

Figure 1

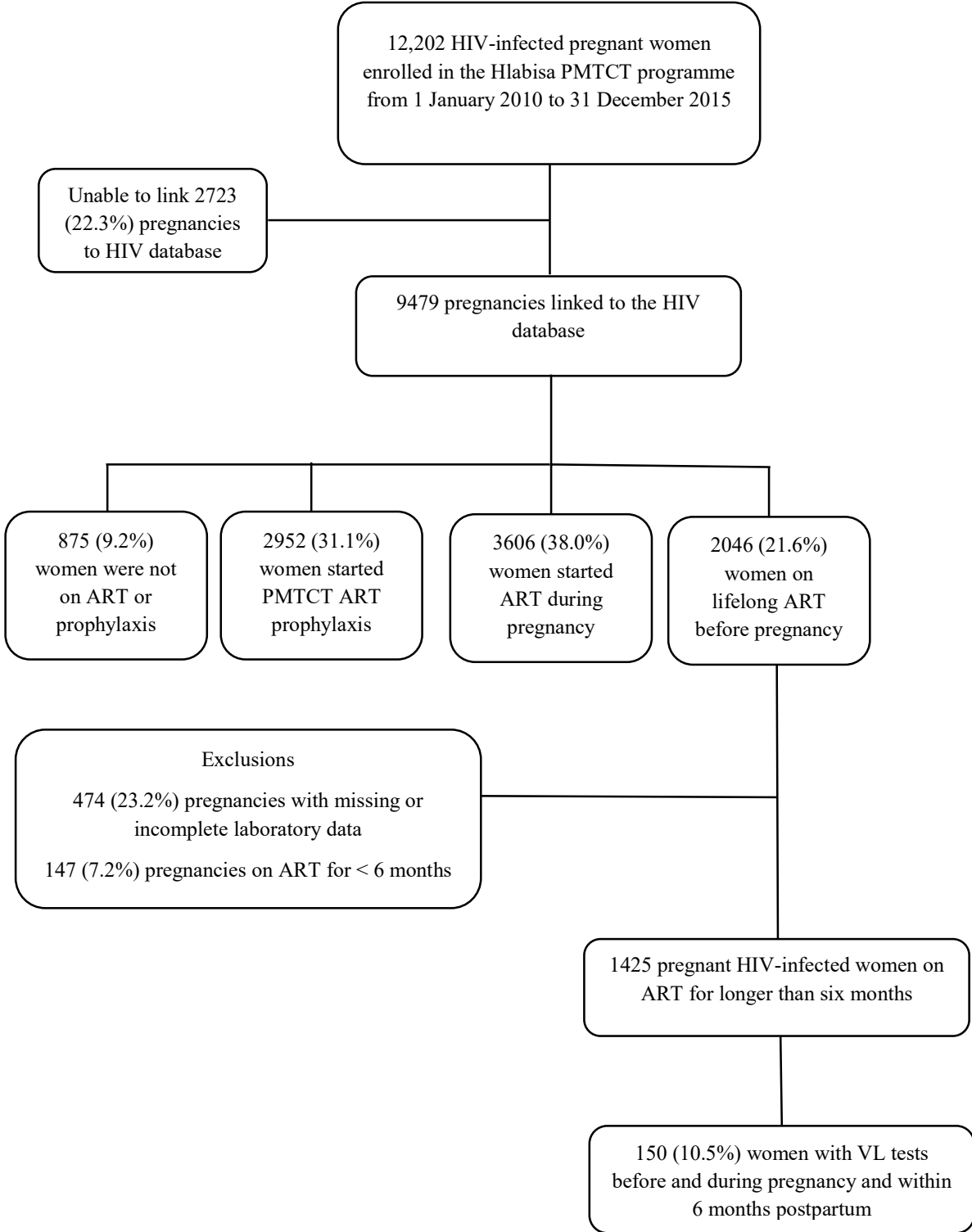


Figure 1: Study inclusions and exclusions

Table 1

**Table 1. Characteristics of HIV-infected women on ART at pregnancy start (N=1425), and a subgroup of women with VL tests before pregnancy start (n=988), January 2010-December 2015, KwaZulu-Natal, South Africa**

Characteristic	Total (N=1425) n (%)	Women by detectable and undetectable VL (n=988)		P value
		Undetectable VL (<50 copies/ml) (n=623) n (%)	Detectable VL (≥50 copies/ml) (n=365) n (%)	
<b>Age at first antenatal visit, median (IQR), years</b>	31 (27-35)	30 (27-34)	32 (29-36)	<0.01
15-24	328 (23.0)	125 (20.1)	65 (17.8)	0.16
25-34	925 (64.9)	403 (64.7)	257 (70.4)	
35-49	172 (12.1)	95 (15.3)	43 (11.8)	
<b>Place of antenatal care</b>				0.07
Peri-urban	370 (26.0)	177 (28.4)	87 (23.8)	
Rural	987 (69.3)	415 (66.6)	267 (73.2)	
Missing	68 (4.8)	31 (5.0)	11 (3.0)	
<b>HIV status disclosure to anyone</b>				<0.01
No	34 (2.4)	12 (1.9)	11 (3.0)	
Yes	936 (65.7)	396 (63.6)	267 (73.2)	
Missing	455 (31.9)	215 (34.5)	87 (23.8)	
<b>Previous PMTCT exposure</b>				0.75
No	425 (29.8)	186 (29.9)	105 (28.8)	
Yes	764 (53.6)	339 (54.4)	196 (53.7)	
Missing	236 (16.6)	98 (15.7)	64 (17.5)	
<b>Gestation at first visit, median (IQR), weeks</b>	23 (16-37)	21 (16-35)	25 (16-38)	0.19
0-19	514 (36.1)	245 (39.3)	125 (34.2)	
≥ 20	859 (60.3)	358 (57.5)	231 (63.3)	
Missing	52 (3.7)	20 (3.2)	9 (2.5)	
<b>Gestation at delivery, median (IQR), weeks</b>	39 (38-40)	39 (38-40)	39 (38-40)	0.56
< 37	120 (8.4)	50 (8.0)	33 (9.0)	
≥ 37	975 (68.4)	425 (68.2)	255 (69.9)	
Missing	330 (23.2)	148 (23.8)	77 (21.1)	
<b>CD4 count in the year prior to pregnancy, median (IQR), cells/mm<sup>3</sup></b>	477 (338-641)	518 (378-671)	424 (299-601)	<0.01
< 350	264 (18.5)	107 (17.2)	101 (27.7)	
≥ 350	722 (50.7)	404 (64.8)	224 (61.4)	
Missing	439 (30.8)	112 (18.0)	40 (11.0)	
<b>Regimen change prior to or during pregnancy</b>				0.17
No	1222 (85.5)	604 (97.0)	359 (98.4)	
Yes	203 (14.3)	19 (3.0)	6 (1.6)	
<b>Duration on ART, median (IQR), years</b>	2.1 (1.3-3.5)	1.9 (1.1-3.0)	3.0 (1.9-4.6)	<0.01
< 3	957 (67.2)	468 (75.1)	177 (48.5)	
≥ 3	468 (32.8)	155 (24.9)	188 (51.5)	
<b>ART regimen</b>				<0.01
TDF-based	791 (55.5)	460 (73.8)	112 (30.7)	
d4T-based	597 (41.9)	145 (23.3)	243 (66.6)	
ZDV-based	37 (2.6)	18 (2.9)	10 (2.7)	
<b>Calendar delivery year</b>				<0.01
2010	58 (4.1)*	19 (3.1)	28 (7.7)	
2011	206 (14.5)	43 (6.9)	66 (18.1)	
2012	297 (20.8)	102 (16.4)	95 (26.0)	
2013	298 (20.9)	148 (23.8)	65 (17.8)	
2014	327 (23.0)	174 (27.9)	68 (18.6)	
2015	239 (16.8)	137 (22.0)	43 (11.8)	

\*Due to rounding up, the percentages in the 1425 women total 100.1%

Table 2

**Table 2. VL tests subsequent to ART start in 1425 women on ART before pregnancy, and subgroup of 150 women with all 3 VL tests in pregnancy period though 6 months postpartum, 2010-2015, Kwa-Zulu-Natal, South Africa**

Viral load (copies/ml)	Overall (N=1425)					Women with all 3 VL tests before and during pregnancy and within 6 months postpartum (N=150)		
	Before pregnancy n=988 (%)	Pregnancy n=854 (%)	Postpartum			Before pregnancy n (%)	Pregnancy n (%)	Postpartum, 6 months n (%)
			6 months n=527 (%)	12 months n=437 (%)	24 months n=656 (%)			
<50	810 (82.0)	657 (76.9)	406 (77.0)	330 (75.5)	497 (75.8)	105 (70.0)	103 (68.7)	107 (71.3)
50-999	67 (6.8)	67 (7.8)	38 (7.2)	29 (6.6)	50 (7.6)	17 (11.3)	13 (8.7)	14 (9.3)
≥ 1000	111 (11.2)	130 (15.2)	83 (15.7)	78 (17.8)	109 (16.6)	28 (18.7)	34 (22.7)	29 (19.3)

Table 3

**Table 3. Risk factors for viraemia subsequent to ART start between 2010 and 2015 in women who initiated ART before pregnancy (n=1425)**

Effect	Unadjusted OR (95% CI)	P	Adjusted OR (95% CI)	P
<b>Pregnancy</b>				
Before pregnancy	Ref	-	Ref	-
During pregnancy	1.29 (0.89–1.86)	0.18	1.31 (0.90-1.92)	0.16
Postpartum, 6 months	1.20 (0.77–1.86)	0.43	1.30 (0.83-2.04)	0.25
Postpartum, 12 months	0.91 (0.55-1.49)	0.70	0.96 (0.58-1.58)	0.86
Postpartum, 24 months	1.26 (0.81-1.96)	0.31	1.40 (0.89-2.22)	0.15
<b>Age (time varying), years</b>				
25-34	Ref	-	Ref	-
15-24	1.10 (0.52–2.31)	0.80	2.01 (0.96-4.20)	0.06
35-49	0.46 (0.28-0.77)	<0.01	0.33 (0.19-0.55)	<0.01
<b>CD4 count at or up to one year before pregnancy, cells/mm<sup>3</sup></b>				
< 350	Ref	-	Ref	-
≥ 350	0.04 (0.02–0.09)	<0.01	0.05 (0.02-0.11)	<0.01
Missing	0.14 (0.07-0.29)	<0.01	0.21 (0.10-0.43)	<0.01
<b>Regimen change (time varying)</b>				
No	Ref	-	Ref	-
Yes	1.09 (0.49–2.44)	0.83	0.82 (0.37-1.81)	0.62
<b>ART regimen</b>				
TDF-based	Ref	-	Ref	-
Non-TDF based	7.11 (3.99–12.65)	<0.01	3.31 (1.61-6.78)	<0.01
<b>ART duration, years</b>				
< 3	Ref	-	Ref	-
≥ 3	1.74 (0.98–3.10)	0.06	3.03 (1.60-5.73)	<0.01
<b>Gestation at first antenatal visit, weeks</b>				
< 20	Ref	-	Ref	-
≥ 20	3.37 (1.85-6.17)	<0.01	2.70 (1.50-4.86)	<0.01
Missing	0.69 (0.13-3.58)	0.66	1.21 (0.26-5.72)	0.81
<b>Calendar year of delivery</b>				
2010	Ref	-	Ref	-
2011	2.08 (0.56-7.73)	0.27	1.93 (0.55-6.74)	0.30
2012	0.45 (0.12-1.62)	0.22	0.74 (0.21-2.62)	0.64
2013	0.28 (0.08-1.02)	0.05	0.85 (0.22-3.34)	0.82
2014	0.16 (0.04-0.60)	<0.01	0.67 (0.17-2.71)	0.58
2015	0.10 (0.02-0.40)	<0.01	0.50 (0.11-2.33)	0.38

Antenatal clinic area, prior PMTCT exposure, birth gestation, and HIV status disclosure were excluded from the model as  $P > 0.2$ .

Table 4

**Table 4.** Multivariable model of viraemia risk in each pregnancy period, **including an interaction term for ART duration and viraemia**, between 2010 and 2015 in women who initiated ART before pregnancy (n=1425)

Effect	Unadjusted OR (95% CI)	P	Adjusted OR (95% CI)	P
<b>Pregnancy</b>				
Before pregnancy	Ref	-	Ref	-
During pregnancy	1.29 (0.89–1.86)	0.18	2.25 (1.33-3.78)	<0.01
Postpartum, 6 months	1.20 (0.77–1.86)	0.43	1.81 (1.00-3.29)	0.05
Postpartum, 12 months	0.91 (0.55-1.49)	0.70	1.54 (0.79-3.0)	0.21
Postpartum, 24 months	1.26 (0.81-1.96)	0.31	2.82 (1.55-5.12)	<0.01
<b>Age (time varying), years</b>				
25-34	Ref	-	Ref	-
15-24	1.10 (0.52–2.31)	0.80	2.19 (1.02-4.72)	0.05
35-49	0.46 (0.28-0.77)	<0.01	0.33 (0.19-0.56)	<0.01
<b>Pregnancy and ART duration, years</b>				
Before pregnancy, < 3	Ref	-	Ref	-
During pregnancy, ≥ 3	0.28 (0.12–0.63)	<0.01	0.28 (0.12-0.64)	0.02
Postpartum 6 months, ≥ 3	0.47 (0.17–1.29)	0.15	0.47 (0.17-1.29)	0.14
Postpartum 12 months, ≥ 3	0.28 (0.09–0.90)	<0.01	0.28 (0.09-0.90)	0.03
Postpartum 24 months, ≥ 3	0.10 (0.03–0.31)	<0.01	0.11 (0.03-0.35)	<0.01
<b>CD4 count at or up to one year before pregnancy, cells/mm<sup>3</sup></b>				
< 350	Ref	-	Ref	-
≥ 350	0.04 (0.02–0.09)	<0.01	0.05 (0.02-0.10)	<0.01
Missing	0.14 (0.07-0.29)	<0.01	0.19 (0.09-0.41)	<0.01
<b>Regimen change (time varying)</b>				
No	Ref	-	Ref	-
Yes	1.09 (0.49–2.44)	0.83	0.82 (0.36-1.84)	0.62
<b>ART regimen</b>				
TDF-based	Ref	-	Ref	-
Non-TDF based	7.11 (3.99–12.65)	<0.01	3.43 (1.63-7.21)	<0.01
<b>ART duration, years</b>				
< 3	Ref	-	Ref	-
≥ 3	1.74 (0.98–3.10)	0.06	7.11 (3.14-16.10)	<0.01
<b>Gestation at first antenatal visit, weeks</b>				
< 20	Ref	-	Ref	-
≥ 20	3.37 (1.85-6.17)	<0.01	2.83 (1.54-5.20)	<0.01
Missing	0.69 (0.13-3.58)	0.66	1.23 (0.25-6.09)	0.80
<b>Calendar year of delivery</b>				
2010	Ref	-	Ref	-
2011	2.08 (0.56-7.73)	0.27	1.98 (0.55-7.15)	0.30
2012	0.45 (0.12-1.62)	0.22	0.74 (0.20-2.71)	0.65
2013	0.28 (0.08-1.02)	0.05	0.83 (0.20-3.37)	0.79
2014	0.16 (0.04-0.60)	<0.01	0.66 (0.16-2.77)	0.57
2015	0.10 (0.02-0.40)	<0.01	0.50 (0.10-2.42)	0.39

Antenatal clinic area, prior PMTCT exposure, birth gestation, and HIV status disclosure were excluded from the model as  $P > 0.2$ .

Table 5

**Table 5.** Multivariable model of viraemia risk in each pregnancy period, **including an interaction term for age at pregnancy start and ART duration**, in women who initiated ART before pregnancy between 2010 and 2015 (n=1425)

Effect	Unadjusted OR (95% CI)	P	Adjusted OR (95% CI)	P
<b>Pregnancy</b>				
Before pregnancy	Ref	-	Ref	-
During pregnancy	1.29 (0.89–1.86)	0.18	1.89 (1.16-3.09)	0.01
Postpartum, 6 months	1.20 (0.77–1.86)	0.43	1.58 (0.88-2.83)	0.13
Postpartum, 12 months	0.91 (0.55-1.49)	0.70	1.16 (0.61-2.23)	0.65
Postpartum, 24 months	1.26 (0.81-1.96)	0.31	1.36 (0.76-2.43)	0.30
<b>Age at pregnancy start, years</b>				
25-34	Ref	-	Ref	-
15-24	1.10 (0.52–2.31)	0.80	2.77 (0.94-8.17)	0.07
35-49	0.46 (0.28-0.77)	<0.01	0.82 (0.36-1.85)	0.63
<b>Age at pregnancy start, years and ART duration, years</b>				
Before pregnancy, 24-35	Ref	-	Ref	-
During pregnancy, 15-24	1.26 (0.39–4.04)	0.70	1.27 (0.39-4.11)	0.69
During pregnancy, 35-49	0.17 (0.07–0.43)	<0.01	0.17 (0.07-0.42)	<0.01
Postpartum 6 months, 15-24	0.68 (0.18–2.61)	0.58	0.65 (0.17-2.45)	0.53
Postpartum 6 months, 35-49	0.39 (0.13–1.14)	0.09	0.38 (0.13-1.11)	0.08
Postpartum 12 months, 15-24	1.28 (0.28-5.88)	0.75	0.99 (0.21-4.55)	0.99
Postpartum 12 months, 35-49	0.25 (0.07-0.83)	0.02	0.25 (0.08-0.86)	0.03
Postpartum 24 months, 15-24	2.37 (0.54-10.34)	0.25	1.66 (0.39-7.13)	0.50
Postpartum 24 months, 35-49	0.36 (0.12-1.03)	0.06	0.36 (0.12-1.03)	0.06
<b>CD4 count at or up to one year before pregnancy, cells/mm<sup>3</sup></b>				
< 350	Ref	-	Ref	-
≥ 350	0.04 (0.02–0.09)	<0.01	0.05 (0.02-0.10)	<0.01
Missing	0.14 (0.07-0.29)	<0.01	0.20 (0.09-0.42)	<0.01
<b>Regimen change (time varying)</b>				
No	Ref	-	Ref	-
Yes	1.09 (0.49–2.44)	0.83	0.82 (0.36-1.84)	0.62
<b>ART regimen</b>				
TDF-based	Ref	-	Ref	-
Non-TDF based	7.11 (3.99–12.65)	<0.01	3.35 (1.60-7.02)	0.01
<b>ART duration, years</b>				
< 3	Ref	-	Ref	-
≥ 3	1.74 (0.98–3.10)	0.06	3.20 (1.65-6.21)	0.01
<b>Gestation at first antenatal visit, weeks</b>				
< 20	Ref	-	Ref	-
≥ 20	3.37 (1.85-6.17)	<0.01	2.78 (1.52-5.10)	0.01
Missing	0.69 (0.13-3.58)	0.66	1.10 (0.22-5.46)	0.91
<b>Calendar year of delivery</b>				
2010	Ref	-	Ref	-
2011	2.08 (0.56-7.73)	0.27	2.17 (0.60-7.87)	0.24
2012	0.45 (0.12-1.62)	0.22	0.75 (0.20-2.78)	0.67
2013	0.28 (0.08-1.02)	0.05	0.89 (0.22-3.62)	0.87
2014	0.16 (0.04-0.60)	<0.01	0.69 (0.16-2.88)	0.61
2015	0.10 (0.02-0.40)	<0.01	0.49 (0.10-2.39)	0.38

Antenatal clinic area, prior PMTCT exposure, calendar birth year, birth gestation, and HIV status disclosure were excluded as  $P > 0.2$ .

Table S1

**Table S1. Risk of viraemia in 150 women on preconception ART with VL tests before pregnancy through six months postpartum, KwaZulu-Natal, South Africa (2010-2015)**

Effect	Unadjusted OR (95% CI)	P	Adjusted OR (95% CI)	P
<b>Pregnancy</b>				
Before pregnancy	Ref	-	Ref	-
During pregnancy	1.17 (0.48–2.87)	0.73	1.28 (0.50-3.28)	0.62
Postpartum, 6 months	0.87 (0.32–2.40)	0.79	0.99 (0.34-2.90)	0.98
<b>Age (time varying), years</b>				
25-34	Ref	-	Ref	-
15-24	1.98 (0.14-28.51)	0.62	2.15 (0.16-29.43)	0.57
35-49	1.20 (0.25–5.67)	0.82	0.72 (0.14-3.59)	0.69
<b>CD4 count at or up to one year before pregnancy, cells/mm<sup>3</sup></b>				
< 350	Ref	-	Ref	-
≥ 350	0.02 (0.003–0.22)	<0.01	0.03 (0.003-0.32)	<0.01
Missing	0.04 (0.002-0.69)	0.03	0.13 (0.006-3.00)	0.20
<b>Regimen change (time varying)</b>				
No	Ref	-	Ref	-
Yes	0.57 (0.06–5.78)	0.64	0.38 (0.04-4.20)	0.43
<b>ART regimen</b>				
TDF-based	Ref	-	Ref	-
Non-TDF based	6.92 (1.04–45.93)	0.06	0.73 (0.06-8.96)	0.81
<b>ART duration, years</b>				
< 3	Ref	-	Ref	-
≥ 3	9.09 (1.25–65.97)	0.03	14.61 (1.56-136.49)	0.02
<b>Gestation at first antenatal visit, weeks</b>				
< 20	Ref	-	Ref	-
≥ 20	1.26 (1.19-8.55)	0.81	0.33 (0.04-2.54)	0.29
Missing	0.28 (0.00-1088.0)	0.76	0.05 (0.01-154.04)	0.46
<b>Calendar year of delivery</b>				
2010	Ref	-	Ref	-
2011	8.78 (<0.001-59027.4)	0.63	7.19 (0.001-48.16)	0.64
2012	0.13 (<0.001-809.84)	0.65	0.20 (0.01-12.74)	0.70
2013	0.11 (<0.001-742.98)	0.63	0.12 (0.01-13.79)	0.63
2014	0.29 (<0.001-1918.07)	0.78	0.67 (0.01-22.42)	0.93
2015	0.03 (<0.001-207.54)	0.44	0.04 (0.01-17.44)	0.48

Antenatal clinic area, prior PMTCT exposure, calendar birth year, birth gestation, and HIV status disclosure were excluded as  $P > 0.2$ .