Abstract Book

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Abstracts
Oral Presentation
Community based Index- and Mobile Testing are complementary and effective in pediatric HIV case finding in Tanzania

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Background: Sauti is a PEPFAR/USAID funded project offering community-based HIV combination prevention services to key and vulnerable populations (KVP) in 14 regions in Tanzania. The project provides HIV testing service (HTS) and linkage to care and treatment to children of KVP and other populations. Per the 2017 HIV Impact Survey, pediatric HIV prevalence is estimated at 0.4%. In fiscal year 19 (FY19: 1 October 2018 to 17 March 2019) compared to fiscal year 18 (FY18: 1 October 2017 to 31 September 2018), the project scaled up targeted testing strategies by introducing index next to mobile testing; training of health care providers on fidelity of testing procedures and beneficiaries’ categorization, and enhancing peer educators’ capacity on demand creation for testing to those at highest risk of HIV.

Materials & Methods: Routine data were recorded in FY18 and FY19. The pediatric population was defined as 18 months – 14 years old, being children of KVP (children of female sex workers, adolescent girls and young women or men who have sex with men) or children of non-KVP (biological parent not from the KVP). Index testing referred to biological children of an HIV positive mother; any other test was categorized as mobile testing. This analysis describes the testing yield and trend by type of population and modality.

Results: In FY18, through mobile testing, Sauti diagnosed 759 HIV positive among 124,199 children of non-KVP (0.6%) and 20 HIV positive among 2,356 children of KVP (0.8%), compared to 137 HIV positive among 7,940 children of non-KVP (1.7%) and 107 HIV positive among 2,035 children of KVP (5.3%) in FY19. Mobile testing yield in FY19 was significantly higher compared to FY18, for children of non-KVP (1.1% increase, 95% CI:0.8-1.4; p<0.0001) and children of KVP (4.5% increase, 95% CI:3.50-5.59; p<0.0001). Index testing yield for children of non-KVP was statistically higher in FY19, 175 new HIV positives among 4,809 children tested (3.6%); compared to FY18, 1,189 new HIV positives among 131,338 tested (0.9%), an increase of 2.7% (95% CI 2.2-3.3, p<0.0001). Likewise, for index testing among children of KVP, FY19 found 197 new HIV positives among 6,197 tested (3.2%); compared to 73 new HIV positive among 7,234 tested (1.0%) in FY18, an increase of 2.2% (95% CI 1.71-2.71, p<0.0001). When comparing testing modalities by type of pediatric population, children of KVP yielded significantly more positives through mobile testing only in FY19 (5.3%), compared to children of non-KVP (1.7%), an increase of 3.6% (95% CI: 2.65-4.69; p<0.0001). Yields for index and mobile testing modalities for children of KVP in FY18 did not differ significantly nor did index testing for children of KVP in FY19.

Conclusion: The significant increase of testing yield over a two year period reflects increased project capacity to support effective demand creation, provision of services with fidelity, and scale-up of targeted testing modalities that are effective in identifying at risk children with HIV. This was particularly true for those children of KVP reached through mobile testing, which in FY19 was a successful complementary strategy to index testing.
The cost-effectiveness of point-of-care platforms for early infant diagnosis of HIV infection in Southern Province, Zambia

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Background: Early infant diagnosis is challenging in sub-Saharan Africa, leading to delays in diagnosis and treatment for HIV-infected infants. Point-of-care (POC) platforms are available that could increase access to early infant diagnosis. This study evaluated the cost-effectiveness of different implementation strategies for POC platforms in Zambia.

Methods: This simulation was performed for Southern Province, Zambia assuming a population of 7,500 infants undergoing testing at birth, 6 weeks and 6 months of age in a given year and 93% PMTCT coverage (range: 73-100%). POC platforms evaluated included GeneXpert (Cepheid Inc.; sensitivity/specificity: 96.80%/99.91%) and mPIMA (Alere Inc.; sensitivity/specificity: 99.00%/99.97%), and utilization by EID programs was assumed to be 100%. Utilization was shared across programs (e.g. for viral load testing) in a sensitivity analysis. The sensitivity and specificity of conventional PCR was assumed to be 100%. Five scenarios were modeled: A) PCR only, with confirmation of positives (standard); B) POC only, with confirmation of positives by PCR with PCR as a tie-breaker for discrepant results; C) POC only, with confirmation of positives by PCR with a third POC as a tie-breaker; D) POC only, no confirmation of positives; and E) POC only, with confirmation of positives by PCR. Health outcomes included the proportion of HIV-infected children initiating ART within 60 days, ever initiating ART (up to age 12 months), and dying prior to ART initiation, and the proportion of children receiving ART who are HIV-uninfected. Total costs included both capital and recurrent costs. All analyses were performed using R software.

Results: In Scenario A, 12.0% and 44.2% of HIV-infected children (n=315) initiated ART within 60 days and ever, respectively, and 25.5% died prior to ART initiation. The total cost was 636,010 USD. Health outcomes improved with all POC scenarios (B-E) and for both mPIMA and GeneXpert. ART initiation outcomes were similar across scenarios but highest for D and E, as confirmation was not required prior to initiation (e.g. ART initiation within 60 days: 78.7% [B] vs. 80.8% [C] vs. 80.9% [D/E] for GeneXpert). However, without any confirmation, scenario D had the highest proportion of children receiving ART who were HIV-uninfected (e.g. 0.004% [B] vs. 0.008% [C] vs. 4.3% [D] vs. 0.5% [E] for GeneXpert). Due to its higher sensitivity and specificity, health outcomes were slightly better for mPIMA than GeneXpert (e.g. 81.5% vs. 78.7% for ART initiation within 60 days [B]). Incremental costs were highest for scenario B and lowest for D (e.g. 123,045 [B] vs. 88,697 [D] USD for GeneXpert) and higher for GeneXpert than mPIMA (e.g. 41,263 USD [D]). POC was more cost-effective in settings with lower PMTCT coverage and with shared utilization of POC platforms. With shared utilization, mPIMA was cost-saving for all scenarios.

Conclusions: Implementation of POC platforms could increase health outcomes for HIV-infected infants by reducing the time to ART initiation. Different POC implementation scenarios had minimal impact on health outcomes, although confirmation of positives reduced the number of HIV-uninfected infants receiving ART. POC testing was more costly than PCR, but cost sharing across programs could reduce costs to such an extent that POC programs become cost-saving.
Virological outcomes and ART discontinuation in children switching to dolutegravir in the UK/Ireland: a propensity score analysis

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Background: Dolutegravir (DTG) was approved in Europe for treatment of HIV-1 for individuals age ≥12 years in January 2014 and extended to 6–<12 year olds in December 2016. It is part of the World Health Organization (WHO) recommended preferred first-line and second/subsequent-line regimens in children. Rapid weight gain has been reported in some adults starting DTG but data on treatment outcomes in routine paediatric care are limited. We assessed virological suppression (VS), treatment failure and weight gain, comparing children switching to DTG with suppressed viral load (VL) to those switching to a new protease inhibitor (PI)-based regimen, in the UK/Ireland.

Materials & Methods: Treatment experienced children/adolescents aged 6–18 years with VS defined as <50 copies/ml or lower limit of detection) at switch to 2NRTIs+DTG or 2NRTIs+PI from 2010-2017 were included. Propensity scores (PS) based on characteristics at start of DTG/PI (age, sex, time since ART initiation, prior treatment failure, prior AIDS event and CD4 count) were derived. After matching on PS differences in proportions with VS, and change in BMI-for-age z-score (zBMI, derived from WHO growth reference) at 6 and 12m after switch were estimated. Time to confirmed VL rebound (2 consecutive VL≥50) or discontinuation of 3rd agent, was calculated with follow-up censored at earliest of last VL date, or 12m after regimen start. Time to VL rebound/discontinuation was modelled using a Weibull model with PS weighting.

Results: Of 216 children ever taking DTG, 153(71%) took DTG+2NRTIs, of whom 17(11%) were ART naive, 18(12%) treatment experienced with detectable VL, and 21(14%) missing VL. The remaining 97(63%) had VS at switch and included in this analysis and were compared to 163 patients with VS at switch to an eligible PI-based regimen. Age at ART initiation were similar in both groups (median 4.7[IQR 1.5,9.3] and 4.4[1.1,8.5] years, respectively) and half were male. Those on DTG were slightly older at switch to DTG (14.9[12.9,16.4] versus 13.7[11.3,15.3] years than in the PI group), with lower CD4 (742[567,974] versus 850[619,1100] cells/mm3) and fewer had previous treatment failure (39% versus 47%). Prior to PS matching, 66/70(94%) and 41/44(93%) on DTG had VS at 6 and 12m compared to 124/159(88%) and 104/140(82%) on PIs. zBMI remained stable; median change 0.00[-0.23,0.09] and 0.05[-0.33,0.23] at 6 and 12m on DTG and 0.00[-0.40,0.93] and 0.01[-0.24,0.26] on PI. Cumulative risk of viral rebound/discontinuation at 12m was lower on DTG at 3.7%(95%CI 1.2,11.2) versus 13.1%(8.7,19.6) on PI.

After matching, characteristics were well balanced and the proportion with VS was 11.8%(4.8,18.8) higher on DTG versus PI at 6m and 10.3%(0.1,20.6) at 12m, respectively. There was no difference in change in zBMI: mean change 0.04(-0.05,0.14) higher on DTG than PI at 6m and 0.05(-0.11,0.21) at 12m, respectively. Average time to viral rebound/discontinuation was 2.8(0.8,2.9) months later on DTG compared to PI.

Conclusions: In our propensity score analysis, a higher proportion of those on DTG had a sustained VS at 6 and 12m compared to those on PI-based regimens. There was no evidence of increases in zBMI after 12m on either regimen but longer-term follow up is needed.
Tenofovir Alafenamide-based regimens: A Pooled Resistance Analysis in Pediatric Participants

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Background: Tenofovir alafenamide (TAF) is a tenofovir (TFV) prodrug achieving lower levels of circulating TFV and higher levels of TFV-diphosphate in lymphocytes compared to tenofovir disoproxil fumarate (TDF), translating into improved renal and bone safety. The TAF-containing single-tablet regimens elvitegravir/cobicistat/emtricitabine/TAF (E/C/F/TAF) and bictegravir/F/TAF (B/F/TAF), as well as the fixed-dose combination F/TAF administered with varying 3rd agents were evaluated in pediatric clinical studies. Virologic success (HIV-1 RNA < 50 copies/mL) rates of TAF-based regimens at Week 24 or 48 using FDA snapshot analysis were high and similar among all studies (90-100%). An integrated resistance analysis across 4 Phase 2/3 pediatric clinical studies is described, including resistance associated mutations (RAMs) to nucleoside reverse transcriptase inhibitors (NRTIs), non-NRTIs (NNRTIs), protease inhibitors (PIs), and integrase strand transfer inhibitors (INSTIs).

Methods: A total of 280 participants were enrolled in 4 clinical studies (E/C/F/TAF: GS-US-292-0106 and GS-US-292-1515; F/TAF: GS-US-311-1269; B/F/TAF: GS-US-380-1474) from sites in South Africa, USA, Uganda, Thailand, and Panama. Treatment-naive (TN) and virologically suppressed (VS) participants were included in the analysis, although the majority were virologically suppressed (82%, 230/280) at study entry. Out of the 280 participants, 100 were 6 to 11 years of age, while the remaining 180 were 12 to 17 years of age. In treatment-naive participants, HIV-1 genotypic testing was conducted pre-treatment using commercial population sequencing (Monogram Biosciences) to assess for HIV-1 protease (PR), reverse transcriptase (RT), and integrase (IN) RAMs. In virologically suppressed participants, historical genotypes were collected when available. For participants with HIV-1 RNA ≥400 copies/mL at time of virologic failure (VF) or early discontinuation, genotypic analysis and phenotypic antiretroviral susceptibility were evaluated.

Results: Out of 280 enrolled pediatric participants, 74 had HIV-1 subtype data available. HIV-1 subtypes included A (3%), A1 (26%), AE (11%), B (27%), C (22%), D (8%), or complex mixtures (4%). HIV-1 subtype distribution correlated with geography (A1, Uganda; AE, Thailand; B, USA; C, South Africa). Out of the 69 participants with baseline data (50 out of 50 [100%] of TN and 19 out of 230 [8%] of VS), pre-existing primary resistance-associated mutations (RAMs) were observed pre-treatment in 22% (n=15) of participants overall (13% [NRTI-RAMs], 13% [NNRTI-RAMs], and 3% [PI-RAMs] of the 69 participants with baseline data). Four had M184V at study entry and were virologic successes at Week 48. Virologic failure resistance analyses were conducted in 6% (16/280) participants across the 4 studies. Four participants on F/TAF + efavirenz had primary resistance to antiretrovirals in their regimen detected at failure in the absence of baseline or historical data (participant 1: Y181Y/C; participant 2: K103K/N; participant 3: K65R, K103K/N; and participant 4: K65R, M184V, K103N). No participant on E/C/F/TAF or B/F/TAF had treatment-emergent resistance.

Conclusions: In this diverse population, resistance development was rare, and there were no cases of treatment-emergent resistance in participants receiving an INSTI-containing TAF regimen. Pediatric participants with the baseline NRTI mutation M184V were successfully treated with TAF-based therapies. Overall, HIV-1 infected pediatric participants achieved a high level of virologic suppression with TAF-containing regimens.
Population pharmacokinetics of nevirapine in preterm infants and prediction of doses needed for treatment in combination with other antiretrovirals

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Background: The only antiretrovirals (ARV) approved to treat HIV- exposed infants below 37 weeks gestational age (GA) are nevirapine (NVP), zidovudine and lamivudine. The NVP concentration target for treatment (3 mcg/mL) is 30-fold that for prophylaxis (0.1 mcg/mL). Preterm infants have reduced NVP clearance compared to term infants; doses of 4 mg/kg QD in IMPAACT P1106 preterm infants consistently gave NVP concentrations above the prophylaxis target. However, there are no NVP pharmacokinetic (PK) data following administration of treatment doses in infants born < 32 weeks GA. We performed a population PK analysis combining PK data from 2 IMPAACT studies (P1106 and P1115) followed by simulations to help determine appropriate NVP treatment dosing in premature infants.

Materials & Methods: A population PK analysis of NVP concentrations from premature infants enrolled in IMPAACT P1106 and P1115 was performed. P1106 included premature and low birth weight (<2500g) infants receiving NVP prophylaxis at 2 different doses (2 mg/kg QD, birth to 14 days of age and 4 mg/kg QD to week 24); 1-3 plasma samples were collected at day 7-14, and again at 4, 6, 10, 16 and 24 weeks of age. P1115 included premature infants (34-37 weeks GA) who received early combination ARV therapy including NVP (4 mg/kg BID in week 1 of life and 6 mg/kg BID thereafter). Dried blood spot and plasma samples were collected at around 7-9 days of life, with a second collection 1 week later if still on NVP. NVP concentrations were analyzed using nonlinear mixed effects modelling (NONMEM ver 7.3). Data were fit to a one-compartment model and PK parameters were allometrically scaled prior to assessing other covariates. The potential effects of GA, postnatal age (PNA) and postmenstrual age (PMA=GA + PNA) on clearance were investigated. Monte Carlo simulations were run for virtual infants between 28 - 37 weeks GA and 5 to 40 weeks PNA with doses of 2-6 mg/kg QD and BID with goal of achieving NVP troughs between 3.0 and 10 mcg/mL.

Results: The population PK model included 304 NVP concentrations from 211 study visits from 71 preterm infants (54 from P1106 and 17 from P1115). The median (IQR) birth weight was 1900 (1500 – 2500g) and GA was 33 (32, 36) weeks. Day of first PK sampling averaged 8 days of life. Inclusion of GA and PNA on apparent clearance (CL/F) significantly improved the model. CL/F was best described as: CL/F (L/h/kg0.75) = 0.117*(GA/34)9.97*(1- MAT) *(MAT) Where MAT is the maturation function described by PNA/(13.5 days + PNA), simulations indicated that initial doses below 4mg/kg BID are needed in premature infants born < 32 weeks GA to avoid NVP concentrations > 10 mcg/mL.

Conclusions: Population pharmacokinetics analysis of combined data P1106 and P1115 data from infants <37 weeks GA, suggest that a NVP dose of 4 mg/kg BID will be too high for premature infants 28-32 weeks GA. Additional studies to assess both PK and safety in this population are needed to determine the appropriate NVP dose for this vulnerable population.
Systemic inflammation and structural brain changes in perinatally HIV+ adolescents

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1Uct

Neurological impairments despite ART are well documented in perinatally-infected HIV+ adolescents (PHIV) but the mechanisms that drive this are not well defined. Systemic inflammation may be one mechanism but this has not been investigated in adolescence when the brain is undergoing rapid development.

Methods: Baseline data were drawn from the Cape Town Adolescent Antiretroviral Cohort (CTAAC). PHIV on ART >6m at public sector facilities completed a comprehensive neurocognitive test battery assessing function in 10 cognitive domains. Diffusion tensor imaging and structural brain magnetic resonance imaging (MRI) was done to determine fractional anisotropy (FA), mean diffusivity (MD), gray and white matter volumes, cortical thickness and cortical surface area. In analysis we examined how neurocognitive and neurostructural measures were associated with a concurrently measured marker of systemic inflammation highly sensitive CRP (hs-CRP).

Results: Overall 204 PHIV ages 9-12 years (mean CD4 cell count 953 cells/µL and 85.3% VL<50 copies/mL) and 44 age-matched HIV-controls completed all assessments. PHIV had higher hs-CRP (p<0.001) vs controls. Among PHIV, hs-CRP negatively correlated with multiple neurocognitive measures including general intelligence (p=0.005), attention (p=0.015), working memory (p=0.003), visual space acuity (p=0.005), processing speed (p<0.001), and executive function (p=0.002); however none of these correlations were apparent among controls. hs-CRP was highest in PHIV with a major neurocognitive disorder (p=0.004). Whole brain MD increased with higher hs-CRP values. Higher MD is suggestive of inflammation and myelin loss.

Conclusion: Markers of systemic inflammation appear associated with both neurocognitive impairment and structural brain changes in PHIV. While further investigation including long-term follow-up is required, this provides novel evidence that inflammatory mechanisms may drive persistent neurological impairment in PHIV.
Abstracts

07

Associations between cholesterol, apolipoprotein E genotype variants, cognition and brain structure in perinatally HIV+ adolescents

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Background: Neurological impairments despite ART are well documented in perinatally-infected HIV+ adolescents (PHIV) but the mechanisms that drive this are not well defined. Apolipoprotein E genotype (ApoE) variants and cholesterol may be some of the mechanisms, but this has not been investigated in adolescence when the brain is undergoing rapid development.

Methods: Baseline data were drawn from the Cape Town Adolescent Antiretroviral Cohort (CTAAC). PHIV on ART >6m at public sector facilities completed a comprehensive neurocognitive test battery assessing function in 10 cognitive domains. In addition, subjects underwent ApoE genotyping. Diffusion tensor imaging and structural brain magnetic resonance imaging (MRI) was done to determine fractional anisotropy (FA), mean diffusivity (MD), gray and white matter volumes, cortical thickness and cortical surface area. In analysis we examined how neurocognitive and neurostructural measures were associated with ApoE genotype and concurrently measured fasting low density lipoprotein-cholesterol (LDL-C).

Results: Overall 204 PHIV ages 9-12 years (mean CD4 cell count 953 cells/µL and 85.3% VL<50 copies/mL) and 44 age-matched HIV-controls (HC) completed all assessments. PHIV had higher LDL (p=0.06) vs controls. Among PHIV, LDL-C negatively correlated with Language (p=0.048), but positively correlated with attention (p=0.023) and working memory (p=0.024); however none of these correlations were apparent among controls. Whole brain mean cortical thickness increased with higher levels of LDL-C in PHIV (p=0.03). Genotyping revealed no ε4 allelic variants in the sample. A total of 232 of 241 subjects were heterozygous for ε3, and, as expected, the majority of subjects (n=156) were homozygous for ε 3. 85 participants were heterozygous for ε2, and 9 were homozygous for ε2. In the combined sample, total cholesterol and LDL-C were significantly different across the ApoE groups. In both total cholesterol and LDL-C ε 3,3 was associated with higher values, ε 2,3 with middle values, and ε 2,2 with the lowest values. This pattern was repeated in both the PHIV and HC groups.

In the PHIV group, triglycerides were highest in the ε 2,3 group, followed by ε 3,3 and ε 2,2 had the lowest presence of triglycerides. Across the cognitive functioning domains, language performance was significantly different (p=0.047), with ε 2,2 having higher scores, followed by ε 2,3 and ε 3,3 having the lowest scores.

Conclusion: This study is the first to examine the effect of ApoE and LDL-C, known risk factors for cognitive decline in middle aged adults in a paediatric population. These data indicate that allelic variants of ApoE are associated language function in PHIV. In addition LDL-C appears associated with both language impairment and structural brain changes in PHIV. While further investigation including long-term follow-up is required, this provides novel evidence that ApoE and LDL-C may drive persistent neurological impairment in PHIV.
Malignancies in children with HIV across Eastern and Western Europe and Thailand

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Background: People living with HIV have increased risk of malignancies, but there are limited longer-term data on incidence among children as they age into adolescence and early adulthood. We analysed incidence of malignancies among children and adolescents from Europe, Russia and Thailand.

Materials & Methods: Children with HIV presenting to paediatric care <18 years of age and with >1 day of follow-up in 17 cohorts across 15 countries were included. Time at risk began at birth for children with vertically-acquired HIV, and from first HIV care visit for others. Children were followed (with data to 01/10/2016) until death, loss-to-follow-up (LTFU), or last visit in paediatric or adult care (where follow-up data were available). Rates of reported malignancies (/1000 person-years(PY)) were calculated overall and for AIDS-defining malignancies (ADM) and non-AIDS-malignancies (NADM) separately. Risk factors for any malignancy were explored using Poisson regression.

Results: Among 9,593 children, 8,311(87%) had vertically-acquired HIV. Calendar year at start of follow-up was <1996 for 3,327(35%), 1996-2003 for 3,424(36%), 2004-2009 for 1,885(20%), and ≥2010 for 957(10%). By end of follow-up, 4,262(44%) remained in paediatric care, 2,411(25%) dropped out, 900(9%) died, and 2,020(21%) transferred to adult care. Median (IQR) duration of follow-up was 13.2(7.2-17.6) years (including 2.8(1.2-5.0) years in adult care for 557(28%) patients), during which 8,720(91%) ever initiated ART.

131 malignancy events were reported: 106(81%) were ADM (80 non-Hodgkin lymphoma, 25 Kaposi Sarcoma, 1 cervical cancer), 22(17%) NADM (13 Hodgkin’s lymphoma, 9 other), and 3(2%) unspecified. Rates of malignancies, ADM and NADM were 1.10[95% confidence interval 0.93-1.30], 0.89[0.74-1.08], and 0.18[0.12-0.28] respectively. Rates of ADM decreased over time from 2.07[1.45-2.96], 1.26[0.93-1.71], 0.47[0.29-0.75] to 0.38[0.22-0.65] (p<0.001), while rates of NADM increased from 0.00, 0.12[0.05-0.32], 0.25[0.13-0.47] to 0.26[0.14-0.50] (p=0.052) in <1996, 1996-2003, 2004-2009 and ≥2010 respectively.

In multivariable analysis, females (adjusted incidence rate ratio (aIRR) 0.61[0.42-0.87] v. males), children from Thailand (0.16[0.04-0.68] v. Thailand, 0.57[0.23-1.42] Russia/Ukraine, 1.00[0.63-1.59] rest of Europe v. UK/Ireland, p=0.054), and those without current severe immunosuppression (0.22[0.14-0.35] v. severe, p<0.001) had lower risk of malignancy. Risk did not change over calendar time in patients currently not on ART (p=0.478) or on ART for <6 months (p=0.945), but decreased in patients on ART for ≥6 months (0.45[0.24-0.85] 1996-2003, 0.25[0.11-0.57] 2004-2009, 0.14[0.05-0.38] ≥2010, v. <1996, p=0.002). Risk increased with current age for those not on ART (2.32[0.89-6.05] 5-<10 years, 5.89[2.07-16.79] 10-<15 years, 3.60[0.41-31.93] ≥15 years, v. <5 years, p=0.001), on ART for <6 months (3.64[0.59-22.43] 5-<10 years, 6.67[1.02-43.61] 10-<15 years, 15.52[1.91-126.31] ≥15 years, v. <5 years, p=0.068) and on ART ≥6 months (0.87[0.47-1.62] 5-<10 years, 0.96[0.46-2.00] 10-<15 years, 2.14[0.96-4.77] ≥15 years, v. <5 years, p=0.048). There was no significant association with mode of infection (p=0.773) or current BMI-for-age z-score (p=0.428). 55(42%) patients with a malignancy died, at median 2.7(0.7-10.2) months post-diagnosis.

Discussion: A higher rate of cancers was observed in children living with HIV compared to the general population of children across Europe (0.14/1000PY). Incidence has fallen in recent years among those on long-term ART, with a smaller increase in risk with age among this group compared to those not on ART.
Shorter telomeres among HIV+ cART-naïve and cART-treated children, and those presenting with abnormal lung function

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Background: A high prevalence of chronic lung disease (CLD) has been reported among African children with perinatally-acquired HIV infection, despite combination antiretroviral therapy (cART). In adults, shorter telomere length (TL) has been reported in association with both chronic lung and HIV disease. Our objective was to measure and compare TL in cART-naïve HIV+, cART -treated HIV+ and HIV -negative older children and adolescents with and without CLD.

Methods: 418 HIV+ children aged 6-16 were enrolled in two cohorts (ZENITH and INHALE) at the Harare Children’s Hospital HIV clinic in Zimbabwe. Participants were either newly diagnosed hence cART naïve (ZENITH), or stable on cART for >6 months (INHALE). 203 age-and sex-matched HIV-negative children were also recruited as population controls. CLD was defined based on spirometry measurements of lung function performed according to the American Thoracic Society standard procedures. Using the global lung function initiative (GLI) 2012 reference ranges (which account for height, sex, age and ethnicity), lung function was considered abnormal if either forced vital capacity (FVC) or the ratio of forced expiratory volume in 1 second (FEV1) to FVC (FEV1: FVC ratio) z scores were less than <-1.64 (below the 10th centile). TL was measured by multiplex qPCR using DNA extracted from packed cells obtained after blood Ficoll Paque separation and values were log-transformed. Univariate associations were investigated through Mann-Whitney and Spearman’s correlation tests. Important factors (p<0.1) were considered in multivariable regression models. Extreme TL values that fell outside the 1.5x interquartile range (IQR) were considered not biologically plausible and excluded in a sensitivity analysis.

Results: TL was obtained from all 621 participants: 237 cART-naïve, 181 HIV+ cART-treated and 203 HIV -. Lung function data was available for 511 participants, of whom 53 (10%) had reduced FVC, 21 (4%) had an obstructive defect (low FVC with normal FEV1: FVC) and 437 (86%) were normal. Both cART-naïve and cART-treated HIV+ children had shorter TL than HIV- children. Among HIV+ children without CLD, cART-naïve participants also had shorter TL than cART-treated peers. There was no association between TL and HIV viral load or CD4 count.

In a multivariable analysis that adjusted for age, HIV/cART status, and CLD status (reduced FVC vs. obstructive defect vs. normal), shorter TL was associated with being HIV+, regardless of cART. Twenty-one/273 ZENITH and 31/389 INHALE outliers were excluded for the sensitivity analysis. In this model, shorter TL was independently associated with older age, being HIV+ and having reduced FVC. For a subset of ZENITH participants (n=21) who had a second specimen available post-cART initiation, a longitudinal increase in TL (p=0.013) was observed. Lastly, there was no relationship between TL and passive smoke exposure at home.

Conclusions: Our results suggest accelerated telomere attrition among HIV+ children, irrespective of cART status, as well as children presenting with CLD defined by reduced FVC. This may be a result of HIV and/or other health stresses, leading to increased immune activation and cellular turnover in response to disease.
Atazanavir exposure in utero and risk of multiple signals of neurodevelopmental dysfunction in 5-year-old HIV-exposed uninfected children

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Background: Toxic effects of antiretroviral medications (ARV) on the brain could be mediated through effects on mitochondrial integrity. Studies have observed Neurodevelopmental (ND) deficits and structural/functional changes in the brains of animals and humans with prenatal exposure to HIV/ARV. Specific ARVs have not been consistently implicated. ND dysfunction typically manifests early in development, often before the child enters grade school, and frequently affects multiple domains. Atazanavir (ATV) is a preferred protease inhibitor recommended by the United States Department of Health and Human Services for pregnant women with HIV. However, some studies have reported associations of ATV with cognitive, social/emotional, language, and behavioral problems in exposed children.

Materials & Methods: Monolingual English-speaking HIV-exposed uninfected (HEU) children from the Surveillance Monitoring of ART Toxicities (SMARTT) Study of the Pediatric HIV/AIDS Cohort Study (PHACS) network were evaluated at 5 years of age using the Behavioral Assessment System for Children (BASC-2), Wechsler Preschool and Primary Scale of Intelligence (WPPSI III) and The Test of Language Development-Primary (TOLD-P:3). “Multiple signals of dysfunction” was defined as having more than one of the following scores at least 1.5 standard deviations worse than population norms: Behavioral Symptom Index of BASC-2, Full Scale IQ of WPPSI-III, and Spoken language Quotient of TOLD-P:3. Separate analyses were conducted for children exposed to ARV at conception and children whose mothers initiated ARVs during pregnancy. Associations between exposure to ATV-containing regimens (versus non-ATV-containing regimens) and risk of multiple signals of ND dysfunction, as compared to no signals, were assessed by log-binomial models. Generalized estimating equation models were used to account for clustering of children within research clinics, adjusting for sex, ethnicity, household income, maternal age, education, IQ, HIV viral load early in pregnancy, marijuana use during the first trimester, family history of language problems, and year of birth (≤2006, 2007-2009, ≥2010).

Results: Among 289 children exposed to ARV at conception, 70 (24%) were exposed to ATV. Of the 571 children whose mothers initiated ARV during pregnancy, 97 (17%) were exposed to ATV. Valid assessments in all 3 domains were available for 228 and 458 children, respectively. Exposure to ATV was not associated with missing or invalid ND assessments. Among children exposed to ARV at conception, 33(14%) had single and 19(8%) multiple signals of dysfunction. Lower risk of multiple signals was observed with exposure to ATV (4% vs 10%, adjusted relative risk [aRR]=0.63, CI: 0.14-2.72). However, among children whose mothers initiated ARVs during pregnancy, 95(21%) had single and 52(11%) multiple signals of dysfunction; those exposed to ATV had a higher risk of multiple signals than those unexposed (23% vs 9%, aRR=1.64, CI:1.16-2.31). Stratified by trimester, the data suggested this association was stronger if their mothers initiated ARVs during pregnancy, 95(21%) had single and 52(11%) multiple signals of dysfunction; those exposed to ATV had a higher risk of multiple signals than those unexposed (23% vs 9%, aRR=1.64, CI:1.16-2.31).
Conclusions: In-utero exposure to atazanavir-containing regimens was associated with higher risk of co-occurrence of neurodevelopmental dysfunction in behavior, cognition and/or language domains, in preschool HEU children whose mothers initiated ARVs during pregnancy.

This abstract was withdrawn.

Periconceptional Antiretroviral Exposure and Central Nervous System (CNS) and Neural Tube Birth Defects – Data from Antiretroviral Pregnancy Registry (APR)

Background: Preliminary data from Tsepamo Botswana birth defects surveillance study identified potential neural tube defect (NTD) teratogenic signal in infants born to HIV-infected women receiving dolutegravir (DTG)-based antiretroviral therapy (ART) during the periconceptional period (before conception and into first trimester), compared with periconceptional non-DTG ART or women without HIV (0.67%, 0.12%, and 0.09%, respectively) (Jul2018 IAS Conference). This analysis aims to 1) describe CNS defect cases reported to APR, a voluntary, international, prospective exposure registry and 2) determine any increased risk by ART drug class.

Methods: Data on prospectively enrolled pregnancies (January 1989 through July 2018) with birth outcome are summarized. Birth defects are reviewed by a dysmorphologist, coded by modified Metropolitan Atlanta Congenital Defects Program criteria, classified by organ system and assigned exposure timing for each antiretroviral. CNS defects include NTD (myelomeningocele/spina bifida, anencephaly) and encephalocele which is reported separately from NTD.

Results: 20,064 prospectively reported pregnancies resulted in 20,413 fetal outcomes including 19,005 live births. Reported pregnancies are from North America (75%), Europe (8%), Africa (7%), South America (6%) and Asia (4%). Of the 19,005 live births with any ART exposure, 8,040 had periconceptional exposure, including 222 birth defect cases and 20 CNS defects (2 NTD and no encephalocele). Both the NTDs reported exposure to NRTI and NtRTI; one with additional exposure to PI and the other to NNRTI.

Conclusions: Twenty CNS defects (2 NTD) were observed among 8,040 birth outcomes with periconceptional ART exposure. Overall and drug class frequencies are consistent with observed low NTD prevalence (0.01%-0.1%) in developed countries where food folic acid fortification and antenatal folic acid supplementation are prevalent, reducing overall NTD occurrence. However, the number of pregnancies enrolled in the APR with exposure to newer drug classes such as integrase inhibitors (InSTIs) are insufficient to rule out or confirm any potential association with NTD. Healthcare providers are encouraged to continue to report pregnancies with periconceptional antiretroviral exposures to the APR, especially those involving newer antiretrovirals.
Effects of dolutegravir and other integrase inhibitors on folate transport pathways

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**Background:** Preliminary analysis of an ongoing birth surveillance study identified evidence of a potential increased risk for neural-tube defects (NTDs) in newborns associated with exposure to dolutegravir at the time of conception. Folate deficiency is a common cause of NTDs. HIV integrase inhibitors were evaluated for inhibition of folate transport pathways: proton-coupled folate transporter (PCFT), reduced folate carrier (RFC), and folate receptor α (FRα) -mediated endocytosis.

**Methods:** Madin-Darby Canine Kidney-II cell monolayers were transfected to express PCFT, RFC, FRα, or vector control. Transport activity was determined by subtraction of cellular uptake of folic acid (PCFT and FRα) or reduced form of folate (RFC) in vector control cells from PCFT, RFC, or FRα overexpressing cells. In vitro transport inhibition was extrapolated to clinic using established approaches for intestinal absorption (PCFT only), as well as distribution and renal sparing by PCFT, RFC, and FRα (2017 FDA in vitro DDI Draft Guidance). Inhibitor concentration 50 (IC50s) are reported where ≥50% inhibition was achieved; otherwise greatest extent of inhibition >25% is reported on the basis that 25-30% reduction in blood folate doubles the risk of NTDs, and pharmacokinetically, >25% cumulative inhibition of folate absorption, distribution, and renal tubular reabsorption (sparing) would decrease fetal folate levels >2-fold.

**Results:** The positive control methotrexate demonstrated clinically-relevant inhibition of PCFT, RFC, and FRα in folate absorption, distribution, and renal sparing. Likewise, the intravenous antifolate, pemetrexed, was flagged as a clinical inhibitor of RFC and FRα folate distribution and renal sparing. Valproic acid was used as a negative control that elicits folate-independent NTDs; >25% inhibition of PCFT, RFC, and FRα was not observed. FRα-mediated folate endocytosis was inhibited in vitro by dolutegravir, cabotegravir, and bictegravir (IC36 = 37.0 μM, IC37 = 25.8 μM, IC50 = 268 μM, respectively); no inhibition was observed by raltegravir and elvitegravir. PCFT folate transport was inhibited in vitro by bictegravir, raltegravir, and elvitegravir (IC50 = 370 μM, IC32 = 564 μM, IC28 = 30 μM, respectively); dolutegravir and cabotegravir did not inhibit PCFT in vitro. All five integrase inhibitors tested did not inhibit RFC in vitro. At clinical exposures, dolutegravir and cabotegravir FRα inhibition was not flagged as clinically relevant [dolutegravir: Cmax,u/IC36=1.002 < 1.1 and < 1.02; cabotegravir: Cmax,u/IC37=1.006 < 1.1 and < 1.02 (below thresholds for clinical inhibition of distribution and renal sparing, respectively)]. Bictegravir inhibition of PCFT and FRα did not reach the criteria for clinical relevance [PCFT Igut/IC50=0.6 < 10; Cmax,u/IC50=1.004 < 1.1 and < 1.02 (below thresholds for clinical inhibition of absorption, distribution, and renal sparing, respectively); FRα Cmax,u/IC50=1.0005 < 1.1 and < 1.02 (below thresholds for clinical inhibition of distribution and renal sparing, respectively)]. Elvitegravir inhibition of PCFT was not extrapolated to be clinically relevant [lgut/IC28=0.02 < 10; Cmax,u/IC28=1.002 < 1.1 and < 1.02 (below thresholds for clinical inhibition of absorption, distribution, and renal sparing, respectively)]. Only raltegravir at the highest 1.2g dose was flagged as a potential clinical inhibitor of PCFT in intestinal folate absorption [lgut/IC32=17.6 > 10 (above threshold for clinical inhibition of absorption); Cmax,u/IC32=1.007 < 1.1 and < 1.02 (below thresholds for distribution and renal sparing, respectively)].

**Conclusions:** These studies do not support dolutegravir as a clinically-relevant inhibitor of folate transport pathways. Dolutegravir is not predicted to elicit clinical decreases in maternal and fetal folate levels. Clinically-relevant integrase inhibitor class effect on folate transport pathways was not observed.
HIV Drug Resistance at Mother-to-Child Transmission and Emergence During Breastfeeding

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Background: Mother-to-child transmission (MTCT) of HIV has decreased with increased coverage of antiretroviral treatment (ART). Conversely, pre-treatment HIV drug resistance (DR) to 1st-line non-nucleoside reverse transcriptase inhibitors (NNRTI) is increasing in low-resource communities due to transmitted/selected drug resistance mutations (DRM) and, in women, from treatment to prevent MTCT. However, whether HIV drug resistance in mothers increases the risk of MTCT or resistance in the infant has not been well-studied. We examined risks of maternal DR on MTCT in a case-control study, and infants' acquisition of DR during breastfeeding (BF) in the PROMISE 1077BF trial.

Methods: 85 HIV-infected infants and their transmitting mothers were compared to 254 HIV-infected, non-transmitting control mothers. MTCT was categorized by time of infants' diagnosis: in utero (IU) at ≤2 weeks or during BF at >2 weeks of age. Controls for each MTCT category were matched for date of delivery and site. Plasma from infant’s date of HIV diagnosis, ART initiation, and last study visit, and mother’s plasma with ≥40c/mL from the nearest date proximate to transmission (controls’ plasma matched to time of case mothers’ specimens) were genotyped by consensus sequencing of HIV pol. Infants and mothers were categorized as wild-type (WT) or DR based on major DRM defined by the Stanford Database. Maternal viral loads (VL) and DR rates were compared using Mann-Whitney and Fisher’s Exact tests. Adjusted analyses used conditional logistic regression.

Results: Proximate to infant diagnosis, case mothers had higher median VL vs. controls (4.28 vs. 3.86 log10 c/mL, p<0.0001). DR was significantly higher in transmitting vs. control mothers (15.8% vs. 7.6%, p=0.048). DR was more prevalent in mothers who transmitted via BF compared to IU (29.7% vs. 4.4%; p=0.002). In a multivariate analysis of genotype, adjusting for VL and antepartum treatment, DR was associated with increased risk of MTCT (OR (95% CI (1.03-5.81)): 2.45, p=0.042).

Of 75 infants genotyped, 5/40 (12.5%) with IU vs. 19/35 (54.3%) with BF transmission had DRM at diagnosis (p<0.001). Of the 24 DR infants, 58.3% had 1 NNRTI DRM, 25% had ≥2 NNRTI DRM, 12.5% had 1 NRTI DRM, and 4.2% had dual-class DRM. Among 72 mother-infant pairs genotyped at infant diagnosis, 46 (64%) were concordant for WT, 7 (9.7%) concordant for DR and 19 (26.3%) were discordant (17/19 pairs were WT mothers with DR infants). Among infants with genotypes available at the last study visit, DRM were detected in an additional 9 and 2 infants with IU and BF MTCT for totals of 12/24 (50%) and 17/23 (73.9%), respectively. Of the 22 infants with genotypic data for all three time points, 18 (81.8%) had DR and 14/18 (77.8%) had DRMs detected prior to ART initiation.

Summary/Conclusions: Maternal DR at infant diagnosis was associated with MTCT during breastfeeding but not with in utero/peripartum transmission. After adjusting for HIV RNA load, DR was significantly associated with increased risk of MTCT. Non-suppression of VL – due to poor drug adherence while breastfeeding – may explain the higher VL and DR in transmitting mothers, thus additional analyses to further investigate the role of HIV DR on MTCT are underway. DR was less prevalent in infants diagnosed with IU vs. BF MTCT, but DR emerged over time. This increase in DR in infants provides a rationale for trials examining alternative regimens with a...
greater barrier to resistance for infant prophylaxis and ART.

Lower birth weight-for-age and length-for-age z-scores in infants with in utero HIV and ARV exposure: a prospective study in Cape Town, South Africa

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Background: Prevention of mother-to-child HIV transmission (PMTCT) programme success has given rise to over 1 million infants born HIV-exposed uninfected (HEU). In recent years a large proportion of HEU infants have also been exposed to antiretroviral therapy (ART) in utero. Although the benefits of PMTCT clearly outweigh the known risks to HEU infants, some studies have reported associations between in utero ART exposure and adverse birth outcomes including impaired fetal growth.

Methods: We compared birth anthropometrics of HEU and HIV unexposed uninfected (HUU) in an observational study in Cape Town, South Africa (B Positive study). All women had gestational age assessed by ultrasound at enrolment and at delivery. All women living with HIV (WLHIV) were enrolled antenatally on ART (tenofovir-emtricitabine-efavirenz) either from conception or initiated during pregnancy. Birth weights and lengths were converted to weight-for-age (WAZ) and length-for-age (LAZ) scores using Intergrowth-21st software, adjusting for infant sex and gestational age at birth. Linear regression was used to compare mean z-scores adjusting for maternal and pregnancy characteristics.

Results: Among 565 mother-infant pairs, 274 infants (49%) were HIV and ART exposed with a median duration of fetal ART exposure of 37 weeks (Interquartile Range (IQR) 26-39), the remaining 51% were born to women without HIV. WLHIV were older [32 years; IQR 27-35] than HIV uninfected women [27 years; IQR 23-33(p<0.001)] and a higher proportion were formally employed (39% vs 30%; p <0.001). The groups were similar with respect to maternal education, marital status and gestational age at delivery. In univariable linear regression analysis, WAZ was lower among HEU infants compared to HUU infants [β = -0.17(95% Confidence Interval (CI): -0.34, -0.001), p-value=0.05]. After adjusting for marital and employment status, HEU infant WAZ at birth remained significantly lower [adjusted β -0.17 (95%CI: -0.35, -0.002), p-value=0.04]. Similar differences were noted for the LAZ comparison with univariable linear regression analysis [β -0.27 (95%CI: -0.55, +0.10), p-value=0.06] and multivariable analysis [β -0.27 (95%CI: -0.56, +0.01), p-value=0.06] after adjusting for the same variables. Infants exposed to HIV and ART from conception had lower WAZ and LAZ compared to those whose mother’s initiated ART later in pregnancy [β -0.12; 95% CI -0.37, 0.13; p = 0.34] and [β -0.28; 95% CI -0.69, 0.12; p = 0.17] respectively. However, the difference was not statistically significant.

Conclusion: In an era when WLHIV are accessing ART prior to conception and in pregnancy, HEU infants present with poorer WAZ at birth compared to infants born to women without HIV. Studies designed to identify the mechanisms and clinical significance of these growth disparities, and to establish the safest ARVs for use in pregnancy are urgently needed.
High uptake and completion of HIV self-testing using a novel community-based delivery strategy for young people in Kenya

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Background: HIV self-testing (HIVST) is a flexible and confidential complement to facility-based testing that may improve testing uptake and engagement in care and prevention among adolescents and young adults (AYA). Kenya is among the first African countries to offer HIVST, however optimal implementation strategies for AYA are unclear. We present preliminary results from an ongoing study evaluating three community-based HIVST delivery channels that target AYA that will inform national scale-up.

Methods: In this cohort study, trained peer mobilizer/HIV test counselor teams recruit AYA through home-based testing (HBT), ‘hot spots’ (nightclubs/bars), or pharmacies. Eligible AYA are ages 15-24 years, report negative or unknown HIV status, and reside in a large informal settlement in Nairobi. Teams administer an enrollment survey, then offer OraQuick HIVST kits and optional assistance and post-test counseling according to national guidelines. Participants self-report test results by phone, text message, or in person. All participants who test reactive are offered confirmatory rapid testing by the study team and, if positive, support linking to care. Enrollment, Month 1 and 4 follow-up surveys assess sociodemographic and risk characteristics, HIVST experiences, willingness to pay, and linkage to care or retesting. The primary outcome is HIVST completion within 30 days by self-report (phone/text, photo) and/or in-person verification of used kits. Secondary outcomes include test acceptance among enrolled, and linkage to care, or retesting, at four months. Test completion by channel is compared using chi-square tests.

Results: Among 313 eligible AYA, 277 (88.5%) enrolled through HBT (44.8%), pharmacies (16.6%), and hot spot (38.6%) channels. Most were ages 18-24 (74.7%), female (64.6%), tested for HIV in the last year (55.2%) and heard of self-testing (53.9%). Among sexually active youth (73.3%), 57.0% reported sex with someone of unknown HIV status in the last 3 months, and 33.6% reported ever using pre-exposure prophylaxis. HIVST acceptance was 100%. Among 251 who completed testing, 91.2% tested within 30 days with median time to test of 3 days (interquartile range: 1-9 days); and, 92% of used kits were returned to study staff to verify results. A significantly higher number of AYA from hotspots (98.0%) completed testing within 30 days (pharmacy, 92.5%, HBT, 84.5%, p<0.01). Most AYA (89.7%) tested without assistance and 49.6% opted for post-test counseling. Of 16 reactive results, only 1 was confirmed positive and linked to care. Most said HIVST was ‘very easy’ to complete, especially older AYA (18-24, 86.3% vs. 15-17, 70.0%); 78.2% would use HIVST again; and >90% would recommend HIVST to a friend or sexual partner. Most (56.8%) would pay $1-15 USD for a self-test especially through pharmacies (68.1%), internet (63.2%), and vending machines (58.8%).

Conclusion: Peer/provider led community-based HIVST distribution is a highly acceptable and efficient strategy to reach a diverse population of AYA at risk of HIV with potential to increase engagement in HIV prevention in high-burden settings.
Describing the characteristics and long-term outcomes of adolescents living with perinatally acquired HIV in the IeDEA-Southern Africa Collaboration: 2004-2017

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Background: There is an emerging population of adolescents living with perinatally acquired HIV (ALPH) who have several unique characteristics resulting from their long-term exposure to HIV and chronic use of antiretroviral drugs. We describe the characteristics and long-term outcomes of ALPH within IeDEA-Southern Africa (IeDEA-SA).

Methods: We analysed routinely collected data from 16 IeDEA-SA sites (2004–2017) of patients entering HIV care aged <13 years without documented non-perinatal HIV acquisition, and who had ≥1 HIV care visits after age 10 years (entry into adolescence). Patient characteristics are described at enrolment into HIV care, initiation of antiretroviral therapy (ART) and during adolescence. Using competing risks analysis, we estimated the outcomes: mortality, loss to follow-up (LTFU: no visit in the 12 months before cohort database closure) and documented transfers. We used Cox Proportional Hazards regression to determine predictors of mortality in the years following their 13th birthday.

Results: Of 25,401 ALPH included, 51% were female. At enrolment, median (interquartile range [IQR]) age was 8.8 (5.9–10.9) years, with 51.8% (95% confidence interval [CI] 51.1–52.6) severely immunosuppressed (WHO 2007 criteria), 42.7% (41.6–43.7) underweight (weight-for-age z-score < -2) and 50.6% (49.3–51.8) stunted (height-for-age z-score (HAZ) < -2). At ART start, median (IQR) CD4 cell count, CD4% (initiating aged<5 years) and CD4 count (initiating aged≥5 years) were 284 (135–469) cells/µL, respectively. Median (IQR) duration of follow-up from ART initiation was 6.0 (3.0–8.6) years.

Over the study period 681 (2.7%) ALPH died, 4007 (15.8%) transferred care and 5497 (21.6%) were LTFU. Overall retention was 59.9%. At the end of follow-up, 7232 (28.5%) of patients were aged 15–19 years while 1175 (4.6%) were aged ≥20 years. Comparing values at the ages of 13 vs. 18 years, the median (IQR) CD4 cell count was 601 (378–848) vs. 488 (296–680) cells/µL, HAZ -2.07 (-2.90–-1.21) vs. -1.48 (-2.29–-0.77), body mass index 16.8 (15.5–18.4) vs. 19.8 (18.0–22.0) kg/m², and proportion (95% CI) with HIV-RNA viral load <400 copies/mL at facilities offering routine annual viral load monitoring was 73% (71.5–74.0) vs. 67% (64.5–70.2), respectively. At 8 years after entry into adolescence, cumulative incidence (95% CI) of mortality, transfers and LTFU for patients who enrolled aged <10 years were 2.4% (2.1–2.8), 26.3% (25.4–27.3) and 25.1% (24.2–26.0) 8 years, respectively. Characteristics at age 13 years associated with mortality were: duration on ART by age 13 (adjusted hazards ratio per year increase [aHR] 0.85 [95%CI 0.79 – 0.93]), being in care at a tertiary care facility (vs. primary care; aHR 1.46 (1.06 – 2.00), being stunted (HAZ < -2 vs. ≥ -2; aHR 1.50 (1.07 – 2.10), being immunosuppressed (CD4 count <350: aHR 4.50 (3.12 – 6.50), CD4 count 350–500: aHR 1.81 (1.12 – 2.95) vs. CD4 >500) and calendar year of 13th birthday (aHR per year increase 0.92 [0.87 – 0.97]).
Conclusions: Children with perinatally acquired HIV have suboptimal retention, viral suppression and survival during adolescence. Those immunosuppressed, stunted or in care at tertiary care facilities during adolescence were the most vulnerable to poor outcomes and could benefit from closer follow-up to optimize treatment success.

Growth and immunodeficiency of ART-treated adolescents living with perinatally acquired HIV: a Collaborative Initiative for Paediatric HIV Education and Research (CIPHER) Cohort Collaboration Analysis.

Background: Adolescents living with perinatally-acquired HIV (APH) represent a growing population worldwide with specific HIV healthcare needs. APH are dealing with severe morbidities, such as growth retardation and immunodeficiency, which need to be well characterized in order to be managed appropriately. Our objective was to describe the growth and immune evolution of APH across adolescence.

Materials & Methods: Through the CIPHER Cohort Collaboration, data collected between 1994 and 2015 from 11 networks in North and South America, Europe, Asia and sub-Saharan Africa were pooled. All adolescents with known perinatally acquired HIV or who entered into care before age 10 years, initiated on ART before age 10, and with at least one available height and CD4 measurement while aged 10 to 19 were included.

Growth was defined using Height-for-Age Z-scores (HAZ) according to the WHO Child Growth Standards. Growth and CD4 evolution between age 10 (baseline) and 19 and their correlates were studied using linear mixed-effects models. Growth models were conducted separately for males and females, including fractional polynomials to model non-linear relationships for time (current age from 10 to 19), age at ART initiation and HAZ at baseline.

Results: Overall, 20,939 APH were included in the growth analysis and 19,557 in the CD4 analysis: 50% were female, 73% were living in sub-Saharan Africa and 11% in Europe. Median age at ART initiation was 6.9 years (Interquartile Range 4.4-8.5). Prevalence of stunting (HAZ<-2 Standard Deviations [SD]) was 48% at ART initiation and 34% at baseline; 33% were severely immunodeficient (CD4% <15 if aged less than 5 or CD4 <350 if older) at ART initiation and 10% at baseline.

Growth evolved differently by sex and region, with higher HAZ for females (mean [SD] at age 15: -1.08 [1.20] vs -1.62 [1.42] for males) and adolescents living in North America and Europe (mean [SD] at age 15: -0.56 [1.14] vs -1.80 [1.28] in sub-Saharan Africa). Adolescents stunted at baseline and those with late ART initiation (after age 5) had larger HAZ gains, but at age 19, neither of these groups achieved the median HAZ level of adolescents without baseline stunting and with early treatment. Overall mean (SD) CD4 count fell from 769 (402) to 588 (338) cells/mm3 between age 10 and 19, and were similar by sex and region. Those with CD4<350 at baseline had substantial initial CD4 count gains, but by age 19 did not reach levels comparable to those with CD4>350 at baseline.

Conclusions: Growth patterns of APH worldwide substantially differed by sex and region, with higher HAZ for females (mean [SD] at age 15: -1.08 [1.20] vs -1.62 [1.42] for males) and adolescents living in North America and Europe (mean [SD] at age 15: -0.56 [1.14] vs -1.80 [1.28] in sub-Saharan Africa). Adolescents stunted at baseline and those with late ART initiation (after age 5) had larger HAZ gains, but at age 19, neither of these groups achieved the median HAZ level of adolescents without baseline stunting and with early treatment. Overall mean (SD) CD4 count fell from 769 (402) to 588 (338) cells/mm3 between age 10 and 19, and were similar by sex and region. Those with CD4<350 at baseline had substantial initial CD4 count gains, but by age 19 did not reach levels comparable to those with CD4>350 at baseline.

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region, with age at ART initiation, severity of stunting and immunodeficiency having strong effects on growth evolution across adolescence. Higher HAZ in high-income regions may be explained by better access to care and low malnutrition risk. CD4 patterns did not appear to be region-specific. Late ART initiation for children with perinatally acquired HIV can lead to high prevalence of stunting and immunodeficiency. Interventions to promote adolescent catch-up growth and immune recovery are needed to avoid them becoming irreversible by the time APH reach adulthood.

19

Hospitalization in Perinatally HIV-infected adolescents on Antiretroviral Therapy in South Africa: a prospective study.

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Background: Little is known about hospitalization in perinatally HIV-infected (PHIV+) African adolescents that started antiretroviral therapy (ART) relatively early. We examined the incidence and causes of hospitalization in participants enrolled in the Cape Town Adolescent Antiretroviral Cohort (CTAAC).

Methods: PHIV+ children and adolescents who were clinically stable on ART for at least 6 months, aged 9-14 years and attending one of 7 public sector ART services and HIV- negative (HIV-) age-matched children and adolescents were enrolled in CTAAC. Data collected from July 2013 through October 2018 were analyzed. Descriptive statistics and time to event analysis were used to describe causes and incidence of hospitalizations. Hospitalization events were obtained from a provincial database.

Results: Overall, median age at enrollment was 12.0 years (IQR:10.6-13.3). Five-hundred and fifteen PHIV+ and 109 HIV- participants had a median follow up of 4.4 years (IQR:4.0-4.7). At enrolment PHIV+ had a median duration of ART of 7.6 years (IQR:4.6-9.2) and >75% had a viral load <50 copies/ml. The crude incidence of any hospitalization event was 6.5 (95%CI: 5.6-7.7) and 2.2 (95%CI:1.2-4.0) events per 100- person years, p=<0.01 in PHIV+ and HIV- adolescents respectively. The cumulative incidence of hospitalization over the study period was 27.4% (95%CI: 23.7- 31.6) and 9.1% (95%CI: 5.0-16.3), p=<0.01 in HIV+ and HIV- participants. One hundred and forty-nine hospitalization events were experienced by 91 HIV+ participants. Age, sex, body mass index and CD4 count at study enrolment and age at ART initiation did not differ between PHIV+ participants that were hospitalized versus those that were not (12.2 years vs 11.9 years, p=0.11; 49.5% vs 51.4% females, p=0.73; 17.6 kg/m2 vs 17.0 kg/m2, p=0.23; 666 cells/mm3 vs 731 cells/mm3, p=0.12; 4.2 years vs 4.4 years, p=0.89) however, the number of participants with a viral load <50 copies/ml was lower in those that were hospitalized versus those that were not (60 (65.9%) vs 333 (78.7%),p=0.01)

Median duration of hospitalization was 2 days (IQR: 1-6) and maximum duration was 116 days; there was one death. In HIV+ participants, 80/149 (53.7%) of admissions were non-infectious, 61/149 (40.9%) were due to infectious causes and 8/149 (5.4%) had no diagnosis documented. Non-infectious causes included hearing loss and ear related admissions (17/80, 21.3%), seizures (7/80, 8.8%), psychiatric diagnoses (4/80, 5.0%), malignancies (2/80, 2.5%) and pregnancy (2/80, 2.5%). Infectious causes included pulmonary tuberculosis (PTB) (16/61, 26.2%), pneumonia (not PTB) (6/619.8 1%) and abscesses (4/61, 6.6%). There was no difference in causes of hospital admissions in those PHIV+ adolescents who maintained viral suppression during follow up time and those that did not.

Conclusions: PHIV+ adolescents on ART have a high incidence of hospitalization. Strategies to address infectious and non- infectious morbidity must be strengthened. Further research on causes of hospital admissions in this unique population is needed especially as
they begin to engage in adult lifestyle risk factors.

20

The Next Generation: Pregnancy outcomes in adolescents and women living with perinatally acquired HIV in South Africa

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Background: Paediatric antiretroviral treatment (ART) programmes have improved life-expectancy in children living with perinatally acquired HIV. An increasing number of girls living with HIV are entering adolescence and adulthood and having pregnancies. Adolescents living with perinatally acquired HIV (ALPHIV) who become pregnant may have HIV-associated infections or complications, long-term exposure to ART, resistance mutations and increased psychosocial challenges, which may adversely affect pregnancy outcomes. There is a lack of published data on the outcomes of pregnancies in ALPHIV in sub-Saharan Africa. We describe the characteristics of pregnant ALPHIV in South Africa, as well as pregnancy and neonatal outcomes.

Materials & Methods: We retrospectively identified pregnancies in ALPHIV who were diagnosed HIV-infected before age 12 and before the index pregnancy (as a proxy for perinatal route of infection) from routinely collected data in the Western Cape province of South Africa between 2007 and 2018 and combined these with pregnancies from known ALPHIV from a cohort in Johannesburg, South Africa. Characteristics of pregnant ALPHIV, laboratory results (CD4 counts and viral loads (VL)), pregnancy and neonatal outcomes were examined.

Results: We identified 258 pregnancies in 232 females living with likely perinatally acquired HIV; 39% of pregnancies occurred in ALPHIV age ≤16 years, 39% at age 17-19 years and 22% were in adults age >20 years. There has been a steady increase in pregnancies in ALPHIV in recent years; over two thirds occurred in the last 3 years. ART commenced prior to pregnancy in 85% of cases, during pregnancy in 7% and had not been commenced by pregnancy end date in 9% of cases. Among the 89% of pregnancies with documented outcomes (n=229), there were 80% live births, 14% terminations, 3% miscarriages and 2% stillbirths. Mother–to-child transmission of HIV occurred in 2% of neonates, 75% were uninfected when last tested and 23% had unknown HIV status. Among those with CD4 counts available close to pregnancy end date (n=202), 37% had optimal immunologic status (CD4 count ≥500 cells/µl) whereas 20% had CD4 count <200 cells/µl and 43% had CD4 count 200-499 cells/µl. Among those with VL available close to pregnancy end date (n=219), 67% had VL<400 copies/ml, 5% had VL 400-999 copies/ml while 28% had VL≥1000 copies/ml. Among 186 known live births, 20% were preterm deliveries (<37 weeks gestation). Among neonates with known birth weights (n=176), mean birth weight was 2900g (95% CI 2747 – 2935g) and 20% of neonates had low birth weight (<2500g). There was 1 case of congenital malformation (musculoskeletal) and 2 cases of neonatal death.

Conclusion: A high proportion of pregnancies was electively terminated suggesting reasonable access to this service. A large proportion of pregnancies occurred in ALPHIV age ≤16 years, although this may reflect that the bulk of South Africa’s ALPHIV population are in this age category, with relatively fewer having aged into the older age categories. The prevalence of elevated VL and poor immunologic status is concerning. Comparison with pregnancies in women with non-perinatally acquired HIV in resource-limited settings is needed to assess whether the
perinatally infected group is at risk of worse outcomes.

The clinical impact and cost-effectiveness of routine HIV screening and testing at infant immunization visits in Côte d’Ivoire (CI), South Africa (SA), and Zimbabwe (Zim)

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Background: Despite scale-up of PMTCT/EID programs, many infants at risk for HIV infection are not tested, due to factors including loss to follow-up between antenatal care (ANC) and EID visits, missed maternal HIV testing in ANC, and incident maternal infection after testing. Considering high vaccination rates, screening for HIV exposure and testing for HIV infection at immunization visits may increase the number of infants tested and improve survival among children with HIV. We investigated the economic value of such programs.

Materials and Methods: We used the validated Cost-effectiveness of Preventing AIDS Complications (CEPAC)-Pediatric microsimulation model of infant HIV infection, disease progression, diagnosis, and treatment to simulate infants born in 2016 in CI, SA, and Zim. We examined two strategies: EID: Nucleic acid testing (NAT) for infants known to be HIV-exposed and presenting to 6-week EID testing visits; and Screen-and-test: 6-week NAT for infants known to be HIV-exposed, plus rapid diagnostic test (RDT)-based screening of mothers of infants not known to be HIV-exposed at 6-week immunization visits, with referrals to NAT (newly-identified exposed infants) and ART (newly-diagnosed mothers, with reduction in subsequent risk of breastfeeding transmission). Data inputs included maternal HIV prevalence in ANC (CI: 3.5%, SA: 30.8%, Zim: 16.0%), maternal incidence during late pregnancy and breastfeeding (0.7/100PY, 3.0/100PY, 1.3/100PY), HIV testing in ANC (58%, 90%, 76%), PMTCT coverage (80%, 95%, 84%), 6-week EID coverage (41%, 73%, 58%), and 6-week immunization coverage (98%, 78%, 95%); we assumed linkage to infant NAT and maternal ART after positive maternal RDT of 60% (all countries). Risks for opportunistic disease (with potential for diagnosis of previously undiagnosed HIV) and mortality were from published data. Full program costs included $24/infant for NAT, $10/mother for screening, $5-30/month for ART, and $20-180/month for HIV care. Model outcomes included MTCT, life expectancy (LE), lifetime HIV-related costs, and incremental cost-effectiveness ratios (ICERs, from discounted [3%/year] LE and costs). We assumed a willingness-to-pay for health of $500-900/year of life saved (YLS), which reflects the ICERs of 2nd-line compared to 1st-line ART in the three countries. We varied data inputs in sensitivity analyses.

Results: Compared to EID, adding Screen-and-test was projected to reduce absolute postnatal MTCT by 0.7% in CI, 0.2% in SA, and 0.7% in Zim, due to maternal HIV diagnosis and ART initiation. Screen-and-test increased undiscounted LE among infants ever acquiring HIV by 3.7 years (CI), 2.0 years (SA), and 2.4 years (Zim). Gains in undiscounted LE for all infants (including HIV-infected, HIV-exposed/uninfected, and HIV-unexposed infants) were 0.4 months (CI), 0.8 months (SA), and 1.2 months (Zim), with increases in discounted costs/person of $15, $15, and $20. The ICERs of Screen-and-test compared to EID were $1,010/YLS (CI), $500/YLS (SA), and $460/YLS (Zim). Screen-and-test was more cost-effective with lower screening program cost, higher linkage to maternal and infant care after positive RDT, or lower maternal HIV testing in pregnancy (becoming cost-effective in CI with testing rates <40%).
Conclusions: Routine maternal screening at the 6-week immunization visit to determine HIV exposure, followed by NAT to diagnose infection, may address gaps in the PMTCT/EID cascade and the increasing contributions of breastfeeding and maternal acute infection to MTCT. Such screen-and-test programs will likely be of good value in high-prevalence settings with current rates of maternal HIV testing, and they may be of good value in low-prevalence settings if maternal HIV testing rates are low.

Safety and efficacy of E/C/F/TAF in virologically suppressed, HIV-infected children through 96 Weeks


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Background: Elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (EVG/COBI/FTC/TAF; E/C/F/TAF) is a once-daily integrase inhibitor-based single tablet regimen (STR) approved for use in pediatric patients ≥6y and weighing ≥25 kg. Week (W) 48 safety data, reported previously, showed no bone or renal toxicity of E/C/F/TAF in 23 children 6–<12y. We now report long-term safety and efficacy data in the full cohort of children (N=52) 6–<12y, weighing ≥25 kg.

Materials & Methods: This prospective, single-arm, open-label, clinical trial evaluated the pharmacokinetics (PK), safety and efficacy of switching to the adult E/C/F/TAF (150/150/200/10 mg) STR once-daily in virologically suppressed children (6–<12y), weighing ≥25 kg. Adverse events (AEs) and laboratory tests were assessed. Bone mineral density (BMD) was measured by dual-energy X-ray absorptiometry. Intensive and sparse PK data were collected throughout the study (up to Week 48). PK parameters of TAF and TFV were estimated by population PK modeling.

Results: We enrolled 52 children; median age 10 y (range 7–11 y), median weight 31 kg (25.5–58.2 kg), 58% female, 71% Black, median CD4 count 926 cells/μL. All but one participant (98%) maintained HIV-1 RNA <50 c/mL at W48. At the time of the data analysis, all 19 participants who had reached W96 were suppressed (HIV RNA <50 c/mL; Missing=Excluded). There was a transient decline in CD4 count at W2, which returned to near baseline values by W48. No participant had a serious AE or AE leading to study drug discontinuation. Median (Q1, Q3) changes from a baseline of 150.3 mL/min/1.73 m2 in eGFRSchwartz at W24, W48, and W96 were −4.6 (−14.1, 9.4) and 0.2 (−14.3, 14.9), −14.1 (−20.8, 9.6; n=18) mL/min/1.73 m2; which is consistent with inhibition of renal tubular creatinine secretion by COBI, observed in adults. Median % change from baseline in BMD at W48 was +3.7% for spine and +4.2% for total body less head (TBLH). At W48, median change from baseline in BMD height-age (HA) adjusted Z-score was -0.12 for spine and -0.08 for TBLH. Median % change from baseline in BMD at W96 was +7.1% for spine and +4.9% for total body less head (TBLH). At W96, median change from baseline in BMD height-age (HA) adjusted Z-score was -0.14 for spine and – 0.35 for TBLH. Mean (CV%) steady-state exposures of TAF (AUCtau: 544.8 [12.5%] h*ng/mL; N=44) and TFV were (AUCtau: 420.5 [19.5%] h*ng/mL; N=52) were within the range of exposures observed in adults.

Conclusion: In HIV-infected children weighing ≥25 kg, E/C/F/TAF was well tolerated and safe as reflected by sustained virologic suppression with persistent favorable safety profile out to W96 and PK exposures within the range of those seen in adults. The long-term safety and efficacy of E/C/F/TAF in children weighing ≥25 kg demonstrates the benefit of this regimen and continued development of E/C/F/TAF in children <25 kg.
Neurodevelopmental outcome at 11 months in perinatally HIV-infected infants: does starting very early antiretroviral therapy help?

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Background: Early initiation of antiretroviral therapy (ART) improves clinical and neurodevelopmental outcomes. The effects of initiating ART before 7 weeks of age in HIV+ infants on neurodevelopment has not been studied. We assessed the early neurodevelopmental outcomes in an HIV+ infant cohort initiating ART within the first few weeks of life.

Materials and Methods: Study participants were enrolled from the public sector birth HIV-diagnosis program in Cape Town, South Africa. Inclusion criteria were birth weight >2000g, ART initiated <6 weeks of age and no cytomegalovirus infection. ART included zidovudine, lamivudine and nevirapine for the first 2 weeks, with nevirapine replaced by lopinavir/ritonavir thereafter. Once body weight >3kg and post-conception age >44 weeks, abacavir replaced zidovudine. Participants were seen as frequently as needed until stable, monthly for 3 months and then 3-monthly. Visits included a medical examination, growth monitoring, adherence support, adverse event assessment, and social work support where needed. HIV viral loads (VL) were measured at baseline, 3, 6 and 12 months of age.

The Griffiths Mental Development Scales (GMDS) were administered between 10 and 12 months of age. Locomotor, Personal-Social, Hearing and Language, Eye and hand Co-ordination, and Performance (visual-motor abilities) scales were assessed. A global General Griffiths Score was also calculated. Correlations between clinical parameters and neurodevelopmental outcomes were assessed with Spearman and Pearson coefficients. GMDS scores at a similar age were compared with participants from the Children with HIV Early Antiretroviral (CHER) trial commencing ART at a median of 7.7 weeks, using Mann-Whitney U tests.

Results: Of the 29 infants (23 females) assessed, 26 (90%) had WHO stage I HIV disease. Median [IQR] birth weight was 2915 [2600;3325]g. Nineteen mothers (66%) had received PMTCT. Twenty-one (72%) infants were diagnosed HIV+ before 7 days of age. Median [IQR] baseline VL was 3904 [259;16922] copies/ml, ART initiation was 6.0 [3;10] days (range 0-21) and time to VL suppression was 19.1 [15;36] weeks. Median [IQR] CD4 at GMDS was 34 [28;39]% and absolute count 2055 [1497;2489]. Nine (31%) participants had detectable VL at the GMDS assessment, performed at a median [IQR] age of 11.5 [10.8;12] months. Mean GMDS quotients were within the average range: Global Griffiths quotient was 103.6±10.9 and mean quotients on the subscales ranged from lowest 95.9±13.4 for Locomotor to highest 112.8±11.3 for Hearing-and-Language. There were no significant correlations between GMDS scores and birth weight, gestation, maternal age, baseline VL, age starting ART, time to VL suppression and CD4 parameters at baseline. GMDS quotients were similar to those from the CHER cohort, where ART was started later at a median of 7.7 weeks of age, apart from personal-social subscale where the CHER cohort scored higher.

Conclusions: Neurodevelopmental assessment suggests a possible window for ART initiation (from birth to age 7 weeks) that may enable to achievement of normal milestones by 11 months of age. Good supportive care and ART adherence are essential. Further investigations on a larger sample will evaluate in utero infection, size of the latent HIV reservoir, social and demographic factors on neurodevelopmental outcomes.
T cell senescence and exhaustion in perinatally HIV infected children (PHIC)

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Background: As successful antiretroviral therapy (ART) allows a larger number of HIV-infected children to reach adulthood, issues such as early immune senescence and exhaustion arise, similar to what is seen in HIV-infected adults. We aimed at evaluating whether time of ART initiation modified patterns of immune activation and senescence in children who acquired HIV infection from their mothers.

Materials & Methods: Cross-sectional, exploratory study that enrolled PHIC in two sites in Sao Paulo, Brazil. We obtained data from the patients’ charts and collected blood for peripheral blood mononuclear cells (PBMC) separation and storage. Eligibility criteria included age < 18 years, ART for at least 6 months and viral load < 50 RNA copies/mL in the last 6 months. We stratified the participants according to age when ART started: < 6 months, ≥ 6 months <1 year, ≥1 year <5 years or >5 years. CD4+ and CD8+ T cells with known markers for senescence (CD57+), anergy (CD28-), apoptosis (CD95+), activation (CD38+, CCR5+, HLA-DR+) and exhaustion (PD-1+) were analyzed by flow cytometry. We used Kruskal-Wallis test for group comparison and when a statistically significant difference was found, we used two-tailed Mann-Whitney test to further compare groups. We examined the correlation between two continuous variables using Pearson or Spearman tests.

Results: From April 2016 to June 2017 a total of 56 children were included, of which 55 fulfilled eligibility criteria. PBMC was available for 43.

At study inclusion children’s median age was 12 years old, median time on ART was 9 years, and their VL was <50 RNA copies/mL for a median of previous 5 years. Median CD4+ T cell counts were 1010 cells/mm3 (p25=746; p75=1275), median of 36,7% (p25=32,0; p75=39,9) and mean CD4+/CD8+ radio was 1.6 (IC 95% 1,3–1,8). Earlier age at ART initiation was negatively correlated with higher absolute and % CD4+ T cells at inclusion, higher total and % nadir CD4+ T cells, and higher CD4+/CD8+ ratio. When looking at children stratified by age at ART initiation, children starting ART <6m had higher total CD4+ cells at inclusion and nadir, and higher CD4+/CD8+ ratio when compared to children starting ART 1-5 years and >5 years. There was positive correlation of age at ART initiation and apoptosis, senescence and exhaustion markers in various subsets of CD4+ and CD8+ T cells, including in cells recently emigrated from the thymus (CD31+). Similarly, children starting ART <6m presented, at study inclusion, lower frequencies of subsets of CD4+ and CD8+ T cells expressing markers related to activation, apoptosis, exhaustion, anergy and senescence. This decreased inflammation profile suggest preservation of the immune system in the context of earlier ART initiation, supporting the preservation of CD4+ T cell pool with earlier initiation of ART.

Conclusions: In this group of HIV infected children successfully on ART, study results suggested significant benefits of early ART initiation in preserving total CD4+ T cells counts and maturation, including when started before 6 months of age.
Chronic maternal depression symptomatology predicts executive behavioral problems in HIV affected children in Uganda

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Background: Parents are often informants of young child behavior and development. However, maternal mental health and depression in particular, may influence how they report on their child’s behavior. Limited research has focused on these influences in Sub-Saharan countries, where pediatric HIV concentrates and impacts child neurodevelopment and maternal mental health.

Materials and Methods: This study examines how latent class trajectories of depression symptoms among mothers living with HIV were associated with behavioral and developmental outcomes in their young children (2-5 years old) in Uganda. Depression was assessed at four time points over the period of two years using the Hopkins Symptom Checklist among 288 women participating in a randomized controlled trial assessing a parenting intervention. Children were evaluated at the same time points (intake, 6, 12, and 24 months) with the Mullen Scales of Early Learning (MSEL-observed developmental assessment) and the Behavior Rating Inventory of Executive Functioning (BRIEF-parent reported behavioral assessment). Mixture modeling with semi-parametric group-based modeling strategy was used to identify groups of women with distinct depression symptoms trajectories over time. The associations between maternal trajectory of depression over 24 months with child behavioral and developmental outcomes at 24 months were evaluated using general linear models adjusting for child’s characteristics including demographics, HIV status, interventions received, and intake BRIEF and MSEL scores.

Results: At intake, children were on average 3 years of age (range: 1.8-4.9), 51% males (n=148), 32% HIV+ (n=92), and 68% HEU (n=196). On average, women were 33 years (range: 18-54), mostly married (69% (n=199), and the biological mother of the child 98% (n=281). Three classes of depression varying in severity and stability were identified: stable-low (53% of women), moderate-sub-clinical (39%), and chronic-high (8%). Compared to the low and moderate-subclinical symptom classes, children of women in the chronic-high depression class had more executive behavioral problems as reflected by three BRIEF indices: Global Executive Component—BRIEF global score, p=0.05; Inhibitory Self-Control Index, p=0.04; Flexibility Index, p=0.02) at 24 months. Although not reaching statistical significance for between depression group differences, the MSEL sub-scales and global cognitive score had a U-shaped relationship with depression group: children of mothers with moderate-subclinical depression symptoms had the lowest MSEL scores compared to mothers with low or chronic-high depression groups.

Conclusions: Executive functioning behaviors appear to worsen over time among HIV-affected children of women with high chronic depression symptomatology, even after accounting for the child’s initial scores that reflect potential parent reporting bias. Neurodevelopment does not seem to be related to maternal depression trajectory over 2 years. The impact of chronic maternal depression symptoms on child executive behavior over and above that of demographic characteristics and child HIV status suggests the importance of developing and funding services to address behavioral needs of affected children.

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Introduction: Data on age-specific trends in advanced HIV disease at antiretroviral therapy (ART) initiation are limited. We examined age and site-specific trends in advanced HIV disease among HIV-infected children initiating ART between 2003-2017 at seven Baylor International Pediatric AIDS Initiative clinics in six Eastern and Southern African countries. We also examined trends in time-to-ART-initiation.

Methods: We retrospectively analyzed records of ART-naïve HIV-infected children aged <15 years who initiated ART. Advanced HIV disease was defined as having WHO clinical disease stage III or IV and/or severe immune suppression for age according to WHO criteria, and time-to-ART-initiation was measured from the date of entry into care. We analyzed age(<2 years, 2-4 years, 5-9 years and 10-14 years) and site-specific trends in the proportion of children initiating ART with advanced disease over seven calendar periods (from 2003 to 2017) using Cochran-Armitage test-for-trend. Trends in time-to-ART initiation and median age were analyzed using Cuzick’s test-for-trend. Median age and proportion with advanced disease were analyzed over ART initiation periods; time-to-ART-initiation was analyzed over periods of entry into care.

Results: A total of 20,605 children (31.6% aged <2 years, 20.2% 2-4 years, 26.6% 5-9 years and 21.6% 10-14 years) were included. Half were girls, 33% were from Uganda, 19.8% from Malawi, 13.9% from Lesotho, 13.3% from Tanzania, 10.8% from Eswatini and 9.2% from Botswana. Between 2003-2017, the proportion of children initiating ART with advanced disease declined among ages 5-9 years (58.3% to 39.9%; p<0.01) and 10-14 years (61.9% to 38.1%; p<0.01), remained the same for ages <2 years (72.7% to 70.6%; p=0.1), and increased slightly for ages 2-4 years (59.4% to 62.3%; p<0.01). By site, the proportion decreased in Eswatini (69% to 33%), Lesotho (80% to 34%), Malawi (94% to 33%), and Tanzania (71% to 69%) (all p<0.01), remained the same in Botswana (70% to 52%, p=0.06) and increased in Uganda (46% to 65%; p<0.01). The trend in median age at ART initiation varied across sites. In Uganda, the median age (IQR) declined from 6.7 (3.8-10.6) to 2.1 (0.8-6.2) years; p<0.01, remained the same in Tanzania [4.2 (1.5-9.5) to 3.3 (1.4-8.9) years; p=0.1], and increased in Botswana [5.1 (2.2-8.1) to 9.6 (1.5-12.6) years; p<0.01], Eswatini [4.3 (1.6-8.1) to 8.5 (1.7-11.7) years; p<0.01], Lesotho [3.9 (1.4-7.9) to 8.4 (2.8-11.5) years; p<0.01] and Malawi [5.4 (2.2 to 8.5) to 6.6 (1.9-10.8) years; p<0.01]. Time-to-ART-initiation reduced among all children [median (IQR): 87 (24-389) to 2 (0-14) days; p<0.01].

Conclusion: Between 2003-2017, disease severity at ART initiation among children aged 5-14 years declined, remained the same in children <2 years, and increased in those aged 2-4 years. Over time, children initiating ART in most southern Africa sites were older and less severely ill; those in Eastern Africa sites were younger and more severely ill. In 2016-2017, children initiated ART within the first week in care but a substantial proportion especially those aged <5yrs still initiated ART with advanced disease. More efforts are required to diagnose and initiate children on ART early.
Closing the Treatment Gap for Children: Global and Regional Trends in Pediatric Antiretroviral Therapy Coverage, 2010-2017

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Background: Antiretroviral therapy (ART) has significantly reduced AIDS-related morbidity and mortality for people living with HIV. Children (<15 years) living with HIV (CLHIV) have benefited from expansion of ART to all populations. In many regions, however, pediatric ART coverage is still low as compared to adults. We reviewed longitudinal (2010-2017) regional and national ART coverage estimates to identify adult and pediatric coverage disparities in order to direct case-finding, linkage, and retention strategies for CLHIV.

Materials & Methods: Secondary data analysis was conducted using publicly accessible UNAIDS Spectrum estimates from 2010 to 2017. Country-level pediatric (0-14 years) and adult (>15 years) ART coverage estimates, defined as the percent of people living with HIV on treatment, were abstracted and merged into a hierarchical data file, segmented by UNAIDS geographic region (n=7). Descriptive statistics were calculated to estimate regional ART coverage disparities by age groups (pediatric, adult). Paired t-tests were calculated to compare regional ART coverage means at each time interval (2010-2017) as well as changes in ART coverage over time. One-way analysis of variance (ANOVA) was performed to determine if national pediatric ART coverage estimates in 2017 differed significantly by region, as determined by one-way ANOVA [F(6,86) = 8.55, p<0.001]. Post-estimation Tukey tests revealed countries in West and Central Africa (n=24) exhibited significantly lower (p<0.05) pediatric ART coverage compared to countries in other regions, with the exception of Middle East and North African countries (n=8). In multivariable analysis, West and Central African countries had, on average, 26.3% lower pediatric HIV coverage than countries in other regions [β = -26.3%, 95% CI: -39.1%, -13.4%, p=0.001].

Conclusions: In spite of significant increases in treatment scale-up globally since 2010, gaps in reaching children and improving pediatric ART coverage still persist. This gap is most noticeable among West and Central African countries where epidemics are more concentrated in high-risk adult populations and significant differences in ART coverage between adults and children persist over time. Priority interventions for mitigating disparities include integrated family-based services and targeted index testing, especially for children of key populations in West and Central Africa, to improve case-finding and reduce missed opportunities for diagnosing CLHIV.
Outcomes of children and adolescents living with HIV considered lost to follow up at IeDEA-SA cohorts in the Western Cape: Linkage to Western Cape Provincial Health Data Centre records.


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Background: Loss to follow up (LTFU) is a challenge to achieving optimal paediatric antiretroviral therapy (ART) outcomes, and limits reporting of programme performance. LTFU may represent unascertained mortality, silent or undocumented transfer or true loss to care. LTFU in children on ART vary widely from 5% to 29% a year after ART initiation, however, there are few studies of outcomes in children LTFU. We aimed to assess the outcomes of children and adolescents living with HIV (CALHIV) considered LTFU in the Western Cape through tracing and factors associated with hospital admissions, silent transfers and being completely lost.

Methods and materials: Children and adolescents living with HIV (CALHIV) considered LTFU, initiated ART at ≤15 years old between 2004-2015 at 4 IeDEA-SA Western Cape sites were included. LTFU was defined as no visit ≥180 days before database closure and not recorded as transferred out or deceased. We linked IeDEA-SA patient records to Western Cape Provincial Health Data Centre visit, laboratory and pharmacy records using unique patient identifier that is implemented at health facilities in the province. We used pooled multinomial logistic regression to assess factors associated with hospital admission, returning to care and being completely lost.

Results: Among 1,057 CALHIV that were LTFU (51% female, median (IQR) age at ART start: 2.4 years (0.60, 6.80), median (IQR) CD4 at LTFU: 861 cells/µL (537, 1319)), 686 (65%) CALHIV were found to have silently transferred to other sites, 240 (23%) had been hospitalised and 131 (12%) were not found. For those silently transferred, median time from last visit to first visit after LTFU was 35 (13,181) days. For hospitalized patients, median time from last visit to admission was 45 (16, 166) days. CALHIV who initiated ART between 10-15 years were more likely to be completely lost compared to being silently transferred (Adj. RRR: 2.63 (1.19, 5.85)) after adjusting for other variables. CALHIV starting ART after 2006 were less likely to be admitted to hospital compared to having silently transferred.

Conclusion: The majority of CALHIV LTFU in our study had been misclassified; most were actually retained in programme in routine care, but a substantial proportion had been admitted to hospital. Data sources beyond the initial facility of ART initiation are needed to accurately assess retention and programme outcomes so as to prevent under ascertainment of mortality estimates among CALHIV.
International Workshop on HIV Pediatrics
Mexico City, Mexico

Abstracts
Poster Presentation
HIV treatment coverage and antenatal care among non-citizen pregnant women in Botswana

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Background: Pregnant women in Botswana have excellent HIV treatment coverage. However, difficult-to-reach populations still exist. One such population may be non-citizens, who are ineligible for free antenatal care or antiretroviral therapy (ART) available to citizens.

Methods: The Tsepamo birth outcomes surveillance study records information on citizenship, HIV status, ART exposure and antenatal care among ~45% of all pregnant women in Botswana. We examined the relationships between citizenship status, antenatal care, and adverse birth outcomes (stillbirth, low birthweight, or neonatal death) among all pregnant women. For multivariate models, we considered potential risk factors for adverse outcomes, including hypertension, smoking, alcohol, age, and having few antenatal visits (3 or fewer). Among HIV-positive women, we examined whether ART access and regimen differed by citizenship status or was associated with adverse outcomes.

Results: From 2014-2018, 104,086 deliveries at 8 government maternity wards were recorded. Maternal citizenship was available for 103,729 (99.7%), with 3,376 (3.3%) reporting foreign citizenship. Non-citizens were older (29.1 vs. 26.9, p<0.001), reported greater gravidity (2.7 vs 2.4, p<0.001), and had lower prevalence of HIV infection (21.3 vs. 24.7%, p<0.001) compared with citizens. Non-citizens were more likely to have unknown HIV status in pregnancy (7.0%) compared with citizens (0.5%) (risk ratio [RR]=13.4, p<0.001), and fewer median antenatal care visits (6.4 vs. 9.6, p<0.001). Non-citizens had increased risk of stillbirth (3.2% vs. 2.3% in citizens, p=0.001) and neonatal death (1.8% vs. 1.4% in citizens, p=0.05) in univariate analyses. However, these relationships were not present in multivariable analyses when adjusted for other risk factors, such as HIV status, hypertension, and number of prenatal visits. Among HIV-positive women with a documented CD4 test, non-citizenship was associated with CD4<200/mm3 (RR=1.8, p=0.01), even when restricted to those on ART (RR=1.8, p=0.02). Among HIV-positive non-citizens, 265 (39.6%) had no ART documented during pregnancy, compared with 1,423 (5.8%) of HIV-positive citizens (RR=6.9, p<0.001). Lack of ART among non-citizens was most common in younger women and those with few antenatal visits (both p<0.001).

Conclusions: Non-citizens in Botswana are more likely to experience adverse pregnancy outcomes, possibly mediated in part through less prenatal care. Compared with citizens, HIV-positive non-citizens are far less likely to receive ART in pregnancy, and may account for a substantial proportion of mother-to-child transmission events.

Too little, too late: Early lessons on MTCT risk from HIV positive infant case investigation in Zimbabwe

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Background: In 2018, Zimbabwe introduced routine case-reporting for all new HIV infections among children 0-24 months. The FACE HIV Program supported MOHCC with entry and analysis of case reports from public health facilities in 6 provinces of Zimbabwe.
from Jan-Sept 2018. Our objective was to describe the characteristics of newly diagnosed HIV positive infants and their mothers.

**Materials and Methods:** Routinely completed paper-based case reporting forms of children testing HIV positive from Jan-Sept 2018 were entered electronically into MS Forms. Anonymised data was abstracted into MS Excel and descriptive analysis with chi-square tests of proportion conducted using StataV13.

**Results:** A total of 106 HIV positive child case investigation forms were entered. Routine laboratory data indicate coverage of retrospective form completion was less than 50%. Maternal characteristics: The median age of mothers of positive infants was 26yrs (IQR: 23-34). Over half of mothers (52%; 55/106) indicated HIV status of their partner was unknown. Few women had a known HIV positive status prior to the current pregnancy (24/106), with 25% (27/106) testing positive in labour and delivery or postnatally (27/106), and 19% testing positive in antenatal care in the current pregnancy (20/106). The majority were initiated on ART less than 8 weeks before delivery or post-delivery, had stopped ART, or were never ART initiated (53%; 56/106). Infant characteristics: The majority of newly diagnosed HIV positive infants recorded were male (56%; 60/106) had a facility-based delivery (78%; 83/106), and were reported to be exclusively breastfed in the first 6 months (71%; 75/106). Median number of days old at time of HIV diagnosis was 89 days (IQR: 43-317 days). Just over half of HIV positive infants were documented as ever having received infant prophylaxis (56/106; 52.8%). The majority of infants had documented ART initiation (77%; 85/106), with a significantly greater proportion of boys initiated on ART than girls (54% vs. 46%, p=0.03). Among the 24 infants not initiated on ART, 50% had undocumented outcomes, with most frequent documented reasons being mother did not return to clinic following results receipt, death of infant, and caregiver refusal.

**Conclusions:** We documented low coverage and high rates of missing data from retrospective case investigation of HIV positive children. Findings have informed development of national electronic case investigation reporting systems using DHIS2 and standard operating procedures for prospective case-based surveillance with quarterly ‘match’ of all positive laboratory diagnoses with completed case investigation forms for monitoring implementation fidelity. Among completed case investigation forms, we document late HIV diagnosis and limited time on ART among mothers that have transmitted HIV to their infants. Active follow up of all HIV-exposed children with unknown outcomes and ensuring all HIV positive children are initiated on sustained ART are required. Our findings underscore countries on the pathway to elimination of pediatric HIV should invest in enhanced efforts to ensure early diagnosis and treatment of all HIV positive women. Future research is required to routinely compare mother-infant characteristics of infected infants with HIV-exposed uninfected infants to inform evidence-based stratified interventions to identify and support women at greater risk of MTCT.

### 31

**Challenges with recognition of newborns at high risk for perinatal HIV transmission in rural Western Cape, South Africa**

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**Background:** Despite tremendous declines in peri-and-postnatal HIV transmission, ±5% of infants born to women living with HIV (WLHIV) in South Africa acquired HIV in 2017. 2015 Western Cape Prevention of Mother-to-Child Transmission (PMTCT) Guidelines stratify infants at birth as high/low-risk for perinatal transmission to identify high-risk infants who may benefit from dual postnatal prophylaxis with zidovudine+nevirapine compared to
nevirapine-alone. High-risk criteria are: maternal antiretroviral therapy (ART) initiated <12 weeks before delivery; unknown/unsuppressed maternal viral load (VL) <12 weeks before delivery; chorioamnionitis; spontaneous preterm labour; prolonged rupture of membranes. Our objectives were to evaluate appropriate identification of and antenatal factors associated with high-risk infants.

Methods: A retrospective cohort study of WLHIV and their infants born at a rural regional hospital in the Western Cape from May 2016-April 2017. Maternal and infant data were extracted from the labour ward PMTCT register (including documentation of assigned high/low risk status), standardized maternity records, National Health Laboratory Service database and Provincial Datacentre. Assigned infant risk was compared with actual infant risk determined from all available information. Maternal antenatal factors were compared between high/low-risk infants and associations with having a high-risk infant were evaluated using multivariable logistic regression.

Results: 216/1762 (12%) infants were born to WLHIV; 202 (94%) with available records were included. Mean[standard deviation] maternal age was 30.2[6.4] years, 19% (39/202) primiparous. Fewer mothers of high-risk compared to low-risk infants had first antenatal visit <20-weeks gestation (57% vs. 77%, p=0.01) and >4 antenatal visits (39% vs. 80%, p<0.001). There was no difference between high- and low-risk infants in timing of maternal HIV diagnosis (75% vs 83% before current pregnancy, p=0.47) or ART initiation (61% vs 70% before current pregnancy p=0.17). Thirty-eight percent (77/202) of infants were assigned as high-risk whereas 71% (143/202) were actually high-risk; 47% (94/202) were assigned as low-risk whereas 29% (59/202) were actually low-risk; 15% (31/202) had undocumented risk. Absence of known viral suppression <12 weeks before delivery, due to non-testing in 49% (98/202) and non-suppression in 10% (21/202), accounted for 83% (119/143) of high-risk exposures and 81% (60/74) of missed high-risk exposures. While 98% (165/168) of infants received postnatal prophylaxis according to assigned risk, only 54% (68/126) of actual high-risk infants received dual prophylaxis. Adjusted for maternal age, parity, gestational age at first visit, timing of HIV diagnosis and ART initiation, only number of antenatal visits (adjusted odds ratio 0.62; 95% confidence interval 0.50-0.76) remained associated with high-risk infants. HIV transmission was confirmed in 4.3% (8/185) of liveborn infants by two years of age, five with correctly assigned high-risk, one with correctly assigned low-risk, one with incorrectly assigned low-risk and one undocumented risk.

Conclusions: Infant high-risk status was driven by suboptimal maternal VL monitoring. Recognition of high-risk infants was frequently missed due to lack of consideration of maternal viral suppression. In light of the association between infant high-risk status and antenatal visit number independent of first visit gestation, reinforcing visit frequency later in pregnancy may improve VL monitoring and VL result availability for appropriate risk assignment and postnatal prophylaxis.

32

Final HIV outcome for exposed infants: Improving mother-baby pair retention in prevention of mother-to-child transmission care in Eswatini through proactive community follow-up

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Background: Determination of final HIV status for HIV-exposed infants (HEIs) after breastfeeding cessation is critical in measuring the success of prevention of mother-to-child transmission (PMTCT) programs and ensuring
early treatment initiation. However, high attrition rates after the six-week postpartum visit negatively affect determination of final HIV status.

**Methods:** The USAID-funded AIDSFree initiative trained, supervised, and compensated community focal mothers (CFMs) to proactively visit mother-baby pairs (MBPs) each month to encourage facility attendance until determination of final HIV status. CFMs visited mothers at home to help them plan for upcoming facility visits. CFMs visited HIV-positive and HIV-negative mothers to educate and encourage all MBPs to complete scheduled child welfare visits. CFMs also provided health workers at three implementing facilities with relevant information on MBP outcomes (e.g. death, transfer-out) for proper documentation in facility registers. Monthly, AIDSFree measured MBP completion of expected facility visits per the Ministry of Health schedule through 18 months postpartum.

**Results:** In the pre-implementation period (January 2014 to December 2015), 36% of expected 292 HEIs in implementing facilities were retained in care at 18 months, and only 32% (93/292) had final HIV status determined. In the CFM implementation period (June 2017 to November 2018), 127 HEIs were enrolled, and 100% (18/18) of HEIs who reached 18 months by November 2018 had final HIV status determined. Two infants tested HIV-positive before the 18-month visit and were both initiated on treatment. Overall, 82% of all enrolled MBPs never missed a scheduled visit; the 18% who did were immediately linked back to care. No enrolled MBPs were lost to follow-up.

**Conclusions:** This initiative demonstrated success in improving MBP retention in PMTCT care through proactive, community-based follow-up with home visits by CFMs, resulting in determination of final HIV status at 18 months, as well as receipt of critical maternal and child health services.

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**33**

**Topic:** Effective Community Engagement and Participation, key to Nigeria achieving the first 90’ target of eMTCT.

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**Background:** Nigeria contributes 30% world burden of Mother to Child Transmission of HIV (MTCT). The entry point to PMTCT is HIV testing which is currently health facility based. Of the estimated nine million pregnancies, only 60% deliver at health facility; the rest accesses services at Traditional Birth Attendants (TBAs). Nigerian body of Obstetrics and Gynecology are opposed to any interface with TBAs. PMTCT programme data (2017) shows that, of 165,474 estimated mothers needing PMTCT, only 64.811 (39.2%) have been identified; only 24,026 (47.2%) delivered at facility offering PMTCT. This intervention was an attempt at finding the pregnant women to make up the first 90’

**Methods:** A draft framework to strengthen interface between the TBAs and health service providers for PMTCT was designed by National stakeholders. A high level advocacy to wives of Governors in 7 selected states ensured non resistance of staff of state ministries of health to interface with TBAs. Three LGAs per state with high HIV prevalence were selected. TBA’s facilities were mapped and linked to health facilities. Community mobilizers selected from the locality and mostly TBAs mobilized pregnant women for testing at the community. Members of HIV networks were on-hand to ensure follow up and enrollment of any identified positive. Testing was provided at the mapped TBAs shops by health facility personals for 5 days. Data set have been validated by National M&E system.

**Result:** A total of 104,576 pregnant women were reached within 5 days. Of which 789 were HIV positive (0.75 positivity). If this is applied to the 774 LGAs in Nigeria, across the two rounds
of MNCH week, 90% of estimated pregnant women will be identified. The TBAs engaged in this exercise now have sustainable interface with the facilities. This also popularized the existence of network groups which have reduced stigmatization and improved uptake of PMTCT services.

Conclusions: This intervention demonstrated clearly that TBAs are patronized by pregnant women. And that strengthening the interface between them and health service providers will improve uptake of PMTCT services. A comprehensive framework for engagement of TBAs as directed by Dakar declaration (Jan,2019) to Nigeria is eminent.

34

Creating Demand for HIV Testing Services (HTS) among School-aged Children

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Background: HIV testing is a critical step in epidemic control. Testing children, especially in the 5-14 years’ age group, is difficult because of a drop in health service engagement between infancy and adulthood. A school-based educational campaign initiative was developed in Eswatini aimed at mobilizing primary school children age 5-14 years to engage in HIV testing.

Methods: EGPAAF developed a strategy with the Ministries of Health and Education (MoE) to conduct school-aged children mobilization campaigns in selected primary schools to encourage and link children for HIV testing. Four schools were identified with MoE and campaigns were launched in two phases; phase one in Matsanjeni and Lulakeni (June-August 2017), phase two in New-Heaven and Ntjanini primary schools (February-April 2018). Prior to each campaign, teachers and grouped pupils selected a topic (e.g. factors inhibiting access to HIV testing) and conducted in-depth research on that topic. On campaign day, groups presented their topics to the whole school; discussions ensued moderated by local nurses. Children who showed interest in HIV testing services (HTS) at the campaigns were referred to two nearby facilities for testing using referral forms. Consent forms were sent home for caregivers sign-off among children under 12 years.

Results: For phase 1, during a 3-month period (January-March 2017) pre-intervention, 371 children (5-14 years) were tested for HIV in two nearby facilities, while during the 3-month intervention period (June-August 2017), 564 children were tested in the two same facilities. For phase 2, during a 3-month period (October-December 2017) pre-intervention, 477 children were tested, while during the 3-month intervention period (February-April 2018), 839 children were tested. Combining phase 1 and phase 2 data, the intervention improved HTS uptake from 848 children before to 1,403 children during the 3-month intervention period. By referral form count, 1,401 children were referred for HIV testing, 1,403 (including peers recruited by those referred) reached the facilities and were tested for HIV. Three (0.2%) children tested HIV-positive and started treatment.

Conclusion: Although the positivity yield was low, this strategy enhanced the number of children (5-14 years) accessing HTS. The MoE is currently adapting this initiative across all regions of Eswatini.

35

Financial incentives increase pediatric HIV testing among HIV positive caregivers

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**Background:** Financial incentives (FI) have been successfully used to motivate desirable health behavior. Testing children of HIV positive adults (index case testing) has high yield for positive tests but uptake is sub-optimal. We hypothesized that FI may motivate HIV-positive caregivers to test their children for HIV.

**Methods:** In February 2017 to September 2018, HIV-positive adults attending HIV clinics in western Kenya, who had children ages 0-12 years of unknown HIV status were randomized with equal allocation to FI of $0, $1.25, $2.50, $5 or $10. Payment was conditional on uptake of child testing (clinic-based) within 2 months. Randomized caregivers received two phone call reminders for their testing visit. Primary analysis was intent-to-treat, with predefined primary outcomes of uptake of child testing and time to testing. Relative risk regression and Cox proportional hazards regression were used to compare FI arms to the $0 arm.

**Results:** 447 caregivers were randomized; 88, 89, 91, 92 and 87 to $0, $1.25, $2.50, $5 and $10, respectively. A majority (300 [67%]) of caregivers were female. Caregiver age, sex and number of children did not differ between arms.

Uptake of child HIV testing by arm was: 31% ($0 arm), 34% ($1.25 arm), 44% ($2.50 arm), 50% ($5 arm) and 57% ($10 arm). Relative to the $0 arm, testing uptake was significantly higher in the $5 and $10 arms, with a 1.7-fold (95%CI: 1.1-2.4, p=0.011) and 1.8-fold (95%CI: 1.3-2.6, p=0.001) increase in testing uptake, respectively, but did not differ significantly in the $1.25 and $2.50 arms (p=0.621, p=0.077, respectively) (Figure 1A).

Median time to testing was 8 days (IQR 4, 23) in the $0 arm, 7 days (IQR 4, 14) in the $1.25 arm, 5 days (IQR 1.5, 17.7) in the $2.50 arm, 5 days (IQR 2, 14) in the $5 arm and 5 days (IQR 2, 8) in the $10 arm. Relative to the $0 arm, time to testing was significantly shorter in the $2.50, $5 and $10 arms (p=0.621, p=0.077, respectively) (Figure 1B).

Of 318 index children tested, median age was 9 years (IQR 6, 11). 7 were HIV positive (HIV prevalence of 2.2% [95%CI: 0.80 to 4.0]).

**Conclusion:** FI values above $2.50 substantially and significantly increased uptake of pediatric HIV testing among HIV positive caregivers.

**Background:** Prevention of mother-to-child transmission of HIV (PMTCT) programs have substantially reduced the number of untested HIV-exposed children. Index case testing has been scaled up in an effort to identify undiagnosed children. For the remaining untested HIV-exposed children, it is critical to identify individual and structural reasons why children remain untested, particularly if their siblings have been tested.

**Methods:** This analysis was nested in a randomized trial to determine whether financial incentives increase uptake of pediatric HIV testing (NCT03049917). Trial eligibility criteria were: HIV positive caregiver in HIV care with 1 or more untested child(ren) aged 0-12 years; families were included in this analysis if they tested 1 or more child(ren) within the trial and had 1 or more previously tested child(ren). At the child testing visit, caregivers were asked about PMTCT, child hospitalizations, and reasons for previously not testing child. Proportions are presented and generalized linear models with random intercepts for family and fixed effects for facility were used to compare untested children to their previously tested siblings.

**Conclusion:** Financial incentives (FI) have been successfully used to motivate desirable health behavior. Testing children of HIV positive adults (index case testing) has high yield for positive tests but uptake is sub-optimal. We hypothesized that FI may motivate HIV-positive caregivers to test their children for HIV.
**Results:** Among 197 families with previously untested children who tested during the trial, 63 (32%) also had children (aged 0-12 years) who had previously been tested for HIV. These 63 families included 176 children aged 0-12 years, 88 (50%) of whom had received an HIV test previously.

Previously tested children were younger than their untested siblings (5.6 vs 9.1 years; PR: 0.91 [95%CI: 0.85, 0.97]; p=0.002) and sex distribution was similar (55% vs 53% female; PR: 0.98 [95%CI: 0.64, 1.49]; p=0.915). During pregnancies with previously tested children, mothers were more likely to have known their HIV status (59% vs 7%; PR: 2.9 [95%CI: 1.9, 4.5]; p<0.001), been enrolled in PMTCT programs (56% vs 5%; PR: 2.9 [95%CI: 1.9, 4.4]; p<0.001), and been on antiretrovirals (55% vs 5% PR: 2.9 [95%CI: 1.9, 4.4]; p<0.001) compared to pregnancies with untested siblings. Previously tested children were more likely to have received infant prophylaxis (56% vs 3%; PR: 3.0 [95%CI: 2.0, 4.6]; p<0.001). Child hospitalization was not associated with previous testing (PR: 1.6 [95%CI: 0.88, 2.76]; p=0.125).

Among previously untested children, caregiver reasons for not testing children included: not thinking the child was HIV positive (49%), child not seeming sick (39%), and not having time to test child (20%).

**Conclusion:** Untested, HIV-exposed children commonly had younger siblings who had been tested for HIV. Untested children were more likely to have experienced gaps in all steps of the PMTCT cascade, predominantly because the mother was not yet diagnosed during the pregnancy. Older children were perceived to have a low likelihood of being HIV positive. Efforts to encourage HIV positive mothers to test all their children may be useful to identify undiagnosed older children.

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**Perception that a child is HIV-positive and fear that the child will be tested are barriers for seeking medical care for the child by HIV-positive caregivers**

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**Background:** HIV-exposed older children sometimes remain untested. Caregivers may avoid seeking health care for these children for fear of a positive HIV test. Understanding these fears and how parents have overcome these barriers is critical in reaching all untested children.

**Methods:** This analysis is nested in a randomized trial to determine whether financial incentives increase uptake of HIV testing among children of HIV-positive adults in Kenya (NCT03049917). Eligible caregivers had at least one child 0-12 years old of unknown HIV status; caregivers were included in this analysis if they completed HIV testing for one child within the trial. Caregivers completed a survey after testing, which asked about their prior perception of their child’s HIV status, and whether they failed to bring their child to a clinic in the past for fear of an HIV test. They were also asked whether they would be more or less likely to seek care for their child in the future, their emotional reaction after testing, and important messages to encourage their peers to test children. Data were summarized using proportions and prevalence ratios (PR) from log-binomial regression, stratified by perceived HIV status and actual HIV status.

**Results:** Of 127 HIV-positive caregivers with untested children, 23% predicted that their child would be HIV-positive, 53% had no prediction, 16% predicted the child would be HIV-negative, and 8% never thought about the child’s HIV status. Following HIV testing, there
were 5 (4%) HIV-positive children; 3 of whom were predicted to be positive. Among 29 children predicted to be infected by their caregivers, 90% were actually HIV-negative on testing.

Twenty-eight (22%) caregivers previously avoided seeking care for their child due to fear of HIV testing. Caregivers who perceived that their child was HIV-positive were more likely to have avoided medical care for children in the past (PR: 7.59 [95% CI: 1.01-57.06]) than those who perceived their child was HIV-negative.

After learning their child’s HIV status, 54% of caregivers were more likely to seek medical care for their child in the future, and even higher among caregivers who had previously avoided medical care (82%). No one reported being less likely to seek care for their child in future.

Among caregivers with an HIV-negative child, 69 (57%) reported being relieved after testing while 3 (2.5%) were shocked or stressed. Among those with an HIV-infected child, one was ‘okay’, 2 of 5 were sad but relieved, while 2 were sad or stressed.

Caregivers found several messages important to share with peers to encourage them to test, including: knowing the child’s result will help you take better care of the child (77%), getting the result was not as bad as I thought (56%), it will be an emotional relief (54%), and the child is more likely to be negative than positive (38%).

Conclusion: Fearing that an untested child is HIV-positive and fear of testing are important barriers among caregivers for seeking other health services for children. Messages that reduce anxiety of the caregiver regarding their child’s possible HIV status may be useful to promote index-case pediatric HIV testing.

Concurrent Implementation of Targeted and Blanket Provider-Initiated Testing and Counseling against Symptom-based Diagnostic HIV Testing among Children and Adolescents in Cameroon: A Comparative Effectiveness Study

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Objectives: Over the past decade, remarkable progress in HIV care and treatment has been made for people living with HIV (PLHIV). However, children (<15 years) have not had proportionate benefits from life-saving antiretroviral therapy (ART) with a coverage of 52%, compared to 59% in adults. To address this gap in the context of generalized HIV epidemic, the World Health Organization (WHO) recommends the concurrent implementation of targeted (tPITC) and blanket provider-initiated-testing and counseling (bPITC) for HIV case finding and treatment among children and adolescents. This study assessed the effectiveness of this intervention compared with the symptom-based diagnostic HIV testing (DHT) in terms of HIV testing uptake, case detection and ART enrollment among children and adolescents in Cameroon.

Methods: In three hospitals in Cameroon where DHT was the commonest clinical practice, we introduced and implemented bPITC+tPITC for a period of 6 months. We implemented this intervention by inviting HIV-positive parents in care in these hospitals to have their biological children (6weeks-19 years) tested for HIV (tPITC). At the same time, we routinely offered HIV testing to children brought by their parents/guardians to the
outpatient departments for any reason (bPITC). We comparing the effectiveness of DHT vs bPITC+tPITC by assessing the mean monthly number of children tested for HIV, identified HIV-positive and ART-enrolled before and after the study.

**Results:** In comparing DHT to bPITC, there was a significant increase in the mean monthly number of children/adolescents tested for HIV (223.0 vs 348.3, p=0.0073), but with no significant increase in the mean monthly number of children/adolescents: testing HIV-positive (10.5 vs 9.7, p=0.7574) and ART-enrolled (7.3 vs 6.3, p=0.5819). In comparing DHT to tPITC, there was no significant difference in the mean monthly number of children/adolescents: tested for HIV (223 vs 193.8, p=0.4648); tested HIV-positive (10.5 vs 10.6, p=0.9544), and ART-enrolled (7.3 vs 5.8, p=0.4672). When comparing DHT versus bPITC+tPITC, there was a significant increase in the mean monthly number of children/adolescents: tested for HIV (223.0 to 542.2, p<0.0001), testing HIV-positive (10.5 vs 20.3, p=0.0256), and ART-enrolled (7.3 vs 12.2, p=0.0388).

**Conclusions:** These findings suggest that concurrent implementation of bPITC+tPITC was more effective compared to DHT in terms of HIV testing uptake, case detection and ART enrolment. However, considering that DHT and bPITC had comparable outcomes with regards to case detection and ART enrolment, bPITC+tPITC may not be efficient. Thus, this finding does not support concurrent bPITC+tPITC implementation as recommended by WHO. Rather, continued DHT+tPITC could effectively and efficiently accelerate HIV case detection and ART coverage among children and adolescents in Cameroon and similar low-prevalence context.

### 39

**Pharmacokinetics, Safety and Tolerability of Doravirine in Adolescents with HIV-1**


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**Background:** Doravirine is a novel nonnucleoside reverse transcriptase inhibitor (NNRTI) active against both wild type virus and the most common NNRTI-resistant variants, recently approved for treatment of HIV-1 infection in antiretroviral-naïve adults with HIV-1. IMPAACT 2014 investigated the pharmacokinetics and safety of 100mg of doravirine in adolescents with HIV-1.

**Materials & Methods:** Adolescents with HIV-1 between the ages of 12 and 18 and weighing at least 35 kg with HIV-1 RNA <40 copies/mL on 2 NRTIs plus either raltegravir or dolutegravir were given a single 100mg dose of doravirine. Doravirine plasma levels were drawn prior to the dose, at 6 timepoints in the first 24 hours post-dose, as well as 48 and 72 hours post-dose. The participants were seen at 2 weeks for a safety assessment. Single dose AUC(0-∞), Cmax, C24, Tmax, and apparent terminal t1/2 were determined. The single dose PK data were used to project steady state AUC(0-24), C24, and Cmax. Individual steady state C24 and Cmax were projected from individual plasma concentration-time profiles using the non-parametric superposition function in WinNonLin v6.3.

**Results:** Nine adolescents between the ages of 12 and 16 years (mean 14.3 years) and weighing 40.3 to 90.8 kg (mean 55.9 kg) received a single-dose of 100mg doravirine and had evaluable pharmacokinetic data. Seven of the 9 (78%) were male and 7/9 (78%) were African American. All participants had HIV-1
RNA < 40 copies/ml at baseline. Mean CD4 count was 788 cells/mm³. The doravirine geometric mean value of the single-dose AUC(0-∞) for the nine participants was 34.8 µM·h (range 20.0 – 73.6 µM·h) which was not different from the AUC(0-24) at steady-state observed in adults taking 100 mg daily; 37.8 µM·h. The geometric mean predicted steady-state trough concentration (C24,ss,pred) was 690 nM (range 335-1721 nM), which exceeded the lower bound for doravirine based on Phase 3 adult studies of 560 nM. There were no clinically significant adverse events. One participant had grade 1 diarrhea on the day of study entry which was assessed as not related to the doravirine.

Conclusion: Single-dose pharmacokinetics of doravirine in adolescents was comparable to that seen in adults. No safety concerns were identified.

Effect of Ready-to-use therapeutic food on efavirenz and nevirapine plasma levels in Malnourished HIV-infected Children in Uganda

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Introduction: The goal of antiretroviral therapy (ART) is to suppress HIV viral replication. Significant causes of virological failure are sub-therapeutic and supra-therapeutic plasma concentrations of ART drugs. Malnutrition affects absorption of drugs, however, little is known about the effect of malnutrition or ready to use therapeutic food (RUTF) on the pharmacokinetics (PK) of efavirenz (EFV) or nevirapine (NVP) in children. The objective of this study was to compare EFV and NVP PK levels of HIV-infected malnourished and well-nourished (WN) children, determine the impact of RUTF on EFV and NVP PK levels after 12 weeks of supplementation and the virological response.

Study design: This was a prospective cohort study of HIV-infected children aged 6 months to 12 years, on ART for at least 3 months between February 2015-March 2016. Malnutrition was defined as weight-for-height z score below 2 standard deviations of that expected for age or mid upper arm circumference <12.5 cm with no edema. Blood samples were collected from children whose caregivers consented and given medication to determine antiretroviral plasmatic mid-dose-concentrations for EFV and C-min for NVP.

Results: Of 120 plasma samples analyzed, 48/120 (40%) were EFV and 72/120 (60%) were NVP. The average age of the children was 7.3 years (SD±3.2) with male: female ratio of 1:1.2. Of the EFV samples analyzed, 23/48 (47.9%) and 25/48 (52.1%) were at baseline and 12-weeks respectively, of whom 7/23 (30.4%) were previously malnourished among the 12 week samples. At baseline 2/23 (8.7%), 11/23 (47.8%), 4/23 (17.4%) had sub-therapeutic, therapeutic and supra-therapeutic EFV concentrations and 8/23 (34.8%) had undetectable levels as they had not initiated ART. At 12 weeks 10/25 (40%), 5/25 (20%), 10/25 (40%) had sub-therapeutic, therapeutic and supra-therapeutic EFV with 10/25 (40%) having no detectable plasma EFV levels.

The EFV levels at baseline were higher among the malnourished compared to WN; 8.1(IQR: 0-12.4) vs 5.4(IQR: 0-11.5), p=0.63. After RUTF supplementation EFV levels among those malnourished at baseline were 8.1(IQR: 0-22.37) and 9.0(IQR: 0-22.4) at 12 weeks;
Of the NVP samples analyzed, 45/72 (62.5%) and 27/72 (37.5%) were at baseline and 12 weeks respectively, of whom 22/45 (48.9%) were malnourished at baseline and 12/27 (44.4%) were previously malnourished but received RUTF by 12 weeks. At baseline 10/45 (43.5%), 11/45 (47.8%), 4/45 (17.4%) had sub-therapeutic, therapeutic and supra-therapeutic NVP concentrations respectively. While at 12 weeks 10/27 (40%), 5/27 (20%), 10/27 (40%) had sub-therapeutic, therapeutic and supra-therapeutic NVP concentration respectively. At baseline, NVP levels were lower among the malnourished compared to the WN: 3.51(IQR: 1.10-7.41) vs 6.83(IQR: 4.06-9.65) (p=0.036).

The majority of the patients 48/68 (70.6%) had detectable viral loads (≥20viral copies/ml) at baseline in comparison to 28/52 (53.9%) at 12 weeks. The median viral load at baseline was 79 copies/mL (IQR: 19-17652) and 221copies/mL (IQR: 19-7155), p-value=0.463 at 12 weeks. The median length of receiving ART was 17 (1-48) months with majority 48/80 (98%) having a self-reported ART adherence score >95%.

Conclusion: Average length of receiving ART was 17 months with high level of undetectable EFV indicating poor adherence. Supra-therapeutic levels of EFV markedly increased after RUTF supplementation indicating possible interaction with EFV metabolism. The malnourished compared to WN have lower NVP at baseline. In addition to viral load monitoring there is need to incorporate routine therapeutic drug monitoring in the pediatric HIV-care-programs. 41

Abacavir use in young infants in the UK and Ireland national paediatric HIV cohort

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**Background:** The World Health Organization recommends abacavir (ABC) as the preferred or alternative NRTI backbone for first line regimens in children with HIV from age 28 days.

For neonates <28 days old the recommended strategy is zidovudine (AZT) plus lamivudine (3TC), with switch to ABC at 28 days. There are limited data available on safety and tolerability of ABC in young infants aged <3 months.

**Materials & methods:** All children in the UK/Ireland Collaborative HIV Paediatric Study (CHIPS) who initiated ABC aged <3 months were included. We describe characteristics at the start of ABC, drug discontinuations, clinical adverse events related to ABC and virological response.

**Results:** Of 100 children in CHIPS who received ART aged<3 months, 53 received an ABC-containing regimen (n=14/50 aged<28 days) and were followed for a median of 11.5[IQR 7.7,14.0] years. Median age at HIV diagnosis was 33[19,53] days and year of birth was 2006[2003,2009]; 21(40%) were male, 38(72%) black African. At first use of ABC, median age was 46[27,71] days, CD4% was 39%[32,49%](n=42) and viral load was <1000c/ml in 10(26%), 1000-<10,000c/ml in 9(23%), 10,000-<100,000c/ml in 14(36%) and ≥100,000c/ml in 6(15%)(n=39). Three (6%) infants received ABC as part of a post-exposure prophylaxis (PEP) regimen (continuing with ABC-containing treatment following diagnosis), 24(45%) initiated ABC-containing ART without PEP exposure, and 26(49%) received other PEP prior to ABC (13 received 3TC+AZT+nevirapine(NVP), 9 AZT, 4 other). Two-thirds (n=33,62%) were taking ABC with 3TC+AZT+NVP. ABC dosing and weight data were available for 32 infants at start of treatment; 22(69%) started on an 8mg/kg twice daily (BD) dose, 3(9%) on >8mg/kg BD, 4(13%) 4-6mg/kg BD and 3(9%) on 2mg/kg BD doses.

At last follow-up, 27(51%) children had taken ABC continuously for 8.9[5.2,12.8] years. Fifteen (28%) children had ≥1 episodes of ABC.
discontinuation but later restarted, and four temporarily interrupted ABC within the first 12 months (3 non-compliance, 1 structured interruption). Fifteen (28%) permanently discontinued ABC after a median of 1.9[0.3,11.1] years (3 simplified treatment available, 2 structured interruption, 2 parents/patients wish, 1 non-compliance, 1 virological failure, 2 unknown); 11 stopped after >1 year on treatment. Three infants (6%) (including 2/14(14%) aged <28 days at ABC start), all on ABC+3TC+AZT+NVP, discontinued after 3, 4 and 7 days due to possible ABC reactions (1 severe metabolic acidosis (possibly ABC reaction); 1 possible HLAB5701 positivity; 1 diarrhoea). All three continued on 3TC+AZT+NVP. Cumulative incidence of permanent discontinuation of ABC was 5.6%(1.9,16.5%) by 3 months, 7.6%(2.9,19.0%) by 6 and 7.6%(2.9,19.0%) by 12 months while 7.6%(2.9,18.9%), 11.4%(5.3,23.6%) and 15.3%(7.9,28.2%) had temporary/ permanent discontinuation of ABC by 3, 6 and 12 months. Overall 30/42(71%) and 29/37(78%) on still ABC-including regimens had viral suppression <400c/ml after 6 and 12 months of therapy. No deaths or other clinical adverse events/reactions associated with ABC were reported.

Conclusions: Half of young infants in CHIPS who received ART aged <3 months took an ABC-containing regimen. Overall, ABC was well tolerated, with ~6% of patients discontinuing ABC due to toxicities possibly related to ABC, most of which occurred early, within 7 days of starting ABC.

Children and adolescents in the UK/Ireland CHIPS cohort on integrase inhibitors: safety and effectiveness

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Background: Integrase inhibitors (INSTI) are recommended as part of the preferred or alternative first and second/subsequent-line regimens in children/adolescents with HIV. However there are limited data on outcomes on INSTI in paediatric care. We assessed the safety and effectiveness of INSTI-based treatment in children in the UK/Ireland CHIPS cohort.

Materials & Methods: Patients aged<18 years in follow-up from 23/01/2008 (first approval of INSTI (raltegravir (RAL)) in children in Europe), who initiated dolutegravir(DTG), RAL or elvitegravir(EVG) aged<18 years were included, with follow-up to 26/09/2018. Patient characteristics at start of the first episode on each INSTI were described. Change in CD4, BMI-for-age z-score (zBMI, WHO growth reference) and viral suppression (VS)(defined as <50c/ml or lower limit of detection) at 6 and 12(+/-3) months after drug start were calculated (overall and in patients who were viraemic (VL>50c/ml) and those with VS (maintenance switch) at start of INSTI), along with clinical adverse events (AEs) and drug discontinuations.

Results: Of 1741 patients, 304(17%) had INSTI exposure, of whom 32(10%) had taken two INSTIs, and one (<1%) three. 216(71%) initiated DTG, 93(31%) RAL and 29(10%) EVG. 54% were female, 92% acquired HIV perinatally. Median [IQR] follow-up on INSTI was 9.9[4.5,17.4], 19.5[7.5,32.3] and 8.3[6.9,12.7] months on DTG, RAL and EVG, respectively. Median age at start of DTG was 15.2[13.0,16.5], RAL 13.1[10.5,15.0] and EVG 14.4[12.7,16.6] years; 19(9%), 10(11%) and 0 were ART- naïve, respectively. Among those ART-experienced, 127(64%), 24(29%) and 20(69%) had VS at drug start, and 40(20%), 53(64%) and 6(21%) had VL≥50c/ml (VL missing for 30(15%), 6(7%), 3(10%), respectively). Overall, 119/132(90%), 43/64(67%) and 15/20(75%) had VS after 6 months on DTG, RAL and EVG and 72/79(91%), 42/51(82%) and 7/8(88%) after 12 months. Among children starting with VS, 82/87(94%), 18/19(95%) and
12/15(80%) maintained VS at 6 months and 46/50(92%), 14/14(100%) and 4/5(80%) at 12 months. For those starting with VL≥50c/ml, 16/21(76%), 22/38(58%) and 2/3(67%) achieved VS by 6 months and 9/11(82%), 23/30(76%) and 2/2(100%) by 12 months. At 12 months, the largest overall gains in CD4 were on RAL (n=53, median increase 138[-69,351] cells/mm3), and in those starting INSTIs with VL≥50c/ml, for whom there was a slight increase of 73[-65,332]cells/mm3(n=7) at 12m on DTG, and 237[32,351]cells/mm3(n=24) on RAL (insufficient data on EVG). Median zBMI at start of INSTI was higher on DTG (0.64[-0.19,1.42](n=167)) and EVG (0.68[0.04,1.07](n=25)) than RAL (0.16[-0.91,1.13](n=93)). There were slight increases in zBMI at 6 and 12 months on RAL with 0.11[-0.19,0.38](n=48) and 0.11[-0.18,0.35](n=40), respectively, but not on DTG (-0.01[-0.15,0.22](n=94) and 0.00[-0.15,0.19](n=60)) or EVG (0.01[-0.25,0.2](n=16), insufficient data at 12 months). Cumulative incidence of discontinuation of INSTI by 12 months was 4.9%(95%CI2.5,9.6) on DTG, 11.3%(6.0,20.8) on RAL and insufficient data on EVG. There were no grade 3 or 4 clinical AEs related to INSTI drugs.

Conclusion: In our national paediatric cohort, most patients starting INSTI were treatment-experienced teenagers, and regimens were generally well tolerated. VS was ≥90% among patients on DTG at 6 and 12months, and there was no evidence of weight gain in the first 12 months, but longer-term data are needed.

43

Lack of Influence of Pubertal Stage on Safety and TFV Pharmacokinetics in TAF-based Regimens

**Background:** Hormonal and physical changes occurring during onset of puberty can potentially influence drug disposition, and possibly affect safety outcomes. PK of tenofovir (TFV) from tenofovir alafenamide (TAF)-based products have been characterized in adolescents and children, and are associated with positive safety outcomes. However, pubertal stage-associated safety has not been evaluated for TAF-based regimens. This is the first analysis evaluating the impact of Tanner Stage on TFV PK and relevant safety outcomes with TAF-based regimens.

**Methods & Materials:** Data were combined from pediatric participants ages 6–18y receiving TAF-based regimens in 4 studies. Participants were grouped according to Tanner Stage 1 (group 1: pre-pubescent), Tanner Stage 2-3 (group 2: early puberty), and Tanner Stage 4-5 (group 3: late puberty) with staging based upon breast or genital development in females and males, respectively. TFV PK parameters were predicted by Population PK modeling. Impact of Tanner stage on TFV AUCtau (PK equivalence boundary 70%-143%) and change in height-age (HA) adjusted BMD Z-score and estimated glomerular filtration rate (eGFR) was assessed using an ANOVA model, adjusting for possible confounding factors as appropriate (eg, age, sex, weight, eGFR, boosted 3rd agent). GLSM ratios and associated 90% CIs for comparisons of TFV AUCtau between groups were estimated. Adjusted mean changes from baseline in HA adjusted spine and total body less head (TBLH) Z-scores and eGFR at Week (W) 48 were estimated for each group.

**Results:** Among 230 participants, median age (range) was 12y (6-17), 133 (58%) were female, and 228 (99%) had an HIV RNA <50 c/mL. At W48, Tanner stage shifts occurred in 65%, 48%, 72%, and 39% of participants who were Tanner 1, 2, 3, and 4 at baseline, respectively. Adjusted

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TFV exposures were similar between groups (GLSM ratios and associated 90% CIs for comparisons between groups 1 and 2 [test] vs. 3 [reference] were within 70%-143%). Adjusted mean changes in spine HA Z-scores at W48 were -0.13, 0.02, and 0.13 for groups 1, 2, and 3, respectively (p=0.098 and 0.35 for groups 1 and 2 vs. 3, respectively). Adjusted mean changes in TBLH HA Z-scores at W48 were -0.07, -0.08, and 0.09 for groups 1, 2, and 3, respectively (p=0.29 and 0.13 for groups 1 and 2 vs. 3, respectively). Mean eGFR at baseline was 158, 162, and 147 mL/min/m² for groups 1, 2, and 3, respectively. Adjusted mean change in eGFR at W48 was -2.1, -10.0, and -22.0 mL/min/m² for groups 1, 2, and 3, respectively (p<0.001 and p=0.005 for group 1 vs. 3, and group 2 vs. 3 respectively).

Conclusions: Tanner stage at baseline had no clinically meaningful influence on TFV PK. Differences in changes in BMD HA Z scores were also not apparent between pubertal groups. Comparison between pre- and early puberty vs. late puberty showed a significant difference in eGFR change from baseline at W48 consistent with differences in growth between pubertal stages. This analysis adds to limited available data evaluating pubertal development with drug exposures and associated safety outcomes. Results support using TAF-based regimens in treatment of HIV infection during all stages of puberty.

44

Maternal factors for adherence in infant isoniazid preventive therapy provision among HIV-exposed uninfected infants (HEU) in Kenya

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Background: Infant isoniazid preventive therapy (IPT) adherence is not well characterized. We assessed prevalence and correlates of infant IPT adherence within an ongoing randomized trial (RCT).

Methods: In an ongoing RCT (NCT02613169) among HIV-exposed uninfected (HEU) infants randomized to 12 months IPT vs. no IPT, we assessed adherence by maternal report within the IPT arm. We determined IPT missed doses, reasons for missed doses, and association between adherence and maternal/infant characteristics using univariate logistic regression. Adherence at the 6-month visit was defined as no missed INH within the last week per maternal report. A questionnaire was administered to mothers to assess influential factors for adherence.

Results: Among 134 HEU infants in the INH arm at 6 months follow-up, 17.9% missed a dose in the last week and 82.1% were adherent (no missed dose within past week). Top reasons for missed doses among non-adherent mothers (n=24) included forgetting to give medicine (33%), running out of medicine (38%), and children vomiting on taking medicine (8%). Adherence was associated with prior maternal TB diagnosis (15% vs. 0%; p=0.047) and initiation of ART during/early post-partum (vs. before this pregnancy; 20% vs. 46%; p=0.008), comparing adherent vs. non-adherent mothers by analysis of variance.

Maternal factors influencing adherence included: understanding the benefit of providing medicine to child (OR 3.6; CI 1.4-8.9; p=0.007), support from research staff (OR 2.6; CI 1.1-6.5; p=0.034), self-identified strategies to remember medication (OR 2.8; CI 1.1-7.3; p=0.021), and disclosure of medication use (OR 2.8; CI 1.1-7.3; p=0.034).

Conclusions: Mothers face challenges in sustaining infant IPT adherence. Mothers with prior TB and recent ART initiation may be concerned about infant TB susceptibility and thus, more likely to adhere. Education and support from healthcare workers to enhance education, adherence strategies and address disclosure could enhance infant IPT adherence.
Burden of Tuberculosis among Children and adolescents on Anti-retroviral Therapy in Myanmar

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Background: One of the common causes of morbidity and mortality among HIV infected children is Tuberculosis and one-third of all deaths of Acquired Immunodeficiency Syndrome (AIDS) are related to TB. Myanmar has been included in the list of 30 countries with the highest TB burden globally. However, little is known about the situation of TB burden among children on anti-retroviral therapy.

Methods: It was a retrospective cohort study with the objective of identifying the burden of Tuberculosis among children and adolescents on anti-retroviral therapy. A total of 3,277 records of children on ART were reviewed. Key informant interviews were conducted with the service providers. Descriptive analysis and Chi-squared test were applied for quantitative data and thematic analysis for qualitative data.

Results: Mean age of children was 8.8 ± 3.4 years and 43% was in the age range of 6 to 10 years. Mean duration of HIV diagnosis was 3.9 ± 2.6 years. Over 93% of children are currently taking first line ART regimen and 74% have been taking ART for 1-5 years. There were more males than females (72/111, 61.5% and 45/111, 38.5%) among children on 2nd line ART (3.4%, 111/3277). TB incidence rate was 12 per 100 person years after excluding death, loss to follow up and transfer out children. Greater proportion of male had ever infected with Tuberculosis during their ART (38% vs. 32%, p=0.02). Higher proportion of incidence of TB was seen among 11 to 15 years old children in comparing to 0-5 years age groups (37.4% vs. 31.9%; p=0.06). Similarly, larger proportion of children on ART duration of >5 years had ever infected with TB than <1 year duration group (41.3% and 28.2%, p=0.001). On the other hand, almost all of the children were treated completely for their TB infection. During discussions with service provider, they mentioned that inadequate supply of medicines for opportunistic infections was one of the challenges.

Conclusions: Older age group, male and children on longer duration of ART were more infected with TB than the other groups. Regular monitoring and comprehensive care is critical to reduce the burden of TB among HIV infected children on ART.

Low Cytomegalovirus (CMV) recurrence among HIV-infected children and adolescents on HAART from a highly CMV-seropositive population

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Background: Although opportunistic infections are less frequent in HIV-infected individuals after HAART, CMV infection is still a challenge because recurrence may occur in adults with adequate control of the HIV infection. Moreover, CMV has demonstrated association with immune activation and immunosenescence in HIV-infected individuals. Knowledge about CMV recurrence among HIV-infected children and adolescents from a highly seropositive population can guide clinical follow-up. We studied the CMV recurrence among HIV-infected children and adolescents on HAART over a period of two years.

Methods: Forty-seven HIV-infected CMV-seropositive adolescents, followed in a reference center, who were 10-18 years old at enrollment in this study were evaluated every three months during a two-year period. Clinical, CD4/CD8 cell count, HIV viral load, and CMV-DNAemia data were obtained periodically. CMV-DNA detection and
quantification in blood and PBMC was performed using CMV Q – PCR Alert KitR (Nanogen Advanced Diagnostic S.P.A.). CMV recurrence incidence was expressed per person-month once few subjects were not completely followed.

**Results:** All of 47 children/adolescents were receiving HAART. Their mean age was 14.2 years. Overall, they had a good control of the HIV infection. Most had >500 CD4+ cells at entry (80.8%) and end (82.9%) of follow-up. HIV viral load results below the detectable limit were found in 52.5% and 47.5% respectively at entry and final evaluation. HIV viral loads ranged from 40 to 400 cps/ml in 17.5% to 22.5% of the adolescents. Almost all of them were classified as stage 1 per the WHO categorization and 90% had not significant immunosuppression. Overall, 411 blood samples were tested with a mean of 9 samples per subject. CMV-DNA was detected in only four samples of three subjects. A single immunodeficient child was symptomatic and died of CMV systemic disease. Thus, CMV recurrence was verified to be a 0.97/ 100 persons-month rate.

**Conclusion:** HIV/CMV coinfected adolescents on HAART with good control of the HIV infection and living in a highly CMV-seropositive population rarely present CMV recurrence. If the primary CMV infection early in the childhood could protect from recurrence at older ages in HIV-infected children deserves further studies.

**Attention deficit hyperactivity disorder in Mexican children and adolescents with perinatally acquired HIV**

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**Background:** Attention deficit disorder hyperactivity disorder (ADHD) is the most common neurobehavioral disorder of childhood in developed countries. There are few reports of this disorder in the pediatric population with HIV in Latin America. **Objective:** To determine the prevalence of ADHD in HIV-infected Mexican children and adolescents.

**Methods:** Clinical records and database of 152 children and adolescents diagnosed with HIV / AIDS in follow up at a tertiary hospital (Children’s Hospital of México) with at least 3 appointments with psychology from January to December 2018 were reviewed. We included patients who, during the semi-structured interviews with the parents and / or caregivers, met the DSM IV and ICD-10 criteria for the diagnosis of ADHD.

**Results:** 50 children (38%) met criteria for ADHD. The most prevalent diagnosis were inattentive type (80%), hyperactive type (6%) and type combined (8%). Median age was 11 years; the female gender was the most frequent; the mother and / or the father were the primary caregiver in 62% of the cases. All patients had ART.

**Conclusions:** The frequency of ADHD (38%) was higher than reported in the pediatric population without HIV (5.7-29.8%) in Latin America including Mexico as well as in cohorts of children with HIV. Mental health interventions should be integrated into medical care.

**Referral Rewards: Impact of strengthening integrated HIV/TB and Malnutrition community-facility referrals among children under 5 in rural Zimbabwe**
Abstracts

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**Background:** Effective referrals between community and facility are recognised as the cornerstone of programs seeking prompt diagnosis and treatment for malnutrition, TB and HIV among children in high burden, low resource settings. Zimbabwe is such a setting, with: an HIV prevalence of 14.1%, estimated 2.1% of children under five years in urgent need of therapeutic treatment for severe acute malnutrition (SAM), and the majority of the population residing in rural communities. To overcome identified gaps in community-facility referrals of children under 5 years to integrated HIV/TB/Malnutrition services, a learning phase implementation of an enhanced community-facility referral system was implemented in rural Mangwe District, Matabeleland South Province, Zimbabwe. Our objective was to evaluate the outcomes of a community-facility referral system upon service uptake rates and integrated HIV, TB and malnutrition screening and treatment among children under 5 years.

**Method:** A mixed method evaluation was conducted from Oct-Dec 2018 to document early outcomes and lessons from implementation of the community-facility referral learning phase consisted of 2 key activities: 1) Process evaluation to assess implementation fidelity and health system stakeholder perceptions and experiences using the referral system through structured health care worker surveys and focus group discussions in 13 health facilities, as well as to capture any case studies of household-level impact 2) Retrospective cohort analysis of community-facility referrals made among children under 5 years from August-Dec 2018. Data were entered into MSExcel and analysed descriptively using MSExcel and StataV13. Qualitative data were analysed thematically.

**Results:** Introduction of the community-facility referral system resulted in a more than 3-fold increase in the number of community-referrals registered at participating health facilities from Aug-Dec 2018. Prior to introduction of the system, there was no functioning mechanism in place for reconciling uptake of community referrals and documentation of integrated services received. The proportion of children referred that received documented screening for malnutrition rose from 90-100% and HIV from 18-79%. While community-facility referral system training placed emphasis on the importance of providing referrals for integrated HIV/TB/Nutrition services, few clients were documented as receiving referrals for these specific services (5.2% (5/96) for nutrition support; 1 (1%) for TB screening and 0 for HIV testing). While the majority of children were referred for immunization or growth monitoring (51%; 49/96), the majority of these children referred had documented screening for malnutrition/HIV/TB on presentation. Significant inter-facility variability was observed in both the number of children referred from community to facility, and provision of integrated screening, testing and treatment at health facilities. Key qualitative themes from health system stakeholders included existence of multiple, parallel referral systems between different implementing partners creating inefficiency and unnecessary burden upon health care workers and voluntary, community health workers.

**Conclusions and Recommendations:** We provide strong preliminary evidence that increasing community-facility referrals increases the proportion of children that receive integrated HIV/TB/Malnutrition screening upon presentation to health facilities in a remote, high burden setting. A harmonization of referral systems between multiple programs under Ministry of Health and Child Care endorsed tools will reduce documentation and reporting burden at multiple health system levels, and improve capacity to document referral uptake and outcomes. Future research is required to explore the sustained impact of community-facility referral systems and contribution to diagnosis and treatment targets malnutrition, HIV and TB among children under 5 years.
Adherence to Anti-retroviral Therapy among children and adolescents in Myanmar: a mixed-methods study

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Background: Comprehensive care and treatment is critical for all the children living with HIV while ensuring adherence is essential to the success of anti-retroviral therapy (ART). Evaluation of care and treatment services for children living with HIV at ART centers from public sector in Myanmar has not done yet.

Methods: A cross-sectional, hospital and clinic-based study applying a mixed-methods design was conducted to identify the situation of adherence to ART among children in Myanmar was done in 2017-2018. Secondary data analysis from ART records covering the period from 2005 to 2016, in-depth interviews with guardians and key-informant interviews with providers were done at 22 public ART centers across the country. Descriptive analysis and Chi-squared test for quantitative data and thematic analysis for qualitative data was done.

Results: A total of 3,277 records were reviewed and age of the children ranged from 0-15 years (mean: 8.8±3.4 years). Mean duration of taking ART was 3.1±2.3 years and many of them (74.1%) have been taking ART for 1-5 years. Retention in ART care at one year was 90.4%. Mean age of children at initiation of ART was 5.4±3.2 years. Mean duration between HIV diagnosis and ART was about 3 months for the children less than 5 years and about 9 months for the older age groups. Nearly 90% of the children had more than 95% adherence to ART within last six months. Considerably higher proportion of children from specialised ART centers had adequate adherence level of 95% than those from non-specialised ART centers (93.1% and 85.7%, p=0.001). Significantly higher proportion of children with more than 5 years duration on ART had better adherence than the children with <1 year duration on ART (94.2% and 84.7%, p=0.001). There was no association between age and sex of children with the adherence status. Providers highlighted that adherence problem was more severe among the children who were not regularly attending the follow-ups and who were orphans. Many guardians expressed that lack of care taker and family’s economic condition were the major challenges hindering for attending regular follow-ups and also for maintaining adherence of the children.

Conclusions: Children from specialized center and children with more than 5 years on ART have better adherence than others. Sustained effort should be made to ensure good adherence level among children on ART from public sector in Myanmar.

Pediatric HIV care at an ambulatory health center in Maputo, Mozambique

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Introduction: In Mozambique, 170,000 children are living with HIV (2017), though antiretroviral treatment coverage in this population is just 51% and retention in care (68%) is poor (Mozambique HIV National Program Report, 2018). In a recent study describing genotypic resistance among pediatric patients from six primary health centers in Maputo, Mozambique, the prevalence of virologic failure (36%) was also high (Vaz, 2018). Taken together, these numbers fall short of the UNAIDS 90% goals for antiretroviral coverage, retention in care and virologic suppression. We report outcomes of a
pediatric cohort from a Ministry of Health-Medecins Sans Frontieres supported primary health care facility in urban context in Maputo, Mozambique.

**Methods:** The Centro Saude de Alto Mae (CSAM) and Centro Referencia de Alto Mae (CRAM) is a combined ambulatory primary care and referral center for patients with advanced HIV infection, as for third line antiretroviral treatment. While CSAM serves its immediate catchment area, CRAM is a city-wide referral center for patients with CD4 count < 100 cells/µL, severe opportunistic infection or other specified medical conditions. We conducted a cross-sectional analysis of children 0-14 years of age receiving care in either clinic, as of January, 2019.

**Results:** The pediatric cohort (n=471) included 330 (70%) patients from CSAM and 141 (30%) patients from the referral center (CRAM). The median age (n=471) of children was 10.0 years (IQR 7.1, 12.2) and 232 (49.3%) were female. All patients were receiving antiretroviral treatment (ART): 320 (68%) on NNRTI-based regimen, 142 (30%) on PI-based regimen, and 6 (1.3%) on INSTI-based regimen. Median CD4 was 679 cell/µL (IQR 388,948), with a lower median CD4 of 451 cell/µL (IQR 166-662) for patients on INSTI-based regimen. Overall 12-month retention in care was 81.4%. With respect to virologic outcomes, 23.3% of children had a viral load greater than 1,000 copies/ml at their most recent measurement.

**Conclusions:** We report high 12-month retention in care within this pediatric cohort, which is especially noteworthy in the context of significant socioeconomic barriers experienced by many children in Mozambique. In addition, this cohort experienced lower rates of virologic failure in all regimens than have been previously reported among children in Maputo. Nonetheless, this indicator remains short of the UNAIDS 90% goal for virologic suppression among patients receiving ART. Innovative approaches to pediatric care, along with further research to better understand causes of virologic failure, including but not limited to treatment resistance and medication adherence, are urgently needed.

**51**

**Virus Load Differentiated Care of HIV-1 infected children and adolescents is feasible and effective in remote rural Zimbabwe**

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**Background:** There are many challenges to ART delivery to children and adolescents in remote communities of rural Africa. The Zimbabwe Population Based HIV Impact Assessment (ZIMPHIA), found rates of Virologic suppression (VS) < 50% among children and adolescents on ART (in 2015-2016). We hypothesized that community-based virus load differentiated care (VLDC), could more readily identify virologic failure (VF), prompting a switch to second-line ART to achieve virologic suppression (VS) among children in rural Africa.

**Materials and Methods** A retrospective longitudinal study of 306 children and adolescents on ART was conducted from 2016 to 2018 in rural Hurungwe Province. ART and VLDC were provided, bimonthly, at youth friendly support clinics or by active outreach to 8 rural ART sites coordinated by Chidamoyo Mission Hospital. Virus load monitoring by central laboratory Roche amplior testing was introduced in 2016. Near POC SAMBA (simplified amplification-based assays), Diagnostics for the Real World, Sunnyvale California were implemented at Chidamoyo hospital in 2018. Virologic failure (VF) was defined as ≥ 1,000 copies/ml. We assessed virologic suppression (VS), defined as < 1,000 c/ml as determined by Roche amplrior at a regional (Provincial) laboratory in 2016 and by POC Samba or Roche amplrior in 2018. A logistic regression model including demographics, care-givers and treatment regimens assessed risks for VF and loss to
Results: Of 306 children and adolescents on ART in 2016, 208 (68%) had viral load <1000 copies/ml. Virologic failure was significantly associated with lower CD4 cells (p<0.001) and non-parental care-givers (p=0.04). Follow-up in 2018 demonstrated that 42 (14%) were no longer receiving care at Chidamoyo and the eight outreach sites, 17 (6%) were lost to follow up (LTFU) and 2 had died. Older age was significantly associated with LTFU (p=0.030). Fifty-eight (22%) had switched to second line in 2017. Of the 264 retested in 2018, 212 (81%) had viral load <1000 copies/ml. The VS rates on first and second line in 2018 were 82% and 72%, respectively. Virologic suppression increased from 68% in 2016 to 81% in 2018 (P < 0.001) following the introduction of VLDC and second line treatment.

Conclusions: Second line ART in children and adolescents with virus load differentiated care is associated with better virologic suppression rates in this vulnerable population. Provision of VLDC including near POC virus load monitoring in remote rural setting is feasible and effective.

Retention and Viral Suppression of Children and Adolescents in HIV Care, Zimbabwe

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Background: Retention in care of children and adolescents is critical in the HIV care continuum with the main goal of achieving 90% viral load suppression. Zimbabwe has an HIV prevalence of 1.8% among 0-14-year olds. The main objective of the assessment was to determine the characteristics, retention and clinical outcomes of children and adolescents currently enrolled in HIV care.

Methods: Retrospective abstraction of routine patient data from EPMS of children and adolescents aged 0-19 enrolled into HIV care from 2004-2018 at 21 purposively selected facilities with > 50 adolescents and children on ART to represent 10 provinces. Retention in care was defined as in care being less than 90 days from last scheduled appointments and viral load as suppressed if viral load is <1000 copies/ml. Data was entered in MSExcel and analyzed using Stata Version 13.

Results: Overall, of the 6,348 children and adolescents living with HIV enrolled in care from January 2004 to May 2018 who had documented dates of ART initiation, 52% were male. Median age at enrolment was 6 years [IQR: 2.03 – 11 years]. Over the period children aged below 5 contributed 40%(2519/6348) on the total enrolments. A five year projection based on service utilization data indicated a proportional increase of the 15-19 year age group from 28% in 2017 to 48% in 2022. Forty three percent (2,710/6,348) of children and adolescents were enrolled in HIV treatment following HIV testing accessed due to illness, and this was more pronounced among those aged 5-9 and 10-14 where hospital illness accounted for 45.7% and 47.8% respectively. About 4 in 10 [41.2%, 95%CI: (40 -42.5)] children and adolescents were at WHO clinical stages 3 and 4 at enrolment in HIV treatment. Median time between HIV diagnosis and ART initiation was 46 days (IQR: 3 -338 days).Further analysis showed an increase in the proportions initiated on ART between 0-30 days after 2016 as compared to those who were initiated after 30 days largely attributed to the Test and Treat strategy rolled out in 2016. A total of 5,105 children and adolescents were retained in care as of May 2018. 51.2% (2,615/5,105) were females, 3.3% (210/6348) were LTFU, 12% (764/6348) transferred out to other facilities and 1.6% (101/6348) were documented as died.

More than half of those retained in care 56% (2856/5105) had no documented VL. Of those with at least one VL documented, 35.3%
(792/2249) had a VL >1000 copies per ml whilst 60% (1351/2249) had a suppressed VL and 4.6% (103/2249) had pending results. Among those with VL > 1000 copies/ml, 76% (599/792) managed to have a subsequent/ or second Viral load assessment.

**Conclusion:** We document high retention of children and adolescents in HIV care in routine public health settings. There is an urgent need to scale up viral load access, repeat VL in case of a high VL and documentation of clinical actions taken among children and adolescents with unsuppressed VL.

53

This abstract was withdrawn.

54

**Virological suppression among HIV infected adolescents and youths receiving ART in the National teaching and referral hospital in Kenya**

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**Background:** HIV virological suppression is poor among the adolescents and youths which may be related to several factors including adherence to antiretroviral therapy. This study aimed to determine the HIV virological response and the associated risk factors among adolescents and youths on ART.

**Methods:** This was a cross-sectional study among adolescents and youths aged 10 to 24 years in Kenyatta National Hospital who were on ART for at least six months. Patient characteristics were captured in a questionnaire and viral load was abstracted from electronic medical records. Viral suppression was presented as a proportion based on viral load less than 1000 copies per milliliter of plasma. Viral suppression rate was associated with categorical independent factors using chi square test and means were compared using independent T-test.

**Results:** The mean age was 17 years (SD 4.3 years) and 55.6% were females. The median CD4 count was 573 cells per micro liter of blood (IQR: 344-1780). A total of 227 (74.2%) HIV infected adolescents and youths were virologically suppressed (viral load less than 1000 copies/ml blood). As compared to children 10-14 years old who had 83.2% suppression rate, adolescents 15-19 years had poorer suppression rate at 69.6% [OR 0.5 (95% CI 0.2-0.9), P= 0.022]. Similarly youths 20-24 years had a lower suppression rate at 70.8% compared to the children [OR 0.5 (95% CI 0.2-0.9), P= 0.022]. Only 56.2% of the study participants had undetectable HIV viral RNA (as per UNAIDS 90-90-90 strategy). RNA Viral suppression rate was lower among ART defaulters (47.2%), those defaulting clinic appointments (51.7%) and those not honoring ART refill (50%). Majority of the participants (86.3%) were in WHO stage I whereas 2% were in WHO stage IV. Among those with unsuppressed viral loads, 20.7% had been diagnosed with Tuberculosis. None of the study participants had Hepatitis B virus infection.

**Conclusions:** HIV viral suppression among adolescents and youths was low and even much lower among 15 to 24 year-olds. Poor ART adherence and non-compliance to clinic appointments increased the risk of poor virological response.
Mental health and its association with metabolic outcomes in youth living with perinatally acquired HIV in the Cape Town Adolescent Antiretroviral Cohort (CTAAC).


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Background: The Cape Town Adolescent Antiretroviral Cohort has demonstrated that youth living with perinatally infected HIV (YLPHIV) have poorer mental health (MH) compared to age- and sex-matched HIV-uninfected (HIV-U) youth. While some adult HIV studies have linked poorer MH to adverse metabolic outcomes, this association has not previously been explored in YLPHIV.

Method: We investigated the association of MH measures with metabolic outcomes including insulin resistance (IR), lipids [Total cholesterol (TC), triglycerides (TG), high density lipo-protein (HDL), low density lipo-protein (LDL)] and albumin. The Beck Youth Inventories were used to assess depression, anxiety, anger, disruptive behaviour (DB) and self-concept, Children’s Motivation Scale to measure motivation levels, Conner’s Parent’s Rating Scale to assess ADHD, and Child Behaviour Checklist (CBCL) to measure internalizing (CBCL-IP), externalizing (CBCL-EP) and total competence (CBCL-TCP) problems. Body mass index z-scores (BMIZ) were calculated using World Health Organization references and abnormal lipids were defined using the National Health and Nutrition Examination Survey. Linear regression models were fit to assess the adjusted association of MH measures with each metabolic outcome.

Result: Overall, 204 YLPHIV were enrolled (median age 10.4 years, 49% male, 10.4% had CD4 count <500 cells/μL, and 82.3% with viral load <50 copies/ml at enrolment). Mean age at antiretroviral therapy (ART) initiation was 3.4 years, mean duration on ART 7.2 years with 53% and 43% on non-nucleoside inhibitor- and protease inhibitor-based ART respectively. Mean BMIZ was -0.12 and median albumin 41g/l. Sixteen percent had hypercholesterolemia, 19% hypertriglyceridemia, 7% high-LDL and 5.3% low-HDL. Clinically significant CBCL-TCP, CBCL-IP and CBCL-EP were found in 39.7%, 30.4 and 15.7% respectively, anxiety in 11%, depression in 6.4%, and DB in 4%.

Higher levels of anger were associated with higher TC and LDL (β=0.010, p=0.041 and β=0.012, p=0.048 respectively), higher DB with higher LDL (β=0.010, p=0.043) and higher CBCL-IP with low albumin (β=-0.067, p=0.052) after adjusting for age, sex, and BMIZ.

Conclusion: This is the first study to investigate the association of MH problems with metabolic profiles among YLPHIV. Greater anger and disruptive behaviour were associated with increased lipid concentration in YLPHIV in South Africa. Further longitudinal studies are needed to evaluate whether modification of MH factors may have long-term effects on metabolic profiles.

Vertically-infected adolescents have poor viral suppression compared to horizontally-infected youth


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Introduction: Sustained viral suppression in adolescents and young adults (AYA) is necessary to optimize benefits of antiretroviral
therapy (ART). Kenya is among the first African countries to launch routine viral load (VL) testing. Using program data, we examined correlates of viral suppression among AYA in HIV care.

Methods: We abstracted electronic medical record and VL data from AYA ages 10-24 at 24 HIV clinics in Kenya from a 15-month period. VLs retrieved from a national database were linked with individual-level data. Viral suppression was defined as last VL<1000 copies/ml (c/ml) among AYA on ART ≥6 months. Vertical infection was defined as age at HIV diagnosis <15 years. Log-binomial regression models estimated adjusted risk ratios (aRRs) and 95% Confidence Intervals (CIs) between correlates and VL suppression at last measure, accounting for clustering by facility. Correlates of sustained VL suppression, defined as any two consecutive results <1000 c/ml, were compared to AYA with suspected virologic failure, or two consecutive results ≥1000 c/ml.

Results: Of 4,335 AYA on ART ≥6 months, 2,085 (48.1%) had VL results; 30.1% were ages 10-14, 23.6% 15-19, and 46.3% 20-24 at first VL. Most were female (70.3%), had vertically acquired HIV (59.7%), initiated ART before age 10 (33.7%) or at ages 20-24 (30.3%), and were on 1st-line regimens (96.4%). Overall, 76.0% were virally suppressed. In multivariable models adjusted for gender, age, time on ART, and pregnancy, horizontally acquired HIV was associated with higher prevalence of viral suppression compared to vertical acquisition (aRR 1.36, 95%CI: 1.20-1.54). Older age at ART initiation was associated with higher prevalence of VL suppression vs. initiation at <10 years (20-24 aRR 1.16, 95%CI:1.03-1.31; 15-19 aRR 1.11, 95%CI:1.00-1.23). Among 525 AYA with 2+ VLs, 63.8% had sustained suppression, 14.9% had only 1 VL suppressed, while 21.3% had suspected VL failure. In adjusted regression models, horizontal acquisition remained associated with sustained VL suppression (aRR 1.77, 95% CI 1.17-2.67).

Conclusion: Nearly 25% of AYA had unsuppressed VL in this programmatic analysis. Vertically infected adolescents had the lowest likelihood of sustained VL suppression. Targeted treatment approaches and improved VL monitoring are critical to achieve 95 percent viral suppression among AYA by 2030.

57

Drug resistance among youth with confirmed virologic failure on first line and response to second line ART in Harare, Zimbabwe.

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Background: Barriers to sustainable virologic suppression in the treatment of HIV infected youth in sub-Saharan Africa include HIV drug resistance (HIVDR), inadequate adherence and limited fixed dose combinations (FDC) as treatment options. We determined patterns of HIV drug resistance mutations (DRMs) among HIV-1 infected young people with virologic failure (VF) on first line non-nucleoside reverse transcriptase inhibitor (NNRTI) based treatment in a setting of optimized adherence counseling and support. Virologic response, after genotyping and then switching to second line boosted protease inhibitor (ATV/r) based treatment were assessed.

Materials and Methods: HIV infected youth (16-24 years old) with confirmed first line VF were genotyped by Sanger sequencing, switched to ATV/r, 3TC and a nucleos(t)ide. Virologic outcomes were determined by 6 monthly virus load by COBAS® Ampliprep/COBAS® Taqman® HIV-1 Test, v2.0.
Confirmed Virologic failure (cVF) was defined as 2 sequential RNA values > 1,000 copies/ml (c/ml), persistent low-level viremia (pLLV) as < 50 c/ml and Virologic Suppression (VS) as < 50 c/ml at ≥48 weeks. Geometric mean titers (GMT) of HIV RNA were expressed as the average of log10 copies /ml. Fisher exact test and Anova were used to test differences between and among groups respectively (Stata 14).

Results: Among 726 young people on first line ART > 2 years at the Newlands clinic, 74 (10%) demonstrated cVF in 2016. DRMs to NNRTI were identified in 72/74 (97%), NRTI DRM in 62/74 (84%) of whom 31 (40%) had K65R, 57 (72%) M184V and 24 (32%) thymidine analog mutations (TAMS). Second-line ATV/r and a new/recycled nucleos(t)ide + 3TC was provided to 62 (86%). Of these, 28/62 (45%) had both K65R and M184V. Mean(±SD) weeks of follow up was 66(±2.1). Those who switched to a new nucleos(t)ide had a significantly greater rate of VS, 32/37 (86%) vs those who continued on the same nucleos(t)ide 14/23 (61%) (p=0.03). Only 7/62 (11%) had cVF (GMT of 4.6 log copies/ml), 7 (11%) had pLLV (GMT of 2.6), while 46/62 (77%) maintained VS. Analysis of nucleoside resistance mutations at the switch to a protease inhibitor (PI) demonstrated higher frequency of M184V; 40/46 (87%) in VS against 14 (57%) in those with VL > 50 c/ml, (p=0.06). K65R was present in only 1/7 (14%) of cVF, 5/7 (70%) among cLLV and 20/46 (53%) in those who achieved virologic suppression (p=0.1) suggesting that VF is associated with inadequate adherence or potency of nucleos(t)ide(s).

Conclusion: With enhanced adherence counseling and aggressive clinic-based support, only 10% of HIV infected youth on first or second line ART had cVF. Switched to a second line ATV/r based regimen for 48 weeks, 89% achieved VS to <1000 c/ml, and 77% to < 50 c/ml. Persistent LLV requires extended follow up and further investigation. Introduction of more potent tenofovir alafenamide (TAF) and emtricitabine (FTC) in FDC may enhance sustainable suppression of HIV among NRTI experienced second line youth in public health ART programs.
Abstracts

copies/ml. VL <1000 copies/ml was not statistically different between females and males (83% vs 81%; p=0.130). A higher proportion of adolescents aged 10-13 years had VL<50 copies/ml (78%) compared to those aged 14-16 and 17-19 years (72% and 68%), respectively (p=0.008).

Conclusions: Though findings represent less than half of ALHIV on ART in Manzini, six-monthly VL testing and viral suppression among these adolescents are sub-optimal for individual patient outcomes and, for epidemic control. Lower rate of suppression of <50 copies/ml among older ALHIV is also of concern as these might be sexually active and could be a source of new HIV infections. Adolescent focused interventions are needed to improve VL testing coverage and to ensure undetectable VL is achieved and maintained in this critical sub-population. In addition, there is an urgent need to accelerate optimization of ARV drug regimens for adolescents.

Second-line Antiretroviral therapy failure and characterization of HIV-1 drug resistance patterns in children in Mali

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Introduction: In recent years, children born to HIV-infected mothers are receiving antiretroviral treatment (ART) with limited or no virologic monitoring which increases the likelihood for development and accumulation of drug resistance mutations which itself may limit the effectiveness of future ART. The objective of this study was to evaluate the prevalence of resistance mutations in children infected with HIV-1 experiencing virological failure to second-line ART in the Pediatric Department of Gabriel Touré Hospital in Mali.

Methods: Children aged from 5 to 18 infected with HIV-1 on second-line antiretroviral therapy and whose viral load was greater than 1000 copies / ml after observance reinforcement were enrolled. The protease and reverse transcriptase genes were sequenced with ViroSeq®. The results were interpreted according to the last version of the Stanford algorithm in 2018. The study was approved by the Ethics Committee of the Faculty of Medicine and dentistry, University of sciences, techniques and technologies of Bamako (Mali).

Results: Among 216 children, 33 (15.3 %) who had a viral load (VL) > 1000 copies / ml in second line were recruited into the study. Plasma viral load median was 77 000 copies/mL [IQR (28 000-290 000)] and the median CD4 cell count was 310 cells / mm3 [IQR (152-412)]. The median age was 12 years; 48.5% of patients were treated with a combination of stavudine/lamivudine/nevirapine (Triomune®) for first-line treatment and 60.6% by abacavir/lamivudine/lopinavir/ritonavir for the second line ART. The median treatment duration was 8.5 years [range, 3-13]. Among the 33 children who failed their treatment, the predominant HIV-1 subtype was CRF02_AG (66.7%). The prevalence of resistance to ART classes was 60.61% (20/33) to NRTIs, 54.51%  (18/33) to NNRTIs and 51.52% (17/33) to PIs. 90.9% of our patients were exposed to LPV/r but only 15.2% (5/33) develop resistance to LPV/r.

Conclusions: This study demonstrated that lopinavir/ritonavir remains active in most patients after second-line ART failure. In children failing to second line ART, a particular attention should be paid about their ART and adherence history when considering the next treatment option.
Dysfunctional natural killer cell subsets correlate with disease progression in HIV-infected Kenyan children

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Natural killer (NK) cells are innate immune cells with cytotoxic and anti-viral effects. NK cells contain viral infection and shape adaptive immune responses via cytotoxic activity and inflammatory cytokine secretion. HIV+ adults display depleted functional and expanded dysfunctional NK cells, yet there is limited data in children. We investigated NK cell frequencies and exhaustion in HIV+ children and correlations with disease progression and adaptive T follicular helper (Tfh) and B cell subsets.

The study cohort included 77 perinatally-infected HIV+ Kenyan children (43 untreated (ART-) and 34 on antiretroviral therapy (ART+)) and 43 HIV uninfected-unexposed controls between ages 5-19 years. NK cells (functional: CD16+CD56+ (NK F1), CD16-CD56++ (NKF2); dysfunctional: CD16+CD56- (NKDF)), exhaustion markers (PD-1, Tim3, CD160) and peripheral Tfh and B cell subsets were evaluated by flow cytometry.

HIV+ have decreased NK cell frequencies compared to HIV- children (ART- p=0.02; ART p=0.0001). ART+ have lower functional NK cells compared to HIV- (NKF1 p<0.0001; NKF2 p=0.01) and ART+ (NKF1 p=0.0006, NKF2 p=0.0001) and higher NKDF cells than HIV- and ART+ (p=0.0001). NKF1 and NKDF2 cells correlated inversely with HIV VL (NKF1 p=0.0002; NKF2 p=0.03) and directly with %CD4 (NKF1 p=0.004; NKF2 p=0.003). NKDF correlated directly with HIV VL (p<0.0001) and inversely with %CD4 (p<0.0001). In prospective analysis, NKDF lowered after 1 year of ART (p=0.001). PD-1+ and CD160+ NK cells correlated inversely with NKF1 cells (PD-1 p=0.0004; CD160 p=0.0002) and directly with NKDF cells (PD-1 p=0.001; CD160 p<0.0001).

Low NKF1 and high NKDF correlated with decreased (p<0.0001) and activated (p=0.01) Tfh cells. Low functional NK cells and high NKDF correlated with decreased naïve (NKF1 p<0.0001; NKDF p<0.0001) and resting B cells (NKF1 p=0.003; NKDF p=0.01; NKDF p<0.0001) and increased activated (NKF1 p=0.02; NKDF p=0.003; NKDF p<0.0001) and tissue-like memory B cells (NKF1 p<0.0001; NKDF p=0.04; NKDF p<0.0001).

HIV+ children have a dysfunctional NK cell profile linked to advancing HIV disease. The loss of functional NK cells correlates with NK cell exhaustion and activated Tfh and B cell states. Restoring NK cell perturbations is critical for therapeutic HIV vaccine strategies bridging innate and adaptive immunity.

Data review and Support supervision as a Quality Improvement approach to improve Viral load Access and Suppression (treatment outcomes) for children and adolescents living with HIV in Uganda

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Background: Viral load (VL) testing has been available and free to patients at all public health facilities in Uganda since 2014. Currently, most (90%) facilities offering ART now provide this service. However, only 69% of the 67,135 HIV-positive children (CLHIV <15yrs) currently in care receive a VL test at intervals specified by the national guidelines, compared to 88% of 1,075,836 HIV-positive adults in care. In order to attain 90-90-90 global targets, VL
coverage needs to improve significantly and children need to be on optimal regimens.

**Methods:** Routinely collected programmatic records of children (<10yrs) and adolescents (10-24yrs) was used to determine the trends of viral load suppression, by age group, ART regimen and repeat testing over time from January 2016 to December 2018.

**Results:** In 2016-2017, national VL testing coverage among children <15yrs significantly increased in Uganda from 50% to 69%. For all ages 0-24, suppression rates at first VL test improved only negligibly, from 78% to 79%. Among children and adolescents who were unsuppressed at first VL test and required to return for a repeat test following 3 months of intensive adherence counselling, the return rate improved from 14% to 21%, and suppression rates during repeat testing improved from 31% to 37%. The currently preferred first line regimen for infants and children (0-<10), ABC+3TC+LPV/r, had suppression rates of 69%. For adolescents (>=10yrs), the preferred first line regimens are TDF-3TC-DTG or TDF-3TC-EFV, with suppression rates of >85% across all 3 years of analysis.

**Conclusions/Next steps** To meet the 90-90-90 targets, the Uganda Ministry of Health (MOH) has adopted a VL Change Package that specifies interventions intended to improve pediatric VL testing coverage, balance resource availability and prioritize areas with the greatest gaps. Closer tracking and follow-up of unsuppressed patients is needed, as well as capacitation among healthcare workers on VL results interpretation and response. Additionally, targeted focus on paediatric and adolescent patients is needed to improve viral suppression in these groups, as adult viral suppression rates remain disproportionately higher at 90%. Impact of the implementation of the VL change package on viral suppression rates for pediatric and adolescent patients will be further analyzed.

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**62**

**Time to viral load suppression and rebound among Canadian infants and children initiating cART in the Early Pediatric Initiation Canada Child Cure Cohort (EPIC4) cohort**

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**Background:** Sustained viral suppression (VS) after early initiation of combination antiretroviral therapy (cART) is a key to limiting the viral reservoir in children. However, the time to, and durability of, VS among early-treated children has not been well described.

**Methods:** Using data from the EPIC4 pediatric HIV cohort, the time to 1) VS (defined as 2 consecutive viral loads (VL) measured undetectable after cART initiation) and 2) Viral rebound (VR) (determined as a single VL measure >10,000 copies/ml after VS achieved) were determined using Kaplan-Meir survival estimates.

**Results:** Out of 226 children enrolled in the EPIC4 cohort, 130 (57.5%) received uninterrupted cART, of whom 52% were initiated on PI-based therapy, 43% on NNRTIs, and 5% on INSTIs. Age at cART initiation was <12 months (28%), between 1-5 years (26%), and greater than 5 years of age (45%). Overall, 127 (97.7%) of those for whom cART was not interrupted achieved VS at any time after treatment initiation. There was a significant difference in median time to viral suppression according to age at cART initiation (shortest among children over 5 years of age initiating cART vs. younger children vs. infants, 0.43 vs. 1.57 vs. 1.17 years, p=0.007), and type of first cART regimen (INSTI vs. PI vs. NNRTI, 0.2 vs. 1.1, and 1.3 vs. 1.2 years respectively, P<0.001). Six months after cART initiation, only 16% of infants had achieved VS, vs. 20% of children 1-
5, and 62% of children over age 5. Thirty-six months after cART initiation, 13% of all children who achieved VS had a their first VL rebound; the risk was lowest among younger children (1-5 years) vs. infants, and older children (17% vs. 16% vs. 24%. P<0.001). Risk factors for VR included gender (male vs. female, 67% vs 33%, p=0.02), recipients of welfare (93% vs. 7%, p=0.02), and being under child protection services (53 vs. 47%, p=0.07).

Conclusion: There was a significant difference time to VS and VR according to age at cART initiation, with longer time to both VS and VR among infants as compared to older children. Social factors, including family disruption and socio-economic status, were further predictors of viral rebound in all age groups.

63

Children’s perceptions of HIV Cure Research: An end of study assessment of the Early Pediatric Initiation, Canada Child Cure Cohort (EPIC4) study

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Background: While the field of pediatric HIV cure research has expanded in recent years, little is known about participants’ perceptions and understanding of such research, or motivations for participating. The objective of this study was to document children’s experiences of participating in an HIV “cure” study, assessing HIV-1 reservoirs.

Methods: The EPIC4 study is a national prospective cohort study of HIV-1 reservoirs in Canadian children. At enrollment, written informed consent was obtained from parents, and assent from children. Study visits were every 3-6 months throughout the 4-year period, and included supplementary blood draws (maximum 100 ml) at the time of routine blood sampling for reservoir assessment. At their last study visit, participants at one site (CHU Sainte-Justine, Montreal, Canada) were asked to complete a standardized questionnaire about their experience. For children who remained undisclosed of their HIV status, this was completed by a parent.

Results: By December 2018, 23 participants had completed the questionnaire: 16 adolescents (age range 15-22 years), and 7 adult parents of children (age range 7-14 years). Overall, 13% could not explain the study’s purpose, 52% mentioned research about HIV, and 35% alluded to research towards an HIV cure (“to find a cure”, “eliminate HIV completely”); none mentioned the word “reservoir.” Only 2 could name the study (EPIC4). When asked why they chose to participate, the majority (78%) explained that they did it to help others living with HIV; other common answers included spending extra time with the clinic team (57%) and the financial compensation provided (48%). While 61% said there was nothing negative about their study experience, 18% listed the blood draws (“too much” or “too painful”), and 21% listed other reasons (including waking up early for clinic, distance from home to clinic). Finally, when asked if they thought an HIV cure would occur in their (or their child’s) lifetime, 74% responded yes, 17% responded they weren’t sure, and only 1 responded no.

Conclusion: Despite a standardized informed consent/assent process at enrollment, not all participants recalled study objectives at conclusion. These results suggest the need for ongoing knowledge translation efforts with pediatric participants and their parents throughout the course of a long-term study. Further probing of participation experiences may also help guide future HIV cure study design and patient engagement.
**Integrating Health Services Provision - Improving HIV testing and treatment for children under five years referred to rural health facilities with Severe Acute Malnutrition**

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**Background:** With an HIV prevalence of 3.5% in children under five years, Zimbabwe is committed to the UNAIDS 90-90-90 targets. Children living with HIV being treated for severe acute malnutrition (SAM) have a significantly higher risk of dying than those uninfected. Yet the baseline revealed only 65% of children referred to rural health centre (RHC) with SAM were being tested for HIV and only 35% of those testing positives were being initiated on ARVs. Our UNICEF funded project in 11 districts of Zimbabwe focussed on integrating service provision for these vulnerable children.

**Methods:** We provide an analysis of routine facility data at 228 health facilities in 11 Districts of Zimbabwe from January-September 2018. Age and sex disaggregated data on rates of SAM diagnosis, HIV tests and yields and treatment outcomes were entered into MS Excel and analysed using StataV13, with chi-square tests for differences in proportion.

**Results**

Between January-September 2018, a total of 2251 children under 5 years were diagnosed with SAM, which comprised of 46% (1033/2251) boys and 54%( 1218/2251) girls. The percentage of children with SAM tested for HIV in the 11 districts increased from 65% to 90.5%. ART initiation rates among children testing positive increased from 35% to 50%. The prevalence of children with SAM living with HIV among those tested was 6.5%. While girls represented had a greater absolute number of SAM diagnoses and HIV tests, boys had a significantly higher HIV test yield than girls (8% vs/ 5% respectively, p< 0.0001)

**Conclusions:** Integration of health service provision reduced missed opportunities for HIV testing and treatment of HIV infected children with SAM. Testing rates and linkage to ART among HIV positive children under 5 improved, however, ART initiation rates remain suboptimal. Gender disparity in HIV test yields requires further research to better understand transmission timing and mode of transmission (antenatal, delivery, feeding practices) as to inform evidence-based EMTCT efforts in Zimbabwe.

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**Adoption of 2018 WHO recommendations on Antiretroviral Therapy preferred First line in Children and Adolescents**

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**Background:** Since 2013 WHO recommended LPVr-based 1-line antiretroviral treatment (ART) for children younger than three years of age. Uptake of this recommendation has been slow with most children in high burden countries still receiving suboptimal regimens, despite the high level of Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTI) resistance. The 2018 WHO ARV guidelines recommend using dolutegravir (DTG)-based regimen as preferred 1st-line therapy for all children with approved DTG dosing. Current dosing information allow use of 50 mg DTG tablets from 20 kg, with LPVr solid formulations preferred for children under 20 kg. These guidelines also support the transition of stable children to optimal regimens and formulations. We here present the status of adoption of these recommendations as of March 2019.
Methods: Starting in September 2019, WHO has provided enhanced technical assistance to support adoption and adaptation of WHO ARV guidelines in key priority countries. Paediatric and adolescents technical working groups (TWG) meetings were convened in collaboration with national governments, to review the use of paediatric ARVs and identify opportunities to improve treatment options for children and optimize national ARV formularies. Group discussion among national stakeholders led to identify transition strategies that were shared with national guidelines committees.

Results: Over 7 months, TWG meetings were convened for ten countries in Sub-Saharan Africa, representing 50% of children living with HIV globally.

DTG was adopted in all countries, but with different approaches. Nine countries decided to introduce DTG-based regimens for children from 20 kg and with the use of fixed dose combination Tenofovir-Lamivudine-Dolutegravir from 30 kg. Following a critical review of global and national NNRTI resistance data, as well as rates of virological suppression, all TWGs agreed to actively phase-out NVP and introduce LPVr solid formulations (pellets or granules or paediatric tablets based on weight and age) for children below 20 kg.

All TWGs agreed on transition to DTG for children over 20 kg and for transition to LPVr for children on NVP below 20 kg. In 5 (5/10) countries upon pre-transition viral load measurement and in two cases only where viral load is feasible.

The use of DTG in adolescent girls posed the biggest challenge to the decision-making process due to the possible teratogenic risk of DTG-exposure during the peri-conception period in the context of poor access to sexual and reproductive health services for adolescents. All countries acknowledged the importance of providing DTG to adolescents and agreed on the need for improving access for these services. Countries with more conservative approach considered to use of DTG up to 15 years and then switch to EFV or combine DTG with contraceptives from 15 years when teenage pregnancy is more frequent.

Conclusion: Enhance technical assistance efforts enabled rapid adoption and adaptation of new WHO ARV guidelines, promoting initiation of active transition to optimal regimen in 2019 for ten countries accountable for half of children living with HIV globally. However, implementation of these guidelines will remain challenging unless key bottlenecks such as supply constrains for LPVr solid formulations and lack of access to SRH services for adolescents will be resolved.

Viral suppression, ART interruptions and switching among children with HIV on ART in KwaZulu-Natal, South Africa, 2010-2016

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Background: Despite recent reductions in the rate of vertical transmission of HIV, high antenatal seroprevalence in South Africa results in a substantial number of infants still being born with HIV. We describe viral suppression, ART interruptions and switching among these children following ART initiation.

Materials & Methods: Data on all children born between 1st June 2010 and 31st December 2016 and on ART were extracted from TIER.net (the national Department of Health ART surveillance system) from the 17 clinics in the Hlabisa health sub-district, KwaZulu-Natal, South Africa. Follow-up data were available to 10th July 2017. A deterministic and probabilistic data linkage algorithm was used to identify children who transferred between clinics.
Among children with known date of ART initiation (who initiated ART within the sub-district), initial ART regimen and the proportion who were CDC immunological stage 3 (defined as CD4<26%/<750 cells/mm3, <22%/<500 cells/mm3 and <14%/<200 cells/mm3 for those aged <1, 1-<6 and ≥6 years respectively, allowing a window of 6 months before and 1 month after initiation) at initiation were summarised.

The frequency of viral load (VL) monitoring, the proportion of children suppressed (≤400 copies/mL) at last measurement, interruptions to ART (calculated based on the duration of prescriptions given at last visit) and switches to second-line (defined as a change to the third agent and of nucleoside reverse transcriptase inhibitor) were summarised.

**Results:** Among 619 children ever on ART, the median (IQR) duration of follow-up was 1.2 (0.3, 3.2) years. Among 466 (75%) with a known date of ART initiation the median (IQR) age at initiation was 10.7 (4.2, 21.0) [0.1, 78.4] months, and 154/229 (67%) of those with an available CD4 measurement were classified as CDC immunological stage 3. Among 447 with a known initial regimen: 308 (69%) initiated on a lopinavir/ritonavir-based regimen (including 4/10 (40%) of those aged <14 days), 136 (30%) on efavirenz-based (including 26/66 (39%) of those aged <3 months), and 3 (1%) on nevirapine-based regimens.

The median (IQR) number of VL measurements per year was 0.6 (0.4, 0.9), varying by clinic from 0.2 to 2.3. Among 277 children with ≥1 VL recorded, 194 (70%) were suppressed at last measurement.

318 (51%) children had an interruption to ART of >1 month, and 38 (6%) of >6 months. Among 447 with a known initial regimen, 42 (9%) switched to second-line, with median time to first switch 2.0 (0.9, 3.8) years.

By the end of the time period, 304 (49%) children were still in follow-up, 119 (19%) had moved to a clinic outside of the sub-district, 163 (29%) were lost-to-follow-up and 33 (5%) were known to have died (median age at death 9.1 (6.7, 16.6) months), with an overall mortality rate of 2.8 (2.0, 4.0) per 100 person-years.

**Discussion:** Sub-optimal regimen choices were observed in TIER among young infants, although data quality is unclear. Half of children experienced an extended interruption to ART, with high loss-to-follow-up and mortality a cause for concern.

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**67**

**Adolescent extrapolation of Efficacy and Safety for Dolutegravir (DTG) 50 mg/ Lamivudine (3TC) 300 mg Fixed Dose Combination (FDC) tablet**

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**Background:** A DTG 50mg/3TC 300mg FDC tablet is under development as a complete, once-daily 2-drug regimen (2DR) for HIV-1 infection. Two identical, double-blind Phase 3 trials GEMINI-1/-2 showed non-inferior efficacy and similar tolerability profile of DTG+3TC single entities (SEs) administered concurrently to a DTG + tenofovir/emtricitabine regimen at 48 weeks. Extrapolation from adults to pediatrics is an important tool that reduces the need for pediatric efficacy trials and accelerates pediatric drug development. This analysis aimed to provide supporting evidence for the extrapolation of efficacy and safety for the use of the adult DTG/3TC FDC in adolescents (12 to <18 years old) weighing ≥40 kg.

**Materials and Methods:** Consistent with the 2016 EMA “Reflection Paper on Extrapolation of Efficacy and Safety in Pediatric Medicine Development”, the extrapolation framework consisted of a) extrapolation of safety and efficacy between populations from adults to adolescents; and b) extrapolation from the co-administered DTG+3TC SEs used in Phase 3 to the DTG/3TC FDC based on similarity in PK exposures between populations and between formulations. Existing information about the
similarity in disease and treatment effects was systematically collated across the source and target populations. Given that the DTG/3TC FDC tablet strength (50mg/300mg) represents the SEs adult doses already authorized in adolescents ≥12 years old weighing ≥40 kg (DTG) or in pediatric patients weighing ≥25 kg (3TC), a systematic review of the existing PK data for DTG HIV-1 infected adolescents (IMPAACT 1093 study) and for 3TC in children and adolescents (Studies NUCA2002, NUCA2005, PENTA 13, PENTA15, and ARROW) was conducted. Lastly, a single-dose, open-label, crossover bioequivalence and food effect study was conducted to compare the PK of the FDC to the co-administration DTG+3TC SEs using mixed effects modeling to construct the test/reference geometric least squares means ratio and associated 90% confidence intervals of key DTG and 3TC PK parameters.

Results: Literature data indicated that the disease dynamics, the virologic and immunologic principles underlying INSTI and NRTI antiretroviral drug use and the PK/PD relationship are sufficiently similar between adults and adolescents to allow extrapolation, provided that drug exposure is similar across populations. For DTG, the geometric mean AUC(0-24) in adolescents was 46 μg*h/mL and the C24h was 0.902 μg/mL, meeting the predefined targeted PK exposure range from adults receiving DTG 50 mg once daily [AUC(0-24) 37 to 67 μg*h/mL and C24 0.77 to 2.26 μg/mL]. For 3TC, CL/F in adolescents following twice-daily administration was comparable to adult values. Furthermore, data in adults and in children 3 months to 12 years of age showed that the same 3TC total daily dose given once daily produces similar AUC(0-24) values compared to twice-daily dosing. Lastly, the bioequivalence and food effect study provided an acceptable PK bridge between the FDC and the DTG+3TC SEs.

Conclusions: This analysis supports the extrapolation from adults to adolescents and from the DTG+3TC SEs to the DTG/3TC FDC for the use of the once-daily DTG/3TC FDC 50mg/300mg 2DR administered with or without food for the treatment of HIV-1 infection in adolescents (12 to <18 years old) weighing ≥40kg.

68


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Background: To assess factors associated with HIV testing uptake, seropositivity and treatment among children and adolescents (6 weeks-19 years) in the implementation of targeted provider-initiated testing and counselling (tPITC) in Cameroon. Methods: Parents living with HIV/AIDS receiving care at three ART clinics in Cameroon to were invited to have their biological children HIV-tested. Children of consenting parents were HIV-tested and positive cases ART-enrolled. Parental and children-level characteristics associated with HIV testing uptake, seropositivity and ART-enrollment were assessed using bivariate and multivariate analysis.

Results: We enrolled 1236 parents through whom 1990 children/adolescents were recruited for HIV testing. Among enrolled parents, 45.5% (562/1236) tested at least one child and 3.2% (39/1236) were found with at least one HIV-positive child. Among enrolled children/adolescents, 56.7% (1129/1990) tested for HIV and 3.5% (40/1129) tested HIV-
positive. Parental predictors of HIV testing uptake in children/adolescents were female gender (aOR=1.5850); office/students occupation [aOR (office work/students vs none) = 1.9785], and ART duration > 5 years [aOR (ART duration: > 5 years vs ≤5 years)=1.9339]. Children-level predictors of HIV testing uptake was younger age [aOR (0-17 months vs 15-19 years =3.6778)]. HIV-positive and ART-enrolled cases were predominantly found among 5-9 years old children (50.0% and 51.4%) and through parents: of female sex (84.6% and 85.3%), with primarily education (59.0% and 64.5%) and on ART for ≤ 5 years (87.1% and 88.2%).

**Conclusions:** tPITC effectiveness and efficiency need to be improved. Research in the development and validation of a screening tool could be considered for that purpose.

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**Auditory Brainstem Neural Responses in Young HIV-Infected and HIV-Uninfected South African Children**

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**Background:** HIV-related central nervous system disease can be a result of perinatal HIV infection (PHIV) and further, it is possible that antiretroviral therapy (ART) for PHIV could also negatively affect the auditory nervous system. Auditory brainstem responses (ABRs) are used to evaluate the afferent neural integrity of auditory nerve fibers from the cochlea to more inferior portions of the central auditory system, specifically the brainstem. Researchers have shown that HIV+ children have decreased ABR peak morphology and low peak amplitude suggesting a lack of neural synchrony. In fact, even children with an AIDS diagnosis and normal hearing were found to have impaired auditory neural function. The purpose of this study is to evaluate ABR data from South African children who are participating in the Auditory Research in Children with HIV: Cape Town (ARCH: Cape Town) study. ARCH: Cape Town is an ongoing study with the purpose of examining the effects of PHIV and ART on various aspects of the auditory system, from the periphery to the auditory cortex.

**Materials & Methods:** One hundred, twenty-eight children currently have ABR data: 74 PHIV (40 girls); 28 perinatally HIV-exposed, but uninfected (PHEU) (7 girls); and 26 HIV-unexposed, uninfected (HUU) (13 girls). All children were assessed between 11-12 years of age. ABRs were obtained using alternating rarefaction/condensation clicks through insert earphones at a rate of 11.1/sec and at 75 decibels (dB) normal hearing level (nHL). A minimum of 2000 clicks were presented and responses were recorded with surface electrodes attached to the child’s vertex or high forehead, the right and left earlobes, and the center of the forehead (ground). The child was instructed to remain as quiet as possible and that they did not need to respond. ABR latencies, in milliseconds (ms), for peaks I, III, and V were determined as well as peak V amplitude, in microvolts (μV). Peak V latency or amplitude of both ears was compared simultaneously between PHIV and combined PHEU/HUU groups using generalized estimation equation models adjusting for age and sex.

**Results:** For both left and right ears, means (standard deviations) were similar between PHIV children and the combined PHEU/HUU children for: peak I latency (1.53 [0.13] vs 1.51 [0.11] ms); peak III latency (3.68 [0.18] vs 3.73 [0.16] ms); peak V latency (5.51 [0.29] vs 5.51 [0.20] ms); and preliminary peak V amplitude (0.49 [0.19] vs 0.49 [0.18] μV). Peak V latency was 0.13 ms shorter in girls than in boys, but the adjusted mean was similar between PHIV and PHEU/HUU children. The adjusted mean peak I-V interpeak latencies were also similar between the two groups.
Conclusions: In preliminary analyses of the ABR data from ARCH: Cape Town, there were no differences in peak I, III or V latencies between PHIV and PHEU/HUU children. Further, peak V amplitude was also similar between PHIV and PHEU/HUU children. There was no association found between HIV and auditory neural function, such that neural processing of auditory stimuli is similar for the groups at least to the level of the brainstem.

Economic vulnerability, inflammation and immune activation in children living with HIV in Uganda

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Introduction: Economic vulnerability is an important component of the social determinants of health. In Uganda, food insecurity and poverty have been associated with poor virologic and immunologic outcomes in adults and youth living with HIV. Here, we aimed to evaluate differences in socio-economic variables in a cohort of HIV+, HIV exposed uninfected (HEU) and HIV unexposed uninfected (HIV-) children and their associations with markers of systemic inflammation, monocyte activation, and gut integrity.

Methods: This is a cross-sectional study in 57 HIV+, 59 HEU and 56 HIV- children aged 2-10 years old enrolled in Uganda. HIV+ children were on stable ART with undetectable viral load. We measured socio-economic variables with a modified questionnaire that incorporated the World Health Organization STEPS instrument and the Demographic and Health Surveys Wealth Index. We measured plasma concentrations of markers of systemic inflammation, monocyte activation, coagulation and gut integrity.

Results: Mean age of all participants was 7 years and 55% were girls. Among HIV+ children, mean %CD4 was 34% and 77% were receiving a non-nucleotide reverse transcriptase based regimen. Compared to HEU and HIV- children, HIV+ children were more likely to have parents that only completed a primary education (p=0.001) and live in a household without electricity (p=0.001). HIV+ children living below the level of poverty (living on < $1.90 per day) also approached marginal significance compared to the other groups (p=0.07). In HIV+ children, but not in the other groups, several factors associated with economic vulnerability correlated with higher biomarkers of inflammation and coagulation. Specifically, living below the level of poverty was correlated with IL-6 (p=0.02), lack of electricity with higher hsCRP, IL-6, sTNFRII and D-dimer (p≤0.01) and having an unprotected water source with higher IL-6 and D-dimer (p≤0.02). Food insecurity, parental education, and parental occupation did not correlate with any biomarkers. No factors of economic vulnerability correlated with markers of gut integrity. After adjusting for age, sex and BMI, IL-6 and D-dimer remained associated with factors of economic vulnerability only in HIV+ children (p<0.02). These associations remained after further adjustment for HIV variables (p<0.01).

Conclusion: Our findings suggest that addressing economic vulnerability may mitigate the persistent high-level inflammation in HIV that lead to many end organ disease. Our findings suggest that longitudinal studies are needed to better understand the impact of socioeconomic factors on HIV inflammation and comorbidities in children living with HIV.
Changes in lipids after switching to boosted Atazanavir in South African youth

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Background: Switching adolescents to Atazanavir/ritonavir (ATV/r)-based regimens may improve lipid profiles but there are no data from sub-Saharan Africa.

Methods: Perinatally HIV-infected children (PHIV) aged 9-14y attending one of 7 public sector ART services were enrolled into the Cape Town Adolescent Antiretroviral Cohort (CTAAC). Participants receiving a LPV/r-based regimen at cohort entry with ≥1 subsequent measurement of fasting lipids over 36 months of follow-up were included in this analysis. In this setting, adolescents are switched from LPV/r to ATV/r to facilitate adherence or if there was sustained dyslipidaemia despite dietary interventions. Laboratory measures included VL and fasting lipid sub-fractions [total cholesterol (TC), triglycerides (TG), high density lipoprotein-C (HDL) and low-density lipoprotein-C (LDL)]. Abnormal TC, HDL, and LDL were defined as >5.18, <1.03 and >3.37 mmol/L, respectively. Abnormal triglycerides were defined as >2.85 mmol/L if age <10 years or >3.89 mmol/L if age ≥10 years. We used linear mixed effect models to examine the effect of a switch to ATV/r on PHIV lipid profiles over time.

Results: Of 143 PHIV included in the analysis, 102 (71%) remained on LPV/r throughout the study period and 41 (29%) switched to ATV/r. At enrollment PHIV switched to ATV/r were older and had higher BMI but there were no differences in lipid profiles or onset of puberty (59% vs 54%, p=0.13). Among PHIV switching, the mean duration of ATV/r use was 7.3 (SD 5.6) months. Mean fasting TC and LDL were lower in children after switching to ATV/r compared to when on LPV/r (3.79 vs. 4.34, p<0.01, and 2.1 vs 2.4, p=0.02, respectively).

However, mean fasting HDL was also lower on ATV/r vs. LPV/r (1.23 vs. 1.45, p<0.01). After adjusting for variation in age, BMI and VL over time, children switched to ATV/r had a 0.3 mmol/L lower TC than those that remained on LPV/r, (95% CI: -0.60 to -0.03, p=0.03) but differences in LDL and HDL did not persist.

Conclusions: Switching PHIV from LPV/r to ATV/r-based regimens resulted in modest improvements in some lipids. With increasing ATV/r use in African settings, long-term lipid changes and their clinical implications require ongoing attention.

Pediatric adaptation of Cause of Death (P-CoDe) methodology to ascertain causes of mortality among hospitalized adolescents with perinatal HIV infection in western Kenya

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Background: In recent years, adolescents (ages 10-19) have been the only age group with increasing HIV-associated mortality. Perinatally-infected adolescents may be particularly vulnerable due to late diagnoses and challenges throughout the care cascade. Limited data exist regarding causes of death in this group in the era of widespread ART.

Methods: Hospitalized adolescents with documented HIV infection, with age at diagnosis ≤12 or documented perinatal route of infection, were comprehensively sampled.
and prospectively enrolled in a mixed-methods study from the pediatric, medicine, surgical, ICU, and oncology wards at Moi Teaching and Referral Hospital in Eldoret, Kenya. Clinical data were abstracted from outpatient and hospital records. Discharged patients were contacted 7 and 30 days after discharge to ascertain post-discharge outcomes. We adapted the Cause of Death methodology to systematically collect pediatric- and adolescent-specific data and evaluate causes of mortality in this group (P-CoDe). Two expert physicians independently reviewed available records on each death and completed a P-CoDe Case Report Form. They then centrally reviewed each case and reached consensus on confirmed or suspected causes of death.

**Results:** Forty-seven hospitalized adolescents with HIV were enrolled in 18 months. Fifteen patients (31.3%) died either during hospitalization or in the post-discharge period. Diagnoses of Kaposi Sarcoma (KS, 4, 26.7%), cryptococcal meningitis (2, 13.3%), and tuberculosis (3, 20.0%) were common, and in some cases coincided, complicating the determination of the direct cause of death. Other cases included myeloid sarcoma and aplastic anemia. In 4 cases, the underlying cause of death could not be definitively determined, due either to incomplete evaluation or to the patient dying at home. Challenges were identified in KS management and in the availability and reliability of diagnostics.

**Conclusions:** Despite massive scale-up of access to ART, adolescents continue to have HIV-associated mortality, and causes of death primarily relate to AIDS-defining illnesses. It is critical to ensure timely diagnosis and optimal HIV management for children and adolescents. There are opportunities to improve prevention and management of OIs; for example, in access to effective chemotherapy against KS. P-CoDe methodology facilitates a systematic approach to evaluating cause of death for pediatric and adolescent populations with HIV.
sufficiently positive to urge others to follow their examples of disclosing their HIV at a higher rate of 71% than boys (47%). The major determinants noticed were fear of unintended or unwanted disclosure by teachers, parents, or friends and fear of negative reactions from family, friends, and the community. Other determinants were universal access to care and medication; transition to and continuity of care; access to provider, family, and peer support; access to informational materials about HIV, sex, and reproductive health; support for disclosure; and safe, youth-friendly, adolescent specific facilities and services.

Conclusions: Governments and organizations need to provide adolescent-friendly and adolescent-focused services that emphasize the development of responsibilities aimed at self-care by engaging them. Disclosure is a gradual process that should be based on the adolescent’s development and readiness to reveal their HIV status to others, and that this process requires a wide range of support – from providers, caregivers, peers, and the community – and skills development to increase self-confidence, self-efficacy, and empowerment. These need to be included in HIV care and support cascade.

Implementing an indeterminate range for more accurate early infant diagnosis: 2018 WHO recommendations

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Background: Mother-to-child transmission rates have decreased considerably with implementation of Option B+ and Treat All policies, resulting in concern for false positive tests results due to lowering positive predictive values. There is limited guidance on how to interpret low levels of viremia in HIV-exposed infants; therefore, a systematic review, meta-analysis, cost-effectiveness model, and acceptability survey were conducted.

Methods: The systematic review identified 32 studies from 14 countries including data from over 1.3 million HIV-exposed infants. The meta-analysis used a random effects model to calculate true positivity and false positivity across various proposed indeterminate thresholds. Additionally, a decision analysis model of 10,000 HIV-exposed infants was developed to estimate the clinical consequences of implementing an indeterminate range.

Results: The optimal indeterminate range was the equivalent of a cycle threshold of 33 on the Roche COBAS TaqMan HIV-1 Qualitative Test v2.0 assay, representing the best trade-off between the proportion of HIV-infected infants who would be incorrectly identified as indeterminate (approximately 8.43%) and the proportion of HIV-uninfected infants who would potentially start treatment unnecessarily (approximately 6.66%). Implementing an indeterminate range was found to be cost-effective across most cycle threshold ranges. Finally, a survey provided to program managers (n=85), health care workers (n=146), and people living with HIV (n=587), established that over 85% of respondents in each group thought the use of an indeterminate range was acceptable in order to prevent unnecessary lifelong treatment.

Conclusions: Implementing an indeterminate range will support more accurate nucleic acid-based early infant diagnosis: it is likely that fewer infants would be put on lifelong treatment unnecessarily as the majority of false positives would fall within the indeterminate range and receive additional testing prior to definitive diagnosis rather than being classified as HIV-infected. Confirmatory testing, retention during the exposure period, and end of exposure testing remain critical.
Rapid antibody tests for determining HIV exposure and infection in infants and children: a systematic review and meta-analysis

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Background: While rapid diagnostic accuracy tests can be considered and used to ascertain HIV exposure in infants, their accuracy depends partly on the timing of maternal infection followed by development and passive transfer of her antibodies as well as variable temporal dynamics of maternal antibody waning in HIV-exposed infants. We assessed the accuracy of rapid antibody tests (RDTs) to determine HIV exposure and infection in infants and children by age.

Methods: Electronic databases and conference websites were searched up to September 2018 for studies that evaluated the use of commercially available rapid antibody tests compared to appropriate reference standards for HIV exposure and infection. Risk of bias was assessed using QUADAS2, and meta-analysis stratified by age at testing.

Results: Ten studies with 5,842 participants were included. Sensitivity and specificity to detect HIV exposure in infants aged 0-3 months were 95.4% (95% CI: 89.3 to 98.1) and 99.7% (92.2 to 100.0), respectively. The sensitivity decreased in older age groups to as low as 50-60% in infants between 7-12 months of age. To detect HIV infection in infants aged 0-3 months sensitivity and specificity were 95.4% (90.3 to 97.9) and 5.8% (2.5 to 12.9), respectively. At 7-9 months, the sensitivity was 92.3% (83.3 to 96.6) and specificity was 81.8% (63.4 to 92.1). To detect HIV infection in infants over 18 months of age, sensitivity and specificity were 98.0% (95.4 to 99.2) and 99.5% (98.0 to 99.9), respectively.

Conclusions: Rapid antibody tests should only be used to determine HIV exposure in infants under three months of age and can be considered around nine months of age to exclude HIV infection but not for diagnosis. Negative rapid antibody test results in infants over three months of age cannot rule out exposure to HIV; therefore, HIV testing of the mother should always be prioritized for this age group. Rapid antibody tests should only be used to determine HIV infection in infants more than 18 months of age.

Substantial antiretroviral non-adherence, non-therapeutic plasma drug levels, longitudinal treatment failure and drug resistance in HIV-infected Kenyan children

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Background: Characterizing pediatric antiretroviral therapy (ART) adherence and viral outcomes in resource-limited settings is critical to sustained viral suppression, care engagement, and intervention development. We investigated associations between ART adherence, plasma drug-levels, and longitudinal viral outcomes among perinatally HIV-infected Kenyan children.

Methods: Participants ≤15 years, on/initiating NNRTI-based 1st-line ART, were recruited in 2010-2014 at the Academic Model Providing Access to Healthcare (AMPATH) in Kenya, with 6-month followup. At two time points (t=1, 1-3 months after enrollment; t=2, 4-6 months after enrollment), we measured caregiver-reported adherence using a validated questionnaire; NNRTI plasma levels (sub-therapeutic=nevirapine <3.0 μg/mL, efavirenz <1.0 μg/mL; therapeutic=nevirapine 3.0-7.6
μg/ml, efavirenz 1.0-4.0 μg/mL; supra-therapeutic=nevirapine >7.6 μg/mL, efavirenz >4.0 μg/mL; viral load; and, for children with virologic failure (VF; >1,000 copies/mL), protease and reverse transcriptase drug resistance. Logistic and Poisson regression models were used to assess associations between adherence and NNRTI levels, and VF and number of NRTI/NNRTI mutations at both time points, adjusting for age, gender, CD4%, ART duration, and, for t=2, VF at t=1. Due to small numbers, resistance accumulation was examined using unadjusted logistic regression. Results are presented as odds ratios (ORs), rate ratios (RR) and 95% confidence intervals (CI).

Results: At t=1, the 227 children were median age 8.4 years (range 1.5-15.7); 55% female; on ART for median 2.0 years (range 0.1-7.9, 79% nevirapine-based); most recent CD4 26% (range 0.0-52.0); and 70% in CDC class B/C. Mothers were most common adherence reporters (61%) and medication providers (66%). At t=1, 49% were adherent, 37% had therapeutic drug levels (17% sub-therapeutic; 46% supra-therapeutic), and 68% were suppressed. Among 62/73 available genotypes, 94% had resistance (94% NNRTI; 92% NRTI). VF at t=1 was associated with younger age, lower CD4%, and longer ART time (p<0.05). Among those with VF, higher resistance was associated with therapeutic (RR=1.8, CI 1.1-2.9, p=0.02) and supra-therapeutic (RR=1.8, CI 1.1-3.0, p=0.02) levels. At t=2, 46% were adherent, 25% had therapeutic levels (16% sub-therapeutic; 59% supra-therapeutic), 81% were suppressed, and among 30/44 available genotypes, 90% had resistance (94% NNRTI; 92% NRTI). VF was associated with lower CD4 (p<0.05). Among those with VF, lower resistance was associated with therapeutic (RR=0.2, CI 0.1-0.9, p=0.03) or supra-therapeutic (RR=0.3, CI 0.1-0.99, p=0.04) levels. Adherence was not associated with VF or resistance at either timepoint. Among those suppressed at t=1, lower VF at t=2 was associated with therapeutic (OR=0.1, CI 0.0-0.7, p=0.02) or supra-therapeutic (OR=0.1, CI 0.0-0.3, p=0.001) drug levels at t=2. Of 227 participants, 62% were suppressed and 14% VF at both timepoints (TP), 6% suppressed at TP1+VF at TP2, and 19% VF at TP1+suppressed at TP2. Among 23 participants with genotypes at both timepoints, 22% accumulated mutations. Those with sub-therapeutic levels at t=1 were 10.5 times more likely to accumulate mutations (combined; CI=1.0-107.2, p=0.047, estimate with high degree of statistical uncertainty.)

Conclusions: Non-adherence, treatment failure and drug resistance among Kenyan children living with HIV are high, with longitudinal implications. Exploring medication-taking patterns and contributors to therapeutic plasma drug levels are critical to maintaining suppression and preventing drug resistance.

77

Effectiveness of a web-based information system to improve HIV early infant diagnosis and hepatitis B immunization at birth in Abidjan, Côte d’Ivoire. The DEPISTNEO project.

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Introduction: Côte d’Ivoire is one of the countries the most affected by the HIV/AIDS epidemic in West Africa. Prevention of mother-to-child-transmission coverage is sub-optimal and new pediatric infections continue to occur. Early infant diagnosis (EID) coverage is also insufficient (40% in 2017, WHO), mainly due to poor linkage between birth and 6-week EID. Additionally, the country is endemic for hepatitis B (HBV). Birth immunization can reduce new HBV pediatric infections however this is not implemented on a routine basis in Cote d’Ivoire. 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.

**Methods:** The DEPISTNEO project was designed to fit in the current standard of routine care. At delivery, mothers were tested for HIV and those infected not yet in care were offered a second opportunity to enroll. All HIV-infected mothers received PMTCT. Mothers were tested for HBV and HBs-Ag-exposed children received immunization at birth. All live-births were recorded in the HIS and HIV or HBV-children were tracked through the continuum of care. Weekly reports alerted social workers in case of a missed visit, who rescheduled. We measured HBV birth immunization coverage among HBV-exposed infants and the 6-week, 9-month and 18-month EID coverage among HIV-exposed infants before and after HIS alert.

**Results:** Between August 2016-December 2018, 38,878 women were offered HIV and HBV RDT (97% screening coverage). Acceptability of maternal HBV testing was 95%; prevalence was 6.0% (95% Confidence Interval (95%CI): 5.7-6.2). Among 1,700 HBV-exposed children, birth immunization coverage was 98.7% (95%: 98.3-99.2). Maternal HIV testing acceptability was 99.4%, HIV prevalence was 3.9% (95%CI: 3.6-4.1); 82% were already on ART and the remaining 18% were offered a second opportunity to enroll into HIV care. Of the 1142 HIV-exposed infants, 59% (95%CI: 57-62) had a DBS for EID by 6 weeks of age. DEPISTNEO significantly increased EID by 12.1% and overall EID was 67% (95%CI: 63-69) (McNemar’s test: p<0.001). Of the 753 6-week PCRs performed, 624 (83%) were returned to families after a median time of 49 days since testing (interquartile interval (IQR): 28-73). We found that turn-around time reduced over time as point of care (POC) testing became available. Among those with at least one PCR result, 15 were positive, 7 (47%) had confirmatory testing and 2 (29%) were false-positive. Among the 13 presumed HIV-infected children, 11 (85%) initiated ART. At 9 months, 13% of HIV-exposed infants were spontaneously tested and DEPISTNEO increased this by 98%; two children were HIV-infected and initiated ART. By 18 months, HIV testing coverage was 6%; one was HIV-infected but did not initiate treatment.

**Conclusions:** Maternal HIV and HBV rapid diagnostic testing at birth is feasible and acceptable. HBV immunization coverage at birth was high and proved a feasible intervention in HBV-exposed infants. Maternal HIV-testing at birth allowed (re)-engaging in care 18% of HIV-infected women. EID uptake was significantly improved by the HIS, though hindered by long turnaround times. As POC is rolled-out in Cote d’Ivoire, the added value of this intervention deserves further investigation. A simple, user-friendly web-based HIS is an effective tool to improve EID coverage in low-prevalent settings however urgent efforts are needed further down to complete the full cascade.

78

Camp Hope Malawi: A game changer for the newly disclosed and challenging adolescent HIV cases.

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**Background:** A study in South Africa by Cluver, LD and others on child disclosure had findings that early and full disclosure is strongly associated with improved adherence, reduced mortality and onwards transmission amongst ART-initiated adolescents. The process however to adolescents accepting their status and living positively leading to improved adherence is a challenge to some of the children managed at the Baylor Malawi Clinic and its outreach clinics. Whether the disclosure was accidental as has been the case in many outreach clinics or planned by the guardian or health worker, at least 30% of these newly
disclosed adolescents present with undesirable outcomes such as anger towards guardians for giving them a disease, depression due to fear of death, suicidal thoughts due to lack of hope for a future, shame and low self-esteem when among peers. All these, if prolonged lead to poor adherence which then may lead to premature death. To avoid the worst, Baylor Malawi in 2008 introduced sleep away retreats which were then named Camp Hope in 2011 for these newly disclosed teens, whose enrolment deliberately target those with difficulty in accepting their HIV status.

**Materials & Methods:** Each session of camp for these newly disclosed teens runs for 5-6 days with 80 campers at the site. Clinicians, Nurses, Psychosocial Counsellors, Social workers, Life Skills mentors, a Medical Doctor and older adolescents also living with HIV that act as peer supporters and/role models support these teens with different activities, all mixed with Serious Fun! All activities are intentional such as a wake up drum beat for morning shower, all campers medication time, engaging breakfast with spreading smiles just to mention a few. Education sessions with topics not limited to HIV knowledge, adherence, peer support, future planning, SRH, internal and external pressure coping techniques, decision making, nutrition and hygiene are delivered. In a child friendly environment, these teens also have fun outdoor physical and mental activities such as spider web challenge games, egg drops, preparation of vertical gardens and outdoor cooking demonstrations. In the evening they either have camp fires or dress up stage nights or talent shows with music and dance all filled with laughter. A single room but fully furnished clinic is also available to manage any emergencies at camp.

**Results:** A total of 1305 newly disclosed adolescents have attended Camp Hope Malawi (2011-17). 2017 post camp results with 60 guardians and their teens showed that; 95% (57/60) reported their campers could recite their Antiretroviral Therapy (ART) names, 97% (58/60) of the campers understood importance of medication adherence, 98% (58) of campers knew the six food groups in Malawi, 90% (54/60) of guardians use the Chichewa recipe book given at camp when preparing meals, and 58(97%) practice good hygiene. Children have also gained resilience as 93% (55) share future career inspiration, 93% (55/60) report a greater sense of hope for the future, 97% (58) have improved concentration in schools, 78% (46) have a peer friend living with HIV, 90% (54) exhibit confidence, 82% (49) feels comfortable talking with their guardians about HIV, 95% (57) have improved self-esteem.

**Conclusions:** Child friendly sleep away retreats that bring together newly disclosed teens to help them realize that they are not alone on lifelong medication should be recommended especially for those teens having difficulty in accepting their HIV status.

**79**

**PMTCT service uptake among adolescents living with HIV**

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**Background:** The HIV burden is disproportionately high among young females and adolescents. The population of adolescents living with HIV is a mix of individuals with both perinatally acquired and sexually acquired HIV. We reviewed the programmatic data in the Centre for Infectious Disease Research in Zambia (CIDRZ)-supported sites to describe uptake of PMTCT services among the adolescent population in 4 provinces of Zambia.

**Methods:** We reviewed the PMTCT programme data to describe the uptake of HIV testing services and ART initiation rates among adolescents living with HIV in 4 provinces of Zambia. HIV testing was offered to all PMTCT clients with unknown HIV status on the day of presentation and ART was offered to all HIV positive clients not on treatment. We calculated HIV prevalence rates and PMTCT ART uptake among the adolescents and did
comparisons with the older age group. We have ethical approval from the University of Zambia Biomedical Research Ethics Committee to use routine programmatic data.

**Results:** Between October 2017 and September 2018, 181,138 women presented for antenatal care services at the CIDRZ-supported health facilities in Western, Eastern, Southern and Lusaka provinces of Zambia. 43,019 (24%) were adolescents and 138,119 (76%) were adults aged 20 years and above. HIV status was established for 42,100 (98%) adolescent and 134,894 (98%) of the =/>20 years old. 1,561 (4%) adolescents were HIV positive compared to 17,066 (13%) =/>20year olds. PMTCT ART uptake among the adolescents was 80% compared to 86% among the =/>20 year olds.

**Conclusion:** Whereas overall PMTCT outcomes are encouraging, pregnant adolescents living with HIV have lower uptake of PMTCT services compared to the older population. Adolescent-friendly interventions targeting this population are critical if we are to eliminate mother to child transmission of HIV.

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**80**

**HIV-related stigma in life trajectories of youths living with HIV**

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**Background:** According to Goffman, stigma is an “attribute that is significantly discrediting” leading someone to social disadvantage. Critical studies about stigma as intrinsic to social interaction argue that stigmatization supports and enhances social inequalities of class, race, gender and sexuality and serves to maintain power differences and social disparities. Thus, the analysis of the impact of HIV-related stigma on health should consider stigma as a complex social process produced at the intersection of different axes of inequality. The aim of this study was to deepen current knowledge about HIV-related stigma among youths living with HIV (YLHIV) transitioning to an adult clinic and those who have transitioned in recent years. The study took place in a public hospital that houses a clinic for adolescents living with HIV (ALHIV) since 2000, with transdisciplinary work and group activities to enhance their capabilities to cope with HIV and other adolescence-related issues.

**Methods:** We collected quantitative and qualitative data; YLHIV in transition to adult clinic (G1) and those who had transitioned in recent years (G2) were submitted to structured questionnaires and invited for focal groups (FG); medical charts were reviewed for laboratory data. The Berger scale for HIV-related stigma was analyzed calculating the score for each of the 4 sub-scales (actual score/total possible score). Thematic analysis of FG contents was conducted to investigate power relations possibly affected by HIV-related stigma in health care settings, family, friendship, romantic interactions and how being HIV+ influenced self-identity.

**Results:** We included 30 YLHIV in G1 and 13 in G2, all from low socioeconomic strata, 86% non-white; 63% were not working; none had post-secondary education. Median age was 22y [IQR=20-25]; 70% female; 65% vertically infected; 49% had viral suppression at last measurement; median CD4% was 20,5 [IQR=14,6-31]; 56% interrupted treatment at least once. Index scores of subscales for HIV-related stigma were 0.57 for “personalized stigma”, 0.58 for “public attitudes”, 0.60 for “negative self image” and 0.73 for “disclosure concerns”. Two FG were performed; mean age of participants was 21y in G1 and 28y in G2; in both groups the theme of stigma-related experiences during childhood and adolescence emerged. While G1 worried about responsibilities of adult life, changes in familial relationships and consequences of disclosure of their HIV status to other people, G2 seemed to have partially overcome HIV-related stigma with the support of romantic partners and children. Both groups valued group activities and support during their follow-up in the
adolescent clinic, although these activities did not impact treatment adherence in that period of life.

**Conclusion:** As all participants belong to similar socioeconomic strata, differences observed in FG possibly reflect different stages of adulthood progression. Raising a family of their own emerged as the most relevant adulthood achievement that contributed to empowerment and wellbeing of YLHIV. Policies to improve care for ALHIV fostered the creation of a support network that positively impacted the study population during early adulthood, even though actual adherence to ART was not directly affected by the transdisciplinary approach and group activities. Through institutional partnerships, health services should favor the reduction of conditions of social vulnerability and HIV related stigma that compromise health care.

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**81**

**Moderate adherence to HIV pre-exposure prophylaxis among men who have sex with men and transgender women aged 15-19 years of age in Thailand**


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**Background:** HIV prevalence among young men who have sex with men (YMSM) receiving HIV testing services in Bangkok is 10.2 per 100 person years. ATN 113 found protective tenofovir diphosphate (TFV-DP) levels between only 28-49% in US YMSM. This study examined adherence to daily PrEP among young MSM and transgender women (TGW) in Bangkok.

**Materials and methods:** Eligible participants were 15-19-year-old MSM and TGW reporting HIV acquisition risk behaviors. Clients self-consented based on informed decisions. Participants were provided daily TDF/FTC, condoms and lubricants at youth-friendly clinics. Clinic visits occurred at months 0, 1, 3, and 6, and phone contact at months 2, 4, and 5. Free services were supported by CIPHER and LINKAGES. Sexual activity, condom use and number of pills taken each week were recorded. Dried blood spots (DBS) were collected for quantification of TFV-DP at months 3 and 6. Adherence to PrEP was calculated using a person-time at-risk approach.

**Results:** Between February-December 2018, 269 YMSM and TGW were screened and 98 enrolled (median age 19.1 years; 87% MSM, 13% TGW). Median number of sex partners and sex acts was 3 (min 0, max 10) and 4 (min 0, max 30) per month, respectively. Laboratory diagnosis of any sexually transmitted infections at baseline was 29%. Retention at months 1, 3 and 6 was 93%, 91% and 66%, respectively. Of 399 person-weeks sexually active, 8% were protected with consistent condom (≥95%) use only, 30% with PrEP (≥4 pills/week) only, and 38% with both PrEP and condoms. Of 49 DBS samples (40 adolescents), 11 (22%) and 19 (39%) had TFV-DP levels 350-700 and >700 fmol/punch, respectively. Among the 33 participants who reported adherence ≥4 pills/week; 8 (24%) and 16 (49%) had TFV-DP levels of 350-700 and >700 fmol/punch, respectively. No HIV seroconversions occurred during the study.

**Conclusions:** High retention in this PrEP program was achieved among YMSM and TGW through maintenance of monthly contact. Seventy-six percent of time spent by YMSM and TGW with sexual activity were reported to be protected by PrEP or condom use. More efforts should be made to roll out PrEP for high-risk adolescents to enable them to stay HIV free.

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**Background:** AIDS-related illnesses are the leading cause of death among adolescent girls and women of reproductive age in Africa, despite treatment availability. Further, only 15% of adolescent girls and young women (AGYW) in sub-Saharan Africa know their HIV status. This analysis was conducted to describe the HIV testing services amongst pregnant AGYW (10-24) attending their 1st antenatal care (ANC) visit between October 2017 and September 2018.

**Methods:** Retrospective cohort data for pregnant AGYW (10-24yrs) booking for 1st ANC between Oct17-Sept18 at 666 public health facilities supported by the FACE-HIV programme were abstracted from the monthly health facility surveillance reports. Descriptive analyses were used to summarise and interpret the data using medians. HIV testing coverages and yields at ANC booking were calculated and analysed by age, sex and geographical location.

**Results:** A total of 175,501 pregnant women booked for 1st ANC at the 666 public health facilities during the 12-month period, 49.9% (87,629) were AGYW, of these, 44.3% (38,812) were aged 10-19 years. The overall proportion of pregnant AGYW with knowledge of their HIV status following the 1st ANC visit was 97.7% (85,646/87,629). Overall HIV test yield was highest amongst young women 20-24 years at 4.3%. Amongst the 6,174 pregnant AGYW who were documented as HIV positive in ANC, 47.3% were newly diagnosed at booking. In the 15-19-year age group, 55.3% (951) of HIV positive (1,719) adolescents were newly identified at booking.

**Conclusion:** Knowledge of HIV status amongst AGYW attending 1st ANC was very high at 97.7%, indicates PMTCT program success to increase coverage of HIV testing in ANC. However, the analysis identified missed opportunities amongst young adolescents (10-14 years). Of all the HIV positive pregnant AGYW attending 1st ANC, nearly half were newly identified at booking, highlighting the importance of HIV testing in ANC as an important vehicle to meeting the 1st 90 UNAIDS target.

83

**Back to basics: Friendly health providers are the key to retaining adolescents living with HIV**

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**Background:** Almost one-third of adolescents on treatment are lost to follow-up. To improve retention, services must be tailored to meet their unique needs. Differentiated approaches tend to focus on structural modifications to the health system – multi-month prescriptions, extended clinic hours, fast-track visits and decentralization. However, although health provider attitudes may impact adolescent service engagement, they receive less attention.

**Materials & Methods:** We conducted cross-sectional surveys with 63 young people living with HIV engaged as peer supporters at clinics in 11 sub-Saharan African countries. Together, they support 55,059 adolescents and young people living with HIV. Surveys set out to quantify and compare the strength of young people’s preferences for specific HIV service features. We provided respondents with a series of choices between hypothetical clinics...
within which the following five attributes were varied: wait time (no wait, or a 1-, 3- or 5-hour wait time), distance from home (1, 10 or 20km), visit frequency (1-, 3- or 6-monthly), clinic hours (weekdays until 16h00, or weekdays until 18h00 plus weekends), and health provider attitudes (“friendly and kind” or “rude and unfriendly”). Data were analysed using univariate statistics to describe central tendencies.

Results: Respondents were 60% female, with a mean age of 22 years, and originated from Southern (56%), East (37%) and West/Central Africa (8%). For each hypothetical choice, young people exhibited a strong preference for the clinic with “friendly and kind” providers, regardless of its wait time, distance from home, visit frequency or operating hours. Young people were willing to accept a longer wait time (5 hours as opposed to no wait), greater distance from home (20km as opposed to 1km), more frequent visits (monthly as opposed to 6-monthly), and shorter operating hours (weekdays until 16h00 as opposed to weekdays until 18h00 and weekends) in order to access “friendly and kind” providers.

Conclusions: Findings suggest that for young people, positive provider attitudes are the most desired feature of care. Moreover, young people are willing to relinquish convenience to access client-centred providers. To satisfy young people’s preferences and enhance the quality of the client experience, programmes should invest in health provider training and sensitization.

84

Mortality and loss to follow-up among HIV positive adolescents and young adults in program settings in Kenya


Background: Mortality among HIV-infected adolescents in sub-Saharan Africa remains high compared to other age-groups. Within programs, little is known about characteristics of adolescent mortality.

Materials and Methods: As part of an ongoing trial (NCT03574129), we abstracted routine adolescent and young adult (AYA) (ages 10-24 years) records from 87 HIV clinics in Kenya, randomly selected from a national pool of clinics using electronic medical records. Records of AYA who had ≥1 clinic visit between January 2016 and December 2017 were reviewed to identify AYA outcomes among AYA with at least 6 months potential follow-up time. AYA who died or were LTFU were compared to AYA continuing follow-up using logistic regression.

Results: Of 6537 AYA with ≥1 clinic visit between January 2016 and June 2017, 191 (3%) died, 1654 (25%) were lost to follow-up, 601 (9%) transferred out and 4091 (63%) continued to attend clinic. Among 191 AYA who died, median age was 18 years (IQR 14, 22), with 30%, 32% and 38% in the 10-14, 15-19 and 20-24 year age-groups, respectively. Fifty percent were female, 84% were single, and 54% reported a parent as a support person.

Comparing those who died to those in follow-up, those in the 15-19 and 20-24 year age-group had 1.35 (95% CI 0.93, 1.94; p=0.11) and 1.97 (95% CI 1.38, 2.81; p <0.001) higher odds of death than those in the 10-14 year age-group. Male AYA were more likely to die (6% vs. 4%; OR: 1.48 95% CI 1.20, 1.99; p =0.009).

Comparing lost to follow-up to those still in follow-up, those in 15-19 and 20-24 year age-groups had a significantly higher odds of becoming lost to follow-up than those in the 10-14 year age group (p<0.001 for both). In contrast to mortality, females were more likely to become lost to follow-up (32% vs. 23%, p<0.001).
Conclusion: In this programmatic analysis, mortality and loss to follow-up among AYA in HIV care was high. Mortality was higher and retention lower among older AYA (ages 15-24). Males were more likely to die while females had higher non-retention. Defining determinants of mortality and non-retention in youth will be important to tailoring interventions.

"They will look at you with eyes that will make you want to run away:" A qualitative assessment of transition experiences and expectations among Kenyan adolescents and their primary caregivers

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Introduction: Transition from child-centered to independent adult care is important to optimize HIV outcomes among adolescents and young adults (AYA) living with HIV (ALHIV). Understanding beliefs, experiences and expectations of ALHIV and their caregivers can inform development of transition interventions.

Methods: Between June and August 2018, we conducted focus group discussions (FGDs) with ALHIV ages 14-24 and caregivers of ALHIV from 4 large HIV programs in Kenya. We purposively included ALHIV who were preparing to transition and ALHIV who had completed transition. Transition involved switching from the adolescent to adult day at the same clinic or completely changing clinics. Topic guides explored anticipated or actual transition experiences, and desired or actual support systems. An analysis of detailed debrief reports and a subset of full transcripts was conducted to identify key attributes impeding or facilitating transition to adult care.

Results: Overall, 89 ALHIV participated in 16 FGDs (8 with non-transitioned ALHIV and 8 with recently transitioned ALHIV) and 49 caregivers participated in 8 FGDs. ALHIV valued support from healthcare workers (HCWs) and caregivers during their transition. ALHIV wanted HCWs to prepare them early for transition, tell them what to expect in adult clinic, and teach them the skills needed in advance of transitioning. ALHIV identified HCW guidance as critical, noting that clinic may be the only place adolescents get support. ALHIV want caregivers to be involved, but struggle with what caregiver support should entail as they mature. Adolescents noted that sudden decreases in caregiver involvement should be avoided, since ALHIV interpret sudden changes as loss of interest in their lives. Caregivers felt that the move to adult care should be the adolescent’s decision, encouraged by caregivers and HCWs. Caregivers also felt adolescents need to be informed about the reason for transition so that they don’t feel abandoned by the adolescent clinic. ALHIV and caregivers identified that self-care management indicators were more useful than age in deciding when transition should occur. Indicators identified by ALHIV included: 1) healthcare providers talking to them like adults, including discussing sexual and reproductive health services, and 2) ownership of illness management including attending clinic and taking medications independently. Caregivers also noted the importance of ALHIV knowing the names of their drugs and reaching sexual debut or getting married as markers for maturity.

ALHIV and caregivers identified several factors facilitating and impeding transition. Non-transitioned adolescents were excited about future transition, valuing receipt of adult-level HIV information and conversations, having role models, and no longer receiving services with young children. Non-transitioned and already transitioned ALHIV noted that fears of “the unknown,” long queues, harsh and disinterested HCW demeanor, stigma from adults in the clinic, and feeling a lack of community with older adults were barriers.
There was also concern about inadvertent disclosure to others in the community by being seen at the adult HIV clinic.

**Conclusions:** ALHIV and their caregivers agreed that a planned, supported transition process, guided by developmental maturity, can improve transition experiences for ALHIV. These results informed development of a transition intervention that will be tested in an RCT.

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**Improving Health and Social Outcomes of Adolescents - Addressing the Parallel Risks of Pregnancy and HIV though a Home Visiting Program in Kenya**


**Background:** The parallel risks of pregnancy and HIV for young women, and of vertical HIV transmission for their infants, make girls and adolescents aged 10–19 years a critically important group. The Strengthening High Impact Interventions for an AIDS-free Generation (AIDSFree) Project developed an innovative home visiting intervention to improve health and social outcomes for this highly vulnerable and neglected group—pregnant adolescents, adolescent mothers, and their infants.

**Materials & Methods:** The AIDSFree Jielimishe Uzazi na Afya (JUA) program design used a case management model; male and female home visiting teams (HVTs) provided individualized services for more than 380 adolescent clients and their households in two counties in western Kenya and in Nairobi’s urban informal settlements. The HVTs focused on three goals: ensuring that the adolescents receive antenatal, postnatal, and HIV prevention services; ensuring that babies receive services for their health and development; and building the adolescents’ resilience and empowerment. Working through community-based organizations, the model included peer-led individual mentoring of pregnant adolescents/mothers on skills needed to access, use, and remain in antenatal and postnatal care, including prevention of mother-to-child transmission services. It also included targeted support for caregivers, households, and partners of adolescents to address structural barriers to care, decrease stigma and discrimination, and mobilize support. Supervisory support to ensure a team-based approach grounded in quality assurance was included as well.

**Results:** In 2018, the AIDSFree JUA program trained 166 mentors, household facilitators, and supervisors. Using a vulnerability screening tool, the teams identified and engaged with 960 adolescents, enrolling 384 of them in the JUA program. Nearly all (94%) who gave birth delivered their babies with the support of a skilled birth attendant—higher than the Kenyan national average of 61%. All enrolled pregnant/breastfeeding adolescents received HIV testing services—20 were identified as HIV-positive. All 20 received antiretroviral therapy during pregnancy and after delivery, and all (20/20) infants received HIV prophylaxis. With program support and follow-up, viral suppression among enrolled adolescents improved from 29% (4/14) at program initiation, to 85% (17/20). Early infant diagnosis increased from 40% (4/10) to 100% (19/19); one infant was known-positive at enrollment. HVTs linked adolescents to crucial health and social services, providing 1,275 referrals and working with their clients to access the services. The HVTs also enabled school re-entry for 42 postnatal adolescents, and helped 54 additional girls at risk of dropping out to stay in school.

**Conclusions:** The innovative AIDSFree home visiting program builds on global evidence on what works for adolescent populations, addressing the barriers adolescent girls often face when using and accessing services, such as harmful social norms which may keep young
Abstracts 80

Developing a pediatric and adolescent HIV-screening tool in outpatient settings in Uganda

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Background: Facilitating targeted HIV testing in outpatient settings has the potential to identify children more likely to be HIV-positive. Using known risk factors and symptoms, we developed a 10-question HIV risk screening tool to support targeted testing. The purpose of this analysis was to identify predictive questions to validate in facility and community settings in Uganda.

Methods: The screening tool was administered by health workers to children/adolescents (aged 18 months – 15 years) without documented HIV-positive status and/or their caregivers in 14 study facilities in eight regions (July-November 2018). All child/adolescent participants were referred for HIV testing with results abstracted from laboratory records. Participants and caregivers provided informed assent and consent per regulatory guidelines. We calculated each question’s sensitivity and specificity. To identify a subset of questions with overall sensitivity and specificity of approximately 80% and 70% respectively for the final tool validation, we used stepwise multivariate logistic regression model of HIV-positive status, excluding screening items with p-values > 0.1.

Results: The screening tool was administered to 2,657 children/adolescents (HIV-positive, 56; female, 51.9%; median age, 7 years). Having a mother who was HIV-positive or of unknown status was highly predictive of child HIV-positive status, with 94.6% (CI 85.1–98.9) tool sensitivity and 52.9% (CI 50.9–54.8) specificity. For children with HIV-positive mothers or with any two of five specific risk factors (sick in the last 3 months, recurring skin problems, not growing well, weight loss in the last 3 months, ever had tuberculosis), tool sensitivity was 83.9% (95% CI: 71.7 – 92.4) with a specificity of 62.4% (95% CI: 60.5 – 64.2). This will comprise the six-question tool for validation. The other 4 screening items, (hospitalization in the last 3 months, death of one or both of the child’s biological parents, child experiencing difficulty in performing daily activities, discharge or sores in the child’s private parts), did not meet the threshold level and were excluded from the final tool.

Conclusions: Our findings suggest that children and young adolescents of unknown HIV status should be screened for maternal HIV status and offered HIV testing if their mother is HIV-positive. A tool that screens for maternal HIV status and child HIV symptoms and co-morbidities may help to prioritize children most at risk of HIV for testing and identify undiagnosed HIV-positive children to achieve the 95% target of people living with HIV who know their status.

Evaluating technology-based methods for collecting self-reported sexual risk behaviour in adolescent girls and young women at high risk of HIV infection

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Background: Obtaining accurate information on sensitive behaviours is crucial to understand HIV and STI transmission dynamics in adolescents. However, acquiring these data is challenging, as it relies often on self-report where confidentiality concerns likely cause reporting bias. We aimed to compare HIV risk behaviours in adolescent girls and young women (AGYW) in two geographically separate peri-urban settings in South Africa, and to evaluate the usefulness of technology-based methods to obtain sexual risk behaviour data.

Materials & Methods: Between 2013 and 2015, the Women’s Initiative in Sexual Health (WISH) study enrolled 298 adolescent women (16-22 years) from low-income communities in Cape Town and Soweto, South Africa. A questionnaire, completed at enrolment, elicited data on: (i) demographics and socio-economic status, (ii) health care and support services utilization, (iii) emotional wellbeing and resiliency, (iv) reproductive, and (v) sexual health. This questionnaire was either tablet-based (129/298; developed using Survey Gizmo version 4 (Boulder, CO, United States) or paper-based (96/298) with manual data entry by a trained interviewer. Logistic regressions were used to investigate the relationship between questionnaire method and reporting of demographic/behavioural factors, adjusting for possible risk factors, including participant age, currently in secondary school and having parents as main source of income.

Results: Adolescents using the paper-based questionnaire completed 99.7% of questions (2392/2400) compared to 98.7% on tablet (3184/3225; p=0.0003). Those completing the paper-based survey were ~3-fold less likely to report using injected drugs or having a tattoo (5% vs 14%; p=0.044), and ~2-fold less likely to report using condoms most of the time (as opposed to always or never using a condom; 26% vs. 40%; p=0.032) than those completing the tablet survey. Irrespective of method of questioning, a large proportion of these participants in both cohorts reported behaviour increasing their risk for HIV infection. The majority of AGYW (57%) did not know their partners’ HIV status, 40% reported unprotected sex in the last three months, and 20% were reportedly in HIV serodiscordant relationships (having an HIV positive partner). AGYW from Soweto reported more risky behavior than their Cape Town counterparts, with a higher frequency of discordant relationships (33% vs. 9% p<0.001), higher rates of intergenerational relationships (>10 year age difference, 14% vs. 4%, p=0.008), higher rates of unprotected vaginal sex in the last three months (52% vs. 31%, p=0.003), and were more likely to report use of injected drugs/tattoos (15% vs. 6%, p=0.044).

Conclusions: Technology-based methods to obtain sensitive risk-behaviour data did not influence reporting. High levels of risk were seen overall, with differences in sexual risk behaviour reporting being better explained by socio-geographic factors (site) than by method of questioning. These findings emphasize the need to develop context-sensitive behavioural interventions in this vulnerable population.

A Qualitative Assessment of Barriers, Facilitators, and Areas of Intervention for Adolescent Retention in HIV Care

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Background: Adolescents living with HIV (ALHIV, ages 10-19) have low rates of retention in care. Strategies to improve retention must
be rooted in ALHIV experiences in care and unmet needs. Youth peer mentors (YPM) in the Academic Model Providing Access to Healthcare (AMPATH) partner with ALHIV to provide HIV education, disclosure and adherence support, and to facilitate peer support groups. We sought to define central barriers and facilitators to retention of ALHIV, and explore needed interventions and their potential implementation, through engagement with ALHIV and YPM.

Methods: This qualitative study was performed at the Rafiki Centre for Excellence in Adolescent Health at AMPATH, in Eldoret, Kenya. We comprehensively sampled YPM for semi-structured key informant interviews regarding barriers and facilitators to ALHIV retention, and areas of needed intervention. We then partnered with YPM to co-facilitate focus group discussions (FGDs) with disclosed ALHIV engaged in care. FGDs elicited ALHIV perspectives regarding key areas of needed intervention to improve retention and their implementation. YPM were interviewed in either Kiswahili or English, and FGDs were conducted in Kiswahili. Sessions were recorded, and transcripts were analyzed through thematic analysis.

Results: We interviewed 19 YPM in a total of 32 interviews, and conducted 8 FGDs with 52 ALHIV, stratified by age and gender. The most central barriers to ALHIV retention included stigma, isolation, mental health issues and trauma. Stigma experienced at school or among peers was particularly difficult to navigate. Key facilitators enabled ALHIV to overcome stigma and isolation; through peer support, adolescent-friendly clinic services, and attending clinic in a space that is not only for HIV care. Areas of intervention to support retention include: expanding peer support and adolescent-friendly services, partnering with educators to address school-based stigma, and financial interventions, such as job training or microloans.

Conclusions: It is essential that adolescent and youth voices are heard in research to improve ALHIV retention in care. ALHIV highlight the barriers posed by stigma and isolation, and favored expanding peer support interventions, key elements of adolescent-friendly care, and financial interventions to improve retention. Research is needed to evaluate the implementation and effects interventions in these areas.

90

Resource utilization in adolescents and young adults with HIV in the HIV Research Network

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Background: Nearly 61,000 adolescents and young adults (AYA) are living with HIV in the US and experience poorer health outcomes than adults living with HIV. Little is known about AYA patterns of utilization of costly healthcare resources.

Methods: We estimated utilization of outpatient, emergency department (ED), and inpatient services among 13-30-year-olds in care at HIV Research Network sites from 2006 to 2015. We stratified average outpatient visits, ED visits and inpatient days per person-year (PY) by mode of transmission (perinatal (PHIVY) versus non-perinatal (NPHIVY), age (13-17, 18-23, 24-30 years), CD4 strata (<200, 200-499, ≥500 cells/µL) and presence or absence of viral load (VL) suppression combined with antiretroviral (ARV) use (< or ≥400 copies/mL; ARVs or no ARVs). We also quantified outpatient, ED, and inpatient services associated with specific AIDS-defining conditions.

Results: Among 4,450 AYA (PHIVY:15%; NPHIVY:85%), there were 12,641 person-years of active outpatient care. Mean (SD) follow-up was 4.2y (3.1) and 2.5y (2.3); baseline mean age was 16.9y and 22.3y; female sex was 52% and
23%; and cumulative loss to follow-up was 8% and 20%. There were 17 deaths (PHIVY:6; NPHIVY:11). Among PHIVY, the majority of person-time was spent between ages 13-23y (13-17y: 43%; 18-23y: 45%), CD4 ≥500cells/µL (61%), and with suppressed VL (69%). Among NPHIVY, the majority of person-time was spent between ages 24-30y (56%), CD4 ≥500cells/µL (54%), and with suppressed VL (66%). Person-time spent while prescribed combination antiretroviral therapy and with unsuppressed VL was 30% (PHIVY) and 24% (NPHIVY). Of PHIVY and NPHIVY, 87% and 71% of participants ever had suppressed VL during the entire period of follow-up. Person-time spent off ARVs was 2% (PHIVY) and 10% (NPHIVY). For both PHIVY and NPHIVY, primary care outpatient visit rates were higher during person-time spent at younger ages (13-17y and 18-23y), at lower CD4 counts (<200, 200-499cells/µL), and while prescribed ARVs. Rates of ED visits and inpatient days were higher during person-time spent at older ages (18-23y, 24-30y), at lower CD4 counts (<200, 200-499cells/µL), and with unsuppressed VL. Overall utilization was higher among PHIVY than NPHIVY (outpatient: 12.1 vs. 6.0/PY; ED visits: 0.4 vs. 0.3/PY; inpatient days: 1.5 vs. 0.8/PY). The rate of AIDS-defining conditions was 4.5/100PY. AIDS-defining conditions associated with the greatest number of visits or days/event included: malignant cervical neoplasm (6.0), mycobacterial disease (4.0) and Kaposi’s sarcoma (3.4) for primary care outpatient; disseminated mycobacterium avium complex (0.6), progressive multifocal leukoencephalopathy (0.6) and dementia (0.6) for ED; Burkitt’s lymphoma (28.0), disseminated Mycobacterium avium complex (24.7) and progressive multifocal leukoencephalopathy (19.6) for inpatient.

Conclusions: Among AYA with HIV, more frequent ED visits and a greater number of inpatient days were observed during time spent at older ages, lower CD4 counts, and unsuppressed viral loads. Overall utilization was higher among PHIVY than NPHIVY. While AIDS-defining conditions were rare, associated resource utilization was substantial. Interventions to improve retention in care, virologic suppression, and immune response may improve outcomes, and thus decrease costly resource utilization, for AYA with HIV as they transition to adulthood.

91

AHEAD Study: a pilot randomised controlled trial of a music intervention aiming to improve executive function in adolescents with HIV

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Background: HIV-positive adolescents have increased risk of executive function (EF) deficits. Musical training has been associated with superior EF. We hypothesised that a group drumming programme would be a feasible and acceptable intervention to improve EF, mental health and perceived social support in HIV-positive adolescents in rural South Africa. The primary objective was to assess intervention feasibility and acceptability in the context. Secondary objectives were to assess the proof-of-concept of an effect on EF, mental health and perceived social support.

Methods: AHEAD (Adolescent HIV Executive Function and Drumming) was a non-blind pilot individually randomised controlled trial (PACTR201804003332337). We recruited 12-19-year-old adolescents (known HIV status) and caregivers at four primary care facilities in the MRC/Wits Agincourt rural HDSS site. Those randomised to the intervention received weekly hour-long sessions (with telephonic reminders) led by a trained facilitator for eight weeks. Controls received no intervention. All participants received snacks and transport fare reimbursement for visits. All participants
completed baseline and endline tablet-based assessments in Xitsonga involving REDCAP electronic questionnaires (including Self-Reporting Questionnaire-20, self-report and caregiver-report Strengths and Difficulties Questionnaire [SDQ], Multidimensional Scale of Perceived Social Support) and OCS-EF and RACER cognitive tasks (trails, Iowa Gambling Task, emotional go/no-go, rule-finding, digit span, spatial delayed match-to-sample, Simon). Feasibility and acceptability were assessed by logging logistical problems, session attendance, non-attendance reasons, pre-intervention expectations, and endline acceptability (including qualitative open-ended questions). Intervention participant data were only analysed if their intervention compliance was ≥ 75%. Cognitive and socio-emotional scale outcomes were analysed using linear regression (controlling for assets, education, baseline scores), and qualitative data using thematic analysis.

**Results:** 77 adolescents were screened; 68 (34 per arm) enrolled (mean age 15.4 years; 68% female; 94% school-enrolled; 90% perinatally acquired; median CD4 count 429 cells/mm³; median viral load 199 copies/ml; 100% ART-experienced; median ART duration 3.95 years). Pre-intervention acceptability was high in the 29 participants attending first session (≥ 90% felt positive and anticipated improved mood and concentration). Weekly attendance was 62-74%. 65% of intervention arm (n=22) received 75% of intervention. Reasons reported for non-attendance were logistical (e.g. transport) or personal (e.g. illness). There were no adverse events. There were no treatment effects on cognition, mental or social scales (n=56; p’s>0.05); however, participants reported subjective improvements. Of those who received half the intervention: 92% felt their concentration improved; 96% felt their mood improved. Participants’ favourite elements were programme components (music, games, snacks, facilitator) and perceived socio-emotional and cognitive benefits (acceptance; increased positive affect and self-worth; decreased disease-related anxiety and suicidality). Post-intervention, 90% felt positive towards programme, 82% recommended it, and 97% would participate again. On SDQ study impact question: more intervention than control participants felt their problems were better (82% vs 53%, p=0.036). Control participants also reported benefits (confidant; increased disease-related knowledge and adherence; decreased self-stigma).

**Conclusions:** Group drumming is a feasible and acceptable intervention amongst HIV-positive adolescents in rural South Africa with subjective socio-emotional benefits described in qualitative data; however, no effect on cognition or socio-emotional scales were found in this pilot. A full-scale trial with longer intervention duration would be more definitive.

92

**Scalability of Point-of-Care Early Infant HIV Diagnosis (POC EID) in Eight Sub-Saharan Countries: Comparing Key EID Outcomes in Introductory and Scale-up Phases.**


**Background:** Routine POC EID testing in sub-Saharan countries has been shown to provide superior clinical and EID outcomes compared to conventional early infant testing. We assessed the scalability of POC EID in eight countries comparing key EID outcomes between the introductory and scale-up phases, during which site enrollment into the POC EID network and network monitoring increased significantly.
Methods: 184 and 1,289 sites were enrolled during the introductory phase (first 6 months following POC EID introduction) and scale-up phase, respectively, in Cameroon, Côte d’Ivoire, Kenya, Lesotho, Mozambique, Rwanda, Eswatini, and Zimbabwe. Introductory phases started between December 2016 and March 2017. Scale-up occur in progressive phases started as early as July 2017. Scale-up data were available until November 2018. All sites received three supervision visits by project and/or ministry of health staff in the first 12 weeks following their enrollment, with quarterly visits thereafter. Human resource, training, and supervision remained the same across both phases although the number of sites requiring support increased throughout scale-up, adding network-monitoring complexities due to additional number of sites and faster enrolment pace. Data were collected prospectively from December 2016 until November 2018 and disaggregated by enrollment phase to compare changes in key EID outcomes (HIV test results returned to caregiver, treatment initiation rates, and turnaround times (TATs) from sample collection to caregiver receipt of results and to treatment initiation). Median TATs were compared between introductory and scale-up phases.

Results: Despite a minor decrease (-1.5%) in results returned within 30 days during scale-up phase as compared to the introductory phase, there were no significant differences in treatment initiation. The median turnaround times to caregiver receipt of result and to treatment initiation both remained at 0 days when moving into scale-up phase (Table 1).

Conclusions: Despite a three-time faster enrollment pace and greater overall network size, performance was sustained during scale-up. This POC EID implementation model can be scaled-up without compromising quality outcomes through strategic use of technical assistance.

Implementation challenges and strategies in integration of PrEP into maternal and child health and family planning services: Experiences of frontline health care workers in Kenya

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Background: Delivering PrEP to adolescent girls and young women (AGYW) through maternal and child health (MCH) and family planning (FP) clinics in Africa may substantially reduce HIV acquisition in this population. Evaluation of implementation challenges and strategies within health systems are critical to inform future scale-up.

Methods: We conducted focus group discussions (FGDs) with healthcare workers (HCWs) offering PrEP in MCH and FP clinics as part of the PrEP Implementation for Young Women and Adolescents (PriYA) Program in Kisumu, Kenya. Topic guides were based on the Consolidated Framework for Implementation Research (CFIR). An analysis of FGD audio and debrief reports was conducted to identify implementation challenges and employed strategies.

Results: Overall, 50 HCWs from 26 facilities participated in 8 FGDs. HCWs felt that PrEP met the needs of AGYW by providing a female controlled prevention strategy, and aligned with policy priorities of elimination of mother-to-child HIV transmission. They were universally enthusiastic about PrEP provision to AGYW through MCH clinics, noting the relative advantage of this approach because it: 1) enabled high coverage, 2) harmonized PrEP and MCH visits, and 3) lowered stigma compared to PrEP offered through HIV care clinics. HCWs noted implementation challenges including: 1) increased workload and documentation burden amid healthcare workforce shortages, 2) physical space
constraints, 3) drug and paperwork stockouts, 4) multiple implementing partners with different PrEP priorities and documentation practices at the same site, and 5) increased HIV testing sessions.

HCWs employed various implementation strategies to overcome implementation challenges, including task shifting from nurses to HIV Testing Service (HTS) providers, facility-specific patient flow modifications (including fast-tracking PrEP clients to reduce wait times), PrEP demand-generation and myth-busting during health talks, provider education, dedicated PrEP delivery rooms, and coordination with adolescent friendly services. Additional suggested strategies to improve PrEP integration included community education to increase broader PrEP awareness and enable shorter counseling sessions, and task-shifting data entry and client risk assessments.

Conclusions: HCWs were enthusiastic about the feasibility, acceptability, and potential sustainability of integrating PrEP services into MCH and FP clinics. Challenges and strategies focused on overcoming provider time and space constraints, and addressing provider and client knowledge.

94

Relationship between Proximity of Health Facilities to Referral Laboratories and Early Infant Diagnosis (EID) Turnaround Time (TAT) and Percent of Results Returned

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Background: Significant gaps remain in the EID testing cascade in sub-Saharan Africa and most results do not return to caregivers within the WHO-recommended 30 days. Testing of EID samples is primarily performed at referral laboratories, resulting in long TAT and low result return to caregivers. Use of point-of-care EID technologies has significantly reduced TAT and increased result return to caregivers. The optimal geographic placement of these products is un-defined and proximity of a facility to a referral laboratory may be used to plan POC EID placement.

Methods: As part of a nine-country pre- and post-POC EID introduction evaluation, data on key EID indicators during the pre-intervention phase (referral laboratory EID testing) were retrospectively extracted from EID registers in purposively selected sites in each country. A sub-analysis was undertaken from facility data in countries with more than one facility located ≤10 km from a referral laboratory and more than one facility located >80 km from a referral laboratory. Four sub-Saharan African countries (Cameroon, Cote d’Ivoire, Rwanda, Zimbabwe) were included which met these criteria. Using the facility as the unit of analysis, facilities ≤10 km (“near sites”) from a referral laboratory were compared to those located >80 kilometers away (“far sites”). The Mann-Whitney U test was used to compare TAT; and the Z-test to compare proportion of results returned to caregiver.

Results: 15 near sites (450 infants) and 18 sites far sites (540 infants) were included. The median TAT was 58 days (IQR 30-85) and 65.5 days (IQR 61-110) for near and far sites, respectively. The percentage of results returned to caregivers was 80% and 83% for near and far sites, respectively. Neither median TAT nor percent of results returned to caregivers was significantly different between near and far sites (p=0.16 and 0.83, respectively).

Conclusions: In this sample, proximity of a facility to a referral laboratory does not impact key EID process outcomes when sending EID specimens to referral laboratories, even when comparing facilities very close to referral laboratories (many of which were in the same city as the referral laboratory) to those much farther away. Given the positive impact of POC EID on TAT, result return and ART initiation...
presented previously, national programs and funders should consider using POC EID not only in hard-to-reach facilities, but also in facilities close to referral laboratories.

95

Outcomes of point-of-care maternal HIV viral load testing and early infant diagnosis at delivery: experience from four tertiary obstetric units in Gauteng, South Africa.

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Introduction: We describe outcomes of the implementation of HIV viral load (VL) and early infant diagnosis (EID) PCR point-of-care testing (POCT) among HIV-positive pregnant women and HIV-exposed neonates at time of delivery at four tertiary obstetric units (TOUs) in South Africa.

Methods: Admitted women were offered VL POCT around time of delivery between June–December 2018 as part of routine care. EID POCT was offered to HIV-exposed neonates during the same period, regardless of maternal VL testing. Specimen collection as clinically indicated was done by TOU staff. Research nurses conducted testing in designated POCT rooms 08h00-16h00 weekdays and returned results. Corresponding specimens for centralised laboratory testing were collected. Number of live births to HIV-positive women (denominator for coverage) was obtained from routine records. Data was analysed in Stata® 14.2. Coverage of VL and EID POCT and return of results prior to discharge were determined as proportions of live births and of those tested respectively, while turn-around times (TAT) - specimen collection to result delivery- were determined medians with interquartile ranges overall and by TOU.

Results: During the implementation period, 5764 live births to HIV-positive women were recorded; 2461 (42.6%) mothers and 4627 (80.3%) neonates each had POC VL and EID specimens collected, of which 1993 (34.6%) and 3475 (60.3%) were tested, respectively. The coverage for testing per site ranged from 17.6%-61.7% for POC VL and 46.1%-81.3% for EID. Of those tested, 74.7% mothers [range 32.4 - 95.2%] and 70.9% neonates [ range 41.6% - 97.7%] received POCT results before discharge. The median TAT for maternal VL was 3.2 hours and 7.1 hours for EID, both shorter than corresponding centralized laboratory TATs. There was wide variability in outcomes across TOUs, with better outcomes in the TOU with prior experience of EID POCT and a larger staff complement.

Conclusions: Implementation of VL and EID POCT, by routine TOU staff and one research nurse, yielded suboptimal testing coverage. Higher EID coverage was attributed to birth PCR being established practice since 2015. More than a quarter of tested patients were discharged before receiving their results. Understanding factors behind the variable outcomes will inform scale-up and improve outcomes.

96

HIV prevalence and factors associated with HIV among children 2-14 years presenting to high-risk settings of selected health facilities in Ethiopia

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Background: In Ethiopia, pediatric antiretroviral therapy (ART) coverage significantly lags behind adult ART coverage (34% vs. 75%), mainly due to challenges with pediatric case identification. Lack of data on HIV prevalence limits informed policy development and implementation of optimized pediatric testing strategies. This study aimed to determine pediatric HIV prevalence, testing yield, and factors associated with HIV at high-risk service delivery entry points in low-prevalence settings.

Methods: A cross-sectional study was conducted from May 2017-March 2018 in 29 public health facilities in Amhara and Addis Ababa regions in Ethiopia. Children 2-14 years were enrolled at different entry points. Data collection included abstraction of HIV status and anthropometric measurements from medical records, and interview with caregivers on sociodemographic factors and clinical history. HIV prevalence and yield among newly tested clients was calculated for each entry point. Logistic regression analysis was conducted to identify factors associated with new diagnosis of HIV.

Results: 2166 children (median age 8 years) were enrolled, identifying 54 known positives and 40 new positives. HIV prevalence and testing yield was highest in family index testing (8.2% and 8.2%), followed by TB clinics (7.9% and 1.8%) and children on treatment for severe malnutrition (6.5% and 1.4%), and were lowest in inpatient wards (3.2% and 0.7%) and orphan and vulnerable children (OVC) programs (2.4% and 0.3%). Prevalence and yield increased with age, and was highest in 10-14 year olds (5.9% and 2.3%) and lowest in 2-4 year olds (2.3% and 1.6%). Factors associated with new HIV diagnosis included: maternal orphan status (aOR= 4.49), recurrent skin infections (aOR= 15.73), severe acute malnutrition (aOR= 4.42), and urban residence (aOR = 3.36), using electricity as a proxy.

Conclusion: The highest pediatric HIV prevalence and yield was in children presenting for family index testing, TB clinics, and severe malnutrition. Strategies and resources should be in place to implement universal testing at these key entry points, and ensure older children are included. HIV screening tools to target testing to high-risk children is needed for inpatient wards, moderate malnutrition, and OVC beneficiaries to maximize resources, utilizing the associated factors of orphan status and recurrent skin infections.

Humoral immune response to measles vaccination at 6, 9, and 15 months and antibody persistence during the first five years of age in early treated HIV-infected children in Cameroon.

Background: Measles remains one of the leading threats among young children living in low-income countries despite the availability of safe and cost-effective vaccines. We aimed here to compare the humoral response to measles vaccine (MV) at different time points during the first five years of life between early treated HIV-infected (HI), HIV-exposed uninfected (HEU), and HIV-uninfected children (HUU) and to identify factors associated to poor MV response.

Conclusion: The highest pediatric HIV prevalence and yield was in children presenting for family index testing, TB clinics, and severe malnutrition. Strategies and resources should be in place to implement universal testing at these key entry points, and ensure older children are included. HIV screening tools to target testing to high-risk children is needed for inpatient wards, moderate malnutrition, and OVC beneficiaries to maximize resources, utilizing the associated factors of orphan status and recurrent skin infections.
**Methods:** The ANRS-PEDIACAM study (n=611), an ongoing prospective observational cohort launched in 2007, is constituted of the above-mentioned children groups included before the aged of 7 months in 3 referral hospitals in Cameroon. Vaccinated children with at least one plasma sample within the study period (n=530) were considered. Measles antibodies were measured within 1 to 6 months after each vaccine dose, then at 2, 3, 4, and 5 years of age using Enzygnost ELISA kit. Results were interpreted as positive if ΔOD> 0.2 (Optical density) corresponding to an antibody titer higher than 319-357mIU/mL depending on lot number. Factors associated to children poor response after 9 months MV were identified using logistic regression.

**Results:** Similar humoral responses were observed after 9 months MV between HI (80.77%, n =104), HEU (81.75%, n =126), and HUU (73.81%, n =126) and after 15 months with HI (96.10%, n =100), HEU (96.08%, n =102), and HUU (99.12%, n =113). Same observation was made concerning measles antibodies persistence and titers (IIQ) at 60 months of age: HI (82.43%, n =74, geometric mean titer=1213.71 mUI/ml IC95%(976.17-1509)), HEU (89.74%, n =78, geometric mean titer=1315.43 mUI/ml IC95%(1051.04-1646.3)), and HUU (91.95%, n =80/87, geometric mean titer=1199.64mUI/ml IC95%(979.66-1469.02)). Among HIV- infected children, factors associated to poor humoral response were low CD4%<34 at cART initiation (OR: 4.75; 95%CI [1.33-16.97]), Nevirapine- based regimen at initiation (OR: 3.87 - 95%CI [1.25-11.98]) compared to lopinavir-based, and poor nutritional status (OR: 6.97- 95%CI [1.75-27.67]).

**Conclusions:** This study shows that early follow up and cART could lead to good MV humoral response among HIV infected-children. Factors associated to poor MV response at 9 months were related to advanced disease at cART initiation. There is a need to monitor the evolution of antibody response within the study period using adapted statistical tools.

**Completeness of maternal HIV testing and repeat testing in Cape Town, South Africa: a longitudinal analysis**

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**Background:** The virtual elimination of mother-to-child transmission of HIV cannot be achieved without complete maternal HIV testing. The WHO recommends that women in high HIV prevalent settings be repeat tested in the third trimester or at delivery. Since 2014 the Western Cape Province (South Africa) prevention of mother-to-child transmission (PMTCT) guidelines recommend a repeat HIV test between 32 - 34 weeks gestation and at delivery, in addition to testing at “booking”, the first antenatal visit ideally before 20 weeks gestation. There are few published longitudinal studies on the uptake of initial and repeat maternal HIV testing programmes in sub-Saharan Africa.

**Methods:** Between 2013 and 2016 we established an electronic PMTCT register that consolidated routine data from a primary healthcare facility and its secondary and tertiary referral sites in Cape Town. This provided a single longitudinal record, from first antenatal visit to delivery. Utilizing these data, we conducted a retrospective analysis investigating the completeness (up to and including delivery) of maternal HIV testing according to the PMTCT HIV testing guidelines in Cape Town, and predictors of complete testing, from July 2014 – December 2016. We used descriptive statistics to assess: the coverage and timing of HIV testing during pregnancy at “booking” and within subsequent recommended testing windows (including delivery); and HIV prevalence and incidence at the recommended testing windows. Logistic
regression was used to determine predictors of missed testing opportunities.

Results: Among 8558 women who delivered at either the primary care facility or its referral sites, 7213 (84%) were not known to be HIV-positive at their first visit and thus eligible for testing in pregnancy, 91% of them received ≥1 HIV test during pregnancy including delivery. Testing completeness at “booking” was 98% among the 85% of women who “booked” for antenatal care, however only 43% “booked” ≤20 weeks gestation. Among women eligible to receive tests at all 3 recommended timepoints, only 10% were tested according to the guidelines. At delivery, HIV testing completion among all women without an HIV-positive diagnosis was 23%. Out of the women who had known HIV status at delivery, 21% were HIV-positive of whom 95% were known HIV-positive before current pregnancy and 4% were diagnosed at their first visit. Overall, HIV incidence in those with ≥2 HIV tests during pregnancy/at delivery was estimated to be 0.2% between “booking” and delivery (i.e. seroconversion during pregnancy). Women who enrolled after 2014 were more likely to receive the three recommended tests (aOR 1.43; 95%CI 1.11–1.83) and to test at delivery (aOR 1.60; 95%CI 1.40–1.82).

Conclusions: HIV testing completion at “booking” was high, but women tended to seek antenatal care late resulting in late initial testing and missed opportunities for early HIV diagnosis. Implementation of repeat HIV testing is poor, particularly at delivery. HIV incidence between first negative antenatal test and delivery is very low and further research is required to assess the most cost–effective and feasible frequency of HIV tests. Overall, maternal HIV testing within the PMTCT programme in Cape Town has matured post 2014 with improved implementation over time.

99

This abstract was withdrawn.

100

Confirmatory testing of HIV-positive status before initiation of antiretroviral treatment: caregiver and healthcare worker experience in Ethiopian facilities

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Background: Since 2014, WHO guidance has recommended confirmatory HIV testing for all people newly diagnosed before antiretroviral treatment (ART) initiation. Ethiopia adopted these recommendations in 2016 and began implementation at HIV testing sites. However, there is little published about confirmatory HIV testing from the perspectives of caregivers and healthcare workers (HCWs). We aimed to assess the experiences of caregivers and HCWs with confirmatory HIV testing of children before ART initiation.

Methods: A cross-sectional study was conducted from May 2017-March 2018 in 29 public health facilities in Amhara and Addis Ababa regions in Ethiopia, enrolling children 2-14 years at high-risk HIV testing entry points. Data collection included abstraction of HIV status from medical records and interview with caregivers on sociodemographic factors and clinical history. Caregivers of children newly testing positive during the study were interviewed after 3 months, and data gathered on experiences of confirmatory testing. Forty HCWs at eight sites were also interviewed about performing confirmatory testing. Descriptive results are described.

Results: Among 40 children newly diagnosed HIV-positive and 1 previously known HIV-positive child not yet on ART, confirmatory testing was done for 34 (83%) by 3 months.
Abstracts

There were no discordant results. Confirmatory tests were conducted within one week of diagnosis for two-thirds (23/41). Less than half (16/41) had their test done the same day of diagnosis. Reasons given for not receiving confirmatory testing included: results were confusing (n=2), test not offered (n=1) non-linkage to ART service (n=1), misunderstanding on the needs for testing (n=1), and death of the child (n=1). The majority (88%) of caregivers of children who received confirmatory testing were satisfied with their experience. Thirty-six (95%) HCWs felt better about starting children on ART after the confirmatory test. Thirty-two HCWs (80%) believed that doing a confirmatory test made caregivers feel better.

Conclusion: Discordant results during confirmatory HIV testing at ART initiation was not observed in this study; however, delays in conducting the confirmatory test was seen, resulting in delayed ART initiation in some children. Caregivers and HCWs had high acceptance rates of confirmatory testing, and both felt better about results of HIV tests and ART initiation after the confirmatory test.

101

Feasibility of Point-of-Care Viral Load Testing in Postpartum HIV-positive Women in South Africa: Interim Results

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Background: Elevated maternal viral load (VL) increases HIV transmission risk for infants during breastfeeding. Although VL testing should be done 6-month post-partum, feedback and action of results are frequently delayed. We describe early results from a non-blinded randomised controlled trial in Johannesburg comparing point-of-care (POC) testing (arm 2), to standard-of-care (SOC) laboratory-based VL testing (arm 1) in HIV-positive post-partum women on first-line antiretroviral treatment.

Methods: Data from the enrolment visit (infant 6, 10, or 14 week clinic visit) was included for 150 mothers and 143 infants enrolled between 4 July 2018 and 23 October 2018. Using the Cepheid GeneXpert IV POC device, trained nurse clinicians and field workers conducted POC HIV-VL in arm 2 women and POC HIV-Qual infant polymerase chain reaction (PCR) testing in arm 1 and 2. Patient demographics, laboratory, and clinical data were captured in REDCap and analysed using STATA 13.1. Chi-square test was used for categorical and t-test for continuous variables.

Results: There were no statistically significant differences in enrolment characteristics between women in arm 1 and arm 2. Median infant age at enrolment was 10 weeks (IQR: 6.4-10.3). 39 (26%) women had previous VL available, 97% were virally suppressed (VL <1000 copies/ml). At enrolment, 16 (10.7%) women had a VL ≥1000 copies/ml, 5 (31%) in arm 1 and 11 (69%) in arm 2. 100% women in arm 2 received POC VL results on the same day as study visit. The median time for VL results available and returned to the mother was 2 days (IQR 2-4) and 45.5 days (IQR: 17-103) in arm 1. In arm 1, two women had appropriate management within one month and three were not contactable. In arm 2, one woman was not contactable to return for a repeat VL. All 143 enrolled infants tested POC PCR negative; 100% received POC PCR results on same day as study visit.

Conclusions: Findings to date show that POC VL testing in postpartum women, conducted by field workers and nurses, is possible with same day results allowing immediate and tailored
clinical management of HIV in maternal populations. This may reduce challenges experienced with feedback of laboratory-based results to the patient.

102

Comparison of qPCR and ddPCR methods to investigate the latent HIV reservoir in a paediatric population with long viral suppression on therapy

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Background: Children with perinatal HIV infection currently have a life-long requirement for antiretroviral therapy (ART). Despite effective therapy, HIV can persist as integrated provirus generating latent viral reservoirs even in the absence of detectable plasma viremia. Latently infected cells, primarily CD4+ T cells, have the potential to release progeny virus and contribute to viral rebound after treatment interruption. Robust assays to monitor the chosen markers of the reservoir are therefore essential and may guide treatment interruption in emerging therapeutic approaches in the future. Here we compare two methods, established qPCR and droplet digital PCR (dPCR), to quantify total HIV-1 DNA, a marker that although known to overestimate the reservoir is extensively used. dPCR offers a theoretical advantage in precision given the fact that a calibration curve is not required. We additionally investigated the role of normalising the HIV DNA value to a cellular genome marker in order to more accurately report HIV DNA copies per million cells.

Materials & Methods: Forty European children and adolescents aged ≥5 years, perinatally infected with HIV-1 receiving suppressive ART (viral suppression <50 c/ml maintained for a minimum of 5 years) were recruited into the CARMA study. Total HIV-1 DNA was measured in purified PBMCs by both dPCR and qPCR. Total nucleic acids were extracted from PBMCs on the Qiasymphony platform using the DSP virus/pathogen mini kit (Qiagen) according to the manufacturer’s protocol. Primers were designed for HIV LTR and genomic reference gene PDH. Quantification of cell-associated HIV-1 DNA with qPCR was determined using 20 µl of extract and a standard curve with known copy numbers in 10 fold dilutions. Samples from the same extract were analysed by dPCR using identical primer sets. Twenty µl (11% CV) of each sample was analysed using the QX200™ Droplet Digital™ PCR System. For comparison between qPCR and dPCR HIV-1 copy numbers were calculated as copies per 10^6 PBMCs. No-template controls were included.

Results: HIV-1 DNA was detected in 34 of the 40 patients, 26 by qPCR and 28 by dPCR, overlap of 22 in paired extracts. HIV-1 DNA was calculated per million cells based on PDH values (0-410 copies per 10^6 PBMCs by qPCR and 0-1420 copies per 10^6 PBMCs by dPCR). Further extractions and qPCR were performed and an additional 10 samples showed detectable HIV-1 DNA at very low levels, below 10 copies per million cells. Thus, a total of 36 of the 40 patients had detectable DNA with a range of 0.1-410 copies per 10^6 PBMCs. Seven of these were below 10 copies per million cells.

Conclusion: Data generated by dPCR indicate a sensitivity of 10 molecules and, at very low HIV-1 DNA levels such as those measured in our patient cohort, may be more accurate than qPCR due to the necessity of a calibrator in the latter. However, the stochastic nature of molecules at this level may preclude meaningful quantification. Further, when employing a qPCR assay, we highlight that caution should be used when normalising to a cellular genome marker.
Point-of-care HIV testing at birth for high-risk vs. all HIV-exposed infants: preliminary results from a pilot study in Zimbabwe

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Background: Birth testing may identify infants infected with HIV in utero and increase early antiretroviral therapy (ART) initiation. National guidance in Zimbabwe recommends that newborns testing negative at birth return for a 6-week test; newborns testing positive should start nevirapine-based ART and return at 14 days to begin lopinavir/ritonavir-based ART. Since April 2017, Zimbabwe has offered point-of-care (POC) birth testing at 35 sites for newborns considered high-risk according to a set of maternal factors. Beginning 1 November 2018 in 10 selected sites, POC birth testing was offered to all HIV-exposed infants, regardless of risk assessment. We evaluated the use of POC birth testing to identify and initiate infected infants on treatment, and compared key service delivery outcomes between the sites offering birth testing to high-risk vs. all HIV-exposed infants.

Methods: Prospective data were collected on all POC tests administered from 1 April 2017-18 February 2019. Variables included: number and percent of infants tested at birth at each site, percent of caregivers receiving results, turn-around-time (TAT) from sample collection to result receipt, positivity yields, percentage of infected infants initiated on treatment, TAT from diagnosis to treatment initiation, percentage of infants testing negative at birth who received a subsequent test at 6-weeks, and treatment retention among those who initiated.

Results: From April 2017 - October 2018, 557 high-risk infants received a birth test and 100% of their caregivers received results. Median TAT from sample collection to caregiver receipt of results was 0 days (IQR 0-2.75). 26 HIV-infected newborns were identified (positivity 4.7%) and 23 were initiated on treatment (88.5%); 21 were initiated within 14 days of diagnosis and all 23 by 60 days. Mean TAT from diagnosis to treatment initiation was 3.5 days (Median 0; IQR 0-2). From 1 November 2018 – 18 February 2019, at sites offering birth testing regardless of risk, 616 infants received a birth test. 97.4% of their caregivers received results, with a median TAT of 0 days (IQR 0-0). 11 HIV-infected infants were identified (positivity 1.8%) and 8 were initiated on treatment (72.7%); all within 14 days of diagnosis. Mean TAT from diagnosis to treatment initiation was 0 days (Median 0; IQR 0-0). Further comparisons between high-risk infants and all HIV-exposed infants, as well as analyses of subsequent tests of newborns who tested negative at birth and treatment retention for those who tested positive at birth and initiated treatment, are ongoing (and will be available for presentation at IAS and the pediatric workshop).

Conclusions: POC EID at birth is a feasible strategy in this setting, and could be an important tool in identifying and initiating infants before the highest mortality period (two months of age for those infected during pregnancy or childbirth). In this study at selected health facilities in Zimbabwe, when compared to POC testing at birth for only high-risk infants, testing all HIV-exposed infants did not appear to negatively affect turnaround times, receipt of results, or other key service delivery indicators. Testing all HIV-exposed infants may allow for faster identification of more infected infants than only high-risk testing. In this study, almost all tested infants received results immediately and, regardless of assessed risk, the majority of identified HIV-infected infants were successfully linked to care and rapidly initiated on treatment.
Dolutegravir does not induce neural tube defects in a rat whole embryo culture system

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A rat whole embryo culture study was conducted to investigate whether direct exposure of dolutegravir to a rat embryo during a critical period for neural tube development would result in abnormal development. Rat embryos were removed from the dams and individually cultured in media containing test article from Gestation Day 9 to 11 (approximately 40 hrs). Vehicle control, Valproic acid (VPA: positive control), Penicillin G (Pen G: negative control) or concentrations of dolutegravir were added to the culture media for the entire culture period. Concentrations of the negative and positive controls were based on previous published work (VPA concentration is close to the therapeutic range; Pen G concentration is in a typical range for detection of malformations). Dolutegravir was evaluated at two concentrations that were similar to the maximum plasma concentration observed in humans at the recommended clinical dose (50mg QD or 50mg BID); also, the higher concentration was slightly lower than concentrations previously shown to be cellularly toxic in another mammalian in vitro assay. 16 embryos/group were cultured with either vehicle control (heat inactivated rat serum with Tyrodes buffer, streptomycin and 0.04% DMSO), dolutegravir (6 or 10 uM, 2.5 or 4.2 ug/mL, respectively), VPA (800 uM) or Pen G (1uM). Statistically significant decreases in visceral yolk sac and embryo size and somite number were seen with VPA. In addition, effects on embryonic morphology (exencephaly, open neuropore, brain segment narrowing and/or spinal cord effects) were seen in all VPA-treated embryos. No effects on size, somite count or neural tube defects were seen at either concentration of dolutegravir, the vehicle or negative controls. In conclusion, as expected from lack of evidence of NTD in DTG non-clinical toxicology studies, no neural tube defects were detected in rat embryos cultured with dolutegravir independent of maternal influence in an embryo culture system. All studies were conducted in accordance with the GSK Policy on the Care, Welfare and Treatment of Laboratory Animals and were reviewed the Institutional Animal Care and Use Committee either at GSK or by the ethical review process at the institution where the work was performed.

Laboratory evaluation of the Xpert® HIV-1 Qual Assay as a point of care technology for HIV early infant diagnosis in Kenya

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**Background:** A prompt return of results in early infant diagnosis (EID) of HIV among HIV exposed infants (HEI) is essential for rapid initiation of antiretroviral therapy (ART). Point of care (POC) technologies can significantly improve the turn-around-time for HIV diagnosis in infants, thereby increasing both retention rates and the proportion of pediatrics that are linked to care. Further to this, these technologies are expected to accelerate the uptake of HIV diagnosis in line with the first ‘90’ of the UNAIDS global 90-90-90 targets. In Kenya, EID is currently centralized, and current projections have it that this system may not meet the aforementioned targets, therefore necessitating the need to scale up access to EID. Xpert® HIV-1 Qual Assay is one of the WHO
prequalified nucleic acid (NAT) based POC assay for the detection of HIV in infants born to HIV infected mothers. The objective of this evaluation was therefore to assess the performance characteristics of the assay, before roll out into the public health care set up.

**Methods:** Performance characteristics for Xpert® HIV-1 Qual Assay were compared to the existing ‘gold’ standard (Roche CobasTaqMan assay) at the National HIV Reference Laboratory, Kenya using routinely collected EDTA whole blood from 200 infants (114 female, 86 male) attending the Kenyatta National Hospital elimination of mother to child transmission (eMTCT) clinic. Statistical analysis was done using statistical analysis system (SAS) version 9.4 to assess the sensitivity, specificity, positive and negative predictive values, and the kappa value in comparison to the gold standard.

**Results:** A sensitivity of 98% with a perfect specificity of 100% was observed for Xpert® HIV-1 Qual Assay. Positive and negative predictive values were 100% (95% CI: 96.4-100) and 98% (95% CI: 93-99.8) respectively. The assay time to result for Xpert® HIV-1 Qual Assay was <2 hours while that of the reference method is 5 hours. Kappa value of 0.98 (95% CI: 0.952 - 1.000) was observed, denoting a near-perfect agreement between the two assays.

**Conclusion:** Xpert® HIV-1 Qual Assay reported an acceptable laboratory performance making its upcoming roll-out a great initiative for Kenya in the race towards the UNAIDS 90-90-90 targets. Its ability to relay results to patients in a single visit could greatly improve patient retention rates, provide better linkage to care, and ultimately improve treatment outcomes.

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**Pediatric HIV case identification: Missed opportunities along the PMTCT cascade in Kenya and Uganda**

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**Background:** A large number of HIV-infected children remain undiagnosed due to missed opportunities along the prevention of mother-to-child HIV transmission (PMTCT) cascade. This study addresses some programmatic gaps by describing maternal profiles of children identified as HIV-positive through active case finding in Kenya and Uganda.

**Methods:** In November 2017-October 2018, we enrolled caregivers of newly diagnosed HIV-positive children <15 years of age, in 45 facilities and surrounding communities (Homa Bay County, Kenya: 15, Southwest Uganda: 30). Caregivers were interviewed about mothers’ utilization of health services, including antenatal care (ANC), HIV testing and antiretroviral (ARV) use. Results were summarized using descriptive statistics.

**Results:** Median age of all children enrolled (n=174) was 2.4 years (interquartile range 0.9-6.2). In Kenya, median age was 3.6 years (1.4-8.8); in Uganda, median age was 2.0 years (0.9-4.5). Overall, 51.7% were female. Of 174 caregivers interviewed, 134 (77.0%) were biological mothers and fathers (n=60 in Kenya, n=74 in Uganda). ANC attendance rates were 80.0% (48/60) and 86.5% (64/74) in Kenya and Uganda, respectively; four known HIV-positive women did not attend ANC. In total, 62 women (65.3%) tested HIV-negative in ANC. Of 41 and 56 HIV-positive women during pregnancy and breastfeeding respectively, 17 (41.5%) and 15 (26.8%) did not receive ARV prophylaxis or treatment. Reasons included clinic not offering ARVs (n=7 during pregnancy, 5 during breastfeeding), defaulting from clinic (n=4,2),

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Reviews in Antiviral Therapy & Infectious Diseases 2019_7
home delivery (n=0.3), HIV status denial (n=1.2) and other/unknown reasons (n=5.3). Of the 41 mothers who were known or tested HIV-positive during pregnancy, 15 (36.6%) of their infants were diagnosed by six months of age. Eight children (19.5%) were not diagnosed until 5-12 years of age, though we did not confirm transmission mode and three caregivers reported previous child testing. Of the mother-child pairs with complete HIV diagnosis information and maternal diagnosis after delivery, 43/75 (57.3%) children were diagnosed as HIV-positive within 14 days of the mother testing HIV-positive; 13/75 children (17.3%) were reportedly tested previously. In Kenya, an additional three children were diagnosed before the mother.

Conclusions: Findings identify program weaknesses in which mothers of newly identified HIV-positive children missed services to prevent vertical transmission and may have resulted in children’s delayed diagnosis and treatment. There were also gaps between maternal and child diagnoses, indicating possible delays in delivery of HIV testing services to HIV-exposed children. ANC attendance was slightly lower than national rates. Two-thirds of women tested HIV-negative in ANC, highlighting the importance of retesting during pregnancy and postpartum and prevention messages for those testing HIV-negative. Finally, some newly diagnosed and known HIV-positive women did not receive ARVs, suggesting inter-facility referral and follow-up systems need to be strengthened.

Monitoring and Supporting Women Living with HIV Who Choose to Breastfeed their HIV-Exposed Infants in Botswana

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Background: Within the current context of guidelines in high-income countries recommending formula feeding for women living with HIV (WLHIV), there is emerging interest in this setting on how best to support WLHIV who choose to breastfeed. We report an approach to monitoring and supporting WLHIV choosing to breastfeed in a research cohort in Botswana.

Methods: Botswana guidelines promote exclusive breastfeeding among WLHIV on antiretroviral treatment (ART) and virally suppressed at delivery. Free infant formula is provided through the government for women choosing not to breastfeed. The Tshilo Dikotla study enrolls pregnant WLHIV with breastfeeding intentions. WLHIV must be on tenofovir/emtricitabine plus dolutegravir or efavirenz in pregnancy; infants are randomized to receive zidovudine or nevirapine prophylaxis for 4 weeks. Maternal viral load (VL) is obtained at enrollment, then repeated in pregnancy and at delivery if initially detectable (>40 copies/mL). WLHIV are counseled on safe infant feeding practices and encouraged to select formula feeding if VL is detectable at delivery or postpartum. When breastfeeding is elected and ongoing, VL monitoring and ART adherence education occur at each study visit (1, 2, 4-6, 9-12, 18, 24 months postpartum). For breastfed infants, HIV DNA PCR testing is performed up to 6 weeks after breastfeeding cessation. This analysis includes singleton infants of WLHIV who completed breastfeeding. Prevalence rates of breastmilk-associated mother-to-child transmission of HIV (MTCT) were calculated with 95% confidence intervals (CI).

Results: Overall, 129 WLHIV/infant dyads (n=86 WLHIV on dolutegravir-based ART, n=62 infants randomized to zidovudine prophylaxis) completed breastfeeding. Median [interquartile range (IQR)] age, gravidity, and duration of breastfeeding was 30 years (IQR:26-35), 3 (IQR:2-4) and 4.03 months (IQR:1.72-6.03) respectively. Thirteen women had a detectable VL (median detectable VL:
611 copies/mL, range: 56-32,183 copies/mL) at any point during breastfeeding; of these, 8 switched to formula feeding. The prevalence rate of MTCT during breastfeeding was 0.00% (95% CI: 0.00, 0.03).

**Conclusion:** In this small research cohort, no breastmilk-associated MTCT occurred. Though further studies are warranted in larger populations, the approach of frequent VL and adherence monitoring coupled with counseling on feeding choices may inform the dialogue in high-income countries surrounding how best to support WLHIV who choose to breastfeed.

108

**HIV vaccination in infancy to achieve lifelong protection- a real possibility?**

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**Background:** Young adults aged 15-24 represent a high-risk for HIV-1 infection, and the only population in which HIV infection continue to rise. Women account for two thirds of these young adults, thereby directly linking the epidemics in young adults and pediatric HIV infections. Despite successful implementation of HIV prevention and treatment strategies worldwide, young adults have some of the lowest rates for HIV testing and adherence to antiretroviral therapy when HIV positive. Thus, a vaccine is needed to stop HIV infection. As a model of early life immunization for long term immunity, we tested the hypothesis that immunization of infant rhesus macaques with HIV Env vaccines can induce potent and durable HIV Env-specific antibodies.

**Methods:** Utilizing the rhesus macaque model, we tested distinct HIV Env vaccine regimens and intervals, compared several adjuvants to optimize HIV Env-specific antibody responses, and evaluated whether passive administration of a broadly-neutralizing Env-specific antibody would interfere with the development of active antibody responses by infant vaccination. Antibody responses were evaluated for magnitude, avidity, neutralization, and for Fc-mediated effector functions.

**Results:** The combined administration of an MVA-HIV Env 1086.C/ 1086.C Env protein vaccine in an extended interval of weeks 0, 6, and 12 in infant rhesus macaques induced high magnitude Env-specific plasma antibody responses with strong avidity, measured by SPR. Env-specific antibody responses could be significantly enhanced in magnitude and function when the Env-protein was adjuvanted with 3M-052-SE compared to STS adjuvant. Of note, responses persisted for up to 20 weeks after the last immunization. A late boost at week 32 further increased antibody binding to infected cells, ADCC, and ADCP. These vaccine-induced responses were unaffected by passive administration of the bnAb CH31 at the first immunization. We also observed that infants mounted potent follicular T helper cell responses associated with germinal center B cell activation.

**Conclusion:** Our combined results of multiple infant macaque studies are consistent with human data and support the idea that an HIV vaccine with initiated in infancy and boosted in childhood should be tested as a strategy to protect against sexual acquisition of HIV in adolescence and to potentially provide lifelong immunity.

109

**A systematic review and meta-analysis of HIV incidence during pregnancy and breastfeeding in sub-Saharan Africa**

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**Background:** Women in sub-Saharan Africa face a high risk of HIV acquisition during pregnancy and breastfeeding, and those who seroconvert during these periods are more likely to transmit HIV to their infants than women with a confirmed HIV infection. However, in recent years, the widespread adoption and scale-up of combination HIV prevention (including treatment as prevention) may have reduced HIV incidence during these at-risk periods.

**Methods:** We systematically searched four electronic databases and relevant HIV conferences between January 1, 1980 and December 1, 2018 for literature on the incidence of HIV during pregnancy and breastfeeding in sub-Saharan Africa. Inverse-variance weighted random-effects models were used to estimate pooled incidence rates and examine trends over time. Calendar time was defined as the midpoint of study implementation and examined continuously and categorically. Our categorical time windows corresponded roughly to eras of combination HIV prevention: pre-implementation (pre-2010), early adoption (2010-2014), and program expansion (post-2014).

**Results:** Forty-one studies met our inclusion criteria. These represented 35 independent cohorts that contributed 104,203 person-years (PY) of follow-up and 36 estimates of the incidence rate of HIV during pregnancy and breastfeeding. Twenty-three estimates were generated before 2010, nine between 2010 and 2014, and four after 2014. The overall pooled incidence rate was 3.7/100PY (95%CI: 3.0-4.5). We observed high heterogeneity of the incidence rate (95% prediction interval: 1.2-11.6), and no apparent difference between pregnancy and breastfeeding periods (ratio of stratum-specific pooled incidence rates: 1.0, 95%CI: 0.6-1.7). Combined, HIV incidence during pregnancy and breastfeeding appeared to decline over calendar time. The pooled estimate of the incidence rate was highest during pre-implementation (4.3/100PY, 95%CI: 2.7-6.8), followed by early adoption (3.0/100PY, 95%CI: 1.7-5.2), and program expansion (1.7/100PY, 95%CI: 0.9-3.0).

**Conclusion:** Declines in HIV incidence among pregnant and breastfeeding women in sub-Saharan Africa over the past decade coincide with the implementation and expansion of combination HIV prevention. Overall rates remain high, however, underscoring the need for novel intervention efforts tailored to pregnancy and breastfeeding.

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**A systematic review of risk factors for HIV acquisition during pregnancy and breastfeeding in sub-Saharan Africa**

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**Background:** Numerous studies have reported high HIV incidence rates during pregnancy and breastfeeding in sub-Saharan Africa. Understanding factors affecting HIV acquisition risk in this population could inform targeted HIV prevention strategies. However, individual studies of potential risk factors often have limited statistical power and uncertain generalizability. Considering the evidence-base as a whole is therefore important.

**Methods:** We systematically searched four electronic databases and relevant conferences from January 1980 to December 2018 for studies that examined risk factors for HIV acquisition during pregnancy and breastfeeding in sub-Saharan Africa. Two reviewers independently assessed studies for inclusion and abstracted data into standardized forms; disagreements were resolved with a third reviewer. As heterogeneity was observed in the types and definitions of risk factors, results are narratively synthesized.

**Results:** Of 5,182 citations identified, 33 met our inclusion criteria. In these, 69 different risk
Factors were assessed. Most studies were implemented in southern and eastern Africa (n=31). Increasing maternal age was inversely associated with incident HIV in 16 of 23 studies. These studies typically distinguished between adolescent girls, young women, and women ≥25 years. Relationship status was also frequently associated with HIV acquisition, with 12 of 15 studies reporting a lower incidence of HIV among married compared to non-married women. Eleven of 12 studies reported an association between incident HIV infection and a current or previous sexually transmitted infection (STI). An increased risk of HIV acquisition persisted irrespective of causative agent and measurement approach. All nine studies that measured number of sex partners reported an increased risk of HIV associated with multiple partners. While knowledge of partner’s HIV status was inconsistently associated with HIV seroconversion, known HIV serodiscordancy was associated with increased risk of incident HIV (three of three studies). Finally, reported associations between condom use and HIV seroconversion were mixed; three studies reported lower risk while six studies observed an increased risk of seroconversion associated with condom use.

Conclusions: Despite inherent variability between studies, several factors routinely assessed during antenatal and postpartum care were associated with incident maternal HIV infection. These factors should be incorporated into risk assessments to identify and prioritize high-risk women for HIV prevention intervention.

Reasons for new paediatric HIV infections: findings from a cohort of HIV infected children screened at Harare Family Care Clinical Research Site.

Background: While the Zimbabwe national ART role out program has reduced mother to child transmission (MTCT) rates of HIV from more than 25000 new infections per year in 1996 to less than 5000 new infection per year in 2017, the country is still to achieve the <5% targets for elimination of mother to child transmission of HIV(eMTCT). To achieve these minimum eMTCT targets, it is acknowledged that effective implementation of the eMTCT agenda requires interventions beyond biomedical approaches as socioeconomic and psychological factors also play a role. There is need to strengthen PMTCT services by shifting to a case finding, response and elimination approach.

We set out to identify reasons for new pediatric HIV infections in children screened for possible enrolment into IMPAACT protocols at Harare Family Care Clinical Research Site (HFC CRS) from 2014-2017. For all HIV infected children screened at the CRS, baseline background sociodemographic, pregnancy and birth and developmental history is routinely collected.

Materials & Methods: Data was abstracted from charts of children 0-3years screened at the CRS during the period Jan 2014 and July 2018 using a structured tool. This data included socio-demographics, pregnancy and birth history, PMTCT and child development history. Data was captured and analysed using EPI INFO version 7.2.2.1.

Results: 40 participant charts were reviewed. The mothers’ age range was 19-41yrs (median 25.5years). Children age range at the first HIV positive test was 0-38 months (median 11.5months). 17/40 of the mothers (42%) attended at least one ante-natal (ANC) visit of which 14 of these registered during the third trimester. 22 children whose mothers were HIV negative at delivery acquired HIV during breastfeeding. After the first negative HIV test, repeat testing was not done for 17/22 mothers. Five mothers...
had repeat HIV testing done regularly during breastfeeding but by the time they got a positive HIV diagnosis, their infants had already acquired HIV infection.

12 infants whose mothers did not access antenatal care services had evidence of intrauterine transmission. These women could not afford to pay the required ANC registration fees.

6 mothers who were HIV infected at the time of ANC registration had infants who acquired HIV infection (Four mother infant pairs were not adherent to their ART regimens, 1 opted out of PMTCT procedures, 1 never started ART).

Condoms use was reported by 1/40(2%) during pregnancy and 0/40 during breastfeeding. Only 4/40 male partners were involved in clinic visits at some point during pregnancy and breastfeeding.

Conclusions: 55% of the new paediatric infections occurred in infants born to women who were HIV uninfected at first contact with a health facility (during pregnancy or delivery). Strengthening serial testing algorithms as well as HIV prevention packages like providing pre-exposure prophylaxis for women at high risk of HIV infection may avert these infections. Making ANC services free may help averting new HIV infections in infants born women who fail to access PMTCT services due to unaffordable user fees. Offering comprehensive ART adherence support to mothers known to be HIV infected during pregnancy and/or breastfeeding is also very important.

Background: Early infant diagnosis (EID) remains a challenge in Mozambique, where only 50% of HIV-exposed infants (HEI) received virologic HIV testing at 4-8 weeks of age in 2017. ICAP reviewed EID data from supported sites in Nampula and Zambezia. From October through December 2017, HIV positivity at 8 weeks in Nampula (4%) and Zambezia (10%) was high, surpassing the global target of <5%. EID testing coverage was also low (52% in Nampula and 31% in Zambezia). Challenges through the maternal and child health (MCH) continuum of care can influence EID success. In order to address challenges, ICAP implemented ICAP’s I-Surge multi-pronged approach to target key areas to improve EID coverage.

Methods: In January 2018, ICAP’s I-Surge was implemented at 56 high volume health facilities (HF) (defined as HF with largest numbers of HIV positive pregnant women in MCH) in both provinces. As part of this approach, ICAP allocated HF based focal points providing continuous technical assistance to healthcare providers and routine intervention implementation monitoring. EID daily targets for each HF were set and strategies to identify missed testing opportunities and implementation of key interventions established. Strategies included identification of HEI at immunization services not linked to care, with immediate enrollment into HEI follow-up consultation including virologic testing; allocation of mentor-mothers to provide monthly home visits to mom-baby pairs and patient tracking for missed appointments.

Routinely reported aggregate facility-level data for 34 HF in Nampula and 22 HF in Zambezia using Ministry of Health monthly reports and PEPFAR indicators were reviewed. Data on the number of HEI receiving a virologic test, age at testing and overall EID coverage using proxy measure of 95% of HIV positive pregnant women in the period for expected number of HEI. Pre and post I-Surge implementation periods (October-December 2017 and April-June 2018) were compared.

Results: HIV testing coverage among HEI <12 months of age increased from 66%
(1,300/1,964) to 94% (1,873/1,999) (P<0.0001) in Nampula and from 75% (774/1,028) to 88% (943/1,072) (P<0.0001) in Zambezia. EID coverage among HEI <8 weeks of age improved from 48% (938/1,964) to 71% (1,422/1,999) (P<0.0001) in Nampula and from 62% (641/1,028) to 73% (780/1,072) (P<0.0001) in Zambezia. The proportion of HEI testing positive was 10% (136/1,300) to 12% (234/1,873) in Nampula and 10% (78/774) to 7% (62/943) (P<0.0001) in Zambezia. Linkage to ART among HIV-positive HEI in sites implementing the I-Surge approach remained high: 89% (209/234) in Nampula and 89% (55/62) in Zambezia in the post implementation period.

**Conclusions:** Enhanced technical support using ICAP’s I-Surge approach led to substantial improvements in EID coverage among HEI. Lessons learned are currently being scaled-up across ICAP-supported HF in Mozambique. While the number of HEI testing positive remains high, the proportion of those who initiated treatment improved. ICAP is scaling-up additional strategies to improve adherence and retention of moms within the PMTCT cascade to further improve infant outcomes. Strategies such as community health talks, outreach and home visits by community and religious leaders, and mentor mother-led demand creation and retention in the MCH continuum of care have now been implemented.

**Adoption of 2018 recommendations on infant diagnosis of HIV**

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**1**World Health Organization, **2**World Health Organization

**Introduction:** Increasing complexity of early infant diagnosis (EID) as a result of reduced viremia in infants and decreasing positive predictive values due to reduction in mother to child transmission rates resulted in new guidance for infant diagnosis. WHO recommends nucleic acid-based testing (NAT) to diagnose HIV in infants <18 months. However, in sub-Saharan Africa, less than 10% of infants with an initial positive test result receive a confirmatory test, resulting in a significant proportion (12.5%) of infants starting lifelong treatment unnecessarily. Therefore, the WHO now strongly recommends introduction of an indeterminate range, to minimize false-positive results. Furthermore, with increasing postnatal transmission and lower sensitivity of rapid diagnostic tests to confirm HIV exposure in high risk infants, the WHO suggests the use of NAT to diagnose infants at 9 months of age. Here we describe outcomes of WHO’s enhanced technical assistance (TA) to monitor national policy revision and support development of accelerated plans for quality infant testing in AIDS FREE priority countries.

**Methods:** Since September 2018, the WHO provided enhanced TA to support ministries of health in 11 of the 21 AIDS Free countries. The support aimed at convening the national paediatric Technical Working Group (TWG) in each country to address gaps in infant diagnosis with a view of optimising testing strategies and maximizing earlier identification of infants and children living with HIV.

**Results:** Over the 6 months’ period, the WHO provided TA to Angola, Eswatini, Ghana, Kenya, Lesotho, Malawi, Mozambique, Nigeria, Tanzania, Uganda and Zambia. All countries, except two, were using both conventional and point of care platforms for early infant diagnosis (EID). Although, confirmatory testing for all positive results prior to ART was included in the national testing polices of all countries, with the exception of Angola and Ghana, implementation of confirmatory testing varied. Based on review of EID implementation and discussions held in country and subsequent virtual follow-ups, all countries agreed to implement NAT at 9 months whilst those using the Roche COBAS® Ampliprep/TaqMan® assay agreed to implement an indeterminate range. However, member states requested
interpretation of cycle threshold values for other WHO prequalified EID platforms. Countries also agreed with adopting WHO-SOP for management of indeterminate range as well as for management of discordant results and are at various stages of updating their guidelines. Additionally, challenges identified included low EID coverage, ineffective sample referral systems, limited clinical acumen for confirmatory testing, limited budgets, and the lack of unique identifiers for longitudinal data analysis of the infant testing cascade of care.

**Conclusion:** Rapid dissemination of new WHO policies and close follow up with countries facilitated a critical review of EID programmes and supported adoption of the updated EID recommendations. It is expected that adoption of the 2018 recommendations will ensure quality EID, but linking those infected to care and ensuring appropriate follow up of HIV negative exposed infants will remain critical to reduce HIV-related infant morbidity and mortality. More follow up will be required to support implementation of these policy changes and ensure impact of WHO guidelines.

### 114

**Assessing Final Infant Outcomes for Two Birth Cohorts of HIV Exposed Infants (HEI) in Manzini region of Eswatini**

**Background:** WHO recommends routine monitoring of final outcomes to determine the final HIV status of HEI for patient management and tracking of progress towards elimination of MTCT. However, many countries struggle to ascertain HEI final outcomes due to disparate reporting systems, poor infant follow-up and poor documentation of breastfeeding practices. We describe the final outcomes for HEI before and after targeted mentorship on HEI follow up in Manzini, Eswatini.

**Methods:** Using national birth cohort registries for HEI, we conducted a retrospective cohort analysis of two birth cohorts who were enrolled in follow-up services at 36 sites. Outcomes for infants aged 18-24 months were aggregated and analyzed for final outcomes (defined as percentage of final outcomes among HIV exposed infants registered in a birth cohort). Final outcomes included HIV-infection status post-breastfeeding cessation, infant death and ART initiation among infants determined to be HIV-infected. Chi square tests were used to test for significance between proportions.

**Results:** A total of 6500 HEI were enrolled in HEI follow-up services in both the 2014/15 and 2015/16 birth cohorts. Overall, only 60% (3929) had a documented final outcome among the two birth cohorts with significant improvements made between the 2014/15 and 2015/16 birth cohort from 53% to 68% (p<0.001). The proportion of HEI testing HIV positive among those with documented outcome was 3% (121) with 83% (101/121) initiated on ART. At 24 months, of all HEI enrolled in care, 3772 (58%) infants were determined HIV negative and 121 (1.9%) HIV positive, there were 36 documented deaths (<1%), 844 (13%) were still breastfeeding (indeterminate status) and 1727 (27%) were lost to follow-up or not tested.

**Conclusions:** It is feasible to improve HEI final outcome determination through enhanced site level mentorship, proper documentation and active follow-up of every HEI using birth cohort registers. The number of infants documented with new infections is low, but a large number of HEI are not retained in care throughout the period of risk. Continued effort to determine final outcomes of HEI birth cohorts, prevent loss to follow-up and ART initiation remain imperative for tracking progress towards elimination of MTCT.
Reducing HIV Exposed Babies Early Infant Diagnosis Cascade Loss: The Shoe Rack Strategy

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Background: Nigeria is the highest contributor to the global pediatric HIV burden. Maternal to child transmission (MTCT) of HIV accounts for over 90% of Pediatric HIV in Nigeria. Nigeria’s of elimination of Mother To Child Transmission (eMTCT) program had been plagued with missed opportunities through cascade losses. Though the introduction of case managers (mentors mothers) significantly reduced cascade losses and improved outcomes, challenge with early diagnosis of HIV exposed infants (HEI) persisted. The objective of the shoe rack strategy was to aid case managers to closely follow up HEI for timely early diagnosis.

Method: Facilities were provided with a shoe rack and the mentor mothers (MM) and providers were mentored on use. The months of the year (January- to- December) were labeled on each pocket of the shoe rack. The MM or provider calculated the expected date for sample collection of every infant which is usually 6 weeks after birth. The date/appointment is communicated to the caregiver and noted on the MM notebook. A slip is filled and inserted into the pocket of the shoe rack whose labeled month corresponds with the expected month for EID on the slip. At the beginning of every month, the MM is expected to pick all slips from that month’s pocket of the shoe rack and track all infants in that pocket reminding the caregivers of their scheduled appointment.

Findings: 385 (primary, secondary, tertiary) facilities in Kano, Katsina, FCT and Nasarawa states are supported to provide prevention services. A total of 6,793 babies were tested in January to December 2017 and 5,175 in 2018. Proportion of HEIs tested at less than two months increased from 63% (4,290) in 2017 to 77% (3,990) in 2018. Number of HEI tested positive were 95 (0.14%) and 106 (0.02%) in 2017 and 2018 respectively. Linkage was also optimal (104% in 2017 [due to transfer-in] vs 92% in 2018) . Almost all 9 infants not linked were accounted for - dead, moved/relocated due to security challenges in their community. Common challenges were; Migration due to communal crisis, babies being turned away when they visit facility earlier than 6 weeks, deliveries outside the facilities by some positive pregnant women (PPW), some PPW attend ANC in a different facilities from where they access ART especially those with previously known status and human resources shortage across all cadre of health care workers (HCWs).

Conclusion: Observed improved early sample collection at less than 2 months and reduced missed opportunities and/or delays, simplified HEI tracking and monitoring system by the Mentor Mothers (MM) and decreased infant mortality by early diagnosis and prompt intervention. Intensifying engagement of mentor mothers for tracking of HEI ahead of due dates, providing hands – on capacity building for HCWs on identifying HEI at all relevant points of entry to address missed opportunities and ensuring scale up the shoe rack strategy in monitoring EID for HEI is recommended.

The Challenges of HIV PMTCT Programming among Sex Workers – Experience of AIDS Information Centre (AIC) – Uganda

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Background: Evidenced based programming involves HIV testing among key and priority populations. Key populations (KPs) who include Sex workers (SWs) are disproportionately infected with HIV and are more at risk for
contracting HIV than the general population. SWs were found to have 12 times the prevalence of HIV than the general population (Uganda 2014) and together with MSM contribute significantly to new HIV infections. It is on this background therefore that it was supposed that children born to SWs are more exposed to the risk of HIV infection. Targeted HIV testing and dialogues to provide information about HIV including PMTCT were carried out for SWs living and operating in different areas of Kampala city central division.

**Methods:** AIDS Information Centre through the CDC funded Kampala Region HIV Project began scale up of integrated HIV Testing Services (HTS) for KPs in April 2018. Under this project, integrated targeted HTS was implemented including dialogues on access to HTS, HIV care including PMTCT and prevention services. Furthermore, male and female condom distribution, treatment for sexually transmitted infections and sexual and reproductive health education was carried out.

**Results:** Between April –September 2018, 60 female SWs attended two dialogue meetings held within the community. HTS was carried out during the dialogues and also in the community at mapped hotspots.

Of 847 CSWs tested, 74 tested HIV positive (47 known and 27 new). Among these newly diagnosed HIV positive SWs were pregnant women as well as mothers with untested children. All new positives were referred to and 21 successfully linked to treatment centres. The other 6 either declined treatment or had not yet reported to the treatment centres.

Children of SWs are typically kept with grandparents because of the SWs time of operation and mobile nature. It is therefore challenging to test their children in the presence of non-disclosure of their HIV status to these caretakers.

A number of SWs are still not aware of prevention strategies including PEP and PrEP and those who are aware may not be willing to partake of them for an undefined duration of time.

The irregular use of/ poor uptake of condoms and family planning among the SWs leaves them at risk of unplanned pregnancy and HIV infection.

**Conclusions:** The nature of the commercial sex trade makes SWs mobile and also attracts new entrants therefore regular, targeted, audience-appropriate health education is required for SWs in community hotspots.

The formulation of targeted community appropriate interventions/services are required for follow up of pregnant and breast feeding HIV positive SWs as well as their exposed children.

117

**Characterizing viral load burden among HIV-infected women at time of delivery: Findings from four tertiary obstetric units in Gauteng, South Africa.**

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**Background:** Within the South African public health sector, it is estimated that antiretroviral therapy (ART) coverage amongst antenatal clients is >95% and 90% of all women on ART are virologically suppressed. We describe maternal viral load (VL)-suppression and intra-uterine (IU)-transmission rates around time-of-delivery from four tertiary obstetric units in Gauteng, South Africa.

**Methods:** Between June-December 2018, routine point-of-care (POC) VL and early infant diagnosis (EID) PCR testing was introduced at four tertiary obstetric units in Gauteng.
province-three in Johannesburg (subdistricts B, D, F) and one in Tshwane. Testing was restricted to normal working hours (08h00-16h00) during weekdays. All HIV-infected women were eligible for HIV-1 VL testing around time-of-delivery using Cepheid Xpert® HIV-1 VL. Similarly, all HIV-exposed infants were eligible for HIV-1 EID PCR testing at birth, defined as <72 hours after delivery, using either Cepheid Xpert® HIV-1 or AlereQ EID assays. Proportions of viraemic women at delivery were calculated at VL cut-offs of ≥50, ≥400 and ≥1000 copies/millilitre (cps/mL) among women with a valid result. Proportions of EID-positive results were calculated as percentage of EID tests with a valid result.

Percentage POC testing coverage of maternal VL and neonatal EID were calculated using 5/7x live-births to HIV-positive women as denominator, obtained from routine records. Overall and site-specific monthly VL-suppression (>1000 cps/ml) and IU-transmission rates were calculated and Pearson’s Chi-square test used to compare VL-suppression and IU-transmission rates at different testing coverages.

**Results:** Among an estimated 4117 HIV-positive women who gave birth, 1892 (46.0%) had a valid POC VL result. Overall monthly VL and EID testing coverage ranged from 33.6%-53.0% and 58.0%-85.5%, respectively. Maternal VL testing coverage was 914/1092 (83.7%), 376/1641 (22.9%), 268/838 (32.0%) and 334/546 (61.1%) in Johannesburg B, D, F and Tshwane units, respectively.3151 (76.5%) neonates had a valid EID test result of whom 987 (90.4%), 955 (58.2%), 663 (79.1%) and 546 (100%) were tested in Johannesburg B, D, F and Tshwane units, respectively. Coverage was likely overestimated due to duplicate-testing or under-estimation of total live-births. The overall median maternal VL was <40 cps/mL (interquartile range: 0-483 cps/mL). Overall, the proportion of women with a VL ≥50, ≥400 and ≥1000 cps/mL was 37.1%, 25.4% and 22.7%, respectively. The proportion of women with a VL >1000 cps/mL was similar among Johannesburg units (21.2%, 21.5%, 19.4%) but significantly higher in Tshwane (30.5%) (p=0.001). The proportion of IU-infected neonates ranged between 1.3%-1.7% in the Johannesburg units while the Tshwane unit had a significantly higher IU-rate of 2.5% (p=0.001). Despite varying monthly VL & EID testing coverage, VL-suppression (p=0.128) and IU-transmission (p=0.210) rates remained constant overall and across sites suggesting representative results.

**Conclusion:** Overall, >20% (n=429) HIV-infected women at time-of-delivery had a VL ≥1000 cps/mL suggesting a high VL-burden at the sites investigated. Viral-suppression rates were lower than the targeted 95% in the general and female population rate. Both the proportion of viraemic women and IU-transmission rates remained constant monthly, despite variable testing coverage suggesting the population of women tested were similar throughout the implementation period. However, we cannot exclude targeted-testing of some patients. Scale-up of VL monitoring, and improving quality of antenatal care including adherence to ART is required for elimination of mother-to-child transmission of HIV.

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**118**

**Supported breastfeeding among women with diagnosed HIV in the UK- the current picture**

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1 UCL

**Background:** The HIV vertical transmission (VT) rate was 0.28% among births to diagnosed women living with HIV (WLHIV) in the UK/Ireland in 2015-16. The British HIV Association (BHIVA) recommends formula-feeding infants born to WLHIV, eliminating postnatal transmission, but also states that virologically-suppressed treated women with good adherence choosing to breastfeed may be clinically supported in this. Guidelines on diagnostics for breastfed infants and maternal viral load (VL) monitoring reflect this, but current clinical practices are uncertain. Data
are lacking on breastfeeding (BF) by WLHIV in resource-rich settings; the National Surveillance of HIV in Pregnancy and Childhood (NSHPC) is placed to collect this data on a population level.

Methods: The NSHPC conducts surveillance of all pregnancies to diagnosed WLHIV in the UK/Ireland and of HIV-infected children <16yrs. Data on supported BF (i.e. woman chooses BF and is supported per BHIVA guidelines) has been collected since 2012 and enhanced surveillance conducted since 08/2018. We describe cases reported by March 2019.

Results: Among 7187 livebirth deliveries, 135 were reported as having planned and/or supported breastfeeding; 18/135 were in women with supported BF in ≥1 pregnancy. Of these 135 pregnancies, 125 (93%) were in women diagnosed pre-pregnancy, 84% (112/133) in women born abroad, median age at delivery was 35yrs (IQR: 31,40) and BF duration ranged from 1day-2years. Enhanced data collection been conducted for 102 supported BF cases to date. Reason(s) for BF were known in 81 cases and included: bonding (36), health benefits (36), family pressures (14), disclosure concerns (14) and finance (2) (>1 reason may be reported). Partners were unaware of maternal HIV status in 11/102 cases and GP was unaware in 10/100 (in 2/11 both GP and partner were unaware). There were problems with attendance for monthly VL testing in 22/102 cases. BF was reported to have stopped in 90/102, ongoing in 9/102 and unknown in 3/102 (LTFU). Among the 90 with BF cessation, 57 infants had confirmed negative antibody test (≥18 months); 28 are in follow-up awaiting confirmatory testing and 5 were LTFU before infection status was confirmed. BF was reported to have stopped owing to maternal VL rebound in 4/90 (2 infants confirmed negative, 2 awaiting confirmatory antibody). A further 3 reported ≥1 detectable VL during BF (1 had a negative antibody test, 1 still in follow-up and 1 LTFU). Among the 9 ongoing BF cases, there was 1 reported VL blip.

Challenges to data collection included access to maternal monthly test results by paediatric respondents and obtaining infant test results where care is transferred during BF.

Conclusions: Numbers of supported BF cases remain small (but growing). Cases have been diverse, particularly regarding duration, and cessation due to detectable VL was rare. Although these results show no VT among supported BF cases so far, in the wider surveillance there was one postnatal transmission in 2015-16 (likely covert BF by a woman with undetectable VL throughout pregnancy). Findings underscore the need for careful monitoring, including early identification of VL blips and establishment of infection status post-BF cessation.

Electronic Health Record (EHR) review of infant outcomes for Neural Tube Defects (NTD) born to HIV+ pregnant women in the US

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Background: Antiretroviral (ARV) therapy has drastically reduced mother to child transmission of HIV. Dolutegravir (DTG), a recently approved integrase inhibitor has moved into first line therapy of all adults including women in their child bearing years. An unplanned analysis of women in Botswana who started DTG preconception revealed an increased prevalence of neural tube defects (NTD) of 0.67 (4/596 95%CI 0.26-1.7%) compared to non-DTG regimens at 0.12% (14/11,300, 95%CI 0.07-0.21%); for women exposed to efavirenz it was 0.05% (95%CI 0.02-0.05%), and for HIV negative women prevalence was 0.09% (95%CI 0.07-0.12). The global estimated prevalence of NTD 15-23/10,000, 0.19%. We sought to review US data via a large electronic medical record
Methods: Data was extracted from Health Facts Database from 1/1/01-12/31/17 to identify HIV+ pregnant women aged 13-50 years and their pregnancy outcomes. The Health Facts Database is a large multi-institutional database derived from Cerner based EHR in the United States. Specific ICD-9 and ICD-10 codes were extracted, including NTD and other congenital malformation as well as any miscarriage, fetal demise or abortion. We compared the pregnancy outcomes in the pre-DTG (before 6/1/2014) and the post-DTG era. Data on specific maternal ARV timing and use are not known.

Results: 1,617 HIV+ pregnant women were identified, with 1,882 pregnancies; 868 in the pre-DTG and 1,014 in the post-DTG era. Forty-eight (2.6%) of these pregnancies ended in a termination, 20 in the pre-DTG and 28 in the post-DTG era, p=0.53. Overall, 35 pregnancies (1.8%) had a diagnosis associated with a congenital defect code, 10 in the pre-DTG and 25 in the post-DTG era. One NTD (1/868, 0.11%, 95%CI -0.11%-0.33%) was identified in the pre-DTG era and 2 NTDs (2/1,014, 0.2%, 96%CI -0.07%-0.47%) in the post-DTG era, p=0.66. Among the post-DTG NTD, one was a live birth with the other a termination (holoprosencephaly). In regards to other congenital malformations, which were categorized as cardiac, renal, genitourinary, gastrointestinal, chromosomal and other, only findings for the cardiac malformations suggest a trend towards an increase in the post-DTG era; 2/868, 0.23% (95%CI -0.09% – 0.55%) pre-DTG, and 7/1014, 0.69% (95%CI 0.18% – 1.20%), post-DTG, p=0.15.

Conclusion: NTD occurrences were rare in both the pre and post-DTG era and were not above the global prevalence in all pregnant women regardless of HIV status. These data require further investigation and replication.

Point-of-care testing for early infant diagnosis of HIV in rural Zambia: Experience from the field

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Background: Early infant diagnosis (EID) is challenging in sub-Saharan Africa, leading to delays in diagnosis and treatment for HIV-infected infants. Point-of-care (POC) platforms could increase access to EID. This study evaluated the feasibility of implementing POC testing for EID in rural Zambia.

Methods: This study was conducted in Macha, Zambia using a hub-and-spoke model starting in September 2018. POC hubs were created at a district level hospital and zonal health center, and one GeneXpert (Cepheid Inc.) machine was placed in each lab. At the hubs, testing was performed in real time using whole blood samples. Three rural health centers also participated and dried blood spot (DBS) cards were collected and transported to one of the hubs on a weekly basis. Test results were provided to mothers and providers and used for clinical decision making. Test results and turnaround times for both POC and HIV DNA testing were compared. For children testing positive, linkage to care and ART initiation were documented.

Results: At the zonal health center hub, upgrades to the lab included new ceiling boards, air conditioner, and electrical and plumbing fittings (cost of $2153 USD), and two training sessions for lab technicians were needed due to staff turnover. Weekly supervisory visits from the hospital hub to the health center hub were necessary in the first month of implementation to troubleshoot issues with testing and review the protocols, with regular support available thereafter. During the study, testing at the health center hub was halted for a week due to malfunctioning of the computer and printer,
which were sent to Lusaka for repair. As of February 25, 2019, 179 samples were tested, including 129 and 43 whole blood and DBS samples, respectively, at the hospital hub and 7 whole blood samples at the health center hub. The turnaround time from sample collection to availability of results at the clinic was a median of 2.0 hours (range: 1.7-49.0 hours) for testing at the hubs and 9.1 days (5.2-22 days) for DBS. The turnaround time from sample collection to when the result was given to the mother was a median of 2.6 hours (2.0 hours-46 days), 4 days (1.9 hours-20 days), and 21 days (7-71 days) for the hospital hub, health center hub, and DBS, respectively. At the hubs, 81% of mothers received their results the same day. A total of 201 tests were run, as 9.5% of samples yielded an invalid result and needed to be re-tested. Among all samples, 174 (97.2%) tested negative and 5 (2.8%) were positive. All children testing positive initiated ART a median of 14 days (1-24 days) after sample collection and the same day (0, 1 days) the mother received the results.

Conclusions: POC testing has the potential to reduce delays in diagnosis and treatment for HIV-infected infants. A hub-and-spoke model for POC testing is feasible to increase access to testing for surrounding health centers. However, infrastructure, training and supervisory requirements must be considered prior to implementation to ensure testing programs are successful and sustainable.

Introduction: Tenofovir (TDF) has become a NRTI of choice for treatment of pregnant women living with HIV, although it is still not recommended for younger children due to concerns about potential bone toxicity. Previous studies evaluating bone mineral content among TDF-exposed infants have demonstrated conflicting results. We present results of a prospective evaluation for bone toxicity in infants with in utero TDF exposure.

Methods: Infants born at >/=35 weeks gestation from three Canadian centres to women living with HIV and treated for at least one month in pregnancy were eligible for inclusion. Lumbar spine bone mineral density (LSBMD) was measured at 1, 6 and 18 months, and z-scores were calculated using normative data from published studies. LSBMD z-scores at each time point were compared between TDF-versus non-TDF-exposed infants using the Wilcoxon rank sum test.

Results: Forty-one HIV-exposed infants were enrolled and had at least one BMD performed and maternal treatment data available, including 25 TDF-exposed and 16 non-TDF-exposed (10 abacavir-exposed, 5 zidovudine-exposed, 1 no NRTIs). Median gestational age at birth was 39 weeks in both groups, with 47% females. Over half (56%) were on treatment from conception. 56% of TDF-treated mothers were also treated with a protease inhibitor. Median LSBMD z-scores in TDF-versus non-TDF-exposed infants at 1, 6 and 18 months were -1.5 versus -0.9 (p=0.083), -0.5 versus -0.5 (p=0.345), and 1.3 versus -0.5 (p=0.017), respectively. There were no significant differences in LSBMD z-scores in TDF-exposed infants exposed to protease inhibitors versus other backbone agents at 1 month (-1.3 versus -1.9, p=0.448) and 18 months (1.0 versus 1.6, p=0.965); protease inhibitor exposed infants had significantly higher LSBMD at 6 months (-0.2 versus -0.8, p=0.018).

Conclusions: We found a clear trend towards lower LSBMD z-scores among TDF-exposed infants at 1 month of age, but were likely underpowered to find a statistical difference. Fortunately, recovery of LSBMD seemed to have occurred by 6 months and TDF-exposed
infants had higher z-scores by 19 months, perhaps reflecting a compensatory mechanism. With the majority of infants with in utero antiretroviral exposure globally being exposed to TDF in the Option B+ era, it is essential to understand the true impact of this exposure on children’s bone health and growth.

LB_01

This abstract was withdrawn

LB_02

Murine Reproductive Toxicity Studies to Evaluate Potential Neural Tube Defects and Other Fetal Abnormalities Associated with Dolutegravir Exposure in Pregnancy.

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Background: The benefits of antiretroviral therapy in improving maternal health and preventing vertical HIV transmission are indisputable. However, exposure to any potent drug during pregnancy carries the risk of embryo-fetal toxicities. Dolutegravir (DTG), an integrase strand transfer inhibitor (INSTI), is a WHO-alternative first-line regimen, because of its efficacy, tolerability, and higher genetic barrier to resistance. However, initial findings from an observational study in Botswana showed an increased incidence of neural tube defects (NTDs) with peri-conceptional exposure to DTG. Here we explore potential DTG reproductive toxicities in a mouse model.

Methods: Wild-type female C57BL/6 mice, were mated and randomly allocated to control (water), 1x-DTG (2.5mg/kg DTG+50mg/kg TDF+33.3mg/kg FTC-yielding DTG peak plasma concentration of ~3,000ng/ml), or 5x-DTG (12.5mg/kg DTG+50mg/kg TDF+33.3mg/kg FTC-yielding DTG peak plasma concentration of ~12,000ng/ml) administered once daily by oral gavage from day of plug detection to sacrifice at embryonic day (E) 15.5. Mice were on a folate-sufficient diet. Fetuses were assessed blinded to treatment allocation by two independent reviewers.

Results: 310 litters and 2,776 fetuses were assessed (control n=82 litters, 747 fetuses; 1x-DTG n=125 litters, 1174 fetuses; 5x-DTG n=103 litters, 855 fetuses). Resorption rates, viability, and fetal/placenta weight ratio did not differ between groups. Higher placenta weight, lower maternal weight gain, and a trend towards smaller litter size were observed in the 5x-DTG vs. control and 1x-DTG groups. Fetal weights were lower in the 1x-DTG vs. control and 5x-DTG groups. Two open NTDs were observed in the 1x-DTG group (2/1174=0.17%), with no NTDs in controls or after 5x-DTG (odds ratio (OR) 1x-DTG vs. control=3.2, 95%CI 0.15-66.5, p=0.26). Fetuses exposed to 1x-DTG also had higher rates of anophthalmia/microphthalmia (OR (95%CI): 2.6 (1.3-5.1), p=0.005), severe edema (OR (95%CI): 2.35 (1.2-4.6), p=0.012), vascular/bleeding issues (OR (95%CI): 2.0 (1.4-3.0), p<0.0001), including cranial/spinal bleeds, and enlarged liver (OR (95%CI): 1.68 (1.1-2.6), p=0.023) compared to control and 5x-DTG (all OR vs. control). Higher rates of mandibular aplasia were observed in both the 1x-DTG and 5x-DTG vs. control.

Conclusion: Contrary to expectations, we observed more defects, including 2 NTDs, in fetuses exposed to 1x-DTG compared to the higher dose 5x-DTG or control groups.
**LB_03**

**Transition Pathways out of Paediatric Care and Associated HIV Outcomes for Adolescents Living with HIV in South Africa**

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**Background:** Research on adolescent transitions out of paediatric HIV care has focused on high-income countries, with limited understanding of these transitions in the sub-Saharan African public HIV care sector.

**Methods:** Patient file data was extracted for all 10- to 19-year-olds ever initiated on ART in 52 public healthcare facilities in the Eastern Cape, South Africa (n=951). Adolescent pathways in HIV care were identified by tracing movements across facility and care types. Associations between transition pathways and viral failure (HIV-1 RNA ≥1000 copies/mL), availability of viral load data, mortality, loss to follow-up, and post-transition viral load change were tested in sequential multivariate regression. Analyses controlled for age, gender, urban/rural residence, horizontal/vertical mode of infection, ART initiation year, time on ART, baseline viral load, immunologic instability, facility level, and history of care down-referral. Thematic analyses of semi-structured healthcare provider interviews identified transition support available at included facilities.

**Results:** Only 20.4% of adolescents had transitioned out of paediatric HIV care. Median age at first transition was 14 years. Two main transition pathways were identified: classical transition to adult HIV care (43.3% of transitioning adolescents) and down-referral transition to primary healthcare clinics (56.7% of transitioning adolescents). Across pathways, 27.3% experienced cyclical transition, or repeated movement between paediatric and non-paediatric care. Independent of covariates, adolescents who experienced down-referral transition were less likely to demonstrate viral failure (AOR 0.25 [95%CI 0.12-0.53], p<0.001). Availability of viral load data, mortality and loss to follow-up were not associated with either pathway. Median post-transition viral load change was not clinically significant (0.00 IQR: 0.00-0.35) or associated with transition pathways. Healthcare providers described informal transition “protocols” used to mitigate risk of negative post-transition HIV outcomes.

**Conclusions:** This study proposes a contextually relevant model for adolescent transitions out of paediatric HIV care in South Africa. Feasible and scalable transition “protocols” have the potential to mitigate risk of worsening post-transition HIV outcomes.

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**LB_04**

**Outcomes of HIV-exposed but Uninfected Children in South Africa over 5 Years: Comparison to Unaffected Peers**

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**Background:** While the tasks to Prevent Mother to Child Transmission (PMTCT) are repeatedly examined, the long-term impact of maternal HIV on their children is typically limited to clinic-based samples over the first 12 months post-birth. This study examines the comprehensive outcomes over time for HIV-exposed, but uninfected children (HEU) compared to their community peers not exposed to HIV (NEH).

**Methods:** Pregnant women in 12 Cape Town neighborhoods (N=594) were recruited in pregnancy and reassessed five times over five
years with high retention (91.9%-82.8%). Comprehensive evaluations of HEU children (n=179) were compared over time to neighborhood NEH children (n=405) of mothers without HIV (MWOH).

**Findings:** HEU were hospitalized, received medical care, and experienced behaviour problems at similar rates as NEH children. Weight-for-age Z scores were significantly lower among HEU children compared to NEH children, but not in the malnourished range, and children were similar in height and stunting. The Kaufman scale of cognitive development was about 2.8 points lower among HEU children compared to NEH children, but the entire sample was more than one SD lower than is typical. About 10% of mothers or children died over 5 years, similar across maternal serostatus.

**Conclusions:** Unexpectedly, the outcomes of HEU children are similar to the outcomes of NEH peers. As broad diffusion of antiretroviral therapies occurs and mothers are surviving and living less symptomatic lives, their children appear to be doing well.
International Workshop on HIV Pediatrics
Mexico City, Mexico

Abstracts

Abstract-book only
Enrollment to HIV treatment services and predictors of enrolment among HIV-infected children from high-risk settings in selected health facilities in Ethiopia

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Background: Antiretroviral therapy (ART) coverage among children living with HIV (CLHIV) in Ethiopia remains low at 34%. Linkage to HIV care and treatment services after diagnosis is key to improving ART coverage. We aimed to measure rate of enrollment of CLHIV into HIV treatment, and describe predictors of enrollment.

Methods: A cross-sectional study was conducted from May 2017-March 2018 in 29 public health facilities in Amhara and Addis Ababa regions in Ethiopia. Children 2-14 years were enrolled at different service delivery entry points. Data collection included abstraction of HIV status from medical records and interview with caregivers on sociodemographic factors and clinical history. Three months later, interviews were done with caregivers of newly diagnosed children or known positive children not yet on ART, including questions on enrollment into HIV services and ART initiation. Bayesian regression analysis identified independent predictors of enrollment to HIV treatment and ART initiation.

Results: 2166 children were enrolled in the study. Three months later, 17.1% of 41 children (40 newly diagnosed children plus 1 known diagnosis not yet on ART) had not yet enrolled to HIV treatment services/initiated ART. Reasons for not enrolling or initiating ART included: caregivers did not see need for services (n= 2), preferred alternative methods of HIV treatment (n=4), brought child to the facility but was not enrolled (n=1), lack of psychological readiness (n=1), and death (n=2). Positive predictors of enrollment to HIV treatment included age ≥ 5 years [OR = 0.06 (0.0002-0.38)], maternal orphan [OR = 0.05 (0.0001-0.38)], and children with poor health [OR =0.17 (0.003-0.89)]. Children with severe malnutrition were less likely to be enrolled [OR = 116 (1.98-563.7)].

Conclusion: 17% of newly diagnosed children were not on ART 3 months after diagnosis. There is an urgent need to intensify early follow-up for newly diagnosed children to ensure prompt ART initiation and identify additional services needed to help caregivers with decision-making around treatment initiation for their children. Extra measures are needed to link very sick children to prevent death. Healthcare workers should understand reasons for poor linkage and provide counseling to address common misconceptions and fears.
Infectious Disease Research in Zambia (CIDRZ) supported health facilities.

**Methods:** We reviewed programmatic data for children aged <15 years on ART who had viral loads between January 2017 and January 2018. We collected data on patient demographics, CD4+ count, and viral loads using SmartCare, the electronic medical record system in the public health sector. We estimated proportions of children with suppressed viral loads (VL) at two cut-off points - VL of 1000 copies/ml and 50 copies/ml.

**Results:** Between January 2017 and January 2018, 895 children receiving antiretroviral therapy in CIDRZ-supported sites had a viral load done. 514 (57%) were female, the median age at ART initiation was 7 years and median baseline CD4 count was 619 cells/µL. 349 (39%) were aged 10-14, 227 (25%) were 5-9 years, 246 (27%) were aged 1-4 years and 73 (8%) were <1 year. Median duration on ART was 12 months. 672 (75%) had viral load below 1000 copies/ml. Suppression rates in the various age groups were: 67% for <1 year, 75% for the 1-4 year olds, 81% for the 5-9 year olds and 73% for the 10-14 year olds. 457 (51%) had viral loads below 50 copies/ml.

**Conclusion:** We demonstrated virological suppression in 75% of children on ART in a resource-limited setting; half of the children had undetectable viral loads after a median of 12 months of ART. Suppression rate was lowest among the infants and improved with age until adolescence when it dropped. We recommend intense monitoring and adherence support for infants initiating ART and adolescents in order to improve virological outcomes.

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**Second Line failure and Outcome of Third line therapy among a Cohort of Treatment-Experienced Children and Adolescents at the University Teaching Hospital in Lusaka, Zambia**

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**Background:** With increasing access to ART and longer duration of treatment drug resistance is emerging among young children and adolescents. There is paucity of data in developing countries on 2nd line failure and outcomes of 3rd line therapy, especially in children and adolescents. This is a review of a cohort of pediatric and adolescent patients from the University Teaching Hospital who were initiated on third line between March 2012 and September 2018.

**Methods:** A retrospective file review of patients started on third line ART from the Pediatric cohort at the UTH. Third line regimen included any combination of Raltegravir, Dolutegravir, Darunavir or Etravirine with optimized Nucleoside Reverse Transcriptase Inhibitors (NRTI). Resistance results were interpreted using Stanford HIV Drug Resistance Database and descriptive statistics were used for data analysis.

**Results:** A total of 26 third line patient files reviewed. Male to female ratio was 1:1. First line: mean age at ART initiation 5y8m; mean duration of 1st line was 4y3m; majority were on AZT/d4T backbone 22/26 (85%) and NVP/EVF base. Regarding 2nd line: mean duration 3y 10m; majority, ABC/TDF (77%) and base of LPV/r or ATV/r. Mean age at 3rd line initiation was 13y 4m. Drug Resistance mutations: 25 patients had a Drug Resistance profile. NRTI mutations documented in 84% (21/25) with M184V in 86% and greater than 3 Thymidine Analogue Mutations (TAM’s) in 48%; NNRTI mutations in...
80% (20/25) with the commonest mutation Y181C and K103N (40% and 35% respectively) and 76% (19/25) had PI mutations with 53% having greater than 3 major PI mutations. Delays in result receipt resulted in 6 patients starting 3rd line treatment empirically. TB/HIV was the commonest OI documented. 65% (17/26) patients treated for TB during ART (5 relapse treatment). LPV/r and Rifampicin overlap was noted in 46% (12 patients) with 7/12 not having a dose adjustment. Viral Suppression (VL below 1,000) after an average of 2y 6m 3rd line treatment showed 81% (21/26) suppressed; 19% (5/26) not suppressed.

**Conclusion:** Third-line regimen of DRV/r, RAL/DTG/ETV and optimized NRTI’s are effective in treatment experienced children and adolescents. Prolonged use of D4T and AZT in first line therapy resulted in high rates of accumulated TAM’s. Important to have DR results before any 3rd line switch is made to avoid premature switches.

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**Association of ART regimen with viral suppression in HIV-positive children in Eswatini: Baseline data from the FAM-CARE study**

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**Background:** Viral suppression among individuals on ART lag among children compared to adult populations. Ensuring HIV-positive children are prescribed optimal antiretroviral treatment (ART) remains an area of needed progress to ensure viral suppression reaches the 90% target.

**Methods:** The FAM-CARE study is evaluating the effect of a family-centered care model (provision of HIV care services to an HIV-infected child together with other family members) implemented in four health facilities in Eswatini versus standard of care (separate clinic care) in four comparison health facilities. We used baseline enrollment data for all children to evaluate overall viral suppression and factors (including age, gender, reported adherence, ART drug pick-up, age at ART start, duration of ART, and ART regimen) associated with lack of suppression.

**Results:** 379 children (50% female) enrolled in the study, mean age 8.3 years (sd=3.7years). 99.7% were receiving ART, with 95.2% on first-line; median age at ART initiation was 2.6 years and median ART duration was 4.1 years. 44% of children were receiving nevirapine (NVP)-based ART (mean age 9.2 years), 25% efavirenz (EFV)-based ART (mean age 10.3 years), and 30% lopinavir/ritonavir (LPV/r)-based ART (mean age 5.4 years). Plasma viral load was <1,000 copies/mL in 78% and <400 copies/mL in 74% of children. The only factor associated with lack of viral suppression (RNA >1,000 c/mL) was ART regimen (p=0.03), with a similar but non-significant trend for detectable VL (RNA >400 c/mL) (p=0.20). The lowest rate of suppression was in children on NVP-based ART and the highest rate in those on EFV-based ART.

**Conclusion:** While Eswatini national treatment guidelines recommend EFV-based ART in children age >3 years, significant numbers of children are still on NVP-based ART, which had significantly lower viral suppression than EFV-based ART. These data speak to the importance of monitoring and optimizing ART regimens for children to improve viral suppression rates.
HIV Drug Resistance Patterns among HIV infected children and adolescents failing for second line antiretroviral therapy in Uganda.

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Background: WHO recommends use of Abacavir, Lamivudine and Lopinavir boosted Ritonavir (ABC/3TC/LPV/r) for children failing on a Zidovudine, Lamivudine, and non-nucleoside (AZT/3TC/NVP or EFV) first-line ART. In 2016, Uganda adopted this guidance empirically switching from first to second line, reserving HIV drug resistance testing for second line failures. However, TAMs accumulating in combination with M184V during 1st line failure with AZT/3TC may impact the effectiveness of ABC in 2nd line. This study compares HIV drug resistance mutations, time on ART and viral loads, in HIV infected children and adolescents failing PI base 2nd line ART with ABC/3TC vs TDF/3TC vs AZT/3TC backbones following AZT/3TC/NNRTI first line.

Methods: A cross-sectional retrospective review of data in children and adolescents from the national third-line ART database was conducted from June 2017 to November 2018. Patients with repeat VL>1000 following Intensive Adherence Counselling were tested using In-House antiretroviral drug resistance genotype tests performed on dried blood spots or plasma samples.

Results: 82 resistance tests reviewed from children (0-9 years, n= 12) and adolescents (10-19 years, n= 70). 62.2% (51/82) were on ABC/3TC backbone, 71% (36/51) on TDF/3TC and 4.9% (4/82) on AZT/3TC backbones following AZT/3TC/NNRTI first line. Of patients with NRTI mutations with > 3 TAMs and M184V, 75% (21/27) had been on ABC/3TC/LPV/r. Of children and adolescents with resistance tests, 74.4% (61/82) had NRTI mutations, 96.3% (79/82) NNRTI and 95.1% (78/82) PI. Of patients with NRTI mutations with > 3 TAMs and M184V (n=48), 54% (26/48, P Value = 0.97) were on ABC/3TC backbones, 18% (16/48, P Value = 0.56) TDF/3TC and 2% (2/48, 0.00) AZT/3TC. Median number of TAMs was 3. Among children and adolescents on ABC/3TC backbone the mutations were as follows; 49.0%(25/51)M41L, 33%(17/51)L210W, 71%(36/51)T215Y/F, 37%(19/51)D67N/G, 37%(19/51)K219Q/E, 0%(0/51)Q151M, 12%(6/51)T69S, 31%(6/51)K70R, 12%(6/51)M184V. AZT/3TC backbone: 75%(3/4)M41L, 25%(1/4)L210W, 50%(2/4)T215Y/F, 25%(1/4)D67N/G, 75%(3/4)K219Q/E, 25%(1/4)Q151M, 0%(0/4)T69S, 75%(3/4)K70R, 25%(1/4)K65R, 25%(1/4) L74V, 75%(3/4)M184V. TDF/3TC backbone; 48% (13/27) M41L, 26%(7/27)L210W, 67%(18/27)T215Y/F, 48%(13/27)D67N/G, 37%(10/27)K219Q/E, 0%(0/27)Q151M, 15%(4/27)T69S, 37%(10/27)K70R, 7%(2/27)K65R, 4%(1/27)L74V, and 78%(21/27)M184V. Median duration on first- and second-line ART combined for all NRTI backbones was 5.5 (range 3-8) years for children and 9.0 (range 4-14) years for adolescents. Median duration on first and second-line ART combined for ABC/3TC backbone was 7 years, and 9 for both AZT/3TC and TDF/3TC backbones. Median VL at second line failure for all NRTI backbones combined was 84,463 (70-3,260,000). Median VL at second line failure for ABC/3TC backbone was 146,190 and, 126,672 and 38,257 for AZT/3TC and TDF/3TC backbones respectively. Adolescents aged 10-19 years were 5.5 times likely to have an unsuppressed viral load compared to children 0-9 years (OR 5.5, P Value = 0.02).

Conclusion: There was no statistical significance among patients failing on ABC/3TC backbone with 3 or more TAMs and M184V as compared to other NRTI backbones. Future studies with a bigger sample size should be conducted to understand the effectiveness of ABC/3TC backbones in second line regimens following AZT/3TC/NNRTI first line.
HIV-1 drug resistance patterns during antiretroviral therapy in pediatric population. Experience in two healthcare centers in Mexico City.

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Background: HIV acquired drug resistance is still a challenge in pediatric population. The limited access to pediatric formulations and the social environment of the patients often ease low adherence to treatment and subsequently promotes the selection of resistance associated mutations (RAMs). Morbidity related to replication and immune deficiency are acute problems but drug resistance can also limit future options of treatment and the odds of remain undetectable in the context of life long antiretroviral therapy. The objective was to describe the HIV drug resistance patterns and clinical features in pediatric population from two clinics in Mexico City.

Materials & Methods: From January 2017 to March 2019 we analyzed the drug resistance patterns and clinical features of 18 HIV-1 positive pediatric patients with an indication of drug resistance testing that were coming from two healthcare centers: CLINDI Hospital Infantil de Mexico (HIM) and Clínica para niños con VIH UNAM/HGM. A P < 0.05 was considered statistically significant.

Results: 50% of the patients were female. The average age of the patients was 10.4 (SD, 5.3) years old and with a mean of 7.2 (SD, 5.2) years since HIV diagnosis. The mean RNA viral load was 293,624 (SD, 912106) copies/mL with a CD4+ T cell count of 664.47 (SD, 566.63). The most frequent mutations found were M184V/I (72.2%) and K103N (22.2%). Only two patients had resistance to protease inhibitors despite that 11 patients (61.1%) were using LPV/r. The other 27.8% and 11.1% were under an NNTRI and INSTI-based regimens respectively. The optimized follow-up regimens were 72.2% based on a PI while the other 27.8% combinations included an INSTI (from which RAL was the most frequent). The overall response to the follow-up regimen was 73% of patients achieving undetectable viral load (<40 copies/mL) despite only 10 (66.7%) had ≥ 2 active drugs. Three out of four patients not achieving viral control had specifically documented history of low adherence and having a mean of 3.4 years-old, while patients achieving viral control had a mean of 11.9 years-old. 1 subject was censored due to death and two more for a short period of follow-up.

Conclusions: After the drug resistance testing analysis, the most compromised drugs were nucleoside and non-nucleoside drugs (FTC, 3TC, TDF, EFV and NVP) while the prevalence of protease inhibitors was low. Moreover, most of the follow-up treatment included LPV/r in their combination, following the recommendations of current Mexican guidelines of treatment. Despite the low number of active agents in the salvage regimen, we found a high proportion of virologic control. Having a detectable RNA viral load after treatment was associated with younger age, which might be consequence of adherence problems related with social environment and formulation of drugs among others.

Pediatric HIV Viral Load Suppression: Qualitative Insights of Barriers and Facilitators among Caregivers of Children on ART in High Volume Sites in Kisumu County, Kenya
Introduction: The number of virally suppressed HIV+ children remains unacceptably low; the experiences of caregivers of children on antiretroviral treatment (ART) are critical to developing interventions to achieve maximum viral load (VL) suppression in this population.

Methodology: Eight focus group discussions (FGDs) were conducted among a purposively sampled cohort of 76 caregivers of children (<18 yrs.) on ART (> 6 months) at eight facilities in Kisumu County. A trained qualitative researcher used semi-structured guides to explore VL testing and suppression; translated audio transcriptions were coded using a collaboratively developed framework and Dedoose.

Results: Most caregivers were female (63%), aged 19-85 (median age 40), and biological parents (71%). Caregivers expressed a general understanding of VL; weight-based dosing and medication and appointments adherence were facilitators. VL testing schedules were challenging and ambiguous. HIV-disclosure to children was a facilitator; determining the appropriate age for disclosure, managing anticipated stigma, and disclosure beyond the immediate family were challenges. Medication-specific barriers included timing of pills, management of side effects, medication refusal, and daily pill burden. Health system barriers included long wait times, high frequency of appointments for high VLs, insufficient medications dispersion, and negative provider reactions to missed ART doses. Assisted disclosure and ART management were facilitators; caregivers requested additional disclosure support for school-age children.

Conclusion: Facilitated disclosure and support for caregivers and their children is critical. Facility-level interventions and differentiated care models are needed to improve caregiver-provider interaction. FGDs were conducted with providers and young adults on ART to triangulate findings in this study.

HIV/CMV immunological activation do not progress the cIMT in HIV-infected adolescents

Background: Immunologic activation during HIV infection is known to generate atherosclerotic lesions. Coinfections such as CMV could intensify the chronic inflammation accelerating vascular damage. We hypothesized that the magnitude of the CMV-specific immunological response and/or the activation of T cells and monocytes are associated with the increment of the carotid intima-media thickness (cIMT) in HIV/CMV-coinfected adolescents.

Materials And Methods: Forty HIV/CMV-coinfected 10-18 (mean=14.2) years old adolescents were followed-up for 2 years. Children were periodically characterized for the following parameters: clinical findings, CD4+/CD8+ cells, HIV-RNA, weight, height, abdominal circumference, Body Mass Index, lipoproteins, fasting glucose, fasting insulin, glycosylated hemoglobin, and HOMA IR. Every six months, CMV-specific immunological activation (Quantiferon CMVR assay) and IgM/IgG anti-CMV were quantified. Nonspecific immunological activation of T cells was determined by quantification of sTNFRI, and the presence of HLADR+CD38+CD8+; and that of monocytes by sCD14. cIMT were evaluated by ultrasound at enrollment and after 24 months. cIMT data were analyzed in

References

1. Okoko N, Owino G, Gatahun M, Agen’go L, Omollo M, Okumu I, Bukusi E, Cohen C, Abuogi L. Center for Microbiology Research, Kenya Medical Research Institute (KEMRI), Department of Obstetrics, Gynecology and Reproductive Sciences, University of California San Francisco, Department of Pediatrics, University of Colorado.

absolute and relative values observed at 24 months compared to entry. Simple and multiple log-binomial regression models were adjusted to test the study hypotheses taking the CD4+ cell number as a covariate.

**Results:** All of the 40 subjects were receiving HAART. Overall, they had a good control of the HIV infection. Most (85%) had >500/mm3 CD4+ cells overtime. HIV viral loads below the detectable limit were found in up to 52.5% or ranged from 40 to 400 cps/ml in up to 22.5% of the children. Almost all of them were classified as WHO stage one and 90% had not significant immunosuppression.

No association between the degree of CMV-specific immunity activation nor the unspecific immunological activation markers and the increment of cIMT over 2 years was identified.

**Conclusions:** HIV or CMV immunological activation in co-infected adolescents did not influence the progression of carotid intima-media thickness over a two-year period. Considering that most of these adolescents had abnormally high cIMT at entry, longer observation periods are needed.

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**Characteristics of Children living with HIV who died before ART initiation in Eswatini**

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**Background:** Without HIV diagnosis and early initiation on antiretroviral therapy (ART), 50% of HIV-infected children will die by age two. Early HIV testing and immediate initiation on ART is critical for the survival of children living with HIV. The objective of this evaluation was to describe characteristics of children who died before ART initiation and to learn where gaps and needed progress lie.

**Methods:** We conducted a prospective cohort follow-up of facility registers, collecting and analyzing data of children, aged 0–12 months, diagnosed with HIV between March 2017 and November 2018 from 26 health facilities providing POC EID in Eswatini. For this analysis, we included all children that ever tested HIV-positive, including those lost to follow-up. Data were abstracted from patients’ POC EID testing forms, facility ART registers and electronic medical records. Children were tested either at birth or 6-8 weeks after birth.

**Results:** At study facilities, 107 children tested HIV-positive; 87 (81%) were initiated on ART. Of 20 (19%) children not initiated on ART, 8 (38%) died before ART could be initiated despite a policy of counseling and offering ART on the same day of diagnosis. Of those who died, 63% had their initial test at age 6-8 weeks; 75% of deaths occurred before age 12 weeks. The median age at testing among children who died before ART initiation was 7.6 weeks; 6/8 (75%) children who died had received their HIV results before death. The median time from sample collection to caregiver receipt of results was 0 days, with median time from testing to death 7 days. Among infants who died before ART initiation, 38% of mothers were not receiving ART themselves.

**Conclusion:** Death was not associated with delayed EID testing, lack of caregiver receipt of results, or lack of access to ART. Thirty-eight percent of women whose children died before ART initiation were not on ART themselves; it is unclear if this had a negative influence on the decision for their children to receive ART. Further data are needed to assess how to enhance the policy of and counseling for same-day ART initiation in children.
Factors associated with liver toxicity among HIV infected children and adolescents attending a national referral pediatric HIV clinic in Uganda

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**Background:** Antiretroviral therapy (ART), has drastically reduced progression of HIV and decreased rate of HIV-associated mortality. However, liver disease has become increasingly prevalent among people living with HIV (PLHIV) in Sub-Saharan Africa. In Uganda, Liver Function Tests (LFTs) among PLHIV are not among the recommended routine investigations. Few published studies have been conducted addressing liver toxicity among pediatric and adolescent populations. This study aims to assess factors associated with liver toxicity among HIV infected children and adolescents on ART attending a national referral pediatric HIV clinic in Uganda.

**Methods:** We conducted a retrospective review of 414 patient charts for events occurring Feb - Mar 2017. Eligible patients were aged 0 – 17 years, had been on ART ≥ 6 months, and had had LFTs done as part of routine procedures in a separate observational cohort analysis. One half (206 (49.8%) of the patients had at least one episode of liver toxicity. Variables including gender, age, HIV Viral load (VL), Hepatitis B infection as defined by a positive Hepatitis B surface antigen test and drugs (ART and Anti-TB) at the time of liver toxicity were abstracted from an electronic medical records database. Liver toxicity was characterized by any of the serum liver enzymes levels of Aspartate aminotransferase (AST), Alanine aminotransferase (ALT) and Alkaline phosphatase (ALP) outside normal reference ranges as defined by Cobas Integra 400+ clinical chemistry analyzer manufacturer.

Data generated was fed into Microsoft Excel for cleaning and exported to Stata for analysis using logistic regression model.

**Results:** The study revealed that age was inversely associated with liver toxicity; children 6 - 13 years and 14 -17 years respectively had 74% and 77% lower odds of having liver toxicity compared to children 0-5 years (Adjusted odds ratio, \(aOR(95\%CI); 0.26(0.15-0.45), p<0.01\)), \(aOR(95\%CI):0.23(0.12-0.44), p<0.01\)). Additionally, having an HIV viral load above 75cp/ml was associated with having 2.4 times higher odds of having liver toxicity compared to those who had <75cp/ml. ART regimen was also associated with liver toxicity \((p<0.05)\); patients on second line ART had 74% lower odds of having liver toxicity compared to their counterparts on first line.

**Conclusions:** Liver toxicity in children was strongly associated with younger age, first line ART regimens and non-suppressed viral load. We recommend that clinicians and policy makers consider routine LFTs monitoring for such categories.

Viral load assay performed well when used as a diagnostic for infants


**Background:** While high attrition and mortality account for many of the shortcomings in identifying infants early and putting those on life-saving treatment, fragmented and challenging laboratory systems provide an added barrier. Developing efficient and effective innovations will support greater access to high quality testing.
Abstracts

133

Child development in HIV exposed, uninfected children: Strategies to improve access to developmental services at a Canadian tertiary care center

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Background: HIV exposed uninfected (HEU) children have higher incidences of developmental delay, attributed to HIV exposure, ARV exposure, and social determinants of health. In Canada, mothers living with HIV are more likely than the general population to be new to Canada, Indigenous, and have a history of IV drug use. HEUs in the province of British Columbia are followed by paediatric HIV specialists at the Oak Tree Clinic, which provides HIV surveillance with integrated developmental monitoring. In 2014, concern was raised that many HEUs were not attending recommended developmental services. This precipitated several changes to developmental follow-up, including screening at every visit using the Ages and Stages Questionnaire (ASQ), early referral for developmental concerns, tracking of referral completion, and connecting HEUs with community paediatricians. This quality improvement study sought to understand whether these strategies successfully increased access to developmental services and identify the barriers to access faced by families of HEUs.

Materials and Methods: A retrospective chart review was performed for 169 HEUs, born 2008-2016, with ≥1 clinic visit. Developmental screens, referrals, demographics, and social factors were collected. The adverse childhood experiences (ACE) score was used to measure childhood trauma. HEUs were divided into older and younger cohorts depending on whether they were 18 months of age before or after 2014.
Results: All HEUs were screened for developmental delay at nearly every visit, with 45.6% and 42.9% of the younger and older cohort screening positive at some point before the age of 5 (p=0.653). We found the proportion of children with developmental concern successfully connected to at least one developmental service was higher in the younger cohort (88.5% vs 63.3%, p<0.01), as was the proportion referred to at least one developmental service (88.5% vs 83.7%, p=0.225). Children from the younger cohort had more referrals to (73.1% vs 61.2%, p=0.156) and were more successfully connected with (65.4% vs 44.9%, p<0.05) community paediatricians. Of those 5 or older who continued to be followed at Oak Tree at the time of the study (50.8%), 33.3% had a developmental diagnosis requiring support at school.

The majority of HEUs had ACEs: 70.4% had ≥1, 9.5% had ≥4. Child protective services were involved in 37.3%, 37.8% had financial instability, and 17.1% had housing instability. HEUs with social vulnerabilities had more documented developmental concerns compared to those who did not, including those who had child protective services involvement (71.4% vs 28.3%, p<0.001), ACE ≥4 (78.6% vs 39.9%, p<0.05), financial instability (61.3% vs 35.3%, p<0.001), and housing instability (71.4% vs 39.7%, p<0.05).

Conclusions: Our results support the high rates of developmental delay in children exposed to HIV seen in literature and suggest that social risk factors may play a major role. Strategies initiated at Oak Tree to support development significantly increased access to developmental services. However, there were still HEUs that were unable to access the services they needed. That difficulties persist within a high resource clinic speaks to the developmental and social vulnerability of HEUs.

ART coverage among infants diagnosed with HIV in KwaZulu-Natal, South Africa, 2010-2016

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Background: Since 2010 national guidelines in South Africa have recommended immediate initiation of ART for infants diagnosed with HIV, with birth PCR testing introduced on 01/04/2015. We describe ART coverage among infants born between 01/06/2010 and 31/12/2016 and diagnosed with HIV in the Hlabisa health sub-district, KwaZulu-Natal.

Materials & Methods: Data on all HIV DNA PCR tests (to 17/07/2017) conducted in the 17 clinics in the sub-district were extracted from the National Health Laboratory Service database. A deterministic and probabilistic data linkage algorithm (based on reported first name, surname, date of birth, sex, and clinic) was used to identify repeat tests on the same individuals. Infants testing positive were subsequently linked to those reported to be on ART in the sub-district in TIER.net (the national ART surveillance system). The proportion initiating ART, time from diagnosis to initiation, and age at initiation were summarised by year of birth. Outcomes among the subset of infants who did not initiate ART but had available follow-up data (through linkage to demographic surveillance datasets) were described. Among those born after the introduction of birth testing, ART coverage was compared between those who were diagnosed at birth (first positive test <7 days of age) and those with a first positive result at an older age.

Results: 458 infants ever had a positive PCR test, of whom 244 (53%) initiated ART,
increasing from 45% among those born in 2010 to 70% among those born in 2015 (p<0.001), and 58% in 2016. The decrease in 2016 was likely due to short follow-up time available for this group, with no difference in the proportion initiating ART by 6 months of age (56% in both 2015 and 2016). The median (IQR) [range] time from diagnosis to ART initiation was 5.0 (1.9, 12.4) [-1.0, 175.4] weeks, and age at ART initiation was 25.7 (14.1, 44.7) [1.0, 183.1] weeks, and both decreased over time (p<0.001, <0.001). Among 23 infants who tested positive and did not initiate ART (but had follow-up data available), 10 (43%) died at a median of 12.5 (3.1, 21.0) [1.3, 62.1] weeks later. Of the 458 infants, 68 were born and diagnosed after the introduction of birth testing; a smaller proportion of those diagnosed at birth initiated ART (6/13, 46%) compared to those diagnosed after birth (40/55, 73%) (p=0.065), though numbers were small. The median age at ART initiation was younger in those diagnosed at birth (1.4 (1.3, 2.1) vs. 19.7 (12.4, 31.4) weeks, p=0.020), although there was no difference in the time from diagnosis to ART initiation (p=0.627).

Discussion: ART coverage improved over time although was still far from complete, with high mortality observed among children who did not initiate ART. Infants diagnosed with HIV at birth appeared to be less likely to start treatment compared to those diagnosed later, although mothers’ rather than infants’ names may have been used on some laboratory test forms at birth, which would have prevented successful data linkage among these infants.

Prolonged HIV-1 DBS stability for EID diagnosis confirmed on the new cobas® 6800/8800 qualitative assay

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Background: Nucleic acid-based testing (NAT) is the WHO recommended diagnostic test for HIV in infants younger than 18 months as maternal antibodies. Diagnostic HIV NAT assays are available for highly-automated medium-to high-throughput as well as point-of-care instruments performed on liquid whole blood and dried blood spot (DBS) samples. DBS samples are preferred in resource-constrained settings with logistical challenges as they bear the advantage of having longer stability than liquid samples given that cold chain maintenance is not required during transport and initial storage. Furthermore, DBS samples may provide an additional advantage, since NAT testing for confirmation of HIV diagnosis in infants on stored samples may be necessary. Retesting of stored DBS may be required as an unintended consequence of successful PMTCT programs. Exposure to ARVs could lower the viral burden in infected infants to below the sensitivity of some assays, while the consequently reduced incidence of HIV transmission could increase the risk of false positive results in the uninfected. Therefore, as part of a verification of the cobas® HIV-1/HIV-2 Qualitative nucleic acid test for use on the cobas® 6800/8800 System (cobas), we evaluated the stability of DBS samples beyond the manufacturer recommended storage for up to three months at 15-30°C. Additionally, as this is one of the few NAT assays with diagnostic claims for HIV-2, we verified the plasma HIV-2 limit of detection.

Materials & Methods: This study was performed at a centralised HIV molecular laboratory in Johannesburg, South Africa. Thirty-one DBS samples with at least three spots obtained from infants aged less than 18 months were collected and stored individually in gas impermeable bags with a desiccant sachet. All samples were routinely tested on the Roche COBAS® AmpliPrep/COBAS® TaqMan® HIV-1 Qualitative Test, version 2.0 (CAPCTM) assay on arrival in the lab. These samples were then kept at ambient room temperature which ranged from 15 to 25°C. Samples were then tested on the cobas assay
within 99 days of collection. Retesting on the cobas assay was performed at a mean of nine months following collection (mean of seven months following the first cobas test). We tested thirty samples of 120, 60, 30, 15, 8, 4 and 2 copies/mL for the HIV-2 LOD determination which were produced by serially diluting HIV-2 subtype A/G spiked basematrix.

**Results:** All routine CAPCTM results were positive and reported cycle thresholds (ct)<33. All initial cobas results were reported as positive with cts ranging from 26.14 to 35.96. All the second cobas results were reported as positive with cts ranging from 24.88 to 36.84. The mean Ct difference between the two cobas tests was 0.80. Bland-Altman analysis indicated good agreement between the Cts for the dates tested. The HIV 2 LOD was confirmed to be below the manufacturer’s claimed 27.9 copies/mL.

**Conclusions:** Correctly packaged DBS samples stored at ambient temperature can produce valid results up to nine months after collection, demonstrating that stability may extend beyond the recommended three months. Furthermore, the manufacturer’s claim for HIV-2 plasma LOD has been verified.

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**136**

**Prevalence and Factors Associated with any Depressive Symptom among HIV-Infected Adolescents in the Republic of Congo**

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**Background:** To describe the frequency of any depressive symptom and associated factors among adolescents (10 - 19 years old) living with HIV in Brazzaville and Pointe Noire, Republic of Congo (RoC).

**Methods:** Adolescents aged 10 to 19 years, on antiretroviral treatment, followed in the two Ambulatory Treatment Centers in Brazzaville and Pointe-Noire, RoC were included in this cross-sectional study. Between April 19 and July 9, 2018, face-to-face interviews were conducted with all participants using a standardized questionnaire that include the nine-item of the Patient Health Questionnaire (PHQ-9). Bivariate and multivariable log-binomial model were used to estimate the prevalence ratio (PR) and 95% confidence interval (95%CI) assessing the strength of the association between predictors and presence of depressive symptoms defined as PHQ-9 score ≥ 9.

**Results:** A total of 135 adolescents were interviewed, representing 50% of the adolescent population in active care at the two clinics. Overall, 67 (50%) were male, 81 (60%) were 15-19 years old, 124 (95%) were known to be vertically infected, and 71 (53%) knew their HIV status. PHQ-9 was ≥ 9 among 52 (39%) of participants. In bivariate analysis, the proportion of participants with PHQ-9 score ≥ 9 was higher among participants who learnt about their HIV status after a prolonged illness (PR: 1.66, 95%CI:0.98-2.79), compared to those who knew their HIV status after mother/father’s HIV; those who reported been sexually active (PR:1.71;95CI%: 1.13-2.58), drinking beer (PR:1.47;95CI%:0.82-2.65), aged 15-19 (PR:2.22;95CI%:1.29-3.84), stopped school (PR:1.77;95CI%:1.13-2.78), forget to take antiretroviral treatment more than 2 times in the 7 days preceding the interview (PR:2.20;95CI:1.42-3.41), having lost both parents (PR:1.44; 95CI%: 0.84-2.49) compared to those with both parent alive, and not having family support in taking ART and attending HIV care (PR:1.58; 95CI%:0.98-2.55) compared to those who have support for the two activities. In multivariable analysis, the following factors remained statistically significant: being 15-19 years old (PR:2.07;95CI%:1.06-4.04), having stopped school (PR:1.60;95CI%:1.06-2.42) and reporting instances of omission to take antiretroviral treatment more than 2 times in the 7 days preceding the interview (PR: 2.06;95CI:1.23-3.45).

**Conclusion:** The prevalence of depressive symptoms among HIV-positive adolescents is
high and is associated with older age, poor compliance, and dropping-out of school. Active screening for depression during routine medical visit and proper management is needed.

“"I spend more time on my daughter’s hair than her HIV”: A qualitative study on perceived medical and psychosocial needs among parents from the United States of America who have internationally adopted children with HIV.

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Background: The number of families in the United States of America (USA) pursuing the international adoption of children with HIV infection has steadily increased since 2010. The majority of internationally-adopted children with HIV (IACH) are under the age of 12 and adopted by parents who commonly work with faith-based adoption agencies. Limited research has explored parental views of adoptees’ medical/psychosocial needs.

Materials and Methods: We conducted 60-minute, semi-structured, audio-recorded interviews with a purposive snowball sample of 25 parents of 29 IACH. Recruitment was done at two pediatric infectious diseases clinics in USA where eligible adoptive parents were informed about voluntary participation in the study. Interested parents contacted the research team and arranged an interview. Participants were asked to refer other adoptive parents to the study and recruitment continued through closed social medial groups for parents of IACH. Interview questions included motivations to adopt, as well as their adopted child’s medical/psychosocial needs. Interviews were coded for emergent themes using standard qualitative methods.

Results: All parents identified as white (24 mothers, mean age 37.9 years, from 12 states) and 23 as Christian. Mean age of adoptees was 9.2 years (range 4-19); 14 were females, 17 (59%) were from African countries. Faith was a guiding factor that influenced most parents’ decisions to adopt a child with HIV from another country. Few serious medical concerns were noted; the most common included hearing issues (4), vitamin D deficiency (4), and short stature (4). Many participants indicated, “HIV is no big deal” and few struggled with antiretroviral medication adherence. Adoption-related issues related to perceived inadequate pre-adoption care, trauma and language barriers were of greater to concern to adoptive parents than HIV-related medical issues. Associated psychosocial problems included attention deficit disorder (5), learning disability (3), and reactive attachment disorder (3). Participants described the initial challenges that their IACH experienced due to cultural differences between their country of origin and their new home. Concerns related to the disclosure of the child’s HIV status to others, as well as to the IACH child themselves, were common. Parents sought to protect their child from HIV-related stigma by carefully limiting those who were informed of the child’s status outside of the immediate family, and some had medications delivered to the home via mail, rather than picked up from a local pharmacy to avoid accidental disclosure. The majority of participants received emotional and/or financial support from family, and reported that they were well-connected to medical care. Most participants reported anticipating challenges during adolescence related to sexuality and disclosure; some reported religious beliefs that supported abstinence-only education.

Conclusions: Adoptive parents of IACH cite religious faith as a motivating factor in their adoption decision. These parents uncommonly reported serious medical issues relating to HIV. However, adjustment and attachment issues emerged as pressing concerns, highlighting the
importance of behavioral health care of IACH. Parents of IACH could benefit from support and education by healthcare providers around issues of disclosure, even before the child matures into adolescence.

138

Tracking Integrated Malnutrition and HIV Outcomes: Cohort Analysis of Integrated Service Provision, Gweru District, Zimbabwe

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Background: With a mother-to-child HIV transmission rate of 6.7% and 2.1% of children under five years in urgent need of therapeutic treatment for Severe Acute Malnutrition (SAM) in Zimbabwe, effective integration of HIV/TB and malnutrition services is a national priority. UNICEF and OPHID implemented a program to strengthen integrated services in 11 Districts of Zimbabwe. Our objective was to trace uptake of integrated HIV/Nutrition services and treatment outcomes among children under 5 newly diagnosed with SAM and HIV.

Methods: We conducted a retrospective cohort analysis of all children under 5 years admitted to the Gweru Provincial Hospital malnutrition stabilising treatment centre for SAM treatment and/or diagnosed HIV positive from Jan-Oct 2018. Individual case review was conducted to document malnutrition screening, HIV testing, TB investigation and malnutrition services received and final outcome status. Data were entered into MSExcel and analysed descriptively to generate service cascades starting from HIV diagnosis and SAM treatment for children under 5.

Results: From January-October 2018, a total of 40 children were admitted for SAM treatment and 35 children diagnosed HIV positive at Gweru Provincial Hospital (N=75). The majority were older than 12 months of age at the time of diagnosis (84%; 63/75). All children newly diagnosed with HIV were screened for malnutrition, and vice versa, with an HIV test yield among children with SAM of 5% (2/40), and diagnosis of malnutrition among 11.4% of HIV positive children (4/35). While 100% of children diagnosed with HIV were TB screened (one positive case identified); only 47.5% of children with SAM were screened for TB (19/40). Child death was documented in 4% (3/75) of children recently diagnosed with HIV or SAM at the time of data collection.

Conclusions: We document strong service integration and yields for diagnosis of co-morbidities among children under 5. Late HIV diagnosis and high mortality indicate missed opportunities for early diagnosis and treatment. While integration of TB screening was strong in HIV services, fewer than half of all children with SAM had documented TB screening. Future research is required to understand the interaction of social and biological risk factors for HIV, malnutrition and TB among young children.

139

Clinical outcomes of HIV-infected children in Pediatric HIV programs in resource-constrained-settings: Implications of achieving HIV viral suppression

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Introduction: Perinatally acquired HIV infection and malnutrition remain major public health challenges for sub-Saharan Africa health systems. The introduction of antiretroviral therapy (ART) and ready to use therapeutic food (RUTF) have significantly reduced morbidity and mortality rates in pediatric HIV programs.

Objectives: We describe the clinical status before and after nutritional supplementation using RUTF in malnourished children and virological response in our pediatric HIV programs.

Methods: We carried out a prospective study of HIV-infected ART-naive (ART-N) children initiating ART and ART-experienced (ART-E) children aged between 6 months and 12 years. We examined their clinical outcomes. At each visit, children had a complete clinical and anthropometric assessment and biological samples were taken to measure markers indicative of clinical responses at baseline and 12 weeks. The malnourished children received RUTF. This study received ethical approval in Uganda and Ireland.

Results: We screened 278 HIV-infected children between January 2015 and December 2017, of whom 156 fulfilled the study criteria. These included 66 ART-N and 90 ART-E HIV-infected children 9 months to 12 years of age. Overall, 41 of 66 (62.1%) of ART-N and 44/90 (48.9%) of the ART-E children were acutely malnourished. The median length of time on ART at baseline for the ART-E children was 42 months (IQR: 15-66 months) Most (85.5%) of the ART-N children had severe immunosuppression with median CD4+ T cell percentage <30% of lymphocytes and an absolute count <1000 cells/ml and a median viral load of 114 viral copies/ml. Virologic failure occurred in 80% of children with severe acute malnutrition (SAM), 50% of moderate acute malnutrition (MAM) and 58.5% of well-nourished (WN) patients. The hospitalisation rate was 35/156 (23.3%), highest at baseline at hospitalisation 25/156 (16%) in comparison to no hospitalisation at 12 weeks. The mortality rate was 5/156 (3.2%) while comorbidities occurred in 103/156 (66%) of the HIV-infected children. The majority were dermatopathies (60/156), candidiasis (14/156), and tuberculosis (TB) (14/156). The opportunistic infection (OI) rate was 30/156 (19.2%) and all OI episodes were diagnosed at baseline, except for the immune reconstitution inflammatory syndrome (IRIS) episodes that were diagnosed during the course of the study. At 12 weeks 81/84 (96.4%) had a self-reported adherence score to ART of >95%. The loss to follow up in this study was 72/156 (46.2%).

Conclusion: The use of ART in HIV-infected children significantly reduces hospitalizations, OIs and mortality rates; however the programs still suffer from high rates of loss to follow up. We have unfortunately also shown that ART-N children attending HIV programs are still presenting very late with severe immunosuppression. The majority of the children had high rates of virologic failure despite high rates of self-reported excellent adherence. We recommend virological monitoring in Pediatric programs is utilized as a marker of adherence.

Performance characteristics of GeneXpert and Alere Q point of care Technologies for HIV early infant diagnosis in Kenya

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Background: In Kenya, early infant HIV diagnosis (EID) among HIV exposed infants (HEIs) is achieved through centralized testing using dried blood spots (DBS). However, only 67% of HEIs accessed EID testing in the first half of 2017, suggesting suboptimal performance of the centralized testing system in meeting EID testing demand. Point of care technologies (POCT) could potentially increase accessibility to EID due to their proximity to the clinics and shortened turn-around time of EID results. We describe performance characteristics of GeneXpert HIV-1 and Alere Q HIV 1/2 as EID POCT in Kenya.

Method: Whole blood was collected from 200 HEIs attending Kenyatta National Hospital (KNH) elimination of mother to child HIV transmission clinic between June 2017 to August 2017. EID testing was conducted on Alere-Q HIV-1/2 and GeneXpert HIV-1 POCTs as well as on Roche CAP-CTM HIV-1 V.2 assay (gold standard). Data was analyzed for sensitivity, specificity, error rates and overall test agreement using SAS version 9.4.

Results: Of the 200 samples, 102/105 tested positive on Alere-Q and 104/105 on GeneXpert. Alere-Q and GeneXpert achieved a sensitivity of 97.1% (95% CI: 93.6% - 100%) and 99.1% (95% CI: 95.8% - 100%) with a specificity of 100% (95% CI: 96.1% - 100%) and 98.9% (95% CI: 94.7 – 100%) respectively. The PPV for Alere Q and GeneXpert was 100% and 98.9%, while the NPV was 96.9% and 99.1% respectively. In comparison to Roche, test agreement kappa value was 0.967 for Alere Q and 0.988 for GeneXpert. The equipment reported an uninterpretable error rate of 6% and 2% for Alere-Q and GeneXpert respectively (Table 1).

Conclusion & Recommendations: Alere Q HIV-1/2 and GeneXpert HIV-1 EID POCT had excellent test agreement with Roche CAP-CTM HIV-1 V.2 assay and therefore suitable to complement the existing centralized testing system, especially in hard to reach areas. Evaluation of long-term cost-effectiveness and monitoring of error rates are recommended before full-blown scale-up.

Retention among adolescents and young people enrolled in a faith-based HIV program in Kenya; A retrospective cohort study

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Background: In sub-Saharan Africa, adolescents and young people living with HIV (AYPLHIV) have worse treatment outcomes and retention rates compared to other age groups. Kenya is among 6 countries that contribute to half of the global deaths due to AIDS-related illnesses among AYPLHIV. To avert these deaths, AYPLHIV must be linked to care, initiated on antiretroviral therapy (ART), and retained in care to ensure viral suppression is achieved. Looking at predictors of non-retention in care provides an opportunity for the Christian Health Association of Kenya HIV/AIDS project (CHAP Uzima) to develop interventions to mitigate attrition from care. CHAP Uzima provides HIV care and treatment to approximately 47,000 people living with HIV of whom 5,003 are AYPLHIV in 79 faith-based health facilities across 19 of the 47 counties in Kenya.

Materials & Methods: We conducted a retrospective cohort study using de-identified electronic medical records from CHAP Uzima database. We enrolled all AYPLHIV aged 10-24 years on ART and active as of 30th September 2017. AYPLHIV were considered admitted to care if they had enough antiretroviral drugs to last through the end of 30th September 2018 based on the last drug pick-up date. Reasons for non-retention studied were death and lost to follow-up (LTFU). Descriptive statistics were computed for the study population. We conducted a bivariate and multivariable logistic regression analysis to identify predictors of non-retention in care.
analysis to determine predictors of non-retention. Predictor variables included age, sex, duration on ART, duration prior to start of ART, disclosure, adherence, baseline World Health Organization (WHO) stage, viral suppression and orphan status. Results are presented as odds ratios (OR) and corresponding 95% confidence intervals (CI).

**Results:** We included 4,646 AYPLHIV of whom 55.1% were female. Nearly half (45%) of the participants were orphans and 1,025 (22.1%) had advanced HIV disease at enrollment due to either a WHO stage 3 or 4 disease. Median age, months on ART and days prior to ART initiation was 16.7 years (Interquartile range (IQR) 13.7-20.4), 90 (IQR 47-118) and 75 (IQR 15-384) respectively. The overall twelve-month retention rate was 97%. Those aged 20-24 years had a lower retention rate of 95.8% compared to those aged 10-14 and 15-19 years, whose retention rate was 98.6% and 96.5% respectively. The odds of non-retention doubled among AYPLHIV aged 15-19 years [aOR=2.3, (95% CI 1.2-4.5), p=0.02] and 20-24 years [aOR=2.2, (95% CI 1.0-5.0), p=0.05]. Being male was associated with higher odds of non-retention [aOR 1.7, (95% CI 1.0-3.0), p=0.05] whereas poor ART adherence increased attrition rates eight-fold [aOR=8.6 (95% CI 3.0-24.7), p=0.001]. We did not find an association between advanced HIV disease at baseline with non-retention in care [OR=1.2, (95% CI 0.7-2.8), p=1.2].

**Conclusions:** The project will implement specific and tailored interventions to address the needs of the older AYPLHIV and more so focus on boys while optimizing adherence to ART to ensure better retention in care.

**Interventions for the perinatally HIV infected youth in sub-Saharan Africa: A systematic review**

**Background:** In sub-Saharan Africa, 90% of youth living with HIV were infected at birth. Perinatally HIV infected youth have health needs that differ from those infected through other routes. Interventions exist for youth living with HIV, but little is known about interventions for the perinatally HIV infected youth in sub-Saharan Africa. The purpose of this systematic literature review was to describe interventions unique to the perinatally HIV infected youth aged 10-24 years in sub-Saharan Africa.

**Methods:** We searched PubMed, CINAHL, ProQuest, Evidence Based Nursing, Psych Info, Science Direct, Embase and Scopus databases for peer-reviewed articles. The Preferred Reporting Items for Systematic Reviews (PRISMA) statement guided this review. The search was limited to studies targeting interventions for youth, aged 10-24 years who were infected with HIV from their mothers. We assessed each article for theoretical relevance and quality.

**Results:** Of the 3739 articles we retrieved, only 10 met inclusion criteria, reflecting a dearth in published studies in the area of interventions targeting the perinatally HIV infected youth in sub-Saharan Africa. We identified seven interventions. Six interventions attempted to improve psychosocial health; three were for promoting adherence, sexual health, cognitive and academic function, while one intervention was for reproductive health. Findings were diverse regarding the effectiveness of the interventions. Some interventions registered positive outcomes including improving adherence to medication, reducing stigma and discrimination as well as anxiety and depression. Other interventions registered limited effectiveness including very few youths reaching full disclosure of their HIV status, and persistent fear and misconceptions about sex among the perinatally HIV infected youth.

**Conclusion:** Further research and more substantial investment in programs for perinatally HIV infected youth in sub-Saharan Africa are needed to establish effective
interventions for the complex health care needs of the perinatally HIV infected youth. Intervention studies should recruit larger samples, have more randomized designs, and use attention-control groups.

The Youth Peer Mentor Role in Supporting Adolescent HIV Care: A Qualitative Study

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Background: Adolescents living with HIV (ALHIV) experience poor outcomes due to complex challenges and unmet needs in care. Scalable strategies are needed to mitigate these challenges for vulnerable adolescents. Youth peer mentors (YPM) in the Academic Model Providing Access to Healthcare (AMPATH) liaise with ALHIV and clinicians to facilitate care. We sought to investigate YPM roles supporting ALHIV to navigate HIV care, as well as critical supports for YPM.

Methods: This qualitative study was performed at the MTRH Rafiki Centre for Excellence in Adolescent Health at AMPATH, in Eldoret, Kenya. We comprehensively sampled YPM for semi-structured key informant interviews (KIIIs). KIIIs investigated the role(s) of YPM in ALHIV care, and needed supports for this work. A trained interviewer conducted KIIIs with YPM in either Kiswahili or English. Sessions were recorded, and transcripts were coded and analyzed through thematic analysis.

Results: We interviewed 19 YPM in a total of 32 interviews. YPM described their own past traumatic experiences in HIV care—in contexts of e.g. severe illness, unsupported disclosure, and intense stigma—and discussed how these experiences motivate them to engage with ALHIV and provide support which they themselves may not have had. As such, they highly value peer mentorship and recognize its importance in ALHIV care. YPM roles include counseling for HIV education and adherence, disclosure, mental health, and sexual and reproductive health. They advise on navigating peer and romantic relationships and overcoming stigma. YPM frequently field questions and help manage challenges that otherwise may not be brought to the clinician. Much of their work extends beyond the clinical setting, through texts, calls, and in-person meetings. YPM were supported by committed clinicians, a comprehensive adolescent care program, and by the use of mobile applications.

Conclusions: YPM perform multiple roles to “fill” gaps in care and support vulnerable ALHIV through individualized support. YPM can be supported by establishing effective and supportive partnerships with HIV clinicians, technological supports, and by empowering YPM to address current gaps in the care program. Research is needed to learn how to best scale up YPM programs and evaluate their impact on ALHIV outcomes.

Perinatally HIV-infected adolescents transition to adult care: a natural experiment

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Background: The transition from pediatric to adult care is a vulnerable time for adolescents
with perinatal HIV infection and is often associated with poor clinical outcomes. To help inform transition guidelines, we evaluated retention in care and viral suppression during a natural experiment in which a policy change led to the cessation of transfers of adolescents living with HIV from the pediatric clinic to the adult clinic.

**Methods:** We performed a retrospective cohort analysis of adolescents with perinatal HIV infection receiving care in a government-supported, hospital-based antiretroviral clinic in KwaZulu-Natal, South Africa. Prior to 2012, all adolescents transitioned to adult care at 12 years (“old policy”). Due to a change in policy, all adolescents were subsequently retained in pediatric care (“new policy”). We analyzed adolescents two years before and two years after this policy change. Outcomes were retention in care (defined as one clinic visit, pharmacy refill, or viral load result in the prior 3 months) and HIV viral suppression (defined as <400 copies/ml) one year after transition to adult care or the 13th birthday if remaining in pediatric care. Analyses included bivariate and multivariable regression models, adjusting for sex, ART regimen, history of tuberculosis, and pre-ART CD4.

**Results:** A total of 183 adolescents who turned 12 years between 2011 and 2014 were evaluated; 50 (27%) transitioned to adult care under the old policy and 133 (73%) remained in pediatric care under the new policy. Adolescents who transitioned to the adult clinic had lower retention in care (92%; 46/50) compared to adolescents remaining in the pediatric clinic (99%; 132/133; p=0.02). In the multivariable regression model, retention in care remained lower for adolescents who transitioned to adult care (AOR 0.04; 95%CI 0.01–0.33; p=0.003) compared to those who remained in pediatric care. Viral suppression among adolescents who transferred to the adult clinic (72%; 36/50) was lower than among adolescents remaining in the pediatric clinic (83%; 110/133), although not significantly (p=0.15). Similarly, no significant association was seen in the multivariable regression model (AOR=0.63, 95%CI 0.28-1.39; p=0.25).

**Conclusion:** Adolescents with perinatal HIV infection have higher retention in care when attending pediatric clinics compared those transitioning to adult clinics at age 12. Research should explore the factors leading to the optimal timing of transition to adult care.

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**145**

**Achieving the third 90: Keeping adolescents living with HIV virally suppressed in rural Nigeria in the era of test and treat using Continuous Quality Improvement (CQI) Model of Peer Counseling & Support Group**

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**Background:** In 2016, Nigeria transitioned to “Test & Treat”, a policy where all people living with HIV (PLHIV) are treated with lifelong antiretroviral therapy (ART) regardless of clinical or immunological status. The policy has associated concerns for linkage to ART & subsequently viral suppression, with particular concern for adolescents living with HIV (ALHIV) ages 10 to 19 years. There are unique challenges achieving viral suppression in ALHIV mainly due to developmental changes, increased stigma, discrimination & rejection or lack of social support. Hypothesis tested was antiretroviral therapy adherence effect on viral load outcome. We examined viral suppression among adolescents living with HIV in rural Western Nigeria.

**Methods:** This study was an observational prospective cohort study of adolescents living with HIV (ALHIV) already initiated on antiretroviral therapy for at least six months, enrolled in health facilities across supported facilities in rural parts of Western Nigeria, during a 12-month observation period starting October 2016 till September 2017.
Quantitative viral load analysis was done using Polymerase Chain Reaction, Roche Cobas Taqman 96 Analyzer. All data were collected using Epidata & statistically analyzed using Statistical Package for the Social Sciences (SPSS) version 23.0, with multiple comparisons done using Post Hoc Bonferroni test.

**Results:** A total of 126 (64 males & 62 females) subjects eligible for the study were recruited. Most of them are in the age range of 10 – 16 years, with a mean age of 13.58 ± 4.26 years. 83 (65.9%) & 71 (56.3%) of the subjects had viral suppression of <1000 RNA copies per ml and <50 RNA copies per ml respectively. The 43 subjects went through peer counseling by trained ALHIV and enhanced adherence counseling (EAC) for three months and viral load test repeated three further months after, which made 113 (89.7%) & 101 (80.1%) of the subjects have <1000 RNA copies per ml and <50 RNA copies per ml respectively during the period of observation. The ALHIVs in the process joined the institutionalized social-media driven support group & adolescent decentralized care model ensuring they achieve the third 90 at an undetectable viral load level. ART adherence has significant effect on viral load outcome ($\chi^2 = 6.42$, df = 1, $P = 0.001$).

**Conclusion:** Antiretroviral therapy (ART) treatment adherence counseling is key to the achieving viral suppression and determine infection prognosis, thus, developing robust continuous quality improvement (CQI) plans to address issues across the cascade ultimately helping in the monitoring of HIV/AIDS disease progression and decrease treatment failure tendencies. This will help more patients stay on first line regimen and prolong their life expectancy, indicating that the UNAIDS last 90 target is achievable in adolescents.
(83%) adolescents had enrolled in HIV care and treatment services, including the 8 who had received disclosure. None of the 3 adolescents not yet linked to HIV care had received disclosure. Caregiver reasons for not yet disclosing to the child included: feeling the age was not appropriate (n=3), afraid to tell their child (n=5), and afraid of psychologically traumatizing the child (n=2).

**Conclusions:** This study shows some progress in disclosing HIV status to young adolescents; however, over half had not yet received disclosure 3 months after diagnosis. National programs need to ensure healthcare workers have the skills to assess disclosure status, provide appropriate counseling to caregivers to address their concerns, and support the disclosure process. Newly diagnosed young adolescents should be actively followed to ensure the disclosure process has begun.

**Comparison of transition outcomes of HIV-infected adolescents to a HIV-adult care and a Youth-Friendly care**

**Introduction:** As HIV-infected children are reaching adolescence it is important to prepare those adolescents to be capable to take care of themselves after transitioning to a HIV-adult care. Little is know about the impact of the transitioning to a HIV-adult care with limit adolescent-specific training. Our aim is to described the outcomes of HIV-infected adolescents to a HIV adult and to a youth friendly care.

**Methodology:** We compared 68 HIV-infected adolescents that were transferred to a HIV-adult care in the period 2004-2014 to 86 adolescents transferred to a youth friendly care during the period 2014-2018. Outcomes measures were: retention to care, lost-to-follow-up (LTFU), death and probable death. Definition of youth-friendly facilities was: the presence of a multidisciplinary team to work on barriers and facilitators of transitioning, and skill training for assuming responsibilities for treatment and continuing of care.

**Results:** Retention to care was obtained in 51.5% of the patients transferred to HIV-adult care as opposed to 84.9% in the youth-friendly care. Comparison of LTFU, death and probable death between transition to HIV-adult care and youth-friendly care were: 10.3% vs 7.0%; 20.6% vs 5.8% and 17.6% vs 2.3%, respectively.

**Conclusion:** Transition of HIV-infected adolescents needs to be well planned and the “receiving” facility needs to be able to provide special support for this population in order to increase retention to care and decrease mortality.

**Advocates in Action: peer supporters driving change on the frontlines of service delivery**

**Background:** Adolescents are the only age group for whom AIDS-related deaths are increasing. Engaging young people living with HIV (YPLHIV) as peer supporters has shown to improve facility-level health outcomes and viral suppression through improved linkage, adherence, retention and psychosocial support. However, the potential power of young peer supporters to act as drivers of change and influence service delivery has not been explored.
Methods: In 2018, Paediatric-Adolescent Treatment Africa (PATA) conducted a cross-sectional semi-structured survey with 63 YPLHIV engaged as peer supporters in 49 health facilities across 12 sub-Saharan African countries. Surveys aimed to better understand young peer supporters’ perspectives and experience of power to influence adolescent programmes. Univariate statistics and thematic coding were used to analyse quantitative and qualitative data.

Results: Respondents were 60% female, with a mean age of 22 years. Almost all (98%) peer supporters considered themselves advocates. Advocacy activities included community outreach and awareness-raising, peer representation on various platforms and providing peer-to-peer education and support. Most felt they had a major (53%) or fair amount (41%) of influence on improving services. The majority (90%) reported they frequently inform health providers about challenges peers face or make recommendations on adolescent-friendly health services. Most (81%) reported that these lead to service improvement. Examples of changes resulting from their advocacy include improvements in existing services and facility procedures, as well as additional services being introduced.

Conclusions: Findings suggest that peer supporters understand themselves to be agents of change beyond their better-understood role of task-shifting and supporting service delivery. Young peer supporters report being advocates for their peers, and frequently leverage their experience to proactively raise issues, challenge existing practice, provide feedback and make recommendations. Peer supporters are well-placed to mobilise and facilitate patient, health provider and facility-level advocacy. With linkage to peer-led networks and community structures, peer supporters can participate in broader health system advocacy. Advocacy training should be integrated into peer support curricula to build skills and capacity to successfully effect change. Additionally, health facility staff should be orientated toward receiving feedback from peer supporters, with facilities establishing mechanisms for intergenerational dialogue between service users and providers to leverage this advocacy potential.

149

Using assisted partner services to identify children at high risk of HIV in Kenya

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Background: Assisted partner services (aPS) is an effective HIV testing strategy that involves soliciting contact information for sexual partners of newly diagnosed HIV-positive individuals and then offering these partners HIV testing and referrals for HIV prevention and care. aPS is being successfully introduced and scaled up across Kenya. It is not known whether the aPS framework can also be used to identify and trace HIV-exposed children who would benefit from HIV testing.

Methods: As part of an ongoing study of aPS optimization and scale-up, newly diagnosed HIV-positive women were offered aPS and asked to provide contact information that would facilitate HIV testing of their sexual partners. Women were also asked about their children and their children’s HIV testing history. Those with children of unknown HIV status were offered home or clinic-based testing. We used descriptive statistics and chi-squared test to determine proportions of undiagnosed HIV-exposed children and index-level factors associated with their testing status.

Results: In May-September 2018, 133 women were enrolled. Median age was 27 (Interquartile range [IQR] 23-31), and the majority were married (63%), employed (58%), had completed primary school (55%), and had previously tested for HIV (84%). One hundred seven (81%) of the 133 women reported having
children, of whom 47 (44%) had children who were known HIV-negative and one (1%) had several HIV-positive children not yet linked to care. Fifty-nine (55%) women had children of unknown HIV status. Women with children of unknown status were less likely to be employed compared to those who had tested all their children (p=0.03), but did not differ in age, education, marital status, monthly household income or HIV testing history. Among the 59 women with children of unknown status, 34 (58%) preferred clinic-based pediatric testing and 25 (42%) preferred home-based testing.

**Conclusions:** A large proportion of newly diagnosed HIV-positive women offered aPS had children of unknown HIV status, despite successful scale-up of pediatric testing in HIV care and treatment centers across Kenya. aPS may provide a unique and novel opportunity to identify and test HIV-exposed children and link them to appropriate referral services.

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**"You should stand for your right and know that your child will be breastfed exclusively."
Exclusive breastfeeding experiences among HIV- positive and HIV- negative women in Kenya: A qualitative study**


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**Background:** Exclusive breastfeeding (EBF) is the optimal way to feed young infants. Guidelines recommend that HIV-positive mothers on antiretroviral therapy (ART) should EBF for 6 months to reduce the risk of mother to child transmission of HIV (MTCT) and continue breastfeeding up to 2 years. Mothers may face social or logistic barriers making it difficult to EBF.

**Methods:** This qualitative research was nested within a longitudinal study of intensive maternal counseling to increase EBF rates. HIV-negative and HIV-positive mothers were recruited from public clinics in Nairobi to participate in focus group discussions (FGDs) exploring beliefs about and experiences with infant feeding practices. Conventional content analysis was used to describe and compare barriers and facilitators that influence HIV-positive and HIV-negative women’s experiences with EBF.

**Results:** We conducted 17 FGDs with a total of 80 HIV-positive and 53 HIV-negative women between October 2009-March 2012. Overall, mothers agreed that breastmilk is good for infants, however, early mixed feeding was a common cultural practice. HIV-positive women were more likely to EBF for 6 months and education at the clinic was identified as a facilitator. HIV-positive women perceived that type and duration of infant feeding is their decision. Autonomy in decision-making was facilitated by receiving EBF counseling and support from family, especially male partners. As a result, they perceived their infants to be healthier. In contrast, most of the HIV-negative women reported less autonomy and followed mixed feeding cultural practices, in large part due to peer pressure from neighbors. A main barrier to EBF, regardless of HIV status, was low milk production, perceived to be from poor maternal nutrition. Other barriers included mother returning to work, pressure to follow cultural feeding practices, infant perceived hungry despite breastfeeding, cost, and belief that male infants need more food.

**Conclusions:** Despite EBF challenges for both groups of women, rates of EBF were high and related to counseling at the health center which empowered HIV-positive women to...
advocate for EBF with spouses and family members. To promote EBF and improve child health, both HIV-positive and HIV-negative women would benefit from interventions that advocate for women’s autonomy and foster support from community and partners.

151

Factors influencing effectiveness of prevention of mother-to-child transmission (PMTCT) of HIV - 13-year observation of the Polish cohort

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Background: Mother-to-child transmission (MTCT) is the most common source of HIV infection in children. Factors influencing the effectiveness of MTCT prevention (PMTCT) of HIV were analyzed.

Materials & Methods: 328 mother-child pairs were prospectively analyzed between 2006 and 2018. Diagnosis of infection in the child was conducted in accordance with the current guidelines. Maternal HIV infection was detected no later than perinatally. The duration and the type of the prophylaxis, the maternal HIV viral load during pregnancy, and the type of labor were analyzed.

Results: HIV infection in women was diagnosed before pregnancy in 75% of cases, during pregnancy in 20% of mothers, and during labor in 5% of cases. Complete prophylaxis (during pregnancy, birth, and in the newborn) was adapted in 202/328 (62%) of cases, in 8/328 (2%) of cases no prophylaxis was administered. 287/328 (88%) of women received antiretroviral treatment during pregnancy, 213/328 (65%) received ZDV during labor, and the prophylaxis was administered in 321/328 (98%) of the newborns. Ten (3%) of the children were HIV-infected. No child became infected when the full prophylaxis was applied, or when maternal treatment was initiated before the 14th week of gestation, and in none of 219 mothers who had undetectable HIV viral load in the last weeks of gestation. The child infection rate was 4% for children of mothers in which the treatment was initiated after 14th week of gestation, 14% for cases when the prophylaxis was used only in neonate and/or during labor, and 38% in children without any prophylaxis. Inclusion of the antiretroviral drugs in later weeks of gestation was associated with a higher risk for infection (p = 0.005). Among 109 women with detectable or unknown viral load before delivery, the risk for the child infection was lower when a planned caesarean section was performed (6%) compared to the vaginal delivery (19%, p = 0.04).

Conclusions: The risk of vertical HIV transmission is low. An effective treatment of a woman before pregnancy or initiation of the treatment from the beginning of the second trimester of pregnancy are the most important factors for prevention of MTCT of HIV.
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Author Index
<table>
<thead>
<tr>
<th>Author Name</th>
<th>Abstract Title</th>
<th>Abstract #</th>
<th>Page #</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abuya, D.</td>
<td>Performance characteristics of GeneXpert and Alere Q point of care technologies for HIV early infant diagnosis in Kenya</td>
<td>140</td>
<td>128</td>
</tr>
<tr>
<td>Ajaykumar, A.</td>
<td>Shorter telomeres among HIV+ cART-naive and cART-treated children, and those presenting with abnormal lung function</td>
<td>09</td>
<td>11</td>
</tr>
<tr>
<td>Alankar, A.</td>
<td>Dysfunctional Natural Killer Cell Subsets Correlate With Disease Progression In HIV-Infected Kenyan Children</td>
<td>60</td>
<td>58</td>
</tr>
<tr>
<td>Anderson, K.</td>
<td>The Next Generation: Pregnancy outcomes in adolescents and women living with perinatally acquired HIV in South Africa</td>
<td>20</td>
<td>21</td>
</tr>
<tr>
<td>Barnabas, S.</td>
<td>Evaluating technology-based methods for collecting self-reported sexual risk behaviour in adolescent girls and young women at high risk of HIV infection</td>
<td>88</td>
<td>80</td>
</tr>
<tr>
<td>Beima-sofie, K.</td>
<td>They will look at you with eyes that will make you want to run away: A qualitative assessment of transition experiences and expectations among Kenyan adolescents and their primary caregivers</td>
<td>85</td>
<td>78</td>
</tr>
<tr>
<td>Beima-sofie, K.</td>
<td>Implementation challenges and strategies in integration of PrEP into maternal and child health and family planning services: Experiences of frontline health care workers in Kenya</td>
<td>93</td>
<td>85</td>
</tr>
<tr>
<td>Bekker, A.</td>
<td>Population pharmacokinetics of nevirapine in preterm infants and prediction of doses needed for treatment in combination with other antiretrovirals</td>
<td>05</td>
<td>7</td>
</tr>
<tr>
<td>Beneri, C.</td>
<td>Electronic Health Record (EHR) review of infant outcomes for Neural Tube Defects (NTD) born to HIV+ pregnant women in the US</td>
<td>119</td>
<td>106</td>
</tr>
<tr>
<td>Black, D.</td>
<td>Maternal factors for adherence in infant isoniazid preventive therapy provision among HIV-exposed uninfected infants (HEU) in Kenya</td>
<td>44</td>
<td>46</td>
</tr>
<tr>
<td>Borges, P.</td>
<td>Identifying HIV disclosure determinants in adolescents living with HIV on ART in late adolescence (15-19 years): A Study in Goa, India</td>
<td>73</td>
<td>68</td>
</tr>
<tr>
<td>Boyce, C.</td>
<td>HIV Drug Resistance at Mother-to-Child Transmission and Emergence During Breastfeeding</td>
<td>14</td>
<td>15</td>
</tr>
<tr>
<td>Brophy, J.</td>
<td>Evaluation of Bone Mineral Density Among Infants With and Without Perinatal Tenofovir Exposure</td>
<td>121</td>
<td>108</td>
</tr>
<tr>
<td>Brusamento, S.</td>
<td>Adoption of 2018 WHO recommendations on Antiretroviral Therapy preferred First line in Children and Adolescents</td>
<td>65</td>
<td>61</td>
</tr>
<tr>
<td>Busobozi, H.</td>
<td>Data review and Support supervision as a Quality Improvement approach to improve Viral load Access and Suppression (treatment outcomes) for children and adolescents living with HIV in Uganda</td>
<td>61</td>
<td>58</td>
</tr>
<tr>
<td>Casalini, C.</td>
<td>Community based Index- and Mobile testing are complementary and effective in pediatric HIV case finding in Tanzania</td>
<td>01</td>
<td>3</td>
</tr>
<tr>
<td>Chakezha, T.</td>
<td>Outcomes of point-of-care maternal HIV viral load testing and early infant diagnosis at delivery: experience from four tertiary obstetric units in Gauteng, South Africa.</td>
<td>95</td>
<td>87</td>
</tr>
<tr>
<td>Chappell, E.</td>
<td>Viral suppression, ART interruptions and switching among children with HIV on ART in KwaZulu-Natal, South Africa, 2010-2016</td>
<td>66</td>
<td>62</td>
</tr>
<tr>
<td>Chappell, E.</td>
<td>ART coverage among infants diagnosed with HIV in KwaZulu-Natal, South Africa, 2010-2016</td>
<td>134</td>
<td>123</td>
</tr>
<tr>
<td>Chouraya, C.</td>
<td>Association of ART regimen with viral suppression in HIV-positive children in Eswatini: Baseline data from the FAM-CARE study</td>
<td>125</td>
<td>116</td>
</tr>
<tr>
<td>Ciaranello, A.</td>
<td>The clinical impact and cost-effectiveness of routine HIV screening and testing at infant immunization visits in Côte d’Ivoire (CI), South Africa (SA), and Zimbabwe (Zim)</td>
<td>21</td>
<td>22</td>
</tr>
<tr>
<td>Cohn, J.</td>
<td>Relationship between Proximity of Health Facilities to Referral Laboratories and Early Infant Diagnosis (EID) Turnaround Time (TAT) and Percent of Results Returned on ART</td>
<td>94</td>
<td>86</td>
</tr>
<tr>
<td>Coombs, A.</td>
<td>Improving Health and Social Outcomes of Adolescents - Addressing the Parallel Risks of Pregnancy and HIV though a Home Visiting Program in Kenya</td>
<td>86</td>
<td>79</td>
</tr>
<tr>
<td>Cox, S.</td>
<td>Tenofovir Alafenamide-based regimens: A Pooled Resistance Analysis in Pediatric Participants</td>
<td>04</td>
<td>6</td>
</tr>
<tr>
<td>Crichton, S.</td>
<td>Virological outcomes and ART discontinuation in children switching to dolutegravir in the UK/Ireland: a propensity score analysis</td>
<td>03</td>
<td>4</td>
</tr>
<tr>
<td>Crichton, S.</td>
<td>Abacavir use in young infants in the UK and Ireland national paediatric HIV cohort</td>
<td>41</td>
<td>43</td>
</tr>
<tr>
<td>Crichton, S.</td>
<td>Children and adolescents in the UK/ Ireland CHIPS cohort on integrase inhibitors: safety and effectiveness</td>
<td>42</td>
<td>44</td>
</tr>
<tr>
<td>Cummings, T.</td>
<td>Challenges with recognition of newborns at high risk for perinatal HIV transmission in rural Western Cape, South Africa</td>
<td>31</td>
<td>34</td>
</tr>
<tr>
<td>De Beer, S.</td>
<td>Completeness of maternal HIV testing and repeat testing in Cape Town, South Africa: a longitudinal analysis</td>
<td>98</td>
<td>89</td>
</tr>
<tr>
<td>De Paris, K.</td>
<td>HIV vaccination in infancy to achieve lifelong protection- a real possibility?</td>
<td>108</td>
<td>97</td>
</tr>
<tr>
<td>Desmonde, S.</td>
<td>Effectiveness of a web-based information system to improve HIV early infant diagnosis and hepatitis B immunization at birth in Abidjan, Côte d'Ivoire. The DEPSTNEO project.</td>
<td>77</td>
<td>71</td>
</tr>
<tr>
<td>Desselas, E.</td>
<td>Humoral immune response to measles vaccination at 6, 9, and 15 months and antibody persistence during the first five years of age in early treated HIV-infected children in Cameroon.</td>
<td>97</td>
<td>88</td>
</tr>
<tr>
<td>Dirajjal-fargo, S.</td>
<td>Economic vulnerability, inflammation and immune activation in children living with HIV in Uganda</td>
<td>70</td>
<td>66</td>
</tr>
<tr>
<td>Author Name</td>
<td>Abstract Title</td>
<td>Abstract #</td>
<td>Page #</td>
</tr>
<tr>
<td>-------------</td>
<td>----------------</td>
<td>------------</td>
<td>--------</td>
</tr>
<tr>
<td>Duran, M.</td>
<td>&quot;You should stand for your right and that your child will be breastfed exclusively:&quot; Exclusive breastfeeding experiences among HIV-positive and HIV-negative women in Kenya: A qualitative study</td>
<td>150</td>
<td>136</td>
</tr>
<tr>
<td>Ekat, M.</td>
<td>Prevalence and Factors Associated with any Depressive Symptom among HIV-Infected Adolescents in the Republic of Congo</td>
<td>136</td>
<td>125</td>
</tr>
<tr>
<td>Enane, L.</td>
<td>Pediatric adaptation of Cause of Death (P-CoDe) methodology to ascertain causes of mortality among hospitalized adolescents with perinatal HIV infection in western Kenya</td>
<td>72</td>
<td>67</td>
</tr>
<tr>
<td>Enane, L.</td>
<td>A Qualitative Assessment of Barriers, Facilitators, and Areas of Intervention for Adolescent Retention in HIV Care</td>
<td>89</td>
<td>81</td>
</tr>
<tr>
<td>Enane, L.</td>
<td>The Youth Peer Mentor Role in Supporting Adolescent HIV Care: A Qualitative Study</td>
<td>143</td>
<td>131</td>
</tr>
<tr>
<td>Escudero, D.</td>
<td>HIV treatment coverage and antenatal care among non-citizen pregnant women in Botswana</td>
<td>29</td>
<td>33</td>
</tr>
<tr>
<td>Fairlie, L.</td>
<td>Feasibility of Point-of-Care Viral Load Testing in Postpartum HIV-positive Women in South Africa: Interim Results</td>
<td>101</td>
<td>91</td>
</tr>
<tr>
<td>Familiar, I.</td>
<td>Chronic maternal depression symptomatology predicts executive behavioral problems in HIV affected children in Uganda</td>
<td>25</td>
<td>26</td>
</tr>
<tr>
<td>Frigati, L.</td>
<td>Hospitalization in Perinatally HIV-infected adolescents on Antiretroviral Therapy in South Africa: a prospective study.</td>
<td>19</td>
<td>20</td>
</tr>
<tr>
<td>Frigati, L.</td>
<td>Changes in lipids after switching to boosted Atazanavir in South African youth</td>
<td>71</td>
<td>67</td>
</tr>
<tr>
<td>Gaitho, D.</td>
<td>Retention among adolescents and young people enrolled in a faith-based HIV program in Kenya; A retrospective cohort study</td>
<td>141</td>
<td>129</td>
</tr>
<tr>
<td>Gill, M.</td>
<td>Developing a pediatric and adolescent HIV-screening tool in outpatient settings in Uganda</td>
<td>87</td>
<td>80</td>
</tr>
<tr>
<td>Gill, M.</td>
<td>Pediatric HIV case identification: Missed opportunities along the PMTCT cascade in Kenya and Uganda</td>
<td>106</td>
<td>95</td>
</tr>
<tr>
<td>Ginindza, M.</td>
<td>Final HIV outcome for exposed infants: Improving mother-baby pair retention in prevention of mother-to-child transmission care in Eswatini through proactive community follow-up</td>
<td>32</td>
<td>35</td>
</tr>
<tr>
<td>Ginindza, M.</td>
<td>Creating Demand for HIV Testing Services (HTS) among School-aged Children</td>
<td>34</td>
<td>37</td>
</tr>
<tr>
<td>Ginwalla-Lakhi, R.</td>
<td>Second Line failure and Outcome of Third line therapy among a Cohort of Treatment-Experienced Children and Adolescents at the University Teaching Hospital in Lusaka, Zambia</td>
<td>124</td>
<td>115</td>
</tr>
<tr>
<td>Graybill, L.</td>
<td>A systematic review and meta-analysis of HIV incidence during pregnancy and breastfeeding in sub-Saharan Africa</td>
<td>109</td>
<td>97</td>
</tr>
<tr>
<td>Graybill, L.</td>
<td>A systematic review of risk factors for HIV acquisition during pregnancy and breastfeeding in sub-Saharan Africa</td>
<td>110</td>
<td>98</td>
</tr>
<tr>
<td>Gutierrez Zamudio, A.</td>
<td>Pediatric HIV care at an ambulatory health center in Maputo, Mozambique</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>Haghighat, R.</td>
<td>Transition Pathways out of Paediatric Care and Associated HIV Outcomes for Adolescents Living with HIV in South Africa</td>
<td>LB_3</td>
<td>110</td>
</tr>
<tr>
<td>Hans, L.</td>
<td>Prolonged HIV-1 DBS stability for EID diagnosis confirmed on the new cobas® 6800/8800 qualitative assay</td>
<td>135</td>
<td>124</td>
</tr>
<tr>
<td>Heaney, J.</td>
<td>Comparison of qPCR and ddPCR methods to investigate the latent HIV reservoir in a paediatric population with long viral suppression on therapy</td>
<td>102</td>
<td>92</td>
</tr>
<tr>
<td>Hoare, J.</td>
<td>Systemic inflammation and structural brain changes in perinatally HIV+ adolescents</td>
<td>06</td>
<td>8</td>
</tr>
<tr>
<td>Hoare, J.</td>
<td>Associations between cholesterol, apolipoprotein E genotype variants, cognition and brain structure in perinatally HIV+ adolescents</td>
<td>07</td>
<td>9</td>
</tr>
<tr>
<td>Hrapcak, S.</td>
<td>HIV prevalence and factors associated with HIV among children 2-14 years presenting to high-risk settings of selected health facilities in Ethiopia</td>
<td>96</td>
<td>87</td>
</tr>
<tr>
<td>Hrapcak, S.</td>
<td>Confirmatory testing of HIV-positive status before initiation of antiretroviral treatment: caregiver and healthcare worker experience in Ethiopian facilities</td>
<td>100</td>
<td>90</td>
</tr>
<tr>
<td>Hrapcak, S.</td>
<td>Enrollment to HIV treatment services and predictors of enrolment among HIV-infected children from high-risk settings in selected health facilities in Ethiopia</td>
<td>122</td>
<td>114</td>
</tr>
<tr>
<td>Hrapcak, S.</td>
<td>Disclosure status among newly diagnosed HIV-infected adolescents aged 10-14 years: Findings from a facility-based study in Ethiopia</td>
<td>146</td>
<td>133</td>
</tr>
<tr>
<td>Htut, K.</td>
<td>Burden of Tuberculosis among Children and adolescents on Anti-retroviral Therapy in Myanmar</td>
<td>45</td>
<td>47</td>
</tr>
<tr>
<td>Htut, K.</td>
<td>Adherence to Anti-retroviral Therapy among children and adolescents in Myanmar: a mixed-methods study</td>
<td>49</td>
<td>50</td>
</tr>
<tr>
<td>Jao, J.</td>
<td>Monitoring and Supporting Women Living with HIV Who Choose to Breastfeed their HIV-Exposed Infants in Botswana</td>
<td>107</td>
<td>96</td>
</tr>
<tr>
<td>Jesson, J.</td>
<td>Growth and immunodeficiency of ART-treated adolescents living with perinatally acquired HIV: A Collaborative Initiative for Paediatric HIV Education and Research (CIPHER) Cohort Collaboration Analysis.</td>
<td>18</td>
<td>19</td>
</tr>
<tr>
<td>Judd, A.</td>
<td>Malignancies in children with HIV across Eastern and Western Europe and Thailand</td>
<td>08</td>
<td>10</td>
</tr>
<tr>
<td>Kakkar, F.</td>
<td>Time to viral load suppression and rebound among Canadian infants and children initiating cART in the Early Pediatric Initiation Canada Child Care Cohort (EPIC4) cohort</td>
<td>62</td>
<td>59</td>
</tr>
<tr>
<td>Author Name</td>
<td>Abstract Title</td>
<td>Abstract #</td>
<td>Page #</td>
</tr>
<tr>
<td>-------------</td>
<td>----------------</td>
<td>------------</td>
<td>--------</td>
</tr>
<tr>
<td>Kakkar, F.</td>
<td>Children’s perceptions of HIV Cure Research: An end of study assessment of the Early Pediatric Initiation, Canada Child Care Cohort (EPIC4) study</td>
<td>63</td>
<td>60</td>
</tr>
<tr>
<td>Kangoth, J.</td>
<td>Virological suppression among HIV infected adolescents and youths receiving ART in the National teaching and referral hospital in Kenya</td>
<td>54</td>
<td>53</td>
</tr>
<tr>
<td>Kido, A.</td>
<td>Safety and efficacy of E/C/F/TAF in virologically suppressed, HIV-infected children through 96 Weeks</td>
<td>22</td>
<td>23</td>
</tr>
<tr>
<td>Kido, A.</td>
<td>Lack of Influence of Pubertal Stage on Safety and TFV Pharmacokinetics in TAF-based Regimens</td>
<td>43</td>
<td>45</td>
</tr>
<tr>
<td>Kizito, H.</td>
<td>The Challenges of HIV PMTCT Programming among Sex Workers – Experience of AIDS Information Centre (AIC) – Uganda</td>
<td>116</td>
<td>103</td>
</tr>
<tr>
<td>Kouamou, V.</td>
<td>Drug resistance among youth with confirmed virologic failure on first line and response to second line ART in Harare, Zimbabwe.</td>
<td>57</td>
<td>55</td>
</tr>
<tr>
<td>Laughton, B.</td>
<td>Neurodevelopmental outcome at 11 months in perinatally HIV-infected infants: does starting very early antiretroviral therapy help?</td>
<td>23</td>
<td>24</td>
</tr>
<tr>
<td>Lemaire, J.</td>
<td>Scalability of Point-of-Care Early Infant HIV Diagnosis (POC EID) in Eight Sub-Saharan Countries: Comparing Key EID Outcomes in Introductory and Scale-up Phases.</td>
<td>92</td>
<td>84</td>
</tr>
<tr>
<td>Lungu, J.</td>
<td>Camp Hope Malawi: A game changer for the newly disclosed and challenging adolescent HIV cases.</td>
<td>78</td>
<td>72</td>
</tr>
<tr>
<td>Machado, E.</td>
<td>Comparision of transition outcomes of HIV-infected adolescents to a HIV-adult care and a Youth-Friendly care</td>
<td>147</td>
<td>134</td>
</tr>
<tr>
<td>Mahtab, S.</td>
<td>Mental health and its association with metabolic outcomes in youth living with perinatally acquired HIV in the Cape Town Adolescent Antiretroviral Cohort (CTAAAC).</td>
<td>55</td>
<td>54</td>
</tr>
<tr>
<td>Maiga, A.</td>
<td>Second-line Antiretroviral therapy failure and characterization of HIV-1 drug resistance patterns in children in Mali</td>
<td>59</td>
<td>57</td>
</tr>
<tr>
<td>Mapangisana, T.</td>
<td>Virus Load Differentiated Care of HIV-1 infected children and adolescents is feasible and effective in remote rural Zimbabwe</td>
<td>51</td>
<td>51</td>
</tr>
<tr>
<td>Mark, D.</td>
<td>Back to basics: Friendly health providers are the key to retaining adolescents living with HIV</td>
<td>83</td>
<td>76</td>
</tr>
<tr>
<td>Masuku, T.</td>
<td>Characteristics of Children living with HIV who died before ART initiation in Eswatini</td>
<td>130</td>
<td>120</td>
</tr>
<tr>
<td>Melvin, A.</td>
<td>Pharmacokinetics, Safety and Tolerability of Doravirine in Adolescents with HIV-1</td>
<td>39</td>
<td>41</td>
</tr>
<tr>
<td>Morales Pérez, D.</td>
<td>ATTENTION DEFICIT HYPERACTIVITY DISORDER IN MEXICAN CHILDREN AND ADOLESCENTS WITH PERINATALY ACQUIRED HIV</td>
<td>47</td>
<td>48</td>
</tr>
<tr>
<td>Mosha, S.</td>
<td>ADOPTION OF 2018 RECOMMENDATIONS ON INFANT DIAGNOSIS OF HIV</td>
<td>113</td>
<td>101</td>
</tr>
<tr>
<td>Moyo, F.</td>
<td>Characterizing viral load burden among HIV-infected women at time of delivery: Findings from four tertiary obstetric units in Gauteng, South Africa.</td>
<td>117</td>
<td>104</td>
</tr>
<tr>
<td>Mubiana, M.</td>
<td>PMTCT service uptake among adolescents living with HIV</td>
<td>79</td>
<td>73</td>
</tr>
<tr>
<td>Mubiana, M.</td>
<td>Virological outcomes among children receiving ART in the public health sector in Zambia; 2017-2018</td>
<td>123</td>
<td>114</td>
</tr>
<tr>
<td>Mudekereza, R.</td>
<td>Assessing Final Infant Outcomes for Two Birth Cohorts of HIV Exposed Infants (HEI) in Manzini region of Eswatini</td>
<td>114</td>
<td>102</td>
</tr>
<tr>
<td>Muheriwa, S.</td>
<td>Interventions for the perinatally HIV infected youth in sub-Saharan Africa: A systematic review</td>
<td>142</td>
<td>130</td>
</tr>
<tr>
<td>Mulindwa, B.</td>
<td>Factors associated with liver toxicity among HIV infected children and adolescents attending a national referral pediatric HIV clinic in Uganda</td>
<td>131</td>
<td>121</td>
</tr>
<tr>
<td>Mutanga, J.</td>
<td>Point-of-care testing for early infant diagnosis of HIV in rural Zambia: Experience from the field</td>
<td>120</td>
<td>107</td>
</tr>
<tr>
<td>Mutiti, A.</td>
<td>Towards Achieving Undetectable Viral Load: Viral Load Outcomes Among Adolescents Living With HIV on ART in the Manzini Region of Eswatini</td>
<td>58</td>
<td>56</td>
</tr>
<tr>
<td>Namusoke,-</td>
<td>HIV Drug Resistance Patterns among HIV infected children and adolescents failing for second line Antiretroviral therapy in Uganda.</td>
<td>126</td>
<td>117</td>
</tr>
<tr>
<td>Neary, J.</td>
<td>Untested children reached through index case testing often have previously tested siblings and poor historic PMTCT engagement</td>
<td>36</td>
<td>38</td>
</tr>
<tr>
<td>Neillan, A.</td>
<td>Resource utilization in adolescents and young adults with HIV in the HIV Research Network</td>
<td>90</td>
<td>82</td>
</tr>
<tr>
<td>Njuguna, I.</td>
<td>Financial incentives increase pediatric HIV testing among HIV positive caregivers</td>
<td>35</td>
<td>37</td>
</tr>
<tr>
<td>Njuguna, I.</td>
<td>Mortality and loss to follow-up among HIV positive adolescents and young adults in program settings in Kenya</td>
<td>84</td>
<td>77</td>
</tr>
<tr>
<td>Nowicka, K.</td>
<td>Factors influencing effectiveness of prevention of mother-to-child transmission (PMTCT) of HIV - 13-year observation of the Polish cohort</td>
<td>151</td>
<td>137</td>
</tr>
<tr>
<td>Nyakato, P.</td>
<td>Outcomes of children and adolescents living with HIV considered lost to follow up at ieDEA-SA cohorts in the Western Cape: Linkage to Western Cape Provincial Health Data Centre records.</td>
<td>28</td>
<td>29</td>
</tr>
<tr>
<td>Nyemba, D.</td>
<td>Lower birth weight-for-age and length-for-age z-scores in infants with in utero HIV and ARV exposure: a prospective study in Cape Town, South Africa</td>
<td>15</td>
<td>16</td>
</tr>
<tr>
<td>Nzomo, T.</td>
<td>Laboratory evaluation of the Xpert® HIV-1 Qual Assay as a point of care technology for HIV early infant diagnosis in Kenya</td>
<td>105</td>
<td>94</td>
</tr>
<tr>
<td>Author Name</td>
<td>Abstract Title</td>
<td>Abstract #</td>
<td>Page #</td>
</tr>
<tr>
<td>-------------</td>
<td>--------------------------------------------------------------------------------</td>
<td>------------</td>
<td>--------</td>
</tr>
<tr>
<td>Okoko, N.</td>
<td>Pediatric HIV Viral Load Suppression: Qualitative Insights of Barriers and Facilitators among Caregivers of Children on ART in High Volume Sites in Kisumu, Kenya</td>
<td>128</td>
<td>118</td>
</tr>
<tr>
<td>Okorie, G.</td>
<td>Topic: Effective Community Engagement and Participation, key to Nigeria achieving the first 90' target of eMTCT.</td>
<td>33</td>
<td>36</td>
</tr>
<tr>
<td>Olivero, R.</td>
<td>“I spend more time on my daughter’s hair than her HIV”: A qualitative study on perceived medical and psychosocial needs among parents from the United States of America who have internationally adopted children with HIV.</td>
<td>137</td>
<td>126</td>
</tr>
<tr>
<td>Omuh, H.</td>
<td>Reducing HIV Exposed Babies Early Infant Diagnosis Cascade Loss: The Shoe Rack Strategy</td>
<td>115</td>
<td>103</td>
</tr>
<tr>
<td>Orkiiriza, J.</td>
<td>Effect of Ready-to-use therapeutic food on efavirenz and nevirapine plasma levels in Malnourished HIV-infected Children in Uganda</td>
<td>40</td>
<td>42</td>
</tr>
<tr>
<td>Orkiiriza, J.</td>
<td>Clinical outcomes of HIV-infected children in Pediatric HIV programs in resource-constrained-settings: Implications of achieving HIV viral suppression</td>
<td>139</td>
<td>127</td>
</tr>
<tr>
<td>Pene Dumitrescu, T.</td>
<td>Adolescent extrapolation of Efficacy and Safety for Dolutegravir (DTG) 50 mg/ Lamivudine (3TC) 300 mg Fixed Dose Combination (FDC) tablet</td>
<td>67</td>
<td>63</td>
</tr>
<tr>
<td>Pimentel De Gusmao, E.</td>
<td>Intensive Technical Assistance supporting Early Infant Diagnosis for HIV-Exposed Infants in Mozambique</td>
<td>112</td>
<td>100</td>
</tr>
<tr>
<td>Posobicie, L.</td>
<td>DOLUTEGRAVIR DOES NOT INDUCE NEURAL TUBE DEFECTS IN A RAT WHOLE EMBRYO CULTURE SYSTEM</td>
<td>104</td>
<td>94</td>
</tr>
<tr>
<td>Rancis, K.</td>
<td>Supported breastfeeding among women with diagnosed HIV in the UK: the current picture</td>
<td>118</td>
<td>105</td>
</tr>
<tr>
<td>Rodriguez, R.</td>
<td>HIV-1 drug resistance patterns during antiretroviral therapy in pediatric population. Experience in two healthcare centers in Mexico City.</td>
<td>127</td>
<td>118</td>
</tr>
<tr>
<td>Rosen, J.</td>
<td>Closing the Treatment Gap for Children: Global and Regional Trends in Pediatric Antiretroviral Therapy Coverage, 2010-2017</td>
<td>27</td>
<td>28</td>
</tr>
<tr>
<td>Rotheram-Borus, M.</td>
<td>Outcomes of HIV-exposed but Uninfected Children in South Africa over 5 Years: Comparison to Unaffected Peers</td>
<td>LB_4</td>
<td>110</td>
</tr>
<tr>
<td>Rowe, E.</td>
<td>AHEAD Study: a pilot randomised controlled trial of a music intervention aiming to improve executive function in adolescents with HIV</td>
<td>91</td>
<td>83</td>
</tr>
<tr>
<td>Sacks, E.</td>
<td>Point-of-care HIV testing at birth for high-risk vs. all HIV-exposed infants: preliminary results from a pilot study in Zimbabwe</td>
<td>103</td>
<td>93</td>
</tr>
<tr>
<td>Santos Cruz, M.</td>
<td>HIV-related stigma in life trajectories of youths living with HIV</td>
<td>80</td>
<td>74</td>
</tr>
<tr>
<td>Serghides, L.</td>
<td>Murine Reproductive Toxicity Studies to Evaluate Potential Neural Tube Defects and Other Fetal Abnormalities Associated with Dolutegravir Exposure in Pregnancy.</td>
<td>LB_2</td>
<td>109</td>
</tr>
<tr>
<td>Shava, A.</td>
<td>Retention and Viral Suppression of Children and Adolescents in HIV Care, Zimbabwe</td>
<td>52</td>
<td>52</td>
</tr>
<tr>
<td>Shava, A.</td>
<td>Integrating Health Services Provision - Improving HIV testing and treatment for children under five years referred to rural health facilities with Severe Acute Malnutrition</td>
<td>64</td>
<td>61</td>
</tr>
<tr>
<td>Shava, A.</td>
<td>Tracking Integrated Malnutrition and HIV Outcomes: Cohort Analysis of Integrated Service Provision, Gweru District, Zimbabwe</td>
<td>138</td>
<td>127</td>
</tr>
<tr>
<td>Soetens, H.</td>
<td>Advocates in Action: peer supporters driving change on the frontlines of service delivery</td>
<td>148</td>
<td>134</td>
</tr>
<tr>
<td>Songtaweesin, W.</td>
<td>Moderate adherence to HIV pre-exposure prophylaxis among men who have sex with men and transgender women aged 15-19 years of age in Thailand</td>
<td>81</td>
<td>75</td>
</tr>
<tr>
<td>Sturzbecher, F.</td>
<td>Low Cytomegalovirus (CMV) recurrence among HIV-infected children and adolescents on HAART from a highly CMV-seropositive population</td>
<td>46</td>
<td>47</td>
</tr>
<tr>
<td>Sturzbecher, F.</td>
<td>HIV/CMV immunological activation do not progress the cIMT in HIV-infected adolescents</td>
<td>129</td>
<td>119</td>
</tr>
<tr>
<td>Sutcliffe, C.</td>
<td>The cost-effectiveness of point-of-care platforms for early infant diagnosis of HIV infection in Southern Province, Zambia</td>
<td>02</td>
<td>4</td>
</tr>
<tr>
<td>Thorne, B.</td>
<td>T cell senescence and exhaustion in perinatally HIV infected children (PHIC)</td>
<td>24</td>
<td>25</td>
</tr>
<tr>
<td>Torre, P.</td>
<td>Auditory Brainstem Neural Responses in Young HIV-Infected and HIV-Uninfected South African Children</td>
<td>69</td>
<td>65</td>
</tr>
<tr>
<td>Tsondai, P.</td>
<td>Describing the characteristics and long-term outcomes of adolescents living with perinatally acquired HIV in the IeDEA-Southern Africa Collaboration: 2004-2017</td>
<td>17</td>
<td>18</td>
</tr>
<tr>
<td>Usman, S.</td>
<td>Achieving the third 90: Keeping adolescents living with HIV virally suppressed in rural Nigeria in the era of test and treat using Continuous Quality Improvement (CQI) Model of Peer Counseling &amp; Support Group</td>
<td>145</td>
<td>132</td>
</tr>
<tr>
<td>Mofenson, L.</td>
<td>Periconception Antiretroviral Exposure and Central Nervous System (CNS) and Neural Tube Birth Defects – Data from Antiretroviral Pregnancy Registry (APR)</td>
<td>12</td>
<td>13</td>
</tr>
<tr>
<td>Vhembo, T.</td>
<td>Reasons for new paediatric HIV infections: findings from a cohort of HIV infected children screened at Harare Family Care Clinical Research Site.</td>
<td>111</td>
<td>99</td>
</tr>
<tr>
<td>Vojnov, L.</td>
<td>Implementing an indeterminate range for more accurate early infant diagnosis: 2018 WHO recommendations</td>
<td>74</td>
<td>69</td>
</tr>
<tr>
<td>Vojnov, L.</td>
<td>Rapid antibody tests for determining HIV exposure and infection in infants and children: a systematic review and meta-analysis</td>
<td>75</td>
<td>70</td>
</tr>
<tr>
<td>Vojnov, L.</td>
<td>Viral load assay performed well when used as a diagnostic for infants</td>
<td>132</td>
<td>121</td>
</tr>
<tr>
<td>Vreeman, R.</td>
<td>Substantial antiretroviral non-adherence, non-therapeutic plasma drug levels, longitudinal treatment failure and drug resistance in HIV-infected Kenyan children</td>
<td>76</td>
<td>70</td>
</tr>
<tr>
<td>Author Name</td>
<td>Abstract Title</td>
<td>Abstract #</td>
<td>Page #</td>
</tr>
<tr>
<td>---------------------</td>
<td>--------------------------------------------------------------------------------</td>
<td>------------</td>
<td>--------</td>
</tr>
<tr>
<td>Wachira, C.</td>
<td>Perception that a child is HIV-positive and fear that the child will be tested are barriers for seeking medical care for the child by HIV-positive caregivers</td>
<td>37</td>
<td>39</td>
</tr>
<tr>
<td>Wagner, A.</td>
<td>Using assisted partner services to identify children at high risk of HIV in Kenya</td>
<td>149</td>
<td>135</td>
</tr>
<tr>
<td>Webb, K.</td>
<td>Too little, too late: Early lessons on MTCT risk from HIV positive infant case investigation in Zimbabwe</td>
<td>30</td>
<td>33</td>
</tr>
<tr>
<td>Wilson, K.</td>
<td>High uptake and completion of HIV self-testing using a novel community-based delivery strategy for young people in Kenya</td>
<td>16</td>
<td>17</td>
</tr>
<tr>
<td>Wilson, K.</td>
<td>Vertically-infected adolescents have poor viral suppression compared to horizontally-infected youth</td>
<td>56</td>
<td>54</td>
</tr>
<tr>
<td>Yang, L.</td>
<td>Child development in HIV exposed, uninfected children: Strategies to improve access to developmental services at a Canadian tertiary care center</td>
<td>133</td>
<td>122</td>
</tr>
<tr>
<td>Yao, T.</td>
<td>Atazanavir exposure in utero and risk of multiple signals of neurodevelopmental dysfunction in 5-year-old HIV-exposed uninfected children</td>
<td>10</td>
<td>12</td>
</tr>
<tr>
<td>Yumo, H.</td>
<td>Reaching out Children of People Living with HIV/AIDS with HIV Services: Parental and Children-level Characteristics of HIV Testing, Seropositivity and Treatment among Children and Adolescents in Cameroon.</td>
<td>68</td>
<td>64</td>
</tr>
<tr>
<td>Zamek-Gliszczynski, M.</td>
<td>Effects of dolutegravir and other integrase inhibitors on folate transport pathways</td>
<td>13</td>
<td>14</td>
</tr>
<tr>
<td>Zanoni, B.</td>
<td>Perinatally HIV-infected adolescents transition to adult care: a natural experiment</td>
<td>144</td>
<td>131</td>
</tr>
</tbody>
</table>
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