

# DO HIV+ WOMEN ON PROTEASE INHIBITORS DELIVER PRETERM? FINDINGS FROM A UK STUDY

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## Background

- HIV-infected women on ritonavir-boosted protease inhibitor (PI/r) based ART regimens in pregnancy may be at higher risk of preterm delivery (PTD, <37weeks gestation) but evidence is inconsistent.
- Conflicting evidence around how timing of ART start, immune status (e.g. CD4 cell count) and interaction with other ART drugs may affect the risk
- The UK and Ireland National Study of HIV in Pregnancy and Childhood (NSHPC) previously reported an increased PTD risk in women on combination ART (14%) versus mono/dual therapy (10%) delivering between 1990-2005 (Townsend et al, AIDS 2007)

## Aims

- To assess whether antenatal PI/r-based, and in particular LPV/r-based regimens increase the risk of PTD compared with NNRTI-based regimens in women delivering between 2007 and 2015
- To examine whether ART at conception and first antenatal CD4 count affect these associations

## Methods

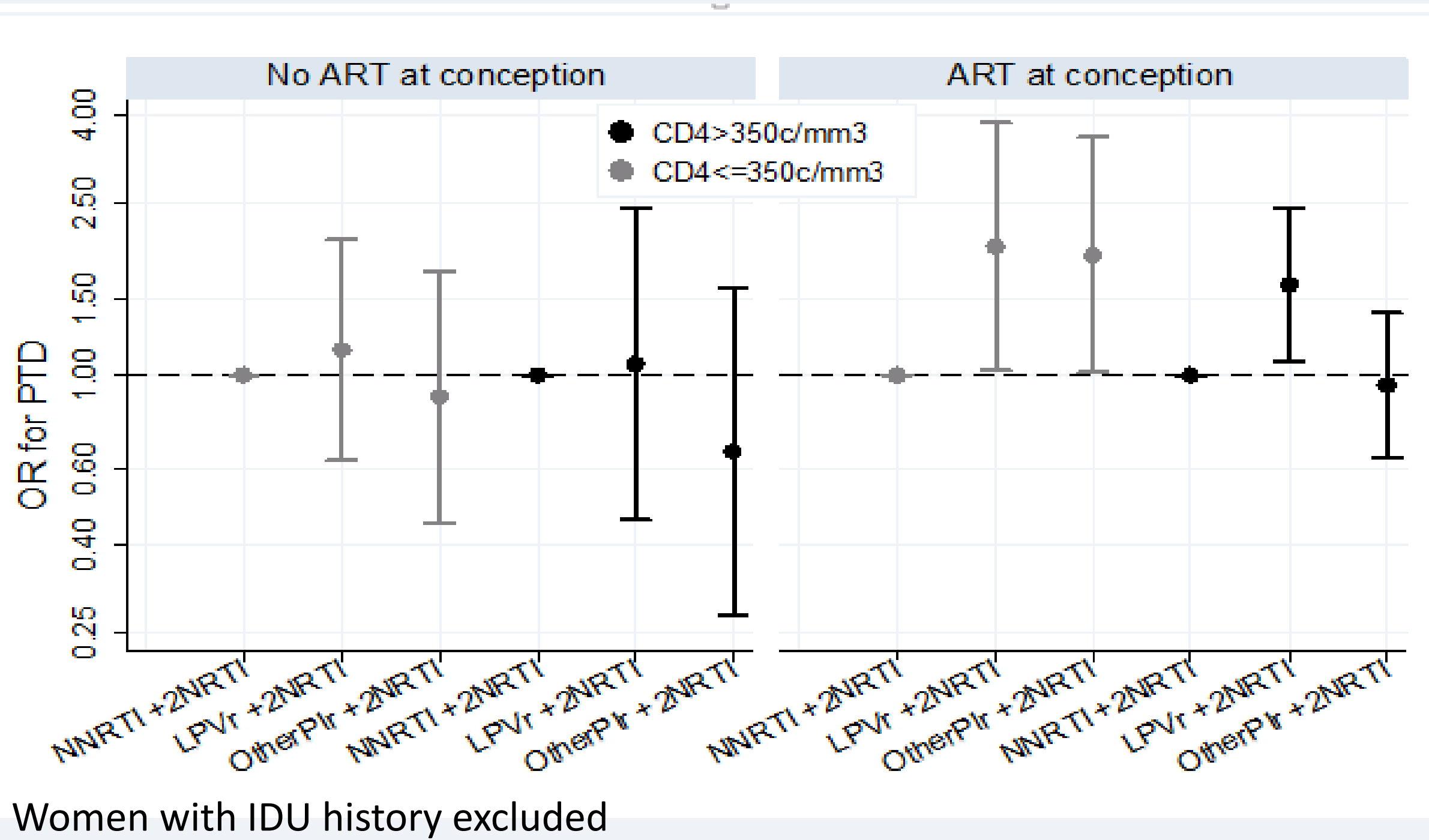
- The NSHPC is a large national study that collects comprehensive population-based surveillance data on all HIV-positive pregnant women and their children seen for care in the UK and Ireland
- Inclusion criteria for analysis:
  - Singleton live births to diagnosed women delivering between 2007 and 2015
  - For women with repeated pregnancies, the most recent pregnancy was included
  - Women on NNRTI+2NRTI or PI/r+2NRTI who did not switch any ARV during pregnancy
- Logistic regression to examine the associations of PTD with LPV/r-, other PI/r- and NNRTI-based regimens adjusted for calendar year, maternal age, region of origin, parity, and stratified by CD4 count (≤350, >350 cells/mm<sup>3</sup>) and ART at conception (yes, no)

## Results

**Table 1** Maternal characteristics of pregnancies (n= 6037)

	NNRTI+2NRTI	LPV/r+2NRTI	Other PI/r+2NRTI
	N (%)	N (%)	N (%)
PTD (<37 GW)	1889 (31.1)	2368 (39.0)	1816 (29.9)
Year of Delivery			
2007-2009	466 (24.7)	1192 (50.3)	338 (18.6)
2010-2012	704 (37.3)	952 (40.2)	637 (35.1)
2013-2015	719 (38.1)	224 (9.5)	841 (46.3)
Maternal age at delivery			
<28 years	305 (16.2)	724 (30.6)	430 (23.7)
28-32 years	415 (22.0)	644 (27.2)	455 (25.1)
33-36 years	575 (30.4)	568 (24.0)	475 (26.2)
>36 years	594 (31.5)	432 (18.2)	456 (25.1)
Parity (n=5945)			
Primiparous	506 (26.8)	743 (31.4)	535 (29.5)
Multiparous	1330 (70.4)	1615 (68.2)	1216 (67.0)
History of IDU	14 (0.7)	44 (1.9)	47 (2.6)
First antenatal CD4 (cells/mm <sup>3</sup> ) (n=5945)			
Median (IQR)	456 (325-610)	430 (303-582)	441 (317-605)
CD4≤350	426 (28.9)	635 (34.1)	44 (30.8)
ART at conception	1577 (83.5)	565 (23.9)	948 (52.2)

**Fig 1** Adjusted OR for PTD stratified by ART at conception and CD4 count (≤350 and >350 cells/mm<sup>3</sup>)



**Table 2** Factors associated with preterm deliveries in women (n=2385) on ART at conception stratified by CD4 count

	CD4≤350c/mm <sup>3</sup>			CD4>350c/mm <sup>3</sup>		
	N	%PTD	aOR*(95%CI)	N	%PTD	aOR*(95%CI)
<b>ART Regimen</b>	504	13.7		1881	8.8	
NNRTI+2NRTI	263	10.3	1.00	973	8.2	1.00
LPV/r+2NRTI	90	21.1	2.01(1.03, 3.91)	338	12.1	1.64(1.08, 2.47)
Other PI/r+2NRTI	151	15.2	2.05(1.07, 3.89)	570	7.9	0.98(0.66, 1.46)
<b>Calendar year</b>						
2007-2009	152	20.4	-	335	7.8	-
2010-2012	200	12.5	-	754	10.0	-
2013-2015	152	8.6	-	732	8.2	-
per 1yr increase	-	-	0.84(0.74, 0.95)	-	-	0.99(0.92, 1.07)
<b>Maternal age</b>						
<28years	87	12.6	1.00	270	6.3	1.00
28-32years	121	15.7	1.42(0.63, 3.22)	422	10.4	1.69(0.94, 3.05)
32-36years	142	12.0	1.00(0.43, 2.33)	582	7.6	1.11(0.61, 2.01)
>36years	154	14.3	1.22(0.54, 2.76)	607	10.1	1.64(0.92, 2.90)

Women with IDU history excluded (n=36); \*Odds ratios all mutually adjusted + parity and region of origin.

- Overall, women on LPV/r-containing regimens but not those on other PI regimens had higher risk of PTD vs. women on NNRTI-regimens. Increased PTD risk was also associated with first antenatal CD4≤350 (aOR 1.28 [95%CI 1.04, 1.58]), older age (>36 vs <28 years) (aOR 1.41 [1.05, 1.89]) and ART at conception (aOR 1.27 [1.01, 1.61])
- Stratified analysis suggested that women on LPV/r- (irrespective of CD4) and women on other PI (CD4≤350 only) at conception were still at higher risk of PTD compared with women on NNRTI-regimens at conception with similar CD4 count. (Fig 1 and Table 2).

## Conclusion

- In this national UK/Ireland study, pregnant women on LPV/r-based regimens were at higher risk of PTD vs. those on NNRTI-based regimens but the association was only apparent in women on ART at conception. Results suggest that women on other PI/r- at conception may also be at higher risk if CD4 ≤ 350.