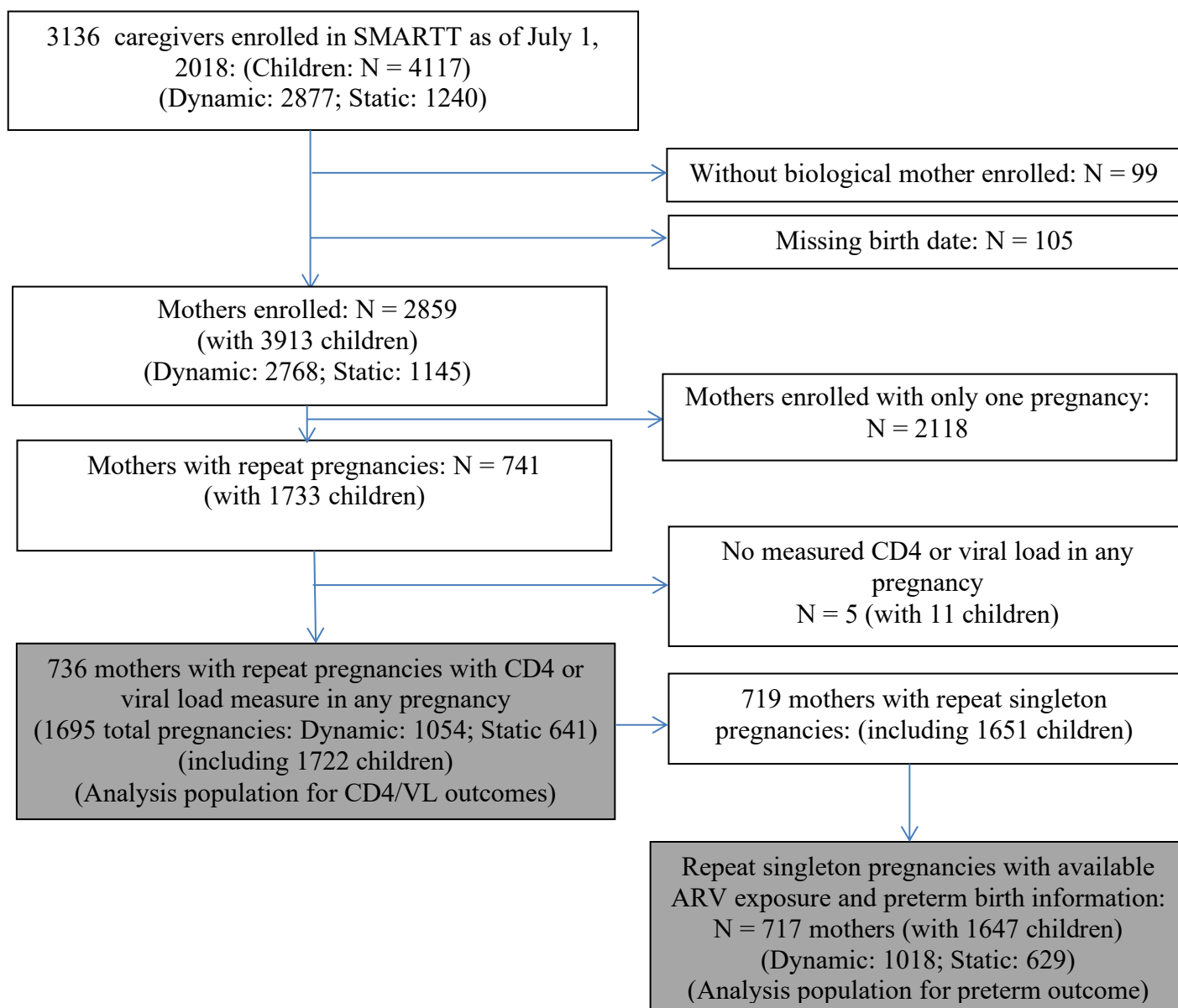


Figure Legend:

Supplemental Figure 1S:

Abbreviations: SMARRT= Surveillance Monitoring for ART Toxicities Study; VL= viral load; ARV= antiretroviral



Supplemental Digital Content Figure 1S. Derivation of Study Population of Women with Repeat Pregnancies

Supplemental Digital Content Table 1S. Maternal ARV Taken During Pregnancy for the First Three Pregnancies Among 736 Women with Repeat Pregnancies

Characteristic	Pregnancy		
	1 st pregnancy (N=736)	2 nd pregnancy (N=736)	3 rd pregnancy (N=177)
ARV taken during pregnancy ¹			
Protease Inhibitor			
Lopinavir	187 (25%)	157 (21%)	49 (28%)
Atazanavir	91 (12%)	145 (20%)	30 (17%)
Darunavir	45 (6%)	71 (10%)	24 (14%)
Nelfinavir	162 (22%)	124 (17%)	16 (9%)
Other	44 (6%)	48 (7%)	8 (5%)
Integrase Inhibitor			
Raltegravir	19 (3%)	42 (6%)	16 (9%)
Dolutegravir	5 (1%)	27 (4%)	9 (5%)
Elvitegravir	4 (1%)	29 (4%)	8 (5%)
NNRTI			
Rilpivirine	18 (2%)	76 (10%)	18 (10%)
Nevirapine	80 (11%)	51 (7%)	10 (6%)
Efavirenz	32 (4%)	23 (3%)	8 (5%)
Etravirine	6 (1%)	7 (1%)	2 (1%)
Timing of ARV initiation in pregnancy			
No ARV at any time	17 (2%)	10 (1%)	5 (3%)
On ARV at conception	193 (26%)	343 (47%)	88 (50%)
1st trimester	115 (16%)	143 (19%)	39 (22%)
2nd trimester	308 (42%)	188 (26%)	38 (21%)
3rd trimester	62 (8%)	23 (3%)	3 (2%)
Unknown	41 (6%)	29 (4%)	4 (2%)

Statistics shown are median (IQR) or count (%). ARV=antiretroviral.

¹ In addition to NRTI backbone.

Supplemental Digital Content Table 2S: Birth Outcomes from the First Three Singleton Pregnancies Enrolled in PHACS SMARTT Cohort

		Singleton Pregnancy		
		1 st pregnancy (N=717)	2 nd pregnancy (N=717)	3 rd pregnancy (N=170)
Gestational age (weeks) ¹	N	677	690	164
	Mean (s.d.)	38.3 (2.0)	38.1 (1.8)	37.9 (2.0)
	Median (Q1, Q3)	38.6 (37.7, 39.7)	38.1 (37.4, 39.1)	38 (37, 39)
	Min, Max	25.9, 42.6	24.1, 42.4	30.7, 42.0
Preterm birth (< 37 weeks gestation)	Yes	102 (14%)	111 (15%)	36 (21%)
	No	595 (83%)	598 (83%)	132 (78%)
	Unknown	20 (3%)	8 (1%)	2 (1%)
Low birth weight (< 2500 g)	Yes	105 (15%)	89 (12%)	23 (14%)
	No	599 (84%)	620 (86%)	145 (85%)
	Unknown	13 (2%)	8 (1%)	2 (1%)
Small for gestational age (birth weight z-score < 10th percentile)	No	562 (78%)	597 (83%)	140 (82%)
	Yes	132 (18%)	106 (15%)	27 (16%)
	Unknown	23 (3%)	14 (2%)	3 (2%)
Very Small for gestational age (birth weight z-score < 3rd percentile)	No	663 (92%)	683 (95%)	165 (97%)
	Yes	31 (4%)	20 (3%)	2 (1%)
	Unknown	23 (3%)	14 (2%)	3 (2%)

¹Of the total 1,647 pregnancies included, 76 were missing gestational age, of which 3 were reported as preterm and 42 were reported as term based on provider exam. Calculations were based on unique pregnancies.

Birth weight z-score adjusted for preterm birth using Fenton 2013 growth algorithms.

Supplemental Digital Content Table 3S. Preterm Birth by Paired ARV Use from Index to Subsequent Singleton Pregnancy

ARV Exposure	Paired ARV Group (1 st pregnancy/ 2 nd pregnancy)	Total (N=664)	Preterm Birth, 1 st Pregnancy N (%)	Preterm Birth, 2 nd Pregnancy N (%)	Difference in Preterm Birth Rate	Odds Ratio* of Preterm Birth (95% CI)	P-value
PI use in pregnancy						1.09 (0.59, 2.00)	0.89
	Not on PI/Not on PI	111	12 (10.8%)	9 (8.1%)	-2.7%		
	Not on PI/On PI	93	14 (15.1%)	15 (16.1%)	1.1%		
	On PI/Not on PI	97	16 (16.5%)	15 (15.5%)	-1.0%		
	On PI/Stayed on PI	363	54 (14.9%)	68 (18.7%)	3.9%		
PI use at conception						1.05 (0.55, 2.00)	1.00
	Not on PI/Not on PI	412	59 (14.3%)	63 (15.3%)	1.0%		
	Not on PI/On PI	135	21 (15.6%)	23 (17.0%)	1.5%		
	On PI/Not on PI	55	7 (12.7%)	8 (14.5%)	1.8%		
	On PI/Stayed on PI	61	9 (14.8%)	13 (21.3%)	6.6%		
PI use in 1st trimester						1.39 (0.79, 2.49)	0.28
	Not on PI/Not on PI	305	40 (13.1%)	38 (12.5%)	-0.7%		
	Not on PI/On PI	156	25 (16.0%)	33 (21.2%)	5.1%		
	On PI/Not on PI	73	10 (13.7%)	9 (12.3%)	-1.4%		
	On PI/Stayed on PI	129	21 (16.3%)	27 (20.9%)	4.7%		
INSTI use in pregnancy						0.75 (0.28, 1.94)	0.66
	Not on INSTI/Not on INSTI	569	82 (14.4%)	93 (16.3%)	1.9%		
	Not on INSTI/On INSTI	71	14 (19.7%)	12 (16.9%)	-2.8%		
	On INSTI/Not on INSTI	5	0 (0.0%)	1 (20.0%)	20.0%		
	On INSTI/Stayed on INSTI	19	0 (0.0%)	1 (5.3%)	5.3%		
INSTI use at conception						0.40 (0.04, 2.44)	0.45
	Not on INSTI/Not on INSTI	624	91 (14.6%)	105 (16.8%)	2.2%		
	Not on INSTI/On INSTI	33	5 (15.2%)	2 (6.1%)	-9.1%		
	On INSTI/Not on INSTI	3	0 (0.0%)	0 (0.0%)	0.0%		
	On INSTI/Stayed on INSTI	4	0 (0.0%)	0 (0.0%)	0.0%		
INSTI use in 1st trimester						0.70 (0.23, 2.04)	0.63
	Not on INSTI/Not on INSTI	599	86 (14.4%)	98 (16.4%)	2.0%		
	Not on INSTI/On INSTI	53	10 (18.9%)	8 (15.1%)	-3.8%		
	On INSTI/Not on INSTI	4	0 (0.0%)	1 (25.0%)	25.0%		
	On INSTI/Stayed on INSTI	8	0 (0.0%)	0 (0.0%)	0.0%		

*Odds Ratio of preterm birth comparing women exposed vs. not exposed to a specific ARV, from exact conditional logistic regression model. ARV= antiretroviral, CI= confidence interval; PI= protease inhibitor; INSTI= integrase strand transfer inhibitor