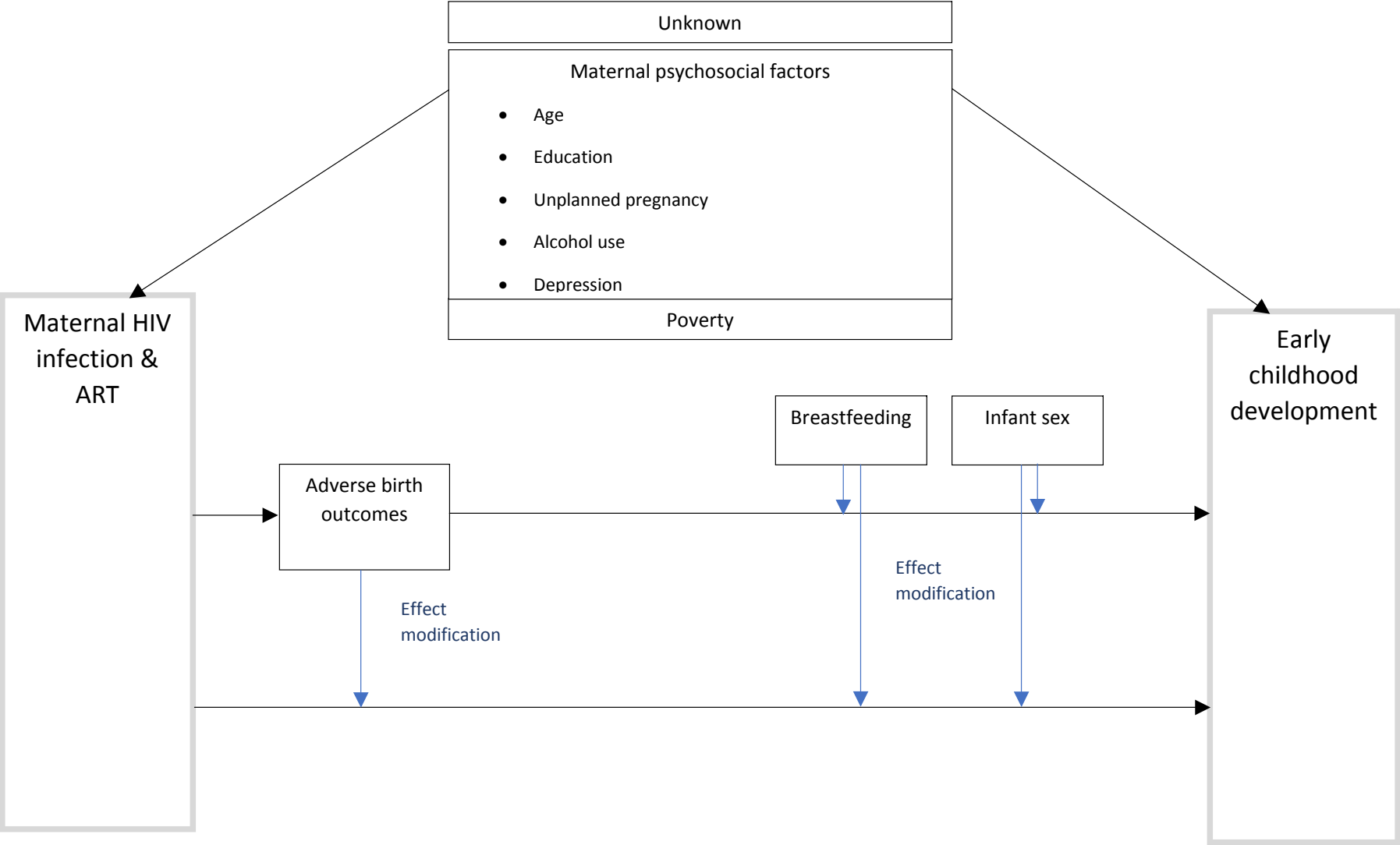


SUPPLEMENTAL DIGITAL CONTENT 1. Directed acyclic graph: Maternal HIV infection and early childhood development



**SUPPLEMENTAL DIGITAL CONTENT 2, TABLE. Maternal and infant characteristics by categories of preterm delivery and HIV exposure status, limited to HIV-uninfected infants with developmental assessment data**

	TOTAL N=521	Term infants		Preterm infants		<i>p</i> -value
		HIV-unexposed n=278	HIV-exposed n=187	HIV-unexposed n=28	HIV-exposed n=28	
Maternal characteristics						
Age in years	28 (24-33)	28 (23-33)	29 (25-33)	29 (24-33)	29 (27-34)	0.25
Married/cohabiting	227 (44%)	125 (45%)	75 (40%)	13 (46%)	14 (50%)	0.64
Completed secondary schooling	202 (39%)	130 (47%)	48 (26%)	13 (46%)	11 (39%)	<0.0001
Employed	225 (43%)	134 (48%)	69 (37%)	10 (36%)	12 (43%)	0.09
Informal housing	240 (46%)	132 (48%)	89 (48%)	12 (43%)	7 (25%)	0.14
Unplanned pregnancy	358 (69%)	176 (63%)	142 (76%)	21 (75%)	19 (68%)	0.03
Antenatal depression	17 (3%)	6 (2%)	9 (5%)	2 (7%)	0	0.20
Risky drinking, enrolment <sup>1</sup>	85 (16%)	18 (6%)	53 (29%)	6 (21%)	8 (30%)	<0.0001
Risky drinking, 3 <sup>rd</sup> trimester <sup>1</sup>	27 (5%)	2 (<1%)	22 (12%)	0	3 (11%)	<0.0001
Intimate partner violence, enrolment <sup>2</sup>	66 (13%)	21 (8%)	37 (20%)	2 (7%)	6 (22%)	<0.0001
Birth and infant characteristics						
Gestation at delivery (weeks)	39 (38-40)	39 (39-40)	40 (39-40)	35 (34-35)	35 (32-36)	0.0001
Male gender	252 (48%)	125 (45%)	102 (55%)	13 (46%)	12 (43%)	0.21

		Term infants		Preterm infants		
Weight for age Z-score at birth <sup>3</sup>	-0.1 (-0.8; 0.5)	0.0 ( -0.7; 0.6)	-0.2 (-0.9; 0.4)	-0.2 (-1.1; 0.4)	-0.4 (-1.0; 0.3)	0.06
<i>Small for gestational age</i> <sup>3</sup>	64 (12%)	29 (10%)	24 (13%)	6 (21%)	5 (18%)	0.27
Length for age Z-score at birth <sup>3</sup>	0.3 (-0.7; 1.5)	0.6 (-0.5; 1.9)	0.2 (-0.7; 1.3)	0.0 (-1.7; 1.1)	-0.2 (-1.3; 0.7)	0.002
Head circumference for age Z-score at birth <sup>3</sup>	0.7 (-0.3; 1.5)	0.9 (-0.2; 1.8)	0.5 (-0.4; 1.4)	0.1 (-0.5; 0.6)	-0.3 (-1.0; 1.5)	0.0002
Breastfeeding (months) <sup>4</sup>	9 (3-12)	10 (3-12)	6 (1-12)	10 (3-12)	6 (2-12)	0.005
Attending creche at time of assessment	71 (14%)	44 (16%)	18 (10%)	4 (15%)	5 (18%)	0.27

Values are median (interquartile range) or n (column %); p-values obtained from Chi<sup>2</sup> or Kruskal-Wallis, no correction for multiple comparisons. Antenatal depression, defined as EPDS (Edinburgh postnatal depression scale) score of  $\geq 13$  at enrolment study visit; <sup>1</sup> Risky drinking, defined as Alcohol use disorders identification test (AUDIT-C) score  $\geq 3$  as reported at first antenatal visit and at approximately 34 weeks' gestational age; <sup>2</sup> Any physical, sexual or psychological violence as measured with World Health Organization violence against women questionnaire at study enrolment; <sup>3</sup> calculated using Intergrowth-21<sup>st</sup> reference standards; SGA defined as weight percentile at birth  $<10$ ; <sup>4</sup> Last visit at which mother reported breastfeeding taken as breastfeeding cessation date.



**SUPPLEMENTAL DIGITAL CONTENT 3, TABLE: Maternal and infant characteristics by availability of developmental outcome data**

	HIV-exposed uninfected children				HIV-unexposed children			
	Total (N=471)	Completed developmental assessment (n=215)	Did not complete developmental assessment (n=256)	<i>p</i>	Total (N=414)	Completed developmental assessment (n=306)	Did not complete developmental assessment (n=108)	<i>p</i>
<b>Maternal characteristics</b>								
Age in years	28 (24-32)	29 (25-33)	27 (24-31)	0.01	27 (23-32)	28 (24-33)	26 (22-31)	0.01
Married/cohabiting	215 (46%)	89 (46%)	126 (45%)	0.87	306 (74%)	138 (75%)	168 (73%)	0.65
Matriculated	117 (25%)	59 (27%)	58 (23%)	0.23	185 (45%)	143 (47%)	42 (39%)	0.16
Employed	184 (39%)	81 (37%)	103 (40%)	0.57	195 (47%)	144 (47%)	51 (47%)	0.98
Informal housing	247 (52%)	96 (45%)	151 (59%)	0.002	197 (48%)	144 (47%)	53 (49%)	0.72
Unplanned pregnancy	338 (72%)	161 (75%)	177 (69%)	0.17	275 (66%)	197 (64%)	78 (72%)	0.14
Risky drinking, enrolment <sup>1</sup>	118 (25%)	61 (29%)	57 (22%)	0.11	30 (7%)	24 (8%)	6 (6%)	0.43
Risky drinking, 3 <sup>rd</sup> trimester <sup>1</sup>	42 (9%)	24 (11%)	18 (7%)	0.10	3 (<1%)	2 (<1%)	1 (1%)	0.76
Intimate partner violence <sup>2</sup>	105 (23%)	43 (20%)	62 (24%)	0.30	33 (8%)	23 (7%)	10 (9%)	0.57
CD4 cell count at ART initiation (cells/mm <sup>3</sup> )	354 (248-517)	346 (235-522)	360 (253-511)	0.53	-	-	-	-
Log <sup>10</sup> HIV viral load at ART initiation (copies/mL)	4.0 (3.4-4.6)	4.0 (3.6-4.7)	3.9 (3.1-4.5)	0.01	-	-	-	-

	HIV-exposed uninfected children				HIV-unexposed children			
	Total (N=471)	Completed developmental assessment (n=215)	Did not complete developmental assessment (n=256)	<i>p</i>	Total (N=414)	Completed developmental assessment (n=306)	Did not complete developmental assessment (n=108)	<i>p</i>
<b>Infant and postpartum maternal characteristics</b>								
Gestational age at birth (weeks)	39 (38-40)	39 (38-40)	39 (38-40)	0.13	39 (38-40)	39 (38-40)	39 (38-40)	0.92
<i>Preterm (&lt;37 weeks)</i>	57 (12%)	28 (13%)	29 (11%)	0.57	39 (9%)	28 (9%)	11 (10%)	0.75
Male	233 (49%)	114 (53%)	119 (47%)	0.16	213 (52%)	168 (55%)	45 (43%)	0.03
Small for gestational age <sup>3</sup>	70 (15%)	29 (13%)	41 (16%)	0.44	46 (11%)	35 (11%)	11 (11%)	0.79
Postpartum depression <sup>4</sup>	19 (4%)	9 (4%)	10 (4%)	0.99	12 (3%)	8 (3%)	4 (4%)	0.44
Breastfeeding (months) <sup>5</sup>	4 (1-12)	6 (1-12)	3 (1-9)	0.001	9 (3-12)	10 (3-12)	3 (2-9)	0.0001

Values are median (interquartile range) or n (column %); p-values obtained from Chi<sup>2</sup> or Kruskal-Wallis, no correction for multiple comparisons.

<sup>1</sup> Risky drinking, defined as Alcohol use disorders identification test (AUDIT-C) score  $\geq 3$  as reported at first antenatal visit and at approximately 34 weeks' gestational age; <sup>2</sup> Any physical, sexual or psychological violence as measured with World Health Organization violence against women questionnaire at study enrolment; <sup>3</sup> Weight percentile at birth  $<10$ , calculated using Intergrowth-21<sup>st</sup> reference standards; <sup>4</sup> Maternal depression, EPDS (Edinburgh postnatal depression scale) score of  $\geq 13$  at 6 weeks' postpartum study visit; <sup>5</sup> Last visit at which mother reported breastfeeding taken as breastfeeding cessation date.

**SUPPLEMENTAL DIGITAL CONTENT 4, TABLE. Summary of Bayley Scales of Infant Developmental scores at 10-18 months of age, by maternal HIV status**

	<b>Total (N=521)</b>	<b>HIV-exposed uninfected infants (n=215)</b>	<b>HIV-unexposed uninfected infants (n=306)</b>	<b><i>p</i>-value<sup>1</sup></b>
<b>Cognitive</b>				
Cognitive composite score	100 (95-110)	100 (95-110)	100 (95-110)	0.99
Cognitive composite score <85	35 (7%)	21 (10%)	14 (5%)	0.02
<b>Motor</b>				
Motor composite score	97 (91-103)	97 (89-107)	97 (91-103)	0.79
Motor composite score <85	33 (6%)	19 (9%)	14 (5%)	0.04
<b>Language*</b>				
Language* composite score	100 (89-106)	94 (89-112)	100 (94-106)	0.46
Language* composite score <85	82 (16%)	38 (18%)	44 (14%)	0.31

\* Based on expressive language scaled scores only; <sup>1</sup>Kruskal-Wallis and Chi<sup>2</sup>

**SUPPLEMENTAL DIGITAL CONTENT 5, TABLE.**

**Maternal and infant characteristics by degree of COGNITIVE developmental delay as measured with BSID-III composite cognitive scores:**

	<b>TOTAL</b>	<b>No delay (BSID-III composite cognitive score ≥85)</b>	<b>Mild/moderate delay (BSID-III composite cognitive score 71-84)</b>	<b>Severe delay (BSID-III composite cognitive score &lt;70)</b>	<b><i>p-value</i></b>
<b>HIV-uninfected women</b>	306	292 (95%)	12 (4%)	2 (1%)	-
<b>HIV-infected women</b>	213	192 (90%)	19 (9%)	2 (1%)	-
Log <sup>10</sup> HIV viral load at ART initiation in pregnancy	4.1 (3.6-4.6)	4.0 (3.6-4.6)	4.2 (3.6-4.7)	5.0 (4.7-5.3)	0.22
<i>Suppressed HIV viral load (&lt;50 copies/uL) at delivery</i>	160 (75%)	144 (75%)	15 (79%)	1 (50%)	0.66
CD4 cell count at ART initiation in pregnancy (cells/mm <sup>3</sup> )	345 (235-512)	349 (232 – 524)	327 (257-436)	259 (213-305)	0.58
Age in years	29 (25-33)	29 (25-33)	32 (27-34)	27 (27–28)	0.25
Married/cohabiting	88 (41%)	73 (38%)	15 (79%)	0	0.001
Completed secondary education	58 (27%)	55 (29%)	3 (16%)	0	0.33
Employed	81 (38%)	76 (40%)	4 (21%)	1 (50%)	0.27
Informal housing	95 (45%)	85 (44%)	9 (47%)	1 (50%)	0.96
Risky drinking <sup>1</sup>	61 (29%)	57 (30%)	3 (16%)	1 (50%)	0.34
Intimate partner violence <sup>2</sup>	42 (20%)	38 (20%)	2 (10%)	2 (100%)	0.01
Depression at 6 weeks postpartum <sup>3</sup>	19 (9%)	15 (8%)	3 (16%)	1 (50%)	0.06
Maternal self-reported smoking at time of assessment	72 (34%)	63 (33%)	7 (37%)	2 (100%)	0.13
Gestational age at delivery (weeks)	39 (38-40)	39 (38-40)	39 (35-40)	37 (35-40)	0.13

	<b>TOTAL</b>	<b>No delay (BSID-III composite cognitive score ≥85)</b>	<b>Mild/moderate delay (BSID-III composite cognitive score 71-84)</b>	<b>Severe delay (BSID-III composite cognitive score &lt;70)</b>	<b><i>p-value</i></b>
<i>Preterm (&lt;37)</i>	28 (13%)	22 (12%)	5 (26%)	1 (50%)	0.06
Male	112 (53%)	102 (53%)	10 (53%)	0	0.32
Birth weight for age, Z-score <sup>4</sup>	-0.2 (-0.9; 0.3)	-0.2 (-0.9; 0.4)	-0.9 (-0.5; 0.2)	-0.3 (0.0; 0.3)	0.65
<i>Small for gestational age (&lt;10<sup>th</sup> percentile)</i>	29 (14%)	26 (14%)	3 (16%)	0	0.82
Birth head circumference for age, Z-score <sup>4</sup>	0.5 (-0.6; 1.4)	0.5 (-0.6; 1.4)	0.5 (-0.8; 1.4)	-0.5 (0.5; 1.5)	0.98
Duration of any breastfeeding (months)	6 (1-12)	6 (1-12)	12 (1-12)	7 (1-12)	0.86
Attends nursery/creche at time of assessment	23 (11%)	22 (12%)	1 (5%)	0	0.62

Values are median (interquartile range) or n (column %); p-values are based on Kruskal-Wallis or chi<sup>2</sup> and are not corrected for multiple testing

Allocation of categories of delay: (a) No delay: composite score ≥85; (b) mild/moderate delay: ≥70<85; (c) severe delay: <70

<sup>1</sup> Risky drinking, defined as Alcohol use disorders identification tool (AUDIT-C) score ≥3 as reported at first antenatal visit

<sup>2</sup> Any physical, sexual or psychological violence as measured with World Health Organization violence against women questionnaire at first antenatal visit

<sup>3</sup> Maternal depression, EPDS (Edinburgh postnatal depression scale) score of ≥ 13 at 6 weeks' postpartum study visit

<sup>4</sup> Corrected for gestational age at birth, calculated using Intergrowth-21<sup>st</sup> reference standards

## SUPPLEMENTAL DIGITAL CONTENT 6, TABLE.

Maternal and infant characteristics by degree of MOTOR developmental delay as measured with BSID-III composite scores:

	TOTAL	No delay (BSID-III composite motor score ≥85)	Mild/moderate delay (BSID-III composite motor score 71-84)	Severe delay (BSID-III composite motor score <70)	<i>p-value</i>
<b>HIV-uninfected women (HIV-unexposed children)</b>	306	292 (95%)	13 (4%)	1 (<1%)	-
<b>HIV-infected women (HIV-exposed uninfected children)</b>	208	189 (91%)	15 (7%)	4 (2%)	-
Log <sup>10</sup> HIV viral load at ART initiation in pregnancy	4.1 (3.6-4.6)	4.0 (3.6-4.6)	4.4 (3.7-4.7)	4.9 (4.3-5.2)	0.10
<i>Suppressed HIV viral load (&lt;50 copies/uL) at delivery</i>	155 (75%)	144 (76%)	10 (67%)	1 (25%)	0.05
CD4 cell count at ART initiation in pregnancy (cells/mm <sup>3</sup> )	344 (231-515)	352 (239-517)	306 (223-502)	254 (126-550)	0.69
Age in years	29 (25-33)	29 (25-33)	29 (28-33)	28 (27-33)	0.82
Married/cohabiting	87 (42%)	79 (42%)	7 (47%)	1 (25%)	0.73
Completed secondary education	57 (27%)	52 (28%)	4 (27%)	1 (25%)	0.99
Employed	79 (38%)	72 (38%)	4 (27%)	3 (75%)	0.21
Informal housing	94 (45%)	87 (46%)	6 (40%)	1 (25%)	0.65
Risky drinking <sup>1</sup>	58 (28%)	52 (28%)	4 (27%)	2 (50%)	0.62
Intimate partner violence <sup>2</sup>	42 (20%)	34 (18%)	6 (40%)	2 (50%)	0.04
Depression at 6 weeks postpartum <sup>3</sup>	19 (9%)	16 (8%)	3 (20%)	0	0.27
Maternal self-reported smoking at time of assessment	68 (33%)	60 (32%)	5 (33%)	3 (75%)	0.19
Gestational age at delivery (weeks)	39 (38-40)	39 (38-40)	37 (31-39)	36 (34-39)	<0.001

	<b>TOTAL</b>	<b>No delay (BSID-III composite motor score ≥85)</b>	<b>Mild/moderate delay (BSID-III composite motor score 71-84)</b>	<b>Severe delay (BSID-III composite motor score &lt;70)</b>	<b><i>p-value</i></b>
<i>Preterm (&lt;37)</i>	26 (13%)	17 (9%)	7 (47%)	2 (50%)	<0.001
Male	108 (52%)	98 (52%)	8 (53%)	2 (50%)	0.99
Birth weight for age, Z-score <sup>4</sup>	-0.2 (-0.9; 0.3)	-0.3 (-0.9; 0.3)	-0.1 (-1.1; 0.6)	-0.4 (-0.9; 0.5)	0.91
<i>Small for gestational age (&lt;10<sup>th</sup> percentile)</i>	27 (13%)	23 (12%)	3 (20%)	1 (25%)	0.52
Birth head circumference for age, Z-score <sup>4</sup>	0.5 (-0.5; 1.4)	0.4 (-0.4; 1.4)	1.4 (-0.7; 1.9)	-0.2 (-0.7; 0.7)	0.22
Duration of any breastfeeding (months)	6 (1-12)	7 (1-12)	4 (1-12)	3 (2-7)	0.61
Attends nursery/creche at time of assessment	23 (11%)	21 (11%)	1 (7%)	1 (25%)	0.58

Values are median (interquartile range) or n (column %); p-values are based on Kruskal-Wallis or chi<sup>2</sup> and are not corrected for multiple testing

Allocation of categories of delay: (a) No delay: composite score ≥85; (b) mild/moderate delay: ≥70<85; (c) severe delay: <70

<sup>1</sup> Risky drinking, defined as Alcohol use disorders identification test (AUDIT-C) score ≥3 as reported at first antenatal visit

<sup>2</sup> Any physical, sexual or psychological violence as measured with World Health Organization violence against women questionnaire at first antenatal visit

<sup>3</sup> Maternal depression, EPDS (Edinburgh postnatal depression scale) score of ≥ 13 at 6 weeks' postpartum study visit

<sup>4</sup> Corrected for gestational age at birth, calculated using Intergrowth-21<sup>st</sup> reference standards

**SUPPLEMENTAL DIGITAL CONTENT 7, TABLE.**

**Maternal and infant characteristics by degree of LANGUAGE\* developmental delay as measured with BSID-III composite scores:**

	<b>TOTAL</b>	<b>No delay (BSID-III composite language* score ≥85)</b>	<b>Mild/moderate delay (BSID-III composite language* score 71-84)</b>	<b>Severe delay (BSID-III composite language* score &lt;70)</b>	<b><i>p-value</i></b>
<b>HIV-uninfected women (HIV-unexposed children)</b>	306	262 (86%)	41 (13%)	3 (1%)	-
<b>HIV-infected women (HIV-exposed uninfected children)</b>	215	177 (82%)	36 (17%)	2 (1%)	-
Log <sup>10</sup> HIV viral load at ART initiation in pregnancy	4.1 (3.6-4.6)	3.9 (3.5-4.5)	4.5 (4.2-5.0)	4.5 (3.7-5.3)	0.0001
<i>Suppressed HIV viral load (&lt;50 copies/uL) at delivery</i>	162 (75%)	138 (78%)	22 (61%)	2 (100%)	0.07
CD4 cell count at ART initiation in pregnancy (cells/mm <sup>3</sup> )	346 (235-522)	358 (261-552)	291 (197-399)	292 (148-436)	0.01
Age in years	29 (25-33)	29 (25-33)	28 (24-32)	30 (26-34)	0.87
Married/cohabiting	89 (41%)	75 (42%)	13 (36%)	1 (50%)	0.76
Completed secondary education	59 (27%)	53 (30%)	6 (17%)	0	0.18
Employed	81 (38%)	70 (40%)	11 (30%)	0	0.32
Informal housing	96 (45%)	82 (46%)	13 (36%)	1 (50)	0.53
Risky drinking <sup>1</sup>	61 (29%)	47 (27%)	13 (36%)	1 (50%)	0.43
Intimate partner violence <sup>2</sup>	43 (20%)	36 (21%)	1 (19%)	0	0.76
Depression at 6 weeks postpartum <sup>3</sup>	19 (9%)	13 (7%)	6 (17%)	0	0.19
Maternal self-reported smoking at time of assessment	73 (34%)	56 (32%)	15 (42%)	2 (100%)	0.08
Gestational age at delivery (weeks)	39 (38-40)	39 (38-40)	40 (39-41)	40 (40-41)	0.08

	<b>TOTAL</b>	<b>No delay (BSID-III composite language* score ≥85)</b>	<b>Mild/moderate delay (BSID-III composite language* score 71-84)</b>	<b>Severe delay (BSID-III composite language* score &lt;70)</b>	<b><i>p-value</i></b>
<i>Preterm (&lt;37)</i>	28 (13%)	25 (14%)	3 (8%)	0	0.55
Male	114 (53%)	94 (53%)	18 (50%)	2 (100%)	0.39
Birth weight for age, Z-score <sup>4</sup>	-0.2 (-0.9; 0.4)	-0.3 (-0.8; 0.3)	-0.1 (-1.0; 0.5)	-0.4 (-1.4; 0.5)	0.95
<i>Small for gestational age (&lt;10<sup>th</sup> percentile)</i>	29 (14%)	21 (12%)	7 (19%)	1 (50%)	0.15
Birth head circumference for age, Z-score <sup>4</sup>	0.4 (-0.6; 1.4)	0.3 (-0.5; 1.4)	1.0 (-0.7; 1.6)	0.4 (-1.1; 2.0)	0.63
Duration of any breastfeeding (months)	6 (1-12)	7 (1-12)	5 (1-12)	10 (3-18)	0.62
Attends nursery/creche at time of assessment	23 (11%)	19 (11%)	4 (11%)	0	0.88

Values are median (interquartile range) or n (column %); p-values are based on Kruskal-Wallis or chi<sup>2</sup> and are not corrected for multiple testing

Allocation of categories of delay: (a) No delay: composite score ≥85; (b) mild/moderate delay: ≥70<85; (c) severe delay: <70

<sup>1</sup> Risky drinking, defined as Alcohol use disorders identification test (AUDIT-C) score ≥3 as reported at first antenatal visit

<sup>2</sup> Any physical, sexual or psychological violence as measured with World Health Organization violence against women questionnaire at first antenatal visit

<sup>3</sup> Maternal depression, EPDS (Edinburgh postnatal depression scale) score of ≥ 13 at 6 weeks' postpartum study visit

<sup>4</sup> Corrected for gestational age at birth, calculated using Intergrowth-21<sup>st</sup> reference standards

**SUPPLEMENTAL DIGITAL CONTENT 8, TABLE. Restricted logistic regression analysis of relative odds of delay (BSID-III composite score<85) across cognitive, motor and language domains: HIV-exposed uninfected compared to HIV-unexposed children**

	<b>Total N= 208</b>	<b>HEU children n=48</b>	<b>HU children n=160</b>	<b>OR</b>	<b>95% CI</b>	<b><i>p</i>-value</b>
Cognitive delay	13 (6%)	5 (10%)	8 (5%)	2.21	0.69-7.10	0.18
Motor delay	5 (2%)	2 (4%)	3 (2%)	2.28	0.37-14.03	0.38
Language* delay	28 (13%)	8 (17%)	20 (13%)	1.40	0.57-3.42	0.46

HEU, HIV-exposed uninfected; HU, HIV-unexposed.

Subgroup: all infants term (≥37 weeks gestational age), AGA (birthweight ≥10<sup>th</sup> centile for gestational age), breastfed for ≥6 months; no risky drinking or intimate partner violence reported at enrolment; HIV-infected mothers limited to those with pre-ART CD4 cell count >200 cells/mm<sup>3</sup>

**SUPPLEMENTAL DIGITAL CONTENT 9, TABLE. Relative odds for developmental delay comparing HIV-exposed uninfected (HEU) to HIV-unexposed (HU) children, stratified by maternal/infant characteristics**

Maternal/infant characteristics	Strata	Cognitive delay		Motor delay		Language delay*	
		OR (95% CI) <sup>1</sup>	<sup>2</sup> <i>p</i> -value for interaction	OR (95% CI) <sup>1</sup>	<sup>2</sup> <i>p</i> -value for interaction	OR (95% CI) <sup>1</sup>	<sup>2</sup> <i>p</i> -value for interaction
Unadjusted estimate	n/a	2.28 (1.13-4.60)	n/a	2.10 (1.03-4.28)	n/a	1.28 (0.80-2.05)	n/a
Breastfeeding duration	< 9 months	2.41 (0.80-7.26)	0.98	1.32 (0.54-3.24)	0.16	1.04 (0.55-1.97)	0.43
	≥ 9 months	2.36 (0.94-5.91)		3.93 (1.15-13.42)		1.53 (0.75-3.11)	
Pregnancy intentions	Unplanned	2.16 (0.92-5.08)	0.79	1.71 (0.73-4.02)	0.40	1.69 (0.97-2.94)	0.04
	Planned	2.66 (0.77-9.14)		3.35 (0.90-12.43)		0.43 (0.14-1.37)	
Maternal age	< 30 years	2.50 (0.93-6.76)	0.71	1.95 (0.80-4.75)	0.75	2.00 (1.04-3.84)	0.03
	≥ 30 years	1.91 (0.71-5.15)		2.51 (0.73-8.61)		0.71 (0.35-1.43)	
Relationship status	Single	1.16 (0.38-3.54)	0.11	3.26 (1.10-9.64)	0.28	1.48 (0.79-2.77)	0.47
	Married	3.85 (1.50-9.86)		1.45 (0.54-3.92)		1.04 (0.50-2.17)	
Employment	Unemployed	3.59 (1.36-9.45)	0.13	2.27 (0.87-5.95)	0.81	1.79 (0.95-3.36)	0.11
	Employed	1.12 (0.35-3.54)		1.90 (0.64-5.63)		0.79 (0.36-1.70)	
Education	No matric	5.22 (1.73-15.80)	0.03	1.75 (0.73-4.17)	0.60	1.14 (0.66-1.99)	0.88
	Matriculated	0.73 (0.19-2.74)		2.65 (0.74-9.54)		1.04 (0.38-2.86)	
Housing	Formal	3.29 (1.09-9.56)	0.41	9.41 (2.06-42.92)	0.01	2.02 (1.04-3.92)	0.05

Maternal/infant characteristics	Strata	Cognitive delay		Motor delay		Language delay*	
		OR (95% CI) <sup>1</sup>	<sup>2</sup> p-value for interaction	OR (95% CI) <sup>1</sup>	<sup>2</sup> p-value for interaction	OR (95% CI) <sup>1</sup>	<sup>2</sup> p-value for interaction
	Informal	1.76 (0.69-4.52)		0.89 (0.34-2.34)		0.77 (0.38-1.57)	
Intimate partner violence <sup>3</sup>	No	2.33 (1.11-4.95)	0.99	1.63 (0.70-3.79)	0.66	1.41 (0.84-2.35)	0.32
	Yes	2.32 (0.24-22.04)		2.47 (0.48-12.76)		0.70 (0.19-2.52)	
Birth size	AGA	2.15 (1.03-4.51)	0.63	1.79 (0.83-3.86)	0.33	1.18 (0.70-1.98)	0.50
	SGA	3.92 (0.39-39.92)		5.92 (0.62-56.34)		0.84 (0.56-6.10)	
Gender	Female	3.3 (1.18-9.22)	0.31	1.75 (0.67-4.56)	0.55	1.37 (0.70-2.68)	0.77
	Male	1.59 (0.61-4.18)		2.71 (0.90-8.19)		1.19 (0.61-2.32)	
Risky drinking <sup>4</sup>	Yes	- <sup>5</sup>	0.99	0.81 (0.18-3.52)	0.21	1.49 (0.44-5.09)	0.69
	No	2.45 (1.17-5.11)		2.37 (1.04-5.43)		1.13 (0.65-1.97)	

Abbreviations: OR, odds ratio; AGA, appropriate for gestational age; SGA, small for gestational age (birthweight < 10<sup>th</sup> centile); \* Based on expressive language only

<sup>1</sup> Obtained from logistic regression analysis: stratum-specific estimates; <sup>2</sup> obtained from logistic regression analysis with interaction term

<sup>3</sup> any physical, sexual or psychological violence as measured with World Health Organization violence against women questionnaire at study enrolment; <sup>4</sup> Alcohol use disorders identification test (AUDIT-C) score ≥3 as reported at first antenatal visit; <sup>5</sup> Unable to determine due to null cell in sub-group (no HU children with cognitive delay and maternal risky drinking)

**SUPPLEMENTAL DIGITAL CONTENT 10, TABLE. Relative odds for developmental delay comparing children in categories of study population characteristics, stratified by maternal HIV status**

Maternal/infant characteristics	Strata	Cognitive delay OR (95% CI) <sup>1</sup>	Motor delay OR (95% CI) <sup>1</sup>	Language <sup>2</sup> delay OR (95% CI) <sup>1</sup>
Planned pregnancy	HEU	1.23 (0.45-3.36)	1.39 (0.50-3.87)	1.16 (0.60-2.25)
	HU	1.00 (0.33-3.08)	0.71 (0.22-2.32)	0.30 (0.10-0.89)
Maternal age ≥ 30 years	HEU	1.44 (0.59 – 3.56)	0.93 (0.36-2.41)	0.90 (0.44-1.83)
	HU	1.89 (0.64 – 5.54)	0.72 (0.22-2.36)	2.54 (1.33-4.86)
Married	HEU	4.08 (1.51-10.97)	1.01 (0.39-2.63)	0.79 (0.38-1.64)
	HU	1.23 (0.42-3.59)	2.27 (0.74-6.95)	1.13 (0.60-2.14)
Employed	HEU	0.48 (0.17-1.36)	0.95 (0.36-2.52)	0.62 (0.29-1.33)
	HU	1.53 (0.52-4.52)	0.95 (0.36-2.52)	1.42 (0.75 – 2.70)
Matriculated	HEU	0.42 (0.12-1.47)	0.94 (0.32-2.74)	0.44 (0.17-1.11)
	HU	2.99 (0.92-9.75)	0.62 (0.20-1.89)	0.48 (0.24-0.95)
Informal housing	HEU	1.14 (0.46-2.82)	0.68 (0.26-1.81)	0.67 (0.33-1.39)
	HU	2.09 (0.68-6.40)	7.27 (1.60-33.07)	1.76 (0.92-3.37)
Intimate partner violence <sup>3</sup>	HEU	0.93 (0.30-2.94)	3.25 (1.22-8.70)	0.86 (0.35-2.12)
	HU	0.94 (0.12-7.56)	2.15 (0.45-10.25)	1.74 (0.61-4.95)
Risky drinking <sup>4</sup>	HEU	0.55 (0.18-1.70)	1.20 (0.43-3.32)	1.59 (0.76-3.33)
	HU	n/a <sup>5</sup>	3.52 (0.91-13.60)	1.21 (0.39-3.72)

Maternal/infant characteristics	Strata	Cognitive delay OR (95% CI) <sup>1</sup>	Motor delay OR (95% CI) <sup>1</sup>	Language <sup>2</sup> delay OR (95% CI) <sup>1</sup>
SGA	HEU	1.06 (0.29-3.87)	1.92 (0.59-6.30)	1.98 (0.80-4.89)
	HU	0.58 (0.07-4.60)	0.58 (0.07-4.60)	1.27 (0.49-3.26)
Male	HEU	0.80 (0.33-1.98)	1.03 (0.40-2.65)	0.98 (0.49-1.98)
	HU	1.66 (0.56-4.91)	0.66 (0.22-2.03)	1.13 (0.60-2.14)
Breastfed ≥ 9 months	HEU	1.41 (0.57-3.49)	0.89 (0.34-2.31)	0.90 (0.44-1.83)
	HU	1.44 (0.47-4.42)	0.30 (0.09-0.98)	0.61 (0.32-1.16)
Preterm birth (<37 weeks)	HEU	3.09 (1.09-8.80)	9.11 (3.25-25.49)	0.52 (0.15-1.82)
	HU	2.91 (0.76-11.13)	4.47 (1.30-15.32)	2.69 (1.10-6.56)
Gestational age at delivery (weeks)	HEU	0.80 (0.68-0.93)	0.63 (0.53-0.76)	1.15 (0.96-1.38)
	HU	0.89 (0.70-1.14)	0.77 (0.62-0.95)	0.87 (0.75-1.01)

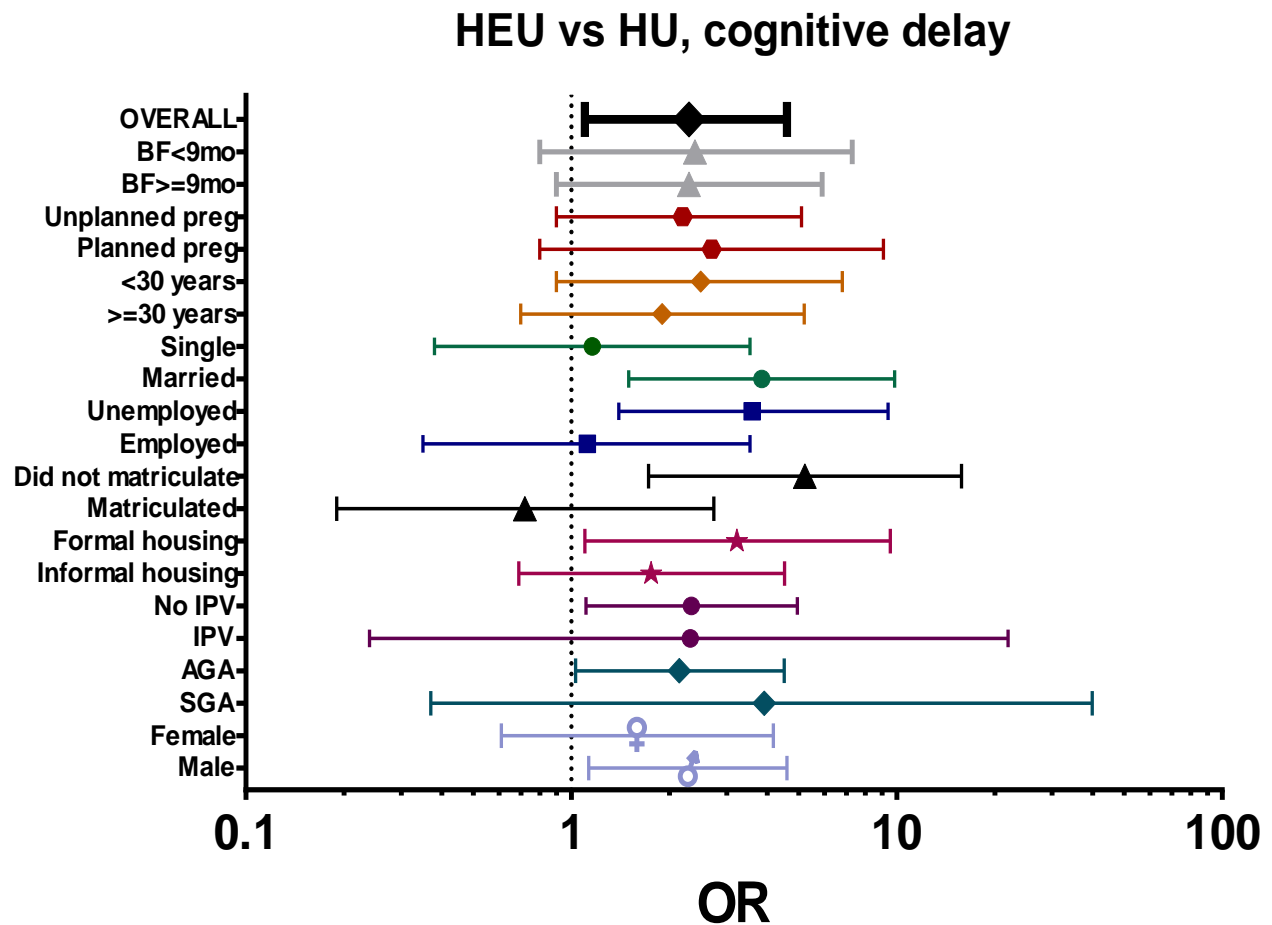
Abbreviations: HEU, HIV-exposed uninfected children; HU, HIV-unexposed children; OR, odds ratio; AGA, appropriate for gestational age; SGA, small for gestational age (birthweight < 10<sup>th</sup> centile);

<sup>1</sup> Obtained from logistic regression analysis: stratum-specific estimates; <sup>2</sup> Based on expressive language only

<sup>3</sup> any physical, sexual or psychological violence as measured with World Health Organization violence against women questionnaire at study enrolment; <sup>4</sup> Alcohol use disorders identification test (AUDIT-C) score ≥3 as reported at first antenatal visit; <sup>5</sup> Unable to determine due to null cell in sub-group (no HU children with cognitive delay and maternal risky drinking)

SUPPLEMENTAL DIGITAL CONTENT 11, FIGURE.

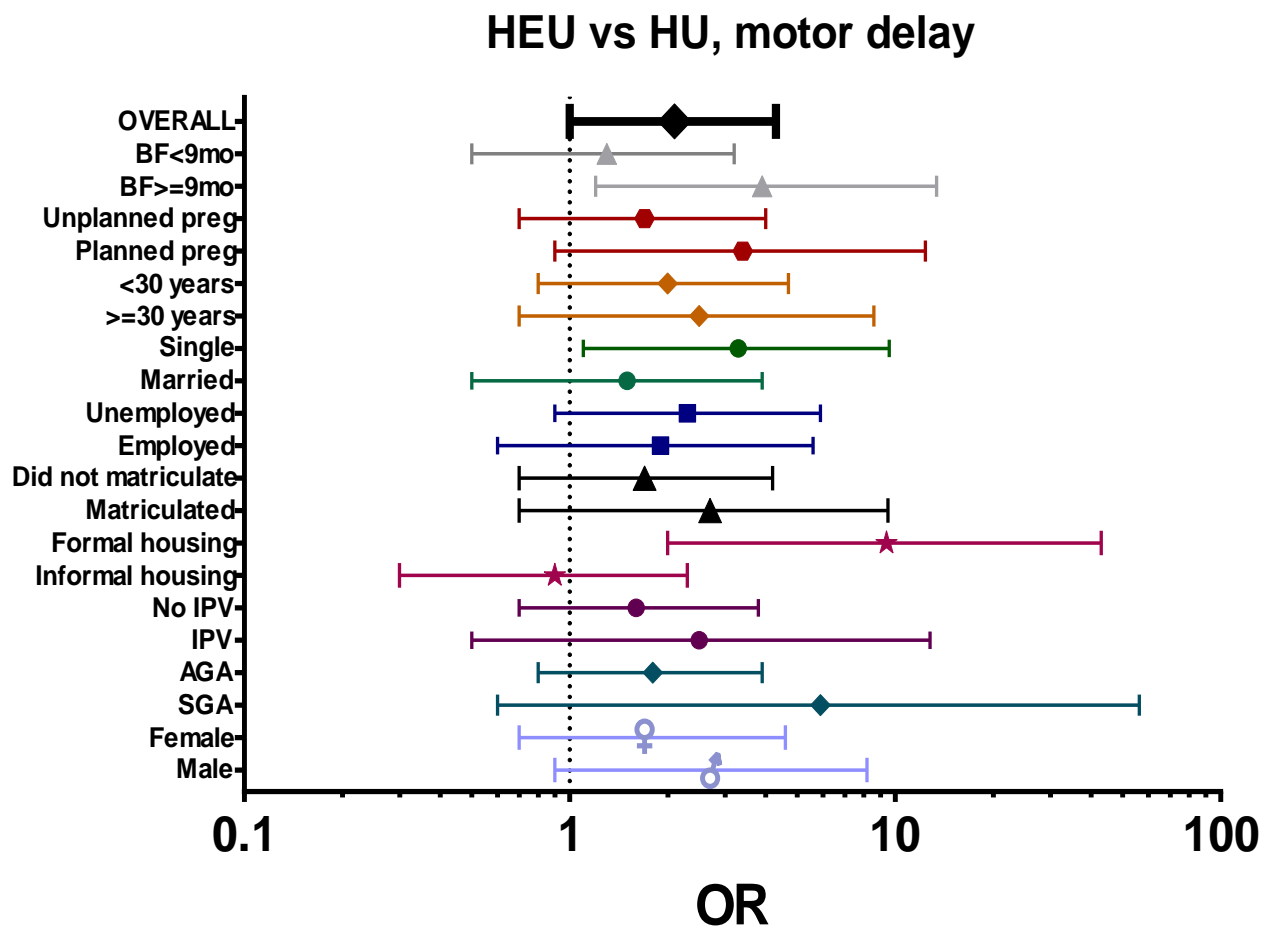
Interaction forest plot of odds ratios for COGNITIVE delay comparing HIV-exposed uninfected to HIV-unexposed infants within strata of maternal and infant characteristics



Abbreviations: HEU, HIV-exposed uninfected children; HU, HIV-unexposed children; OR, odds ratio; BF, Breastfeeding; preg, pregnancy; IPV, intimate partner violence; AGA, appropriate for gestational age; SGA, small for gestational age (birthweight < 10<sup>th</sup> centile)

## SUPPLEMENTAL DIGITAL CONTENT 12, FIGURE.

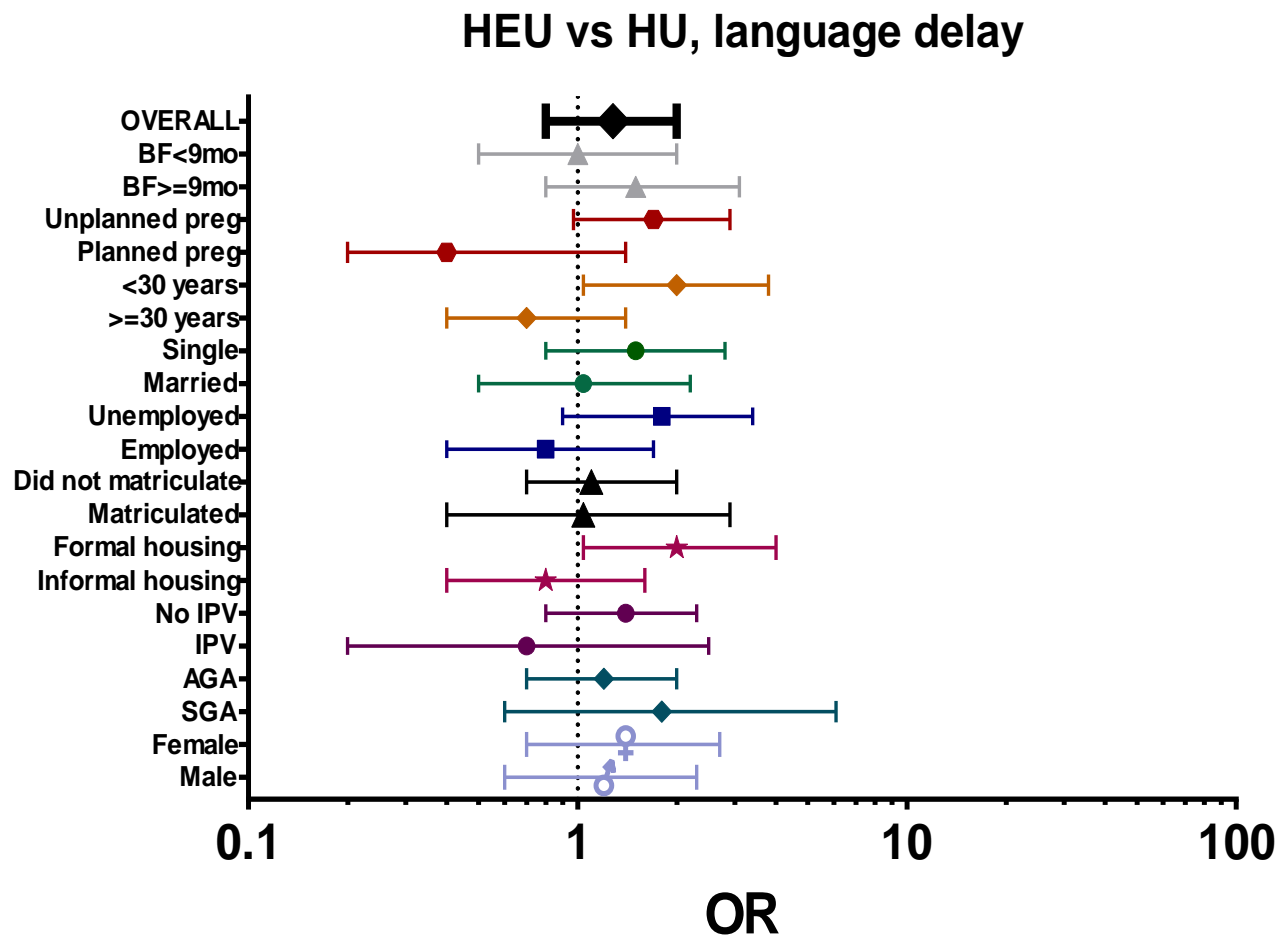
Interaction forest plot of odds ratios for MOTOR delay comparing HIV-exposed uninfected to HIV-unexposed infants within strata of maternal and infant characteristics



Abbreviations: HEU, HIV-exposed uninfected children; HU, HIV-unexposed children; OR, odds ratio; BF, Breastfeeding; preg, pregnancy; IPV, intimate partner violence; AGA, appropriate for gestational age; SGA, small for gestational age (birthweight < 10<sup>th</sup> centile)

## SUPPLEMENTAL DIGITAL CONTENT 13, FIGURE.

Interaction forest plot of odds ratios for LANGUAGE delay comparing HIV-exposed uninfected to HIV-unexposed infants within strata of maternal and infant characteristics



Abbreviations: HEU, HIV-exposed uninfected children; HU, HIV-unexposed children; OR, odds ratio; BF, Breastfeeding; preg, pregnancy; IPV, intimate partner violence; AGA, appropriate for gestational age; SGA, small for gestational age (birthweight < 10<sup>th</sup> centile)