

Table 1. Review of associations between cognitive development and HIV exposure among infants and children without any reported antiretroviral exposure, by type of cognitive assessment

Author (Year)	Title	Setting	Study design	Sample size and description	Cognitive assessment tool	Results ^a	Limitations
Mellins, CA., et al. (1994)	Effects of pediatric HIV infection and prenatal drug exposure on mental and psychomotor development	Hospital, New York City	Cross-sectional	77 infants, 4-30 months of age (HIV+, n=24; HEU, n=30; HU, n=23) *ART exposure not indicated for HIV+ or HEU	Bayley Scales of Infant Development	HIV+ infants exhibited lower psychomotor scores than HEU and HU [t(74)=2.8, p=0.007; t(74)=2.6, p=0.01]	Small sample
Noyzce, M. et al. (1994)	Effect of perinatally acquired human immunodeficiency virus infection on neurodevelopment in children during the first two years of life.	Unknown	Prospective cohort	181 infants, 0-24 months of age (HIV+, n=21; HEU, n=65; HU, n=95) *ART exposure not indicated for HIV+ or HEU	Bayley Scales of Infant Development	HIV+ infants exhibited lower mental development and psychomotor scores than HEU and HU	n/a
Chase, C., et al. (1995)	Early neurodevelopmental growth in children with vertically transmitted human immunodeficiency virus infection	Pediatric Immunodeficiency Clinic at Boston (Mass) City Hospital, Boston University Medical Center	Prospective cohort	51 infants, 17-30 months of age (HIV+, n=24; HEU, n=27) *ART exposure not indicated for HIV+ or HEU	Bayley Scales of Infant Development	HIV+ infants exhibited lower motor development scores than HEU [3-16mo: HIV+, mean (SD) 85.2±11.6; HEU, mean (SD) 97.8±14.5; p=0.001; 17-30mo HIV+, mean (SD) 85.8±16.4; HEU 97.8±16.7; p=0.01]	Non-blinding of HIV status may have biased scoring of developmental tests
Drotar, D., et al. (1999)	Neurodevelopmental outcomes of Ugandan infants with HIV infection: an application of growth curve analysis	Makerere University prenatal clinic at New Mulago Hospital in Kampala, Uganda	Cross-sectional	410 infants, 0-24 months of age (HIV+ nART, n=61; HEU, n=234; HU, n=115)	Bayley Scales of Infant Development	HIV+ nART infants had lower mental and motor development scores than HEU and HU [t (1, 719)=3.1; p<0.01; t (1, 720)=4.6; p<0.0001]	Two-year follow-up of cohort
Knight, WG., et al. (2000)	Effects of pediatric HIV infection on mental and psychomotor development	Hospital, New York City	Cross-sectional	45 infants, 3-30 months of age (HIV+, n=20; HEU, n=25) *ART exposure not indicated for HIV+ or HEU	Bayley Scales of Infant Development	HIV+ infants exhibited lower baseline (3-21mo) mental development and follow-up (7.9-27.7mo) performance scores than HEU [t=2.6; p≤0.05; t=2.2; p≤0.05]	Small sample size, did not collect data on medication use, data collected prior to initiation of HAART
Blanchette, N., et al. (2001)	Cognitive and motor development in children with	HIV/AIDS Program, Hospital for	Cross-sectional	50 infants, 2-3 years of age (HIV+, n=25; HEU, n=25)	Bayley Scales of Infant Development	HIV+ infants exhibited lower mental development and psychomotor scores than HEU [F	Small sample size

Author (Year)	Title	Setting	Study design	Sample size and description	Cognitive assessment tool	Results ^a	Limitations
	vertically transmitted HIV infection	Sick Children, Toronto, Canada		*ART exposure not indicated for HIV+ or HEU		(4, 48)=8.0; p<0.001; F(2, 44)=14.3; p<0.001]	
McGrath et al. (2006)	The timing of mother-to-child transmission of human immunodeficiency virus infection and neurodevelopment of children in Tanzania	Dar es Salaam, Tanzania	Randomized, double-blind placebo controlled	327 children, 6-12 months of age (sample size not parsed by HIV status) *ART exposure not indicated for HIV+ or HEU	Bayley Scales of Infant Development	HIV+ children exhibited lower performance and mental development scores than HEU [mean 1.4, 95% CI, 0.0, 2.7; 1.1, 95% CI ,0.4, 1.8]	Cultural bias of Bayley, no measure of caregiver capabilities or home environment
Van Rie, A., et al. (2008)	Impact of HIV/AIDS Epidemic on the Neurodevelopment of Preschool-Aged Children in Kinshasa, Democratic Republic of Congo	Primary care clinics, Kinshasa, Democratic Republic of Congo	Cross-sectional	160 children, 18 months to 6 years of age (HIV+ nART, n=35; HEU, n=35; HU, n=90)	Bayley Scales of Infant Development	HIV+ nART children exhibited worse motor, mental, language comprehension and expression delays than HEU and HU [Motor: HIV+ nART 28.6% severe delay; HEU 14.3% severe delay; p=0.003; HU 0% severe delay; p<0.0001; Mental: HIV+ nART 25.7% moderate delay, 60% severe delay; HU 26.7% moderate delay, 24.4% severe delay; p<0.0001; Language comprehension: HIV+ nART 76.9%; HEU 10.5% p=0.0002; HU 12.9%, p <0.0001; Language expression: HIV+ nART 84.6%; HU 12.9%; p<0.001]	Small sample size (couldn't model impact of covariates), cross-sectional nature
Baillieu, N., et al. (2008)	The extent of delay of language, motor, and cognitive development in HIV-positive infants	HIV clinics in Johannesburg, South Africa	Cross-sectional	40 infants, 18-30 months of age, HIV+ nART	Bayley Scales of Infant Development	HIV+ nART infants exhibited worse cognitive and motor delays [7.6 months delayed; p<0.001; 9.7 months delayed; p<0.001]	Small sample size
Kandawasvika, G., et al. (2011)	Neurodevelopmental impairment among infants born to mothers infected with human immunodeficiency virus and uninfected mothers from three peri-urban primary care clinics in Harare, Zimbabwe	Primary care clinics, Harare Zimbabwe	Prospective cohort (1-year follow-up)	598 infants, 3-12 months of age (HIV+ nART n=65; HEU, n=188; HU, n=58)	Bayley Infant Neurodevelopmental Screener	HIV+ infants exhibited worse neurodevelopmental impairment than HU infants [OR 2.1, 95% CI 1.0-4.3]	Skewed sample (high mortality among HIV+, high drop-out among uninfected mothers)

Author (Year)	Title	Setting	Study design	Sample size and description	Cognitive assessment tool	Results ^a	Limitations
McDonald, CM., et al. (2013)	Stunting and wasting are associated with poorer psychomotor and mental development in HIV-exposed Tanzanian infants	Antenatal clinics, Dar es Salaam	Randomized, double-blind, placebo-controlled trial	311 infants, 6-18 months of age (HIV+ nART, n=32, HEU, n=279)	Bayley Infant Neurodevelopmental Screener	HIV+ nART infants exhibited lower psychomotor and mental development scores than HEU [mean 5.9 points lower; 95% CI=-8.9, -2.3; p=0.0001; mean 2.5 points lower; 95% CI=-4.9, -0.2; p=0.03]	Sample size did not permit for longitudinal analysis of developmental status over time, did not include reference group of HIV-unexposed infants
Kerr et al. (2014)	Neurodevelopment outcomes in HIV-exposed-uninfected children versus those not exposed to HIV	Thailand and Cambodia	Multicenter neurodevelopment study in Thailand and Cambodia, cross-sectional	327 children 1-12 years of age (HEU, n=160; HU, n=167) *ART exposure not indicated for HEU	Beery Visual Motor Integration (VMI), Perdue Pegboard, Color Trails and Child Behavioral Checklist, Wechsler Intelligence Scale, and Stanford Binet Memory test	HEU children exhibited lower verbal and full scale IQ and memory than HU (Mean (95% CI) differences: Verbal -6.1 (-10.3 to -1.96; p=0.004); full scale IQ: -4.57 (-8.80 to -0.35), p = 0.03; Binet Bead Memory: -3.72 (-6.57 to -0.88), p = 0.0)	Full scale IQ is comprised of verbal and performance IQ, scores highly influenced by verbal IQ. Cross-sectional design. Data not collected on maternal ART exposure
Wachtel, RC., et al. (1994)	Neurodevelopment in pediatric HIV infection: The use of CAT/CLAMS	University of Maryland	Prospective cohort	137 children 6-18 months of age (HIV+, n=35; HEU, n=58, HU, n=44) *ART exposure not indicated for HIV+ or HEU	Clinical Adaptive Test/Clinical Linguistic and Auditory Milestone Scale	HIV+ children exhibited lower than normal neurocognitive development scores (6mo: HIV+ 6% with lower than normal scores; 12mo 23.5% with lower than normal scores; 18mo 6% with lower than normal scores)	n/a
Msellati et al. (1993)	Neurodevelopmental testing of children born to Human Immunodeficiency Virus Type 1 seropositive and seronegative mothers: a prospective cohort study in Kigali, Rwanda	Kigali, Rwanda	Prospective cohort	436 infants 6-24 months of age (HIV+, n=50; HEU, n=136, HEU-indeterminable HIV status, n=32; HU, n=218) *ART exposure not indicated for HIV+ or HEU	Denver Developmental Screening Test	HIV+ infants exhibited lower gross motor development scores at all ages (6mo: HIV+ mean (SD) 3.0 (1.28); HEU 3.6 (0.6); HU 3.5 (.7); p=0.0001; 12mo HIV+ mean (SD) 1.0 (0.9); HEU 1.8 (0.9); HU 1.8 (0.9); p=0.0001; 18mo: HIV+ mean (SD) 1.8 (1.3); HEU 2.6 (0.7); HU 2.7 (0.7); p=0.0001; 24mo: HIV+ mean (SD) 3.2 (1.4); HEU 4.4 (0.8); HU 4.2 (1.2); p=0.0002) lower	

Author (Year)	Title	Setting	Study design	Sample size and description	Cognitive assessment tool	Results ^a	Limitations
						<p>fine motor development at 6 and 12 months of age (6mo: HIV+ mean (SD) 3.2 (1.3); HEU 3.8 (1.1); HU 3.8 (1); 12mo HIV+ mean (SD) 1.5 (0.8); HEU 1.7 (0.4); HU 1.7; 0.5), lower language acquisition scores at 24 months of age (24mo HIV+ mean (SD) 1.4 (1.1); HEU (2.0 (0.9); HU 2.2 (0.8); p=0.002), and lower social contacts scores at 6 and 24 months (6mo HIV+ mean (SD) 2.3 (0.8); HEU 2.6 (0.6); HU 2.6 (0.5) p=0.004; 24mo HIV+ mean (SD) 1.8 (0.5); HEU 1.9 (0.1); HU 2 (0); p=0.0001) than HEU and HEU</p>	
Boivin et al. (1995)	A preliminary evaluation of cognitive and motor effects of pediatric HIV infection in Zairian children	Hospital near Kimpese, Zaire	Longitudinal	50 infants 0-18 months of age (HIV+, n=14; HEU, n=20; HU, n=16) *ART exposure not indicated for HIV+ or HEU	Denver Developmental Screening Test	HIV+ infants exhibited lower motor development scores than HEU and HU [Fisher's protected least significant differences HEU=21.1 and HU 21.4; p<0.001]	Screening tool, not intended to monitor developmental effects of infection
Bruck et al. (2001)	Developmental milestones of vertically HIV infected and seroreverter children	Clinical Hospital of the Federal University of Paraná (UFPR)	Prospective cohort	150 infants 1->72 months of age (HIV+ n=43; HEU, n=40; HU, n=67) *ART exposure not indicated for HIV+ or HEU	Denver I and II Developmental Screening Test	HIV+ infants exhibited higher rates of developmental screening test failure than HEU and HU (1-13mo: HIV+, 78% failure, HEU, 30% failure; p=0.01; 25-36mo: HIV+ 62.5%, HEU, 23.8%; p=0.02]	Small sample size
Tahan, T. et al. (2006)	Neurological profile and neurodevelopment of 88 children infected with HIV and 84 seroreverter children followed from 1995 to 2002	Clinical Hospital of the Federal University of Paraná (UFPR)	Prospective and cross-sectional	172 children 1->72 months of age (HIV+, n=88; HEU, n=84) *ART exposure not indicated for HIV+ or HEU	Denver I and II Developmental Screening Test	HIV+ children exhibited higher rates of developmental screening test failure than HEU [Denver I: HIV+, 43% failed; HEU, 16%; p=0.008; Denver II: HIV+, 77% failed; HEU, 30% failed; p=0.01]	Low rate of participant return

Author (Year)	Title	Setting	Study design	Sample size and description	Cognitive assessment tool	Results ^a	Limitations
Ruel, TD., et al. (2012)	Neurocognitive and motor deficits in HIV-infected Ugandan children with CD4 cell counts	Kampala, Uganda	Observational cohort	199 children, 7.4-10.1 years of age (HIV+ nART, n=93; HU, n=106)	Kaufman Assessment Battery for Children, Bruininks-Oseretsky Test of Motor Proficiency, second edition	HIV+ nART children exhibited lower cognitive and motor scores than HU [Cognitive: HIV+, mean (SD) 184.7±63.7; HU, mean (SD) 200.6±68.7; p=0.02; Motor: HIV+, mean (SD) 187.8±34.3; HU, mean (SD) 198.3 ±33.9; p=0.003]	Restricted to WHO stages 1 and 2 children
Abubakar, A., et al. (2013)	The performance of children prenatally exposed to HIV on the A-Not-B Task in Kilifi, Kenya: a preliminary study	Kilifi District Hospital, Kilifi, Kenya	Cross-sectional	367 infants/children 6-35 months of age (HIV+ nART, n=31; HEU n=17; HU, n=319)	Kilifi Developmental Inventory	HIV+ nART children exhibited lower psychomotor scores than HEU and HU [HIV+ -0.91 (1.86); HEU: 0.11 (0.6); HU 0.08 (08.4)] ^b	Small sample size of HIV+ and HIV-exposed uninfected groups
Van Rie, A., et al. (2009)	Neurodevelopmental trajectory of HIV-infected children accessing care in Kinshasa, Democratic Republic of Congo	Primary care clinics, Kinshasa, Democratic Republic of Congo	Prospective cohort (1-year follow-up)	160 children 18-71 months of age (HIV+ nART, n=35; HEU, n=35; HU, n=90)	Mullen Scales of Early Learning	HIV+ infants exhibited similar cognitive development scores to HEU and lower cognitive development scores than HU [HIV+ 84.3±7.2; HU 96.5 ±5.0; p<0.01; HEU 87.6 ±6.6]	Wide age range, high mortality rate during follow-up
^a Scores reported as mean (SD) Abbreviations: HIV+: HIV-infected, HEU: HIV-exposed uninfected, HU: HIV-unexposed Blue text indicates no differences between groups; red text indicates worse outcomes among HIV+ and/or HEU							

Table 2. Systematic review of associations between cognitive development and HIV exposure among infants and children exposed to antiretroviral therapy, by type of cognitive assessment

Author (Year)	Title	Setting	Study design	Sample size and description	Cognitive assessment tool used	Results ^a	Limitations
Gay, CL., et al. (1995)	The effects of HIV on cognitive and motor development in children born to HIV-seropositive women with no reported drug use: birth to 24 months	Haiti	Prospective cohort	130 infants/children, 0-24 months of age (HIV+ receiving ART (AZT), n=28; HEU, n=98)	Bayley Scales of Infant Development (BSID)	HIV+ infants exhibited lower mental development and performance scores than HEU [Z=5.9; p<0.001; Z=7.1; p<0.001]	None listed
Pollack, H., et al (1996)	Neurodevelopment, growth, and viral load in HIV-infected infants	United States	Prospective cohort	65 infants, 0-24 months of age (HIV+ nART, n=7, HIV+ receiving ART (AZT), n=11; HEU, n=29; HU, n=18]	Bayley Scales of Infant Development (BSID)	HIV+ infants had lower mental and motor development scores than HEU and HU at 12 months [$\chi^2=9.2$, $df=2$, $p=0.01$; [$\chi^2=7.1$, $df=2$, $p=0.03$].	Small sample size
Culnane, M., et al. (1999)	Lack of long-term effects of <i>in utero</i> exposure to Zidovudine among uninfected children born to HIV-infected women	United States	Prospective cohort, double-blind, placebo-controlled trial	234 children, 30 months-6 years of age, (All HEU 1:1 ART-exposed (AZT) <i>in utero</i> and at 6weeks of age, n=122; ART-unexposed, n=112)	Bayley Scales of Infant Development (BSID) and McCarthy Scales of Children's Ability	HEU ART-exposed children and HEU ART-unexposed exhibited no differences in Bayley Scales of Infant Development and McCarthy Scales of Children's Ability	Two-thirds of enrolled children are be followed up for late-effects, expected loss to follow-up of 10% per year.
Alimenti et al. (2006)	A prospective controlled study of neurodevelopment in HIV-uninfected children exposed to combination antiretroviral drugs in pregnancy	n.s.	Prospective controlled cross-sectional study	63 children, 18-36 months of age (All HEU; exposed to HAART, n=39, not-exposed to HAART, n=24)	Bayley Scales of Infant Development (BSID)	HEU ART-exposed children and HEU ART-unexposed exhibited no differences after controlling for maternal substance abuse	
Foster et al. (2006)	Neurodevelopmental outcomes in children with HIV infection under 3 years of age	Family Clinic at St Mary's Hospital, London, UK	Retrospective case note	62 children <3 years of age, all HIV+ (Group A/B receiving HAART (n.s.), n=23; Group C receiving sub-optimal mono/dual therapy, n=12; ART-unexposed, n=27)	Bayley Scales of Infant Development (BSID)	All HIV+ children exhibited lower performance and mental development scores than published norms [mean (SD) 100±15]. Group C infants, receiving sub-optimal mono/dual therapy exhibited lower performance and mental development scores than Group A/B receiving HAART [mean (SD) 74.9 (15.5), $p=0.002$].	Small sample size

Author (Year)	Title	Setting	Study design	Sample size and description	Cognitive assessment tool used	Results ^a	Limitations
Williams et al. (2010)	Neurodevelopment and <i>in utero</i> antiretroviral exposure of HIV-exposed uninfected infants	United States, including Puerto Rico	Multisite prospective cohort	1840 infants, 12-24 months of age, all HEU (ART-exposed, n=1694; ART-unexposed, n=146)	Bayley Scales of Infant Development (BSID I & II)	HEU infants exhibited no differences in development scores at 9-15 across ART exposure groups.	
Sirois et al. (2014)	Safety of perinatal exposure to antiretroviral medications: developmental outcomes in infants	Pediatric HIV/AIDS Cohort Study (PHACS), United States and Puerto Rico	Prospective cohort	423 infants, 9-15 months of age, (HEU ART-exposed <i>in utero</i> , PI with/without NNRTIs, n=297; NNRTI-containing without PIs, n=19, NRTI alone, n=53; ART-unexposed, n=5; HU, n=49)	Bayley Scales of Infant and Toddler Development, Third Edition (Bayley-III)	HEU infants exhibited no differences in development scores at 9-15 months across ART treatment groups.	
Whitehead et al. (2014)	The neurodevelopment of HIV-infected infants on HAART compared to HIV-exposed but uninfected infants	Empilweni Clinic at Rahima Moosa Mother and Child Hospital, Johannesburg, South Africa	Longitudinal comparative	56 infants 0-12 months of age (HIV+, receiving HAART (n.s.) n=27; HEU, n=29)	Bayley Scales of Infant and Toddler Development, Third Edition (Bayley-III)	HIV+ infants receiving ART exhibited lower language and motor scores than HEU ^b [Language: baseline: HIV+, mean (SD) 87.8±12.8; HEU, 100.3±7.8; p<0.001; 3-month follow-up: HIV+ 85.4±10.9; HEU 97.2±10.0; p<0.001; 6-month follow-up: HIV+ 90.3±1.9; HEU 100.2±10.1; p=0.004; Motor: baseline: HIV+ 93.1±19.3; HEU106.5; p=0.004; 3mo: HIV+ 91.3±15.9; HEU 108.1±13.1; p=0.001; 6mo: HIV+ 93.7±10.9; HEU 105.6±10.9; p=0.002]	Small sample size, high loss to follow-up (30.4%)
Da Silva et al. (2016)	Evaluation of motor and cognitive development among infants exposed to HIV	AIDS referra center, Santos/São Paulo, Brazil	Cross-sectional	80 infants, 4-18 months of age (HEU ART-exposed (n.s.) <i>in utero</i> and 6weeks after birth, n=40; HU, n=40)	Bayley Scales of Infant and Toddler Development, Third Edition (Bayley-III)	HEU infants exposed <i>in utero</i> and receiving ART exhibited lower composite scores than HU [(F(3,72) = 5.3, p = 0.002)]	Lack of follow-up, small sample size
Chaudhury, S. et al. (2017)	Neurodevelopment of HIV-exposed and HIV-unexposed uninfected children at 24 months	Gaborone and Mochudi, Botswana	Prospective cohort (2-year follow-up)	670 children, 24 months of age (HEU ART-exposed <i>in utero</i> to either AZT/3TC/NVP or AZT, after birth to a single dose of NVP, and AZT at 1mo), n=313; HU, n=357)	Bayley Scales of Infant and Toddler Development, Third Edition (Bayley-III) & Development	HEU children exposed <i>in utero</i> and receiving ART exhibited lower expressive language, cognitive, and personal-social scores than HU [expressive language: adj. mean difference - 0.6; p=0.09; cognitive: adj. mean	Did not adjust for effects of breastfeeding

Author (Year)	Title	Setting	Study design	Sample size and description	Cognitive assessment tool used	Results ^a	Limitations
					Milestones Checklist (DMC)	difference 0.6; p=0.03; personal-social: adj mean difference 0.7; p=0.03]	
Caniglia et al. (2017)	Atazanavir exposure <i>in utero</i> and neurodevelopment in infants: a comparative safety study	US and Puerto Rico	Prospective cohort	575 infants, 9-15 months of age (All HEU ART-exposed <i>in utero</i> , (ATV) n=118; (non-ATV), n=457)	Bayley Scales of Infant and Toddler Development, Third Edition (Bayley-III)	HEU children exposed <i>in utero</i> to atazanavir exhibited lower cognitive scores than HEU exposed <i>in utero</i> to non-atazanavir regimen [Adj. mean difference (95% CI), cognitive: -1.5 (-6.2, 3.2), language: -3.3 (-7.6, 1.0), motor: -2.9 (-7.7, 1.9), social-emotional: 0.1 (-6.2, 6.4), adaptive behavior -0.1 (-4.3, 4.0)]	Unable to separate results of atazanavir and tenofovir
Pthanakit, T., et al. (2013)	Cognitive function and neurodevelopmental outcomes in HIV-infected children older than 1 year of age randomized to early versus deferred antiretroviral therapy: the PREDICT neurodevelopmental study	Thailand and Cambodia	Multicenter randomized, open-label trial	603 children 1-12 years of age (HIV+ early ART, n=139; HIV+ deferred ART, n=145 (ART regimens: AZT/3TC/NVP, n=141; AZT/3TC/LPV, n=25, n.s., n=42); HEU, n=155; HU, n=164)	Beery Visual Motor Integration (VMI), Perdue Pegboard, Color Trails and Child Behavioral Checklist (CBCL), Wechsler Intelligence Scale (IQ) and Stanford Binet Memory test	HIV+ children exhibited lower cognitive scores than HEU and HU (p<0.001). HIV+ children exhibited no differences across ART exposure arms.	No baseline neurodevelopmental assessments

Author (Year)	Title	Setting	Study design	Sample size and description	Cognitive assessment tool used	Results ^a	Limitations
Ngoma, M.S., et al. (2014)	Cognitive and language outcomes in HIV-uninfected infants exposed to combined antiretroviral therapy <i>in utero</i> and through extended breastfeeding	District clinics, Lusaka, Zambia	Double cohort	200 infants/children, 15-36 months of age (HEU ART-exposed (AZT/3TC/LPVr) <i>in utero</i> and via breastmilk for 1year, n=97; HU, n=103)	Capute Full-Scale Developmental Quotient (standardized Capute Scales)	HEU and HU infants exhibited no differences in Full-Scale Developmental Quotient	Limited capacity of test to detect specific cognitive or language delays, Capute Scales are a screening tool (non-diagnostic)
Govender, R., et al. (2011)	Neurologic and neurobehavioral sequelae in children with Human Immunodeficiency Virus (HIV-I) infection	Red Cross War Memorial Children's Hospital and Groote Schuur Hospital, Cape Town, South Africa	Cross-sectional	78 children, 3 months-12 years of age, (All HIV+; receiving ART, n=61 [AZT, n=2; D4T, n=1])	Denver II Developmental Screening Test	HIV+ children exhibited high rates of developmental screening test failure [6mo-7yr 48.8% failed; 6-7yr 100% failed]	Developmental delays may not be HIV-specific, no comparison group for environmental factors
Brahmbhatt, H., et al. (2014)	Neurodevelopmental benefits of antiretroviral therapy in Ugandan children aged 0-6 years with HIV	Rakai, Uganda	Prospective cohort	329 infants/children, 0-6 years of age (HIV+ receiving ART; AZT/3TC/NVP or D4T/3TC/NVP, n=116; HEU, n=105; HU, n=108)	Mullen Scales of Early Learning (MSEL)	HIV+ children exhibited lower fine motor, visual reception, receptive language, expressive language, and early learning composite scores than HEU [Fine motor: adj. PRR=2.39; CI: 1.15–4.95; Visual reception: adj. PRR=5.86, CI:2.30–14.92; Receptive language: adj. PRR=4.20; CI: 1.83–9.64; Expressive language: adj. PRR=2.27; CI: 2.27–1.15–4.50; Early learning composite adj. PRR=6.87; CI: 2.54–18.58] HEU children exhibited lower receptive language and early learning composite scores than HU [Receptive language: adj. PRR=2.67, CI: 1.08, 6.60; Early learning composite: adj. PPR=2.94, CI:1.11, 7.82]	Did not include other environmental or parental factor as co-variables

Author (Year)	Title	Setting	Study design	Sample size and description	Cognitive assessment tool used	Results ^a	Limitations
^a Scores reported as mean (SD) Abbreviations: HIV+: HIV-infected, HEU: HIV-exposed uninfected, HU: HIV-unexposed; AZT: azidothymidine, zidovudine; D4T: stavudine; NVP: nevirapine; 3TC: lamivudine, epivir; LPVr: lopinavir/ritonavir; ATV: atazanavir; n.s.: not specified, HAART: highly active antiretroviral therapy (combination of ≥3 antiretroviral medications), PI: protease inhibitor (ex. amprenavir/fosamprenavir, ATV, darunavir (DRV), indinavir (IDV), LPV, nelfinavir, ritonavir, saquinavir, tipranavir (TPV)); NNRTI: non-nucleoside reverse transcriptase inhibitor (ex. Etravirine, efavirenz (EFV), NVP, rilpivirine (RPV), delavirdine (DLV)); NRTI: nucleoside reverse transcriptase inhibitors (ex. emtricitabine, 3TC, AZT, didanosine, tenofovir, D4T, abacavir) Blue text indicates no differences between groups; red text indicates worse outcomes among HIV+ and/or HEU							