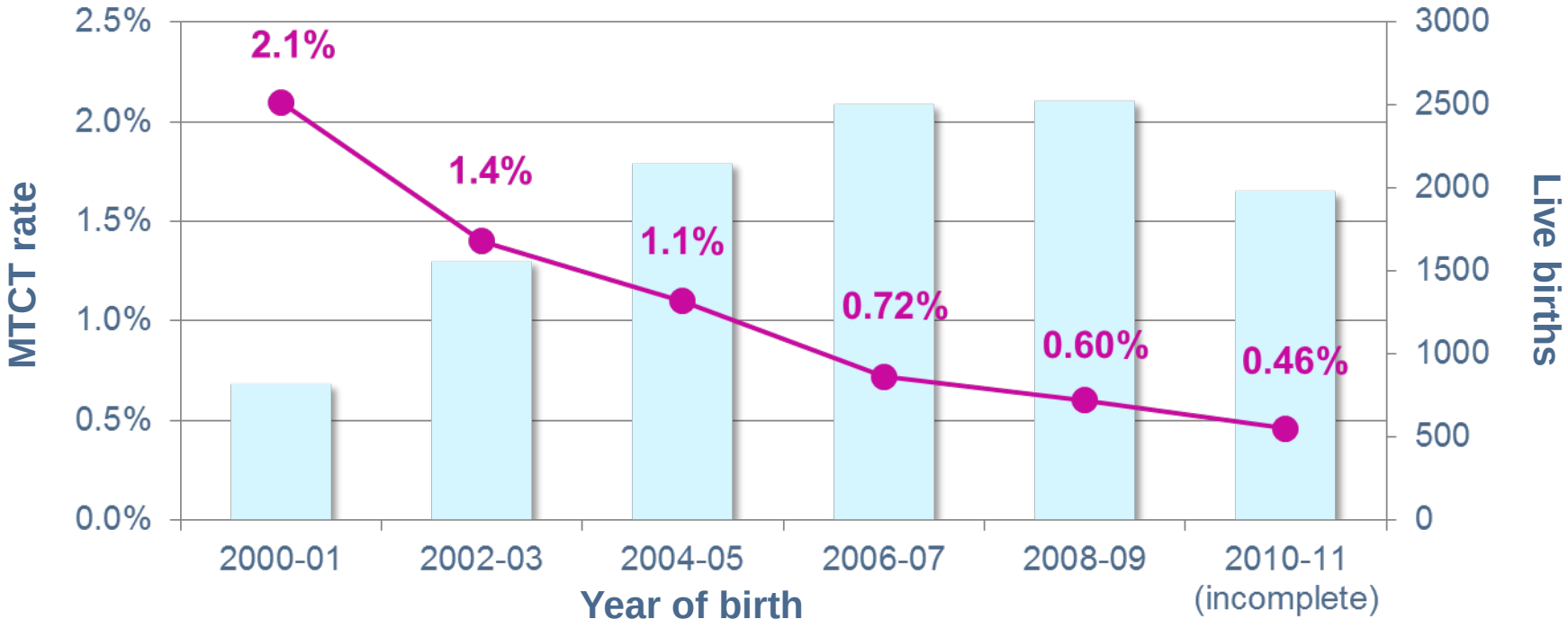
Neonatal PEP start < 4 hours after birth
Neonatal PEP continue for 4 weeks

PCP prophylaxis - co-trimoxazole, from 4 weeks only if:
- HIV infected or,
- mother's VL at 36 weeks / delivery >1000 or unknown

National Study of HIV in Pregnancy and Childhood

NSHPC

HIV MTCT in antenatally diagnosed women, UK & Ireland 2000-2011



~12,500 singleton births; significant decline in MTCT over time ($p<0.001$)

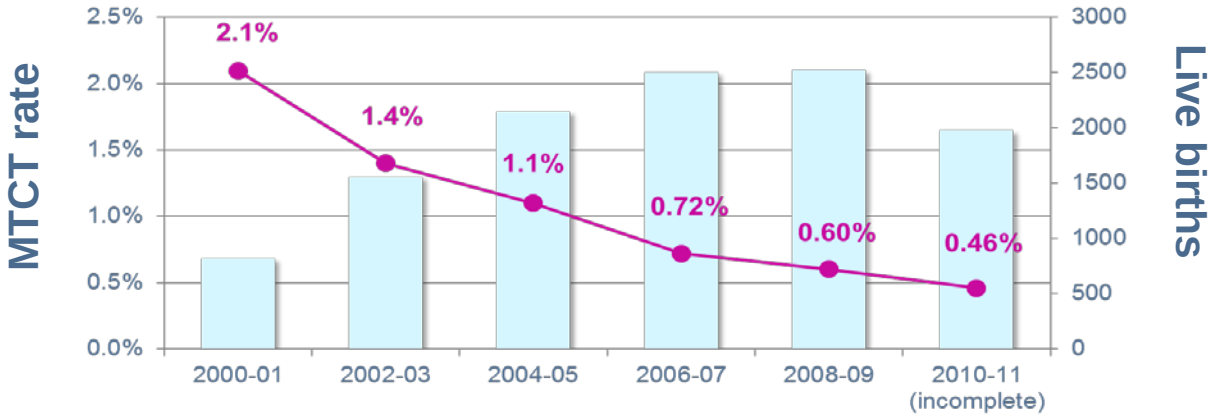
Graph derived from data in Townsend *et al*. Earlier initiation of ART and further decline in mother-to-child HIV transmission rates, 2000-2011. AIDS 2014; 28:1049–1057

Efficacy of triple PEP in neonates?

UK cohort – Triple PEP only for High Risk

National Study of HIV in Pregnancy and Childhood

NSHPC



Use of neonatal PEP UK & Ireland, 2001-2008 (n = 8205)

99% infants received PEP (86% single; 3% dual; 11% triple)

Use of triple increased over time	2001-2004	2005-2008
Untreated women	43% (41/95)	71% (45/63)
Women viraemic despite ART	13% (114/883)	32% (344/1088)

Factors associated with receipt of Triple PEP (MVA)→

later time period, shorter duration / no ART, maternal VL > 50, low CD4, preterm delivery, unplanned delivery (emergency C/S or vaginal)

Low rates of mother-to-child transmission of HIV: UK & Ireland 2000-2006

Townsend *et al.* AIDS 2008; 22:973-81

Group	Number of transmissions	MTCT rate
Overall	61/5151	**1.2%** (CI 0.9-1.5%)
2000-2002	23/1456	**1.6%**
2003-2006	38/3695	**1.0%**
At least 14 days HAART	40/4864	**0.8%**
ZDV monotherapy + PLCS	0/464	**0.0%**
HAART + PLCS	16/2286	**0.7%**
HAART + SVD	4/559	**0.7%**
VL<50 copies/ml	3/2117 (*2 with evidence of in utero transmission)	**0.1%**

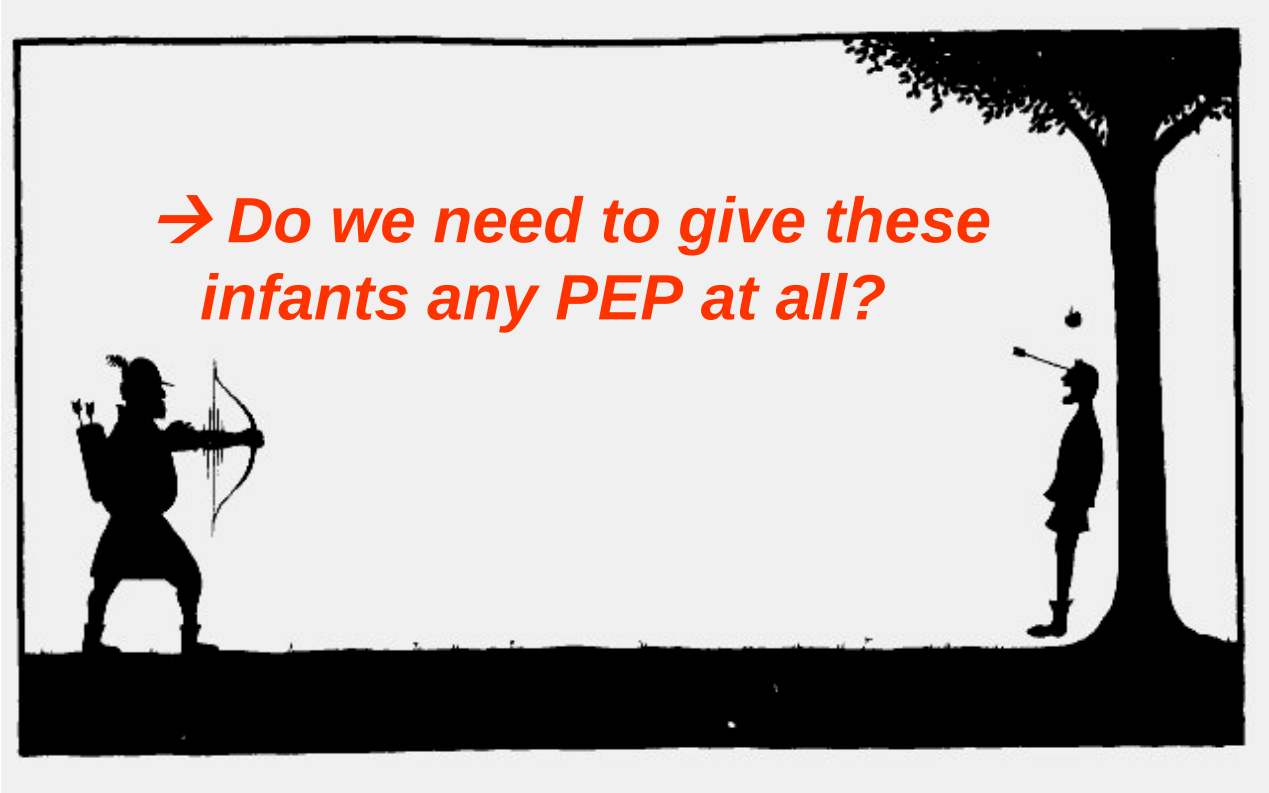
ZDV: zidovudine
PLCS: planned lower caesarean section
SVD: spontaneous vaginal delivery
VL: HIV viral load

National Study of HIV in Pregnancy and Childhood

no maternal viraemia in pregnancy

The **"Swiss Statement"** for neonates?

Mother fully suppressed on ART
ART with good transplacental transmission to infant
ART with good duration of plasma levels in the infant



NO PEP for the low risk infant?

Mother with VL < 50 pre-conception

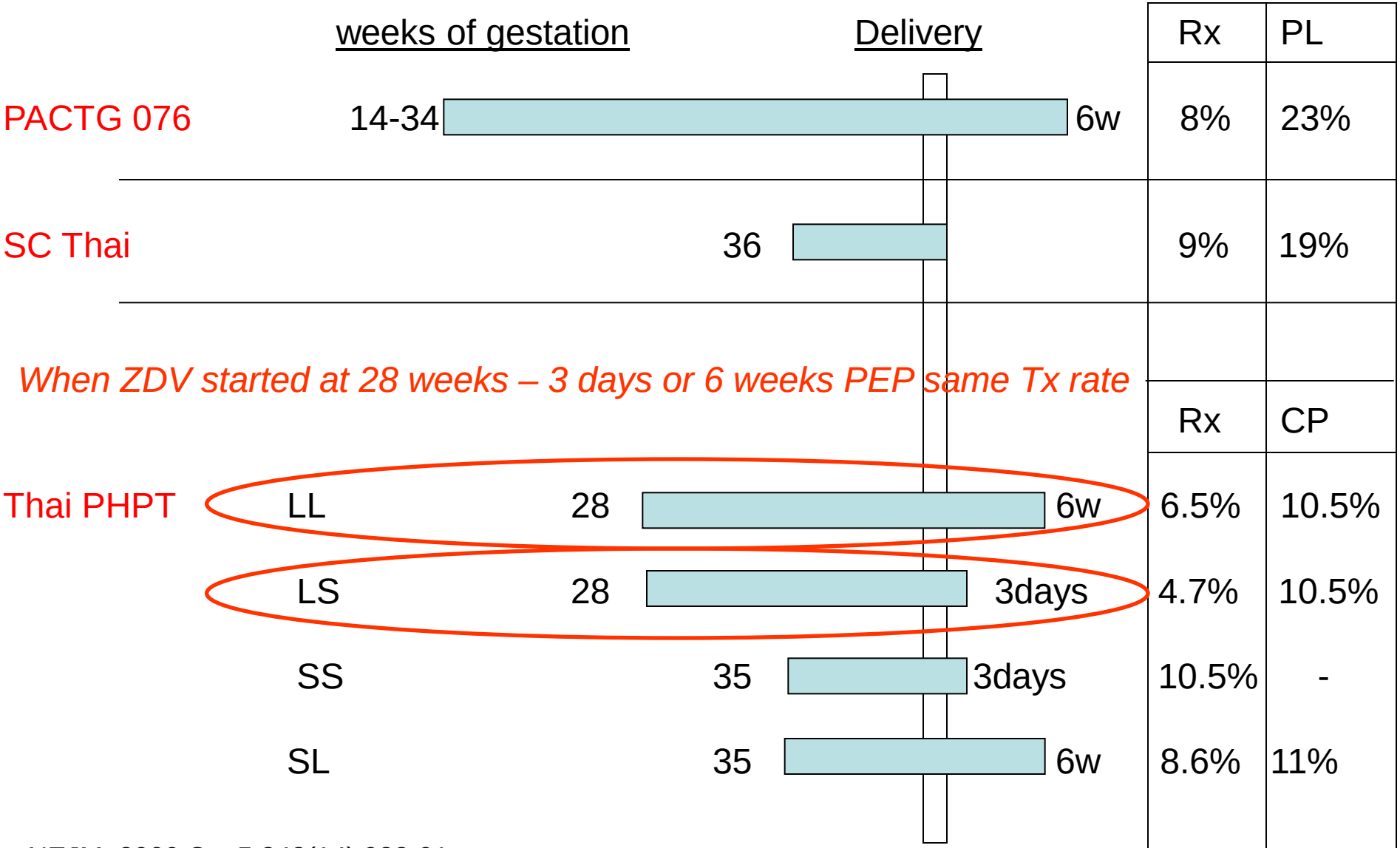
Mother with VL < 50 from 28 weeks

Mother with VL < 50 from 36 weeks

SHOW of HANDS

Can we shorten the duration of infant PEP?

Historic ZDV Monotherapy - Randomised Controlled trials



	Rx	PL
PACTG 076	8%	23%
SC Thai	9%	19%

	Rx	CP
Thai PHPT LL	6.5%	10.5%
Thai PHPT LS	4.7%	10.5%
Thai PHPT SS	10.5%	-
Thai PHPT SL	8.6%	11%

NEJM 2000 Oct 5;343(14):982-91

Bearing in mind PHPT – 3 days v 6 weeks

Mother with VL < 50 pre-conception

→ 1 week mono PEP

Mother with VL < 50 from 36 weeks

→ 4 weeks mono PEP

Mother with VL > 50 at 36 weeks

→ 4 weeks triple PEP

Could there ever be a randomised controlled trial?

Target Prevention for HIV Transmission – Save triple PEP for high risk infants

Scenarios	Post Exposure Prophylaxis - Non Breast feeding infant	Post Exposure Prophylaxis - Breast Feeding infant – mother on ART
No maternal Rx – very high risk	Triple 4 weeks	Triple how long?
VL > 50 (VL at 36 wks) – higher risk	Triple 4 weeks	Triple how long?
VL < 50 (VL at 36 wks) – low risk	Mono 4 weeks	Mono 4-6 weeks
VL < 50 since conception – lowest risk	None ???	None ???

Reduce toxicity - Reduce drug errors - Reduce cost -
Do not give unnecessary Triple PEP to low risk infants