

Pregnancy outcomes in HIV-infected women using non-zidovudine HAART in Europe: 2000 to 2009



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Introduction

- Zidovudine (ZDV) is the only antiretroviral drug licensed for use in pregnancy.
- There is declining use of ZDV in HIV-infected adults in resource-rich settings due to well recognised side effects.
- Increasing numbers of pregnant women will therefore conceive or be initiated on highly active antiretroviral therapy (HAART) that does not contain ZDV ("non-ZDV HAART").
- Data on non-ZDV HAART use in pregnancy and outcomes are sparse.

Aim: To investigate the risk of detectable maternal HIV viral load (VL) at delivery, congenital abnormality and mother-to-child transmission (MTCT) of HIV in pregnancies in women taking non-ZDV HAART compared with ZDV HAART.

Methods

Combined analysis of data from:

National Study of HIV in Pregnancy and Childhood (NSHPC)¹

- Population-based surveillance (1990-2009).
- Maternity units in the United Kingdom & Ireland.

European Collaborative Study (ECS)²

- Consented cohort study (1990-2009).
- 26 centres in ten European countries.

Inclusion criteria: Live singleton births 2000-2009 to diagnosed HIV-infected women with ≥ 14 days of HAART documented in pregnancy (reported by June 2009).

- HAART:** ≥ 3 antiretroviral drugs including a protease inhibitor (PI) and/or a non-nucleoside reverse transcriptase inhibitor (NNRTI)
- 7353** pregnancies were included (NSHPC=6310, ECS=1263).
- 95% power** to detect a true odds ratio (OR) of 1.40 for detectable maternal VL at delivery; **90%** power for a true OR for congenital abnormality of 1.75; **80%** power for a true OR of 2.50 for MTCT.
- All analyses were conducted in Stata 10.0.

Baseline characteristics: Table 1

		ZDV HAART (n=6374) %	Non-ZDV HAART (n=1199) %
Ethnicity*	Black	78.3	73.8
	White	17.1	22.5
	Asian/other	4.6	3.8
History of injecting drug use*	No	96.1	93.9
	Yes	3.9	6.1
Maternal age at delivery (years)*	Median (interquartile range)	30.3 (26.7-34.2)	33.0 (29.1-36.4)
	Mode of delivery		
Mode of delivery	Elective CS	56.5	54.0
	Emergency CS	18.2	20.7
	Vaginal	25.3	15.3
1 st recorded HIV viral load (copies/ml) in pregnancy*	Undetectable	25.6	58.5
	50-999	15.3	11.7
	1000-9999	26.1	13.4
	≥ 10000	34.1	16.4
	Initial CD4 (cells/mm ³)		
Initial CD4 (cells/mm ³)	≥ 500	25.9	28.4
	200-499	58.3	57.2
	< 200	15.9	14.4
Type of HAART *	PI	56.9	53.4
	NNRTI	37.1	3.6
	PI+NNRTI	6.0	10.0
Preconception HAART *	Yes	23.2	71.3
	No	76.8	28.7
Duration of HAART (weeks)*	≥ 24	27.5	75.6
	12-23	44.3	16.4
	8-11	17.6	4.9
	2-7	10.6	3.1
Gestational age (weeks)*	≥ 37	86.6	83.6
	34-36	9.3	10.9
	< 34	4.2	5.4
Year of delivery*	2000-2002	19.6	17.1
	2003-2005	39.1	24.2
	2006-2009	41.4	58.7

CS, caesarean section; * $p < 0.05$

Results

Patterns of non-ZDV HAART use

Figure 1. Use of non-ZDV HAART over time

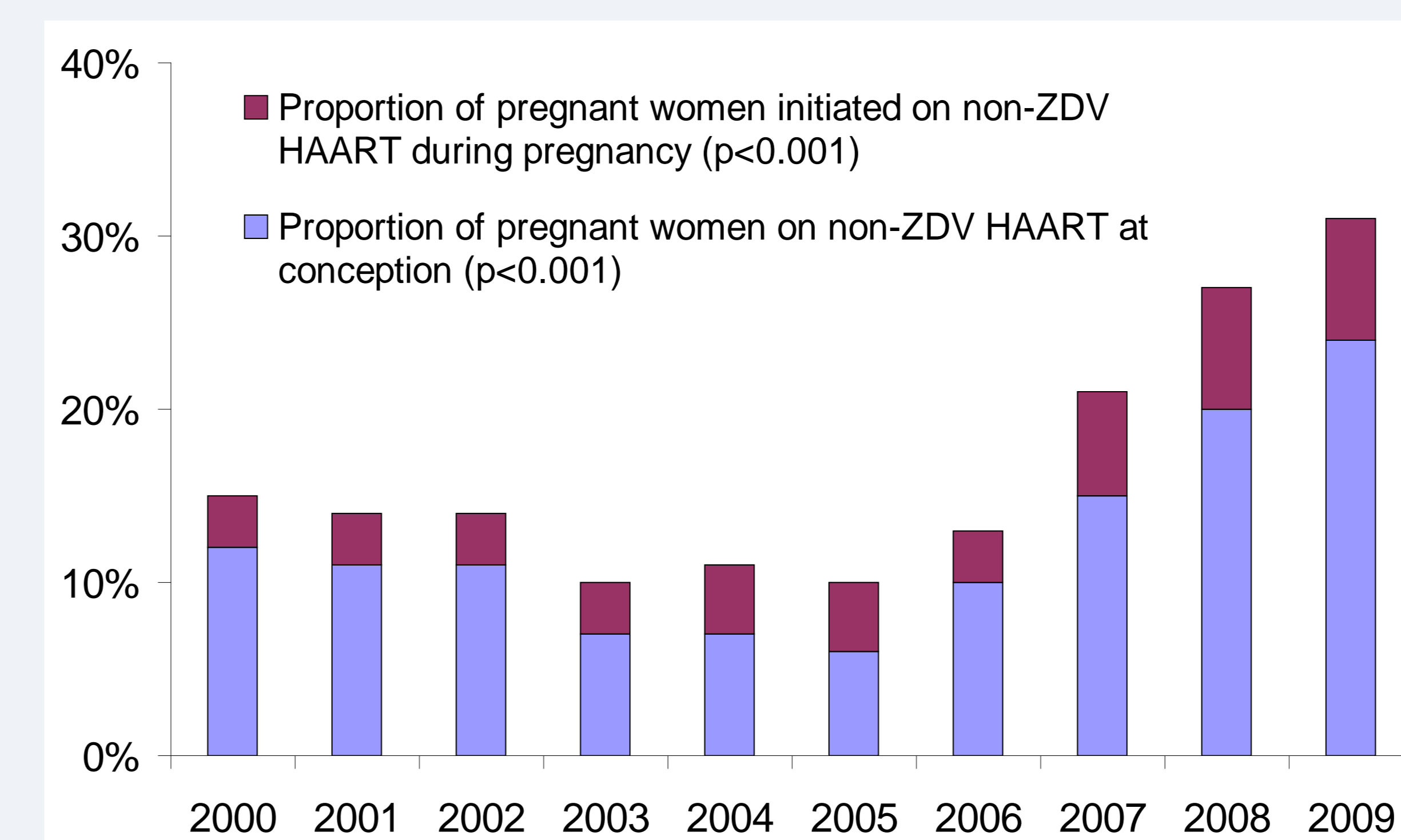
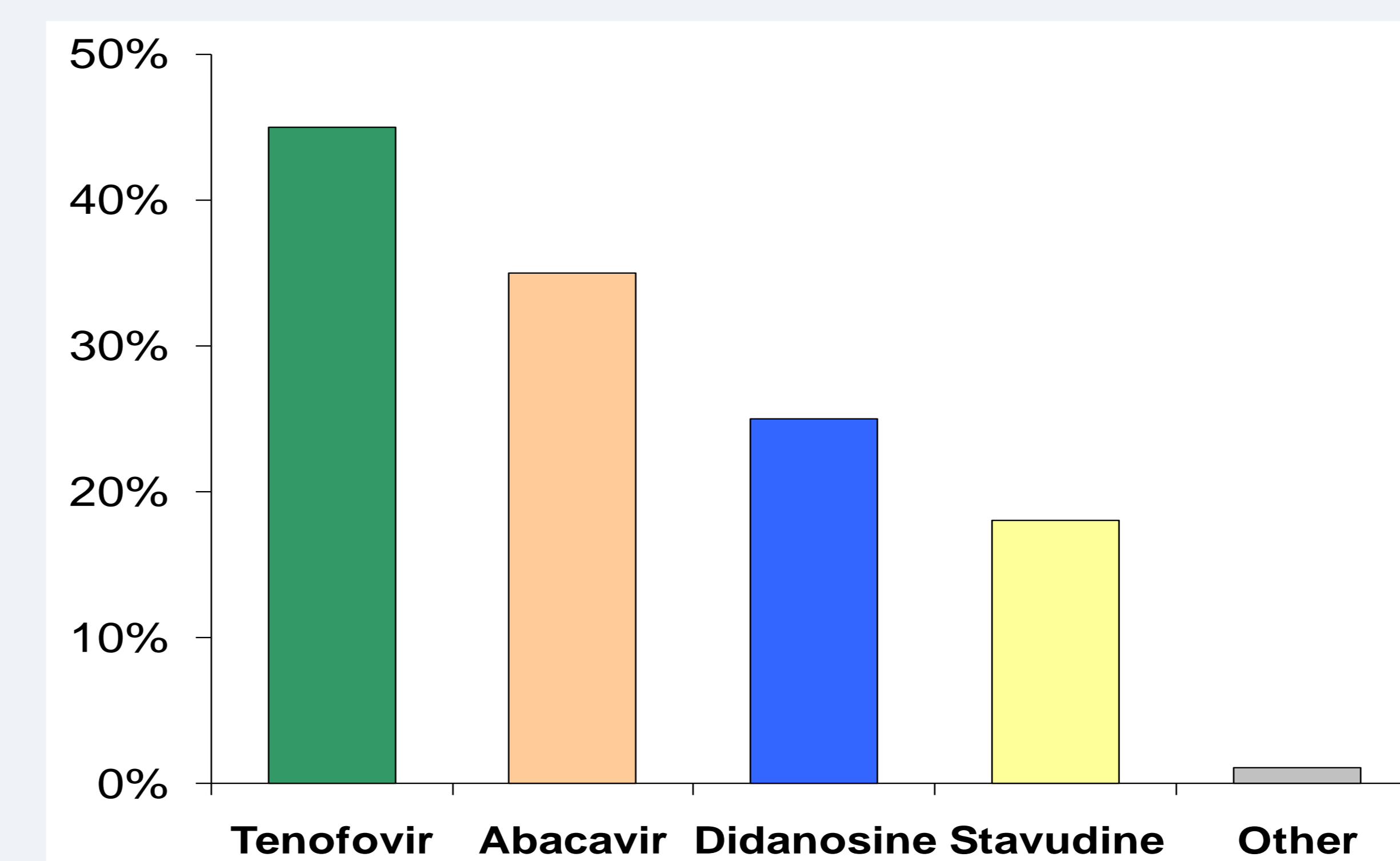


Figure 2. Non-ZDV drugs used in pregnancy



Maternal and infant outcomes: Table 2

	Detectable maternal VL at delivery n=4212		Congenital abnormality (all pregnancies) n=7383		Congenital abnormality (1st trimester exposure to HAART) n=1930		Mother-to-child transmission n=6111	
	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p
Univariate								
ZDV HAART	1		1		1		1	
Non-ZDV HAART	0.60 (0.49,0.73)	<0.01	1.00 (0.68,1.48)	0.98	0.77 (0.47,1.27)	0.31	0.81 (0.37,1.80)	0.61
Multivariable								
ZDV HAART	1		1		1		1	
Non-ZDV HAART	0.90 (0.72,1.11)¹	0.33	0.95 (0.64,1.41)²	0.80	0.76 (0.46,1.25)³	0.28	1.81 (0.77,4.26)⁴	0.18

¹ Adjusted for study and duration of HAART; ² Adjusted for study and maternal age; ³ Adjusted for maternal age; ⁴ Adjusted for Study and mode of delivery.

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Publications: 1. Townsend CL, Cortina-Borja M, Peckham CS, Tookey PA. Trends in management and outcome of pregnancies in HIV-infected women in the UK and Ireland, 1990-2006. *BJOG* 2008 Aug;115(9):1078-86.
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3. Townsend CL, Cortina-Borja M, Peckham CS, de Ruiter A, Lyall H, Tookey PA. Low rates of mother-to-child transmission of HIV following effective pregnancy interventions in the United Kingdom and Ireland, 2000-2006. *AIDS* 2008 May 11;22(8):973-81.

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NSHPC team: Pat Tookey (PI), Janet Masters, Hiwot Haile-Selassie, Clare French, Icina Shakes. Contact nshpc@ich.ucl.ac.uk Website www.nshpc.ucl.ac.uk
ECS collaborators: Please see a recent ECS publication for list of collaborators

- Overall 16% (1199/7773) of women were prescribed non-ZDV HAART during pregnancy.
- Use of non-ZDV HAART (including initiation) in pregnancy has increased since 2000 ($p < 0.001$).
- In multivariable analysis the odds of detectable maternal VL at delivery were similar in those treated with non-ZDV and ZDV HAART ($p = 0.33$) (Table 2).
- There was no difference in odds of congenital abnormality comparing the non-ZDV and ZDV groups ($p = 0.80$).
- In women on HAART in first trimester there was no evidence of a difference in congenital abnormality risk between non-ZDV and ZDV HAART ($p = 0.28$).
- MTCT rates were 0.8% and 0.9% in the non-ZDV and ZDV groups respectively. The odds of MTCT were similar in both groups ($p = 0.18$).
- Information on maternal VL at delivery was missing for 45% of pregnancies; however proportions of missing data were similar in ZDV and non-ZDV groups therefore estimates were unlikely to be biased.
- HIV status was not yet reported for 20% of infants; mainly those born recently. Previous work has shown that this is unlikely to introduce bias³.

Conclusions

- Use of non-ZDV HAART increased over time in this combined observational dataset, particularly in early pregnancy (Figure 1).
- Tenofovir and abacavir were the most commonly used non-ZDV drugs in pregnancy (Figure 2).
- It was reassuring that there was no difference in risk of **detectable maternal HIV viral load at delivery, congenital abnormality or mother-to-child transmission** when comparing non-ZDV with ZDV HAART.
- Continued monitoring of pregnancy outcomes and longer term consequences of *in utero* exposure to these antiretroviral drugs is required.