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Abstracts
Oral Presentations
Low-to-undetectable initial viral loads in in-utero HIV-infected infants in the era of antenatal anti-retroviral therapy.

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Background: Several studies have suggested that very early antiretroviral therapy (ART) initiation in in-utero HIV infected infants may provide potential for cure or remission. We designed a study, Ucwaningo Lwabantwana, to explore the feasibility of ART initiation within 48hrs of birth for infants with in-utero HIV infection and to investigate its impact on viral suppression.

Materials and Methods: Between August 2015 and April 2018, in-utero HIV infected infants were identified from 4 hospitals in KwaZulu-Natal South Africa using point-of-care testing (GeneXpert Qualitative HIV PCR, Cepheid), viral load measurement (Nuclisens EasyQ v2.0 HIV-1 RNA PCR, bioMérieux) and standard of care dried blood spot (DBS) testing (COBAS AmpliPrep /COBAS TaqMan HIV-1 Qualitative PCR, Roche) at birth. ART was initiated as per South African guidelines. Infant follow up occurred monthly for 6 months then 3 monthly. Viral suppression was defined as viral load <20 viral RNA copies per millilitre (cpm), and viral rebound as >1000cpm or two consecutive detectable viral loads. The Mann-Whitney test, Kaplan Meier analysis and Log-rank test were used for statistical analysis.

Results: Maternal HIV seroprevalence was 39.2%. 108 in-utero HIV-infected infants were identified; 59 (55%) infants were diagnosed very early via point-of-care testing and ART initiated at a median 27 hours; 49 (45%) infants were diagnosed by DBS and ART initiated at a median 10 days. 80 (74%) mothers were prescribed ART antenatally, with a median duration of 19 weeks prior to delivery (interquartile range 6-29 weeks), but half self-reported missing doses. 24 mothers (22%) had chronic HIV infection of whom 4 (3.7%) had themselves been infected perinatally. At least 28 mothers (26%) seroconverted, with a documented negative test preceding a positive test, during the pregnancy. Initial infant viral load was lower than found in a historical cohort in KwaZulu-Natal in the era of no antenatal ART (median 12,000cpm versus 155,000cpm (p<0.0001)). 10 infants (9.3%) had undetectable initial viral loads. Median time to viral suppression was 4 months, with 25% unsuppressed at 1 year. Of those suppressed, median time to viral rebound was 15.2 months. Treatment was protease-inhibitor based and no cases of virological failure resulted from protease-inhibitor resistance. 56% of infants who rebounded did not regain viral suppression. 11 infants (10.1%) were lost to follow up or disenrolled. 11 infants (10.1%) died.

Conclusion: In-utero ART exposure significantly lowers the initial viral load in HIV-infected infants, 9% of whom had undetectable viraemia. Despite the potential for rapid viral suppression, 20% of infants were lost to follow up, disenrolled or died, median time to suppression was as long as 4 months, and median time to virological rebound was 15 months. Virological failure did not result from clinically significant drug resistance. These data demonstrate that, although there is potential for in-utero HIV-infected infants to be identified and ART initiated within the first 48hrs of life, with rapid suppression of viraemia, in practice there are major challenges to achieving ART adherence in children in whom mother to child transmission has in many cases arisen as a result of maternal non-adherence.
Pharmacokinetic and 4-week safety/efficacy of dolutegravir (S/GSK1349572) dispersible tablets in HIV-infected children aged 4 weeks to <6 years: Results from IMPAACT P1093

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Background: Dolutegravir (DTG) is recommended for first-line treatment of HIV-1 infected adults due to its potency, high barrier to resistance, and tolerability. A 5 mg dispersible tablet (DTG-DT) pediatric formulation is being evaluated in IMPAACT P1093, an ongoing phase 1/2 open-label pharmacokinetic (PK), safety, and dose-finding study. Here we present intensive PK and 4-week safety (primary outcome) and efficacy of the first doses of DTG-DT tested in the youngest age-defined cohorts (V: ≥4 weeks to <6 months, IV: ≥6 months to <2 years, III: ≥ 2 to <6 years).

Methods: On enrollment, children received DTG-DT as monotherapy, or added to stable-failing or empiric initial background regimens and dosed using weight-band tables. Intensive 24-hour PK sampling was completed between days 5-10, after which background regimens were optimized based on enrollment genotypes. Safety, tolerability, and plasma HIV-1 RNA levels were assessed through 4 weeks. From adult data, targets (range) for geometric mean (GM) exposures were AUC24h 46 (37-86) mgxh/L and C24h 750 (500-2260) ng/mL.

Results: Thirty-two children were enrolled to achieve 30 (10 per age cohort) with evaluable data, of whom 17/30 (57%) were female, 27/30 (90%) had CD4% >14, with baseline median (range) HIV-1 RNA of 4.9 (2.8 to 7.0) log10 (copies/ml). The GM AUC24h and C24h of each cohort were within target ranges. The median (range) age (in years) and doses (in mg/kg), followed by the GM (arithmetic CV%) AUC24h (mgxh/L) and C24h (ng/mL) were as follows: Cohort III [4.0 (2.1-5.9), 1.1 (0.8-1.6), 40 (36%) and 461 (59%)]; Cohort IV [1.2 (0.9-1.9), 1.2 (1.0-1.4), 51 (38%) and 711 (60%)]; Cohort V [0.34 (0.28-0.39), 1.2 (0.9-1.7), 61 (44%) and 1207 (55%)]. However, DTG exposures demonstrated moderate inter-subject PK variability; 8/10 in each of cohorts IV and V achieved C24h above the lower acceptable limit (>500 ng/mL), but only 4/10 achieved the lower limit in cohort III. DTG-DT was well-tolerated, with no Grade 3 or 4 adverse events or study drug discontinuations. At 4 weeks, 24/30 (80%) participants had attained HIV-1 RNA of <400 copies/ml or a >2 log10 decrease.

Conclusions: In P1093, once daily dosing of DTG-DT at median dose of ~ 1.2 mg/kg was well-tolerated, achieving mean AUC24 and C24h results within target range with universal declines in plasma HIV-1 RNA. Given the moderate inter-subject PK variability, higher dosing will likely be needed for children 2 to <6 years of age to reliably achieve a C24h within the acceptable range. This hypothesis is currently being explored.
Steady-state pharmacokinetics and early safety data in HIV-infected African children weighing ≥25kg after switching to 50mg film-coated dolutegravir tablets in the ODYSSEY trial


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Background: ODYSSEY is an ongoing international randomised trial evaluating dolutegravir (DTG)-based antiretroviral therapy (ART) versus standard-of-care in HIV-infected children starting first- or second-line ART. This cross-over pharmacokinetic (PK) substudy aimed to provide within-patient comparative PK and safety data in children weighing 25-<40kg, switching from current EMA-approved DTG doses (requiring a mix of 25mg and 10mg tablets) to 50mg (adult dose), in order to simplify DTG administration.

Methods: Steady-state 24-hour PK curves (t=0, 1, 2, 3, 4, 6 and 24h) were constructed from data in children (≥3h fasted) observed taking film-coated DTG as 25mg and 35mg (10mg+25mg) tablets in 25-<30kg and 30-<40kg weight bands respectively. At least one week after all children switched to single daily 50mg film-coated DTG tablet, a second 24h PK curve was constructed. Informed consent was obtained for all children. We aimed to achieve DTG exposures comparable to adult data for DTG 50mg film-coated tablets QD under fasted conditions (geometric mean (GM): C trough 0.83 mg/L, AUC0-24h 43.4 h*mg/L, C max 3.34 mg/L). Additionally, results were compared to PK data for DTG 50mg BID in adults (GM ranges: C trough 2.41 to 2.72 mg/L, AUC0-24h 93.4 to 92.7 h*mg/L, C max 5.41 to 5.55 mg/L). Dolutegravir plasma concentrations were measured using a validated UPLC-MS/MS method.

Non-compartmental PK analysis was performed to calculate PK parameters with WinNonlin 6.3 software. Laboratory and clinical safety were evaluated after switch to the 50mg dose at 2, 4 and 12 weeks and then every 12 weeks.

Results: 27 black-African children from Uganda and Zimbabwe (59% male) with a median (IQR) age 11.1(10.0-12.4) years and weight 29.2(27.0-30.7) kg were included in the analysis. 23 children (25-<30kg: n=14 30-<40kg, n=9) had evaluable PK curves on both PK days allowing for within-child PK comparison. For two additional children on 25mg, and one on 50mg in each weight band, a single PK-curve was available. For children weighing 25-<30kg on DTG 25mg (n=16) GM with coefficient of variation (CV) for C trough and AUC0-24h were 0.37(44) mg/L and 32.4(22) h*mg/L respectively, and after switch to DTG 50mg (n=15) values were 0.70(32) mg/L and 56.1(21) h*mg/L, respectively. For children weighing 30-<40kg on DTG 35mg (n=9), C trough and AUC0-24h were 0.45(63) mg/L and 40.3(35) h*mg/L, and after switch to DTG 50mg (n=10) values 0.63(49) mg/L and 53.5(32) h*mg/L, respectively. Administration of the higher 50mg dose resulted in C max values of 5.26(23) mg/L and 5.22(25) mg/L in weight bands 25-<30kg and 30-<40kg, respectively. After a median (IQR) follow-up of 21.3(15.6-23.1) weeks on the 50mg dose one SAE (cryptococcal meningitis) and one grade 3 laboratory event (asymptomatic anaemia) were reported; both were considered unrelated to DTG.

Conclusions: In children weighing 25-<40kg DTG 50mg film-coated tablets achieve appropriate DTG plasma exposures, as C trough and AUC0-24h are comparable to DTG exposures in adults on 50mg QD, and provide a practical way of dosing in children weighing ≥25kg. Short term safety data is acceptable in this PK substudy. Children in the main ODYSSEY trial will switch to 50mg tablets and longer-term safety data will be evaluated.
Pharmacokinetics, safety, and efficacy of bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) single-tablet regimen in HIV-1-infected children (6 to <12 years)

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Background: Bictegravir (BIC, B), a novel, unboosted integrase strand transfer inhibitor (INSTI) with a high barrier to resistance and low potential for drug interactions, has been coformulated with the recommended NRTI backbone of emtricitabine (F, FTC) and tenofovir alafenamide (TAF) (B/F/TAF) into a once-daily (QD), single-tablet regimen (STR). We report pharmacokinetics (PK), safety and efficacy in children who switched from a stable antiretroviral regimen to B/F/TAF.

Methods & Methods: We conducted a prospective, single-arm, open-label, 2-part, 48-week (W) clinical trial to evaluate switching to the adult formulation of B/F/TAF (50/200/25 mg) QD in virologically suppressed children (6 to <12 years) weighing ≥25 kg. Intensive PK was evaluated at W2 or W4. To confirm BIC dose, PK parameters were compared to B/F/TAF-treated adults were made using geometric least-squares mean (GLSM) ratios and associated 90% confidence intervals (CI) with PK equivalence. Adverse events (AE), laboratory tests, HIV-1 RNA, were assessed. We report follow up data through W12.

Results: 25 children enrolled; median (range) age 10 (6-11) yrs, median (range) weight 28.4 (25.0-39.0) kg, 52% female, 64% Black, median CD4 count 928 cells/μL. BIC AUCtau was similar, Cmax 77% higher, and Ctau 22% lower in children ≥25 kg than adults. BIC Ctau was well above protein-adjusted effective concentration for wild-type virus (162 ng/mL) in all children. FTC and TAF exposures were within safe and efficacious ranges of adults. Through median (Q1, Q3) exposure to study drug of 16.1 (15.9, 17.7) weeks, most common AEs were grade 1 diarrhea and upper respiratory tract infection (each 16%, 4/25); no other AE occurred in >2 participants. No participant discontinued for an AE. All (100%) had HIV-1 RNA <50 c/mL at W12; none met criteria for resistance testing.

Conclusions: B/F/TAF maintained virologic suppression and was well tolerated in children through at least 12 weeks. Similar to adults, therapeutic plasma concentrations of all B/F/TAF components of B/F/TAF were achieved. Efficacy and safety in children are consistent with phase 3 B/F/TAF results in adults and adolescents, showing high proportions with viral suppression, excellent tolerability, and no resistance. B/F/TAF may be an important unboosted INSTI, STR option for HIV-infected children due to its small tablet size, high barrier to resistance and lack of food requirement.
Outcomes of second-line antiretroviral therapy (ART) in HIV-infected children: a CIPHER cohort collaboration global analysis

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Background: There are limited data describing characteristics at initiation of second-line ART and subsequent immunological and clinical outcomes among children, particularly in resource-limited settings.

Materials & Methods: Follow-up data through 2015 on children aged <18 years initiating combination ART from 11 cohort networks within CIPHER were pooled. Characteristics at start of second-line ART and outcomes at one and two years after second-line ART initiation were summarized by region: North America, Latin America (Caribbean, Central & South America), Europe, Asia, Southern Africa (South Africa & Botswana) and the rest of sub-Saharan Africa (SSA). AIDS was defined as WHO Stage 3/4 or CDC Stage C. Cumulative incidences of mortality and loss to follow-up (LTFU) were estimated with LTFU as a competing risk for mortality and vice-versa.

Results: Of 85,389 children who started first-line ART, 3,555 (4%) switched to second-line ART, primarily with protease inhibitors (92%). Median [interquartile range (IQR)] age at second-line ART initiation varied from 4.1 [1.9-7.5] years in North America to 10.3 [6.7, 13.8] years in Latin America. The lowest CD4 counts at second-line start were in SSA and Latin America (235 [81, 561] and 239 [63, 661] cells/mm3 respectively). Routine CD4 monitoring was available in the majority of cohorts during follow-up, though the proportions of children with CD4 count measurement at initiation of second-line varied from 70% in SSA to 89% in Europe. Overall, the median [IQR] follow-up after second-line ART initiation was 29 [12,51] months, with the shortest follow-up in SSA (21 [8,39] months) and the longest follow-up in North America (63 [32,101] months). By one year after initiating second-line ART, mortality estimates varied from 0% in North America to 5.0% in Latin America (95% CI: 2.0%, 9.8%); LTFU by one year ranged from 0% in North America to 4.8% (3.6%, 6.3%) in SSA. Among those AIDS-free at initiation of second-line, progression to AIDS by one year was highest in SSA (12.1% [9.4%, 15.4%]) followed by Asia (4.6% [2.2%, 8.4%]). Median CD4 counts at one year after second-line start improved from start of second-line to >500 cells/mm3 in all regions; proportions of children with CD4 data available, however, varied from 56% in SSA to 88% in Europe and Asia. By two years after second-line ART initiation, there remained no deaths in North America, while cumulative mortality in other regions ranged from 1.4-5.7%; LTFU by two years ranged from 1.6% (0.1%, 7.7%) in North America to 7.6% (6.0%, 9.4%) in SSA. Progression to AIDS was highest in SSA at 17%. There were continued improvements in CD4 counts with median CD4 counts >600 cells/mm3 in all regions. SSA (39%) and Southern Africa (49%) had the lowest proportions of children with CD4 counts available at two years.

Conclusions: We found wide regional variations in age and CD4 count at start of second-line ART among children. Outcomes at one and two years of follow-up after second-line ART initiation showed continued mortality in some regions after switch. Immunological restoration was observed in all regions though CD4 availability varied over time.
Alendronate improves bone mineral density in perinatally HIV-infected children and adolescents

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Background: Bisphosphonate therapy has not been well-studied in perinatally HIV-infected children and adolescents (PHIV) with low bone mineral density (BMD).

Materials and Methods: IMPAACT P1076 was a randomized, placebo-controlled, double-blind, crossover study to assess safety and efficacy of 48/96 weeks of once-weekly Alendronate in PHIV 11-25 years of age. Participants from sites in US and Brazil on stable antiretroviral therapy (ART), with dual-energy-X-ray absorptiometry lumbar spine BMD z-score (LS_BMDZ) < -1.5 SD or history of fragility fracture, were randomized to three groups: A/A - Alendronate for 96 weeks (70 mg >30 kg or 35 mg if < 30 kg); A/P - Alendronate (48 weeks) followed by Placebo (48 weeks); P/A - Placebo (48 weeks) followed by Alendronate (48 weeks). Participants received daily calcium/vitamin D and instructions for one hour of weight-bearing exercise daily, and were followed for 144 weeks. We present 48-week results comparing the combined A/A and A/P Arms (Alendronate) to the P/P Arm (Placebo). The primary safety outcome was development of new or worsening ≥ grade 3 laboratory values, signs or symptoms, or new targeted diagnoses (jaw osteonecrosis, atrial fibrillation, or non-healing fractures). The proportion of participants with ≥1 safety outcome was compared between Arms using Fisher’s exact test. The primary efficacy outcome of percent change in LS_BMD to weeks 24 and 48 was compared between Arms using two-sample t-tests. Secondary outcomes included absolute change in LS_BMDZ and whole body BMD z-scores (WB_BMDZ), and percent change in whole body BMD (WB_BMD). Linear regression was used to assess effect modification of treatment differences by age group (11-<15, 15-<19, ≥19 years).

Results: Fifty participants (Alendronate: n=32; Placebo: n=18) started treatment: 68% male, median (min, max) age 16.1 (11.1-23.4) yrs, all on ART, CD4 count 728 (268, 1699) cells/mm3, 82% with HIV-1 RNA <400 copies/ml, LS_BMDZ -2.40 (-5.60, -1.40) and WB_BMDZ -2.50 (-5.10, -0.50). Five Alendronate participants (16%; 95% Confidence Interval (CI): 5%, 33%) experienced 4 grade 3 (1 possibly treatment-related) and 1 grade 4 safety outcomes compared to two (grade 2) Placebo participants (11%; 95%CI: 1%, 35%, p>0.99). There were no new targeted diagnoses. LS_BMD increased significantly more in the alendronate Arm: mean changes of 14% and 20% on Alendronate compared to 4% and 7% on Placebo at 24 and 48 weeks, respectively. Mean (95% CI; p-value) treatment differences in percent change from baseline (Alendronate minus Placebo) were 10% (6%; 14%; p<0.001) at week 24 and 13% (7%; 19%; p<0.001) at week 48. LS_BMDZ also increased more on Alendronate than Placebo (Alendronate minus Placebo): 0.60 (0.36, 0.85; p=0.001) at week 24 and 0.73 (0.41, 1.05; p<0.001) at week 48. Similar increases on Alendronate were seen for WB_BMD and WB_BMDZ. Alendronate use was associated with larger improvements in LS_BMD in children < 15 years (effect modification p=0.02).

Conclusions: There were no safety concerns with 48 weeks of Alendronate treatment in PHIV children and adolescents with low BMD, and greater increases in LS and WB on Alendronate compared to Placebo, especially in younger children.
Persistence of myeloid cell-associated inflammation in HIV-infected children after 8 years on early initiated therapy - The key role players in HIV persistence?

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Background: Combination antiretroviral therapy (ART) does not completely eradicate HIV latently infected cells. Resting CD4+ T cells remain the most studied source of residual viremia. Research evaluating the role of myeloid lineage cells, such as monocytes and macrophages, in HIV persistence is limited. These long-lived cell types provide optimal hideouts for the virus and are less susceptible to HIV-induced cytopathic effects and death. Evaluating the interplay of the immune mechanisms of myeloid cells and HIV persistence within a pediatric population may provide valuable insight into therapeutic targets for eradicating latent reservoirs.

Methods: Plasma samples originating from the Children with HIV-Early Antiretroviral Therapy (CHER) trial were evaluated. ART was initiated at <1 year of age and children sustained viral suppression at 7-8 years. Cytokines (IL-1β, IL-6, IL-8, IL-10, INF-γ, TNF-α, TGFβ1,2,3, sCD14, sCD163, GCSF, CMCSF, LBP, and VEGF) and chemokines (MCP-1, MIP-1α, MIP-1β, LBP) involved in monocyte/macrophage activation and trafficking were measured using Luminex® Multiplex assays. Age-matched controls were measured for the same biomarkers. A subset of HIV-infected participants was tested for total HIV-1 DNA using qPCR targeting a conserved region in HIV integrase. Statistical analysis employed a Wilcoxon matched paired test for nonparametric data.

Results: 163 samples (88 HIV-infected and 75 HIV-uninfected controls) were evaluated. The median baseline viral load at ART initiation was 738,500.5 copies/ml. Median CD4-percentage at baseline was 36.9% (range: 23.1-57.1%). At 7-8 years of age, there were no significant differences between the CD4-percentage of the HIV-infected (38.3%) and control groups (40.0%) (p=0.261). HIV-infected children showed highly significant (p<0.001) levels of IL-1β, IL-6, TGFβ3, sCD14, sCD163, MCP-1, MIP-1α, MIP-1β, GCSF, CMCSF, LBP, and VEGF when compared to controls. Significant increase in IL-8 (p=0.0450), TNFα (p=0.0033), TGFβ1 (p=0.0140) and TGFβ2 (p=0.0042) were also observed. Among 32 children assessed for HIV-1 DNA at follow-up, a median of 32.5 copies/million cells (range: 0-562.6) was observed at 7-8 years of age.

Conclusions: Despite early therapy initiation, long-term viral suppression, low cell-associated HIV-1 DNA detection and normalized CD4 counts, HIV-infected children display persistent myeloid-cell associated inflammation which may drive ongoing low-level replication. The increase in sCD14 and LBP levels implicate bacterial gut translocation.
Prevalence of depressive symptoms among Thai adolescents living with HIV using the Patient Health Questionnaire-9 (PHQ-9) screening tool

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Background: Depression is a major mental health disorder contributing to illness and disabilities among HIV-infected persons. A simple screening measure for depressive disorders plays a crucial role in assisting healthcare professionals at identifying suspected cases in clinical practice. This study aimed to investigate the prevalence and associated factors of depressive symptoms, using the Patient Health Questionnaire-9 (PHQ-9) as a screening tool, among HIV-infected Thai adolescents.

Methods: A multicenter, cross-sectional study was conducted in Thailand. HIV-infected adolescents aged 15-25 years, and age- and sex-matched healthy, HIV-uninfected participants were recruited (ratio 1:1). The Thai version of PHQ-9, a simple, brief, and validated depression screening tool based on the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV) criteria for major depressive disorder, was used to screen for depressive symptoms. It is a 9-item, self-administered questionnaire that takes <5 minutes to complete. Scores for each item range from 0-3, giving a maximum score of 27. Participants with PHQ-9 scores ≥9 and/or with suicidal thoughts within the past 2 weeks were defined as having depressive symptoms. All participants with a positive screening test were referred to a psychiatrist to confirm the presence of a psychiatric disorder. The 10-item Alcohol Use Disorders Identification Test (AUDIT) was used to screen for excessive alcohol drinking. AUDIT scores ≥8 out of 40 indicate hazardous alcohol use. Logistic regression analysis was performed to identify factors associated with depressive symptoms among our HIV-infected adolescents.

Results: Between February and April 2018, 150 HIV-infected and 150 healthy, HIV-uninfected adolescents were enrolled. The median age of participants was 19.0 (interquartile range: 16.8-21.8) years, and 50% were male. Of the total cohort, 32 (11%) reported to ever having suicidal thoughts, and 64 (21%) had hazardous alcohol use within the past year. Among HIV-infected participants, the majority (94%) had perinatal HIV infection, 59 (39%) were currently on efavirenz-based regimens, and 109 (73%) had virologic suppression (HIV RNA <50 copies/ml).

Overall, depressive symptoms were identified in 46 participants (15%; 95% CI: 11-19%), of whom 22 (15%; 95% CI: 9-20%) were HIV-infected, and 24 (16%; 95% CI: 10-22%) were healthy adolescents (P=0.75). In the multivariable analysis among HIV-infected adolescents, AUDIT scores ≥8 (adjusted odds ratio: 3.8; 95% CI: 1.2-12.4) were independently associated with depressive symptoms, whereas HIV-related characteristics did not reveal any significant associations (P>0.05). HIV-infected participants with depressive symptoms tended to have lower proportions of virologic suppression compared to those without (64% versus 74%; P=0.30). Among 42 participants with depressive symptoms who were evaluated by psychiatrists, 25 (60%); 9 HIV-infected and 16 healthy had a definite psychiatric disorder which included adjustment disorder (n=14; 5 HIV-infected and 9 healthy), depressive disorder (n=7; 4 HIV-infected and 3 healthy), and anxiety disorder (n=4; all were healthy).

Conclusions: Using the PHQ-9, a simple mental health screening tool, 15% of our HIV-infected adolescents with depressive symptoms were detected and linked to a formal psychiatric assessment. The prevalence of depressive symptoms was comparable between HIV-infected and general Thai youth. Hazardous alcohol drinking was associated with depressive symptoms among this population.
Caregiver depression and child neuropsychological outcomes in an observational study carried out in four Sub-Saharan countries

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Background: Depression symptoms in caregivers may influence their young children’s behavior and cognitive development. Few research studies have focused on Sub-Saharan countries where high prevalence of pediatric HIV may impact child neuropsychological development and caregiver mental health.

Methods: We investigated cross-sectional associations between caregivers’ depressive symptoms and child neuropsychological outcomes in P1104s; a multi-center study in sub-Saharan Africa sponsored by the International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) Network. 611 children between 5-11 years (246 HIV+, 183 HIV exposed, uninfected, and 182 HIV unexposed, uninfected) completed assessments at 6 research sites: South Africa (3), Malawi, Uganda and Zimbabwe. Children were assessed with the Bruininks-Oseretsky Tests of Motor Proficiency 2 (BOT-2 total score), the Kauffman Assessment Battery for Children II (KABC-II mental processing index -MPI) and the Tests of Variables of Attention (TOVA). Caregivers responded to the Hopkins Symptom Check List (HSCL-25) depression subscale and evaluated their child with the Behavior Rating Inventory of Executive Function (BRIEF) and the UNICEF Multiple Indicators Cluster Survey-4 (MICS) Questionnaire for Children. Associations were evaluated with Pearson correlations and with unadjusted and adjusted (for study design, caregiver and child characteristics) linear regression using generalized estimating equations (GEE).

Results: Children’s mean age was 7.2 years (SD= 1.4) and 290 (47%) were boys. Most caregivers (68%) were HIV+ and 36% had an HSCL-25 score above 1.75. Caregiver depression scores were comparable across groups. Of HIV+ children, 96% had suppressed viral load. In adjusted GEE models, caregivers with high (>1.75 mean score) levels of depression reported higher BRIEF scores (e.g. more executive function problems) by an average 5 to 7 points (p<.001) and almost 3 point lower average MICS development scores (p=0.01; e.g. less development for age). BOT-2 and TOVA scores were not significantly associated with caregiver depression symptoms. Exploratory regression models with interactions between caregiver depression and child HIV status showed a trend; with adjusted KABC MPI mean scores decreased with increasing levels of caregiver depression in HIV+ children (adjusted p=0.12).

Conclusions: High depressive symptomatology in caregivers was a significant predictor of child behavioral problems and poorer development. Cognitive performance was not associated with caregiver’s depressive symptoms. Considering the mental health of the caregiver should be part of integral neuropsychological evaluations and care in the context of HIV disease.
A randomized, controlled trial of a patient-centered disclosure counseling intervention for Kenyan children living with HIV

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Background: For children living with HIV, learning about their HIV status (“disclosure”) is a critical process within their transition to adulthood. Caregivers of perinatally HIV-infected children frequently worry about the impact of disclosure, while also reporting delayed disclosure can hurt medication adherence. We evaluated the impact of a patient-centered, culturally- and age-appropriate disclosure counseling intervention among Kenyan children and their caregivers.

Methods: We conducted a prospective, clinic-cluster randomized trial in which we followed child-caregiver dyads (children ages 10-14) attending eight clinics (randomized to intervention or control) at a large HIV treatment program in Kenya. All patients at the intervention clinics had access to intensive counseling (family, one-on-one, and peer group sessions) with trained disclosure counselors and culturally-tailored materials, compared to control clinics with standard care. Disclosure was treated as a time-to-event outcome, measured on a discrete time scale, with assessments at 0, 6, 12, 18, and 24 months. Mental health and psychosocial outcomes were assessed using standardized questionnaires.

Results: The 285 children were mean age 12.3 years, 52% female, with average time-on-treatment of 4.4 years. At baseline, 32% of the children reported that they knew their HIV status already (no difference between control and intervention groups). Disclosures in both control and intervention arms increased over follow-up, but the intervention arm had significantly more disclosures. Using child-reported disclosure, the prevalence of disclosure increased significantly between the baseline and 24 months of follow-up from 29.2% to 58.5% in the control arm and from 33.2% to 74.0% in the intervention arm (difference of 15.5%, 95% confidence interval: 3.7, 27.3). Overall, there were not significant differences in mental and behavioral health outcomes, although trends suggested mental and behavioral distress increased at month 6 in the intervention group as disclosures increased, and then decreased compared to controls thereafter.

Conclusion: This study provides evidence for an effective, clinic-based intervention to increase disclosure of HIV status to children living with HIV. Making counseling support available throughout the disclosure process may be particularly important to navigate increased psychological distress immediately after disclosure and move towards resilience.
PrEP uptake among pregnant and postpartum women: Results from a large implementation program within routine maternal child health (MCH) clinics in Kenya

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Background: Very few examples of PrEP delivery to pregnant and postpartum women have been reported. The PrEP Implementation for Young Women and Adolescents (PrIYA) Program provides real-world evidence on delivering PrEP to pregnant and postpartum women in Western Kenya.

Methods: PrIYA is part of the DREAMS Innovation Challenge funded by PEPFAR managed by JSI Research & Training Institute, Inc. We approached HIV-uninfected pregnant women seeking routine antenatal (ANC) and postnatal (PNC) services at 16 maternal and child health clinics in Kisumu County, Kenya from June to December 2017. At each patient encounter, screening for behavioral risk factors and willingness to consider PrEP was conducted per national PrEP guidelines. Those who were willing to consider PrEP were assessed for medical eligibility and those eligible were offered PrEP at the same visit. Logistic regression models determined correlates of PrEP initiation.

Results: In total, we conducted 9,704 assessments among pregnant and postpartum clients for behavioral risk factors and willingness to consider PrEP. The median age was 24 years (IQR 21-28); 31% did not know their male partner’s HIV status and 84% were married. Overall, 1,856 (19%) of encounters led to PrEP initiation; only 6 women (<0.01%) were medically ineligible (creatinine clearance <50 min/mL). Frequency of PrEP initiation differed by male partner HIV status (HIV-negative 7%, unknown 43%, HIV-positive 79%, p<0.001). PrEP initiation was more common in the postpartum period than during pregnancy (23% vs 16%, p<0.001). Women younger than 24 years of age were more likely than older women to initiate PrEP (OR=1.18, 95% CI 1.08-1.28, p=<0.001). Initiating PrEP was also associated with having an STI (OR=2.66, 95% CI 1.48-4.77, p=0.001) and being forced to have sex in the last 6 months (OR=3.69, 95% CI 1.69-8.06, p=0.001). The most frequently reported reasons for declining PrEP were the perception that HIV risk was low (46%) and the partner was HIV-negative (43%); few women accepting PrEP feared intimate partner violence as a result (2%).

Conclusions: In this pregnant and postpartum population, a substantial number of women desired and started PrEP. PrEP initiators were younger and more likely to have HIV risk factors than those who declined PrEP.
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Role of Maternal Viral Load and CD4 Count on Perinatal HIV-1 Transmission during Breastfeeding in the PROMISE Postpartum Component

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Background: In the PROMISE 1077BF trial, breastfeeding women with CD4 > 350 cells/mm³ (or >country-specific ART threshold if higher) and their uninfected neonates were randomized to maternal ART (mART) or infant nevirapine prophylaxis (iNVP) until breastfeeding cessation or 18 months post-delivery, (whichever occurred first) and had low infant HIV-1 infection rates (0.7% overall). We assessed whether maternal viral load (MVL) or CD4 were associated with perinatal HIV transmission risk.

Methods: MVL was measured retrospectively on batched specimens collected at entry (7-14 days postpartum) and weeks 6, 14, 26, and 50 postpartum. CD4 was measured real-time at entry and weeks 14, 26, 38, and 50 postpartum. Infant HIV-1 NAT was obtained at weeks 1, 6, every 4 weeks until week 26, then every 12 weeks. Infant infection was defined as a positive HIV-1 NAT at any two post-entry timepoints. The associations of baseline and time-varying MVL and CD4 with transmission risk were assessed using proportional hazards regression models by randomized treatment arm, with MVL categorized as < 1000 or ≥ 1,000 copies/ml and CD4 categorized as < 500 or ≥ 500 cells/mm³, and adjustment for mART receipt during pregnancy.

Results: 2431 mother-infant pairs were randomized. Baseline MVL and CD4 did not differ by randomized arm. Among women randomized to mART (n=1,220), baseline CD4 count was < 500 cells/mm³ in 162 (13%) and ≥ 500 cells/mm³ in 1,058 (87%) and baseline MVL was < 400 copies/ml in 672 (55%), 400 – 1,000 copies/ml in 239 (20%), and ≥ 1,000 copies/ml in 309 (25%). Among women randomized to the iNVP arm (n=1,211), baseline CD4 count was < 500 cells/mm³ in 170 (14%) and ≥ 500 cells/mm³ in 1,041 (86%) and baseline MVL was < 400 copies/ml in 604 (50%), 400 – 1,000 copies/ml in 210 (17%), and ≥ 1,000 copies/ml in 397 (33%). Baseline MVL (p = 0.11) and CD4 (p = 0.51) were not significantly associated with infant HIV-1 infection. Time-varying MVL was significantly associated with infant HIV-1 infection in the mART arm (hazard ratio (95% CI): 12.04 (2.54, 57.06) but not in the iNVP arm (hazard ratio (95% CI): 1.04 (0.20 – 5.52)). Time-varying CD4 was not significantly associated with infant HIV-1 infection in either arm (hazard ratio (95% CI): 0.29 (0.05-1.59) in mART arm and 0.33 (0.07-1.57) in iNVP arm). Of 7 postnatal infections in mART arm, 2 had proximal MVL < 40 copies/ml.

Conclusions: With iNVP, MVL was not significantly associated with HIV-1 transmission during
breastfeeding. However, among women receiving mART, increased MVL during breastfeeding was associated with increased risk of infant HIV-1 infection. These data emphasize the important role of adherence to mART in controlling MVL and preventing infant infection and suggest that iNVP should be considered in situations with documented poor maternal ART adherence.
Diagnosing and treating more infants, faster: Findings from the first multi-country evaluation of routine point-of-care early infant diagnosis in eight sub-Saharan countries.

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Background: Point-of-care early infant diagnosis (POC-EID) may improve the care of HIV-exposed infants compared to conventional testing. POC-EID is being implemented in eight sub-Saharan African countries at POC (“testing”) and near-POC (“spoke”) sites. A program evaluation was undertaken to assess the impact of POC- or near POC-EID implemented as part of routine care, compared with conventional testing.

Materials and Methods: Using a pre-post intervention design, key EID outcomes were compared in each country. Pre-intervention conventional EID data were collected retrospectively from registers across a purposively sampled sub-set of sites. Post-intervention data for specimens processed between December 2016 and December 2017 were collected prospectively using a POC-EID testing form. Median turnaround times (TATs) were compared using Wilcoxon rank-sum test, and proportions with Pearson chi-square test. Kaplan-Meier Estimator was used for the proportion of caregivers who received results within 30 days of sample collection. Prospective data were analyzed by entry point and compared between testing/hub and spoke sites. The cost per test result returned was calculated using Global Fund’s total cost of ownership estimates for POC and conventional EID.

Results: POC-EID resulted in a significantly higher percentage of results returned to caregiver and percentage of infants started on treatment sooner, as compared to conventional EID. There were no significant differences in percent results returned between testing and spoke sites. Valid, non-confirmatory tests from different entry points revealed 3.2%, 19.6%, 15.5%, and 2.5% HIV- positivity rates from prevention of mother-to-child transmission entry points, pediatric inpatient, outpatient, and vaccination clinics, respectively. The cost per test result returned (regardless of TAT) was $20-38 for POC and $21-33 for conventional.

Conclusions: Routine use of POC-EID in sub-Saharan Africa is feasible and significantly improves key patient outcomes. Spoke sites can expand access to POC-EID, with minimal differences in patient-level outcomes. POC-EID is particularly important for high-yield entry points such as pediatric wards, where patients may be less likely to receive results from conventional testing with long TATs. Given similar costs per test result returned to caregiver for conventional testing, POC-EID represents an efficient and effective way to identify HIV-infected infants and initiate on antiretroviral treatment.
Impact of the introduction of HIV testing at birth on early infant diagnosis in KwaZulu-Natal, South Africa, 2010-2017

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Background: Guidelines for the timing of infant HIV testing in South Africa changed on 01/04/2015 from testing at age 6 weeks, to birth testing with repeat testing at 10-18 weeks of age (depending on the duration of prophylaxis received). In both time periods testing at 6 weeks after cessation of breastfeeding was maintained. We examined the impact of the introduction of birth testing in the rural Hlabisa health sub-district in KwaZulu-Natal, South Africa. We describe the number of tests per infant, age at diagnosis, receipt of confirmatory testing, and testing coverage, by guideline time period.

Materials & Methods:
Data on all HIV DNA PCR tests conducted from 01/06/2010 to 17/07/2017 at 17 clinics in the sub-district were extracted from the National Health Laboratory Service database. A deterministic and probabilistic data linkage algorithm using infant first name, surname, date of birth, sex, clinic and clinic ID was used to identify repeat tests on the same child. Children born between 01/06/2010 and 31/12/2016 were included. A window of +1 week was used to identify tests at birth, and ±2 weeks for tests at other times. As no data on prophylaxis use were available, all tests from 10-18 weeks were considered follow-up tests as recommended after 01/04/2015. Testing coverage was estimated using the number of live births and antenatal seroprevalence data from Statistics South Africa.

Results: Among 17,361 PCR tests, 15,006 unique infants were identified, of whom 4529 (30%) were born after 01/04/2015. The proportion of infants ever testing PCR positive declined from 6.7% among those born in 2010 to 1.0% among those born in 2016. Among those born before 01/04/2015, 13% received >1 test. The median (IQR) ages at first test and first positive test (n=390) were 7.0 (6.1-11.0) and 10.6 (6.7-27.4) weeks respectively. Among those born after 01/04/2015, 18% received >1 test, ranging from 9%-43% by clinic. The median ages at first test and first positive test (n=67) were 0.6 (0.0-10.7) and 13.1 (1.9-29.1) weeks, respectively. Among 2383 (53%) infants tested at birth, 11 (0.5%) tested PCR positive. Among 2355 testing negative at birth, 547 (23%) were ever repeat tested (with no change in the proportion over calendar time) at a median age of 10.9 (9.9-14.9) weeks, of whom 5 (1%) tested positive. Children tested at birth were less likely than those not tested at birth to have a test at 10-18 weeks (15% vs. 59%, p<0.001). Of those born after 01/04/2015 and testing positive at any time, 45% (30/67) received a confirmatory PCR test a median 13 (7-19) days later.

The estimated number of HIV-exposed infants born during the whole time period was 20,840, resulting in an overall estimated testing coverage of 72%.

Conclusion: Our results suggest that under a quarter of infants testing negative at birth received a follow-up test; given the low sensitivity of birth tests this may result in high numbers of missed infections. Poor linkage due to limited data may have contributed to underestimates of testing coverage and repeat testing; a future validation study is planned.
Growth patterns of HIV-exposed uninfected versus HIV-unexposed children in the context of breastfeeding and universal maternal antiretroviral therapy: a prospective study

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Background: HIV-exposed uninfected (HEU) children comprise a growing proportion of child populations across sub-Saharan Africa, but little is known about the comparative growth of HEU children with breastfeeding in the context of universal maternal antiretroviral therapy (ART).

Materials & Methods: A prospective cohort of HIV-infected pregnant women initiating ART (TDF+FTC+3TC), and a parallel cohort of HIV-uninfected pregnant women, were enrolled at first antenatal visit, followed through delivery and until 12-18 months postpartum with their breastfed HIV-uninfected children in Cape Town, South Africa. Infant feeding practices and maternal risk factors were assessed using standard questionnaires. Anthropometry was measured at birth, 6 weeks; and 3, 6, 9 and 12 months(m) using standardized methods; analysis was limited to singletons and first-born twins. Age- and gestation-adjusted Z-scores were generated using Intergrowth-21st and World Health Organization reference standards. Weight-for-age (WAZ), length-for-age (LAZ) and head circumference-for-age (HCAZ) Z-scores were compared over time using mixed effects linear models with adjustment for confounders.

Results: Overall, 873 mother-infant pairs [HEU, n=461; HIV-unexposed (HU), n=412] attended 4542 anthropometry visits. All HIV-infected women initiated ART in pregnancy (at initiation: median log10 HIV viral load: 4.0 copies/mL; median CD4: 354 cells/mm3). HIV-infected (vs. HIV-uninfected) women were less likely to have completed high school (25% vs 45%); be employed (40% vs 47%); and live in a home with toilet and running water (27% vs. 38%). Median (interquartile range, IQR) gestation at birth was 39 (38-40) weeks and birthweight, 3180g (2820-3460g); proportions preterm delivery (PTD, <37 weeks) and small-for-gestational-age (SGA, birth weight <10th centile) were similar for HEU and HU children (12% vs 9%, p=0.20; 11% vs 10%, p=0.28, PTD and SGA respectively). Compared to HU, HEU children were breastfed for shorter periods (median 4 vs 9 months). At birth, HEU (vs. HU) children had lower mean WAZ [β [-0.24 (95%CI -0.37; -0.12)], LAZ [-0.34 (-0.55; -0.12)] and HCAZ [-0.46 (-0.65; -0.26)]. Lower Z-scores among HEU (vs. HU) persisted across follow-up: aβ (95%CI) WAZ, -0.25 (95%CI -0.37; -0.12); LAZ, -0.14 (-0.28; -0.02); HCAZ, -0.27 (-0.40; -0.14), adjusting for socio-economic factors, maternal alcohol use, intimate partner violence, SGA, preterm birth, infant feeding and child age. Over time, magnitude of Z-score differences (HEU vs. HU children) increased for LAZ [at ±12m, aβ -0.29 (95%CI -0.48; -0.10]) but remained similar for WAZ and HCAZ. Inferences were unchanged in analysis restricted to term, appropriate-for-gestational-age (AGA) children. SGA predicted lower WAZ, LAZ and HCAZ, with lowest scores observed in children both HEU and SGA. Among HEU children, pre-ART maternal viral load predicted lower WAZ [per log10 increase, aβ -0.10 (95%CI -0.21; -0.02)], but not LAZ or HCAZ.

Conclusions: Even with universal maternal ART and breastfeeding, HEU children have small but clinically meaningful deficits in early growth trajectories versus otherwise comparable HIV-unexposed children. Mitigating the population-level impact of growth failure in this expanding group of children will require a better understanding of the drivers of these differences.
Multisystem chronic disease in perinatally HIV-infected South African adolescents on antiretroviral therapy

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Background: Perinatally HIV-infected adolescents (PHIVA) are at risk of chronic disease due to early and ongoing immune suppression as well as long-term ART toxicity. There are little data on multisystem involvement in PHIVA, especially in African populations. We investigated the overlapping burden of neurocognitive, cardiovascular, respiratory or renal impairment in PHIVA in the Cape Town Antiretroviral Cohort (CTAAC).

Methods: PHIVA aged 9-14 years on ART for >6 months were recruited from seven sites across Cape Town, with age-matched HIV negative adolescents. Disease assessed at enrolment was: Neurocognitive impairment defined as an International HIV Dementia Scale score of <10; cardiac impairment based on echocardiogram abnormality; respiratory impairment based on impaired spirometry with either obstructive, restrictive or mixed patterns; renal impairment defined as abnormal glomerular filtration rate (GFR). Single, dual or multi-system impairment was defined as having impairment of one, two or 3 or more of the 4 systems measured, respectively. Baseline variables were compared between groups using t-tests, Wilcoxon, and Chi-square tests as appropriate.

Results: Overall, 430 PHIVA and 95 HIV- adolescents were included (mean age,12 years; 49% female). Median age of ART initiation was 4.3 years (IQR: 1.8-7.7), median CD4 count was 710 (IQR:564-951) with 63% of PHIVA being virologically suppressed at enrollment. Abacavir and Zidovudine were the most commonly used NRTIs with 60% on NNRTI based regimen and 38% on a PI based regimen. Almost half (45%) the PHIVA cohort had single system impairment while 33% had two or more systems involved. Of these 33 (8%) PHIVA had 3 or 4 systems involved. Of those with single system impairment 43%, 3% 40% and 34% of adolescents had cardiac, renal, neurocognitive, respiratory respectively. Of PHIVA with dual system morbidity (n=141), the most common pattern was cardiac and neurological comorbidity (n=73, 52%), followed by cardiac and respiratory morbidity (n=66, 47%). There was no difference in viral suppression at enrollment or duration of ART regimen in those that had dual or multisystem impairment versus those that had single or no system impairment (p=0.27 and p=0.71 respectively). Of 33 PHIVA with multisystem impairment, the median CD4 count was 734 (IQR: 520-1089) and 51% were virally suppressed. Median age of ART initiation was 3.7 years (IQR: 0.95-8.11) with a median duration on ART of 8.3 years. The most common pattern of multisystem disease was the combination of the cardiovascular, respiratory and neurological system. Two (0.5%) participants had impairment of all 4 systems. Eighty-eight percent had abnormal right heart echocardiogram parameters. The most common spirometry pattern was restrictive (67%). 25% reported repeating at least 1 year of school.

Conclusions: In this cohort of PHIV+ youth almost a third of adolescents had two system impairment with a smaller proportion having multisystem impairment. Despite relatively early ART initiation some adolescents will still have significant systemic morbidity that will require increasing clinical attention as PHIVA age into adulthood.
Virologic outcomes of perinatally infected adolescents in the period of early adolescence (10-15 years) in South Africa

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Background: HIV infected adolescents are at high risk of poor treatment outcomes compared to adults or children both due to their developmental stage and because the transition from paediatric to adult/adolescent care can be very challenging with impacts on adherence and retention. We sought to describe the virologic outcomes of adolescents that started antiretroviral therapy (ART) before the age of 10 years in the period of early adolescence (10-15 years).

Methods: We included all adolescents aged 10-15 years who initiated ART before age 10 years (as a proxy for being perinatally infected) from 2004-2015 in 9 IeDEA-SA collaborative cohorts and had at least 1 viral load (VL) measurement after the age of 10 years. We examined viral non-suppression (VL≥400 copies/ml). Mixed effects logistic regression models were used to explore the association between age and viral non-suppression adjusting for patient characteristics and time on ART as potential confounders. We excluded all adolescents that were non-suppressed at 10 years.

Results: The median age at ART start among 4,297 adolescent children (49% female) who started ART before the age of 10 years was 7.29 years (Interquartile range (IQR): 6.8, 8.9). After the age of 10 years, 16.5% of these adolescents had VL ≥400 copies/ml. The probability of non-suppression increased with increasing age on treatment above 10 years (adjusted Odds Ratio [aOR]: 2.30 per year increase in age; 95% CI: 2.00, 2.65) and was higher in those who started ART in more recent years (compared to reference period of 2004-2006 aOR: 2.72; (95% CI 1.58, 4.66) for years 2007-2009, 4.31; (95% CI: 2.38, 7.79) for years 2010-2012 and aOR9.20 (95%CI: 2.68, 31.63) for years 2013-2015.

Conclusions: As perinatally infected children progress into adolescence, the likelihood of poor virologic outcomes increases with increasing age on treatment. It is a concern that children that initiated ART in the later years after 2010 are also at a higher risk.
Stunting and growth development for adolescents perinatally infected by HIV: males and females evolve differently. A multiregional analysis from the IeDEA global pediatric collaboration.

**Background:** Perinatally HIV-infected adolescents (PHA) are a growing population that faces many challenges, both physically and psychologically, due to their lifelong infection. Stunting and pubertal delay are key issues among PHA that need to be better understood. As part of the IeDEA multinational consortium, we described growth evolution during adolescence for PHA, looking at the differences between males and females.

**Methods:** We included data from sub-Saharan Africa, Asia-Pacific, and Caribbean, Central and South America regions collected between 2003 and 2016. The inclusion criteria were as follows: HIV-infected patients on antiretroviral therapy (ART); reported perinatally acquired infection or entering HIV care before 10 years of age; >1 height measurement between 10-16 years of age; and followed in care until at least 14 years of age.

Growth was described using sex-specific Height-for-Age Z-scores (HAZ) according to the WHO Child Growth Standards. Characteristics at ART initiation and at 10 years of age were compared by sex. Correlates of growth between ages 10-19 years were studied separately for males and females, using linear mixed models. Analyses were adjusted by region, age at ART initiation, CD4 cell count and stunting (HAZ < -2 SD) at ART initiation and at 10 years of age.

**Results:** Overall, 8737 PHA were included, with 46% from Southern Africa. Median age at ART initiation was 8.1 years (Interquartile Range [IQR] 6.1-9.6), 50% were female, and 41% were stunted at ART initiation. Males and females did not differ by age and stunting at ART initiation, by CD4 count over time and by retention in care. At 10 years of age, 34% of males were stunted vs. 39% of females (p<0.001); then, growth showed better improvement for females while it slowed for males, resulting in a higher prevalence of stunting for males compared to females (48% vs. 25% at 15 years of age, 31% vs. 15% at 18 years of age). This difference in growth trajectory by sex was seen in every region. In linear mixed models, those most stunted at 10 years of age were those initiating ART after five years of age or with more advanced HIV disease (CD4 count <250 cells/mm3, moderately or severely stunted at ART initiation). Growth evolution during adolescence was subsequently greater for those who were most stunted at 10 years, with results at 19 years of age varying by sex: while the most stunted females had catch-up growth, reaching similar HAZ values at 19 years of age (vs. non-stunted females), the most stunted males at 10 years still experienced growth failure at 19 years of age.

**Conclusions:** Substantial sex-based differences in growth evolution during adolescence were observed in this global cohort but could not be explained by differences in age of access to HIV care, HIV disease advancement or settings. Except for growth, males and females had similar characteristics in this study. Growth differences could be explained by other data not recorded here, such as differences in pubertal development among HIV-infected adolescents, with potentially greater pubertal delays for males, resulting in longer term growth delays throughout adolescence.
Severe immunosuppression and viral failure in adult care among antiretroviral therapy-experienced young people with perinatal HIV in the UK

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Background: Adolescence and transition to adult care is a vulnerable time with increased risk of poor adherence to antiretroviral therapy (ART). Previous work on the UK’s paediatric HIV cohort reported a declining CD4 trend prior to transition. We update this work by assessing cumulative incidence and predictors of severe immunosuppression and viral failure (VF) post-transition in young people with perinatal HIV (PHIV).

Methods: Patients aged ≥13 years on 01/04/2017 in the national UK/Ireland paediatric HIV cohort (CHIPS) were linked to the adult UK CHIC cohort. Cumulative incidence and risk factors of severe immunosuppression (first CD4 count <200c/mm3) and VF (2 consecutive VL >400c/ml) in adult care for patients on ART for ≥6 months prior to transition (last visit in paediatric care) were calculated separately using Kaplan-Meier and Cox regression. Potential risk factors were demographic, clinical and treatment characteristics at ART initiation and at transition. Analyses of severe immunosuppression were restricted to those with ≥1 CD4 measurements in UK CHIC and CD4 >200cells/mm3 at transition; analyses of VF were restricted to those with ≥2 VL in UK CHIC and VL<400c/ml at transition. Time at risk was from transition until earliest of: severe immunosuppression/VF, death or last adult care follow-up.

Results: Among 1,911 eligible CHIPS patients, 474 were linked to UK CHIC with follow-up data post-transition. Of 441 (93%) who were on ART, 216 (49%) were female, 353 (82%) were black ethnicity and 260 (60%) born abroad. At transition, median age was 18 [interquartile range 17,19] years, median CD4 was 480 [278,672]c/mm3 and 65% had VL<400c/ml. Median duration of follow-up in adult care was 3.4 [1.4,6.2] years. Fourteen (3%) patients died post-transition. Overall, 334 (76%) and 273 (62%) met the inclusion criteria for severe immunosuppression and VF analyses, respectively. In adult care, 57/334 (20%) and 98/273 (36%) experienced severe immunosuppression and VF, respectively. Out of 263 who had CD4 and VL data, 50 (19%) experienced both outcomes. Kaplan-Meier cumulative probability of severe immunosuppression was 19% (95%CI 15%-24%) and 29% (23-35%) at 2 and 4 years post-transition, and similarly for VF was 25% (20-30%) and 36% (30-43%), respectively. In adjusted analyses, predictors of severe immunosuppression in adult care were: experiencing VF in last year of paediatric care (adjusted hazard ratio 2.03 (95%CI 1.12-3.68) vs no VF), ever CDC stage C diagnosis (1.72 (1.45-1.93) vs never) and lower CD4 count at transition (1.67 (1.44-1.93)/100c/mm3 lower). Predictors of VF in adult care were black ethnicity (2.20 (1.20-4.03) vs white/other), female sex (1.99 (1.24-3.18) vs male), non-combination ART initial regimen (mono/dual, triple NRTI or triple unboosted-PI) (1.65 (1.05-2.59) vs cART), and VF in last year of paediatric care (3.90 (2.46-6.18) vs no VF).

Conclusion: Over 4 years of follow-up in adult care, quarter and one-third of patients experienced severe immunosuppression or VF, respectively. Female or black patients had twice the risk of VF post-transition. Poor virological and immunological status in prior to transition were predictive of both poor outcomes in adult care, suggesting the need to focus additional adult care resources to patients with pre-existing problems with disease management in paediatric care.
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Abstracts
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IMPAACT P1110: Raltegravir Pharmacokinetics and Safety in HIV-1 Exposed Neonates: Dose-Finding Study in Infants born to Mothers receiving Raltegravir-containing ART

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Background: The FDA approved dosing for raltegravir (RAL) oral granules for suspension in full-term neonates is based on P1110 pharmacokinetic (PK) and safety results from infants born to mothers with HIV infection who did not receive RAL during pregnancy. Data previously reported from a washout PK study of RAL in neonates born to pregnant women with HIV (IMPAACT P1097) demonstrated that RAL readily crosses the placenta and RAL elimination in neonates is highly variable and extremely prolonged in some infants. Direct administration of RAL to a neonate with in utero RAL exposure poses the potential risk of accumulation of RAL to excessive concentrations. Based on PK modeling and simulations, the FDA recommends that initial neonatal RAL doses should be delayed until 24-48 hours after birth if a pregnant woman receives RAL 2-24 hours before delivery. We now report the pharmacokinetic and safety analyses of daily RAL dosing in neonates enrolled in P1110 whose mothers received RAL prior to delivery.

Materials and Methods: Infants initiated RAL dosing with oral granules for suspension between 12 and 60 hours of delivery: 1.5 mg/kg once daily through Day 7 of life; 3 mg/kg twice daily on Days 8 to 28 of life; and 6 mg/kg twice daily from 4-6 weeks. All infants also received standard antiretroviral prophylaxis against perinatal HIV transmission. PK evaluations included intensive sampling after the first dose and at 15-18 days of life plus sparse sampling at times of dose changes. Samples were analyzed for RAL concentrations using a validated HPLC-MS-MS method. AUC was estimated using the trapezoidal method. Protocol exposure targets were AUC24 12-40 mg*h/L, AUC12 6-20 mg*h/L, C12 or C24 > 33 ng/mL. Infants were followed with clinical and laboratory safety evaluations through age 24 weeks.

Results: Ten infants were enrolled and data are available for 9. Geometric Mean (GM) RAL plasma concentration prior to the first dose was 394.9 ng/mL (range 62.9-1045.4 ng/mL) demonstrating significant transplacental transfer of RAL from in utero exposure. After the first dose of 1.5 mg/kg, GM (range) RAL AUC24 was 42.7 mg*h/L (27.4-63.9) and C24 was 910.5 ng/mL (251.9-2005.4). On 3 mg/kg twice daily dosing, the GM (range) RAL AUC12 was 18.3 mg*h/L (6.0-38.2) and C12 estimated to be 273.6 ng/mL (26.7-1016.2). There were no safety concerns associated with daily RAL administration through 6 weeks of life.

Conclusions: Daily RAL beginning at 12-60 hours of age through age 6 weeks was safe and well tolerated in infants born to mothers receiving RAL prior to delivery. While the GM for RAL PK parameters met protocol exposure targets, some individual infants had AUC24 following the initial dose slightly exceeding the target range. This transient overexposure was considered safe and acceptable given the rapid increase in RAL metabolism over the first week of life. Our findings confirm that the current FDA dosing recommendations based on PK modeling and simulations are appropriate for use in neonates with in utero RAL exposure.
P1101: Phase I/II Study Of Raltegravir-Containing Regimen In HIV And TB Co-Treated Children Aged 6–<12 Years

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Background: Current antiretroviral (ARV) treatment options for HIV-infected children with TB disease are limited. Rifampin (RIF) induces UDP-glucuronosyltransferase activity, accelerating the clearance of raltegravir (RAL). In adults, doubling the RAL dose partially overcame this pharmacokinetic (PK) interaction without safety concerns. We sought to establish the optimal and safe dose of RAL when administered with RIF-containing anti-TB therapy in HIV-infected children.

Methods: P1101 is a dose finding study of RAL in HIV-infected children from 4 sites in South Africa receiving RIF-containing TB therapy for at least one week, with three age cohorts: Cohort 1: 2 to <6 years (closed), Cohort 2: 6 to <12 years of age (closed) and Cohort 3: 4 weeks to <2 years, aiming to enroll 12 evaluable participants for PK and safety in each cohort. At enrollment participants start 3 ARVs, including chewable RAL formulation at 12 mg/kg/dose twice daily (twice the recommended pediatric dose) and 2 nucleoside reverse transcriptase inhibitors. Intensive RAL PK sampling is conducted 5-8 days after ARV therapy is initiated, and then a 4th ARV is added. Clinical and laboratory assessments are routinely completed. RAL is stopped at TB treatment completion and participants are followed for another 3 months. PK targets are a geometric mean (GM) AUC12h of 14-45 μMxh and GM C12h ≥75 nM. Here we report the results from Cohort 2.

Results: Among 14 participants who received RAL, 7 (50%) were male, median age 8 years (IQR: 7–9), median baseline Log10 RNA copies/mL 4.55 (IQR: 4.21–5.09), median CD4 count/μL 575 (IQR: 142–704), median CD4 percent 21% (IQR: 7–25). PK for all 14 children at Week 1 showed GM AUC12h (%CV) of 38.8 μMxh (38%); the GM C12h was 227.6 nM (78%). 1/14 (7%; 95% exact confidence interval (CI) [0%, 34%]) developed a Grade 4 AST and ALT, and Grade 3 Total Bilirubin, deemed possibly treatment-related, although consistent with an IRIS event and possibly due to concomitant medication; RAL was permanently discontinued. No other significant adverse events related to RAL were reported. 12/14 had evaluable efficacy data at week 8 (2/14 discontinued RAL prior to the week 8 visit, but after PK collection). 11/12 (92%; 95% CI [62%, 100%]) were virologically suppressed by Week 8. 1/12 had virologic failure with documented non-adherence, requiring discontinuation of RAL at 15 weeks. At Week 8, median changes from baseline were: log10RNA copies/mL -2.78 (IQR: -3.41 to -2.09), CD4 count 162.5 cells/μL (IQR: 29–351.5), and CD4 percent 5% (IQR: 0.7–7.65). RAL was permanently discontinued in 4/14 participants because: 2/14 had AUC12h >63 μMxh, meeting the PK end point despite being asymptomatic, 1 was non-adherent and 1 developed liver toxicity as mentioned above.

Conclusions: A 12mg/kg dose twice daily of the oral chewable formulation of RAL appears to achieve PK targets safely in HIV-infected children 6 to <12 years with TB disease who are also receiving rifampin.
Steady-state pharmacokinetics and early safety data in HIV-infected African children weighing 14 to <25kg on film-coated dolutegravir 25mg tablets in the ODYSSEY trial

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Background: ODYSSEY is an ongoing international randomised trial evaluating dolutegravir (DTG)-based antiretroviral therapy (ART) versus standard-of-care in HIV-infected children starting first- or second-line ART. In this pharmacokinetic (PK) substudy simplified doses of DTG were assessed for children in WHO weight bands 14 to <20kg and 20 to <25kg and safety was evaluated.

Methods: Steady-state 24-hour PK curves (t=0, 1, 2, 3, 4, 6 and 24h) were constructed from data on children weighing 14 to <25kg observed taking a film-coated 25mg DTG tablet under fasted conditions (≥3 hours). Informed consent was obtained for all children. The aim was to compare DTG exposures to those achieved in adults taking DTG 50mg film-coated tablets QD under fasted conditions (geometric mean(GM): Ctrough 0.83 mg/L, AUC0-24h 43.4 h*mg/L, Cmax 3.34 mg/L). DTG plasma concentrations were measured using a validated UPLC-MS/MS method with a lower limit of quantification of 0.01 mg/L. Non-compartmental PK analysis was performed to calculate PK parameters with WinNonlin 6.3 software. Laboratory and clinical safety were evaluated at 2 (mandatory for 14 to <20kg), 4 and 12 weeks, and then every 12 weeks on DTG.

Results: 20 black-African children from Zimbabwe and Uganda (50% male) with median (IQR) age 7.6 (6.0-9.5) years and weight 22.4 (17.2-23.4) kg were included in the analysis. For children weighing 14 to <20kg (n=8), GM with coefficient of variation (CV) for Ctrough, AUC0-24h and Cmax were 0.48 (67) mg/L, 42.3 (44) h*mg/L and 4.27 (37) mg/L respectively. For children weighing 20 to <25kg (n=12), Ctrough, AUC0-24h and Cmax were 0.29 (97) mg/L, 28.7 (40) h*mg/L and 3.12 (40) mg/L, respectively. After a median (IQR) follow-up of 23.3 (12.4-33.1) weeks on the 25mg tablet dose, three patients had reportable adverse events: one child had an SAE (acute sinusitus, grade 3), one had asymptomatic raised liver enzymes with thrombocytopenia (grade 3) and one had asymptomatic neutropenia (grade 3). All events were considered unrelated to DTG by an independent blinded endpoint review committee.

Conclusions: The 25mg film-coated DTG dose results in lower exposure to DTG in children weighing 14 to <25kg when compared with fasted adults on DTG 50mg QD. This is more marked in children weighing 20 to <25kg (65% lower GM Ctrough values compared with fasted adults) than in those weighing 14 to <20kg (42% lower GM Ctrough vs adults). Short-term safety data were acceptable. A follow-up study with higher DTG doses and different DTG formulations is planned for children in these weight bands and will also provide data on longer term safety within ODYSSEY.

Exposure-Safety of Tenofovir in Pediatric HIV-Infected Participants: Comparison of Tenofovir Alafenamide & Tenofovir Disoproxil Fumarate

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Background: Tenofovir alafenamide (TAF) and tenofovir disoproxil fumarate (TDF) are both prodrugs of tenofovir (TFV). TAF provides higher intracellular concentrations of the active metabolite TFV-diphosphate, and markedly lower plasma TFV.
levels compared to TDF. TAF-containing fixed-dose combinations (FDCs) such as emtricitabine/TAF (F/TAF, 200/10 or 200/25 mg with boosted or unboosted third agents, respectively) and elvitegravir/cobicistat/F/TAF (E/C/F/TAF, 150/150/200/10 mg) have been examined in global pediatric clinical trials. Safety data over 4 years in approximately 220 participants ≥25 kg are currently available. This work represents the first comparison of the exposure-safety (renal and bone outcomes) profile of TFV in pediatric participants receiving TAF-based regimens versus TDF-based regimens, with the overall objective of simplifying dosing recommendations for TAF in pediatrics.

Materials & Methods: Safety (Week [W] 48) and TFV PK data, following TAF (E/C/F/TAF [N=73] or F/TAF [N=25]) or TDF (alone [N=11] or E/C/F/TDF [N=14]), in 6 to <18-year-old (≥ 25kg) pediatric HIV participants were included in the analysis. TFV exposures (AUC₂₄h) were estimated based on population PK modeling and simulations. A linear regression-based model was developed to evaluate the relationship between observed TFV exposure (AUC₂₄h; following administration of TAF 25 mg unboosted, TAF 10 mg boosted, or TDF) versus selected safety endpoints. The established exposure-safety relationship was used to assess the TFV safety profile associated with increasing TFV exposures.

Results: For all safety endpoints, the slope of the regression line was negative indicating a larger decline in safety parameters (relative to baseline) at higher plasma TFV exposures (associated with TDF) compared to those following TAF; differences (absolute) in change from baseline (ΔBSLN) for height-age (HA) spine/total body less head (TBLH) Z-scores and eGFR(Schwartz) at W48 for TDF versus TAF were approximately -0.10 and -7.49 mL/min/1.73 m², respectively. Furthermore, changes from baseline in the safety endpoints following TAF 25 mg with boosted third agents (e.g. LPV/r) were smaller than those noted with TDF-containing regimens (ΔBSLN differences of ≥0.03 for Z-score, ≥3.74 mL/min/1.73 m² for eGFR(Schwartz)). This favorable safety profile of TAF 25 mg (with or without boosting agents) is further supported by longitudinal data through W108 (in 6 to <12-year-old, ≥25 kg participants who received E/C/F/TAF), albeit in a limited number of participants; no clinically relevant changes from baseline were observed in bone and renal: mean (SD) change of -0.05 (0.829, N=15) and -0.38 (0.498; N=16) in spine and TBLH BMD HA Z-scores at W96, % mean ± SD spine (9.7±8.7; N=16) and TBLH (5.6±5.1; N=18) BMD at W96, median (Q1, Q3) increase of 0.06 (0.03, 0.11; N=17) mg/dL in serum creatinine at W108, and decrease of -3.1 (-29.1, 10.4; N=17) mL/min/1.73 m² in eGFR(Schwartz) at W108.

Conclusions: These analyses demonstrate the improved risk-benefit profile of TAF-based regimens relative to TDF in children. Furthermore, the results suggest the appropriateness of simplifying dosing options and evaluating a single dose of 25 mg TAF (with boosted or unboosted third agents) in HIV-1 infected pediatric individuals 6 to <12 years of age and weighing ≥25 kg.

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Optimizing HIV case finding and linkage to care and treatment among adolescents in western Kenya through a comprehensive case finding intervention package

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Introduction: Low HIV testing uptake among adolescents affects identification of those living with HIV and challenges effective linkage to care and treatment services. To address this gap, an innovative package was implemented to improve HIV testing uptake and linkage to care among adolescents aged 10-19 years in Western Kenya.

Methods: This quasi-experimental study used program data at pre- and post-intervention periods to describe the effects of an innovative adolescent case finding and linkage to care and treatment package at 139 health care facilities (HCFs). The study population consisted of adolescents aged 10-19 years divided into an early age cohort (10-14 years) and a late age cohort (15-19 years). Three types of HCFs were included: hospitals, health centers and dispensaries. The innovative case finding package, which began to be implemented in July 2016, was comprised of staff capacity building, program performance monitoring tools, an
adolescent-focused HIV risk screening tool, and implementation of adolescent-friendly HCF hours. Collected data, including numbers of adolescents who tested for HIV, were HIV-positive, and were linked to care and treatment services, were analyzed with descriptive statistics. Demographic and testing data in the pre- and post-intervention evaluation periods were compared using the Poisson mean test, while the Chi-square test was used to compare the linkage to care rates.

Results: Pre-intervention data were collected from January to March 2016 and post-intervention data were collected from January to March 2017. During the pre-intervention period, 25,520 adolescents were tested and 198 were HIV-positive (0.8%) compared to 77,644 adolescents tested with 534 being HIV-positive (0.7%) during the post-intervention period. (p<0.001 for numbers tested, respectively). The proportion of HIV-positive adolescents linked to care increased from 61.6% in the pre-intervention period to 94.0% in the post-intervention period (p<0.001). The increase in linkage to care and treatment was observed among both the early and late adolescent cohorts and within each facility type (p-values <0.001).

Conclusion: The innovative intervention package led to a significant increase in both HIV testing uptake and linkage to care and treatment services among adolescents in Western Kenya and is considered for the scale up in the region.

Addressing Sexual and Gender-Based Violence in Pediatric and Adolescent Populations as Part of a Comprehensive HIV Testing and Treatment Program in the Democratic Republic of Congo

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Background: Over half of all females in the Democratic Republic of Congo (DRC) have experienced sexual or physical violence. Underlying gender discrimination in the country has been compounded by population displacement and ongoing violence in eastern DRC, where sexual violence has been used as a tool of war. Children are vulnerable to sexual and physical violence by both armed forces and members of their communities. The high rates of sexual and gender-based violence (SGBV) have far-reaching public health effects, influencing both HIV transmission rates and HIV treatment retention. SGBV has been found to reduce HIV testing uptake and both violence and fear of violence have been found to reduce antiretroviral therapy adherence.

Materials & Methods: ICAP at Columbia University supports the implementation of SGBV screening, care, and referral services as part of its PEPFAR-supported comprehensive HIV programs in Kinshasa and Haut-Katanga provinces. ICAP’s post-SGBV care services try to address both health and social consequences of violence, and aim to reach SGBV survivors, including infants and children, within 72 hours of experiencing violence, when the initiation of HIV post exposure prophylaxis (PEP) is most effective. In addition to health facility-based care, lay community healthcare workers conduct SGBV screenings in the field. Through close partnerships with police, the judicial system, and local organizations, ICAP facilitates referrals to social, legal, psychosocial, and other community services for both children and adults. We reviewed routinely collected aggregate data to understand SGBV demographics, and to compare the number of encounters among children and adolescents versus adults.

Results: From January 1, 2016 to December 31, 2017, there were 561 SGBV-related appointments at ICAP-supported medical facilities within 72 hours of experiencing violence: 375 (66%) were with new patients and 186 (33%) were with clients already enrolled in care at these facilities. Of all 561 reported events, 543 (97%) were reported by females and 18 (3%) were reported by males. Among all patients seen for SGBV services, 7 (1%) were <1 years old, 37 (7%) aged 1-4, 147 (26%) aged 5-9, 168 (30%) aged 10-14, 191 (34%) aged 15-19, 34 (6%) aged 20-24, 38 (7%) aged 25-49, and 2 (0.3%) aged ≥50.

Conclusions: The high proportion of children and adolescents experiencing SGBV suggests a need for age-specific SGBV support for these groups, including education for families and SGBV screening and outreach for adolescents. Given the established link between SGBV and HIV treatment adherence
and retention, addressing SGBV is critical in all HIV care settings. These findings suggest that this need is particularly acute among adolescents who both experience SGBV in greater numbers and who also face other barriers to adherence and retention. Addressing SGBV is also an important aspect of preventing HIV acquisition, and SGBV services should be a part of prevention packages for children and adolescents in DRC.

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Characterizing the double-sided cascade of care for HIV-infected adolescents transitioning to adult-centered care in the iDea Southern Africa Collaboration

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Background: As adolescents living with HIV (ALHIV) age, they face a “transition cascade”, a series of steps associated with transitions in their care as they become responsible for their own healthcare. In high-income countries, this frequently involves transfer from a predominantly pediatric/adolescent setting to an adult clinic. However, in resource-limited settings, pediatric HIV care is mostly provided in decentralized, non-specialist primary care clinics, with “transition” not usually involving a physical movement or change in provider. Unlike conventional HIV cascades, the adolescent transition cascade needs to be double-sided, comparing outcomes both before and after transition. We aimed to evaluate the pre- and post-transition cascade in ALHIV using different age thresholds as a proxy for when “transition” to autonomy might occur.

Methods: We included ALHIV aged <16 years at enrolment who received antiretroviral therapy at iDea Southern Africa sites from 2002-2017, and did not transfer to a different facility as they aged up. We used 2 ages to identify “transition”: 18 and 20 years; and compared the following outcomes in the 12 months before and after these ages: retention (≥2 visits in the 12-month period), and viral suppression (VS) (HIV-RNA <400 copies/ml). For each age threshold, we included adolescents with >12 months potential follow-up after the threshold.

Results: We assessed “transition” at 18 and 20 years in 3946 (53% female) (transition-18y cohort) and 1514 (55% female) (transition-20y cohort) ALHIV, respectively. The proportions enrolled at <10 years old (proxy for perinatal infection) were 14% (transition-18y) and 5% (transition-20y). Among adolescents overall, post-transition retention was lower after age 20 years vs. after age 18 years (71% vs. 74%; Risk Difference [RD]: -2.9; 95% CI: -5.6-0.3%). At both age thresholds, retention consistently declined post-when compared to pre-transition (83% vs. 74% (transition-18y); RD: 9.0; 95% CI: 7.2-10.8%; and 79% vs. 71% (transition-20y); RD: 8.3; 95% CI: 5.2-11.3%), but there was no difference in proportion with VS (65% vs. 62% (transition-18y); and 63% vs. 65% (transition-20y)). In the subset of adolescents who enrolled before age 10, VS was similar before and after both age thresholds. However, retention worsened post- vs pre-transition (86% vs. 76%; RD: 9.4; 95% CI 4.9-14.0% at age 18 years; and 86% vs. 69%; RD: 16.7; 95% CI: 3.4-30.0% at age 20 years). Using logistic regression, patients were more likely to be retained post-transition if they had sustained retention in the year pre-transition (adjusted odds ratio [aOR] 5.17; 95% confidence interval [CI] 4.34-6.18 at age 18 years; and aOR 4.84; 95% CI 3.72-6.30 at age 20), while patients enrolling at older ages were less likely
to be retained post-transition for the age 18 years threshold (aOR for each additional year 0.96; 95% CI, 0.93-0.99).

**Conclusion:** Among all ALHIV, retention, but not VS, was worse post- vs. pre-transition for both transition age thresholds. Differentiated care models are required for ALHIV as they take on greater responsibility for their healthcare in settings where transition may not involve transfer of care, to guide them through this period.

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**Mortality and AIDS-defining events among young people with perinatal HIV following transition to adult care in the UK**

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**Background:** The UK/Ireland has an ageing cohort of patients living with perinatal HIV (PHIV) who are now surviving to adulthood. We aimed to investigate long-term mortality and AIDS events after transition to adult care in this cohort.

**Methods:** Patients aged ≥13 years on 01/04/2017 in the national UK/Ireland paediatric HIV cohort (CHIPS) were linked to the adult UK CHIC cohort. Cumulative incidence of and risk factors for the composite endpoint of mortality or new AIDS event post-transition were calculated using Kaplan-Meier and Cox regression for patients with ≥1 CD4, viral load (VL) or ART date in adult care and ≥30 days of follow-up post-transition. Potential risk factors were: sex, ethnicity, place of birth, nadir CD4 count; CD4, VL, and initial regimen at ART initiation; age, duration on ART, calendar year, ever CDC stage C, CD4 and VL at transition (defined as last date in paediatric care); and length of gap between last paediatric and first adult care visit. Time at risk was from transition date until the earliest of the composite endpoint or end of follow-up.

**Results:** Among 1,911 eligible CHIPS participants, 474 were linked to UK CHIC with follow-up data post-transition, of whom 387 (82%) met the inclusion criteria for analysis. Half (51%) were female, 82% were of black ethnicity and 61% born abroad. At transition, median age was 18 (interquartile range 17,19) years, 88% were on ART (any regimen) of whom 23% had switched to a third or later ART line, 231 (60%) had VL <400 copies/ml, median CD4 was 477 [289,660] cells/mm3, 55 (14%) had a CD4 <200 cells/mm3 and 108 (28%) ever had a CDC stage C diagnosis. Median duration of follow-up was 3.3 [1.2,6.0] years in adult care. At last follow-up, 270 (70%) had VL<400 copies/ml and 56 (15%) had CD4 <200 cells/mm3. In adult care, 27 (7%) patients experienced a new AIDS event, 12 (3%) died, overall 30 (8%) patients had the composite endpoint of AIDS or death. Age at death ranged from 19-24 years, and occurred a median of 4 years post-transition, 9/12 (75%) had viral failure (>400c/ml) at last follow-up. Causes of death were advanced HIV disease (n=3), HIV wasting (n=1), non-HIV/AIDS related (n=1), suicide (n=1), renal failure (n=1), respiratory disease (n=1) and unknown/missing (n=4). Cumulative incidence of mortality/AIDS was 3% (95% confidence interval 1-5%), 6% (4-10%) and 11% (7-16%) by 2, 4 and 6 years in adult care, respectively. In adjusted analyses, predictors of mortality/AIDS in adult care were: earlier calendar year of transition (adjusted hazard ratio 1.20 (1.05-1.37) per earlier year) and ever CDC stage C diagnosis at transition (2.93 (1.34-6.42) vs never).

**Conclusion:** These findings highlight the clinical complexities of this population with one in ten progressing to mortality/AIDS by 6 years in adult care. Patients with prior AIDS diagnosis in paediatric care or transitioning in earlier calendar years were at higher risk for mortality/AIDS post-transition. The high risk of mortality and morbidity in this cohort suggest the need for greater investment in multidisciplinary specialised services in adult care.
The EU Pediatric legislation delivers first successes for children’s HIV care

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Background: In 2007, the integrase inhibitor raltegravir was approved by regulators, providing the first approval for a member of this novel ARV class. Several integrase inhibitors have since been approved and are now recommended as preferred first line agents in multiple national and international medical guidelines. This new treatment option for adults came just after the European Commission adopted a new Paediatric Regulation (EC No 1901/2006) which included incentives for research and development of new medicines for children with a balanced system of obligations and rewards in Europe. The Regulation built upon and extended the paediatric requirements that had previously been put in place by legislation in the United States.

Materials and Methods: This case study presentation on raltegravir will provide insights into the developer’s experiences from the clinical research and development program in collaboration with the IMPAACT clinical research network that led to approval of the drug for the pediatric population, which addresses an important unmet medical need in children. It will discuss the pediatric regulatory requirements in EU and US, the study program and the amount and types of data that were necessary for regulatory approvals. It will also highlight the importance of appropriate formulations that are required to ensure that the medication reaches all subsets of the paediatric population.

Results: After a decade long research, clinical development and regulatory process, raltegravir has now been approved for use across the entire paediatric age range, from birth (full-term, at least 2kg in weight) through adolescence in the US, EU and other countries. These regulatory approvals took place in a stepwise fashion, with the most recent approval in neonates in the EU in March 2018. As a result appropriate pharmacokinetic, safety and dosing information for raltegravir is available for every subset of the paediatric population except low birth weight infants. The US and EU approvals can now facilitate the availability of raltegravir as the first integrase inhibitor throughout the paediatric age spectrum in many other countries.

This experience made clear that there is an urgent need for new global efforts to collaborate and accelerate paediatric development. Various stakeholders recognize this need and new projects in collaboration with WHO, UNITAID, PEPFAR and others are already underway to accelerate availability of new treatment options in many more countries. The presentation will describe some of these new initiatives.

Conclusions: Regulations in the EU and US are driving paediatric drug development today. To comply with these regulations, developers must navigate significant challenges related to scientific and clinical outcomes, development cost, and safety surveillance during long development cycles. The presentation will discuss the successful experience of MSD and IMPAACT in navigating the paediatric development cycle for raltegravir. Our experience may serve as a model for accelerating paediatric drug development for new products and efficiently obtaining the US and EU regulatory authority approvals necessary for these new products to become clinically available for children throughout the world.

Safety and nevirapine concentrations of 6-week triple antiretroviral prophylaxis in high risk HIV-exposed infants

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Background: Triple-drug antiretroviral prophylaxis of zidovudine (AZT)/lamivudine (3TC)/nevirapine (NVP) is preferred among HIV-exposed neonates with high-risk of transmission in many countries, including Thailand. This study aimed to assess safety of triple-drug neonatal prophylaxis and NVP trough concentrations (C24) over the first 28 days of life.

Methods: A prospective cohort of 200 HIV-exposed infants was conducted at 5 clinical sites in Thailand. We enrolled 100 high-risk HIV-exposed neonates (maternal HIV RNA >50 copies/mL prior to delivery or received antiretroviral therapy (ART) <12 weeks) who received AZT/3TC twice daily, plus NVP (4 mg/kg/dose) once daily, from birth for 6 weeks, and 100 standard-risk HIV-exposed neonates who received a 4-week regimen of AZT. Blood tests to assess hematologic and liver toxicities were performed at birth, 1, 2 and 4 months of life. Sparse plasma NVP concentrations were collected at day 1, 2, 7, 14, and 28 and assayed by a validated liquid chromatography-mass spectrometry assay.

Results: From October 2015 to November 2017, 200 infants were enrolled. Median (IQR) gestational age and birth weight were 38 (37-39) weeks and 2,873 (2,590-3,184) g, respectively. Common maternal ART regimens were TDF/3TC or FTC (58%), AZT/3TC (32%) in combination with EFV (50%), ritonavir boosted protease inhibitor (31%). Overall, there was no significant difference of hematotoxicity and hepatotoxicity between ZDV/3TC/NVP prophylaxis and ZDV alone; all grade anemia (41.1% vs 38.6%, p=0.72), all grade neutropenia (5.0% vs 6.2% p=0.47), elevated AST (0.8% vs. 0.5%. p=0.61), and elevated ALT (3.4% vs. 3.1%, p=0.82). Median (IQR) hemoglobin level among infants who received triple prophylaxis were 9.9 (9.0-11.4) g/dL, 10.1 (9.3-11.0), and 11.7 (11.0-12.3) at aged 1, 2, and 4 months, respectively, which did not significantly differ between groups. No infants required blood transfusion. NVP concentrations were available from 48 infants (135 samples); median predicted NVP C24 were 1.34 mg/L, 2.24, 2.78, 2.20, and 0.81 on days 1, 2, 7, 14, and 28 of life, respectively. All infants maintained NVP concentrations above the proposed prophylactic target threshold of 0.1 mg/L during the first 4 weeks. Maternal EFV treatment did not affect infant NVP levels.

Conclusions: Six-weeks of AZT/3TC/NVP in HIV-exposed infants did not increase the risk of toxicity compared with an AZT regimen. Administration of 4 mg/kg of NVP from birth provided adequate NVP concentrations for prophylaxis during the first 4 weeks of life.

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Safety & efficacy of elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide single-tablet regimen in HIV-1 infected virologically suppressed adolescents

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Background: Elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (E/C/F/TAF) is a once-daily, integrase strand transfer inhibitor (INSTI)-based single-tablet regimen (STR) approved for use in adolescents and children ≥25 kg. Whereas efficacy and safety of E/C/F/TAF have been previously reported in treatment-naïve adolescents, this is the first study of E/C/F/TAF in virologically suppressed, treatment-experienced adolescents.

Methods & Materials: We conducted a prospective, single-arm, open-label, 2-part, 48-week clinical trial to evaluate the safety and efficacy of switching from a suppressive antiretroviral regimen (on a stable regimen and HIV-1 RNA <50 copies/mL for ≥ 6
months prior to baseline) to E/C/F/TAF (150/150/200/10 mg) once daily in adolescents (12 to <18 years; ≥35 kg). Adverse events (AEs) and laboratory tests, including HIV-1 RNA and renal biomarkers, were assessed. Bone mineral density (BMD) was measured by dual-energy X-ray absorptiometry. We report data through Week 48.

Results: We enrolled 50 adolescents; median age 15y (range 12-17y), median weight 52.2 kg, median weight z-score -0.36, median of 12 years since diagnosis (range 0-17y), median CD4 count 742 cells/μL; 64% female, 98% Black, and 80% vertically infected. At Week 48, 45 (90%) participants maintained HIV-1 RNA <50 copies/mL. Through median exposure of 111.6 weeks, E/C/F/TAF was well tolerated, with most AEs and laboratory abnormalities of grade 1 or 2 in severity. The most common AEs were cough, upper respiratory tract infection, and vomiting. Three participants had serious AEs (grade 4, unrelated electrocution [n=1]; grade 2, related vomiting [n=1]; grade 1, unrelated spontaneous abortion [n=1]); two had AEs leading to study drug discontinuation (grade 1, related iridocyclitis [n=1]; grade 1, unrelated pulmonary tuberculosis [n=1]). One death was reported (grade 4, electrocution). No participant developed phenotypic or genotypic resistance to any component of the study drug. No participant developed proximal renal tubulopathy or discontinued study drug due to a renal AE. An initial decrease in estimated GFR (Schwartz formula) occurred between Weeks 1 and 8 and remained stable through Week 48 (median [IQR] change at Week 48: -19.4 [-32.1, -4.4] mL/min/1.73 m²), consistent with inhibition of renal tubular creatinine (Cr) secretion by cobicistat. Renal biomarkers (retinol binding protein to Cr ratio, beta-2-microglobulin to Cr ratio) remained relatively stable or declined from baseline throughout the study. Median % change in BMD at Week 48 was +3.6% for spine and +2.8% for total body less head (TBLH).

BMD decreases of ≥4% occurred in one participant for spine (which increased at subsequent visits) and none for TBLH by Week 48. Median change in BMD height-adjusted Z-score at Week 48 was +0.05 for spine and +0.09 for TBLH. One participant had a bone fracture (grade 1 foot [metatarsal] fracture, unrelated to study drug).

Conclusions: In HIV-infected adolescents 12 to <18 years of age on suppressive ART, switching to E/C/F/TAF maintained high rates of virologic suppression at Week 48. E/C/F/TAF was generally well tolerated through 48 weeks with a favorable bone and renal safety profile. These findings support use of E/C/F/TAF in treatment-experienced, virologically suppressed adolescents, complementing its use in treatment-naïve adolescents.

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Pellets’ Formulation Of Lopinavir/Ritonavir In Children: 48-Week Evolution Of Viral Suppression Across Age Categories In The Living Study


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Background: The pellets’ formulation of LPV/r which is palatable, heat-stable and easy-to-administer has received tentative USFDA approval for use in infants and young children. However, there is a paucity of clinical data on its effectiveness and safety in routine care. The LIVING study is evaluating the effectiveness, safety, PK and acceptability of LPV/r pellets + ABC/3TC (or AZT/3TC) dispersible tablets, in HIV+ children unable to swallow tablets in Kenya and Uganda.

Methods: An open-label, single-arm, prospective, multi-centre, phase-3b implementation study. Inclusion criteria: ARV naïve, on liquid LPV/r-based or failing NNRTI based ART; Weight ≥3 and <25kg. ART dosing based on WHO weight bands. Children assessed at baseline, 1 month then 3-monthly. AEs were graded using DAIDS tables. We evaluated viral suppression across 4 age categories (months): 5-11, 12-24, 25-48 and ≥49.

Results: As of 31/10/2017, 723 patients had been enrolled, of whom 459 and 303 had reached WK24 and WK48 respectively, with a cohort retention of 88.6% (follow-up on going, 7 deaths.). Baseline and
**Background:** The development of pediatric fixed-dose combinations (FDCs) for all lines of therapy has become a priority to simplify dosing, increase adherence and thus improve pediatric care. The use of LPV oral solution is limited by taste aversion and short storage period, alternative solid formulations for small children are wanted. The objective of this study was to evaluate the relative oral bioavailability and safety profiles of Lopinavir/Ritonavir Granules 40 mg/10mg (2 Sachets with 40/10mg, Mylan Laboratories Limited, India) with KALETRA® (Lopinavir/Ritonavir, AbbVie Inc.) Oral Solution 80mg/20mg per mL.

**Methods:** In this open label, 1:1 randomized, two-period, two-treatment, cross-over, single dose evaluation, the relative oral bioequivalence was tested in 68 healthy adult subjects under fed conditions. In each study period, a single oral dose of either test product (T) or reference product (R) was administered orally under fed conditions. Subjects were monitored for safety and tolerability until completion of the study. Serial blood samples from pre-dose 0.00 hour up to post-dose 36.00 hours were collected in each period. Drug concentrations in plasma were quantified by using a validated method for test product (T) and reference product (R). Pharmacokinetic parameters (Cmax, AUC0-to-inf, Tmax, Kel, t½ and AUC_%Extrap_obs) were computed using the non-compartmental model of Phoenix® WinNonlin® software version 6.3 (Pharsight Corporation, USA) for T and R. Statistical comparison of the pharmacokinetic parameters of both formulations were carried out by using PROC GLM from SAS® statistical software version 9.2 to assess the bioequivalence of T and R.

**Results:** The 90% confidence interval for the ratio of the test and reference product averages pharmacokinetic parameters Cmax, AUC0-to-inf and AUC0-to-inf were between 80% and 125% for the In-transformed data with respect to Lopinavir and Ritonavir.

Lopinavir test product (T):
Geometric least squares means of:
Cmax 389.809 ng/mL, AUC0-to-inf 3144.695 ng·hr/mL, AUC0-to-inf 3215.917 ng·hr/mL
Lopinavir reference product (R):
Geometric least squares means of:
Cmax 369.967ng/mL, AUC0-to-inf 2955.001 ng·hr/mL, AUC0-to-inf 3076.989 ng·hr/mL
Lopinavir T vs. R % (90% CI)
Cmax 105.36 (94.15-117.91), AUC0-to-inf 106.42 (94.48-119.86), AUC0-to-inf 104.52 (92.58-117.99)

Ritonavir test product (T):
Geometric least squares means of:
Cmax 27.859 ng/mL, AUC0-to-inf 219.562 ng·hr/mL, AUC0-to-inf 226.160 ng·hr/mL
Ritonavir reference product (R): Geometric least squares means of:
Cmax 119.860 ng/mL, AUC0-to-inf 104.52 (92.58-117.99)

**Conclusion:** LPV/r-based ART in children is associated with very levels of HIV viral suppression regardless of age at initiation.

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**A randomized, open-label, balanced, two-treatment, single-dose, crossover oral bioequivalence study of Lopinavir/Ritonavir Granules 40mg/10mg with KALETRA® (Lopinavir/Ritonavir) Oral Solution 80 mg/20mg per mL in healthy adults under fed conditions**

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Acceptability and palatability of the single-tablet regimens of B/F/TAF and E/C/F/TAF in children (6-12 years) living with HIV infection

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Background: Various factors, such as need for multiple individual pediatric antiretroviral (ARV) drugs, poorly palatable ARV formulations, and twice daily dosing frequency, have been associated with suboptimal adherence and treatment failure in children living with HIV. Development of acceptable and palatable fixed-dose combinations (FDCs) that facilitate daily HIV treatment in children is therefore needed. Bictegravir, a novel unboosted integrase strand transfer inhibitor (INSTI), has been coformulated with emtricitabine and tenofovir alafenamide (B/F/TAF). Elvitegravir, an INSTI boosted by cobicistat, was also coformulated with F/TAF (E/C/F/TAF). Both FDCs represent once-daily, single-tablet regimens (STRs). We report data on acceptability, palatability, adherence and efficacy of B/F/TAF and E/C/F/TAF in children 6 to <12 years of age.

Materials & Methods: Two prospective, single-arm, open-label, 2-part, 48-week clinical studies evaluated safety and efficacy of switching from a suppressive multi-drug ARV regimen to the STR of either B/F/TAF (50/200/25 mg, 15mm x 8mm) or E/C/F/TAF (150/150/200/10 mg, 19mm x 8.5mm) in children (6 to <12 years, ≥25 kg). Palatability (normal vs abnormal) and acceptability (acceptable vs not acceptable) were assessed by investigator administered questions on product taste and shape/size conducted at baseline and week (W) 4. Plasma HIV-RNA levels were assessed at each study visit. Adherence was calculated as number of pills taken divided by number of pills prescribed.

Results: For B/F/TAF, 25 children were enrolled; median age 10 years (range 6-11 years), median weight 28.4 kg, 52% female, 64% Black, 92% vertically infected with median years since diagnosis of 8 years (range 2-11 years). For E/C/F/TAF, 23 children were enrolled; median age 10 years (range 8-11 years), median weight 30.5 kg, 61% female, 78% Black, 100% vertically infected with median years since diagnosis of 8 years (range 6-11 years).

For B/F/TAF, all 25 participants reported product taste normal and product size acceptable at both baseline and W4. For E/C/F/TAF, only 1 (4%) participant reported product taste abnormal (at BL) and product size not acceptable (at both baseline and W4) but continued taking the study drug through end of study.

At W12, all 25 participants on B/F/TAF maintained HIV-1 RNA <50 c/mL, and at W24, all given E/C/F/TAF maintained HIV-1 RNA <50 c/mL. At median (Q1, Q3) exposures of 16.1 (15.9, 17.7) weeks (B/F/TAF) and 32.1 (31.7, 32.1) weeks (E/C/F/TAF), study drug adherence was 98.8% (90.4%, 100%) and 98.1% (94.6%, 98.8%), respectively. Study drug adherence was ≥90% for all participants and ≥95% for 23 and 16 (92% and 70%) on B/F/TAF and E/C/F/TAF, respectively.

No participant discontinued study drug.

Conclusions: A high percentage of treatment-experienced children aged 6 to <12 years, switching from a multi-drug ARV regimen, reported either B/F/TAF or E/C/F/TAF to be palatable and acceptable. The majority maintained high rates of adherence and virologic suppression and with no

Cmax 25.242 ng/mL, AUC0-t 201.972 ng-hr/mL, AUC0-inf 208.668 ng-hr/mL
Ritonavir T vs. R % (90% CI) Cmax 110.37 (100.91-120.72), AUC0-t 108.71 (98.53-119.94), AUC0-inf 108.38 (98.36-119.42)

Both the test and reference products were well tolerated, when administered as single dose under fed conditions.

Conclusions: Under fed conditions, the test product (T) Lopinavir/Ritonavir Granules 40 mg/10 mg of Mylan Laboratories Limited, India was bioequivalent to the Reference product (R) KALETRA® (Lopinavir/Ritonavir) Oral Solution 80 mg/20mg per mL of AbbVie Inc., USA, with regard to rate and extent of absorption. This new pediatric FDC could provide an easy-to-use treatment for small children.
product issues leading to study drug discontinuation. These findings demonstrate potential benefits of using F/TAF-based STRs in children and their continued evaluation in the pediatric populations living with HIV.

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ODYSSEY: A randomised trial evaluating the efficacy and toxicity of dolutegravir-based antiretroviral therapy compared to standard of care in HIV-infected children starting first-line or second-line therapy: design, current status and baseline characteristics

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Background: Dolutegravir (DTG)-based antiretroviral therapy (ART) is highly effective, safe and well-tolerated in adults. A number of sub-Saharan African countries have initiated DTG procurement, with Clinton Health Access Initiative predicting a 59% market share by 2021. DTG needs evaluating in first-line and second-line ART regimens in children.

Materials & Methods: ODYSSEY (Once-daily DTG based ART in Young people vs. Standard thErapY) is a multi-site, open-label, randomised, non-inferiority basket trial to compare the efficacy and toxicity of DTG plus 2 nucleos(t)ides (NRTIs) vs. standard of care (SOC) in HIV-infected children <18 years starting first-line ART (ODYSSEY A) or switching to second-line ART (ODYSSEY B). Children will be followed for ≥96 weeks; the primary endpoint is clinical or virological failure by 96 weeks. Assuming a failure rate of 18% overall, 700 children will provide 90% power to exclude a difference of >10% between arms; enrolling 310 children in ODYSSEY A and 390 in ODYSSEY B will provide 80% power to exclude a difference >12% between arms in both subgroups. European Medicines Agency approved DTG dosing is used (including, from May 2017, DTG 20mg QD in children ≥6 years weighing 15-<20kg); in nested pharmacokinetic (PK) sub-studies at sites in Uganda and Zimbabwe more pragmatic dosing (aligning with WHO weight-bands) has been tested (DTG 25mg QD for children 14-<25kg; DTG 50mg QD for children ≥25kg).

Results: Between September 2016 and April 2018, 674 children (96% of target) were enrolled, including 282 (91%) in ODYSSEY A and 392 (100%) in ODYSSEY B. 47% of children are in Uganda, 21% Zimbabwe, 19% South Africa, 9% Thailand, 4% Europe. 348 (52%) participants are male; 571 (85%) were vertically-infected; median age [range] at enrolment was 12.3 years [2.9-18.0] (similar in A and B). 76 (11%) children weighed 14-<20kg, 119 (18%) 20-<25kg, 197 (29%) 25-<35kg, 282 (42%) ≥35kg. 121 (18%) had WHO stage 3 and 55 (8%) WHO stage 4 disease. Median [IQR] CD4 was 433 cells/mm3 [218, 651] in ODYSSEY A and 474 cells/mm3 [241, 737] in ODYSSEY B; 49 (18%) and 54 (14%) had CD4<100 cells/mm3 respectively. Median [IQR] log viral load was 4.6 copies/mL [3.9, 5.2] in ODYSSEY A and 4.3 copies/mL [3.8, 4.8] in ODYSSEY B; 83 (34%) and 71 (18%) had viral load ≥100,000 copies/mL respectively. ODYSSEY B participants had median 5.5 years prior exposure to ART, almost all (96%) NNRTI-based ART. SOC is primarily efavirenz-based ART for ART-naive children and lopinavir/ritonavir-based ART for children switching to second-line with abacavir + lamivudine or tenofovir + lamivudine/emtricitabine.

Conclusions: ODYSSEY has recruited on target. By employing a basket design (to include ART-naive children and children starting second-line ART) and nested PK sub-studies the ODYSSEY trial efficiently evaluates multiple scientific questions regarding dosing and effectiveness of DTG-based ART in HIV-infected children. Protocol version 4.0 (undergoing
ethics review) allows recruitment of 60 additional children weighing ≥3kg to <14kg and aged ≥28days using dispersible DTG (with associated PK sub-studies); randomisation of children <14kg will be stratified by weight-band (3–<6, 6–<10, 10–<14kg) and will not delay the end of follow-up for the main trial.

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Safety and effectiveness of dolutegravir (DTG) in children and adolescents with HIV in the UK/Ireland

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Background: Dolutegravir (DTG) is approved for the treatment of HIV-1 in children/adolescents aged ≥6 years, weighing ≥15kg in Europe. There are scarce data on paediatric DTG use and outcomes in routine care. We assessed the safety and effectiveness of DTG in children/adolescents with HIV in the UK/Ireland.

Methods: Children/adolescents followed in the CHIPS cohort in the UK/Ireland who initiated DTG aged 6–<18 years were included, with data from 01/01/2014-31/03/2018. Characteristics at start of DTG, CD4 and viral load (VL) response at 6 and 12(+/-3) months after DTG start, clinical adverse events (AEs) and reasons for discontinuation, were described. Viral suppression (VS) was defined as VL<50c/mL.

Results: Of 994 patients aged 6–<18 years in follow-up from 2014 (DTG approval Europe), 174(18%) initiated DTG; 53% female, 91% perinatal HIV, 27% prior CDC C diagnosis. Ten (6%) were naïve when starting DTG, with median age 15.2[IQR 14.1,15.7] years, CD4 481[298,581] cells/mm3. Of the 164 treatment-experienced patients, median age was 5.4[1.7,10.2] years at ART initiation and 15.5[13.5,16.7] years at DTG start, 58(35%) had previous triple class exposure (NRTIs, NNRTIs and PIs), median CD4 (n=124) was 656[473,849] cells/mm3, and 90/128(70%) had VS at DTG start.

164(94%) took DTG in a ≥3 drug regimen (106(65%) Triumeq fixed dose combination (DTG+ABC+3TC)), the rest were dual therapy. 153/174 patients had dose/weight data; one took an unlicensed DTG dose.

Median duration on DTG was 10.9[4.6,17.3] months. Overall 9(5%) patients discontinued DTG at median 8.3[4.6,25.8] months. Cumulative risk of discontinuation was 3.9%(95%CI 1.8-9.2%) at 12 months. Reasons for discontinuation were: toxicity (n=3, 1 kidney-related, 1 hypertension, 1 raised ALT), alternative regimen available (n=3), other/missing (n=3).

121 patients were on DTG for ≥6 and 79 for ≥12 months, for whom 80/95(84%) and 41/49(84%) had VS at these time points, respectively. All naïve patients had VS (n=3/3, 2/2) at both time points. Among treatment-experienced patients, 58/62(94%) and 28/34(82%) with VS at DTG start had VS at 6 and 12 months respectively, and similarly 11/19(58%) and 8/8(100%) of those not VS at DTG start.

Change in CD4 cells/mm3 from DTG start was -9[-67,112](n=81) at 6 months and 47[-68,171](n=49) at 12 months of DTG. In naïve patients it was 207[79,281](n=5) at 6 months, with insufficient numbers at 12 months. In treatment experienced patients, it was -22[-74,91](n=41) and 62[-103,153](n=26) in those VS at DTG start and 3[-24,175](n=19) and 150[-29,332](n=6) in those not VS at DTG start, respectively.

There were five grade 2 clinical AEs, four possibly related to DTG. Three events in two patients were headache, which resolved without DTG discontinuation. The fourth was raised ALT, the fifth was hypertension (unknown if related to DTG), both patients discontinued DTG.

Conclusion: Almost a fifth of children aged ≥6 years in CHIPS took DTG. DTG was generally well tolerated; 4% discontinued DTG by 12 months, few were for toxicity and there were no serious AEs. Viral suppression was high in naïve patients and those virally suppressed at DTG start but was lower in patients not VS at DTG start. Data on longer term outcomes in routine care are needed.
Emergence of Resistance in HIV-1 Integrase Following Dolutegravir Treatment in 6 to <18-Year-Old Participants Enrolled in the P1093 Study

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Background: P1093 is a phase I/II, multicenter, open-label pharmacokinetics (PK), safety, and dose-finding study of dolutegravir (DTG) plus optimized Background regimen in adolescents and children. Cohorts I and II (12 to<18 and 6 to<12 years old) have completed recruitment. Herein we provide an instream review of virologic failure (VF) for Cohorts I and II and the emergence of integrase strand transfer inhibitor resistance (INsti) among children receiving a DTG containing regimen.

Methods: VF for P1093 is defined as confirmed decrease in HIV-1 RNA (VL) of <$1.0 \log_{10}$ at/after week 12 (unless <$400c/mL$) or confirmed $>400c/mL$ at/after Week 24, or confirmed $>400c/mL$ after initial confirmed $<400c/mL$ or confirmed $>1 \log_{10}$ increase above VL nadir (nadir $\geq400c/mL$) At confirmed VF, population and clonal integrase (IN) genotypes and phenotypes and IN replication capacity (RC) were investigated. Adherence was assessed by 3-day recall per participant, and through communication with site PI.

Results: P1093 recruited 23 participants each in Cohort I (tablets), and Cohort IIA (tablets) and 15 participants in Cohort IIB (granules). VF rates were 12/23, 6/23, and 1/15, respectively. VF was associated with lack of adherence in most cases. For each cohort, treatment emergent INsti resistance was detected in 2/12, 0/6, and 1/1, respectively. One participant (Cohort I) acquired R263R/K and remained on study for an additional >2 years. A clonal analysis at longitudinal timepoints post VF showed a subsequent accumulation of additional linked IN substitutions and a modest increase in DTG susceptibility over time. Two participants acquired G118R mutations, one with L74M, G118R (Cohort I) and one with G118R, E138E/K (Cohort IIB). For each of these latter two participants, DTG susceptibility was decreased to 22- and 10-fold, respectively. A clonal analysis of integrase for these two participants showed the viral population at VF had linked IN substitutions. Clonal RC was performed on HIV-1 IN and showed longitudinal decreases in RC for all three patients, however, measurement of RC for the integrase coding region only may not provide a complete characterization of viral fitness.

Conclusion: Among 6 to<18-year-old participants receiving a DTG containing regimen, INSTI resistance developed in 3 of the 19 who experienced VF. INSTI resistance in these participants followed either of two integrase mutational pathways, R263K and G118R, the latter having a greater impact on reduced DTG susceptibility.

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Outcomes of Integrase Inhibitor-Based ART in Treatment-Experienced Children, Adolescents and Young Adults with HIV Infection

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Background: Currently the data on integrase inhibitor (INsti)-based antiretroviral treatment (ART) in children, adolescents and young adults (AYA) are limited. The objective of this study was to evaluate outcomes of INsti-based ART prescribed as a standard of care to treatment-experienced children and AYA receiving clinical care in Washington, DC, USA.

Methods: We conducted a sub-study of HIV-infected patients enrolled in the DC Cohort study, a multi-center prospective observational study of individuals receiving HIV care in Washington, DC. Treatment-experienced children and AYA 0-24
years of age who had ever initiated INSTI-based ART during 2011-2017 were included in this analysis. We calculated descriptive statistics for demographic, ART, immunologic (CD4 count), and virologic (HIV RNA) parameters at the start of INSTI-based ART (baseline) and during subsequent follow up.

**Results:** During the study period, 160 treatment-experienced pediatric and AYA patients (43.8% Female; 89.4% Black; 58.1% perinatally infected) were newly prescribed INSTI-based ART. Dolutegravir was the most commonly prescribed INSTI (53.8%), followed by elvitegravir (36.9%) and raltegravir (9.4%). At baseline, median age was 20.0 years (IQR 16.3-22.5) and 14.4% were ≤12 years old. Median baseline CD4 count was 507 cells/μL (IQR 326-765) and median baseline HIV RNA was 651 copies/mL (IQR non-detectable-22,524), with 107 (66.9%) having had detectable HIV RNA. Of all 160 patients, 117 had ≥1 follow-up HIV RNA result available, which included 34 patients who were virologically suppressed and 83 who were not virologically suppressed at baseline; the median duration of follow up on INSTI-based ART was 33.4 weeks (IQR 16.0-65.0). Among the 34 patients who were virologically suppressed at baseline, 19 (55.9%) consistently maintained undetectable viral load after a median of 25.3 weeks (IQR 13.1-59.7), and 15 (44.1%) had at least one detectable HIV RNA after a median of 21.0 weeks (IQR 6.3-38.4), based on a median of 3 follow-up test results (IQR 1-4) while on INSTI-based ART; 12 of 15 (80.0%) patients with viremic blips became re-suppressed at a later date. Among the 83 children and AYA with detectable viremia at baseline, 50 (60.2%) did not achieve undetectable HIV RNA after a median of 23.1 weeks (IQR 11.0-50.3), while 33 (39.8%) achieved viral suppression after a median of 12.1 weeks (IQR 6.1-18.0), based on a median of 2 follow-up test results (IQR 1-5) while on INSTI-based ART; however, of the 26 patients with ≥1 additional result available after initial viral suppression, 19 (73.1%) had ≥1 episode of recurrent detectable viremia, while 7 (26.9%) remained sustainably suppressed. The majority of patients (n=107; 66.9%) stayed on the initial INSTI regimen, while 32 (20.0%) switched to a different INSTI formulation.

**Conclusion:** In our cohort of treatment-experienced children and AYA on INSTI-based ART, more than half of patients with detectable viremia at baseline did not achieve viral suppression. Transient viremia among virologically suppressed patients was also observed among those who switched from previous ART regimen. Further evaluation of long-term outcomes of INSTI-based second and third line ART in treatment-experienced children and AYA is warranted and is ongoing within our cohort.

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**Pregnancy rates and postpartum virologic control among young women living with perinatal HIV infection in the US.**

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**Background:** There is limited data describing rates of pregnancy and postpartum health among perinatally HIV-infected (PHIV) young women. We compared pregnancy rates among PHIV and perinatally HIV-exposed, uninfected (PHEU) women, and describe pre-conception and postpartum trajectories of HIV-1 RNA among PHIV women.

**Materials & Methods:** Pregnancy rates from onset of sexual debut were calculated by HIV status among women in the Pediatric HIV/AIDS Cohort Study (PHACS) AMP Up protocol which enrolls PHIV and PHEU participants ≥18 years of age in the US. LOESS plots described trends in HIV-1 RNA starting one year prior to conception, during pregnancy, and through one-year postpartum for all pregnancies among PHIV women by pregnancy outcome (live-birth or spontaneous/elective abortion). Linear mixed-effects models were used to estimate HIV-1 RNA slopes prior to conception, from delivery to 24 weeks postpartum, and from 24 weeks to one year postpartum.

**Results:** Of 323 young women enrolled in AMP UP, 273 (234 PHIV, 39 PHEU) who reported age at sexual debut and history of heterosexual vaginal intercourse were included in analyses. Pregnancy rates were higher among PHEU compared to PHIV women (IR per 100 person-years [95% CI]: 16.5 [11.4, 23.8] vs. 10.2 [8.4, 12.3]). Median age at sexual debut was one year earlier among the 99 PHIV women who ever reported a pregnancy compared to the 135 who did not. The median [IQR] percent of HIV-1 RNA measurements ≥ 400 copies/mL was 765 (22.5) and 14.4% were ≤12 years old.
copies/mL up through date of sexual debut was also higher among PHIV women with a pregnancy (70% [44, 89] vs 50% [22,81]). Of the 99 PHIV women with at least one pregnancy, 60% had 1 pregnancy, 20% had 2, 12% had 3, 4% had 4, 3% had 5, and 1% had 6, with a total of 172 reported pregnancies. 72% of the pregnancies resulted in a live-birth, 9% were spontaneous abortions, and 19% were elective abortions. At one year prior to conception the average HIV-1 RNA was 475 copies/mL in all women and slowly increased over time up through conception. During pregnancy, HIV-1 RNA levels decreased with average HIV-1 RNA <400 copies/mL at delivery. In the first 24 weeks postpartum, HIV-1 RNA levels increased by 1.3 (0.4, 2.2) log10 copies/mL per year after a live birth and subsequently stabilized with a small decreasing slope from 24 weeks to one-year postpartum (slope: -0.3 [-0.8, 0.1] log10 copies/mL per year). In comparison, the average postpartum trajectory of HIV-1 RNA after a spontaneous/induced abortion remained at levels <400 copies/mL.

**Conclusion:** Compared to PHEU women, PHIV women had lower pregnancy rates. Among PHIV women however, HIV-1 RNA levels increased after a live birth in the first 6 months post-partum, potentially indicating a vulnerable time period for HIV progression among new mothers and the importance of continued engagement in HIV care.

### Raltegravir use in HIV-infected children and adolescents, and outcomes as a third-line combination antiretroviral therapy (cART) option in the IeDEA consortium

**Background:** As integrase inhibitors become available in low- and middle-income countries (LMICs), they offer the potential to expand extremely limited treatment options available to children. In LMICs, small numbers of children and adolescents have used raltegravir primarily as part of third-line regimens. Using data from the IeDEA global consortium, we aim to describe the characteristics of children on raltegravir-containing regimens and the outcomes of those on third-line.

**Methods:** We included data from children and adolescents (age <18 years) initiating combination antiretroviral therapy (cART) between 1997 and 2017, from four IeDEA regions, who received raltegravir for at least 90 days at any time during their treatment history. Database closure was between January and August 2017. We describe their characteristics, and immunologic and virologic outcomes for those on raltegravir as part of third-line/salvage regimens, which we defined as a regimen following exposure to PI-based cART, which included a change in or addition of at least one drug class.

**Results:** Among 62 children and adolescents, 37 (60%) were female. At raltegravir start, median age was 14.3 years (IQR 11.2-15.8), with a median duration on cART of 8.6 years (IQR 6.2-10.8), and median CD4, CD4% and log10 VL of 275.5 cells/μL (IQR 68-494, n=50), 14.95% (IQR 5.05-22.2, n=44), and 4.7 (IQR 3.7-5.2, n=46), respectively.

At database closure, median time on raltegravir was 2.0 years (IQR 0.8-3.0); one patient died, six were lost to follow-up. Of the 21 (34%) who had stopped using raltegravir, 15 had documented reasons: lack...
Dynamics of immunological and viral profile of HIV-1 chronically infected children under cART

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Background: HIV-1 infection is characterized by progressive loss of CD4+ T lymphocytes and immune dysfunction. Defective immune response against HIV-1 results in a chronic immune activation that plays a crucial role in the disease progression; its impact on premature aging and immune senescence, particularly in young patients who lack persistent viral suppression, is under discussion. We evaluated the correlation between viral load and immunological profile in HIV-1 chronically infected children over 5 years of cART.

Methods: 45 HIV-1 perinatally infected children (median[IQR] 14[10-19] years old) were studied at baseline (complete response to cART, i.e. HIV-1 RNA <50 copies/ml) and after 5 years of cART. 11 age-matched HIV-1 infected children with poor response to cART were included in the study. Peripheral blood mononuclear cells (PBMCs) were analyzed by flow cytometry to evaluate CD4+ and CD8+ T cells subsets for the expression of memory (CD45RA, CD27, CCR7), activation (CD38, HLADR) and senescence (CD28, CD57) markers. HIV-1 DNA copies were determined by Droplet Digital PCR assay. Statistical analyses were performed by non-parametric tests (comparisons by Wilcoxon test, Mann-Whitney U test or Kruskal-Wallis test, where appropriate; correlations by Spearman’s rho test).

Results: HIV-1 infected children were divided into subgroups according to their HIV-1 plasma viremia level over time: complete responders at baseline were divided into group 1 (n=32, persistent HIV-1 RNA <50 copies/ml) and group 2 (n=13, with 1-3 spikes of viremia); group 3, poor responders (n=11, HIV-1 RNA >50 copies/ml). At baseline, groups 1 and 2 did not significantly differ for any of the studied parameters, while both differed from group 3 for: i) CD4/CD8% ratio (1.1[0.9-1.4], 0.9[0.6-1.3] vs 0.7[0.2-0.8], p=0.055); ii) percentage of activated CD8+ T cells (2.0[0.9-3.8], 3.3[2.2-9.8] vs 5.5[3.3-9.2], p=0.003); iii) percentage of CD8+ senescent T cells (26[17-40], 40[17-54] vs 48[42-58], p=0.002). After 5 years, HIV-1 DNA level tended to decrease in group 1 (56[0-100] vs 0[0-99] copies/106 cells), while it remained constant in group 2 (35[0-319] vs 43[0-438]), and tended to increase in group 3 (20[0-284] vs 266[65-1008]). CD4/CD8% ratio remained persistently lower in group 3 than in groups 1 and 2 (0.5[0.2-0.8] vs 1.0[0.7-1.6] and 1.2[0.8-1.7], p=0.002). Group 3 also showed a significant increase of CD8+ memory T cell subset (36[26-52] vs 47[38-69], p=0.040). Additionally, the percentage of
activated CD8+ T cells tended to increase only in group 3 (5.5[3.3-9.2] vs 9.8[4.4-16.3], p=0.080) and the percentage of CD8+ senescent T cells remained significantly higher in group 3 than in groups 1 and 2 (44[31-50] vs 29[14-41] and 21[10-40], p=0.024).

Conclusions: These results indicate that persistence of high level of chronic activation is associated with expansion of memory CD8+ T cell subset and premature immune senescence. Interestingly, sporadic spikes of viremia do not significantly impact immune activation and senescence, as persistent viremia does; however, they impair the reduction of viral reservoir.

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Challenges to achieving and maintaining sustained viral suppression among HIV infected Canadian children

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Background: One of the keys to post-treatment control (viral remission) is sustained viral suppression (SVS) after early initiation of combination antiretroviral therapy (cART.). The objective of this study was to identify predictors of SVS among children in the Early Pediatric Initiation of CART Canada Child Cure Cohort (EPIC4).

Methods: Retrospective case-control study. Using data from the EPIC4 pediatric HIV cohort, the proportion of children who did vs. did not achieve SVS with their first cART regimen were compared, and predictors of SVS determined. Non-SVS was defined as ≥ 1 viral load rebound after ≥ 2 consecutive undetectable viral load (VL) measures. Only patients with a minimum 1-year of follow-up data were included.

Results: 211 children were enrolled in the EPIC4 cohort; mean age was 11.7 years (range 2.2-23 years). Nineteen children had not yet initiated cART; among those on treatment, 44% were on NNRTI, 30% on protease inhibitor, and 26% on integrase inhibitor-based regimens. Only 18.8% were on their initial cART regimen, 21.6% were on their second, and 59.6% had had three or more regimen changes. Mean age at cART initiation was 4.0 years (SD=4.2) and mean proportion of life on effective cART was 46% (SD: 0.31). Among the 49 children who initiated cART in the first year of life, only 32.7% had achieved SVS, with 41% having had documented difficulty with adherence in infancy. Overall in the entire cohort, 56% of children had achieved SVS after cART initiation (at any age), and 33% reported at least one period of previously poor adherence. Children with SVS were more likely to be foreign born than Canadian born (85% vs. 67%, p=0.03), and less likely to have received social assistance (9% vs. 29%, p=0.01) or to have child protection services involvement (60% vs. 85%, p<0.01). There was no significant difference in SVS according to gender or baseline viral load. There was a higher proportion of SVS among those with any protective HLA allele (from among HLA B57, HLAB81, HLA B27 vs. none, 90 vs. 73%), though not statistically significant (p=0.12).

Conclusion: Only 56% of children enrolled in the EPIC4 cohort achieved SVS. While adherence remains the overwhelming barrier to SVS, broader social determinants including income level and family disruption were identified important issues to address in this setting.
Factors associated with poor immune reconstitution despite virologically suppressive ART in children in Europe and Thailand

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Background: On commencing ART, a small proportion of children with HIV fail to achieve a satisfactory increase in CD4 count (i.e. poor immune reconstitution) despite virological control. This study aimed to identify factors associated with poor immune reconstitution in children in Europe and Thailand receiving ART.

Methods: Children with perinatal HIV with >1 CD4 measurement after ART start were included. Random effects asymptotic regression models explored the effect of characteristics (age, gender, ever CDC C (AIDS) and VL at ART start, and region of cohort (Thailand, UK/Ireland, Russia/Ukraine and rest of Europe (ROE)) on estimated ln(CD4-for-age) at ART initiation and 6 years later (long-term), and rate of ln(CD4-for-age) change. Predicted long-term CD4 counts were compared to WHO HIV-associated immunodeficiency criteria (advanced: CD4 count 200-<350 cells/µL; severe: CD4 count<200 cells/µL). Characteristics of advanced/severe immunosuppressed children (poor-responders) and responders with sustained viral suppression (SVS: VL<400 copies/ml within first year of ART start & no subsequent confirmed rebound >400 copies/ml) were compared, excluding children with no VL measurements >2 years of ART.

Results: Overall, 2204 children from 16 cohorts were included, contributing ~30,000 VL and CD4 measurements. Patients were from UK/Ireland (39%), Thailand (18%), Russia/Ukraine (12%) and ROE 31%; 54% were female. At ART start, median [IQR] age was 5.6[1.4,9.9] years, CD4 count 423[200,977] cells/µL and VL 5.0[4.5,5.6] log10 copies/µL; 12% had an AIDS event. Around a third of children started an efavirenz (31%), nevirapine (30%) or protease inhibitor (34%) based ART. Median follow-up was 5.8[3.1,6.0] years; 20 (1%) children died and 154 (6.7%) were lost to follow-up.

At ART start ln(CD4-for-age) was lower in those with prior AIDS diagnosis, lower VL or older age at ART start, and in children from Thailand and Russia/Ukraine (all p<0.001). Only age at ART start predicted long-term ln(CD4-for-age), with lower ln(CD4-for-age) in older children (p<0.001). There were no significant effects of any covariates on the rate of increase in ln(CD4-for-age).

Based on the long-term predicted CD4 count, 105 (4.8%) children were classified as having WHO advanced and 58 (2.6%) severe immunodeficiency. Median predicted final CD4 count in these poor-responders was 252[151,305] cells/µL, similar to their observed final CD4 count of 224[103,298] cells/µL. In comparison, responders had a median predicted final CD4 count of 839[628,1147] cells/µL, again close to the observed 823[605,1187] cells/µL.

In children with VL measurements, the number of poor-responders dropped to 25/66 (1.6% overall) advanced and 2/34 (0.1% overall) severe respectively when considering only children who had SVS. These 27 “discordant” poor-responders were older at ART initiation than the responders (n=995) with SVS (median age 12.2[8.8,14.1] vs 5.9[2.2,10.0] years, p<0.001) and had lower CD4 count 123[24,232] vs 406[192,914] cells/µL , p<0.001) and lower VL 4.6[4.1,5.3] vs 5.0[4.4,5.6] log10 copies/µL , p=0.050) at ART initiation. There were no significant differences in initial ART regimen, region or AIDS at ART start between the two groups.

Conclusions: Older age at start of ART is the strongest predictor of poor CD4 recovery in virologically suppressed children on ART.
Cofactors of mortality among hospitalized HIV infected children newly initiating ART in Kenya

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Background: Early diagnosis and initiation of antiretroviral therapy (ART) among HIV-infected children is associated with a dramatic reduction in mortality. However, many HIV-infected children in sub-Saharan Africa first present to care with advanced HIV disease and severe co-infections. Identifying factors associated with mortality among acutely ill HIV-infected children may help clinicians prioritize and optimize care for those at higher risk of death.

Materials & Methods: The Pediatric Urgent Start of Highly active antiretroviral therapy (PUSH) study (NCT02063880) was a randomized clinical trial of urgent (within 48 hours) versus post-stabilization ART (within 7-14 days), among HIV-infected, hospitalized, ART-naïve Kenyan children aged 0-12 years. Between April 2013 and May 2015, children were enrolled from 4 hospitals in Kenya and followed for 6 months for primary study outcomes: mortality, drug toxicity and immune reconstitution inflammatory syndrome (IRIS). At enrollment, detailed demographic, clinical and laboratory data were collected. We evaluated cofactors of mortality including: age, severe immunosuppression (WHO stage and CD4%), viral load, and weight for age Z-scores (WAZ) selected apriori, and orphaned and vulnerable child (OVC) status, persistent diarrhea (more than 2 weeks), visible wasting, oral thrush, oxygen saturation, confirmed TB, albumin, hemoglobin, and C-reactive protein (CRP) in exploratory analysis. Multivariate analysis was used only for apriori defined correlates with adjustments for hypothesized confounders per model. We used Kaplan-Meier survival analysis to summarize probability of survival and Cox proportional hazards regression univariate and multivariate analysis to estimate hazard ratios and 95% confidence intervals (CI).

Results: Of 181 enrolled children, 39 (22%) died within 6 months. Median age among children who died was 1.3 years (interquartile range [IQR] 0.5-2.1). Of these, 7 (18%) died 1 day after enrollment and 33 (85%) by one month. Cumulative probability of 6-month survival was 0.78 (95% CI 0.71-0.83). Common primary diagnoses at death were pneumonia (18 [46%]), gastroenteritis (9 [23%]), and suspected pulmonary tuberculosis (2 [5%]). Factors associated with mortality in unadjusted univariate analysis were age (HR 2.8 [95% CI 1.4 to 5.8]), log10 viral load (HR 2.2 [95% CI 1.4 to 3.5]), OVC status (HR 2.0 [95%CI 1.1 to 3.9]), persistent diarrhea (HR 3.8 [95% CI 1.9 to 7.7]), oxygen saturation <92% (HR 2.0 [95% CI 1.0 to 4.1]) and oral thrush (HR 2.2 [95% CI 1.2 to 4.1]) (p<0.05 for each). In multivariate analysis, adjusting for site, children <2 years had a 2.8 fold higher hazard of death compared to older children (95% CI 1.4 to 5.8, p=0.006). Adjusting for CD4 count, confirmed TB, and history of persistent diarrhea at enrollment, WAZ score <-2 was not significantly associated with a higher hazard of death. Severe immunosuppression was not associated with mortality, after adjusting for site and log10 viral load. Viral load models remained unadjusted.

Conclusions: Age and viral load predicted mortality among hospitalized HIV-infected children. OVC status, persistent diarrhea, low oxygen saturation and oral thrush may be important clinical predictors of mortality in children. Strategies to enhance early infant diagnosis and improve hospital management of HIV-infected children are needed.

Mortality and virologic outcomes between two and five years of antiretroviral treatment initiated during the first year of life: experience of the 1240 ANRS-PEDIACAM study (Cameroon)

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Introduction: In most of the studies, virologic response is assessed during the first 2 years of antiretroviral treatment initiated in HIV-infected infants. Instead, early initiation of antiretroviral therapy exposes infants to very long-lasting treatment. Moreover, maintaining viral suppression in children is very difficult. We aimed to describe virologic response and mortality after two years of antiretroviral treatment initiated during the first year of life, and identify factors associated with success in a Sub-Saharan African children.

Methods: We included 149 children of the ANRS 12140-PEDIACAM study still alive after two years of antiretroviral treatment initiated during the first year of life. The study population was organized in two groups according to virologic status at two years of antiretroviral treatment initiation: 1) group 1: children with viral load <400 copies/mL; 2) group 2: children with viral load ≥400 copies/mL or whose viral load was not measured. The probability of maintaining virologic success between two and five years antiretroviral treatment in group 1, or achieving virologic success at least once in group 2, was estimated using survival models. The study of factors associated with viral load <400 copies/mL in children still alive at five years of antiretroviral treatment (versus ≥ 400 copies/mL or not measured) was performed using univariate and multivariate logistic regression.

Results: At five years of early antiretroviral treatment, viral load was suppressed in 66.4% [58.7-74.1]) of the 144 children still alive and in care, but viral load was not measured in 15.4%. Five deaths (3.3% [IC95%: 0.4-6.2]) were recorded during the study period. Among the children with viral suppression at two years of treatment initiation, the probability of maintaining viral suppression at five years of treatment was 64.0% [48.5-79.6]. Among the children with detectable or unknown viral load at 2 years of treatment initiation, the probability of achieving viral load < 400 copies/mL at least once between two and five years of treatment initiation was 76.0% [53.5-98.5]. The only factor associated with viral suppression at five years of treatment initiation was virologic success at two years of treatment initiation.

Conclusion: The probability of maintaining viral suppression between two and five years of early initiated antiretroviral treatment in HIV-infected children is unsatisfactory, stressing difficulties of parents for daily long-term adherence to treatment. Thus, it is necessary to routinely monitor viral load and resistance to antiretroviral drugs in order to optimize treatment response in Sub-Sahara African children.

Neurodevelopmental and behavioral outcomes in perinatally HIV infected children who initiated antiretroviral therapy within 3 months of age

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Background: Data regarding neurodevelopmental and behavioral outcomes among children who initiated antiretroviral therapy (ART) within 3 months old are limited. This study compares neurodevelopmental and behavioral outcomes among children with perinatally-acquired HIV infection (PHIV) and perinatally HIV-exposed uninfected children (PHEU).

Materials & Methods: This is an observational study of children aged 12-56 months. PHIV children with 2 positive HIV DNA PCR were classified as early PHIV
Cohort study of HIV+ children in Southern Africa returning to care

if they commenced ART within 3 months old, and late PHIV if ART began between 3 and 12 months. Age-matched PHEU children had negative HIV DNA PCR at age > 4 months or anti-HIV negative at age > 12 months. Neurodevelopmental outcomes were assessed with the Mullen Scale of Early Learning (MSEL). Behavioral outcomes were evaluated by Child Behavioral Checklist (CBCL). Global developmental impairment was defined by MSEL Early Learning Composite (ELC) Score of < 70. Prevalence of development impairment and behavioral problems were compared by Chi-square test. Predictors of ELC scores were analyzed by multiple linear regression models.

Results: From 2016 to 2017, 150 children were enrolled (27 early PHIV, 23 late PHIV and 100 PHEU children). Median (IQR) age was 28 (19-41) months. 37/50 (74%) of PHIV children had undetectable HIV-RNA.

Prevalence of global developmental impairment was 26% in late PHIV, 7.4% in early PHIV, and 8% in PHEU, p=0.047. Mean (SD) ELC scores were 80 (18) in late PHIV, 83 (11) in early PHIV, and 90 (16) in PHEU, p =0.005. Late PHIV had significantly lower scores in gross motor and visual reception domains, p <0.05. Predictors of ELC score were ART initiation after 3 months old [mean difference -8.6, 95% CI (-16.3) – (-0.9) p=0.03] and no nursery school attendance [mean difference -5.9, 95% CI (-11.4) – (-0.3) p=0.04].

No significant differences were observed in CBCL internalizing, externalizing or total behavioral problems. Among individual behavioral problems, somatic complaints were reported more often in late PHIV (64% in late ART, 48% in early ART and 33% in PHEU, p=0.02).

Conclusions: Late PHIV had higher rate of developmental impairment when compare to early PHIV and PHEU. Early initiation ART and nursery school attendance mitigated neurodevelopmental scores in PHIV children.

after being lost to follow up: Effect of interrupting care on mortality


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Background: Although patients initiating antiretroviral therapy (ART) should ideally have sustained engagement in care after ART start, it is increasingly recognized that a large proportion of patients experience care interruptions for a range of reasons. However, few studies have assessed the long-term outcomes of children with a care interruption (CI), during which the child’s health status and use of medication is unknown. We evaluated the characteristics and outcomes of HIV-infected children that have care interruptions (i.e. >180 days without a clinic visit).

Materials and Methods: We included data on children <16 years old initiating antiretroviral therapy (ART) since 2004 at an International Epidemiologic Databases to Evaluate AIDS (IeDEA) Southern Africa (IeDEA-SA) cohort with >180 days potential follow-up. Children who died within 180 days of ART start were excluded. A CI was defined as >180 days without a clinic visit and loss to follow-up (LTFU) was defined as no visit within 180 days of database closure. The main outcome was all cause mortality. Two exposed groups were considered: those with a first CI within the first 6 months on ART, and those with a first CI after >6 months on ART. Children who died >180 days after last clinic visit were recorded as having a care interruption prior to
Results: Among 46,356 children included, 24,280 (52%) had at least one CI, of which 10,998 (24%) had a first CI within 6 months on ART and 13,282 (29%) had a first CI after 6 months on ART. Children with a CI before 6 months on ART were more likely to have longer first care interruptions than children with an interruption after 6 months on ART (median duration 322 days compared to 244 days, p<0.001). After adjusting for sex, current age, age at ART initiation, year of ART initiation, CD4% at ART initiation, time in/out of care and cohort, the results showed that having a CI within the first 6 months on ART was associated with increased mortality (adjusted rate ratio (ARR) = 2.70, 95% CI 2.13 - 3.43), but there was no association between a first CI after 6 months on ART and mortality (ARR = 1.01, 95% CI 0.77 - 1.31).

Conclusion: The findings suggest that strengthening retention of children in care in the early period after ART initiation is critical to improving paediatric ART outcomes. Care interruptions at different durations may significantly affect ART outcomes and need to be taken into account when assessing factors associated with mortality.

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Constructing a treatment cascade from routine laboratory data for HIV-PCR positive children in two districts in South Africa.

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Background: Retention-in-care is associated with improved virological control and survival amongst HIV-infected children. Currently there is no system for longitudinal monitoring of newly diagnosed HIV-infected infants. Using routine laboratory data, we followed the retention-in-care and virological outcomes of HIV-PCR positive children aged <18-months in urban and rural district in South Africa.

Methods: HIV-PCR positive results of children tested between April 2015-May 2016 from Tshwane (urban) and uMkhanyakude (rural) districts, were extracted from the National Health Laboratory Service’s Corporate Data Warehouse (CDW). HIV test-data (PCR, viral load (VL), CD4) are routinely collected into the CDW near real-time after authorization. HIV test-data were collected for ≥13-months after the initial HIV-PCR positive result per infant using both an automated patient-linking algorithm and manually searching demographics within the CDW. Test-sets were linked if ≥2 demographics (surname, name, date of birth, folder number) matched exactly. Programmatic indicators evaluated included age at HIV diagnosis, transmission route, result return-rate and retention-in-care at 6 and 12-months.

Results: In Tshwane and uMkhanyakude, 304 and 94 children tested HIV-PCR positive respectively. Median age (interquartile range) at HIV diagnosis was 2.3-months (0.1-6.7) for Tshwane and 3.6-months (1.4-7.1) for uMkhanyakude. Mode of transmission in Tshwane compared to uMkhanyakude was 90 (30%) vs. 17 (18%) in-utero, 23 (8%) vs.11 (12%) postnatal, 16 (5%) vs. 3 (3%) either intra-partum or postnatal and could not be determined in 175 (57%) vs. 63 (67%) cases due to the first HIV-PCR test being performed at >3-months of age. In both districts, loss-to-follow-up (LTFU) rates (per 1000 person-months) were lower in children diagnosed at birth (<7-days) compared to children diagnosed at older ages (≥7-days) at 126 vs. 149 (p<0.001) in Tshwane and 72 vs. 90 (p<0.001) in uMkhanyakude. While no statistically significant differences in median time-to-return for HIV-PCR positive result were observed in uMkhanyakude, children diagnosed at birth took longer to return for their results compared to their counterparts in Tshwane (34 vs.14 days respectively, p=0.003). In Tshwane, 218 (72%) children returned for their initial HIV-PCR positive result; 192 (63%) had a confirmatory HIV test; 58 (19%) were retained in care at 6-months; 50 (16%) had a VL test and 24 (8%)
were virologically suppressed. 40 (13%) children retained in care at 6-months had subsequent follow-up. In uMkhanakude, 73 (78%) children returned for their initial HIV-PCR positive result; 59 (63%) had a confirmatory HIV test; 30 (32%) were retained in care at 6-months; 25 (27%) had a VL and 15 (16%) were virologically suppressed. 21 (13%) children retained-in-care at 6-months had subsequent follow-up.

LTFU rates presented here may be overestimated if children are accessing clinical care without VL monitoring.

Conclusion: We demonstrate the value of routine laboratory data for constructing a near real-time treatment cascade of HIV-infected children and identify LTFU rates of 70-80% between returning for follow-up after the first HIV-PCR positive result and the 6-month VL test. However, children retained at 6-months are mostly retained at 12-months. Strengthening systems for tracking HIV-infected children in the first 6-months of treatment must be prioritized to improve retention-in-care.

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Evaluation of a comprehensive approach to close the paediatric HIV programme gap in Johannesburg, South Africa

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Background: Since the rollout of the South African HIV programme, the country has made tremendous progress in expanding paediatric treatment coverage. Despite this, considerable effort is required to ensure that all HIV-infected children are linked to treatment. The Paediatric and Adolescent Scale-up Project collaborative aimed to close this programme gap.

Materials/Methods: We implemented a comprehensive approach of technical assistance and direct service delivery by roving teams to target children (<15 years of age) missing from the HIV programme in sub-districts CDEG in Johannesburg Health District, between September 2015 and December 2017. Interventions included case-finding strategies, data driven linkage to care support, paediatric case management strengthening and data systems improvement. Routine operational and programme data were collected and analysed.

Results: Over a two-year period, a total of 84097 children were tested for HIV at facilities in the supported sub-districts; 2317 (2.8%) of whom tested HIV-positive. 69.6% (n=58544) of the total tests were in under-five children, and 51.4% (n=1192) of the positive tests were in this age group. Project implementation resulted in a significant increase in testing uptake (from 1050 to 3504/month; p<0.001) and number of children testing positive (from 61 to 96/month; p<0.001); test positivity rate dropped from 4.0% to 2.3% (p<0.05). The absolute number of children initiated on ART remained in similar range, at around 800 per year, illustrating reduction in linkage to care. Despite intensive efforts, programme retention rate decreased over time with one-year loss to follow-up increasing from 18% to 21% overall, but 27% in under-fives; one-year viral suppression rate also decreased from 72% to 56%.

Conclusions: Our comprehensive model has successfully enhanced scale-up of paediatric HIV testing and case finding in regions CDEG of Johannesburg over time, although other factors could also have played a role. The high rate of loss to follow-up and low rate of viral suppression warrant attention, especially in children under 5. In order to close the paediatric HIV programme gap, focus of effort should shift from case finding strategies to strengthening the quality of care and psychosocial adherence support to dramatically improve linkage and retention in care.
Progress toward a pediatric 90-90-90: 2016 Lesotho population-based HIV impact assessment results

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Background: Lesotho remains disproportionately impacted by the HIV epidemic. To date, understanding of the pediatric HIV burden in Lesotho has been limited. Recent UNAIDS publications (2016) estimate 13,000 children living with HIV and 56% antiretroviral therapy (ART) coverage. The 2016 Lesotho Population-based HIV Impact Assessment (LePHIA) was conducted in all ten districts across Lesotho and was designed, in part, to measure national pediatric HIV prevalence and viral load suppression (VLS).

Methods: A nationally representative sample of children, 0-14 years, participated in household-based, rapid HIV testing between November 2016 and May 2017. Children <18 months with a reactive rapid test underwent DNA PCR testing for HIV diagnosis. Parents or legal guardians provided information on children's clinical history. Children 10-14 years of age answered socio-demographic and behavioral questions. HIV-seropositive results among children 18 months to 14 years of age were confirmed via a supplemental assay and viral load was performed on all HIV+ samples at the central lab. VLS was defined at HIV RNA <1000 copies/ml. Analyses account for study design.

Results: In total, 3,996 children were tested for HIV. Overall, HIV prevalence was 2.1% (95% CI 1.5, 2.6), corresponding to approximately 13,000 children living with HIV. VLS among all HIV-positive children regardless of ART use was 62.7% (95% CI 50.6, 74.8). Among children who tested HIV positive during the survey, median age was nine years (95% CI 8, 11) and parents or legal guardians reported that overall, 74.0% (95% CI 61.9, 86.2) already knew the child’s HIV status (1st 90), of whom 97.7% (95% CI 93.1, 100.0) reported ART use (2nd 90), and 74.2% (95% CI 60.7, 87.6) of those on ART were virally suppressed (3rd 90). For females, parents or legal guardians reported that 77.2% (95% CI 62.3, 91.2) already knew the child’s HIV status (1st 90), of whom 96.4% (95% CI 89.5, 100.0) reported ART use (2nd 90), and 80.9% (95% CI 63.9, 98.0) of those on ART were virally suppressed (3rd 90). For males, parents or legal guardians reported that 68.7% (95% CI 47.7, 89.7) already knew the child’s HIV status (1st 90), of whom 100.0% (95% CI 100.0, 100.0) reported ART use (2nd 90), and 62.0% (95% CI 37.9, 86.0) of those on ART were virally suppressed (3rd 90). Median time on ART was 30 months (95% CI 19, 42).

Conclusions: Pediatric HIV prevalence remains high. Awareness of status is low although once children are aware of their status ART use is high. Despite high ART use, VLS remains low with much room for improvement. Aggressively targeting children for HIV testing, treatment, and adherence counseling may contribute to reduced morbidity and mortality from HIV among children in Lesotho.

Trends in the characteristics of HIV-infected children initiating antiretroviral therapy in sub-Saharan Africa: Reassessing progress

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Background: Sub-Saharan Africa has experienced an expansion in access to antiretroviral therapy (ART) for HIV-infected children over time, with particular attention to the early initiation of ART for
infants and young children. Few studies have described regionally representative data assessing the ongoing scale-up of paediatric ART programs in routine care settings. We aim to explore the trends in ART initiation characteristics among HIV-infected children ≤5-years-old accessing ART over 10 years of implementing expanded ART initiation guidelines in sub-Saharan Africa.

Methods: We examined data from HIV-infected children 0-5 years of age, initiating cART at 30 IeDEA sites within 13 countries across West and Southern Africa, from 2006-2017. We described and compared ART initiation characteristics according to time-period of initiation: 2006-2010, 2011-2013 and 2014-17.

Results: Overall, 32,635 HIV-infected children were included (West Africa; 7%, Southern Africa; 78%, East Africa; 15%), 50% were female. Forty-five percent, 30% and 25% of all children initiated ART between 2006-10, 2011-13 and 2014-17, respectively. The median age at ART initiation was 1.7 years (interquartile range (IQR): 0.7-2.9) overall, and 2.1 years (IQR:1.2-3.4) in West Africa, 1.8 years (IQR: 0.8-3.1) in Southern Africa, and 2.4 years (IQR:1.4-3.6) in East Africa. There was a slight decrease in the median age of ART start over time from 1.7 years (IQR: 0.7-3.0) in 2006-10 to 1.5 years (IQR: 0.7-2.8) 2014-17 (p<0.001). Among 10,535 (32.2%) infants (<12 months old), the median age of ART initiation was 5.4 months (IQR: 3.2-8.5), and this decreased slightly across consecutive time periods from 6.4 months (IQR: 4.0-9.1) to 5.0 months (IQR: 2.6-8.8) (p<0.001). Among infants across all regions, the proportion of those initiating ART ≤3 months of age progressively increased over time from 17.0% in 2006-10 to 22.2% in 2011-13 and to 32.2% in 2014-17 (p<0.001).

Conclusions: Over time, HIV-infected children started ART at progressively earlier ages and with better health states, as reflected by an improvement in nutritional and immune status. While the global regions are achieving earlier ART initiation among HIV-infected infants in the first few months of life, effort still needs to be focused on identifying barriers to early infant diagnosis, linkage to care and initiating this critical group of children earlier on ART.

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Same Day ART Initiation Does Not Reduce 12-Month Retention Among HIV-Infected Children In Uganda

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Introduction: Countries have adapted the WHO Test and START guidelines for antiretroviral therapy (ART) initiation, but there is limited evidence on how soon to start ART in children without jeopardizing retention. Uganda has implemented Test and START guidelines for children which included same day initiation since 2014. We compared 12-month probability of retention in HIV-infected children aged <15yrs initiated on ART on the same day of diagnosis versus 2-14 days or >14 days from diagnosis during HIV Test and START policy implementation in Uganda.

Methods: We retrospectively reviewed clinic charts for HIV-infected children diagnosed and initiated on ART from June 2014 to March 2015 in 42 health facilities in Uganda. Retention was defined as being alive and on ART during the 12th month on ART. Kaplan-Meier estimates were used to calculate the 12-month probability of retention (overall and stratified by health facility level and age at diagnosis) and the log-rank test to compare groups

Results: Of 899 HIV infected children, 115(12.8%) were excluded for missing diagnosis date and 784(87.2%) were included in the analysis. Of these 784 children, 56% were girls, median ages (IQR) at diagnosis and ART initiation was 3(1, 7) years and
Three hundred and seventeen (40.4%) children started ART on the same day they were diagnosed, 155(19.8%) started within 2 to 14 days and 312(39.8%) started after 14 days. The overall probability of one-year retention was 89.9%; Retention was similar among children who initiated ART on the same day (89.7%) compared to those initiated 2-14 day’s (94.0 %) and >14 days (90.2 %), p=0.3. Retention was highest in those diagnosed at age 5-14yrs (93.5%) and at health centres (96.0%); and lowest in children under 2 years of age (85.9%) and regional referral hospitals (89.7%). Retention in each age and health facility stratum did not differ by time from diagnosis to initiation (table 1).

Conclusion: Starting ART in children on the same day of diagnosis does not jeopardize retention on treatment.

Background: In the Democratic Republic of Congo (DRC), a country with one of the highest tuberculosis (TB) burdens in the world, 12% of TB patients are also living with HIV, and TB incidence among children less than 15 years of age is 32%. HIV seropositivity is an important predictor of mortality among pediatric TB patients in DRC, underscoring the need for timely diagnosis and integrated HIV and TB care and treatment. Children and adolescents in DRC also face unique vulnerabilities to both HIV and TB, due to the country’s political instability and ongoing violence, low rates of school attendance, and high rates of orphaned children. In addition, children in DRC face barriers to accessing care and treatment. As of 2017, antiretroviral therapy (ART) coverage among children less than 15 was only 30%.

Materials & Methods: From 2015 to 2017, ICAP supported the expansion of pediatric HIV care and treatment in Kinshasa and Haut-Katanga regions under the ACT initiative, a public-private partnership aimed at doubling the number of children receiving ART. As part of a holistic approach, ACT activities included integrated TB care, education for families, mentorship to health facility staff, collaborations with orphanages, quality improvement activities, and birth testing for HIV-exposed infants. To describe linkage to care among both HIV and TB patients, we reviewed routinely collected aggregate data from ICAP-supported sites across 49 health zones in the two regions from April 2016 to March 2018, a time period spanning six months after the initiation of ACT programming through six-months following its completion.

Results: Between April 2016 and March 2018, 1,552 children and adolescents aged ≤19 years newly enrolled in HIV care at 202 ICAP-supported facilities: 512 (33%) were under 5 years, 378 (24%) 5-9 years, 226 (15%) 10-14 years, and 436 (28%) 14-19 years. Among all pediatric patients, 1,485 (96%) were screened for TB during their first HIV clinic visit, 96 (7%) had a laboratory confirmed TB diagnosis, and 78 (81%) were initiated on TB therapy. In Katanga, a rural province, 100% of 1,020 new HIV patients were screened for TB, while in Kinshasa, 87% (464/532) were screened. During the same period, 1997 new pediatric patients with confirmed TB diagnoses enrolled in care at ICAP-supported TB clinics; of the 1,912 (96%) with unknown HIV status, 1,896 (99%) received an HIV test, and 45 (2.4%) were identified as HIV positive. All patients (100%) newly diagnosed with HIV at TB clinics were enrolled in care and initiated on ART.

Conclusions: Pediatric HIV clinics in DRC serve as important avenues for diagnosing TB and initiating treatment among children and adolescents. Similarly, pediatric TB clinics have demonstrated a critical role in diagnosing HIV and initiating ART. These results indicate that successful HIV-TB cross-linkage services for children can be achieved, which may contribute to reducing mortality and morbidity in this particularly vulnerable population.
adolescents living with HIV — Kenya, 2016–2017

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Background: HIV infected children (0–14 years) and adolescents (15–19 years) on Antiretroviral Treatment (ART) in Kenya have lower viral suppression at 67% and 65%, respectively, compared to adults at 83%. Our study evaluated the relationship between child and adolescent viral suppression and primary caregiver characteristics.

Methods: We used HIV program data from HIV treatment facilities in Nairobi, central Kenya, and selected faith-based facilities across Kenya. Data were collected for the period January 1, 2016–September 30, 2017. Viral suppression was defined as viral load (VL) < 1000 copies/ml. The primary care giver was identified from child/adolescent clinical records. We used chi-square tests to compare differences in proportions and ordinary logistic regression to identify factors associated with virologic non-suppression.

Results: We analyzed 9789 records of children and adolescents with HIV; 51% were female. A primary caregiver was documented for 8173 of these children and adolescents; 4709 (57.6%) primary caregivers were mothers, 720 (8.8%) fathers, and 2777 (33.5%) guardians. 56% (4758) of caregivers were HIV-infected. Overall, 77.8% of children and adolescents were virologically suppressed, as were 86% of HIV-infected primary caregivers. Children and adolescents with HIV-negative caregivers had 79.2% viral suppression compared to 76.7% of those with an HIV-infected primary caregiver (p=0.007). Children and adolescents with HIV-infected/non-suppressed caregivers were nearly three times more likely to have non-suppression compared to those with HIV-infected/suppressed caregivers (48.0% vs. 18.7%, respectively; aOR 2.67, 95% confidence interval [CI] 2.11-3.38). Children and adolescents whose primary caregivers had poor ART adherence were more likely to have viral non-suppression than children and adolescents with primary caregivers who had satisfactory ART adherence (aOR 1.46, 95% CI 1.02–2.09). Primary caregiver relationship, caregiver support group attendance, sex of child/adolescent, and disclosure of HIV status to the child/adolescent were not significantly associated with viral suppression.

Conclusions: Children and adolescents with caregivers who are HIV-negative are more likely to achieve viral suppression. Children and adolescents on ART are less likely to be suppressed if they have a HIV-infected primary caregiver with non-suppression and/or poor adherence to ART. Family-centered approaches to support caregivers who have not achieved virologic suppression should be investigated to determine effects on virologic suppression for their children and adolescents.

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Newly diagnosed HIV-infected children: a unique index case to improve HIV diagnosis and linkage to care of parents


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Background: Newly diagnosed HIV-infected children may be unique index cases to identify parents with undiagnosed HIV infection. However, parental uptake of HIV testing and treatment services may be poor due to complex relationship dynamics, non-disclosure, and the emotional burden of a new pediatric HIV diagnosis. Understanding gaps in the care cascade of parents of HIV-infected children may inform interventions to improve HIV diagnosis and linkage to care.

Methods: We used data from the Pediatric Urgent Start of HAART (PUSH; NCT02063880) study, a randomized clinical trial comparing urgent to post-stabilization ART among hospitalized, ART-naïve,
HIV-infected children ages 0-12 years at four hospitals in Kenya. We assessed parental HIV testing, linkage to care, and ART initiation at enrollment and 6 months post-enrollment. We restricted this analysis to the families of newly diagnosed HIV-infected children who completed 6 months of follow-up. Information was collected from the caregiver present at interview at baseline or 6 months. We used McNemar’s tests to compare differences over time (baseline vs. 6 months) in the proportions of mothers and fathers tested for HIV (yes vs. no/don’t know), linked to care (yes vs. no/don’t know), and on ART (yes vs. no/don’t know).

Results: Of the 181 children enrolled in the trial, 152 were newly diagnosed with HIV during the enrollment hospitalization, of whom 87 survived and completed 6 months of follow-up. Of these 87, 78 (90%) had two living parents, 5 (6%) had only a living mother, 2 (3%) had only a living father, and 2 (3%) did not have living parents. Most caregiver survey respondents were the child’s mother (82 [94%]). Among children with living parents, 26 (33%) fathers and 2 (2%) mothers were not fulfilling parental duties, or were not residing in the same household as the child.

Among 83 children with living mothers, 30 (36%) mothers were in HIV care at baseline compared to 65 (78%) at 6 months (p<0.0001). Eighteen (22%) were on ART at baseline compared to 45 (54%) at 6 months (p<0.0001). Among 80 children with living fathers, the number of fathers who knew the child’s HIV positive status increased from 27 (34%) at baseline to 62 (78%) after 6 months (p<0.0001). The reported proportion of fathers ever tested for HIV increased from 34 (43%) at baseline to 52 (65%) after 6 months (p<0.0001), with 18 (23%) of fathers ever testing HIV positive at baseline compared to 32 (40%) fathers ever testing HIV positive at 6 months (p=0.0002). Among the 80 living fathers, there was an increase in the number of HIV-infected fathers ever linked to care from baseline to 6 months (12 [15%] vs. 26 [33%], p=0.0002), and 9 (11%) fathers had ever initiated ART at baseline compared to 15 (19%) fathers had ever initiated ART at 6 months (p=0.0082).

Conclusion: Using newly diagnosed HIV-infected children as index cases identified a substantial number of parents with previously undiagnosed HIV infection or poor engagement with HIV care. Significant improvements across the HIV care cascade were noted for both mothers and fathers.

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Successful same day ART initiation in newly diagnosed HIV-positive children and adolescents: encouraging Results and outcomes from a pediatric HIV clinic in Mbeya, Tanzania.

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Background: Same day HIV testing and antiretroviral therapy (ART) initiation has been shown to improve retention to care, virologic suppression, and survival in HIV+ adults. However, there are sparse data in HIV-positive children and adolescents on the impact of same day HIV testing and ART. This study describes clinical characteristics and treatment outcomes of HIV+ children and adolescents who had same day HIV testing and ART initiation in a pediatric HIV clinic in Mbeya, Tanzania.

Materials and Methods: Retrospective chart review was conducted to describe baseline characteristics and treatment outcomes of children and adolescents initiating ART at the Baylor College of Medicine Children’s Foundation – Tanzania Centre of Excellence (COE) in Mbeya, Tanzania between 1 January 2016 and 31 December 2017. Newly diagnosed clients and their caregivers were assessed by COE clinicians and counselors per national protocols to determine if eligible and ready for same day ART initiation versus standard pre-ART counseling later followed by ART initiation (non-same day). Most recent post-ART viral loads and current chart status were extracted to determine virologic suppression (VL<1000 copies/mL) and treatment outcomes.

Results: Between 2016 and 2017, there were 151 children and adolescents (ages 0-19yo) with same day HIV testing and ART initiation, and 101 with non-same day ART initiation. At baseline, same day ART initiations were significantly older (7.3 yr vs 4.3 yr, p<0.001), less disease burdened by WHO stage (51.7% vs 76.2% WHO Stage 3/4, p<0.001), and less...
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imunosuppressed (50.3% vs 25.7% WHO immune suppression of “Not Significant or Mild”, p<0.001), compared to their non-same day ART initiation counterparts. All newly diagnosed patients were started on either ABC-3TC-LPV/r, ABC-3TC-EFV, or TDF-3TC-EFV depending on their age as recommended by current national guidelines.

Same day ART initiations had higher rates of viral suppression (82.7% vs 67.2%, p=0.03) and lower mortality (2.0% vs 8.9%, p=0.01) than non-same day ART initiations. All newly diagnosed patients were started on either ABC-3TC-LPV/r, ABC-3TC-EFV, or TDF-3TC-EFV depending on their age as recommended by current national guidelines.

Conclusion: Our findings demonstrate that same day HIV testing and ART initiation was feasible in newly diagnosed HIV+ children and adolescents in Mbeya, Tanzania, and these clients had good retention to care, high levels of virological suppression and low mortality.

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Pediatric HIV treatment gaps in seven East and Southern African Countries: Examination of modeled data, survey data, and routine program data

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Background: Remarkable success in prevention and treatment of HIV infection in children has been achieved in the past decade. Large differences remain between estimated number of children living with HIV (CLHIV) and those that are identified through the national HIV programs. We evaluated the number of CLHIV and those on treatment in Lesotho, Malawi, Swaziland, Tanzania, Uganda, Zambia and Zimbabwe.

Methods: We assessed the total number of CLHIV, CLHIV on antiretroviral treatment (ART) and national and regional ART coverage gaps using three data sources, including 1) UNAIDS model-based estimates as well as national program data used as input values in the models, 2) Population-based HIV impact surveys (PHIA), and 3) Program data from PEPFAR supported clinics.

Results: Across the 7 countries, HIV prevalence among children 0-14 years ranged from 0.4% (0.2%-0.6%) to 2.8% (2.2%-3.4%) according to the PHIA surveys, resulting in estimates of 520,000 (460,000 – 580,000) CLHIV in 2016-2017 in the 7 countries. This compared to Spectrum estimates of pediatric HIV prevalence ranging from 0.5% (0.4% – 0.6%) to 3.5% (3.0% – 4.0%) with 470,000 (370,000 – 540,000). CLHIV not on treatment according to PEPFAR, PHIA, and Spectrum for the 7 countries stood at 48% (25% – 60%), 49% (37% – 50%), and 37% (22% – 48%), respectively. Of the 78 regions examined across the 7 countries, 33% of regions according to PHIA data and 41% of regions according to PEPFAR data had met the ART coverage target of 81%.

Conclusion: There are substantial gaps in the coverage of HIV treatment in CLHIV in the 7 countries included in the study according to all sources examined. There is continued need to identify, engage and treat infants and children. Important inconsistencies still existed in estimates across the three sources that warrant future in-depth investigation.
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Linking HIV-infected children to care and support: a data driven strategy implemented in Johannesburg, South Africa

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Background: South Africa has made significant improvements in the diagnosis and care of HIV-positive children. Despite this, delays in management of laboratory results remain a challenge. We describe the implementation of a data driven strategy to improve use of laboratory results, using weekly ‘results for Action’ reports generated by the National Health Laboratory Services. These provide individual-level details on: a) HIV diagnosis in infants under 18 months (HIV-PCR), and b) detectable viral loads (HIV-viral load) in children on antiretroviral therapy (ART).

Materials/Methods: On a weekly basis we matched individual names and birth dates in the ‘results for Action’ reports to health facility data sources, between July 2016 and Sept 2017. HIV-infected infants not on ART (HIV-PCR reports) were traced and treatment initiation supported at facility level. To address detectable viral loads in children on ART (HIV-viral load reports), we implemented a strategy of psychosocial and clinical management support. We collected and analysed routine operational data to determine the relevance and impact of our strategy.

Results: Through the HIV PCR reports, 1025 HIV-infected infants were matched to facility records. 63% (n=652) ultimately accessed HIV-care (approximately 50% of which were through active tracing), 33% (n=340) were not found and 2.5% (n=26) had died. Of the total number of infants testing HIV-positive, the percentage of children accessing care increased over the reporting period (59% to 68%). Management of children with detectable viral load was more complex and required several follow-up steps: 1324 children with detectable viral loads were included in the reports, 33% (n=439) were found and received an intervention and 24% (n=322) could not be traced (file or patient not found). The remaining 42.5% (n=563) have not been reached due to capacity challenges.

Conclusions: Laboratory generated HIV-PCR reports were a useful tool for patient level linkage and outcome verification. Viral load reports, however, required considerable capacity and were more complex to manage. The large proportion of patients that are not traced is of concern; improvement and scale-up of the strategy is required to ensure management and outcome verification of all children with detectable viral loads.

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Prevalence and predictors of bone mineral density among perinatally HIV-infected adolescents on antiretroviral therapy (ART) in the Cape Town Adolescent Antiretroviral Cohort (CTAAC).

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Background: Access to ART has reduced morbidity and mortality in perinatally HIV-infected adolescents (PHIVA), but long-term complications including low bone mineral density (BMD) remains a concern. In high income countries, low BMD has been reported in 10-54% of HIV-infected adolescents. We studied the prevalence and predictors of low BMD among South African PHIVA on ART.

Method: We evaluated calcaneus stiffness index (SI) in a cross-sectional analysis using Quantitative Ultrasoundonography (QUS), a reliable and non-invasive method to screen BMD. Adolescents 11-17 years old were included. SI was considered low if z-score < -2 SD using age and sex matched HIV-uninfected controls (HIV-) as a reference. Multiple logistic regression was used to examine the adjusted association between low SI and both HIV-related and traditional risk factors in PHIVA.
Result: Overall 407 PHIVA (median age: 14 years; 50% female; median age at ART initiation: 4.2 years) and 92 HIV- (median age: 14 years; 54% female) were included. Median duration on ART was 9.8 years (IQR 6.8-11.5) with 38% initiating ART at ≤2 years of age. PHIV+ had low mean SI and BMI z-score compared to HIV- (99 vs 105, p<0.001) and (-0.19 vs 0.43, p<0.001) respectively. At Tanner Stage I, the mean SI between PHIVA and HIV- were similar (93 vs 94, p=0.832). During puberty, mean SI increased with Tanner Stage in both PHIVA and HIV- but there was more significant increase among HIV- controls; Tanner Stage II-III (96 vs 101, p=0.009) and Tanner Stage IV-V (104 vs 112, p=0.001).

Among PHIVA on ART, 52 (13%) had low SI. After adjusting for age, gender and Tanner stage, exposure to Lopinavir/Ritonavir (LPV/r) (OR=2.31, p=0.012) and viral load >50 copies/ml (OR=2.06, p=0.023) were associated with increased risk of low SI. However, exposure to Efavirenz (EFV) (OR=0.41, p=0.009) was associated with decreased risk of low SI.

Conclusion: In South African PHIVA, SI appears significantly different from HIV-controls especially in late puberty. LPV/r exposure and high viral load are risk factors for low SI and exposure to EFV seems to be associated with better SI. Longitudinal study of BMD is needed to evaluate long term effects.

Utility of calcaneal quantitative ultrasound to detect and monitor bone acquisition deficits in HIV-infected children in Johannesburg, South Africa

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Background: HIV-infected children and adolescents have decreased bone mass accrual and alterations in bone microarchitecture, thus affecting skeletal growth. We previously reported lower bone mineral content (BMC) in HIV-infected children who initiated antiretroviral therapy (ART) before 2 years of age and who had sustained virologic control on ART. Disruption of bone accrual during critical periods of development can compromise adult peak bone mass and increase fracture risk later in life. The goal of this study was to evaluate whether bone quality could be adequately assessed and monitored using quantitative ultrasound (QUS) of the calcaneus, an inexpensive, radiation-free device. QUS assesses bone quality by measuring the Broadband Ultrasound Attenuation (BUA) and Speed of Sound (SOS) of the transmitted ultrasound wave propagation through bone and combines these values into a composite measure, Stiffness Index (SI).

Methods: This longitudinal analysis included 121 HIV-infected children with viral suppression on ART and 151 HIV-negative children enrolled in the CHANGES Bone Study conducted in Johannesburg, South Africa. Dual X-ray Absorptiometry (DXA) was done at baseline and 1 year and QUS evaluations at baseline, 1 year, and 2 years. The Lunar Achilles Insight QUS device was utilized to measure SOS (m/s), BUA (dB/MHz), and SI of the left calcaneus. QUS indices were compared to bone mineral content (BMC) of the whole body (WB) and lumbar spine (LS) measured with a Hologic QDR DXA. Multivariable generalized linear regression models with an identity link to account for correlation between visits were used to examine the relationship between HIV status and the ultrasound bone quality measures and to stratify by sex. BMI- and height-for-age z-score were accounted for in the analytic models.

Results: At baseline, the median age of the children was 7.1 years, 47% were female, mean BMI-for-age z-score was 0.2 and mean height-for-age z-score was -0.9. Compared to HIV-negative controls, HIV-infected children had lower calcaneal BUA, SOS and SI, as well as lower WB and LS BMC at baseline and 1 year. Similar relationships were observed when stratified by sex. HIV-infected children were an average 13.1% (p<.0001) lower for WB BMC and 7.8% (p<.01) lower for LS BMC than HIV-negative children. Children who were HIV-infected were an average of 6.5 dB/MHz lower in BUA (p<.0001), 7.8 m/s lower in SOS (p<.0001), and 6.3 points lower in SI (p<.0001) than their HIV-negative counterparts. On average, female children were 5.3 m/s lower in SOS (p<.01), 2.3 points lower in SI (p<.02), and 1.8 dB/MHz lower in BUA (p<.0001).
Presentation of chronic lung disease in children and adolescents living with HIV

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Background: The use of antiretroviral therapy (ART) and co-trimoxazole prophylaxis has reduced risk of acute respiratory tract infections among children living with HIV but a high prevalence of chronic respiratory disease has been reported in recent years. We investigated factors associated with a Forced Expiratory Volume in one second z-score (FEV1 z-score) < -1 in a case-control study of children and adolescents taking ART in southern Africa.

Methods: Perinatally HIV-infected participants aged 6-19 years and taking ART for at least 6 months were recruited from HIV clinics in Harare, Zimbabwe and Blantyre, Malawi. Exclusion criteria were current tuberculosis (TB) and acute respiratory tract infection, pregnancy or breastfeeding. We enrolled all cases with an FEV1 z-score < -1, with no reversibility (<12% improvement in FEV1 after salbutamol 200 μg inhaled using a spacer), at screening, and an age and sex frequency-matched sample of controls with an FEV1 z-score ≥ -1 in a 4:1 allocation ratio. Logistic regression was used to determine factors associated with FEV1 z-score < -1 at enrolment. The model which minimised Akaike’s Information Criteria (AIC) was chosen as the best predictive model.

Results: Between June 2016 and March 2018, 261 cases (54% male, 70% aged ≥13 years) were enrolled with mean FEV1 z-score of -2.06 (standard deviation (SD): 0.75) and 45 (40% male, 69% aged ≥13 years) were enrolled in the control group with mean FEV1 z-score of 0.72 (SD: 1.23).

Among cases with FEV1 z-score<1, unadjusted mean FEV1 z-score was lower (worse lung function) in those on ART for longer periods, with lower CD4 cell count, with higher viral loads, with lower body mass index (BMI)-for-age and weight-for-age z-scores (poor anthropometry), on second line ART regimen and not attending school. A history of admission in the last 12 months for chest problems was reported by 5 (2%) cases, past TB treatment history was reported in 82 (31%) cases and 28 (11%) cases presented with a current cough and 26 (10%) cases had significant breathlessness MRC Dyspnoea Score ≥2).

In a multivariable model, factors associated with low FEV1 z-score (< -1 compared to ≥ -1) were being on 2nd line ART (OR=2.6, 95%C1:0.97-6.83, p=0.06), younger age (6-9 years, 10-12 years or 13-16 years compared to 17-19 year olds: p=0.02), not attending school (OR=5.20, 95%C1:1.31-20.7, p=0.02), and low weight-for-age z-score (OR=4.1, 95%C1:1.6-10.5, p=0.003). The model which minimised the AIC also controlled for duration on ART (p=0.14), low body mass index (p=0.15) and viral suppression (p=0.60).

Conclusion: Poor lung function was associated with poorer general health, lower BMI- and weight-for-age z-scores and not attending school. Strategies for treatment of chronic respiratory disease among children and adolescents living with HIV are urgently needed.
Prevalence and associated factors of proximal renal tubular dysfunction among perinatally HIV-infected Thai adolescents

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Background: People living with HIV are at increased risk of developing kidney disease in the course of their lifetime. This co-morbidity which might arise from HIV infection or nephrotoxicity of combination antiretroviral treatment (cART) can accelerate a progression towards mortality. Yet, the information regarding renal tubular disorders among HIV-infected youth, particularly in resource-constrained settings, are limited. This study aimed to assess the prevalence and associated factors of proximal renal tubular dysfunction (PRTD) among perinatally HIV-infected Thai adolescents.

Methods: This was a sub-study of a multicenter, prospective cohort study evaluating kidney disease among HIV-infected Thai adolescents. Participants with (1) perinatally acquired HIV infection, (2) aged 10-25 years, and (3) were on cART for ≥12 months, together with their age- and sex-matched healthy, HIV-uninfected controls were enrolled in the ratio of 2:1. HIV-infected participants were categorized as tenofovir disoproxil fumarate (TDF) users versus non-TDF users, according to their current cART regimens. At enrollment, proximal renal tubular function parameters, including urine β2-microglobulin to creatinine ratio (Uβ2M/UCr), tubular reabsorption of phosphate (TRP), fractional excretion of uric acid (FEUa), and fasting urine glucose levels were measured and calculated. PRTD was defined as the presence of ≥1 abnormalities in the following criteria: (1) β2-microglobulinuria (tubular proteinuria): Uβ2M/UCr >1,000 mcg/g Cr; (2) phosphaturia: TRP <80%; (3) uricosuria: FEUa >15%; or (4) normoglycemic glycosuria: fasting urine glucose >25 mg/dL, while fasting plasma glucose <100 mg/dL. Logistic regression analysis was conducted to identify factors associated with PRTD among our HIV-infected adolescents.

Results: Between December 2016 and June 2017, 210 participants (140 HIV-infected and 70 healthy), with a median age of 17.8 years (interquartile range: 15.0-21.4 years), were enrolled. Half of them (50.0%) were male. Among HIV-infected adolescents, 70 (50.0%) were TDF users, of whom 35 were concurrently receiving protease inhibitors (PI)-based regimens. Almost all (98.6%) had World Health Organization (WHO) clinical stage 1-2, 124 (88.6%) had CD4 cell count ≥350 cells/mm3, and 116 (83.0%) had virologic suppression (HIV RNA <50 copies/mL) at enrollment. For proximal renal tubular function evaluations, β2-microglobulinuria was identified in 10 TDF users (14.3%), 4 non-TDF users (5.7%), and 1 healthy participants (1.4%) (P=0.01). However, phosphaturia (n=1; 1.4%), uricosuria (n=2; 2.9%), and normoglycemic glycosuria (n=1; 1.4%) were noted in only TDF users. Overall, PRTD was identified in 18 participants (8.6%), which was significantly higher among TDF users (n=13; 18.6%) compared with non-TDF users (n=4; 5.7%) and healthy controls (n=1; 1.4%) (P=0.001). Focusing on TDF users, the prevalence of PRTD was not different between those concurrently receiving PI-based (n=7; 20.0%) versus non-nucleoside reverse transcriptase inhibitor (NNRTI)-based regimens (n=6; 17.1%) (P=0.76). In the multivariable analysis among HIV-infected adolescents, TDF use (adjusted odds ratio: 3.6; 95% CI: 1.1-12.1) was significantly associated with PRTD, controlling for current WHO clinical stage, immunologic status, and virologic status.

Conclusions: PRTD is relatively common among our perinatally HIV-infected adolescents. TDF use is strongly associated with this co-morbidity. Routine evaluations of renal tubular function, particularly among TDF users, are necessary to promptly identify kidney function abnormalities in this population.
Height and timing of growth spurt during puberty in children and adolescents with perinatal HIV in Europe and Thailand

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Background: Children with perinatal HIV (PHIV) may experience delayed puberty and poor growth in comparison to normative populations. We explore factors associated with growth during puberty in children and adolescents with PHIV.

Materials & Methods: Data from 12 cohorts with routinely collected height data, in 11 European countries and Thailand, were included. Children with PHIV initiating ART aged 1-10 years on an NNRTI- or boosted PI-based regimen with height measures at ART initiation (baseline) and >8 years of age were included. Height-for-age z-scores (HAZ) were calculated using the WHO Growth Standard and 2007 growth reference.

SITAR (Super Imposition by Translation And Rotation) models, describing growth through adolescence using 3 parameters (mean height, timing and shape of the growth spurt), were applied with growth allowed to vary by baseline age, HAZ and their interaction (optimal model selected using AIC). Multivariate regression was used to explore characteristics (geographical region, year of ART initiation, initial regimen class, BMI z-score and WHO immunological status) associated with unexplained variation in these 3 growth parameters. The effect of being born outside the cohort country was explored in the subset of the cohort initiated ART with height close to the WHO reference regardless of age at ART start; there was a 1.6(95%CI 1.2,1.9) year delay in those with baseline HAZ<3 compared to baseline HAZ>1. Later growth spurts resulted in continued growth into later adolescence. In males with baseline HAZ<1 who started ART aged 6-10 years there was a trend towards later growth spurts than in those starting at younger ages. Children who initiated ART with height close to the WHO reference mean (HAZ≥-1) maintained a similar mean height to the reference throughout adolescence.

After controlling for baseline HAZ and age, children from Thailand were on average -3.3(-4.7,-1.9) cm shorter throughout adolescence but had a growth spurt at a similar time to adolescents from elsewhere. Females born abroad were -2.4(-3.9,-1.0) cm shorter and experienced an earlier growth spurt -0.3(-0.6,-0.04) years than those born domestically; there were no differences in males.

Conclusions: The delayed growth spurt observed in females who were stunted at ART initiation translated into continued growth in this group further into later adolescence, allowing females who were severely stunted to ‘catch-up’. Growth curves of children who were not stunted at ART initiation were similar to the mean WHO reference suggesting they grew at a similar rate to that expected in an uninfected population.

Long term growth after initiation of ART in children and adolescents with perinatal HIV in Europe and Thailand

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Background: Poor growth is associated with increased morbidity and mortality in children with HIV. Catch-up growth after starting antiretroviral therapy (ART) has been shown in numerous studies but long-term growth has not been well described. We describe long-term growth after ART initiation and associated factors.

Materials & Methods: Data from 12 cohorts in 11 European countries and Thailand which routinely collected height data were included. Children were eligible if they had perinatal HIV, initiated ART aged <19 years old on an NNRTI- or boosted PI-based regimen and had height available at ART initiation. Height-for-age z-scores (HAZ) were calculated using the WHO Growth Standard and WHO 2007 growth reference. Thai-specific growth reference data were used for the Thai cohort in sensitivity analyses.

A mixed-effects model was used to describe HAZ over time from ART initiation. Fractional polynomials modelled non-linear relationships and potential interactions (optimal model selected using likelihood ratio tests). Geographical region, year of ART initiation, initial regimen class, BMI z-score and WHO immunological status at ART initiation were also included. The effect of being born outside the cohort country (born abroad) was explored in sensitivity analyses of the subset of cohorts with >5% and <95% of children born abroad.

Results: Of 2679 children who initiated an eligible regimen, 1775(66%) had a height measurement at initiation; children without a height measurement were younger, more likely to be from Europe (other than UK/Ireland) and more likely to have been born abroad. Of those included 46% were male, 48% from UK/Ireland, 29% from Thailand, and 22% from elsewhere in Europe. At ART initiation median age was 7.4[IQR 2.8,11.0] years, HAZ -1.1[-2.3,-0.1] and 57% were severely immunologically compromised for age. Median follow-up after ART start was 6.8[3.8,10.0] years, with 22[10,38] height measurements recorded per child.

In multivariable modelling there was a four-way interaction between time on ART, sex and both age and HAZ at ART initiation (p<0.001). Children starting ART with a baseline HAZ of 0 maintained this score throughout follow up. Those who started ART with HAZ<0 experienced an initial gain; however, the magnitude of this gain decreased with increasing age at ART start. In the children with the largest initial gain (i.e. those age <5 with baseline HAZ<2 at ART start) the initial increase was followed by a decline in HAZ as they entered adolescence (age 10+ years).

In sensitivity analyses including 1044 children, 58% were born abroad. Children born abroad were shorter (adjusted mean difference in HAZ: -0.09 (95%CI -0.17,-0.01), p=0.025) than those born domestically. Similarly, children from Thailand (-0.29, (-0.37,-0.21), p<0.001) were shorter compared to those in Europe. Using Thai-specific reference data, this difference disappeared while interpretations of other parameters remained unchanged.

Conclusions: Age and height at ART initiation are strong predictors of growth after starting ART. While the largest initial gains in height were observed in children who started ART early with a low HAZ, falling HAZ scores during adolescence suggest these early gains may not be maintained and may be indicative of delayed puberty.

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A Complex Coexistence: Facilitators and Barriers for Pediatric HIV & Nutrition Integration in 4 Districts of Zimbabwe

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Background: Integration of HIV and malnutrition services is recognized as an important programmatic pathway for achieving accelerated progress towards 90-90-90 and Sustainable Development Goals among children, however, it is recognized that gaps remain to achieving this in practice. Zimbabwe has an HIV prevalence of 16.1% among women in antenatal care and Moderate Acute Malnutrition (MAM) and Severe Acute Malnutrition (SAM) rates among children under 5 of 1.6% and 1.4%, respectively. Our objective was to explore existing barriers and enablers to the
provision of quality integrated HIV and MAM/SAM services for children under 5 years.

Materials & Methods: We conducted a mixed-method health systems assessment at 20 public health facilities in 4 districts of Zimbabwe implementing the UNICEF ‘Supporting life-saving multi-sectoral interventions to prevent the escalation of malnutrition in Zimbabwe’ project. Facilities were selected using purposive stratified sampling based on level and type of services (SAM referral centres, tertiary and randomly selected primary care facilities). Structured questionnaires were used to document site level operational characteristics influencing provision of integrated HIV/MAM/SAM services. Retrospective health service data for HIV/MAM/SAM services provided to children under 5 years at selected health facilities were collected from Oct 2016-Oct 2017. Key stakeholder surveys were implemented among District Health managers, nurses and community-health workers to explore key themes among perceived facilitators and barriers to provision of integrated SAM/MAM/HIV services for children under 5 years.

Results: Serving an estimated catchment population of 42,760 children under 5, selected facilities diagnosed 82 HIV positive children; and 628 children with MAM/SAM from Oct 2016-Oct 2017. The most commonly treated conditions in children under five included acute respiratory illness, diarrhea and skin conditions. Per facility, an average of 7.7 health care workers (range 2-18) were trained in HIV services, compared to 4.4 trained in malnutrition services (range 1-8), with an average of 3.5 trained in both. Only 50% (6/12) of rural primary care facilities had all current HIV and nutrition guidelines available. There was no cost for HIV or malnutrition services at any site, however, average distance to referral facilities for SAM was 51 km. Facility stock outs of essential HIV testing commodities (30%; 6/20) and ready-to-use therapeutic foods for malnutrition (60%; 12/20) were documented. Key themes regarding barriers to provision of integrated HIV/MAM/SAM services included transport costs, consent to test children and community awareness of the relationship between HIV and malnutrition in children; key facilitators included integrated service outreach and strengthening of community-facility referral, defaulter tracing systems and outcome documentation.

Conclusions: Existing data indicate HIV and malnutrition are underdiagnosed in children under 5. Decentralization of policy to practice, health care worker capacity to provide integrated services and strengthening of commodity chains are required to improve quality of facility-based HIV/MAM/SAM service delivery. Community engagement, service outreach to reach the most vulnerable, and strengthening of community-facility linkages are central to increasing access and uptake of integrated HIV and malnutrition screening and treatment among children under 5 in high prevalence, low resource settings.

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Effect of caregiver training on the neurocognition of school-age siblings of preschool HIV-exposed uninfected target children: a Ugandan cluster randomized controlled trial

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Background: Early childhood development (ECD) programs typically combine healthy nutrition and cognitive stimulation in an integrated model. We separately delivered these two components in a clinical trial to evaluate their comparative effectiveness. This is the first study to evaluate whether older siblings of preschool target children benefit from training intervention for their HIV-infected mothers.

Methods: 210 school-age siblings (5-12 years old) in ECD intervention households with target children 2-3 years of age were evaluated on neurocognitive outcomes using the Kaufman Assessment Battery for Children (KABC), computerized Tests of Variables of Attention (TOVA), the Behavior Rating Inventory for Executive Function (BRIEF; parent) and an ADHD-R-IV questionnaire completed by the mother. Households from 18 geographic clusters in eastern Uganda were cluster-randomized to biweekly individualized sessions of either: 1) Mediational Intervention for Sensitizing Caregivers
Early age at ART initiation may mitigate educational delays associated with HIV

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Background: Education can support child survival, growth, development, and well-being and is a predictor of later life health. Educational outcomes are influenced by cognitive, behavioral, and social factors and chronic disease, but little is known about how growing up with HIV impacts educational outcomes in sub-Saharan Africa. We investigated educational delay, defined as being below expected school grade-for-age, in a cohort of school-aged children living with and without HIV in South Africa.

Methods: The cohort included 553 children living with HIV and 339 children without HIV enrolled at two sites: Empilweni Service and Research Unit (ESRU), Rahima Moosa Mother and Child Hospital and Perinatal HIV Research Unit (PHRU), Chris Hani Baragwanath Hospital, Johannesburg, South Africa. HIV-infected children were former participants in clinical trials and initiated ART at a median of 4.7 months of age (IQR: 2.0–9.6); 186 (33.6%) initiated ART >6 months of age and 367 (66.4%) ≤6 months of age. Study visits were scheduled every 6 months and visits occurred between ages 4.0 to 13.5 years between February 2013 and August 2017. Uninfected children were recruited from household members of participants or those attending services for routine health care. At each visit, caregivers reported the child’s current grade. Expected grade-for-age for each child at each visit was calculated based on the South African Schools Act 84 of 1996. We defined educational delay as the number of years the child was below their expected grade-for-age. Generalized estimating equation (GEE) models were used to examine associations between educational delay and HIV status, age at ART initiation, and other factors.

Results: Overall, 51.5% of children living with HIV ever had educational delay (i.e. 1 or more years below expected grade-for-age) compared to 31.6% of uninfected children (p<0.01). More children living with HIV were ever 1 year (41.4% vs. 27.7%), 2 years (6.9% vs. 3.2%), or ≥3 years (3.3% vs. 0.6%) behind their expected grade-for-age compared to uninfected children (p<0.01). After adjusting for sex, site, and caregiver education, children living with HIV were more likely to have educational delay than uninfected children (adjusted OR [aOR]: 2.30; 95%CI: 1.74–3.06). Educational delay was more common in boys (aOR: 1.51; 95%CI: 1.17–1.96) and...
less common with more maternal education (aOR: 0.74; 95%CI: 0.57–0.95). Stratifying by age at ART initiation, 61.1% who initiated ART >6 months ever had educational delay compared to 46.6% who initiated ≤6 months (p<0.01). Children who initiated ART >6 months (aOR: 2.59; 95%CI: 1.79–3.74) and who initiated ≤6 months (aOR: 2.00; 95%CI: 1.42–2.82) were more likely to have educational delay than uninfected children, adjusted for age, sex, site, and caregiver education.

Conclusions: High rates of educational delay were observed in a cohort of school-aged children in South Africa, with significantly higher rates among children living with HIV who started treatment within the first 3 years of life. Initiation of ART before 6 months of age partially mitigated the adverse HIV effect, although it remains unclear if this was due to biological factors, social factors, or other confounders.

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Functional and structural brain imaging findings support early ART initiation in vertically transmitted HIV

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Background: There is evidence of HIV status affecting neurocognitive processing, including executive function, in adolescents, but little is known of the corresponding neural correlates during this important developmental stage. Additionally, age of ART initiation has been associated with lower health outcomes in HIV positive children. This study investigates working memory related brain activity in South African HIV positive and negative adolescents, while also considering age of ART initiation.

Methods: Sixty four perinatally infected adolescents (ages 9-12) and 20 demographically matched controls (ages 9-13) underwent functional magnetic resonance imaging (fMRI) while completing the n-back working memory task with alternating 1-back and 0-back blocks. Whole brain analyses comparing the two groups in working memory conditions were run using SPM12.

Results: At an uncorrected p value threshold of 0.001, differences were detected, with the HIV positive group showing decreased activation during working memory conditions in the following regions: left superior temporal gyrus, left pre and postcentral gyri extending to the insula, bilateral hippocampus, putamen, and mid cingulum. When the HIV positive group was stratified according to age of antiretroviral treatment initiation, those who started treatment after the age of two showed less activation during task conditions vs rest in the mid cingulum, left inferior parietal gyrus, as well as right frontal, bilateral thalamic, and superior temporal regions, extending into the right insula. When these regions were tested for structural group differences, the mid cingulum, right inferior frontal gyrus, right insula, and right thalamus were found to be smaller in the group with the later age of ART initiation, in terms of cortical thickness, surface area, or regional volume.

Conclusions: Regional differences between adolescents living with HIV and healthy controls are consistent with impairments in structures involved in executive function. These data also support early ART initiation in perinatally infected individuals.

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Antiretroviral therapy (ART) interruption is associated with reduced cortical structures than uninterrupted ART at age 5 years in HIV-infected children on early ART.

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Introduction: ART interruption (ATI) has been studied in HIV-infected (HIV+) children and adolescents and may occur due to poor adherence, stock-outs and ART intolerance. Although ATI in early treated children may not affect immune health, neurocognition and quality of health in the short term, its effect on brain development is not clear. Here, we investigated the effect of ATI on brain morphometry - cortical thickness (CT) and local gyrification indices (LGIs) – in healthy 5 year-old children who initiated ART before 18 months of age.

Method: MRI scans were acquired from participants in the Children with HIV Early Antiretroviral therapy (CHER) trial follow-on study according to protocols approved by the ethics committees of the Universities of Cape Town and Stellenbosch. FreeSurfer software v6.0 (http://freesurfer.net/) was used for automated reconstruction and segmentation. Whole-brain CT and LGIs – a measure of cortical folding - were compared between HIV+ children and uninfected controls (HIV-), and between children with ATI who restarted when CD4% <25% or CDC severe Stage B and children on continuous ART using a linear regression model controlling for sex, age at scan and age at ART initiation.

Result: Forty-six HIV+ children (24 ART-interrupted – interruption age (median ± IQR = 49.14 ± 36.18 weeks), ART initiation - median ± IQR = 9.14 ± 2.93 weeks, 22 ART-uninterrupted, ART initiation - median ± IQR = 11.86 ± 22.14 weeks) and 18 age-matched uninfected controls (9 boys) (age: mean ± std. = 5.58 ± 0.31 years) were included. HIV+ children showed thicker cortex than controls in bilateral frontal and post central regions and lower gyriation in bilateral anterior cingulate, superior parietal and left superior frontal regions. ATI had thinner cortex than continuous therapy in a left lateral occipital (cluster size: 812.30 mm2) region. ATI showed lower gyriation than continuous therapy in bilateral superior parietal (cluster size: left – 2970.70 mm2, right – 865.97 mm2) regions (figure 1).

Conclusion: ART interruption at a young age may affect the development of cortical structures, leading to parietal gyriification decrease and occipital cortical thinning at age 5 years. The neuropsychological implications of these effects in HIV+ children requires further investigation.

Ongoing white matter alterations in HIV infected and HIV exposed children: a DTI study at 9 years.

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Background: An increasing number of perinatally HIV-infected (HIV+) infants are growing up on ART. Examination of diffusion tensor imaging (DTI) measures over time can identify the impact of HIV exposure, infection and/or treatment on white matter (WM) maturation. DTI studies report WM regions with reduced fractional anisotropy (FA) and increased mean diffusivity (MD) in HIV+ children on ART, which point to demyelination and/or axonal damage.

In the Children with HIV Early Antiretroviral therapy (CHER) substudy, we reported persistent WM abnormalities in the inferior/superior longitudinal fasciculus (ILF/SLF), inferior fronto-occipital fasciculus (IFOF), forceps minor and corticospinal tract (CST) at ages 5 and 7, despite early ART. Here, we further investigate voxelwise group differences of MD and FA in this cohort at age 9.

Methods: Participants are 51 HIV+ and 36 HIV-infected/EX (42 Females; mean age:sd: 9.4±0.4; 11 Cape Coloured/76 Xhosa) scanned in Cape Town, South Africa on a 3T Siemens Skyra MRI scanner (Erlangen, Germany).

Structural T1-weighted images and two DWI sets with opposite phase encodings were acquired. Data were processed using TORTOISE (version 3.1.0) and AFNI. Voxelwise group comparisons of FA and MD were performed in FSL using a general linear model (GLM) with gender, age and ethnicity as confounders. Axial diffusivity (AD), and radial diffusivity (RD) were extracted for each subject in surviving clusters (threshold pth=0.005 and α=0.05)
and compared between groups using a student’s t-test.

**Results:** HIV+ children demonstrated lower FA in bilateral CST, right IFOF and corpus callosum (CC), and higher MD bilaterally in CST and ILF, left IFOF and right anterior thalamic radiation (ATR). Differences were largely attributable to higher RD.

**Conclusions:** Our results indicate that despite early ART, persistent WM alterations in the IFOF, ILF and CST are present from age 5 to 9. Furthermore, although we did not observe CC abnormalities at 5 or 7 years, microstructural abnormalities in CC at 9 years suggest early ART may not prevent ongoing damage.

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**White matter abnormalities in children with spastic diplegia due to HIV Encephalopathy or Cerebral Palsy: is there a difference?**

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**Background:** HIV encephalopathy (HIVE) is one of the most common primary paediatric HIV-related Central Nervous System disorders, with about 60% of these children presenting with spastic diplegia (HIV neurology clinic, Cape Town, South Africa). The gait pattern of children with spastic diplegia secondary to HIVE shows similarities to spastic diplegic cerebral palsy (CP), including stiff knee gait and equinus ankle. However, the etiology is different and this may be reflected in brain microstructural differences between children with HIVE and CP. The aim of the study is to determine white matter (WM) differences between children with spastic diplegia due to HIVE and due to CP using diffusion tensor imaging (DTI). In addition, associations of DTI parameters to knee flexion/extension range of motion (ROM) and maximum ankle dorsiflexion parameters were investigated in these two study-cohorts.

**Materials & Methods** Twenty-seven children with HIVE (mean age: 8.7±2.2 years, 11 boys) and 14 children with CP (mean age: 8.7±2.1 years, 9 boys) were recruited from Red Cross War Memorial Children’s Hospital, Tygerberg Hospital and special needs schools in Cape Town, South Africa. DTI images were acquired on a 1.5 T Phillips scanner located at Red Cross War Memorial Children’s Hospital and were processed using TORTOISE. DTI parameter maps (FA and MD) were co-registered to an MNI pediatric template using AFNI. To identify regions showing differences between groups, voxelwise comparisons were performed using FSL-randomise. Type I error was controlled by cluster size correction at p<0.01 using AFNI-phSim [5]. Gait parameters were recorded using three-dimensional gait analyses (3DGA), including sagittal plane knee flexion/extension ROM and maximum ankle dorsiflexion parameters. Mean DTI parameters in each cluster showing significant group differences were extracted and associations with gait parameters examined in the HIVE and CP-groups separately using Pearson’s correlation.

**Results:** Based on the DTI, voxelwise analyses revealed lower FA and higher MD in children with HIVE within right (R) corticospinal tract (RCST) compared to children with CP. Conversely, children with CP showed reduced FA in children with CP compared to children with HIVE in 3 regions—R anterior thalamic radiation (ATR), body of corpus callosum (BCC) and splenium of corpus callosum (SCC). Higher MD was also seen in left (L) ATR and l superior longitudinal fasciculus (LSF) in children with CP. In the HIVE-group no significant correlations were found between the DTI parameters and gait parameters, while in the CP-group mean FA in the BCC cluster was associated with both knee flexion/extension ROM (r=0.79; p=0.001) and ankle maximum dorsiflexion (r=0.67; p=0.009).

**Conclusions:** Children with HIVE and spastic diplegia might present with similar clinical features to children with spastic diplegic CP, differences in WM microstructure are evident. The HIVE-group present with WM alterations in RCST, which is involved in motor control function and may relate to the typical spastic diplegic gait pattern, though no associations were found with the selected gait parameters. This in contrast to the CP-group, who showed abnormalities in ART, BCC, SLF and SCC and an
association between BCC and stiff knee gait and equinus ankle parameters.

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Disability in HIV-Infected Children Attending an Urban Paediatric HIV Clinic in South Africa

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Background: With the success of evolving antiretroviral therapy (ART), human immunodeficiency virus (HIV) has become a chronic condition. Results from studies conducted in Malawi and South Africa suggest that the prevalence of disability in young children infected with HIV is very high. Developmental delay and HIV encephalopathy has been documented in infants infected with HIV, however less is known about the challenges experienced by slightly older children and what rehabilitation services they may require. This study aimed to investigate the extent of disability among a group of HIV infected children, between two and ten years of age, in South Africa and whether they are being referred and accessing rehabilitative services.

Materials and Methods: A cross-sectional study was conducted at an HIV clinic in Johannesburg. Caregivers were interviewed about their child, using the Ten Question Screen for Disability Questionnaire (TQSD). They also completed a questionnaire on medical history, services referred to and accessed and socioeconomic status (SES). Clinical data and anthropometric data were recorded from the child’s clinic file. Data were evaluated for omitted values and outliers. Counts were used to establish the prevalence of disability among the cohort of HIV-positive children. WHO Anthro (version 3.3.2) was used to calculate anthropometric Z-scores. Data were analysed using STATA 14 (DataCorp) USA and Microsoft Excel 2013. Levene’s test was used to assess quality of variances. The Chi-square test, Fisher’s Exact test, t-Test and Mann–Whitney U test were used to calculate the significance of association between disability and clinical and socioeconomic factors. A logistic regression was used to analyse any factors significantly associated with the presence of disability.

Results: The caregivers of 200 children between two and nine years were interviewed. Ninety five percent of children were on ART and the majority were virally suppressed. Of the 200 children, 101 (50.5%) experienced disabilities, 61 (58.4%) of those had more than one co-existing disability. When analysing the distribution of different types of disability; developmental delay was the most frequently reported difficulty (27%). The next most common were cognitive and behavioural (20.5%) followed by communication difficulties (16.5%). Of the children who reported disability only 46% had been referred for an appropriate rehabilitation assessment even though these services were available. Previous diagnosis of tuberculosis (TB) (p=0.003), lower respiratory tract infections (LRTI) (0.049) and low pre-treatment CD4% (p=0.021) were found to be factors associated with disability.

Conclusion: This study confirms the results of previous work done in sub-Saharan Africa. The prevalence of disability in children with HIV is high even when access to ART is relatively good. These children are not accessing appropriate support services. Government policy and clinic practice need to shift their focus of management of children living with HIV, in order to integrate services that can assist children to reach their developmental potential and improve their quality of life. Screening with the TQSD is quick and easy and could be easily integrated into clinic visits.
Probability of depression among HIV-infected and HIV-exposed uninfected adolescents in Thailand and Cambodia

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Background: HIV is a well-known risk factor for depression. Depression impacts overall well-being, personal functioning and behavioural issues in adolescents. This study sets out to investigate the prevalence of depression in a longitudinal cohort of Thai/Cambodian HIV-infected and HIV-exposed uninfected adolescents in order to inform the need for performing depression screening tests in routine HIV adolescent care.

Methods: Adolescents with perinatally acquired HIV (PHIV) and HIV-exposed but uninfected (HEU) and HIV-unexposed (HUU) adolescents in Thailand and Cambodia, aged > 10 years were followed in the PREDICT and RESILIENCE longitudinal cohort studies. Depression screening tests, the Child Depression Inventory (CDI) for adolescents aged ≤ 15 years and the Center for Epidemiological Studies Depression Scale (CES-D) for those > 15 years were performed annually. The prevalence of persistent positive screening scores as defined by CDI ≥ 16 or CES-D ≥ 16 for depression in at least 2 consecutive visits was determined. Risk factors associated with persistence of depression were analyzed, including age, gender, nationality, WISC/WAIS (Wechsler Intelligence Scale for Children / Wechsler Adult Intelligence Scale) processing speed, viral load (VL), CD4 count, and primary caregiver.

Results: A total of 422 adolescents were included for analyses with 211, 92 and 199 adolescents in the PHIV, HEU and HUU groups respectively. Two-hundred and fifty-one (59%) were male. Median age was 14.9 years in PHIV compared to HEU (13.1) and HUU adolescents (13.3). Two-hundred and sixty-nine (61%) were Thai. For PHIV adolescents, median (IQR) CD4 at baseline was 766 (582-970) cells/mm3 with 88% having viral loads < 50 copies/mL.

Depression screening tests were done at 2 visits among 282 (67%) and 3 visits among 140 (33%) annually. Prevalence of abnormal depression screening tests at ≥2 consecutive visits was 18%, 14% and 10% (p = 0.18) in the PHIV, HEU and HUU groups respectively.

The older the adolescent, the more likely they were to have positive depression screening scores (aOR 1.27, p <0.001). Gender, HIV status, primary caregiver and nationality did not affect risk of having positive screening tests. Among the 62 adolescents with abnormal screening tests, 25 were by CDI and 37 by CES-D. Median (IQR) onset of depression was at age 16.9 (14.3-18.6) years. Cases scored a median of 20 (17-21) and 23 (19-27) in the CDI and CES-D groups respectively. There was no difference between rates of depression between Thai and Cambodian children (17% vs 11% p=0.12). Adolescents with positive depression screening tests had lower processing speed indices than those that did not; however, there was no difference in VL suppression (89% vs 88% respectively). Median (IQR) processing speed indices in adolescents with and without depression were 91 (91-114) vs 101 (79-104) respectively (p=0.001).

Conclusions: There is similar risk of depression in PHIV and HEU compared to HUU adolescents. Screening and managing depression at follow-up health visits may improve overall well-being and personal functioning in this population.
Adverse childhood experiences and associations with mental health, adherence and viraemia among HIV-positive mothers in Cape Town, South Africa

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Background: Adverse childhood experiences (ACE) can result in a negative trajectory of poor physical and mental health into adulthood. Among women, ACE may later be associated with poor parenting practices, with negative effects on child development. However, there are few data exploring ACE among HIV-positive women in low- and middle-income settings. We examined reported ACE among HIV-positive mothers; and explored associations with mental health, antiretroviral therapy (ART) adherence and viral load (VL) in Cape Town, South Africa.

Materials & Methods: ART-eligible pregnant women entering antenatal care were recruited and followed through delivery; women who opted to breastfeed were followed through 18 months postpartum as part of an intervention study evaluating strategies for delivering HIV care. Women were asked to return for one additional study visit between 36–48 months postpartum. At this visit, we administered the World Health Organization (WHO) Adverse Childhood Experiences International Questionnaire and summed categories of reported ACE (maximum=13). We used multivariable logistic regression to explore associations between ACE scores and each of past-week depressive symptoms (Edinburgh Postnatal Depression Scale score ≥13); past-year risky alcohol use (Alcohol Use Disorders Identification Test – Consumption score ≥3); past-year IPV (any violence reported on the WHO Violence Against Women questionnaire); self-reported suboptimal adherence (missed ART dose(s) on ≥1 day during the past 30 days); and elevated VL (Abbott RealTime HIV-1; ≥50 copies/mL).

Results: A total of 353 women (mean age: 32.1 years; mean time postpartum: 44.1 months) participated between May 2017–April 2018. Depressive symptoms, risky alcohol use and IPV were reported by 4%, 14% and 4% of women, respectively; 29% reported suboptimal adherence, and 44% had elevated VL. Women reported experiencing a median [inter-quartile range] of 2 [1-3] ACE categories. The most frequently reported ACE categories were parental separation/divorce and witnessing community violence, each reported by 52% of participants. Physical, emotional and sexual abuse during childhood were reported by 7%, 6% and 4% of women, respectively; and emotional and physical neglect by 22% and 6%, respectively. After adjustment for sociodemographic factors, a higher ACE score was strongly associated with depressive symptoms [adjusted odds ratio (aOR) for each additional ACE category reported: 1.68; 95% confidence interval (CI): 1.33-2.12], risky alcohol use (aOR: 1.20; 95% CI: 1.03-1.40) and IPV (aOR: 1.40; 95% CI: 1.12-1.75). Similarly, a higher ACE score was strongly associated with suboptimal adherence (aOR: 1.25; 95% CI: 1.10-1.43) after adjustment for sociodemographic factors and time since ART initiation; the association between ACE score and elevated VL did not reach statistical significance (aOR: 1.11; 95% CI: 0.99-1.26). Results were unchanged when suboptimal adherence and elevated VL were defined as missed doses on ≥2 days and VL ≥1000 copies/mL, respectively.

Conclusions: Poor mental health, suboptimal adherence and elevated VL are prevalent in this population, and appear to be associated with increased adversity during childhood. These novel data suggest that the negative trajectory initiated by ACE may include adverse effects on ART treatment outcomes during adulthood, and that a better understanding of the impact of early adversity on adult ART outcomes is needed.
Accelerated epigenetic aging in perinatally acquired HIV infected South African adolescents is related to altered development of brain structures

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Objective: We recently demonstrated that vertical infection with the Human Immunodeficiency Virus-1 (HIV) is associated with accelerated aging effects in young adolescents according to a highly accurate epigenetic biomarker of aging known as the epigenetic clock. These epigenetic changes also accompanied poorer attention, working memory, executive functioning, and processing speed. It has not yet been investigated whether epigenetic age acceleration in adolescents living with HIV impacts brain development and neurostructural differences.

Design: Observational study of PHIV and HIV-uninfected adolescents enrolled in the Cape Town Adolescent Antiretroviral Cohort (CTAAC) Study.

Methods: The Illumina EPIC array was used to generate blood DNA methylation data from 204 PHIV and 44 age-matched, uninfected (HIV-) adolescents aged 9 to 12 years old. The epigenetic clock software and method was used to estimate two measures of epigenetic age acceleration. Each participant completed Diffusion tensor imaging (DTI) and structural brain magnetic resonance imaging (MRI) to determine fractional anisotropy (FA), mean diffusivity (MD), gray and white matter volumes, cortical thickness and cortical surface area. We made backward elimination stepwise multiple regression models in ‘R’ for brain region surface area, cortical thickness, volume, FA, and MD values, to determine the amount of variance caused by the interaction of HIV status and epigenetic age acceleration.

Results: The interaction of HIV status and epigenetic age acceleration accounted for significant variance in FA, MD, gray and white matter volumes, cortical thickness and cortical surface area in a number of brain regions. Cortical surface areas with the most explained variance were the left hemisphere total white matter surface area (R2=0.106), anterior cingulate area (R2=0.117), middle frontal lobe area (R2=0.127). Cortical thickness with the most explained variance was the left hemisphere middle temporal lobe (R2=0.056). Left hemisphere cortical volume demonstrated the most explained volumetric variance (R2=0.074). Variance in white matter microstructure as measured FA and MD were most significant in the internal capsule (R2=0.128) and the posterior corona radiata (R2=0.1).

Conclusions: Overall, our results indicate that epigenetic age acceleration in blood can be observed in adolescents as young as 9-12 years and that these epigenetic changes accompany poorer cognitive functioning. The interaction of HIV status and epigenetic age acceleration accounted for significant variance in FA, MD, gray and white matter volumes, cortical thickness and cortical surface area in a number of brain regions, suggesting that epigenetic age acceleration in adolescents living with HIV impacts brain development and neurostructural differences.

Community-based HIV-free survival in high prevalence settings after introduction of Option B+: Results from Lesotho

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Background: Population-based HIV-free survival (HFS) at 18-24 months among HIV-exposed infants (HEI) in high prevalence settings with Option B+ is largely unknown. We conducted a community-based survey to determine outcomes of HEI at 18-24 months in Lesotho.

Methods: From November 2015 to December 2016, we conducted a survey among households with a child born 18-24 months before study initiation.
Facility catchment areas from 25 health facilities in Butha-Buthe, Maseru, Thaba-Tseka and Mohale’s Hoek districts were randomly selected using probability proportional to size sampling. Consecutive households were visited and eligible consenting caregivers were enrolled. Rapid HIV antibody testing was performed for mothers of unknown HIV status (never tested or HIV-negative > 3 months prior) and children of HIV-positive or unknown status mothers. Mortality information for mothers and children who died were captured. Categorical variables were summarized by frequencies and proportions in each category. Continuous variables were summarized using means and standard deviations or medians and interquartile range. The difference in survival between sub-groups of the sample was determined using the log-rank test. Comparisons included HIV-unexposed versus HIV-exposed children.

Results: Of the 11,169 households visited, 2,190 were eligible and 1,852 (84.6%) were enrolled. Of the 374 women documented to be on antiretroviral treatment, 36% (135/374) started ART before ANC and 88% (329/374) were still on treatment at the time of the study. The mother-to-child HIV transmission rate was 5.7% [95% CI: 4.0–8.0]. The mortality rate was 2.6% [95% CI: 1.6–4.2] and 1.4% [95% CI: 0.9–2.3] among HIV-exposed and HIV-unexposed children respectively. HFS was 91.8% [95% CI: 89.2 – 93.8] among HEI. Disclosure of mother’s HIV status (aOR = 4.9, 95% CI: 1.3 – 18.2) and initiation of cotrimoxazole prophylaxis in the child (aOR = 3.9, 95% CI: 1.2 – 12.6) were independently associated with increased HIV-free survival while child growth problems (aOR = 0.2, 95% CI: 0.09 – 0.5) was independently associated with reduced HIV-free survival.

Conclusion: Even with Option B+, Lesotho has not reached elimination of mother-to-child transmission. With mortality of HIV-exposed children twice that of HIV-unexposed children, HIV-free survival was only 91.8%. Disclosure of maternal HIV status was associated with survival.

Birth outcomes and HIV-free survival with Option B+ in Lesotho: Results from an observational prospective cohort study.

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Background: Combination antiretroviral therapy (cART) reduces mother-to-child transmission of HIV and improves maternal health. Since introduction of option B+, there are scant data on birth outcomes of HIV-exposed compared to unexposed infants. We assessed birth outcomes and six-week HIV free survival among HIV-exposed infants (HEI) and HIV-unexposed infants (HUI).

Methods: 941 HIV-negative and 653 HIV-positive pregnant women were enrolled in an observational cohort to evaluate effectiveness of universal maternal cART (Option B+) rolled out within routine programs in 13 health facilities in Lesotho. Birth outcomes included infant birth weight (IBW), maturity, congenital anomalies, and mortality. Infant HIV birth testing by DNA PCR within two weeks of birth was introduced at study sites alongside routine six-week testing. Data were analysed to determine birth outcomes, HIV transmission, and HIV-free survival rates at six weeks.

Results: HIV-positive women were older, 28.7 vs. 24.4 years (p<0.001) and presented for antenatal care earlier at 23 weeks vs. 25.3 weeks gestation (p<0.001). Mean IBWs were similar: 3.0 kgs for HEIs vs 3.1 kgs for HUI. HEI were more likely to be premature, 8.3% vs. 4.0% (p=0.001). Neither Age (median age: 26 vs 25) nor parity (median: 1 vs 1) was associated with prematurity. No differences in stillbirths or congenital anomalies were noted. Six infants were HIV-infected by six weeks: cumulative HIV transmission was 0.9% (N=4) at birth (95%CI: 0.25%-2.36%) and 1.03% (N=6) (95%CI: 0.38%-2.23%) by six weeks. Infant mortality was 4.4% and 4.3% for HUI and HEI respectively (p=0.93). The estimated six-week HIV free survival was 91.5%
Postnatal transmission or rebound of in utero HIV infection treated by ARVs in maternal breastmilk?

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Abstracts

Results: An HIV-exposed infant had indeterminate NAAT results on day 1, 7 and 22 of life and negative NAAT results on day 15, 28, 64, 106, 148, 232, and 324. VL assays at these time points were target not detected (TND). The mother initiated efavirenz, tenofovir and emtricitabine 80 days prior to delivery and had low VL during follow-up (range <20-1630 copies/ml). The infant was breastfed and given daily nevirapine prophylaxis until 43 days of age. At age 12 months (day 357), 18 days after breastfeeding cessation, the child presented with pyrexia, tachycardia, tachypnoea and weight loss. At this time the NAAT was positive and plasma VL >10 million copies/ml, confirmed 3 days later. The child’s virus was a phylogenetic match to the mother and no drug resistance was detected. Lopinavir/ritonavir-based ART was started and VL declined rapidly. Tests on a stored child plasma sample taken at 8 months detected 0.29mg/L efavirenz (therapeutic mid-dose interval 1.0-4.0mg/L). Two child samples from the first month of life tested using an in-house nested PCR method optimised to detect low levels of HIV DNA yielded weak positive results.

Background: Prompt initiation of antiretroviral therapy (ART) for infants diagnosed with HIV is strongly recommended. Diagnostic confirmation is important as committing children to life-long ART carries serious health and social implications.

Methods: As part of screening for early treatment studies at Rahima Moosa Mother and Child Hospital in Johannesburg, South Africa, blood was collected from HIV-exposed newborns and tested at the national laboratory with a standard Roche diagnostic nucleic acid amplification test (NAAT). Positive or indeterminate tests were followed up with repeat NAAT (Roche COBAS®Ampliprep/COBAS TaqMan® HIV-1 Qualitative Assay v2.0) and viral load (VL) assays (Roche COBAS®Ampliprep/COBAS TaqMan® HIV-1 Test v2.0, range 20-10 million RNA copies/ml). We describe an unusual trajectory of Results for two cases.

Conclusions: A low HIV transmission rate by six weeks was found among mother-infant pairs enrolled in a universal cART prevention of mother-to-child transmission program, though there were higher rates of prematurity; six-week survival among HIV-exposed infants was comparable to HIV-unexposed infants. It will be important to explore if this trend continues at 12 months and 24 months.
and perhaps even treated, intrauterine infections. These cases raise the importance of repeat testing of HIV-exposed breastfed infants through to after complete weaning.

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HIV mother-to-child transmission in Cameroon: Early infant diagnosis positivity rates by entry point and key risk factors

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Background: Prevention of mother-to-child transmission (PMTCT) programs aimed at reducing pediatric HIV infections are frequently assessed by the MTCT rate collected from PMTCT entry points, but this misses positivity rates in other entry points. Using the opportunity of the introduction of point of care early infant diagnosis (POC EID) in Cameroon, we extended infant HIV testing to several new entry points of health facilities. We assessed HIV positivity by entry point and other key risk factors.

Methods: A cross-sectional study nested within the POC EID project implemented in four priority regions was conducted in 58 health facilities of varying levels. Clinical history of the mother-baby pair or assessment of HIV status of the mother were used as eligibility criteria of infants. In each health facility, all healthcare entry points were considered and categorized as either a PMTCT entry point or a non-PMTCT entry point. Eligible infants presenting to these facilities between December 2016 and December 2017 were tested by POC EID. Variables including demographics, antiretroviral use, and breastfeeding history were extracted from the EID request form. Data were analyzed using multivariate analysis with backward elimination (p>0.20).

Results: Overall, 2,254 HIV-exposed infants were tested using POC EID as first HIV diagnosis. The sex ratio was 1.03 and the median age at blood sample collection was 7.3 weeks (IQR [6.3;19.0]). The main entry points were PMTCT (48.7%), immunization unit (14.3%), Pediatric ward (13.8%). Out Patients Department (6.5%) and maternity ward (6.5%). Of the 2,254 infants tested, 8.7% (197/2,254) were HIV-positive. This rate varied according to entry points (outpatient department, 19.2%; emergency/pediatric ward, 17.7%; PMTCT/antiretroviral treatment (ART), 5.7%; and maternity/antenatal care, 3.5%). In univariate analysis, positive cases were more likely to be found at non-PMTCT entry point, among females, and infants delivered to HIV-positive women who received incomplete ARVs for PMTCT. In multivariate analysis, risk of being HIV-positive was higher when the infant was found at non-PMTCT entry point (OR:2.09; 95%CI: 1.47-2.99; p<0.001), was on mixed feeding mode (OR: 3.74; 95%CI: 2.43-3.47; p<0.001).

Conclusion: Less than half of the yield (47.0%) came from PMTCT as an entry point. EID positivity rates were highest in non-PMTCT entry points and for HIV-exposed infants who had key risk factors for transmission. Strengthening testing in non-PMTCT entry points and more closely tracking these rates may efficiently help to address missed opportunities of PMTCT programs and link more children into ART care.

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Efficacy and Safety of a reduced 2-weeks post-exposure prophylaxis with Zidovudine for HIV-1 exposed infants with low transmission risk

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Antiretroviral prophylaxis for infants of perinatally HIV infected (PHIV) women with drug resistance

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Background: Due to a lifetime of antiretroviral (ART) exposure and often difficulties with adherence, perinatally HIV infected (PHIV) women may be multidrug-resistant once of child-bearing age. However, there are no specific guidelines for the ART prophylaxis of infants born to drug-resistant mothers. The objective of this study was to describe the ART resistance profiles of PHIV women, and specifically, to the drugs recommended for the prophylaxis of HIV-exposed newborns.

Methods: Clinic records from the Centre Maternel et Infantile sur le SIDA (CMIS) mother-child cohort in Montreal, Canada, were reviewed to identify all pregnancies among PHIV women previously followed as children at two tertiary care centers in Montreal, Quebec. Drug resistance was identified using cumulative HIV-1 mutations identified by Virco Type HIV-1 Virtual phenotype (from all available on record), and classified according to the HIV-resistance interpretation algorithm (2011 Agence nationale de recherche sur le SIDA) consensus technique.

Results: Out of 23 pregnancies from among 12 PHIV women, there were 17 live births (5 terminations, and 1 miscarriage.) At the first prenatal visit, 71% had a detectable viral load, 53% were on ART, and 35% were immunosuppressed (absolute CD4 count <200 cells/mm3). While all were prescribed ART during pregnancy, at the time of delivery, 41% continued to have a detectable viral load, and 29% remained immunosuppressed. Cumulative drug resistance profiles were available for 10/12 women. All were resistant to zidovudine (ZDV) and lamivudine (3TC), 8/10 were also resistant to nevirapine (NVP), and 4/10 harbored mutations to protease inhibitors. In the 7 cases determined to be at high-risk of transmission due to detectable viral load at delivery, combination ART (empiric HIV therapy) was used for prophylaxis in the newborns;
specific combinations included AZT and 3TC alone (1), or in combination with raltegravir (3), nelfinavir (1), lopinavir/ritonavir (1) or NVP (1). None of the infants were infected.

**Conclusion:** The majority (80%) PHIV women in the CMIS cohort were resistant to all of the drugs currently recommended for neonatal prophylaxis for prevention of perinatal HIV transmission. While the risk of transmission of drug resistant virus is not clear, these results suggest that for infants of PHIV women at higher risk of transmission due detectable viral load, alternatives to the currently recommended regimens for newborns may be necessary.

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**The vaginal microbiome of HIV-infected pregnant mothers: associations with local inflammation and gestational age at delivery**

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**Background:** Bacterial vaginosis is a known risk factor for preterm birth. In spite the high rate of PTB experienced by HIV-infected mothers, few data are available about the vaginal microbiome of HIV-infected women during pregnancy. We sought to describe the microbiome in a group of HIV-infected pregnant women and explore associations with local cytokine environment and gestational age at delivery.

**Materials and Methods:** A prospective observational multi-site study. Vaginal and cervicovaginal fluid (CVF) were obtained using swabs and menstrual soft cups from HIV-infected and uninfected mothers (Exclusion criteria: <350 cells/mm³, multiple or in-vitro pregnancy and injecting drug user) at 3 time points (12-22, 23-26, 27-31 weeks). MiSeq sequencing of 16S rRNA gene amplicons was used to characterise the vaginal microbiome. Multiplex chemiluminescent assays were used to measure CVF cytokine concentrations. Multivariate modelling was performed to explore associations with bacterial genus/species, CVF cytokine concentrations and clinical data.

**Results:** HIV-infected mothers (n=53) had a median age of 35, 81% were of Black ethnicity and 14% had PTB. In comparison, HIV-uninfected mothers (n=30) had a median age of 33 and 50% were Caucasian. HIV-infected mothers delivering at term had higher abundance of Gardnerella (18% versus 3% p=0.003) and Prevotella genera (4% versus 0.1% p=0.002) and lower proportions of Lactobacillus species (70% versus 93% p=0.009) compared to uninfected mothers. The predominant vaginal community state type (CST) of HIV-infected pregnant women was III (L. iners dominant) 55% (n=23), 20% (16) were CST IV (high diversity, anaerobic), 13% (7) were CST I (L. crispatus dominant) and 2% (1) were CST II (L. gasseri dominant).

Amongst HIV-infected women, PTB was associated with increased proportions of anaerobes: Gardnerella, Peptoniphilus, Aerococcus, Gordinobacter (p<0.0001), Megasphaera (p=0.02) and Prevotella species (p=0.03) compared with term birth. Bi-directional switching of CST type during the second trimester between IV to III was associated with lower gestational age at delivery (p=0.007). Matching CVF cytokine data were available for 79 of the 117 vaginal microbiome samples. Sequence read counts of CST IV associated anaerobes were positively correlated with higher concentrations of CVF proinflammatory cytokines: IFNγ (Gardnerella spp., Atopobium vaginae and Prevotella spp., p<0.02); IL-1β (Gardnerella spp., Atopobium vaginae, Prevotella spp. and Snaethia spp., p<0.0001); IL-8 (Atopobium vaginae and Prevotella spp., p<0.01) and TNFα (Gardnerella spp., Atopobium vaginae, Prevotella spp. and Snaethia spp., p<0.03). Within this small group, no associations between cytokine concentrations and gestational age at delivery were observed.

**Conclusion:** Presence of diverse bacterial communities within the vaginal microbiota in HIV-infected mothers during the second trimester is associated with PTB. The associated local proinflammatory cytokine profile may reflect the pathogenic contribution of these organisms to the early trigger of labour.
Factors Associated With non-Viral Suppression in a Multi-Country Cohort Study of HIV-Infected Women on Life-Long ART: US-PEPFAR PROMOTE Study


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Background: Despite the rapid scale up of lifelong combined Antiretroviral therapy (cART) also known as Option B+ in sub-Saharan Africa; barriers to achieving the UNAIDS 2020 strategy regarding the 3rd ‘90’ persist. There is paucity of data to better understand these barriers and enabling factors to attainment of viral suppression. We sought to determine the association of baseline factors with a detectable viremia threshold of >200 copies/mL in African women on life-long ART.

Methods: The PROMOTE study is a longitudinal cohort assessing long-term safety and effectiveness of ART among 1986 Human Immunodeficiency Virus (HIV)-infected women enrolled from 8 sites in Uganda, Malawi, Zimbabwe and South Africa. Enrolment commenced in December 2016, ending in June 2017. Enrolment viral load data were reviewed at different thresholds of detectable viral load (VL) <50; 50-200; >200-1000; >1000 copies per ml. Trained study workers administered sociodemographic, clinical, and ART adherence questionnaires. Analyses included descriptive and multivariate logistic regression.

Results: At enrolment, 1943/1986 (98%) women reported taking ART. Of these, VL was undetectable in 1652/1943 (85%), and detectable in 291/1943 (15%). Of the 291 women with detectable VL, 24(8.2%) had <50 copies/ml, 53(18.2%) had 50-200 copies/ml, 50(17.2%) had >200-1000 and 164(56.4%) had >1000 copies/ml. The following variables were significantly associated with a lower risk of detectable (>200 copies/ml) viremia in the multivariate regression model: Age per 5 year increase (odds ratio [OR] 0.73; 95% CI 0.63-0.85; p value <0.001); being married (OR 0.59; 0.38-0.90, p value <0.01); higher level of education (college or secondary completed) (OR 0.65;0.44-0.96, p value 0.03); having household electricity (OR 0.59; 0.39-0.88, p value< 0.011); never missed ART dose (OR 0.50; 0.37-0.69; p value <0.001) - while recent hospitalization (OR 2.70; 1.03-7.05, p value< 0.043); and abnormal vaginal discharge (OR 2.11; 1.15-3.89, p value <0.02) were associated with a higher risk of viremia >200 copies/ml. Despite 14% of women not disclosing their HIV status to their male partners, this variable was not statistically associated with high VL in this study.

Conclusion: Majorly sociodemographic factors seemed to significantly affect non-viral suppression in this cohort. It is essential to regularly explore and address sociodemographic barriers to achieving suppressed levels of viremia in women on life-long ART.

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Intracellular Concentrations of Tenofovir Diphosphate (TFV-DP) during Pregnancy in the PROMISE study: Description and Relationship with Adverse Pregnancy Outcomes


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**Background:** Promoting Maternal and Infant Survival Everywhere (PROMISE) a phase-3 randomized controlled trial of antiretroviral therapy (ART) for prevention of mother-to-child transmission of HIV reported an increased risk of adverse pregnancy outcomes among women on ART containing tenofovir disoproxil fumarate (TDF) versus zidovudine alone. This sub-study examined the association between adverse pregnancy outcomes and concentrations of tenofovir diphosphate (TFV-DP) in dried blood spots (DBS), a measure of long-term drug exposure, in women receiving TDF-containing ART.

**Materials and Methods:** Pregnant women randomized to receive TDF-FTC and ritonavir-boosted lopinavir from 14 weeks gestation through delivery; who received at least one dose of TDF-FTC; and had a week-4 DBS sample drawn prior to delivery were included in the analysis. Cases of adverse pregnancy outcomes (preterm delivery (PTD) prior to 34 weeks of gestation, stillbirth at or after 20 weeks gestation, or early infant death (EID) prior to 14 days old) were matched to controls (1:2 ratio) by site and gestational age at randomization. DBS samples collected at weeks 4 and 8 post-ART initiation were assayed for TFV-DP concentrations by liquid chromatography coupled with tandem mass (LC-MS/MS) methods. TFV-DP values below the lower limit of quantification (LLQ) were imputed as ½ LLQ, and in a separate sensitivity analysis imputed using 0 fmol/punch. Wilcoxon Signed Rank Test was used for case-control comparisons of TFV-DP concentrations and conditional logistic regression was applied to examine TFV-DP concentrations as a predictor of individual and composite adverse pregnancy outcomes. Hypothesis testing used 0.05 alpha. Separate analyses were done at weeks 4 and 8.

**Results:** Overall, 22/33 (66.7%) mothers who met the composite outcome definition; 15 for PTDs; and 6 still births; and 23 for EIDs, were included in these analyses. Of the 22 mothers included in the composite outcome analyses, TFV-DP concentrations were comparable: at week 4, overall median (inter-quartile range (IQR)) was 706 (375 – 1,023) fmol/punch and the median (IQR) for the difference between cases and controls TFV-DP concentrations was 15.45 (-232.00 – 142.50) fmol/punch; and at week 8 were 806 (414 – 1,265) fmol/punch and 47.90 (-152.75 – 725.50) fmol/punch, respectively. There was no difference between cases and controls for the composite endpoint matching (p-value of 0.86 and 0.35 for weeks 4 and 8, respectively). For the primary analysis, the Odds Ratio (95% Confidence Interval) of composite adverse pregnancy outcomes was 1.27 (0.74, 2.18) at week 4, and 1.74 (0.66, 4.60) at week 8. Similarly, non-significant differences were observed for individual adverse pregnancy outcomes. Study findings did not differ between LLQ imputation methods.

**Conclusions:** TFV-DP levels in DBS samples were not significantly different between cases and controls at 4 and 8 weeks post-ART initiation, respectively, and were not associated with individual or composite adverse pregnancy outcomes. These findings, based on data from a limited sample size, suggest that intrauterine exposure to TFV-DP concentrations, as measured in DBS, was not significantly associated with the adverse pregnancy outcomes/early infant deaths reported in the PROMISE trial.

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**Background:** The United States (US) Department of Health and Human Services (DHHS) issues guidelines for maternal use of antiretrovirals (ARVs) in pregnancy, providing recommendations that balance risk of HIV transmission with pregnancy safety data. Comparing ARV prescribing patterns with DHHS guidelines may inform future prescribing practices and guideline updates.

**Methods:** The Pediatric HIV/AIDS Cohort Study (PHACS) Surveillance Monitoring for ART Toxicities (SMARTT) study dynamic cohort enrolls pregnant women living with HIV (WLHIV) and their infants in the US, including Puerto Rico, to evaluate ARV
Background: The immune parameters of the placenta of the HIV-infected woman during pregnancy have been linked to the mother-to-child transmission of HIV. The purpose of this study was to investigate the characteristics of the placentas and the expression of the CD14+ and CD68+ receptors in macrophages of the placenta of Russian HIV-infected women and to compare it with the expression of the immune receptors in placentas of women with co-infections and healthy women as controls.

Methods: The study prospectively investigated postpartum placentas obtained from deliveries at two different (general and specializing in HIV-complicated deliveries women) maternity wards in St. Petersburg. Data on maternal age and delivery outcome were collected. The placentas were collected from three groups of patients: Group A – cases with children infected with HIV, Group B – cases with non-infected children born to HIV-infected mother and Group C – placentas from women without any infection.

In morphological analysis routine staining (hematoxylin and eosin) and microscope investigation were used. HIV-infection was confirmed immunohistochemically with use of p24 antibodies (Dako). The DNA-viruses of family Herpesviridae was detected immunohistochemically with use of antibodies against HSV (I and II) and CMV (Diagnostic BioSystems). Receptors expression was studied immunohistochemically with use of monoclonal antibodies CD14 (Novocastra) and CD68 (KP1 clone, Dako) and further morphometric analyses with the program Leica QWin Standard v2.8.

Results: The study collected 11 placentas in Group A, 11 placentas in Group B and Group C had 16 placentas. Placental infection was detected in 91% (n=10) of placentas Group A, 64% (n=7) of Group B. In Group A the majority of placental inflammation (73%; n=8) represented inflammatory changes (chorioamnionitis, placental membrane inflammation), including 46% (n=5) combined bacterial and viral changes, and 18% (n=2) had isolated viral inflammatory changes – HIV and DNA-virus (one with HSV-1, two with CMV, and one with combined HSV-1 + CMV). In Group B the majority of placentas had HIV changes – 55% (n=6) and the smaller proportion – 18% (n=2) had combination of viral and bacterial infection associated changes. The presence of the bacterial and viral inflammatory changes was statistically associated with MTCT (p<0.05). The chronic insufficiency of placenta was detected in Group A in 45.5%, in Group B in 36% (n=4).

Results: 1,884 pregnancies from 1,594 women with complete ARV prescribing data were included in this analysis. Of these, 795 (42%) pregnancies involved maternal ARVs from conception, 651 (35%) resumption of ARVs in pregnancy, 421 (22%) ARVs first initiated in pregnancy, and 17 (1%) had no ARV use. A higher percentage of pregnancies with first ARV initiation involved DHHS designated preferred or alternative treatment compared to pregnancies with ARV resumption or use at conception (70% vs 53% vs 35% respectively; p < 0.001). More pregnancies with ARV use from conception involved ARVs with insufficient safety evidence compared with pregnancies with ARV resumption or initiation (33% vs 25% vs 14% respectively; p < 0.001).

Conclusions: Most women starting ARVs during pregnancy were prescribed preferred or alternative regimens. However, those conceiving on or resuming ARVs in pregnancy were more likely to be prescribed ARVs that deviated from DHHS guidelines, commonly receiving regimens with insufficient safety evidence in pregnancy. Overall, 35% of infants in the cohort had in utero exposure to ARVs with unestablished safety profiles, highlighting the importance of long-term safety monitoring.

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Co-infection of the human placenta and problem of the mother-to-child transmission of HIV

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Abstracts

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Expression of CD14+ in cytoplasm of chorion villi cells and endotheliocytes was the highest in Group A (14.14±1.11%), followed by Group B (10.04±1.37%), when compared with control Group C (3.21±0.43%, p<0.05 for both comparisons). Similarly, the expression of CD68+ was the highest in Group A (13.07±0.83%), followed by Group B (7.21±0.89%) when compared to the control Group C (2.02±0.60%, p<0.05 for both comparisons).

**Conclusion:** In our study there was a significant prevalence of bacterial and combined bacterial and viral inflammatory changes in the placentas of women with MTCT of HIV compared to the placentas of the women without MTCT. The presence of viral infections (HSV and CMV) and HIV was accompanied by the significant increase of CD14+ and CD68+ macrophages in the placenta of Russian women at time of delivery.

**Developmental and cognitive effects of type of antepartum and postpartum ARV exposure for Ugandan and Malawian PROMISE HIV-exposed versus unexposed children at age 12, 24, and 48 months**


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**Background:** Triple ARVs during pregnancy and breastfeeding dramatically decrease the risk of HIV transmission from mothers to infants. However, antepartum and postpartum exposure to Triple-ARV prophylaxis may disrupt infant neurodevelopment. The present study evaluates longitudinal developmental outcomes for HIV-exposed uninfected (HEU) and uninfected (HUU) Ugandan and Malawian children enrolled in the IMPAACT PROMISE RCT study.

**Methods:** Pregnant HIV-infected mothers were randomized to Triple-ARV prophylaxis (3TC-ZDV/LPV-RTV or FTC-TDF/LPV-RTV), versus Zidovudine (ZDV). Postpartum, the mother/newborn dyads were randomized to maternal Triple-ARV or infant Nevirapine (NVP) during breastfeeding. 942 children were enrolled between 9 and 12 months of age: 465 were unexposed/uninfected (HUU) (49%) and 454 (48%) girls. HEU and age-matched HUU children were enrolled at the two IMPAACT PROMISE study sites: 465 (49%) in Blantyre, Malawi, and 477 (51%) in Kampala, Uganda. Mullen Scales of Early Learning (MSEL) was used for developmental assessment at 12, 24, and 48 months of age, and the Kaufman Assessment Battery for Children (KABC) for cognitive assessment at 48 months only.

**Results:** Controlling for sex, study site, and age at assessment, there were no significant MSEL neurodevelopmental differences among PMTCT ante- and post-partum treatment arms at 12 and 24 months. There were significant differences among the treatment arms at 48 months for the MSEL composite cognitive score (p=0.04) and Fine Motor scale (p=0.001). For the KABC at 48 months, there were significant differences among the study groups for all the global scales (Mental processing p=0.03, Sequential processing p=0.02, Simultaneous processing p=0.02, Learning p=0.02) except the nonverbal index. However, the maternal Triple-ARV (antepartum and postpartum) children were not at a significant disadvantage to the HUU group on any of the pairwise comparisons. Only MSEL fine motor at 48 months remained significant after a Bonferroni adjustment for multiple comparisons (p=0.01). Again, the maternal Triple-ARV exposed children were not at a significant disadvantage.

**Conclusions:** Both ante- and postpartum maternal triple-ARV exposure did not result in greater developmental or cognitive risk for their HEU children through 48 months of age compared to HUU children. Overall, HUU and HEU children were comparable. These findings are reassuring as PMTCT programs using maternal ART are widely
rolled out in resource-constrained settings in sub-Saharan Africa and globally.

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HIV exposure without infection impacts early language development: Outcomes from a South African birth cohort study

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Background: Sub-Saharan Africa, where HIV is most prevalent, has the highest proportion of children at risk of not reaching their neurodevelopmental potential. Whereas HIV infection is a known risk factor for developmental delay, effects of HIV and antiretroviral therapy (ART) in exposed HIV-uninfected (HEU) children remain unclear. We compared neurodevelopmental outcomes in HEU and HIV-unexposed uninfected (HUU) children during their first 2 years.

Materials and Methods: The Drakenstein Child Health Study is a population-based birth-cohort in the Western Cape, South Africa. Women were enrolled antenatally from two clinics between 2012-2015. Mothers and children from these two communities received HIV testing and treatment as per the Western Cape prevention of mother-to-child transmission guidelines at the time. Developmental assessments were conducted by trained assessors blinded to HIV/ART status, using the Bayley-III Scales of Infant and Toddler Development (BSID-III) at 6 and 24 months.

Results: A subgroup of 260 children (61 HEU, 199 HUU) had a BSID-III assessment at 6 months and 732 children (168 HEU, 564 HUU) at 24 months. Mean scaled scores of all subscales were within normal range (BSID-III standardised mean 10, SD 3) at 6 months with no differences between HEU and HUU (p>0.1). However, at 24 months, HEU scores were significantly lower than HUU in cognitive mean (SD) [6.80(1.88) vs. 7.14(1.84), p=0.049]; receptive [6.62(1.82) vs. 7.25(1.97), p=0.001] and expressive language [6.94(2.29) vs. 7.57(2.30), p=0.028]; in contrast, fine and gross motor domains were similar (p=0.93 and p=0.53 respectively). HEU had higher risk of delay (>2 SD below the mean) than HUU children in receptive (13.9% vs. 7.2%, odds ratio[OR] 2.09, 95%CI 1.21-3.61) and expressive language (11.4% vs. 5.7%, OR 2.12, 95%CI 1.15-3.90) but not in the cognitive scale (10.8% vs. 9.3%, OR 1.18, 95%CI 0.67-2.09). After adjusting for age, sex, clinic and maternal education, the effect remained for receptive (OR 2.23, 95%CI 1.16-4.30) but not expressive language (OR 1.74, 95%CI 0.86-3.54).

Conclusions: These initial analyses suggest receptive language is impaired in HEU children. Ongoing analyses will focus on disaggregating effects of in-utero exposure to HIV and ART. Given the global focus on child development and the critical importance of language in society, further work is needed to monitor and address the long-term clinical outcomes of HEU children.

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A population-based study of health outcomes of HIV-exposed uninfected children using Ontario’s administrative health databases

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Background: Maternal treatment with combination antiretroviral therapy (cART) in pregnancy has led to a generation of HIV-exposed uninfected children (HEUs) globally and in Canada. Some data suggests increased immunologic, infectious and neurodevelopmental morbidities in HEUs. We utilized Ontario’s administrative health databases to estimate rates of these morbidities in Ontario-born HEUs.

Methods: A retrospective population-based study was conducted comparing diagnoses among
HIV-exposed uninfected children have poorer neurocognitive outcomes than HIV-unexposed children

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Background: The relationship between perinatal HIV-exposure and poor neurocognitive outcomes in HIV-exposed uninfected children (HEU) remains controversial. We compared neurocognitive outcomes in HEU and HIV-unexposed uninfected children (HUU) at school-age.

Methods: Both groups of children were recruited from maternal child health clinics in Nairobi, Kenya. Key inclusion criteria for HEU children were child confirmed HIV seronegative, biological mother confirmed seropositive (both using rapid HIV antibody testing) and mother self-reported knowing HIV status during pregnancy or at delivery. Key inclusion criteria for HUU were child and biological mother confirmed HIV seronegative. Both cohorts were aged 5-12 years. Both groups of children underwent a detailed battery of assessments, including the Kaufman Assessment Battery for Children, 2nd ed., the Test of Variables of Attention, and Behavior Rating Inventory for Executive Function and the Bruininks-Oseretsky Test of Motor Proficiency (Brief Form, 2nd ed.). Raw scores from each test were scaled and standardized compared with a US norm and converted to z-scores. Univariable and multivariable linear regression analyses were used to compare neurocognitive scores between groups. Separate models were evaluated for co-linear potential confounders (food security, body mass index (BMI) for age z-score, paternal status, caregiver education).

Results: Child age was similar for HEU (N=58) and HUU (N=60) children (6.9 vs 6.9 years, respectively; p=0.8); HEU children had trends for lower proportion of females (48.3% vs 61.7%; p=0.1). Most mothers of HEU children (86.2%) had received some prophylaxis for prevention of mother to child transmission, including 25 (50.0%) who received single-dose nevirapine and 18 (36.0%) who received antiretroviral treatment. Households of HEU children had a trend for more moderate or severe food insecurity (43.1% vs 30.0%; p=0.1), but HEU children also had a trend for higher BMI for age (medians, -0.83 vs -1.22, p=0.1). Mothers of HEU children were older (medians, 34.5 vs 29.5 years; p=0.01), but had similar years of education...
Both HEU and HUU children had high proportion with a father who had died or was no longer fulfilling parental duties (34.5% vs 23.3%; p=0.2). In unadjusted analyses, HEU children had lower scores for global cognitive ability (mean z-score difference, -0.32; p=0.01), short-term memory (-0.45; p=0.001), delayed memory (-0.30; p=0.05), non-verbal test performance (-0.31; p=0.04), attention (-0.32; p=0.04), and processing speed (-0.83; p=0.002). Adjusted for maternal age and food insecurity, results were similar (mean adj. differences, global cognitive ability [-0.26; p=0.06], short-term memory [-0.38; p=0.007], delayed memory [-0.24; p=0.1], non-verbal test performance [-0.27; p=0.09], attention [-0.30; p=0.05], and processing speed [-0.78; p=0.007]). Separate models adjusted for paternal status, BMI for age, and caregiver education also gave similar results.

Conclusions: HEU had poor neurocognitive outcomes compared with HUU children. These data suggest ongoing monitoring of neurocognitive outcomes in HEU cohorts remains important.

Factors associated with increased risk of moderate-to-severe diarrhea among HIV-exposed, uninfected infants in Kenya

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**Background:** Children with moderate-to-severe diarrhea (MSD) experience a 9-fold higher risk of death than children without diarrhea. HIV-exposed, uninfected (HEU) children are a growing population at particularly high risk of infection-related death in whom preventing MSD may significantly reduce under-5 morbidity and mortality.

**Methods:** MSD was defined as seeking care for diarrhea with one of the following indicators of severity: dehydration, dysentery, or hospital admission. Associations of MSD with home environment, pregnancy and postpartum maternal morbidity and HIV disease stage, and infant factors, were assessed in a historic cohort (1999-2002) of HIV-infected Kenyan mothers and their infants. Mothers were enrolled during pregnancy, received short-course zidovudine, and mother-infant pairs were followed for 12 months postpartum. HEU infants were included in the analysis and censored at the last HIV-negative test prior to HIV diagnosis. Anderson-Gill Cox models were used to determine correlates of MSD. Potential confounding factors were included in adjusted models and retained if the hazard ratio (HR) of interest differed from the unadjusted by more than 10%.

**Results:** HEU infants (n=373) experienced a mean 2.09 (95% Confidence Interval [CI]: 1.94, 2.25) episodes of diarrhea and 0.46 (95% CI: 0.39, 0.54) episodes of MSD during their first year of life. Infant birthweight was not associated with risk of MSD. Ever breastfed and currently breastfeeding infants had a 34% and 43% lower risk of MSD, respectively (HR: 0.66; 95% CI: 0.46, 0.96; HR: 0.57: 95% CI: 0.38, 0.84). Infants living in households with a pit latrine were 1.51 times more likely to experience MSD relative to those with a flush toilet (HR: 1.51; 95% CI: 1.04, 2.17). Postpartum maternal diarrhea was associated with a 3-fold increased risk of infant MSD after adjusting for crowding, maternal undernutrition and CD4 count during pregnancy (adjusted HR: 3.01; 95% CI: 1.18, 7.99). Higher maternal HIV viral load (4 log10 vs <4 log10) during pregnancy was associated with an increased risk of MSD among infants (HR: 1.81; 95% CI: 1.03, 3.31) although maternal CD4 count, malnutrition, and fever were not.

**Conclusions:** Efforts to reduce diarrheal morbidity among HEU infants may need to target improved sanitation, encouragement of breastfeeding, and interventions to improve maternal health.
Early Infant Diagnosis HIV-1 PCR tests identify infants with high viral loads at birth: findings from a cohort study in Johannesburg, South Africa

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Background: HIV-infected infants with high plasma viral load (VL), in particular VL ≥5 log10 cps/ml, have been associated with poorer clinical outcomes. The ability to predict high VL using early infant diagnosis (EID) PCR cycle threshold (Ct) values provides the opportunity to identify high-risk infants at the time of diagnosis. We describe the association between Ct values of two separate EID assays, one laboratory and one point-of-care (POC), with HIV-1 RNA plasma VL results among a cohort of intra-uterine HIV-infected infants.

Materials & Methods: This study comprised a secondary data analysis of a cohort of intrauterine HIV-infected neonates enrolled between 05 August 2014 to 30 November 2017 at Rahima Moosa Mother and Child Hospital in Johannesburg, South Africa. Neonates were screened with the standard laboratory EID HIV-1 PCR test (COBAS AmpliPrep/COBAS TaqMan [CAP/CTM] HIV-1 Qualitative Test v2.0, Roche Molecular Systems, Branchburg, NJ, USA). Neonates with a positive CAP/CTM PCR result were traced and baseline plasma HIV-1 RNA VL testing performed in a centralized laboratory (CAP/CTM HIV-1 Quantitative Test, v2.0, Roche Molecular Systems, Branchburg, NJ, USA). During the course of the study EID POC testing was introduced simultaneously with the screening CAP/CTM PCR test using Xpert HIV-1 Qualitative assay (Cepheid, Sunnyvale, CA, USA). Ct values for CAP/CTM and Xpert PCR tests were documented. Multivariable linear and binomial regression were used to determine the magnitude and strength of association between EID PCR Ct values and VL. A Bland-Altman plot determined the extent of agreement between screening Xpert PCR Ct value and screening CAP/CTM PCR Ct value. Linear regression models adjusting for times between PCRs (CAP/CTM and Xpert) and VL testing were used to predict log10 of VL measurements for CAP/CTM and Xpert PCR Ct values.

Results: 152 neonates had a positive CAP/CTM HIV-1 PCR result at birth, 77 (51%) of whom had a simultaneous Xpert PCR, and 141 (93%) had a VL. Median age of screening CAP/CTM PCR was 1 day (interquartile range [IQR]:0–1) and VL was 3 days (IQR:1–9). Median VL result was 18500 cps/ml (IQR:964–220410). When analysed as a continuous variable, for every 1 cycle increase in CAP/CTM PCR Ct there was a 0.26 VL log10 RNA decrease (95% CI:0.21–0.32). When CAP/CTM PCR Ct was analysed as a categorical variable, a Ct of ≤25 was independently associated with a 2.1 (95% CI:1.3–2.9) times increased risk of VL ≥5 log10 cps/ml. Bland-Altman comparison of Ct values demonstrated limits of agreement of 4.2–11.0 cycles between laboratory and POC EID assays. Ct values on the Xpert assay were consistently higher than on CAP/CTM PCR, with a median difference of 7.2 cycles (IQR:6.5–8.7). An Xpert Ct of 39, 35, and 30 was associated with VL log10 3 (95% CI:2.6–3.2), log10 4 (95% CI:3.7–4.1), and log10 5 (95% CI:4.7–5.1) cps/ml, respectively.

Conclusions: Both CAP/CTM and Xpert HIV-1 PCR Ct values strongly predicted plasma VL thereby assisting with early identification of HIV-infected infants at high risk of increased morbidity and mortality.

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Birth testing for infant diagnosis in eSwatini: uptake among women with HIV in Manzini Region

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Background: Birth testing of HIV-exposed infants (HEI) may improve identification of infants infected with HIV in utero and accelerate antiretroviral treatment (ART) initiation for these infants who are at high risk for mortality. eSwatini has the highest antenatal HIV prevalence in the world (27.2%) and introduced Option B+ for PMTCT in 2014. By 2017, eSwatini had achieved 95% coverage of antiretrovirals for prevention of mother-to-child transmission (PMTCT) of HIV and had an estimated MTCT rate of 6%. With assistance from the US Centers for Disease Control and Prevention (CDC), ICAP at Columbia University supported the eSwatini Ministry of Health (MOH) to pilot birth testing at the two health facilities that provide delivery services in Manzini Region starting in October 2017.

Methods: In collaboration with MOH and other partners, ICAP developed standard operating procedures, revised monitoring tools and training materials, and conducted trainings and provided ongoing support for birth testing implementation. No additional nursing staff were hired; birth test samples were collected from neonates of HIV-positive mothers and data were recorded by nursing staff in postnatal wards prior to mothers’ discharge. Dried blood spot specimens were sent several times per week to the eSwatini National Molecular Reference Laboratory (NMRL) for DNA PCR testing (ROCHE CAP/CTM 96) for prioritized testing within seven days. Test results were returned to the delivery facility. Per national SOPs, birth testing information was recorded in patient-held health cards so that mothers could receive birth test results at community health clinics where they attend postnatal/infant care; nurses at community clinics could call the NMRL hotline to retrieve results per existing procedures. Mothers of infants with positive birth test results were traced in the community by health facility staff. We report data on birth tests conducted from October 2017 through March 2018.

Results: Among the 4,324 women who delivered at the two delivery facilities, 1,488 (34.4%) were living with HIV. 1,453 HEI were admitted to the postnatal ward (excluding newborn deaths and transfers) and 1,368 (94.2%) received birth testing. Staffing shortages at one of the health facilities resulted in not all mothers being offered birth testing. Results of all birth tests (100.0%) were received at the maternity facilities within one week of testing of specimens arriving at the lab. Four HEIs tested HIV-positive (0.3%); three were successfully traced and linked for follow-up care including confirmatory testing and initiated on ART (median of 3 days from receipt of results by caregiver to ART initiation). Median infant age at ART initiation was 24 days.

Conclusion: In the first six months of a birth testing pilot in eSwatini, there was almost universal acceptance of testing for newborns among HIV-positive mothers using DBS and sample testing at the NMRL using standard of care for EID. Very few infants were found to be infected through birth testing suggesting low incidence of in utero infections. Future analyses will assess receipt of negative results at community health clinics and uptake of 6-8 week testing following the introduction of birth testing.
Task shifting for point-of-care early infant diagnosis testing: Comparison of error rates between nurses and specialized laboratory trained personnel.

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Background: Point-of-care (POC) early infant diagnosis (EID) of HIV allows for sample analysis at peripheral health facility. Unlike conventional testing that requires specialized laboratory personnel, POC EID is near-fully automated and may be operated by non-specialized laboratory personnel. POC EID technologies include internal error controls that detect user errors. High rates of error may suggest inadequate user capacity. To decentralize POC EID, task-shifting to cadres such as nurses is important. We used data from a POC EID project in Zimbabwe to compare the error rates and result return to caregivers for samples run on a POC EID technology (Alere q HIV 1/2 Detect) between nurses and lab personnel (MLSc/Techs) to assess user competence.

Materials & Methods: All ten sites in Zimbabwe providing POC EID for routine clinical use were enrolled. Two sites are operated by MLSc/Techs, six by nurses, and two by both cadres. Data from December 2016 to June 2017 were reviewed. Error rates were downloaded from each POC EID machine and exported to excel to analyze errors by type of operator. Turnaround time (TAT) from sample collection to issuing of results to caregiver was extracted from the EID test request form and uploaded into an Excel-based database for analysis.

Results: A total of 1,847 tests were conducted by 45 testers (12 MLSc/Techs and 33 nurses), including 165 errors. Overall error rate was 8.93% (7.69% vs. 9.24%, for MLSc/Techs and nurses, respectively, p=0.36). User error rate was 6.17% (5.22% vs. 6.41%, for MLSc/Techs and nurses, respectively, p=0.38). There was no statistical difference between error rates for MLSc/Techs and for nurses. Over time, both cadres’ error rates decreased. 98.75% of results were issued to clients versus 98.92% for MLSc/Techs and nurses, respectively. Overall median TAT was same day (Q1=0.5, Q3=2). Tests processed by MLSc/Techs had a TAT of one day (Q1=0.5, Q3=3.5) versus same day (Q1=0.5, Q3=2.5) for nurses.

Conclusions: Similar error rates and TATs between nurses and lab-tech-operators suggest that non-specialized laboratory trained personnel can perform POC EID equally well as specialized laboratory personnel. Nurse-operated POC EID testing will ensure decentralization and timely return of test results without compromising the quality of testing.

Can a short-haul specimen referral system work efficiently to access “point-of-care” early infant diagnosis testing? Lessons from Lesotho and Zimbabwe.

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Background: Specimen referral systems can increase access to diagnostic services but are also vulnerable to logistical and system efficiency challenges. An efficient specimen referral over short distances (<1 hour) was adopted to increase access to point-of-care (POC) early infant diagnosis (EID). We compared key clinical and service delivery outcomes observed within testing facilities (POC model) to those within referring facilities (referral model), in Lesotho and Zimbabwe.

Methods: We used data from 4,746 POC EID testing forms (2,670 in POC model and 2,076 in Referral model) routinely used across all 109 facilities (27 testing facilities; 82 referring facilities) having access to POC EID from February to October 2017 across Lesotho and Zimbabwe combined. Key POC EID clinical outcomes (percentage of results returned to caregivers at facility and percentage of HIV-infected infants initiated on treatment) and key service delivery outcomes, including intermediate turnaround times (TAT) (between specimen
collection, transport, processing, result transmission facility, and return to caregiver) and total TAT (from specimen collection to result return to caregiver at facility) were aggregated per facility. We assess differences between the two delivery models using the Wilcoxon rank-sum test on summary statistics (median, range intervals, proportions) from aggregated facility outcomes. The significance threshold was set at 0.05.

Results: In both POC and referral models, there were no significant differences in percent results returned (100% in both models), or in the proportions of HIV-infected infants initiated on treatment (100% in both models), despite the latter having a small but significant distribution difference (p<0.018). The total TAT median observed in the referral model (2 days [0-28]) was only two days longer than in the POC model (0 days [0-3]), with a significant difference in the TAT groups’ distributions (p<0.001). Whereas both models experienced same-day specimen transportation, same-day specimen processing and testing, as well as same-day return of results to requesting facility; caregivers took significantly longer (1-day vs 0 days; p<0.001) to collect the result from facility in the referral model.

Conclusions: A short-haul POC EID specimen referral system showed no significant differences in key clinical outcomes, and a significant increment of only 2 days in the final TAT, (mostly due to time required for caregivers to collect results) as compared to patients seen at POC testing sites and may be considered to increase access to POC EID.

Introduction: Early infant diagnosis (EID) coverage is insufficient in Abidjan, partially due to poor linkage between birth and 6-week EID on DBS as recommended since 2011. We implemented a novel routine screening strategy that combined rapid diagnostic testing for both maternal HIV and HBV linked to a web-based health information system (HIS) that tracked from birth HIV/HBV-exposed mother-infant pairs through the continuum of postnatal care in Abidjan, Côte d’Ivoire. We describe the cascade of care among the first 20,000 births.

Methods: All mother-infant pairs who gave maternal consent in the five participating maternity clinics were included. At delivery, mothers were tested for HIV, those HIV-infected but unaware of their status were offered a second opportunity to be enrolled in care. All HIV-infected mothers received PMTCT. Mothers were also tested for HBV; HBs-Ag-exposed newborns received immunization at birth. All births were recorded in the HIS; HIV and HBV-exposed infants were tracked through the continuum of postnatal care. Each step of the EID and immunization cascades was recorded in the HIS. Weekly reports alerted social workers in case of a missed visit, who then contacted families to reschedule. HIV-infected infants are followed-up until definite diagnosis, after breastfeeding cessation.

Results: Between August 2016 and January 2018, 19,905 mothers gave birth to 20,000 newborns. Acceptability of maternal HBV testing reached 95% prevalence of HBV was 6.2% (95%Confidence Interval (95%CI): 5.7%-6.6%). Among the 1,070 HBV-exposed newborns, 1059 (99%) were immunized at birth. Maternal HIV testing coverage at time of birth was 99%; maternal prevalence of HIV was 3.8% (95%CI: 3.5%-4.0%). Of those HIV-infected, 79% were already on combined ART, and 21% unaware of their HIV-status. Among the 18,897 live-births >24 hours, 639 were HIV-exposed with follow-up >6 weeks: 59% (95%CI: 55%-63%) had a DBS for 6-week EID. After HIS alerts, this significantly increased to 66% (95%CI: 62%-69%) (McNemar’s test: p<0.001). Among those who did not receive 6-week EID, 11% had died, 6% had withdrawn consent, 1% transferred out and 17%...
had provided fake contact details and were lost-to-follow-up. Among the 418 children tested: 273 (65%) Results were returned to the clinics after a median delay of 52 days (interquartile interval (IQR): 30-74), of which 267 (98%) were subsequently returned to families. Among the 273 children with available PCR results, five came back positive (6-week incidence rate: 1.8%; 95%CI: 0.2%-3.4%). All five children-initiated ART immediately. After confirmatory testing, one was HIV-negative and stopped ART. Among the 291 HIV-exposed infants with 9-month follow-up, HIV serology coverage was 14% (IC95%:10-18) and reached 32% (IC95%: 26-37) after HIS alerts (McNemar’s test: p<0.001); one child was HIV-infected.

Conclusion: Maternal HIV and HBV rapid diagnostic testing at delivery is both feasible and acceptable. HBV immunization coverage at birth was high and proved a feasible intervention to reduce new HBV infections among infants. EID uptake was 59% and was significantly improved by the HIS, however successful EID remained hindered by long turnaround times for results. While the uptake of EID is improving in Cote d’Ivoire, efforts should focus on reducing result turn-around time.

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Monitoring and evaluation of infant virologic testing and linkage to antiretroviral therapy in PEPFAR-supported programs: The challenge of using simple program indicators to monitor a complex process

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Background: Infant virologic testing (IVT) is critical to reducing HIV-related infant deaths through early identification and treatment of HIV-infected infants.

To measure linkage of HIV-infected infants to antiretroviral therapy (ART), programs must report a numerator (number of infants initiated on ART) and denominator (number of HIV-infected infants).

Description: PEPFAR uses standardized indicators to evaluate IVT and infant ART initiation. The PEPFAR IVT indicator counts infants with a first specimen collected by 12 months of age, with disaggregates for age (0-2 months/2-12 months) and results returned within the quarter (positive, negative, unknown). IVT coverage is calculated as number of first IVT collected divided by number of HIV-positive pregnant women in the reporting period. The PEPFAR infant ART initiation indicator reports all infants initiating ART by 12 months of age.

Between 2011 and 2017, the number of HEI receiving a first HIV test by 12 months of age in PEPFAR-supported programs nearly doubled from 422,567 to 809,395. IVT coverage by 12 months of age increased from 62.3% to 102.4%; IVT coverage by 2 months of age increased from 37.7% to 56.7% (Figure 1).

In 2017, 22,624 (2.6%) of first IVT results were positive, 708,124 (87.5%) negative, and 80,010 (9.9%) unknown. The proportion of unknown results varied by country from 0%-53.9%. In 2017, 16,318 infants were initiated on ART (72.1% estimated infant ART linkage).

Lessons learned:
The PEPFAR IVT indicator effectively measures first infant specimen collection, demonstrating improved testing coverage yet persistent need for scale-up of testing by 2 months of age. A high proportion of unknown results in some countries may be due to long turn-around-times, high specimen rejection rates and/or reporting errors. The current indicator does not capture all first IVT results, and it fails to count infants identified as HIV-infected on subsequent tests. As a result, any estimates of linkage to ART using these indicators are likely significant overestimates.

Conclusions/Next Steps: Measuring a complex, multi-step process with a single cross-sectional indicator is challenging. To better evaluate effectiveness of IVT, a new PEPFAR indicator will be launched in FY18 to capture all HIV-infected infants identified each quarter and therefore better estimate linkage to ART.

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Applying Strategic Innovations to Conventional EID Services in 4 States in Nigeria

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Background: Early Infant Diagnosis (EID) of HIV is crucial for early initiation of life-saving anti-retroviral treatment in infants. However, in most resource-constrained settings including Nigeria, where the National EID program utilizes few regional PCR laboratories that serve satellite health facilities within the region, there are numerous logistics challenges along the EID testing cascade that contribute to delays in EID and early initiation of anti-retroviral therapy. Health Strategy and Delivery Foundation (HSDF) is currently implementing the 3-year EID Operation Support Services intervention to address challenges faced in the EID testing cascade and linkage of identified HIV+ infants to care and treatment services. This study presents the strategies, Methods, key achievements and learnings from this program.

Materials & Methods: Prior to the intervention, in January 2015, a baseline retrospective analysis of 1186 infant dried blood sample (DBS) records collected from 49 health facilities in 4 states of Nigeria (Akwa Ibom, Bayelsa, FCT and Rivers) between January 2013 and December 2014 was conducted to determine average infant age at DBS collection, overall turn-around-time (TAT) from DBS collection to results reaching health facilities, the time between results reaching health facilities and the caregivers and linkage rate to pediatric HIV care and treatment.

EID OSS commenced in June 2015 in 20 high volume health facilities in each state. The intervention included stakeholder engagement, logistics support and strategic innovation at each point of the EID testing cascade and data-driven response to challenges encountered along the EID cascade during the period of EID OSS implementation. The intervention was aimed at reducing the average infant age at DBS collection and overall TAT to the Nationally recommended standards of 6 weeks and 4 weeks respectively as well as to improve linkage of identified HIV+ infants to HIV care and treatment.

In January 2018, retrospective analysis of 4500 DBS records collected from the 20 intervention health facilities in the 4 states within two and a half years of the intervention (June 2015 to December 2017) was conducted to measure intervention effectiveness at each point of the EID testing cascade and overall TAT.

Results: Before the intervention, average infant age at DBS collection was 18 weeks (range: 3-72 weeks), overall TAT from DBS collection to results reaching the results facilities was an average of 18 weeks (range: 8-32 weeks) and no information was available for results reaching caregivers and linkage of HIV+ infants to HIV care and treatment.

Following the intervention, the average infant age at DBS collection was reduced to 4 weeks (range: 3-6 weeks), average turn-around-time for DBS reduced to 4 weeks (range: 4-8 weeks), the time between results reaching health facilities and the caregivers was 1 week (range: 1-2 weeks) and 50% of identified HIV+ infants were linked to paediatric ART.

Conclusions: Our findings show that strategic interventions at critical points along the EID testing cascade successfully reduced the TAT to the nationally recommended standards and improved linkage of identified infants to HIV care and treatment.

Malnutrition, orphan hood, and TB diagnosis are strong predictors of HIV positivity among children less than 15 years in Uganda

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Introduction: Despite strides in improving pediatric HIV service coverage in Uganda, it is estimated that 32% of children living with HIV have not been identified. Identifying children with higher risk of HIV infection can improve efficiency of HIV testing among this population sub-group. We describe...
correlates for HIV positivity among children less than 15 years attending health facilities in Uganda.

**Methods:** HIV testing was offered to 3245 children in 8 health facilities from February 2017 to June 2017. Probability proportional to size was used to distribute the number of children recruited in each of the study sites and entry points. Consecutively sampled children who entered through out-patient department (OPD), in-patient department (IPD), malnutrition, TB and special (HIV, sickle cell, young child, and eye) clinics, whether patients themselves or accompanying patients, were reviewed for HIV status and offered a test if their status was unknown. Characteristics of children who tested positive were described and their correlates were analysed using a binominal generalised linear model factoring in level of facility.

**Results:** The HIV test uptake was 96% (3119/3245) with an overall yield of 1.4% (45/3119). Females accounted for 49.5% of the children and 49.5% were under 5 years. Children 10-15 years had significantly higher yield (2.5%) than children 18 months-4 years (1.2%, p = 0.0185) or 5-9 years (1.1%, p=0.0165). Yield did not differ by gender. Correlates for HIV positivity included: malnutrition (adjusted odds ratio (AOR)=2.14; 95% Confidence Interval (95%CI)=[1.6, 2.9]); orphan hood (single orphan: AOR=2.13; 95%CI=[1.02, 4.44], double orphan: AOR=6.97; 95%CI=[1.76, 27.66]); TB diagnosis (presumptive & confirmed: AOR=16.1; 95%CI=[13.57, 19.02]); older age (10-15 years: AOR=1.59; 95%CI=[1.56, 1.63]); children escorting their sick siblings (not sick: AOR=2.02; 95%CI=[1.92, 2.13]); and recurrent illness (AOR =2.71; 95%CI=[2.39, 3.08]).

**Conclusion:** The finding of higher yield in older children reflects the great success of EMTCT efforts in Uganda. Malnutrition, Ophrannhood and TB diagnosis should be prioritized in the screening and identification of HIV in children. Furthermore, the significant HIV positive yield observed among children escorting their sick relatives provides an untapped opportunity to increase HIV identification amongst children.

**Concurrent implementation of targeted and routine provider-initiated-testing and counselling of HIV among children and adolescents: evidence from the Active Search for Pediatric HIV/AIDS (ASPA) study in Cameroon**

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**Background:** The provider-initiated-testing and counselling (PITC) implementation modalities among children and adolescents include the targeted PITC (tPITC) whereby biological children of HIV positive parents in care are targeted for testing and the routine PITC (rPITC) whereby all children attending the health facility are offered an HIV test irrespective of the reason of consultation. The Active Search for Pediatric HIV/AIDS (ASPA) study assessed the effectiveness of the concurrent implementation of both strategies among children and adolescents in Cameroon.

**Methods:** During a 6-month period, the ASPA study was conducted by introducing the tPITC approach in three hospitals in Cameroon. This novel approach was implemented by inviting HIV positive parents receiving HIV care in these hospitals to have their biological children (6 weeks-19 years) tested for HIV either in the hospital or at home. At the same time, the study systematically offered HIV testing to all children attending the outpatient department (OPD) of the same three hospitals (rPITC). We collected prospectively and retrospectively the numbers of: children tested for HIV, children tested HIV positive and children enrolled on ART. We compared the means of these numbers before and after the intervention.

**Results:** During the implementation of tPITC, 2829 eligible children were identified for HIV testing, 1163 tested for HIV and 64 tested HIV+ and 35 enrolled on ART. Before the implementation of rPITC, 5891 children consulted at the OPD, 1338 tested for HIV, 63 tested HIV+ and 44 enrolled on ART. After the implementation of rPITC, 4643 children consulted at the OPD, 2090 tested for HIV, 58 tested HIV+ and 38 enrolled on ART. While the HIV testing uptake was significantly higher after rPITC implementation compared with before (223.0 children tested/month vs 348.3 children tested/month, p<0.0001), the HIV case detection was significantly lower (10.5 children newly diagnosed HIV positive/month vs 9.7 children newly diagnosed
HIV positive/month, p<0.0001) and there was no significant difference on ART enrolment (7.3 children newly enrolled on ART/month vs 6.3 children newly enrolled on ART/month, p= 0.1368). During the concurrent implementation of both tPITC and rPITC, the HIV testing uptake increased significantly by 143% compared with before (223.0 children tested/month vs 542.2 children tested/month, p<0.0001). Likewise, the HIV case detection also increased by 93.7% (10.5 children newly diagnosed HIV positive/month vs 20.3 children newly diagnosed HIV positive/month, p<0.0001) and the ART enrolment by 65.9% (7.3 children newly enrolled on ART/month vs 12.2 children newly enrolled on ART/month, p=0.0001).

Conclusion: The rPITC was effective at increasing HIV testing uptake, but not effective in increasing the HIV case detection and ART enrollment. On the contrary, the tPITC was associated with an increase in HIV testing uptake, a doubling of HIV case detection, and a significant increase on ART enrolment. This highly effective strategy yields more newly HIV cases and increases ART initiation. It could be used to fast-track the achievement of the 90-90-90 targets by 2020 among children and adolescents, especially in West and Central Africa Region.

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Finding children and adolescents living with HIV in Johannesburg: Optimising HIV testing strategies

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Background: In high HIV-prevalence settings such as Johannesburg, South Africa, a substantial number of HIV-positive children may remain undiagnosed until clinical deterioration results in HIV diagnosis. Reasons for delayed diagnosis of older children include missed diagnostic opportunities with the previously less than optimal prevention of mother-to-child transmission (PMTCT) guidelines, poor uptake of paediatric HIV testing services and children that were known to be HIV-positive but dropped out of care. Additionally, high HIV incidence rates in adolescent girls and young women are well described. The Paediatric and Adolescent Scale-up Project (PASP) sought to upscale testing of children and adolescents within primary healthcare (PHC) facilities using different approaches per age group.

Description: Between March 2016 and December 2017, HIV case finding interventions were implemented across 41 PHC facilities in Johannesburg. Children and adolescents were screened and tested when they accessed various service points by facility or PASP staff or were requested to come back for testing through index case finding by using an HIV-positive adult or sibling index patient. This data was then analysed to determine which age groups and entry points showed the highest yield.

Lessons learned: In total 14331 children and adolescents were tested, 376 were HIV-positive (yield=3%). Strategies with the highest yield included HIV testing of adolescents in primary care, (9%, n=110) particularly adolescent girls (15-19 years) accessing contraception services (15%, n=66). Index testing also had a high yield with 112/1885 (6%) HIV-positive siblings or children of HIV-infected patients, however testing uptake was low. Lower yields were seen in those <5 years old and 5-14 years, including in acute care settings such as Integrated Management of childhood illness (IMCI) with the lowest yield in children of 18 months accessing immunisation clinics (1%; n=19).

Conclusions: Current PMTCT implementation and immunization clinic-based early infant diagnosis testing is effective in reducing MTCT and identifying HIV-positive children. Targeted HIV-testing can improve identification of older HIV-positive children and adolescents who should particularly be offered PICT at contraception service points. Improved index case finding and testing is effective in identifying HIV-positive children and adolescents however innovative approaches for index testing are required to increase testing uptake in this high-risk group.

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Innovations in Index Case Contact Testing to Increase Identification of HIV-infected children and Adolescents

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Background: Index-case testing has been identified as a leading strategy to enhance identification of HIV-positive children. However, there is limited data on the positivity across a range of index-case testing approaches. Between November 2016 and January 2018, the Elizabeth Glaser Pediatric AIDS Foundation (EGPAF)-Kenya scaled-up index-case testing through five different approaches in 70 sites in western Kenya. The five approaches varied in individual(s) used as the index client and included the following variations: living adult clients on ART, deceased adults with known HIV status, adolescents on ART to reach siblings, adolescents on ART to reach sexual partners, and families with more than one member on ART.

Materials & Methods: Trained HIV testing service (HTS) providers were placed at 70 facilities, project developed index case contacts’ registers for active and deceased index clients, and sensitized health care workers. The registers were used for line listing active and deceased index clients’ contacts and documenting the contacts by relation to the index case (e.g., child, sibling, sexual partner). HTS providers and HIV clinic staff worked together to ensure line listing of index case contacts at enrolment on care, line listing of contacts of the current clients on care that were previously missed; and checking records of clients who had died in the past 2 years to collect contacts and assess eligibility. HIV testing was performed on contacts with consent. We conducted a descriptive analysis of data on positivity by type of index client.

Results: 27,484 children and adolescents were tested through this initiative, with 446 testing positive with a total positivity of 1.62%, compared to 0.9% of facility-based PITC at the same sites. 22,019 children of living adult clients were tested, 332 testing HIV positive (1.5% positivity). 860 children of deceased clients were tested and 30 tested positive (3.5% positivity). Out of 1,389 adolescents siblings tested 39 were positive (2.8% positivity). 8 out of 290 index adolescents partners tested were positive (2.8% positivity) and 2,925 children/adolescents who have more than one family member on ART were also tested with 37 testing positive (1.3% positivity).

Conclusions: Index case contact testing is an effective approach to identifying undiagnosed children and adolescents with HIV, and should continue to be prioritized and scaled up. This data demonstrates that index case contact testing can be optimized by utilizing a range of individuals as the index clients, including deceased clients with known HIV infection. We hypothesize that deceased individuals with known HIV infection may have been more likely to present with advanced disease, less likely to be retained on ART, and less likely to have disclosed their status to partners and family members. Using living adults on ART as the index client yielded the highest number of children and adolescents tested, as well as the highest number of infected children and adolescents identified, even though the positivity was lower than other approaches.

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Trends in Pediatric/Adolescent Intensified Case Finding: Lessons from Kenya, Swaziland, and Zambia

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Background: From February 2016 to January 2018, the Elizabeth Glaser Pediatric AIDS Foundation (EGPAF) implemented a range of facility and community-based HIV testing approaches for children and adolescents (age 18 months-14 years) at 133 sites across Kenya (78 sites), Swaziland (25 sites), and Zambia (30 sites). The objective of this initiative was to identify targeted testing approaches to reach children and young adolescents missed through prevention of mother-to-child transmission (PMTCT) services. This included optimizing provider-initiated testing and counseling (PITC) at outpatient and children centered facilities based on national eligibility for HIV testing, expanding index case contact testing, and targeted community-based “hotspot” testing. Referrals for testing from school campaigns to facility testing were also introduced.

Materials and Methods: We conducted a retrospective analysis of aggregate programmatic data (February 2016-January 2018) to identify results and trends in HIV testing across the three countries.

Results: 566,159 children and adolescents were tested, with 4,050 testing HIV positive. The highest
proportion of all children/adolescents tested and newly diagnosed were in Kenya (73% and 58% respectively), followed by Zambia (20% and 34%) and Swaziland (7% and 8%). Total HIV positivity was 0.7% across all children/adolescents tested, and total HIV positivity across the three countries ranged from 0.6% (Kenya), 0.9% (Swaziland), and 1.2% (Zambia). 38% of all children/adolescents testing HIV positive were 18 months to 4 years, 29% were five to nine years and 33% were 10-14 years. In Swaziland and Zambia, HIV positivity increased with age. In Swaziland, HIV positivity in children/adolescents aged five to nine years and 10-14 years was 126% to 471% higher than children aged 18 months to four years. In Kenya, HIV positivity was relatively constant across the age ranges. Between the first and second years, HIV positivity in each age group decreased by at least 10%, although the total number of HIV positive children/adolescents newly identified increased during this same period.

Conclusions: Although this initiative utilized targeted testing approaches, including screening children/adolescents using national eligibility criteria for HIV testing, targeting children/adolescents of biological family members with known HIV status, and “hotspot” community testing, HIV positivity was lower than anticipated. HIV positivity decreased between the first and second year of this initiative, as the number of children/adolescents with undiagnosed HIV infection in the catchment area decreased. HIV testing approaches need to be dynamic and regularly reviewed to include newer approaches to identify the decreasing number of HIV-positive children/adolescents who are undiagnosed. Additionally, our initiative demonstrated that specific efforts were required to reach children aged five to nine years and adolescents aged 10-14 years with testing, once they are missed in under five services. Despite the good progress of the PMTCT programs, gaps still exist in PMTCT as evidenced by the substantial number of children who are diagnosed at later age group of 18 months and older. Data, such as through this broad initiative, are important to informing accurate programmatic expectations, targets, and effective approaches.

Pediatric case finding, focusing on high yield entry points: Implementation of index case testing for children of women attending MCH services in Nampula and Zambezia province, Mozambique

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Background: Mozambique, with 1.4% pediatric HIV prevalence and 54% Pediatric ART coverage, is among the countries with the highest number of new pediatric HIV infections. Pediatric case identification remains the main barrier to timely ART initiation, and optimization of provider initiated testing and counseling and identification of high yield entry points has been a Ministry of Health priority. Index case testing (ICT) among children and partners of HIV-positive individuals has been identified as an important intervention to ensure timely identification of HIV-positive and exposed children.

Material & Methods: Between October and December 2017, ICAP piloted ICT within Maternal and Child Health (MCH) services at 26 high volume health facilities (HF). By January 2018, this strategy had been expanded to 79 high volume HF in Nampula (45) and Zambezia (34) Provinces. ICAP developed a screening tool to identify all contacts of HIV-positive pregnant and breastfeeding women was included in the index case registry and form. Testing eligibility was assessed and the option of HF testing or household testing during a home visit conducted by a community activist was offered to all mothers.
Results: Routinely reported data from the index case cascade was reviewed for the 2 periods of implementation. During the pilot phase (Oct-Dec’17), 581 index cases were identified, 551 child-contacts were tested, 43 identified as HIV-positive (7.8% yield) and 37 (86%) linked to care and treatment. During the scale-up period (Jan-Mar’18) out of 5499 index cases, 6137 child-contacts were tested, 454 identified as HIV-positive (7.4% yield) and 429 (95%) linked to care and treatment. Yield of pediatric testing at other entry points during pilot and scale-up phase was 2% and 5% at emergency rooms, 4% and 3% at inpatient consultation respectively. Challenges during initial implementation included shortage of HIV test kits, high refusal rates for household testing and low return to the HF for contacts testing. Considering those challenges, during the pilot phase ICAP worked closely with the regional and HF management team and staff to reinforce supply chain management, engaged key community actors to promote demand for ICT, strengthen quality of counseling provided at MCH and provide close follow-up of strategy implementation.

Conclusion: Index case testing presented as an important strategy for pediatric case identification in Mozambique context, identifying a high number of HIV-positive children and presenting the highest yield among the different testing strategies and entry points for this sub-population. Scale-up and increases in the number of children tested did not substantially reduce testing yield, reinforcing the importance of implementation in large scale to improve pediatric case identification. Close monitoring of early implementation is essential to ensure identification of key gaps, allowing identification of focused interventions to ensure adequate implementation and sustainable scale-up.

The Surge: A targeted, multi-strategy approach to accelerate HIV case finding in Malawi

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Background: The World Health Organization recommends a strategic combination of community- and facility-based HIV testing and Counseling (HTC) service models to improve the identification of people living with HIV (PLHIV). However, there is a paucity of literature describing the impact of an approach that simultaneously implements multiple HIV case finding strategies within routine program delivery. This study describes the impact of “The Surge”, a targeted multi-strategy testing approach on HIV case finding in Malawi; where 27.3% of PLHIV are unaware of their status.

Methods: The Surge was a simultaneous implementation of six HTC strategies (enhanced outpatient department screening, index case testing, extended testing hours on weekends and evenings, testing during mobile outreach clinics, targeted community testing events, and scaled-up facility-based provider initiated testing) over a 6 week period at 19 health facilities in Malawi. The Surge also included increased supervision, infrastructural enhancements to provide additional testing space, and creation of a data feedback loop that provided weekly performance reports to facilitate real-time programming adjustments. Routinely collected, de-identified data from Ministry of Health HTC registers were used to determine number of tests performed and positive cases identified.

Results: In total, 29,533 HIV tests were conducted; 1,051 (3.6%) were positive. Of total tests conducted, 69.6% were amongst women and 23.0% were amongst those 15 years and younger. Yield was 3.3% amongst women, 4.2% amongst men, 1.5% amongst those 15 and younger, and 4.2% amongst those older than 15. The average weekly number of tests performed increased 51.6% during the surge from 3,337 to 6,896 (p=0.002). The average weekly number of positive cases identified increased 34.3% during the surge from 157.6 to 240.0 (p=0.017), and average weekly testing yield decreased from 4.5% pre-surge to 3.6% during surge. Testing yield was 1.6% for males 15 years and younger, and 1.5% for females 15 and younger. Index case testing was the highest-yield strategy for identifying male and female clients <15 years (2.8% for both groups).
Conclusion: This study shows that a multi-strategy approach to HTC can be an effective means of accelerating HIV case finding; index case testing is particularly effective for identifying HIV-infected persons <15 years. Additionally, increased supervision, enhanced infrastructure, and real-time data feedback are critical factors in the success of a surge testing initiative.

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Volume and yield of pediatric HIV testing by modality in 21 PEPFAR-supported African programs

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Background: Case-finding for children living with HIV (CLHIV) remains suboptimal, contributing to persistently lower antiretroviral treatment (ART) coverage for children (<15 years old).

Methods: Volumes and positivity rates of HIV testing for children in PEPFAR-supported programs in Africa (Angola, Botswana, Burundi, Cameroon, Cote d’Ivoire, DRC, Ethiopia, Kenya, Lesotho, Malawi, Mozambique, Namibia, Nigeria, Rwanda, South Africa, South Sudan, Swaziland, Tanzania, Uganda, Zambia, Zimbabwe) during 2017 (fiscal year) were analyzed overall and by four modalities: inpatient wards, index testing, outpatient departments (OPD) and tuberculosis (TB) clinic. Early infant virologic diagnostic testing was excluded. Total testing exceeds the sum of the four selected modalities because we did not break out test results reported under modalities that were difficult to characterize for children (e.g., voluntary testing and counseling) or that were not primarily case-finding channels (e.g., pre-circumcision testing). Results from Ghana were excluded because they were incomplete.

Results: HIV testing volume (volume), contribution to overall testing volume (% of Volume), positivity rates (POS rate), and contribution to country program positive results (% of POS) varied widely across the 21 country programs. Overall, OPD testing contributed the greatest testing volume (49.2%) and cases identified (46.1%); however, on average, the OPD positivity rate (1.6%) was lower than the positivity rate overall (1.9%) and than for all other modalities: inpatient, 2.0%; index, 4.8%; TB, 5.0%. While TB positivity rates were high in many countries, it accounted for <2% of testing volumes (except 5% for South Sudan) and contributed <6% of case-finding. Inpatient POS rate was <5% for all countries except Burundi (6.3%). While index testing POS rates varied greatly, they were as high or higher than the overall POS rate for all but 3 countries (South Africa, Swaziland, Zambia) and accounted for >10% of new cases in 12 countries including >20% of all new cases in six countries (Burundi, Cote d’Ivoire, Ethiopia, Mozambique, Rwanda, South Sudan).

Conclusions: Tracking pediatric testing results overall and by modality can help countries adjust testing programs to optimize identification and treatment of CLHIV. Inpatient testing remains an important but declining source of case identification. Index testing has variable yield that may reflect whether testing is limited to biologic children of parents with HIV; scaling this approach with fidelity is a key strategy for finding children in all settings.

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Intensified case finding and tuberculosis preventive treatment among HIV-infected adolescents in Kenya: Facility and individual-level characteristics

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Background: TB is the leading cause of death among people living with HIV (PLHIV) and contributes to more than 1/3 of deaths among adolescents with HIV. The World Health Organization recommends
intensified case finding (ICF), isoniazid preventive therapy (IPT), and contact investigation for all HIV infected individuals to prevent tuberculosis (TB). However, data remains scarce on their implementation in adolescents and young adults (AYA). Despite AYA comprising approximately 22% of Kenya’s population and >20% of Kenyan PLHIV, TB prevalence and incidence is not reported for this age group. Utilizing individual medical record data and facility surveys from clinics in Kenya, we described ICF and IPT services provided to HIV-infected adolescents.

Materials & Methods: Eligible clinics completed a survey, detailing services provided to HIV-infected AYA, including TB symptom screening (also referred to as ICF) and IPT availability. In addition, we conducted a retrospective analysis of routine individual medical record data collected between January 2016-January 2017 in HIV-infected AYA, age 10-24. We assessed adult and child ICF records for TB symptom screening, presence of symptoms for TB, and use of IPT. We summarized ICF and IPT use, and clinic characteristics using descriptive statistics.

Results: Data were available from 36 facility surveys from large facilities (>500 individuals in care). Most facilities report conducting ICF and/or IPT (89%; 32/36). Among clinics that conducted ICF, most conducted ICF monthly or at every clinic visit (94%; 30/32). Twenty-three clinics (74%; 23/31) provided additional TB services following a positive ICF symptom screen and 23% (7/31) referred AYA to a different TB clinic.

For clinics that provided IPT, most clinics provided one month of IPT per visit (64%; 19/30). Five clinics (17%; 5/30) reported IPT shortage within the last 12 months. Clinics with the most frequent shortages (13%; 4/30 clinics every month or every 6 months) reported distributing shorter duration of IPT to patients due to shortages.

Of 3,321 individual records obtained from 36 facilities, almost all individuals had ICF records (>99%; 3305/3321). Two percent (71/3305) of all adolescents with ICF records had any TB symptoms, including 73% with cough (52/71), 28% with fever (20/71), 45% with weight loss (32/71), 35% with night sweats (25/71), and 3% were contacts of TB cases (2/71). All 71 symptomatic adolescents had confirmatory diagnostic testing with smear microscopy of sputum, resulting in 2 positive results (3%; 2/71). Twenty-five percent of ICF records indicated any IPT use (835/3305), with 49% completion of IPT (410/835), <1% discontinuation of IPT (4/835), and 50% missing values for IPT outcome (421/835).

Conclusions: While most facilities report providing ICF and IPT services, individual IPT uptake among individuals without TB symptoms remains low. Assessment of missingness/discontinuation of IPT may provide further insight into the institutional gaps that exist with universal ICF and IPT delivery. Quantifying ICF and IPT will strengthen TB data among AYA as well as improve reporting on IPT coverage and utilization in Kenya.

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I have made friends with whom we remind and encourage each other: Youth perspectives on and access to a WhatsApp-based HIV treatment support tool in Nairobi, Kenya

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Background: Adolescents and young adults (AYA) are disproportionately affected by HIV infection and experience poor treatment outcomes. Mobile health strategies have shown promise in supporting adult ART adherence but studies in AYA have been limited. Starting in 2014, HIV-infected AYA at two clinics in Nairobi spontaneously established virtual peer support groups using the mobile social media application, WhatsApp. We conducted a mixed-methods analysis of the messaging content of these WhatsApp groups, perspectives of AYA on the groups’ functions, and access to social media among HIV-infected AYA in Nairobi.

Materials & Methods: The study was conducted at two HIV clinics in Nairobi. In-depth interviews were conducted with 35 HIV-infected AYA (age 14-24): 14 members of WhatsApp peer support groups and 21 non-members. The study joined two WhatsApp groups, one at each study clinic, and 6 weeks’ messages were exported for content analysis. Two-hundred HIV-infected AYA attending HIV care (n=100 at each) completed a cross-sectional technology access questionnaire. Interview
The two existing WhatsApp groups included 250 and 60 members respectively. During the 6-week observation period, 52 (21%) of 250 members sent 378 messages in one group and 38 (63%) of 60 members sent 714 messages in the other. Messaging was spontaneous, unfacilitated, and included HIV-unrelated content such as jokes, entertainment and job opportunities, as well as HIV-related encouragement and ART reminders. Interviewed group members and non-members had median ages 20(IQR 17-23) and 18(15-18) respectively. Members viewed the groups as providing companionship, instrumental support, emotional support and behavioral modeling. Non-member-reported barriers to group participation included lack of smartphone and unawareness of the group. Members and non-members were supportive of using WhatsApp for peer treatment support. Desired group characteristics included large size (≥20 members), mixed gender, and age segregation. Desired content included unstructured discussion dynamically driven by member interests, as well as advice on status disclosure, HIV prevention and ART reminders. Some respondents desired healthcare worker involvement, while others opposed inclusion of healthcare workers in the group. The 200 AYA enrolled in the technology survey had median age 17(16-20), median self-reported age at HIV acquisition 4 years(0-12), and 99 (50%) had at least one deceased parent. One-hundred-forty (70%) had access to a mobile phone and 112 (56%) to a smartphone; 123 (62%) had used WhatsApp and 116 (58%) had used Facebook. Smartphone access was significantly higher in young adults (age 20-24) than adolescents (age 14-19) (86% vs. 44%, p<0.0001), but did not differ by gender, orphanhood or parental financial support (p>0.05 for all).

Conclusions: Mobile social media platforms offer a feasible and acceptable platform through which to support HIV treatment in this population of AYA. Access to smartphones and familiarity with social media is substantial, particularly among older youth. These findings offer guidance for development and evaluation of standardized virtual peer support interventions.

Assessment of adolescent HIV service delivery in Kenya: the PHASE study

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Background: Inadequate provision of accessible and acceptable HIV services has been cited as a barrier to engagement and retention in HIV care among adolescents. We assessed provision of adolescent services at HIV treatment facilities throughout Kenya.

Methods: We conducted a survey at 102 large (≥500 HIV-infected patients) facilities in Kenya randomly selected among clinics using electronic medical records. Interviews were conducted with healthcare providers between February-May 2017. Respondents provided information on provision of adolescent (ages 10-19 years) care including: adolescent-dedicated services, workforce training, HIV treatment practices, and reproductive health services.

Results: Facilities reported an average of 110 adolescents (Range: 4-1462) ever enrolled in care with 62 (Range: 3-508) in active follow-up. Forty-four percent of clinics had dedicated pediatric and adolescent clinic staff. Fifty-seven percent saw adolescents only on specific adolescent days rather than integrated into days for adults (23%), children (15%) or combined adult/pediatric days (9%). Most (72%) clinics reported having received training in adolescent HIV service provision while 59% reported receiving training in providing adolescent sexual and reproductive health services. Only 64% of clinics identified themselves as providing “adolescent friendly services.”

Most (81%) clinics offered peer support groups or teen clubs. Adolescents were most often given one month (51%) or three months (22%) of medication. Fifty-one clinics (50%) reported varying medication
delivery based on school schedules and/or medication adherence. Almost all clinics (99%) allowed a proxy to pick up medication for adolescents. One-third (34%) required a parent or primary caregiver to be present when providing HIV care to adolescent minors (ages 10-17) while 47% listed specifications for when care could be provided in the absence of a caregiver, including adolescent maturity and disease severity. Median age for initiating transition from pediatric to adult care was 15 years (IQR: 12-18), and for planned completion of transition was 19 years (IQR: 18-20). Most clinics reported providing condoms (65%), family planning services (60%) and STI screening (67%) to adolescents.

Conclusions: This study demonstrates the implementation landscape for adolescent HIV services in Kenyan clinics. Continued training on adolescent HIV service provision can ensure uniformly high quality of care across regions and facilities.

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Adolescent HIV services: Implementing universal antiretroviral treatment for 10-19 year olds living with HIV in eight African countries

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The Elizabeth Glaser Pediatric AIDS Foundation (EGPAF) supports treatment access in eight countries for >500,000 PLWH, in collaboration with Ministries of Health and various donors. HIV identification, treatment, retention and viral suppression has generally been lower among adolescents living with HIV (ALHIV) than in adults or younger children. We utilize disaggregated data to describe provision of HIV services to ALHIV in eight countries over a 12 month period, and identify remaining challenges.

From October 2016 –September 2017, EGPAF supported adolescent’s care by providing youth-friendly services, peer support, and building provider capacity in Cameroon, Democratic Republic of the Congo, Lesotho, Malawi, Kenya, Swaziland, Tanzania, and Zimbabwe. A total of 40,098 adolescents living with HIV (ALHIV) accessed treatment across 841 sites. Only 18,630 viral load tests were completed for adolescent clients. During this period, 7,574 adolescents were newly initiated on treatment, with surges around campaigns; 3,291 providers were trained in youth-friendly reproductive health, and HIV services and 486 psychosocial and peer support groups were attended by 9,268 ALHIV. Country specific data disaggregated by sex and age cohort (10-14 and 15-19 years) are available. All countries except Cameroon and the Democratic Republic of the Congo developed strategies and supported new country-specific adolescent HIV guidelines in 2017.

Summary: Adolescent HIV Care and Treatment Service Data from October 1, 2016 – September 30, 2017 is available to present by country, number of sites* providing data, total number of adolescents on ART, number of new adolescents initiated on ART in the last 12 months (by sex), number of viral load tests completed, number of providers trained in adolescent services in the last 12 months, and number of peer support/psychological social support groups for adolescents.

Adolescents represent just 4-10% of the total population in HIV care but have more intensive treatment, adherence counselling, and psychosocial support needs. Services are designed according to patient needs and volumes. Clubs and peer support groups are important supplements to clinical care but are not available to all adolescent clients. In one year, new patients represented 10-27% of the total ALHIV population. More providers can be trained at facility level compared to off site, which can build capacity using short courses and to empower multidisciplinary care cadres (clinicians, counsellors, social workers). Viral load testing is critical, but not yet accessible to most ALHIV.

The rapid pace of providing universal treatment will need to anticipate care challenges of unique adolescent patients alongside workforce capacity and resources. Global guidance for universal treatment has catalyzed access to ART for ALHIV.
Abstracts

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Across all eight countries, but access to viral load remains limited, making it difficult to assess the impact of ART on viral suppression.

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Adolescent-specific provider training and provision of services is associated with retention in Kenyan HIV clinics


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Introduction: Over 80% of adolescents and young adults (AYA) with HIV live in Africa. This population has poor clinical outcomes compared to other age groups, attributable to low engagement in care. We measured retention in HIV care, and evaluated correlates of retention, among AYA at 24 large public HIV clinics enrolled in a stepped-wedge randomized trial of standardized patient actor training to improve quality of care and AYA clinical outcomes (SPEED Study).

Materials and Methods: Eligible records were from AYA ages 10-24 enrolled at 24 HIV clinics with ≥40 AYA active clients in Central (Nairobi, Kiambu counties) and Western (Kisumu, Homa Bay counties) Kenya during the 15 months preceding the trial (11/1/2015-3/31/2017). Sociodemographics, clinical characteristics, and visit dates were abstracted from electronic medical records (EMR). Surveys with facility managers assessed whether the site offered any prior AYA-focused training and services. Surveys with individual health providers working in AYA HIV care (3-10 per facility) assessed self-reported history of AYA-specific trainings, experience caring for AYA, and self-rated competency. Facility-level means were derived from individual responses. Retention in care was defined as return for first follow-up visit within 3 months among newly enrolled or recently re-engaged AYA using EMR visit dates. Multi-level regression modeling was used to estimate risk ratios (RRs) and 95% Confidence Intervals (CIs) between facility and individual cofactors and AYA retention.

Results: Among 3,656 AYA records at first eligible visit, most were female (75.0%), older (20-24 years: 54.3%), and on ART (79.5%). Overall, 2,636 AYA were retained (72.1%), with retention higher among females (73.1% vs. males 68.9%), older AYA (20-24 years: 75.0% vs. 10-14: 69.2%, 15-19: 68.0%), and at Western Kenya clinics (82.7% vs. 66.0% Central). Clinics where >20% health providers reported being trained in adolescent-friendly care had higher AYA retention than those with ≤20% of providers trained (85.4% vs. 66.4%, aRR 1.18, 95%CI:1.08-1.29), as did clinics with higher mean provider self-rated competency scores in caring for AYA (aRR 1.03, 95%CI:1.01-1.05). Clinics using the Kenyan government’s new adolescent package of care checklist had significantly higher overall AYA retention (88.9% vs. 69.2%;aRR 1.14, 95%CI:1.06-1.23).

Conclusion: Results suggest sub-optimal retention among HIV-positive AYA in Kenya. This is one of the first studies demonstrating that adolescent-specific health provider training and services may improve AYA retention in care, suggesting that health provider interventions are necessary to achieve the ‘90-90-90’ targets for this priority population.
Improving retention in HIV care of adolescents through provision of adolescent friendly services in Rwenzori region, western Uganda.

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Background: Adolescents living with HIV are an under served population and lack specific programs targeting their needs. Poor retention in HIV health care services and high mortality rates due to HIV have been reported in this age group. Adolescents are the only age group in which deaths due to AIDS are not decreasing. In Rwenzori region, twelve-month retention in HIV care for adolescents was at 73% (October 2015 – March 2016). Baylor Uganda implemented targeted adolescent friendly interventions to improve retention in HIV care for adolescents. We describe best practices learnt in improving retention in HIV care for adolescents.

Description: From February 2016 to March 2018, the following interventions were implemented to strengthen retention in HIV care for adolescents in 5 districts in Rwenzori region:

In February 2016, selected health workers were trained to provide adolescent friendly services at health facilities. These became adolescent focal persons and played an oversight role in provision of adolescent friendly services at the health facilities.

In April 2016, trained adolescent focal persons were supported to establish adolescent-only clinics for HIV care. Previously adolescents had been obtaining HIV services on the same clinic day as adults. In the same period, health facilities were supported to conduct adolescent peer support meetings once every 2 months at which peer to peer psycho-social support was provided.

In September 2016, adolescent peer leaders were trained and engaged in planning and provision of adolescent HIV services including peer to peer health education talks, counselling, file running, routine follow up and follow up of lost adolescents through home visits. Twelve-month retention data for adolescents in HIV care was abstracted from hybrid reporting system (PEPFAR national data system) before intervention (October 2015 –March 2016 cohort) and after the intervention (April 2016 – September 2016, October 2016 – March 2017, April 2017 – September 2017 and October 2017 – March 2018 cohorts).

Lessons learnt: Between April 2016 to March 2018, adolescent-only HIV care clinics increased from 12 to 57 clinics with all the clinics having adolescent peer leaders. Before the intervention, 12-month retention in HIV care for adolescents was at 73% (October 2015 –March 2016) and it dropped to 66% for the April 2016 – September 2016 cohort at the beginning of implementation of the intervention. Progressive increase in 12-month retention was achieved in the cohorts of October 2016 – March 2017 (80%), April 2017 – September 2017 (85%) and October 2017 – March 2018 (93%) following training and engagement of adolescent peer leaders.

Recommendations: Deliberate efforts should be made to train and engage adolescent peer leaders within adolescent-only friendly HIV care clinics as a strategy of improving retention in HIV care for adolescents.

Meaningful engagement of schools and school-based advocates in promoting education on HIV and supporting adolescents living with HIV in Homa Bay, Kenya

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Background: Adolescents living with HIV (ALHIV) spend a significant proportion of their daily lives in schools. In 2016, with support from ViIV Healthcare, the Elizabeth Glaser Pediatric AIDS Foundation implemented the innovative peer-designed fast-track linkage-to-care and early retention Red Carpet Program (RCP) throughout public health care facilities (HCFS) and schools in Kenya. RCP worked closely with the Ministry of Education (MOE) and
Ministry of Health (MOH) to design and implement school-based interventions to promote HIV education and support for ALHIV. The aim of this analysis was to evaluate the implementation of RCP school-based interventions conducted in 2017.

Description: RCP conducted two main interventions in the Homa Bay County boarding schools: a) enhanced partnership between schools and 50 RCP HCFs; b) built capacity of adolescent health advocates (counselling teachers, school matrons, school nurses and boarding in-charge personnel). A sensitization meeting was held with 70 secondary school managers, principals, Teachers Service Commission and MOE officials in August 2017. During August-September 2017, RCP conducted a two-day capacity building workshop for 90 school-based adolescent health advocates from 67 high volume local secondary boarding schools.

Lessons learned: By November 2017, 50 boarding schools in Homa Bay County developed key School based HIV strategies including: a) fostering direct linkages with HCFs; b) formation of School Health Committees (SHC) including counsellors, teachers, school managers, students, parents, HCWs form linked facilities, adolescent health advocates; c) training of adolescent health advocates; and d) support of ALHIV. By December 2017, 50 SHC were formed and >3000 students (both HIV+ and HIV-) were reached with education on HIV, HIV stigma, antiretroviral treatment, pre-exposure prophylaxis, and sexual and reproductive health. A total of 153 ALHIV who have disclosed their HIV status in schools, have been supported with access to clinical care, having access to their antiretroviral medications and being supported staying in care and on treatment. The uptake of the general HIV education and support services for ALHIV was high in 50 schools of Homa Bay County, Kenya. With RCP support, we were able to have high level of collaboration between regional MOE and MOH on the ALHIV agenda. Going forward, RCP works to expand collaboration between HCFs and schools with a goal of increasing long-term retention in care and on treatment, and achieving high levels of virologic suppression among ALHIV.

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Effect of mental health adversities on adherence to antiretroviral medication among adolescents living with HIV and visiting the Comprehensive Care Clinic at Kenyatta National Hospital in Kenya

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Background: Globally adolescents continue to have an upward trend in HIV incidence and AIDS related mortality. The interplay between the rapid physical growth, sexual maturation and enormous albeit slow-evolving cognitive and psychological changes in adolescence may partly explain this trend. Our main purpose was to determine the prevalence of depression and its association with adherence to antiretroviral medication among adolescents living with HIV.

Methodology: The study was a descriptive cross sectional survey conducted between August and December 2016 among 270 adolescents ages 10-19 years attending the HIV clinic at Kenyatta National Hospital in Nairobi. Depression was screened using Patient Health Questionnaire – 9 tool and adherence was self-reported using a validated questionnaire. Univariate and multivariate analysis was done to determine association between depression and poor adherence to antiretroviral medication.

Results: The mean age of our sample of 270 was 14.75 years (SD=2.6 years). This included 125 adolescents aged 10-14 years and 145 aged 15-19 years; of whom 145 (53.7%) were male and 125 (47.3%) female participants. Overall 142 (52.6%) of the adolescents had depression symptoms and 139 (51.5%) reported poor adherence to their medications. Twelve (4.4%) of the adolescents were found to have suicidal ideation in the last two weeks preceding the survey. On univariate analysis adolescents who had experienced symptoms of
depression were significantly more likely to report poor adherence to their medications 89 (62.7%) versus 50 (39.1%), [OR=2.62 (95% CI 1.60, 4.28), p<0.001]. While on multivariate analysis non-adherence to medication increased likelihood of having depression symptoms by almost two fold [OR=1.84 (95% CI 1.08-3.14) p=0.03].

**Conclusion:** Though further studies need to be conducted to determine causal relationship between depression and poor adherence, our work highlights the need to tap and focus on this area if 90% viral suppression is to be achieved.

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**Evaluating an enhanced adherence intervention and defining atazanavir hair concentrations among HIV positive adolescents failing atazanavir/ritonavir-based second line antiretroviral treatment at a public health clinic**

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**Background:** Adequate antiretroviral exposure is crucial for virological suppression. Sustaining virological suppression among HIV-infected adolescents is challenging. Enhanced adherence support may improve treatment outcome. This study evaluated the relationship between a home-based adherence intervention and viral load (VL) response, atazanavir hair concentrations and self-reported adherence among adolescents failing atazanavir/ritonavir-based 2nd line treatment at Harare hospital, Zimbabwe. The study also evaluated drug resistance in the same cohort.

**Methods:** HIV-infected adolescents (10-18 years) on atazanavir/ritonavir-based 2nd line treatment for ≥6 months with virological treatment failure (VL >1 000 copies/ml) were randomised to either standard care (control) or standard care + modified directly administered antiretroviral therapy (mDAART) (intervention) for 90 days. VL was measured and questionnaires administered at baseline and 90 days. Genotyping was done for participants with continued virological failure. Primary outcome was suppression to VL <1 000 copies/ml.

**Results:** Fifty adolescents were enrolled; 23(46%) were randomized to mDAART + standard care, and 27(54%) to standard care only. Fifty-four percent were female; mean age was 15.8 years and mean baseline VL was 4.8 log10 copies/ml; Participants in mDAART: were modestly associated with virological suppression (p=0.105); were significantly associated with VL decrease (p=0.031) and lower VL after follow-up (p=0.04); had higher self-reported average adherence over the past month (p=0.05) and reported adhering to dosing schedule over the past 4 days more (p<0.001). There were no significant differences in atazanavir hair concentration between the 2 arms after follow-up. Atazanavir hair concentration ≤2.35ng/mg (lower inter-quartile range for those with virological suppression) defined a cut-off below which most participants experienced virological failure (p<0.001). Male sex (p=0.03), virological suppression at follow-up (p=0.013), greater reduction in VL (p=0.006), decreased average adherence over the past month (follow-up minus baseline) (p=0.031) and change in average self-reported adherence over the previous month (p=0.031) were associated with adequate (>2.35ng/mg) hair concentrations. Participants with atazanavir hair concentrations ≤2.35ng/mg were: more likely to have virological failure (RR=7.2, 95% CI=1-50.9, p=0.049); more likely to have decreased average adherence over the past month (RR=295, 95% CI=2.6-33 921, p=0.019) and less likely to be male (RR=0.019, 95% CI=0.0008-0.44, p=0.013). Genotyping in 28/30 participants with continued virological failure demonstrated high level atazanavir resistance (I50L, N88S and I84V) in 6(21%).

**Discussion:** mDAART modestly improved virological suppression, significantly decreased VL and significantly increased self-reported adherence among adolescents with atazanavir/ritonavir-based 2nd line failure. It did not increase atazanavir hair concentrations. A threshold of atazanavir concentrations in hair (2.35ng/mg), above which virological suppression was likely, was defined for adolescents. Antiretroviral hair concentrations may serve as a useful tool among adolescents. High level atazanavir resistance was demonstrated.

**Conclusion:** Targeting mDAART to adolescents with virological failure to atazanavir/ritonavir-based 2nd line treatment improves virological outcome and increases self-reported adherence. Increasing...
Availability of 3rd line treatment and antiretroviral resistance testing is important.

Key words: Adolescents, virological 2nd line treatment failure, adherence, drug resistance.

Comparison of Methods to measure ART adherence in children and young people living with HIV: Analysis of data from the BREATHER trial

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Background: Adherence to antiretroviral therapy (ART) is critical to achieve successful clinical outcomes and is known to be problematic during adolescence. Measurement of adherence can be challenging and better understanding of the validity of adherence tools may improve adherence assessment. The BREATHER trial randomised participants to continuous ART versus short cycle therapy (5 days on, 2 days off). Our aim was to compare and evaluate the adherence measures used in the BREATHER trial.

Materials & Methods: Viral load (VL) and 6 measures of adherence (any missed doses in the last week, since last visit and visual analogue scale (VAS), each reported by participant and caregiver) were collected at weeks 4, 12, then 12 weekly up to week 204. The trial’s primary outcome was viral rebound (confirmed VL≥50c/ml) and was used in this analysis as a proxy for “true” adherence. Trial arms were pooled as there were no significant differences between arms for any adherence measure or viral rebound. The association between viral rebound and each adherence measure was analysed using random effects logistic regression, adjusting for visit week and trial arm; baseline variables were examined as predictors of viral rebound.

Results: Of 199 participants, 105(53%) were male, 180(91%) had perinatal HIV, median age at baseline was 13.9 [IQR 11.9,17.4] years and median duration of ART at baseline was 6.0 [4.1,8.3] years. Median follow-up was 188 [155,203] weeks. Viral rebound occurred at 118/2812 (4%) visits and 32(16%) participants. Adherence questionnaire completion rates varied by age (caregivers completed questionnaires for younger participants). Participants and caregivers reported missing doses in the previous week at 172/2487 (7%) and 62/1485 (4%) visits respectively. At 19/94 (20%) visits with viral rebound (and questionnaire data available), the participant reported missed doses in the previous week; the corresponding result for caregiver report was 3/41 (7%). At 19/168 (11%) and 3/61 (5%) visits where the participant and caregiver, respectively, reported missed doses in the previous week and VL data available, viral rebound occurred. After adjusting for visit week and trial arm, participants report of missed doses in the previous week was most strongly associated with viral rebound (odds ratio (OR) 3.88 [95%CI 1.52,9.82], p=0.006); findings were similar in each trial arm (interaction p=1.0). Less than 95% adherence since last visit on the patient VAS (OR 2.50 [1.12,5.66], p=0.054) and caregiver VAS (OR 4.58 [1.33,15.79], p=0.025), and participant report of any doses missed since last visit (OR 2.96 [1.32,6.63] p=0.010) were also associated with viral rebound, albeit less strongly. Age, sex, ethnicity, African/non-African site, duration on ART, mode of HIV infection, baseline ART regimen, and trial arm were not associated with viral rebound.

Conclusions: Self-reported missed doses in the previous week helps to identify young people on ART who require additional adherence support. However, none of the adherence measures used provided a reliable surrogate for viral rebound. Most participants reporting recent missed doses remained virologically suppressed; conversely, there appeared to be under reporting of poor adherence.
adherence to treatment as evidenced by viral rebound in the absence of reported missed doses.

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“I failed to take them as I should and now I’m scared”: How can we support adolescents’ adherence on second line HIV treatment?

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Background: Sustaining optimal adherence is the major challenge facing adolescents living with HIV (adolescents). In low-income settings ‘second-line treatment’ is often the last affordable and accessible option. Given this, how can we best support adolescents to adhere once their treatment has been changed?

Methods: Using qualitative data from ODYSSEY, a large international clinical trial, we examine the adherence experiences of adolescents who are being moved onto second-line treatment, prior to entering the trial. We report on the baseline in-depth interview data from 40 adolescents (aged 10-18) from Uganda and Zimbabwe, we describe their adherence stories, including reasons for their sub-optimal adherence behaviour, as well as identify the implications for their treatment engagement, support needs and self-management of HIV.

Results: Some adolescents explained that poor adherence had been due to a limited understanding of why they were taking the medication and/or the physical side effects of taking ART, such as persistent nausea. There were also more complex explanations, which included feeling frustrated with carers’ lack of transparency about the nature of their condition and uncertainty about their present and future quality of life with HIV. A rapid shift from mediated to autonomous treatment taking appeared to often accompany worsening adherence behaviour, suggesting that relational support was withdrawn too quickly for young people to effectively adapt. Concerned about the reaction of their caregivers and healthcare providers and keen to protect these relationships, adolescents delayed discussing their difficult adherence experiences until a clinical crisis occurred.

The clinical term ‘treatment failure’, frequently used to explain a treatment switch, has been imbued with unintended social meaning. It is interpreted by participants as indicating failed adherence behaviour. Switching treatment is characterised by fear and blame, which further impedes being candid about adherence problems.

Conclusions: Adherence behaviour is not static, especially throughout adolescence as ALHIV encounter multiple changes in circumstances and responsibilities. Fluctuating treatment compliance can be anticipated and ongoing discussion initiated within the clinic. We must reconsider the language used to describe treatment switches and move from the implicit emphasis on individual culpability. Relationally-orientated solutions which involve significant others around the young person appear to show greater potential for supporting adherence than the narrower focus on the individual.

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Background: Eighty percent of adolescents living with HIV (ALHIV) worldwide are in sub-Saharan Africa. We aimed to assess the 24-month outcomes among ALHIV with perinatally acquired HIV, in two sites of the West-African IeDEA paediatric cohort.

Methods: The COHADO cohort, as part of the West African International epidemiologic Database to Evaluate AIDS (IeDEA) Collaboration paediatric cohort, was initiated in 2015. All adolescents aged 10–19 years, included in HIV-care before the age of 10 years (proxy of perinatal infection), on antiretroviral treatment (ART), followed up at Yopougon Teaching Hospital (Abidjan, Côte d’Ivoire) and Sylvanus Olympio Teaching Hospital (Lomé, Togo), and who consent with their parents to be enrolled were included. The 24-month outcome was assessed using clinical, immunological and virological criteria, separately then combined. Adolescent had a favourable combined outcome if he was alive, followed up, did not progress to WHO clinical stage 4 (AIDS), had CD4 count not <10% of the baseline value, and had a viral load undetectable (<50 copies/mL). We performed a backward stepwise logistic regression analysis, to assess factors associated with a favourable outcome after 24 months of follow-up.

Results: A total of 209 adolescents were included. Among them, 52% were in Abidjan, 55% were females. At inclusion, median [interquartile range (IQR)] age was 13[12-15] years and they were younger in Togo (12[11-15] years) than in Côte d’Ivoire (14[12-15] years) (p=0.012). Median [IQR] age at ART start was 7[4-10] years; median [IQR] duration of ART was 6[4-10] years, and it was shorter in Togo (5[2-6] years) than in Côte d’Ivoire (9[7-11] years) (p<0.001); Overall, 54% had a good treatment adherence (>95% of planned doses); 46% were classified WHO clinical stage 1, 80% in Côte d’Ivoire versus 9% in Togo (p<0.001). Median [IQR] CD4 count was 521 [278-755] cell/mm3, 540 [314-753] cell/mm3 in Côte d’Ivoire and 484 [272-760] in Togo (p=0.716). Only 30% had viral load measurement (8%<1000 copies/mL, 3%<50 copies/mL). The frequency of adolescents aware of their HIV status at baseline was 42.4% (95%CI: 35.5-49.2): 54.4% in Côte d’Ivoire and 25.3% in Togo (p<0.01). After 24 months, 4 (1.9%) adolescents were transferred out, 6 (2.9%) adolescents died, 8 (3.8%) were lost to follow-up, 7 (3.4%) progressed to WHO clinical stage 4. 76(36.7%) had CD4 count below 10% of the baseline value (51% in Côte d’Ivoire versus 21% in Togo, p<0.001), and among the 80% with viral load measurements, 52.3% were virologically suppressed (47% in Côte d’Ivoire versus 76% in Togo, p<0.001). The 24-month combined outcome was favourable for 45% of adolescent overall (29.6% in Côte d’Ivoire and 61.4% in Togo, p<0.001). Adjusted on sex, disclosure status, adolescents from Togo are four times more likely to have a favourable outcome compared to those from Côte d’Ivoire (adjusted odds ratio (aOR)=4.36 IC95%:1.18-4.62, p<0.001)

Conclusions: In this West-African cohort of young ALHIV on ART, mortality was high, and only less than half had a favourable combined outcome after 24 month. Efforts are urgently needed to improve their care and reach the 90% target of virological success on ART.

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90-90-48: The Reality of Viral Suppression among ART-initiated Adolescents in South Africa

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Background: Global fast-track targets include 90% viral suppression among all ART-initiated persons. Data suggests adolescents have worse viral suppression rates than children and adults, but little is known on adolescent progression through the HIV treatment cascade, once initiated on ART. This study examines the HIV treatment cascade for a large sample of HIV+ adolescents in South Africa.

Methods: 1,058 ART-initiated adolescents (10-19 years) from 52 urban and rural healthcare facilities in the Eastern Cape were interviewed (March 2014-September 2015). Data were extracted from paper-based medical records from all facilities (including records in multiple facilities) through January 2018. Predictors of progression through cascade were identified using sequential multivariate logistic regressions, with age (10-14/15-19 years), sex, urban/rural residence, mode of infection, decentralised/centralised ART care, and time on ART entered simultaneously. Interactive effects and moderating effects of gender and mode of infection were tested with regressions, corrected with the Benjamini-Hochberg procedure.
Results: 92.5% of adolescents had viral loads available in clinic files. 63.1% had viral loads recorded in the past 2 years. At most recent viral load, 78.5% of measurements were ≤1000 copies/mL, but only 58.8% were undetectable (≤50 copies/mL). Participants were female (54.0%), median age 13 years (IQR 11-16), urban-living (76.8%); and 30.0% attended ≥2 healthcare facilities. Adolescents on ART for <2 years were more likely to lack viral loads from the past 2 years (OR 5.73 [95%CI 1.82-18.08], p=0.003), and decentralised care was protective only for females (OR 2.56 [95%CI 1.40-4.64], p=0.002). Viral load >1000 copies/mL was associated with older age and rural-living (OR 2.18 [95%CI 1.58-3.00], p<0.001; OR 1.48 [95%CI 1.06-2.12], p=0.031). Older adolescents, those on ART for <2 years, and decentralised adolescents were less likely to have undetectable viral loads (OR 0.65 [95%CI 0.49-0.87], p=0.003; OR 0.36 [95%CI 0.13-0.91], p=0.047; OR 0.74 [95%CI 0.57-0.98], p=0.035).

Conclusions: Viral suppression rates remain low among adolescents in South Africa. Older, recently initiated, and decentralised adolescents were least likely to be virally suppressed — potentially due to down-referrals from tertiary paediatric facilities to generalised primary clinics. With 30% of adolescents receiving care in multiple facilities, interventions supporting patient linkages to care may be essential for adolescents transitioning across multiple forms of care.

Virological suppression among young people living with perinatally and behaviourally-acquired HIV infection in Ukraine


Background: Two-thirds of adults in HIV care in Ukraine receive ART, among whom 80% on ART for >6 months have undetectable viral load (VL) (<40c/ml). We aimed to explore virological suppression (VS) among young people in HIV care. Nationally in 2016, this population included 1500 young people with perinatally-acquired (PHIV) and 11,500 with behaviourally-acquired HIV (BHIV) aged 10-24 years.

Methods: The Ukraine Paediatric HIV Cohort has prospectively followed children and young people in paediatric HIV care since 2011, currently active at 13 sites. In 2016-2017, within a linked project on young people, data were collected on BHIV ≤25 year olds at 5 centres including clinical status, ART and VL. Analyses explored VLS<400c/ml at last measure among those on ART for >6 months; Poisson regression models with robust estimates were fitted to explore associated factors.

Results: Of 917 PHIV young people aged ≥10 years at last follow-up, median age was 13.5 [IQR 11.7, 15.8] years, 48% (443) were male, median CD4 count was 740 [535, 975] cells/mm³ and 38% (344) had a history of AIDS. Most (97%, 893) were on ART, initiated at median age 5.5 [2.7, 8.2] years. Of these 893, 68 had been on ART for <6 months (n=13), were aged <10 years (n=26) at last VL, or were missing ART duration (n=29). Of the remainder, 90% (746/825) had VLS<400c/ml at last measure and 81% (667/825) had VL<40c/ml. After adjusting for centre and pre-ART AIDS diagnosis, age ≥9 years at ART start was associated with lower probability of VLS<400c/ml at last measure (AIRR 0.90 [95%CI 0.81-0.99], AIRR 0.99 [0.92-1.06] for 1-3 years and AIRR 0.94 (0.88-1.02) for 4-8 years, all vs age <1 year) as was exposure to ≥5 antiretroviral drugs (AIRR 0.90 (0.85-0.96), AIRR 1.03 (0.98-1.08) for 4 drugs, both vs 3 drugs). Age at VL measure was not associated with VLS<400c/ml (p=0.834 for categories 10-12, 13-15 and 16-20 years) and neither was sex (p=0.300). Among 384 BHIV young people, median age was 23.1 [21.3, 24.2] years. Most (68%, 259/380) were on ART: Median time since HIV diagnosis was 1.4 [0.5, 3.1] years with no difference by ART status (p=0.294). More women were on ART than men (72% [208/290] vs 57% [51/90] respectively.
Background: WHO clinical stage 4 disease history. Median nadir CD4 was 319 [228,445] cells/mm³ for those on ART vs 460 [303,609] cells/mm³ for those not. Median ART duration was 0.9 [0.3, 2.1] years; VL was available for 223/259, at >6 months after ART start for 130/259, of whom 79% (103/130) had VL≤400c/ml and 77% (100/130) VL<40c/ml. In these 130, all 17 males vs 76% (86/113) females had VL≤400c/ml (p=0.023) but VL≤40c/ml was not associated with age (IRR 1.02 (0.97-1.07) per year) or time since HIV diagnosis (IRR 1.00 (0.98-1.03) per 6 months).

Conclusions: PHIV young people were doing well on ART with 90% attaining VS. Rates of VS appeared lower among BHIV young people, although consistent with national figures for adults generally.

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The power of peers: Multi-country analysis of adolescent viral suppression in sub-Saharan Africa

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Background: UNAIDS fast-track targets require 90% of people on ART to be virally suppressed, but we are far from reaching this goal in adolescents and young people. Limited age-disaggregated data from sub-Saharan Africa reflect viral suppression rates of 33-56% in these age groups. Health facility-based adolescent peer supporter programmes have gained recent attention as a promising scaleable intervention. However, we urgently need to examine their effectiveness in real-world settings in sub-Saharan Africa. This is the first known multi-country analysis of the impact of facility-based adolescent peer support on viral suppression.

Materials & Methods: In 2017, Paediatric-Adolescent Treatment Africa (PATA), a network of frontline health providers across sub-Saharan Africa, conducted cross-sectional surveys with 71 health facilities from 13 countries in Southern, Eastern, West and Central Africa to assess facility-level characteristics and past-year adolescent (10-19 years) viral suppression rates. Data were analysed using multivariate logistic regression to measure the impact of ≥1 facility-based adolescent peer supporter on adolescent viral suppression rate, controlling for: country, urban/rural location, public/private facility, level of facility (primary/secondary/tertiary) and physician/non-physician care. UNAIDS Eastern and Southern Africa (ESARO) 2017 data for all people living with HIV were used to define the regional viral suppression rate as 50%.

Results: Facility respondents were from Southern (35.2%), East (54.9%) and West/Central African (9.8%) regions. Two-thirds (74.7%) of facilities were urban/peri-urban and 57.8% public-only. Half (49.3%) provided primary care and 74.7% physician care. Controlling for these facility characteristics, provision of facility-based adolescent peer support was associated with an almost seven-fold increase in the likelihood of aggregate adolescent viral suppression above that of the ESARO regional rate (adjusted OR 6.95, p=0.02, CI 1.28-37.59).

Conclusions: Findings suggest that peer support should be a key service component of the facility-based health response for adolescents living with HIV in sub-Saharan Africa, regardless of where facilities are located, their level of care or health provider profile. However, further operational research is needed to determine how best to implement and integrate peer support programmes. PATA will seek to identify a minimum package of peer-led services for low-resource settings to optimise the power of peers for the health and wellbeing of adolescents living with HIV.

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Post-transition outcomes of adolescents and young adults in Asia highlight need to address chronic viremia and diversify adherence support
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Background: Adolescents and young adults living with HIV (AYHIV) who received care in pediatric HIV clinics will eventually transfer to adult HIV care as they age. Our study aims to assess factors associated with transition outcomes in Asia, and explore barriers and facilitators for successful post-transition retention in care.

Methods: AYHIV who were transferred from pediatric to adult HIV care were consented and enrolled into the Study of Transitioning Asian Youth (STAY) cohort between March 2016-April 2017. Study visits were at four “sending” pediatric clinics in Thailand and Vietnam, or at one “receiving” adult clinic in Malaysia. Demographic and clinical data and self-reported socio-economic and risk behavior data were collected at enrolment and at 48 weeks.

Results: A total of 93 AYHIV from Thailand (81%), Malaysia (11%), and Vietnam (8%) were enrolled: 94% were perinatally infected, 60% were female. At week 48, 87 AYHIV remained in study follow-up; 3 died (disseminated tuberculosis, n=2; septic shock, n=1), 2 discontinued from the study, and 1 was lost to follow-up. Their median age was 20 (18-21) years; median post-transition time was 14 (11-19) months from the first adult clinic visit (n=67) or 16 (12-20) months from the last pediatric clinic visit (n=20). They reported their most recent adult HIV clinic visit was within 6 months (20%), 7-12 months (22%), >12 months (29%), or did not remember (28%). All patients at week 48 were on antiretroviral therapy (ART; median duration 13.7 [10.8-16.2] years), of whom 51% reported 100% 30-day adherence by visual analogue scale. Current ART regimens included non-nucleoside reverse transcriptase inhibitors (57%), protease inhibitors (PI; 42%), or PI plus integrase inhibitor (1%); 62% of regimens included tenofovir and 3.5% included abacavir. Between weeks 0 and 48, the proportion with HIV RNA suppression (<40 copies/mL) was similar (82% to 81%). Of those with detectable HIV RNA at week 48 (median 4,700 [255-26,078] copies/mL), 69% had viremia at week 0. From week 0 to 48, more patients reported living alone (5% to 16%) or with a partner (7% to 15%), working full-time (43% to 66%), and had higher monthly incomes (323-484 USD: 5.4% to 23%). Of the 52% who had sex in the past 3 months, 56% always used condoms. From week 0 to 48, some AYHIV reported rarely or never having someone they trusted to talk with about their problems (26% to 30%), feeling unequal in their relationships with others due to their HIV (11% to 23%), being less confident to deal efficiently with unexpected events (37% to 24%) and needing to keep their HIV status a secret (70% to 63%).

Conclusions: While ~80% of our cohort were virally suppressed after transition, most of the remainder were persistently viremic over the past year. Though reporting greater independence in their personal and professional lives, they continued to have challenges with navigating relationships and finding social support. Interventions to support adherence should be prioritized for those with chronic viremia and expanded beyond drug and regimen simplification to include mental health support.
Transitioning adolescents to adult HIV care: Health facility models of care and transition practices in Kenya

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Introduction: It is urgent to understand and improve transition to adult HIV care systems for adolescents in sub-Saharan Africa. Differences in clinic models may influence transition definitions and procedures. While guidelines often recommend age-based milestones to track transition readiness, specific tools to track individual non-age milestones are often lacking. We determined models of adolescent care, transition definitions and transition tracking practices in HIV clinics in Kenya.

Materials and Methods: We conducted in-person facility surveys with clinic managers from a random sample of 36 large (≥500 total patients in care) HIV clinics. Surveys collected information on models of adolescent care, definitions of transition and availability of transition guidelines and tracking tools. We compared availability of transition guidelines by models of care, adolescent services, and clinic type using Fisher’s exact test.

Results: Of 36 clinics, 3(8%) were county hospitals, 12(33%) sub-county hospitals, 20(56%) health centers or dispensaries and 1(3%) a mission hospital. The majority (72%) of clinics provided adolescent services on dedicated adolescent clinic days. Most clinics (92%) had the same staff providing care for all age-groups, with only 2(3%) reporting specific adolescent staff. Transition definitions were heterogeneous. In almost all (92%) clinics, age defined when transition occurred. Other definitions included: demonstrating independence in managing care (29 [81%]), independently collecting antiretroviral medication (15(42%)), completing an adult clinic visit (9[26%]), completing a formal transition process (8[22%]) and becoming pregnant (3[8%]). Thirty-three (92%) had a specified age at which transition discussions should begin (median: 18 years; IQR: 17-19) and transition be completed (median: 20 years; IQR: 18-23). When assessing readiness for transition, non-age factors considered included viral suppression or adherence in 20 (56%) and mental health in 23 (64%). Twenty-eight (78%) clinics had systems to identify adolescent records that included different folder colors (10 [28%]), stickers (5[14%]) or separate storage (4[11%]). Eleven (31%) clinics used the adolescent checklist, a tool developed by the Kenya Ministry of Health that has one question (yes/no) on transition preparation, as a transition tracking tool. Ten (28%) clinics reported using other tracking documents, including readiness assessment tools, and 15(42%) clinics did not use any tools. Twenty-four clinics (67%) reported tracking adolescents who had completed the transition process, including the adolescent checklist (13[54%]), transition logs (9([38%]), nurse notes (7[29%]), clinic notes (6[26%]), and electronic medical records (1[5%]). Eighteen (50%) clinics documented transfer completion to adult clinics either through patient file transfer (13[33%]), notes in electronic medical records (6[17%]), change in filing (2[6%]), transfer letter (1[3%]) and handover registers (1[3%]). Clinics that reported using transition tools were more likely to have dedicated adolescent clinic days (90% vs. 50%; p=0.02) and were more likely to use the adolescent checklist (89% vs.14%; p=0.001) compared to clinics not using transition tools.

Conclusion: Lack of consensus on adolescent models of care and definitions of transition make it challenging to evaluate transition processes and practices. Research to develop consistent transition definitions and tools to track post-transition outcomes are urgently needed.
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Differential genital inflammation associated with Chlamydia trachomatis sequence types in adolescent girls and young women at high risk of HIV infection

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**Background:** Chlamydia trachomatis is highly prevalent in young people, with significant genetic diversity that may influence pathogenesis. C. trachomatis increases HIV risk in adolescent girls and young women (AGYW), and causes reproductive complications. We hypothesized that different C. trachomatis strains could increase genital inflammation, which could may influence HIV acquisition risk.

**Methods:** We enrolled 298 AGYW (16-22 years) from Cape Town (CPT) and Soweto, Johannesburg (JHB) South Africa (WISH cohort) who were tested for: C. trachomatis (including L-serovars), Neisseria gonorrhoeae, Treponema pallidum using multiplex PCR. Forty-four cytokines were measured in genital secretions by Luminex. The sequence types of C. trachomatis were determined using multilocus sequence typing based on five non-housekeeping and the ompA genes. (CPT n=52; JHB n=23).

**Results:** C. trachomatis was the most prevalent bacterial infection, found in of AGYW 41.6% in Cape Town and 17.4% in Soweto. It was associated with significantly elevated concentrations of 10/44 cytokines compared to their STI/BV-negative counterparts, including IL-1β, IL-6, TNF-α, IP-10, MIG, G-CSF, HGF, SCF, IFN-γ and IL-4. C. trachomatis was more inflammatory in Soweto (n=26) than in Cape Town (n=62). MLST was performed successfully on 75/88 cases, and 34 different sequence types (ST) (including 7 genovars) were detected. Of these, 15 were novel types. The three most common ones were ST12d (n=12), ST530b (n=11) and ST3 (n=9). There were no significant differences (p=0.187) in distribution by geographical site in a minimum spanning tree. Differential inflammation levels were seen, with ST12d being most inflammatory (IL-3, MCP-3, IFN-α2 and β-NFG upregulated). Cytokines were down regulated for ST319 (PDGF-BB, IL-7, HGF, IL-18, GM-CSF, MIP-1β, IL-1β, TRAIL and SDF-1α), ST551 (IL-10, Eotaxin, IL-12(p70), IL-13, FGF basic, IL-9 and IFN-γ) and ST188d (SCGF-β, MCP-3, IL-16, IL-2Rα, IFN-α2, β-NFG, and CTACK) while ST530b was neutral for inflammatory markers compared to uninfected women.

**Conclusions:** C. trachomatis was highly prevalent in this at-risk population and was associated with a robust inflammatory profile, which was sequence type-dependent. Understanding the mechanism through which C. trachomatis may increase inflammation and possibly HIV acquisition could be important in reducing HIV risk. Vaccine development should be encouraged.

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An algorithm to determine likely mode of infection in adolescents living with HIV enrolling in care at age 10-15 years

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**Abstracts**

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Background: Perinatally and non-perinatally HIV-infected adolescents may differ with regards to disease progression, social vulnerabilities, risk behaviours and outcomes. In spite of this, likely mode of infection is often not recorded in routine clinical care in resource-limited settings, with age thresholds at enrolment (e.g., <10 years, <15 years) often used as proxies. This may result in the misclassification of perinatally infected, slower progressors who present in adolescence as being non-perinatally infected. Current UNAIDS models assume that no non-perinatally acquired infections occur between 10-15 years of age. Using data from HIV-infected adolescents with documented mode of infection, we developed an algorithm for classifying their likely mode of infection.

Methods: We included HIV-infected adolescents aged 10-15 years at enrolment, within the IeDEA-Southern Africa (IeDEA-SA) and IeDEA Asia-Pacific (IeDEA-AP) cohorts, which are linked to the GRADUATE (Global fRAmework of Data collection Used for Adolescent HIV Transition Evaluation) project, from 2002-2017. Mode of infection was categorized as perinatal, non-perinatal or unrecorded. Using data from adolescents with recorded mode of infection, we developed logistic regression models using patient characteristics at enrolment that are routinely available in resource-limited settings (i.e., sex, age, height-for-age z-score [HAZ], BMI-for-age z-score [BAZ], CD4 count, viral load) to predict the likely mode of infection. The predictive ability of different models was assessed using the area under the receiver operating characteristic curve (AUROC). We then applied these models to adolescents with unrecorded mode of infection.

Results: We included 10,124 adolescents (9497 from IeDEA-SA and 627 from IeDEA-AP) in the analysis. Among 1920 (19%) with a documented mode of infection, 1875 (98%) were perinatally infected (54% female; median age at enrolment 11.8 [interquartile range (IQR) 10.8-13.0] years), and 45 (2%) were non-perinatally infected (49% female; median age at enrolment 12.7 [IQR 11.5-14.3] years). In logistic regression models, non-perinatal infection was associated with older age (adjusted odds ratio [aOR] for each additional year 1.71; 95% confidence interval [CI] 1.31-2.24), and higher height-for-age z-score (HAZ ≥2 to <1 vs. <2, aOR 3.35; 95% CI 1.43-7.87; and HAZ ≥1 vs. <2, aOR 3.58; 95% CI 1.41-9.10). Compared to a model using age alone (AUROC 0.652), a model including HAZ had higher AUROC (0.7231), with a further increase in predictive ability when including CD4 count (AUROC 0.7495). The proportion of adolescents with unknown mode of infection classified as non-perinatally infected when using a model based on age alone was 14%. This proportion decreased with the addition of HAZ (13%) and CD4 count (7%) to the model. However, addition of HAZ and CD4 count increased the proportion that could not be classified due to missing HAZ and CD4 data (14% and 56%, respectively).

Conclusion: Based on this algorithm, an age threshold of <10 years at enrolment as a proxy for perinatal infection would misclassify most perinatally HIV-infected adolescents 10-15 years of age as non-perinatally infected. Addition of HAZ and CD4 to the model improves its predictive ability. This algorithm needs to be further assessed in cohorts with larger proportions of adolescents with documented mode of infection.

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Health risk behavior clustering among adolescents in an HIV context.

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Background: Close to 83 per cent of adolescents living with HIV reside in sub-Saharan Africa. However, limited research from this region has explicitly explored clustering of multiple forms of health risk behavior (HRB) and underlying factors among this sub-population. The aim of this study was to explore the clustering of HRB, the composition of the clusters and predicting factors among perinatally HIV affected (PHIV+); perinatally HIV exposed uninfected (PHEU); and HIV unexposed uninfected (HUU) adolescents.

Materials & Methods: This was a case control study conducted at the neuro-assessment unit at the Centre for Geographic Medical Research, (CGMRC)
located at the Kenyan coast in Kilifi. The study involved 256 adolescents (111 PHIV+, 62 PHEU and 83 HUU) aged 12-17 years. The PHIV+ and PHEU adolescents were recruited from a specialized HIV care clinic and from households affected by HIV within the community. HUU adolescents were randomly sampled within Kilifi Health and Demographic Surveillance System. All participants completed a locally validated questionnaire on HRB and the Patient Health Questionnaire 9 (PHQ) administered in Swahili language via an audio computer-assisted self-interview. Various socio-demographic characteristics were also captured. Data analysis consisted of latent class analysis (LCA) based on based on 16 behavioral variables within 7 categories of sexual behavior; injury or violence; substance use; hygiene; physical activity; gambling; and diet behavior. A stepwise ordinal logistic regression model was run in STATA15 software to identify the predictors of HRB clustering.

**Results:** LCA generated 4 clusters. Cluster 1 (54%) comprised Low risk takers with no occurrence of risky sexual behavior, lowest substance (alcohol, khat and other drugs) use, good hygiene and lowest reports of injury and violence. Cluster 2 (14%) were Moderate risk takers with moderate reports of bullying, least engagement in gambling but had very low daily fruit intake (3%), high current use of khat (8.6%) and reports of coerced sex. Cluster 3 (14.8%) were mentally and sexually vulnerable substance users who experienced the highest burden of transaction (11%) and coerced sex (24%), the highest burden of suicidal ideation and highest rates of lifetime drug use (95%). Cluster 4 (18%) were high risk takers who reported the highest occurrence of unprotected sex (13.3%), highest occurrence of injury, gambling, current alcohol and khat use. Overall, we did not find significant differences in HIV status across the 4 clusters but it was noteworthy that about 30% and 40% of PHIV+ and PHEU adolescents respectively belonged to the high risk taking clusters (3 and 4).

Being PHEU (p=0.007) and high depression scores (p<0.001) predicted membership to high risk behavioral clusters, whereas higher education attainment (p=0.002) and having a male caretaker (father) predicted lower risk behavioral cluster membership.

**Conclusions:** Our results suggest that HIV status is a potential predictor of HRB clustering in adolescents. Tailored intervention may be useful, should involve caretakers and sustain school attendance and healthy school environment. Multi-component health behavior interventions should simultaneously address multiple forms of HRB and address mental health of the adolescents.

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Characteristics of and risk factors associated with violence reported by Asian youth living with and without HIV through audio computer-assisted self-interview (ACASI)


**Background:** Adolescents and young adults living with HIV are frequently socially vulnerable and at risk for experiencing physical or sexual violence. While exposure to violence can negatively impact HIV treatment outcomes, the nature and perceptions of violence vary by cultural and social contexts.

**Methods:** Data on violence and behavioural risks were collected as part of a study on sexual health among perinatally HIV-infected adolescents (PHIVA) and matched uninfected controls in Thailand and Vietnam between 2013-2017. An audio computer-assisted self-interview (ACASI) was used to collect data at baseline/enrolment, 48, 96, and 144 weeks, and included questions on demographics, sexual behavior, substance use, adherence to antiretroviral therapy (ART), stigma, and violence (physical and sexual). If adolescents reported any violence, the ACASI triggered immediate referral for counselor evaluation and support.

**Results:** A total of 142 PHIVA (65% female; median age 18 years) and 144 uninfected (68% female; median 19 years) adolescents were enrolled. Among PHIVA at baseline, median CD4 was 27% (21-
32), 24% had HIV RNA >1000 copies/mL, and 76% reported ART adherence ≥80%. The reported lifetime prevalence of ever physically being hurt by family members among PHIVA was higher than among uninfected adolescents: 26% vs 15% (p=0.02). Other types of violence reported included ever physically being hurt by friends (21% vs. 19%; p=0.72), ever being physically hurt by a teacher (11% vs. 9%; p=0.53), and ever being forced to have sexual contact (6% vs. 8%; p=0.50). The incidence rate tended to be lower for any type of violence among PHIVA compared to uninfected adolescents (28 vs. 32 per 100 person-years [PY], p=0.97), for physical violence alone (25 vs. 28 per 100 PY, p=0.89), for physical violence by a non-family member (18 vs. 21 per 100 PY, p=0.96), and for sexual violence (2 vs. 3 per 100 PY, p=0.71). Compared to uninfected adolescents, PHIVA were less likely to have a history of either drinking alcohol or smoking cigarettes and other substance use, and more likely to use condoms. In multivariate logistic regression, factors associated with elevated violence rates were younger age (incidence risk ratio [IRR] 4.44, 95% CI 1.83-10.77), ever smoking cigarettes (IRR 1.81, 95% CI 1.27-2.58), ever drinking alcohol (IRR 3.45, 95% CI 1.40-8.49), and not using condoms during sex (IRR 1.96, 95% CI 1.17-3.28).

Conclusions: Although the prevalence of physical and sexual violence reported among PHIVA and uninfected adolescents were similar in this cohort, the incidence tended to be higher among those without HIV, which may be related to differences between living with perinatal vs. non-perinatal infection. Mechanisms to report violence and support those who have been abused should be made available to all adolescents in healthcare settings in Asia, regardless of HIV status.

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Awareness and Acceptance of HIV Self-Testing and PrEP among Adolescents, Young Adults and their Caregivers in Washington, DC, USA

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Background: Adolescents and young adults (AYA) significantly contribute to the HIV epidemic in the USA while demonstrating a decline in HIV testing. In the USA, the self-test for HIV has been approved and available over-the-counter since 2012 and PrEP has been approved for use among AYA ≥ 18 years of age since 2014, with studies underway to approve pre-exposure prophylaxis (PrEP) among those <18 years of age. To date, however, the uptake of self-testing for HIV and PrEP has been limited among AYA in the USA. Our study aimed at evaluating awareness and attitudes towards HIV self-testing and PrEP among inner city AYA and their caregivers in Washington, DC, USA.

Methods: An interactive, anonymous, voluntary survey was administered to AYA ages 13-24 years and to the AYA caregivers during their visit to the community pediatric emergency department in an area of high HIV prevalence in Southeast Washington, DC. Self-reported demographics (e.g. age, gender, race and sexual activity) were collected. Regarding self-testing, participants were asked about having ever heard of HIV self-testing (awareness) and willingness to self-test for HIV (acceptance). Regarding PrEP, the participants were asked about their knowledge of PrEP (awareness) and willingness to consider PrEP (acceptance). Brief education about self-testing and PrEP was provided to all participants. A Likert scale was used to describe virtual PrEP acceptance. Descriptive statistics were used for analysis.

Results: The study enrolled 144 AYA (mean age=16 years; 116 Females/27 Males; 111 sexually active) and 35 caregivers (mean age=40 years; 35 Females). Most AYA (80%; n=115) had not heard of HIV self-testing and almost half of AYA (42%; n=60) reported that the price of the HIV self-test would determine their willingness to use the test, while 46% (n=66) reported that they would be willing to self-test if the self-testing kits were provided free of charge. Majority of AYA (97%; n=140) and caregivers (94%; n=33) reported having never heard of PrEP. Majority of AYA (65%; n=93) and caregivers (74%; n=25) were interested in learning more about PrEP. Almost half of AYA (47%; n=68) reported being potentially interested in taking PrEP, however, only 19% (n=27) of AYA reported being likely to take daily PrEP. The majority of caregivers (74%; n=26) were not interested in taking PrEP themselves. Almost half of caregivers reported being unlikely to let their child take PrEP (46%; n=16), 26% (n=9) reported
being neutral, and 29% (n=10) somewhat likely to let their child take PrEP.

Conclusions: We found low awareness about HIV self-testing among predominantly female AYA from the community with high HIV prevalence. The need for purchasing and price of HIV self-test were perceived as major barriers to considering self-testing. Knowledge of PrEP among AYA and their caregivers was limited and both populations were interested in learning more about PrEP. An ongoing project is aimed at increasing the knowledge and acceptance of self-testing and PrEP among inner city AYA in the USA.

Addressing the needs of pregnant HIV-positive adolescent girls and young women: A growing need

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Background: Lesotho’s adult HIV prevalence is 25.7%. Elizabeth Glaser Pediatric AIDS Foundation (EGPAF) is a clinical implementing partner that provides technical assistance to Lesotho’s Ministry of Health (MOH) and direct, comprehensive HIV/TB service delivery in 120 health facilities in five districts. In January 2017, EGPAF established adolescent and youth-friendly clinics in the Lesotho districts of Maseru, Berea, and Leribe. This abstract describes data collected at these clinics to increase a greater understanding of health needs among a population in sub-Saharan Africa with growing HIV infection and HIV-related mortality rates.

Materials and Methods: The established youth-friendly clinics are focused on scaling-up provision of quality, comprehensive TB/HIV services, sexual and reproductive health (SRH) services (including antenatal care [ANC] and PMTCT), and primary health care for adolescents and young people (AYP) aged 10 to 24 years. Services are provided by specially trained staff (adolescent health-focused pediatricians, nurses, social workers, psychologists, and youth ambassadors) during non-traditional hours and weekends. Data from these clinics are collected routinely through MOH registers and entered into EGPAF electronic data collection tools.

Summary statistics are calculated monthly and quarterly. Data for pregnant adolescent girls and young women (AGYW) at these clinics between June and October 2017 were collected and analyzed.

Results: Between June and October 2017, a total of 789 pregnant adolescents and young women (AGYW) were seen in the five clinics for antenatal care (ANC). 99 (12.5%) of the 789 pregnant AGYW attending came in with known HIV-positive status. Of these, 96% (95/99) were already on ART. Uptake of HIV testing for those with unknown status was 98.7% (681/690). Of those tested for the first time in ANC, 7.6% (52/681) were HIV-positive. Overall positivity (including known positives) was high, at 19.4%. (151/789). Overall ART uptake was high at 96.4% (54/56). The two AGYW who do not start antiretroviral treatment immediately were later put on treatment, after they had received support from significant others.

Conclusions/Next steps: The high HIV prevalence among pregnant AGYW at these clinics poses new challenges for addressing the needs of this population and their new-born infants. This will include better access to family planning to avoid future unplanned pregnancies, counseling on infant feeding and early infant diagnosis for their HIV exposed babies and support for adherence and dealing with possible HIV transmission to newborn infants. Offering testing, diagnosis and treatment services in non-school hour settings to AYP by specialized staff is a clear need and such services should be more widely implemented. EGPAF is currently expanding training of clinicians at all 120 supported health facilities to provide AYP health services, including PrEP, to enable better epidemic control.
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Association of proportionate and disproportionate small for gestational age outcomes with HIV/antiretroviral treatment in an African setting

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Background: The consequences of small for gestational age (SGA) are well known and include higher morbidity and mortality in childhood and possibly later in life. However, the association of SGA with antiretroviral (ART) use during pregnancy is rarely reported. We hypothesized that at birth, HIV-infected women on ART will have rates of SGA similar to rates among HIV-uninfected women. We present rates of SGA and its subcategories of proportionate and disproportionate among HIV-infected women on ART during pregnancy and among HIV-uninfected women from Malawi.

Materials & Methods: This observational study was conducted in Blantyre, Malawi from January 2016 to September 2017. All women giving birth at five health facilities were enrolled at delivery based on confirmed HIV status; written informed consent; singleton births; and for HIV-infected women: CD4>=350 cells/mL, no stage 3 or 4 HIV disease, and exposure to ART during or before pregnancy (first-line regimen in Malawi is TDF, 3TC and EFV). Birth weight (BW) and gestational age ("GA", using Ballard score) were measured at birth. Maternal and newborn questionnaires, physical examination and anthropometric measurements were also completed. SGA and “Very” SGA (VSGA) were defined as BW <10th and <3rd percentiles for GA, respectively. Ponderal Index (PI) was used to classify SGA to proportionate (PI>2.25) and disproportionate (PI<2.25). Logistic regression analyses were used to assess associations between SGA outcomes and HIV infection after adjusting for potential confounders.

Results: 614 HIV-infected and 685 HIV-uninfected woman-infant pairs were concurrently enrolled; the rate of SGA was 17.1% among HIV-infected and 18.4% among HIV-uninfected, p=0.54. There were no overall associations between SGA and HIV infection after controlling for maternal age, gravidity, previous losses/adverse outcomes of pregnancy, maternal education, body-mass-index, hemoglobin level, and socioeconomic status (p=0.88). Of the 231 women-infant pairs with SGA, 182 (78.8%) were proportionate and 49 (21.2%) were disproportionate. Of the 182 proportionate SGA, 32 (18%) were proportionate VSGA and 150 (82%) were not proportionate VSGA. Of the 49 disproportionate SGA, 15 (31%) were disproportionate VSGA and 34 (69%) were not disproportionate VSGA. There was no statistically significant association between HIV infection and proportionate SGA (p=0.30). However, among 49 disproportionate and 1068 appropriate for GA (comparison group), there was a statistically significant association between HIV infection and disproportionate SGA (adjusted odds ratio (ORA) =2.28; p=0.01). There was no association between HIV infection/ART use and the outcomes of proportionate VSGA or Not VSGA. However, there was a strong association between being HIV-infected (on ART) and the outcome of disproportionate VSGA (N=15) after controlling for other factors (ORa =4.95, 95% CI 1.43-17.19). There was no association between disproportionate Not VSGA and HIV infection.

Conclusions: Overall rates of SGA were not statistically different between HIV-infected and HIV-uninfected women. However, exposure to HIV infection/ART use was strongly associated with disproportionate VSGA. This adverse outcome has not been previously reported; whether this association is related to HIV, ART or another factor needs additional evaluations.

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Scaling up Family-based Service Delivery Models: Reaching 95-95-95 for Female Sex Workers and their Children

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Background: Motherhood is common among female sex workers (FSWs) and many have at least one biological child; with low contraceptive use and high burden of unintended pregnancy, they have poor reproductive outcomes and avoidable mother-to-child transmission risk. Globally, there are 2.1 million children living with HIV and antiretroviral therapy (ART) coverage is dismally low at 46%. Without timely diagnosis and treatment, half of all children born with HIV will die by the age of two. By integrating services for FSWs and their children, prevention of mother-to-child transmission of HIV (PMTCT) uptake among FSW mothers and early infant diagnosis can improve and therefore reduce transmission of HIV.

This abstract is a multi-country review of models of care for FSWs and their children from Cameroon, Ethiopia and Tanzania — all have documented promising practices with improved HIV case-finding and coverage of services for children of FSWs.

Methodology: A qualitative and quantitative review of program data from Cameroon, Ethiopia and Tanzania was completed for this analysis. Focus group discussions were conducted with HIV+ and HIV- FSWs and results were aggregated into common themes. A review of service delivery models that address both FSWs and their children together documented best practices being implemented.

Results: Focus group discussions conducted in Cameroon, Ethiopia, and Tanzania reveal the following challenges and vulnerabilities cited by FSW mothers: separation from children, neglect and lack of child care while mothers work, lack of school fees and low school enrollment, poor access to health and social services, food insecurity and malnutrition, poor access to economic strengthening interventions, physical, sexual, and emotional abuse (perpetrated by clients), and social marginalization, stigma and discrimination.

Countries use a mix of facility and community service delivery points and cadres to reach FSWs and their children through coordination by local implementing partners. Children of HIV+ FSWs tested from each country program are reported below:

- Ethiopia: 850 children tested, 30 HIV+, yield 3.5% (December 2017 to April 2018)
- Cameroon: 433 children tested, 26 HIV+, yield 6% from (October 2015 to March 2016)
- Tanzania: 12,710 children tested, 724 HIV+, yield 5.7% from (April 2017 to September 2018)

The variability in number of children tested is in part due to HIV burden and evolution of the model of care for FSW mothers and children. A limitation to note is that there may be a small number of children who were tested whose mothers are not FSWs in Tanzania, however this data point was not fully captured.

Conclusions: The multiple and compounding vulnerabilities cited by FSWs during focus group discussions can impact children’s health and development and have long-term consequences on both their physical and psychological well-being. Furthermore, testing data from Cameroon, Ethiopia, and Tanzania reveals that children of HIV-infected FSWs are at risk for HIV and have high positivity ranging from 3-6%. A combination of efforts and programming is needed to prevent and treat HIV infections among children, reduce missed opportunities for early identification of HIV, and ensure that FSW mothers, their children and families remain healthy.

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Reaching the Unreached HIV Positive Children with Quality Care & Treatment through Telemedicine: An Innovative Pilot Initiative

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Background: The vast Indian state of Maharashtra with many difficult-to-reach areas has a high burden of HIV with over 26807 children living with HIV [CLHA]. Although the recommended pediatric ART formulations are available at the ART centers, most of these centers are not staffed by pediatricians or...
specialists. The complicated cases get referred to the higher center, but failure to access due to financial and other constraints, lead to further deterioration or death. Many challenges remain in the quality of pediatric HIV treatment and care till date, mainly due to the unavailability of expertise at the peripheral levels and the staggering distances for referral services. In order to bridge this gap and to enhance the capacity of the staff of peripheral centers through e-mentoring, an e-decentralized model of expert Pediatric HIV care and referral services was established as a pilot project at the Pediatric-Center-of-Excellence-for-HIV-Care [PCoE] in Maharashtra. This study was designed to compare the outcomes of CLHA receiving care & treatment from ART centres linked to PCoE through telemedicine versus those that are not linked and to determine if the initiative has improved the quality of care in the linked ART Centers compared to the non-linked ART Centers.

Methods: A retrospective analysis of 5411 children upto 18 years of age, from 31 Telemedicine Linked [19 Linked-regular (≥12 video-conference sessions) and 12 Linked-irregular (≤12 video-conference sessions)] centres and 28 Non-Linked centres in the state of Maharashtra, India. We compared CLHA alive on Pre-ART/ ART, lost to followup (LFU) on Pre-ART/ ART, death during the Pre-ART/ ART, eligible but not initiated on ART, baseline CD4 counts (actual and number missing), latest CD4 counts, and regular visits between these three types of centres.

Results: Of the total children, 3676 (68%) were on ART and 1735 (32%) were in the Pre-ART group. In the Pre-ART group, the proportion of children alive was high in the Linked-regular centres compared with Linked-irregular centres, and Non-Linked Centres (79% vs 76% vs 70%, p=0.001) and proportion of children who were LFU was lower in Linked centres (regular and irregular) compared with Non-Linked centres (6% vs 5% vs 8%, p=0.09). In the ART group, the baseline CD4 counts were missing in a significantly lower proportion of children in the Linked-regular centres compared with Linked-irregular centres and Non-Linked centres (6% vs. 11% vs. 7%, p< 0.05) and the latest CD4 counts were missing in a significantly lower proportion in the Linked-regular centres compared with Linked-irregular centres and Non-Linked centres (12% vs. 31% vs. 30%, p < 0.001). Comparison between three groups across all parameters studied showed the Linked-regular centers performing significantly better than the Linked-irregular or Non-linked centers.

Conclusions: Our study showed that the centers linked through regular telemedicine performed better in terms of patient care & treatment with higher proportion of CLHA alive and fewer LFUs. Overall, this pilot project of Telemedicine for Pediatric HIV has proved to be acceptable, feasible, and significantly effective in improving the quality of care for children living with HIV across the state of Maharashtra.

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Screening tools to identify children and adolescents living with HIV: increasing case finding in high HIV prevalence settings

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Background: South Africa has an HIV prevalence of 2.7% in children aged 5–14 years, with at least half of HIV-infected children already diagnosed and on antiretroviral therapy. While there are existing guidelines for testing children for HIV, these are poorly implemented. In response, a screening tool of ten questions derived from the guidelines, integrated management of childhood illnesses manual and other validated tools was developed. It aims at assisting healthcare workers to implement the guidelines to identify high-risk children for being HIV-infected when they presented to health facilities in Johannesburg, South Africa.

Methods: The screening tool was implemented between April and December 2017 by HIV counsellors at twelve high volume, urban health facilities. Pre-screening was performed on a convenient sample of children 0-19 years presenting at health facilities, with a focus on children 5-14 years. Excluded were those known to be HIV-infected and those who had tested HIV-negative in the last six months. An unknown HIV status led to screening using the ten questions with a single positive answer being considered a positive screen. They were then consented, counselled and tested for HIV.

Results: A total of 998 children were pre-screened and results are as follows: 22 (2.2%) were known to be HIV-positive, 89 (9.0%) were HIV-negative and
887 (88.9%) had an unknown HIV status. Of those with an unknown status, 635 (71.6%) had a positive screening question and of these, 478 (75.3%) had an HIV test and 26 had a positive result (test positivity rate=5.4%). The number screened to find one positive child was 38 (screen positivity rate=2.6%). Of the 26 children testing positive, seven were 19-59 months (120 tested, yield 5.1%); 17 were 5-9 years (325, 5.2%) and two were 15-19 years (14, 14.3%). In the target age group, the highest number of HIV positive results came from a positive screening for question one (14 positives of 153 tested, yield 9.1%); followed by question two (2/21, 9.5%); and question eight (1/9, 11.1%). Screening positive for the remaining questions did not yield any positive HIV results. A total of 71 children of all ages were tested despite not having any positive questions and all were found to be HIV negative.

**Conclusions:** Screening tools are essential in high HIV-prevalence settings to promote HIV testing in at risk children. Use of this screening tool led to a positivity rate of twice the expected background HIV prevalence for children in this setting. In the target age group of 5-14 year olds, the positivity rate was similarly high. Reassuringly, in the few children tested despite not screening positive, no HIV-infected children were found. However, screening using the ten questions led to almost three quarters of screened children needing to be tested and suggests the current criteria for testing children are over-inclusive and offer little reduction in children needing to be tested when compared to implementing universal HIV testing. To improve screening efficiency, the guidelines and tool could be reduced to fewer questions. This would lead to less children screening positive and needing testing.

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**Impact of male involvement beyond PMTCT: Male partner practical support associated with improved maternal mental health in rural Zimbabwe**

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**Background:** Zimbabwe has an HIV prevalence among women in antenatal care of 16.1% and HIV is the leading cause of maternal death. Male partner involvement during pregnancy is associated with improved PMTCT uptake and outcomes. While there is evidence that male involvement is associated with improved maternal mental health, this is rarely a focus of male involvement strategies. Our objective was to examine the association between male partner practical support and maternal mental health outcomes.

**Methods:** A cross-sectional baseline survey was conducted June-August 2016 for a community-based health program in rural Mutasa District, Zimbabwe. Trained non-clinical female enumerators administered the survey in eight health facility catchments with women who had given birth in the previous six months. The questionnaire included a Shona-language Edinburgh Postnatal Depression Scale (EPDS), previously validated in Zimbabwe, and questions about male partner practical support during pregnancy, birth and after birth. Survey data was analysed with Stata 13.0, adjusted for clustering effects.

**Results:** Among 459 women enumerated, mean age was 25.5 years and mean number of children 2.4. Using the validated EPDS cut-off of 11, 28.8% (95%CI:24.6-32.9) of women reported symptoms of clinically significant depression and anxiety, while 18.7% (95%CI:14.0-23.4) reported thoughts of self-harm. Mean EPDS score was 7.6 (95%CI:7.1-8.2) out of 30. Across the items of the male partner practical support assessed, there was no difference in level of support provided to HIV positive and HIV negative women. However, multiple items of practical support from male partners, including contributions to food preparation, household chores, and childcare, were significantly associated with improved maternal mental health outcomes related to postnatal depression and anxiety, and thoughts of self harm in the previous seven days, among all women. While effect size varied across different items of practical support, clinically significant symptoms of depression and anxiety were reduced by up to 66.7% (95%CI:37.1-82.4) and recent thoughts of self harm by up to 78.1% (95%CI:69.1-
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84.5), among women whose partners provided practical support.

Conclusions: Male involvement in maternal and child health is increasingly recommended as a PMTCT strategy in high prevalence settings, with a focus on increasing couples’ uptake of HIV testing and access to treatment during pregnancy and breastfeeding. We demonstrate that among vulnerable, rural women in a high prevalence setting, male involvement is also associated with improved mental health outcomes. Investment into programs that meaningfully engage men in maternal, newborn and child health, including PMTCT, can plausibly benefit maternal mental health as well as HIV outcomes.

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Bringing HIV tests to Adolescents aged 15 to 24 years to increase uptake of testing among adolescents: A way to achieve the first 90.90.90 target

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Background: Malawi has made significant strides in the fight against HIV/AIDS, leading to a drop in HIV prevalence from 13% to 8.8% in the general population in 2015. Despite these gains, HIV prevalence rate amongst adolescents aged 15 to 24 years remains very high. According to National Strategic Plan for HIV and AIDS 2015-2020, HIV prevalence rate is 2% amongst adolescent boys and 5.3% for adolescent girls aged 15 to 24 years respectively. The prevailing situation, points to the fact that there is need for more interventions among the adolescents group to ensure that the first 90 is reached. It is against this background that Malawi AIDS Counseling and Resource Organization implemented a 1 year project from August 2016 to July 2017 aiming at increasing uptake of HIV testing amongst adolescents in Lilongwe, Malawi.

Description: Innovative HIV testing strategies such as mobile van outreach and moonlight HIV testing at secondary and tertiary schools was used to provide testing services to adolescents aged 15 to 24 years. Trained HIV testing providers, provided HIV tests using rapid HIV test kits in a customized mobile van fitted with HIV testing rooms.

Lessons learned: Taking HIV testing to adolescents has potential of increasing uptake of HIV testing among this age group and linking those found HIV positive at the right time to ensure high quality life. 10,400 adolescents out of a target of 10,000 got tested and 179 of them tested HIV positive representing 1.7% positivity rate. 158 of the 179 HIV positive adolescents were put on antiretroviral therapy treatment. The remaining 21 refused to start treatment on the spot as they requested more time.

The project further revealed that, the Malawi population and most parents have knowledge gap on the legal age (13 and above) on when adolescents can give consent for HIV testing as most of them at the onset of the project refused their children to get tested which was later clarified through dialogue.

Conclusions/Next steps: Using innovative and multiple approaches to provide HIV testing to adolescents can increase HIV testing uptake and contribute significantly towards the first 90, however better strategies to link them to care have to be in place.

1. Malawi Demographic and Health Survey 2015-2016

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SPARK17 - Unite and Ignite Youth Leadership in the HIV Field


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Background: Youth leaders require business skills for improved campaign development and implementation. The SPARK17 meeting uniquely aimed to develop, unite and empower global HIV
youth leaders by equipping them with such skills, to communicate, inspire and ignite change in their communities. The residential camp intervention model was adapted creating an interactive, peer-to-peer training programme, in a safe space for expression. Although paediatric-HIV interventions (e.g., youth safe spaces, such as clubs and residential camps, and peer to peer support) were debated to inform future initiatives, no HIV education was done. Training occurred over 3 Days at Sentebale, Lesotho. The effectiveness/applicability of training content and meeting model were evaluated.

Methods: Questionnaires were completed immediately before and after training, by 35 delegates (54% self-identified females; 74% aged 18-26, 26% 27-36 years; 54.3% from Sub-Saharan Africa, 20% Europe, 14.3% Central/South-America, 11.4% Asia). Questions were grouped into 4 topics for 5 point Likert scale responses (from strongly disagree to strongly agree): communications/creative writing training (9 questions); effective use of social media training (7 questions); paediatric-HIV interventions workshop (5 questions); confidence living with/changing perceptions about HIV (10 questions). Positive responses were defined as both ‘strongly agree’ and ‘agree’. Sum positive response rates were calculated as follows: total positive responses divided by total number of responses, from all delegates for all questions in each of the four topics above. A fifth topic questioned overall satisfaction with the meeting, requiring yes/no responses or scores on a 0-10 scale. Follow-up at 6-months checked embedding. A 100% delegate response rate was observed for the questionnaire at Day 0 (35/35), a 94% response rate at Day 3 (33/35) and an 83% response rate at Month 6 (29/35).

Results: Positive response rates were high at baseline for communications/creative writing (76%, 239/315) and social media (78%, 192/245). Despite this, at Day 3 there was a 17-19 percentage-point increase in positive response rates for these two skillsets (95% each, 281/297 and 220/231); a 37% increase for paediatric-HIV interventions was also observed (from 51%, 89/175 to 88%, 146/165), indicating improved delegate confidence with these three topics. Positive response rates for confidence living with/changing perceptions about HIV were high at both baseline (87%, 305/350) and Day3 (91%, 301/330). At Day 3, the overall positive effect of SPARK17, satisfaction with the meeting and likeliness to recommend to others (0-10 scale) averaged 9.5, 9.2 and 9.7, respectively. 100% and 94% of delegates planned to use learnings from SPARK17 and/or share these with friends/co-workers. At Month 6, 93% and 83% of delegates had used learnings from SPARK17 and/or had shared these with friends/co-workers. 92-97% of delegates felt confident that they could now influence others and change perceptions about themselves, HIV and/or their work.

Conclusions: SPARK17’s unique model delivered effective business skills training. Affecting change with young-people can be challenging in topics that they perceive to be strengths at baseline. Novel approaches to youth training, beyond HIV education, should continue to be explored.

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Breastfeeding, vertical HIV transmission and implications for accurate monitoring: data from the UK and Ireland

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Background: In 2012-2014, the vertical HIV transmission rate (VTR) was 0.27% among diagnosed women living with HIV (WLHIV) in the UK and Ireland. The British HIV Association (BHIVA) currently recommends formula-feeding infants born to WLHIV, eliminating postnatal transmission risk; however, BHIVA states that virologically suppressed treated women with good adherence to antiretroviral therapy (ART) who choose/plan to breastfeed may be clinically supported to do so. Guidelines on diagnostics for breastfed infants and maternal viral load (VL) monitoring have been updated.

Methods: The National Study of HIV in Pregnancy and Childhood (NSHPC) conducts comprehensive surveillance of all pregnancies to diagnosed pregnant WLHIV in the UK/Ireland. HIV-infected children <16yrs are also reported through a parallel paediatric reporting system. We report maternal characteristics and VTRs among singleton liveborn infants in 2015-16 with infection status reported by 31/03/18 and reports of planned and/or supported breastfeeding [births since 2012].
Results: There were 1914 singleton livebirths, with 71% (1347/1909) born to Black African women and 83% (1552/1878) to women born outside UK/Ireland. Median age at delivery was 34 years (IQR: 30,37). Over 99% (1900/1905) of pregnancies were in women on ART and 70% (1300/1847) were conceived on ART. Among 1230 infants with data on maternal VL within 30 days of delivery, this was undetectable (<50c/ml) in 93% (n=1140). Overall, 47% (894/1896) of infants were delivered vaginally. Infant infection status was confirmed for 75% (1438/1914) of infants. There were four transmissions: two infants whose mothers were diagnosed after 20 weeks gestation following late antenatal care presentation, who achieved an undetectable delivery VL, but where transmission occurred in utero (positive PCR aged ≤3 days); one other in utero transmission was an infant born to a woman diagnosed pre-conception with detectable delivery VL and the final case was a postnatal transmission via likely breastfeeding (PCR negative at 6 weeks, positive aged 18months) where the mother was diagnosed pre-conception with undetectable delivery VL. The overall VTR for 2015-16 was 0.28% [95% CI: 0.08%, 0.71%], with the VTR for women with undetectable delivery VL being 0.35% ([0.07%, 1.00%] 3/868) and that for women diagnosed pre-pregnancy with undetectable VL throughout pregnancy being 0.17% ([0.01, 0.92] 1/586).

Of note, for the likely postnatal transmission, breastfeeding was not communicated to clinicians. There have been 70 reports of planned and/or supported breastfeeding among women on fully suppressive therapy to the NSHPC since 2012 (duration ranging from 1 day to 2 years/ongoing); 36/70 were infants born during 2015-16. Infection status has not yet been confirmed in many of these cases and ongoing monitoring is required.

Conclusions: The VTR among diagnosed WLHIV in the UK/Ireland remains very low and stable at 0.28%, with the proportion of women achieving undetectable delivery VL having increased since 2012-14 from 87% to 93%. The reports of breastfeeding reflect guideline updates, the current ‘U=U’ era and continued strides towards normalisation of maternity experiences for WLHIV. These require careful monitoring, enabled by our paediatric surveillance operating in parallel with maternity reporting, ensuring identification of any late postnatal transmissions and appropriate adjustment of the VTR.

Partnership dynamics limit the reach of index client testing (ICT) approaches for testing children at a population level


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Background: Index client testing (ICT) for children—testing children of HIV-infected index adults—reveals a high prevalence of undiagnosed pediatric HIV. However, uptake of ICT has been sub-optimal in research and programmatic settings.

Methods: During recruitment for an ongoing randomized trial (NCT03049917), data were collected from sequential clients attending HIV care regarding whether they had children ages 0-12 years of unknown HIV status. Female index clients were considered eligible for ICT if they had any children who had never tested for HIV or had not completed testing following breastfeeding cessation. Male index clients were considered eligible for ICT if they met the same requirements, but also knew that the mother of the untested child(ren) was HIV-infected or deceased. Among eligible clients, the frequency of partnership dynamics that limit uptake of ICT was characterized. We compared the proportions of male and female index clients who were eligible and enrolled using Chi-squared tests.

Results: Among 11,945 HIV-infected adults (3,856 male, 8,089 female), 952 (8%) had no children, 7,542 (63%) had tested all their children, 2,960 (25%) had children of unknown status who were all >13 years, and 73 (1%) had female partners of unknown or negative HIV status.

Four hundred eighteen adults (3.5% [418/11,945]) had children eligible for ICT. This differed for male and female clients (4.9% [188/3,856] of all male clients vs 2.8% [230/8,089] of all female clients, p<0.001). Three quarters (76% [317/418]) of eligible clients enrolled in the ICT intervention, which also
differed for male and female clients (58% [109/188] of male clients vs 90% [208/230] of female clients, p<0.001).

Of the 22 female index clients who did not enroll, reasons included: 36% (8/22) parents separated or divorced and female caregiver could not access children, 45% (10/22) female caregiver separated by distance from her children (not divorced), 14% (3/22) not interested or in a rush, and 5% (1/22) wanted to consult with partner before enrollment.

Of the 79 male index clients who did not enroll, reasons included: 71% (56/79) parents separated or divorced and male caregiver could not access his children, 14% (11/79) parents and children separated by distance (not divorced), 11% (9/79) wanted to consult with partner before enrollment, and 4% (3/79) not interested or in a rush.

**Conclusions:** ICT has scaled up in Kenya, but a substantial proportion of those with untested children have partnership challenges related to physical and/or partnership separation, which may limit the extent to which traditional ICT can reach index clients and their children. These dynamics are particularly pronounced in male index clients.

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**Estimating the cost of very early HIV infant diagnosis in Lesotho**

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**Background:** Infants with HIV infection, particularly those infected in utero, who do not receive antiretroviral therapy (ART) have high mortality in the first year of life. With the World Health Organization recommending virologic diagnostic testing between ages 4 and 6 weeks, adding very early infant diagnosis (VEID) testing at birth has recently been suggested to enable earlier diagnosis and rapid treatment of in utero infection. We assessed the costs of adding VEID to standard 6-week testing in Lesotho, where universal maternal ART during pregnancy is standard-of-care.

**Methods:** Retrospective cost data were collected at eight health-care facilities in three districts participating in an observational prospective study that included birth testing and at the National Reference Laboratory in Lesotho, to investigate the cost-per-infection identified. Extrapolating to country-wide HIV-exposed infants, the cost of identifying one infected infant was calculated; averted early infant deaths by VEID with immediate ART if infected was based on an estimated 21% mortality in the first 2 months of life with untreated in utero infection.

**Results:** The unit cost-per-VEID test in Lesotho in 2015 was $40.50. Major cost drivers were supplies/commodities (46%) and clinical labor (22%). In 2015, 66.3% of cohort study infants born at study facilities underwent VEID; one out of 199 infants had a positive HIV DNA PCR test at birth (0.5% potential in utero infection), yielding a cost of $8,059.50 per HIV-positive child identified. Sensitivity analysis showed costs based on Lesotho costing data ranged from $810 to $16,194 per infected child with varying in utero infection rates from 5% and 0.25%, respectively. With 11,157 HIV-exposed births in Lesotho in 2015, assuming 66.3% VEID coverage, and 0.5% in utero infection, if VEID had been offered nationally, 37 infants infected with HIV could have been identified at birth and 8 early infant deaths potentially averted with immediate ART compared with waiting for 6-week testing.

**Conclusions:** If Lesotho costing data from this pilot study were applied to different epidemic circumstances, the cost-per-infected child identified by adding VEID birth testing to standard 6-week testing was lowest when in utero infection rates were high.
Deficiencies in linkage to HIV care and treatment for children enrolled into a pneumonia etiology research project at University Teaching Hospital in Lusaka

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Introduction: The Pneumonia Etiology Research for Child Health (PERCH) project was a 7-country, case-control study to determine the etiology of and risk factors for severe and very severe pneumonia in children 1-59 months of age. The main objectives of the PERCH study were to determine the association between pneumonia and infection with known and putative viral, bacterial, mycobacterial, and fungal pathogens, estimate the fraction of pneumonia attributable to pathogens for which vaccines are currently under development and to assess putative factors for infection and/or disease due to novel or under-recognized pneumonia pathogen

Materials and Methods: Cases and matched controls were enrolled between August 2011 and August 2013 at the University Teaching Hospital in Lusaka and from randomly selected households in the community, respectively. HIV controls were enrolled from the HAART clinics. Demographic, clinical, laboratory data and biological specimens were collected from each case and control. HIV exposure and infection status was determined and whether or not eligible child was on cotrimoxazole (CTX) and nevirapine (NVP) prophylaxis and antiretroviral (HAART) therapy. The analyses for this abstract are limited to HIV status and linkage to care for positive and exposed cases and controls.

Results: PERCH enrolled 617 cases hospitalized with severe or very severe pneumonia according to the WHO definition, 615 community controls and 71 HIV+ controls.103 cases were confirmed to be HIV infected by approved testing protocols, 134 were exposed but uninfected (HEU) and 369 were unexposed uninfected (HUU). 78 of the 103 HIV-infected cases were 12 months or younger and only two (2.5%) were on HAART. In total, only 14 (13.6%) HIV infected cases were on HAART. NVP coverage among all HIV+ and HEU cases was 19%. Of the 157 HEU children who were eligible for CTX prophylaxis, 101 (64%) were receiving it [cases-33/66, controls 70/91]. HEU children who did not take CTX were 4.48 times more likely to present with pneumonia than HEU children who took CTX. Overall inpatient mortality of HIV infected cases was 40%, higher than HEU at 22% and 11% for HUU. Vaccination coverage determined by at least one dose of DTP was 93% for cases and 96% for controls.

Conclusions: Non-initiation to HAART, CTX and nevirapine prophylaxis among HIV-infected children who present with pneumonia is high. Pneumonia mortality among HIV-infected and HEU children is higher than among HIV unexposed children. Linkage to HIV care for HIV-exposed children in Lusaka remains a significant challenge despite successful PMTCT efforts. Our results suggest the need for a more ambitious and rigorous program of linkage to and maintenance in care for HIV+ and HEU to prevent excess morbidity and mortality. Vaccination coverage for these children was high and the EPI appears to be the most logical place for Health Care staff to start care and treatment for HIV+ and HEU children, rather than restricting the availability of these services to HAART clinics only.

Evaluation of PMTCT program performance using HIV Exposed Infant final outcomes at peripheral PMTCT clinics in rural mid-western Uganda.

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Background: Baylor-Uganda with support from the Centres for Disease Control and Prevention (CDC) provides technical assistance in implementation of HIV Exposed Infant (HEI) birth cohort monitoring at 127 health facilities in Mid-western region. Each HEI is registered in a facility held register in their respective birth month/year and followed up for the recommended 18 months. At the end of the follow up period, PMTCT program performance is assessed
based on two key exposed infant final outcomes; proportion discharged HIV negative and proportion tested HIV positive and linked to care. We set out to evaluate PMTCT program performance using exposed infant final outcomes.

**Methodology:** A retrospective review of HIV Exposed Infants final outcomes data from 127 peripheral PMTCT accredited sites for the period January-December 2017. We determined the proportion of HEI tested for HIV within 2 months of age, proportion discharged HIV negative and rate of Mother to Child Transmission (MTCT) of HIV as key PMTCT performance indicators.

**Results:** A total 4697 HIV Exposed Infants were registered in the birth cohort-January to December 2015 and 18 months later, their final outcomes were evaluated to determine the percentage of HEI tested for HIV within 2 months of age, proportion discharged HIV negative and MTCT of HIV. Overall, 81% (3815/4697) of HEI received HIV testing by DNA PCR within six-eight weeks of age; 75.1% (3527/4697) completed the recommended 18 months of follow up; of these, 95.8% (3378/3527) were discharged HIV negative while 4.2% (149/3527) tested HIV positive (96% initiated on ART). A total of 1170 HEI did not complete the 18 months follow up period and of these, 10.5% (123/1170) were reported dead, 36.4% (426/1170) were lost to follow up and 45.9% (538/1170) were referred to another health facility for continuity of care. A small fraction of HEI (83/1170) were active in care at 18 months with missing final HIV status.

**Conclusion:** In a setting where ART is integrated into ANC clinics, 75.1% of HEI completed the recommended 18 months of follow up and of these 95.8% were discharged HIV negative (HIV Free Survival). Majority of HEI that did not complete 18 months of follow up had been referred to another facility for continuity of care.

**Background:** Due to the success of paediatric treatment, children with HIV are surviving into adolescence and adulthood. Adherence to antiretroviral treatment (ART) is poorer among adolescents than other age groups resulting in lower rates of viral suppression. Factors that influence adherence are psychosocial, socioeconomic, individual, and treatment-related. Many young women have become pregnant and face the additional complexities of parenthood. This retrospective cohort study analyses the pregnancy outcomes in a cohort of perinatally infected young women.

**Materials and Methods:** The study population was perinatally infected young women between the ages of 15 to 24 years, with a positive pregnancy test between Jan 2014 and Dec 2017. Medical records of eligible patients were reviewed, pregnancy outcomes were described and infant outcomes analysed using the 6 week and post weaning HIV DNA PCR test results. Three monthly HIV viral load (VL) monitoring was done during pregnancy and breastfeeding. Patients with unsuppressed VL were enrolled in interventions including enhanced adherence counselling, directly observed treatment, and a monthly support group. All infants received ART for PMTCT.

**Results:** Data of 80 women were analysed. Median age was 20 years (IQR:18-22). 50 (63%) women had live births, 13 (16%) early miscarriages, 1 (1%) stillbirth, 2 (3%) induced abortions, 3 (4%) lost to care or transferred out, and 11(14%) were still pregnant. Of the 50 live births, 46 underwent HIV DNA PCR tests at 6 weeks: 42 (91%) were negative, 1 (2%) positive and 3 (7%) results are pending. 27 babies were weaned, and of these 25 (93%) had negative post-weaning HIV tests, 1 had a pending result and 1 had no post weaning HIV test done. One baby was not breastfed, and had a negative test at 6 weeks and was not retested. 21 babies were still receiving breastmilk.

**Conclusion:** The rate of vertical transmission in this cohort of perinatally infected young women was 2%. However post weaning HIV status is still pending for 21 babies. This 2% vertical transmission rate was achieved by regular VL monitoring and the implementation of rigorous adherence support strategies. It is possible to meet the UNAIDS target of < 5% but will require increased efforts in adherence support. The number of unsuccessful pregnancy outcomes was quite significant at 20%, highlighting a potential area of research for a possible etiology of this finding.
Current approaches to managing third-line pediatric antiretroviral therapy among countries in sub-Saharan Africa

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Background: The New Horizons (NH) Advancing Pediatric HIV Care Collaborative is a multi-sectoral partnership mobilizing research and resources for treatment-experienced children and adolescents living with HIV. Built from a darunavir (DRV)/etiravirine (ETR) donation program, NH aims to support national HIV and AIDS programs in access to and management of children and adolescents on second- and third-line antiretroviral therapy (ART). The objective of this analysis is to describe approaches to third-line pediatric ART service delivery among nine sub-Saharan countries.

Materials and Methods: Data were collected in October 2017 during the annual NH workshop in South Africa from nine Ministry of Health representatives/delegates from Cameroon, Kenya, Lesotho, Malawi, Nigeria, Swaziland, Uganda, Zambia, and Zimbabwe. Descriptive data were extracted from country presentations on national approaches, service delivery models, and guidelines for pediatric third-line ART.

Results: All countries described national guidelines, service delivery models, and challenges for pediatric third-line ART. The recommendations for third-line ART generally followed World Health Organization treatment guidelines. In Kenya, Lesotho, Malawi, Uganda, Swaziland, and Zambia, children and adolescents with detectable viral load (VL) on ART were reported to receive intensive adherence counseling interventions for 3-6 months before the VL test is repeated. In case of repeatedly detectable VL, genotypic drug resistance testing (DRT) was done as a standard of care, when feasible, to guide selection of the third-line regimen.

Service delivery for switching patients to third-line ART varied from highly centralized to decentralized models. Pediatric third-line ART is managed at centers of excellence or central hospitals (Lesotho, Swaziland, Zambia, Zimbabwe), provided at regional facilities (Cameroon), managed at facility-level with guidance from regional or national technical working groups (Kenya), or a combination of these approaches (Malawi and Uganda). Pediatric third-line ART is currently unavailable in Nigeria; however, second-line ART is centralized. Some countries noted a lack of age-disaggregated data reporting tools for adolescents (Cameroon and Kenya) or challenges in managing national third-line ART data (Lesotho).

Access to DRT was identified as a common challenge due to: 1) DRT not being routinely available in-country (Lesotho, Swaziland, Malawi, Zimbabwe); 2) delayed turnaround of results (Kenya and Zambia); and 3) insufficient ART and DRT human resources (Cameroon). Barriers to third-line ART included: stock-outs (Kenya, Uganda, Zambia); unavailability of ritonavir (RTV) liquid formulations (Lesotho) or pediatric RTV tablets (all countries) for DRV boosting; and challenges with procurement of pediatric raltegravir (RAL) (Uganda and Zambia). Access to pediatric third-line antiretroviral drugs was limited in West African countries (Cameroon and Nigeria) and Malawi. None of the countries had pediatric 50 milligram RTV tablets available for boosting of DRV.

Conclusions: As pediatric treatment is scaled up in sub-Saharan Africa, the need to manage treatment failure and sequencing of pediatric ART regimens will likely intensify. Challenges in third-line ART service delivery for children and adolescents range from accessibility to pediatric ARV drug formulations and DRT to health system capacity to assess and support adherence. Strengthening of health system capacity, service delivery, monitoring, and evaluation are needed to ensure efficient management of third-line ART in children and adolescents.
Paediatric Outcomes Among Infants Born To HIV Positive Women Disengaged From A PMTCT Program In Uganda

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Background: PMTCT programs have led to a reduction in paediatric HIV/AIDS mother to child transmission rates worldwide. The success of PMTCT is hindered by the high rates of lost to follow-up among mothers. Infants born to mothers who initiate ART, then later drop out of care are potentially at an increased risk of acquiring HIV. Tracing of mothers who drop out is resource intensive, as such there is limited data regarding what happens to their infants. Our aim was to establish outcomes of infants born to mothers who have disengaged from care, in comparison with those whose mothers were retained.

Methodology: Data were collected between July 2016 and March 2018 at six Kampala City Council Authority clinics supported by the infectious Disease Institute (IDI), Uganda. We enrolled a prospective cohort of HIV-infected women initiating ART during pregnancy. We included women aged >18 years and 6-12 weeks postpartum. A woman was considered disengaged (DW) if she was last seen >90 days and had not showed up by week 12 for her 6-week postpartum visit. DW were matched with retained women (RW) by age and duration on ART. A team of community outreach workers traced the DW through telephone calls and home visits to obtain vital status of both mother and baby. Dried Blood Spots were collected to establish infant HIV sero-status (DNA PCR) and maternal HIV viral load. DW and their infants were encouraged to reengage in care. Data were extracted from routine HIV clinical data and structured questionnaires designed to assess current engagement status, reasons for disengagement, infant HIV testing, feeding and immunization practices. We used descriptive statistics to describe the population and estimated proportions of women and infants with different HIV outcomes.

Results: There were 18(9%) infant deaths among the enrolled women, 10(9.7%) disengaged and 8(8.2%) engaged P= 0.112. We enrolled 103 DW with 90 infants and 97 RW with 89 infants, yielding 179 infants. Of the 179 enrolled infants, 83(46.9%) were female, median age 6.1 months (interquartile range (IQR): 5 – 7) with a median weight of 3.2 kgs (IQR 2.9-3.5) at birth. Among the disengaged infants, 40(44.9%) were delivered at the primary facility of HIV care, compared with 61(69.3%) among retained infants; while 7(7.9%) of disengaged infants were delivered from home, versus 2(2.3%) retained infants. Among the disengaged infants tested for HIV 4/90 (4.5%) were found positive compared with none among retained infants, P=0.045. Fewer disengaged infants 25(28.1%) were enrolled into the Early Infant Diagnosis program compared with 83(94.3%) retained infants, P<0.0001. Thirty (34.1%) disengaged infants received Septrin prophylaxis compared to 82(93.2%) of retained infants. Disengaged infants were equally as likely to be immunized as engaged infants 98.9% versus 96.6% respectively (P=0.306). Exclusive breastfeeding was lower among disengaged infant 42.1% compared to 50% among retained infants (p=0.007).

Conclusion: Though not statistically significant we identified a higher rate of HIV transmission in infants born to disengaged women. There is need for interventions to ensure retention in care for HIV positive women and exposed infants in order to improve paediatric HIV care outcomes and eliminate MTCT.
Adolescent to Adult Patient-centered HIV Transition (ADAPT) Study: Adolescents’ perspectives about transition from pediatric to adult HIV care setting in northern Nigeria – findings from a qualitative study

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Background: One of the challenges faced by emerging adults living with HIV is the transition of care from their long-term pediatric HIV providers to treatment within an adult HIV program. Unsuccessful transition can be difficult and catastrophic. Limited studies have been conducted in sub-Saharan Africa incorporating the voices of youth in the design, implementation and interpretation of interventions to assist ALHIV in their transition to the adult HIV care system. This qualitative study explored ALHIV perspectives on the process of transition.

Method: Eighteen Focused Group Discussions (FGDs) were conducted for 15-19 years old ALHIV across 6 healthcare facilities in Northern Nigeria May-July 2017. To be included in the study, ALHIV knew their HIV status and were enrolled in ART clinic for ≥12 months. Participants were interviewed by a researcher using a script containing a series of open-ended questions in key domains: experience of having the health care provider introduce the concept of transition, AHLIV readiness for and importance of transition, advantages and disadvantages of transition, and what constitutes a successful transition. All participants provided written informed consent prior to FGD. Discussions were audio-recorded. FGDs in English were transcribed verbatim, those in Hausa were translated to English after transcription. Thematic analysis was performed using the MAXQDA software; common themes were extracted.

Results: A total of 150 ALHIV participated; 56 preparing for transition, 53 with successful transition, and 41 unsuccessful transition; 57% were female, 79% perinatally-infected, and 46% Muslim. Several themes emerged related to the experience of learning about transition; ALHIV reported feeling unhappy, anxious, confused, and uncomfortable when their health care provider introduced the idea of transition. Consistent themes emerged among all participants related to ALHIV definition of transition readiness: age, maturity/sense of responsibility, and ownership of care. Participants identified the following themes when describing transition success: improved state of their health and physical growth.

Conclusion: The voices of ALHIV are essential to the development of interventions to support their transition from pediatric to adult HIV care. Findings from this study will be presented to inform strategies for the development of transition services in resource-limited settings.

Early versus Late Virological Failure; Results from 48 months of First-line Antiretroviral Treatment among HIV infected Children in Uganda.

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Reviews in Antiviral Therapy & Infectious Diseases 2018_8
Background: HIV drug resistance associated mutations (DRM) are jeopardizing antiretroviral treatment (ART) programs in African children. To preserve the already limited treatment options, prevention of acquiring DRM’s is essential. However, there is limited long term data of African children on ART who later develop Virological Failure (VF) and DRMs. This data is crucial to identify determinants for late (>24 months) VF and acquiring DRM’s during life-long ART, in order to improve long-term outcomes for African children on ART. This study describes the occurrence of early VF (<24 months) and late VF (24-48 months) and the prevalence of acquired DRM’s in HIV-infected children on first line ART during the first 48 months of treatment in Uganda. Secondly, determinants for late VF are investigated.

Method: Children aged ≤12 years initiated on first-line ART in Uganda in 2010-2011 were included. Viral load (VL) and genotypic resistance testing were done at baseline and 6-monthly. DRMs and susceptibility were scored by 2017 IAS-USA mutation list and Stanford algorithm 7.0. Virological failure (VF) was defined as two consecutive VLs>1,000 copies/ml or death after six months of ART. VF was typed early VF if occurring between 0-24 months or late VF when occurring at 25-48 months. Viral suppression was defined as VLs<1,000 copies/ml. Adherence was calculated as the mean thirty-day adherence reports.

Results: 316 Ugandan children were enrolled. Viral suppression was achieved among 194/256(75.8%), 178/249(71.5%), 162/223(72.6%) and 126/182(69.2%) at 12, 24, 36, 48 months respectively. VF occurred in 111/286 children (38.8 %) respectively, 75/111 (67.6%) showed Early VF and 36/111(32.4%) late VF. Early VF was associated with baseline partly active regime (GSS<3) (OR 6.0, 95%CI 1.9-18.5) and poor adherence (OR 3.1, 95%CI 1.3-7.4). Late VF was associated with baseline age above 3 years (OR 3.2, 95% CI 1.4-7.13) and WHO stage 3/4 (OR 5.0, 95% CI1.5-16.3). Acquired DRM occurred among 73/270(27.0%) children at 0-24 months and 39/270(14.4%) at 25-48 months.

Conclusion: Although most VF occurs in the first year of treatment, long-term outcome is important to challenge VF after 24 months as well. Children with an advanced HIV disease stage and age >3 years at start of ART are at risk for late VF. These findings underline the WHO—policy to treat all HIV infected children early, irrespective of age or disease progression. Moreover, given the ambition to maintain these African children on ART for decades, identification of additional factors that challenge treatment sustainability is essential.

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A Systematic Retrospective Loss Analysis Assessing Outcomes for Children on Antiretroviral Therapy in Tanzania

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Objective: According to UNAIDS, as of 2017 there are an estimated 110,000 children living with HIV (<15yo) with only 50% on antiretroviral therapy (ART) in Tanzania. Routinely reported data from Tanzania reveals substantial loss in the number of children on ART over time, but the reasons are not well understood. There are significant concerns about mortality and morbidity among children on ART, and while this likely contributes to poor retention, UNAIDS data suggests that approximately 8% of children on ART are ‘aging out’ of the <15yo age band in Tanzania. This implies that some children not documented on ART may in fact still be on ART, but are no longer counted in the <15yo age band. We conducted a systematic retrospective loss analysis to determine the extent of and reasons for the loss in the number of children <15yo on ART over time in Tanzania.

Methods: We analyzed data for children <15yo current on ART at the beginning of the study period and new on ART during the study period: October 1, 2014 to September 30, 2015. The number of children on ART was assessed at the end of the study period. For this analysis, children were defined as retained if on ART at the start of the study period or newly initiated on ART during the study period and still on ART at the end of the study period in the <15yo age band; children not documented on ART at the end of the study period were defined as ‘not retained’ and further categorized as aged out (>15yo age band), transfer out, died, or LTFU after 3 months.
**Results:** At the beginning of the study period, 7,408 children were current on ART; during the study period, 3,543 children initiated ART and 1,491 children on ART were documented as transferred in. At the end of the study period, 10,222 children were retained on ART and 2,220 were not retained. Of those not retained: 59% (n=1,316) aged out, 23% (n=500) transferred out, 7% (n=163) died, and 11% (n=241) were LTFU. Further disaggregation and review of the data by those children current on ART at the beginning of the study period and newly initiated on ART during the study period was completed. Among 7,408 children current on ART, 1,264 were not retained: 78% (n=993) aged out, 9% (n=109) transferred out, 0.2% (n=2) died, and 13% (n=160) were LTFU. Among 3,543 children newly initiated on ART, 956 were not retained: 34% (n=323) aged out, 41% (n=391) transferred out, 17% (n=161) died, and 8% (n=81) were LTFU.

**Conclusions:** A large proportion of children not retained on ART was due to ‘aging out’ of the <15yo age band, especially for those children already on ART at the beginning of the study period, emphasizing the need for adolescent-friendly services and patient monitoring across age bands. A systematic loss analysis to monitor retention outcomes for children on ART is essential to improve outcomes.

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**Predictive probability models for targeted birth HIV PCR testing**

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**Background:** Many advances have been made towards the global aim of eliminating infant HIV transmission by targeting suboptimal antenatal care, maternal treatment failure and primary HIV infection in pregnancy. Infants born to mothers in high-risk scenarios contribute disproportionally to the HIV transmission rate. Appropriate, accurate and cost-effective HIV diagnostic algorithms are needed to guarantee early HIV treatment success. Targeted birth HIV PCR testing constitutes a potential approach.

**Materials & Methods:** A cross-sectional study was conducted on HIV exposed newborns at Kalafong Provincial Tertiary Hospital (KPTH), South Africa. Maternal and infant characteristics were reviewed, infants clinically evaluated and tested for HIV infection by PCR within 72 hours of birth. Associations between HIV infection and individual parameters were quantified by odds ratios with 95% confidence intervals and p-values from fitting univariate and multivariate logistic regression models. Clinically important risk factors with p < 0.25 in univariate-unweighted models were included in multivariate regression models. The performance of the risk scores was evaluated using the area under the receiver-operating curve. For various cut-points of the derived risk scores, sensitivity and specificity were determined.

**Results:** From August 2014 to December 2016 there were 15 175 live births at KPTH, 3356 (22.12%) to HIV-infected mothers. Of the 1911 infants screened, 1759 (92%) were enrolled. Pregnancy-related characteristics showed that 5.7% (97/1688) had no ANC visits with a significant difference in the number visits between the PCR negative and PCR positive cohorts (p=0.0005). Most mothers knew their HIV status before delivery (98.8%) and were on cART (1626/1704, 95.4%). Virological control varied with HIV viral loads not detectable in 595 (60.15%) and 1 in 5 mothers (217/990, 21.9%) had viral load levels >1000 copies/µL. More than a quarter (432/1655, 26.1%) were born at a gestational age <38weeks. Low birth weight (<2.5kg) was documented in 398/1598 (24.55%) of the PCR negative infants and in 13/32 (40.63%) of the positive group (p=0.0329). Less than 15% were clinically symptomatic at birth. Growth restriction or small for gestational age were documented in 204/1689 (12.08%), six (6/37, 16.22%) of whom were PCR positive. Symptomatic newborns more frequently tested HIV positive (p=0.0042). The newborn HIV PCR positivity rate was 1.8% (31/1759).

Detectable maternal HIV viral load, maternal cART duration of <1 month, and an infant that was symptomatic at birth were the most significant risk factors predicting HIV infection. Small-for-
gestational-age was included with the above three characteristics in multivariate analyses and a two-, three-, and four-risk model for newborn HIV acquisition was developed with a predictive probability score of a newborn PCR positive test at 0.28, 0.498, and 0.57 respectively.

**Conclusions**: Models for targeted birth PCR testing in resource constraint settings are proposed in this study. Access to maternal VL testing is paramount to a targeted birth PCR approach as maternal HIV viral load levels remain one of the most important parameters in predicting mother to child transmission. Maternal cART history and infants’ birthweight, gestation estimates and symptoms are parameters that can be combined in two-, three-, and four-risk modelling to guide a targeted approach algorithm.

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**High HIV testing yield among children at TB, Nutrition, and HIV clinics in Uganda**

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**Background**: Optimizing identification of undiagnosed HIV among children is critical in reducing the global burden of pediatric HIV/AIDS. Understanding the HIV yield among children at different facility-based entry points can inform more efficient pediatric HIV testing strategies. We assessed entry point HIV testing yield among children 18 months to 15 years in 4 regions of Uganda.

**Methods**: HIV testing was offered to 3245 children in 8 health facilities (4 regional referral and 4 district hospitals) from February 2017 to June 2017. All children who entered through outpatient department (OPD), inpatient department (IPD), malnutrition, TB and special (HIV, sickle cell, young child (YCC), and eye) clinics, whether patients themselves or accompanying patients, were reviewed for HIV status and offered a test if their status was unknown. A retest for verification was conducted for those testing HIV positive. HIV testing yield was defined as the proportion of HIV positive children among those tested. Proportions, percentages, chi-square and fisher exact tests were used in the analysis of results.

**Results**: The HIV test uptake was 96% (3119/3245) with an overall yield of 1.4% (45/3119). Among entry points; TB clinics, Nutrition units and special clinics had the highest yield at 5.6% (4/71), 2.2% (2/92) and 2.4% (17/706) respectively (p=0.001). Entry points with relatively low HIV yield included: OPD 1.1% (12/1126) and IPD 1.0% (10/1046). In spite of the relatively low HIV testing yield at OPD and IPD, these two entry points accounted for the highest number of children testing HIV positive. While the HIV clinic had the highest HIV yield 52.9% (9/17) among special clinics, YCC clinic did not yield any HIV infected child and the testing volumes were rather low.

**Conclusions**: TB units/clinics, Nutrition units/clinics and HIV clinic entry points had the highest HIV test yield while, OPD and IPD accounted for the largest number of HIV positive children identified. This finding further emphasizes the need for HIV testing for all children with TB, malnutrition, and those who have family members living with HIV. In OPD and IPD settings, however, introduction of a screening tool could maximize HIV testing yield while more efficiently utilizing limited testing resources.

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**Characteristics and Outcomes of Children, Adolescents, and Young Adults with Kaposi Sarcoma Treated in a Comprehensive Care Program in Mbeya, Tanzania**

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**Background**: Despite increasing availability of antiretroviral therapy (ART), Kaposi sarcoma (KS)
remains an important HIV related malignancy in regions with high human herpes virus 8 seroprevalence, such as Tanzania. To address the needs of pediatric, adolescent and young adult (AYA) patients with KS, a comprehensive care program was established in Mbeya, Tanzania in 2011.

Materials and Methods: A retrospective chart review was conducted to describe characteristics and outcomes of patients diagnosed with KS between 1 March 2011 and 31 Dec 2017. Services provided included chemotherapy, ART, palliative care, nutrition and psychosocial support. All oncology and other clinical services were delivered in an outpatient setting by pediatricians and medical officers at the Baylor Tanzania Centre of Excellence in Mbeya, Tanzania, with offsite technical advise provided by Baylor Houston pediatric oncologists.

Results: The cohort included 60 patients: 58% (35/60) male, median age 12.8 years (2.2-22.1). Clinical diagnosis was supported by histopathology in 36% (22/60). At diagnosis, 35% (21/60) had lymphadenopathic KS, 28% (17/60) had woody edema KS, 26% (16/60) had disseminated KS and 10% (6/60) had moderate cutaneous/oral KS. Severe anemia (Hgb < 8g/dL) was present in 28% (17/60) and severe thrombocytopenia (platelets < 50,000/mm3) was present in 22% (13/60). 97% (58/60) were HIV +, of those, 78% (45/58) were on ART for a median of 11 months (2 days -120 months). IRIS occurred in 24% (11/45). CD4 data was available for 95% (55/58), of whom 64% (35/55) met criteria for WHO severe immunosuppression. 45% (27/60) patients had severe acute malnutrition (SAM).

95% (57/60) patients were treated with chemotherapy; 3 patients died before treatment initiation. 52% (30/57) were treated with bleomycin and vincristine (BV); doxorubicin was added for 39% (22/57). Paclitaxel was given to 21% (12/57) who failed to achieve complete clinical remission (CCR) with BV or BV + doxorubicin; 1 patient was initially treated with paclitaxel. 96% (56/58) of HIV + patients were given ART. At the end of study period, 72% (43/60) patients were alive. No patients were lost to follow up; 7 transferred out. Of living patients, 67% (29/43) achieved CCR. Median follow up for living patients was 25 months (2-78) from diagnosis to end of study.

Conclusion: Despite the resource limitations that exist in southwestern Tanzania, pediatric and AYA patients with KS can be successfully treated with the majority of patients in our clinical oncology program achieving positive outcomes.

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Accessing developmental services: supporting HIV exposed but uninfected children

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Background: The prevalence of developmental delay (DD) in HIV exposed but uninfected children (HEU) born in British Columbia (BC), Canada, is higher than in the general population. This is likely attributable to perinatal exposure to alcohol and drugs, prematurity, social determinants of health and adverse childhood experiences (ACEs). Of ~240 HEUs born in Canada annually, 25-30 come from BC and are followed by pediatric HIV specialists at the Oak Tree Clinic (OTC), a women- and family-centered HIV clinic. HEUs are followed frequently in the first year of life, and less often after age 18 months. In 2014, changes were made to enhance early detection and early intervention (EI) for DD through screening, anticipatory guidance, linkages with developmental services, follow-up of referrals and biannual visits until age 5 for vulnerable children. Our study aims to evaluate HEUs’ access to EIs and the social barriers that exist within this population.

Materials and Methods: A retrospective chart review was performed for HEUs born between 01/2008-05/2014 (older cohort) and 06/2014-06/2016 (younger cohort) with at least one visit. Information about formal DD screening, referral to EIs, demographic variables, and ACEs were collected by chart review. Outcomes including major developmental diagnoses and school problems were collected for the older cohort.

Results: Among 169 HEUs, 89 (52.7%) were male; 112 belonged to the older cohort (age >4years) and 57 to the younger cohort (age 18m-4y). Ethnicity, known for 156 (92.3%), included 40 (23.7%) Indigenous, 47 (27.8%) African/Caribbean/Black and 53 (31.4%) Caucasian. 133 children (78.7%)
were born at term and 79 (46.7%) were exposed in utero to drugs and/or alcohol. 127/169 (77.2%) were in the care of biological parent(s); the remainder were adopted, in foster care, or with extended family. At least 69 (40.8%) had child protection services involvement. The majority (119; 70.4%) had ≥1 ACEs, and 16 (9.5%) had ≥4.

Both cohorts were screened for DD at nearly every visit (100% younger versus 96.3% older, p=0.14). 75 (45.6% younger, 42.9% older) screened positive for a developmental concern; 54/75 (72%) children with DD were followed by EI, 42 of these children (77.8%) had referrals from OTC, with an average completion rate of 63.5%. The remainder of those followed had accessed EI through referral from other developmental services (22.2%). Of the 22 children referred for speech therapy, 8 (36%) did not attend. In the older cohort, 19 (17%) have a developmental diagnosis documented at OTC, with 13 (68.4%) being diagnosed with ADHD, and the majority requiring support at school.

Conclusions: With almost half of the HEU children in BC screening positive for a developmental concern (and the literature suggesting high rates of diagnosed developmental disabilities), HEUs require careful developmental monitoring. Optimally, all children at risk for DD (HEU, prematurity, ACE>3, prenatal drug exposure) would be followed and benefit from EI. However, even with an increased emphasis on early detection and referral within a tertiary HIV clinic setting, referral completion remains less than optimal and many HEUs still face significant challenges and barriers related to services and interventions.

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Acceptability and feasibility of implementing birth testing for early infant diagnosis of HIV infection in Zambia

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Background: Testing for HIV at birth is now recommended in many settings as it can lead to earlier diagnosis and treatment for HIV-infected infants and reduce morbidity and mortality. Testing at birth presents different challenges than later in infancy as it occurs in maternity wards shortly after delivery. This study was conducted to understand the acceptability and feasibility of implementing birth testing in different settings in Zambia.

Materials and Methods: A prospective cohort study of HIV exposed infants undergoing early infant HIV diagnosis was conducted at two urban facilities (one hospital and one clinic) and five rural facilities (one hospital and four clinics) in Southern Province, Zambia from February 2016 to May 2017. All HIV-exposed infants born at the health facilities were eligible to participate. Dried blood spot cards were collected and sent to a central laboratory for HIV DNA testing. Results were documented and provided to the mother.

Results: 864 HIV-exposed infants were identified as eligible and 754 infants (87%) were enrolled in the study. Only 19 (2%) infants did not participate because the mother did not want the child to be tested at birth. More mothers declined birth testing in the hospitals (urban: 1%; rural: 6%) than in the clinics (urban: 0.6%; rural: 0%). Only 1.7% and 0.9% of infants at the urban and rural facilities had detectable HIV DNA, respectively. The proportion of mothers who did not receive the results was high in the urban facilities (hospital: 63%; clinic: 23%) and rural hospital (13%) and low in the rural clinics (<1%). At the urban hospital, the primary reason was that the mother defaulted. At the urban clinic and rural hospital, the primary reason was that the mother had no phone and could not be reached.

Conclusions: Testing at birth was acceptable to the majority of mothers delivering in health facilities. However, returning test results to mothers was challenging, particularly in the urban areas and hospitals, as many women delivered far from home and lacked access to a phone, supporting the need for point-of-care tests for early infant diagnosis.

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Impact of late versus early antiretroviral therapy on PBMCs-associated HIV-DNA levels and naive T lymphocytes percentages in HIV-1
infected children/adolescents – The ANRS-EP59-CLEAC study


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Background: Early combined antiretroviral therapy (cART) initiation reduces progression to AIDS and death and lowers the size of the cell-associated viral reservoir in children infected with HIV-1 in the perinatal period. Currently, few data are available on the persistence of early cART benefit for older children and adolescents. The ANRS-EP59-CLEAC study aims to compare the immunological and virological characteristics, according to early (< 6 months of age) versus late in childhood (≥24 months of age) cART initiation in HIV-1-infected children and adolescents who achieved initial virological suppression.

Methods: Patients’ recruitment was conducted in Paris area between 2016 and 2018. Total cell-associated HIV1-DNA was quantified in blood using ultrasensitive real-time PCR (adapted from Biocentric, Bandol, France). CD4 and CD8 naive T lymphocytes were quantified by flow cytometry with fresh blood and defined by the coexpression of CD45RA and CCR7 molecules. The Kruskal-Wallis test was used to compare the parameters from early/late treated children (5-12 years) and adolescents (13-17 years).

Results: We prospectively enrolled 27 children (E-Ch) and 9 adolescents (E-Ado) in the early cART group, and 19 children (L-Ch) and 21 adolescents (L-Ado) in the late cART group. Patients were mainly girls (54%), born in mainland France (60%) to mother originating from Sub-Saharan African countries (74%). At the time of the study, all patients were receiving ART, 76 % had undetectable plasma HIV-1 RNA and the median (interquartile range) CD4 T-cell count was 824 [660; 1167] cells/µl. Total HIV-1 DNA levels were lower in early treatment than in late treatment groups (medians were 2.2 (E-Ch), 2.9 (L-Ch), 2.3 (E-Ado) and 3.0 (L-Ado) log10 copies/106 PBMCs, P < 0.0001). Naive CD4 and CD8 T-cell percentages were available for 58 subjects. The highest percentages were observed in early treated children (medians in E-Ch, L-Ch, E-Ado and L-Ado groups were 61, 54, 36 and 55% for CD4, P=0.02; and 50, 33, 29, and 29%, for CD8, P = 0.004).

Conclusion: In children and adolescents, cART initiated from infancy is associated with lower PBMCs-associated HIV-1 DNA levels as desired for HIV-1 remission strategies. An immunological benefit of early cART on naive T cells was suggested in children.
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