Abstract Book

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Abstracts
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Abstract: O_01

Implementation research on PMTCT and pediatric treatment programs

Treatment cascade of HIV-infected infants in the Thailand National Program: How close are we to the 90-90-90 target?

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Background: UNAIDS has set 90-90-90 targets for diagnosis, treatment and viral suppression in HIV-infected children by 2020. The Thailand Global AIDS Response Program estimated 4,869 HIV-infected pregnant women and 102 new perinatal HIV–infected children in 2014. We describe the coverage of early infant diagnosis and treatment cascades of perinatally HIV-infected infants in the National Program.

Methods: The national AIDS program provides HIV DNA PCR testing for all HIV-exposed infants and antiretroviral therapy (ART) is provided, free of charge, regardless of CD4 count. Viral load testing is performed at 6 and 12 months after ART initiation. We analyzed national data collected on HIV-infected infants by the Active Case Management Network and the HIV DNA PCR database of 15 laboratories. The coverage of infant diagnosis was calculated against estimated data from 2014.

Results: From August 2014-December 2015 (17-month period), 21,415 HIV DNA PCR tests were performed. Of these, 101 HIV-infected infants were identified, accounting for 70% of the estimated number of newly infected infants per year. ART was initiated in 85 infants (84%); 74 (89%) received the lopinavir/r-based regimen. The median age at ART initiation was 2.5 months (IQR 1.2-4.2). In 46 (55%) infants, ART was initiated the same day that blood was drawn for confirmatory HIV DNA PCR. The median (IQR) CD4 cell count was 2251(1554-3057) cell/mm\textsuperscript{3} and the HIV-RNA prior to ART was 5.5(3.6-6.4) log\textsubscript{10} copies/ml. The overall mortality rate was 16% (11 infants died prior to and 5 infants died after ART initiation) and median age at death was 4.4 months (IQR 2.4-6.2), with pneumonia being the commonest cause of death. Of these 16 deaths, 10 (63%) did not receive neonatal antiretroviral prophylaxis. The proportion of infants on ART with HIV RNA <400 copies/ml were (29/54) 54% (95% CI: 40-67) at 6 months and (17/27) 63% (95% CI: 42-81) at 12 months.

Conclusions: 70% of HIV-infected infants diagnosed, 84% began treatment, and 63% achieved virological suppression. A high mortality rate was noted, particularly among HIV-infected infants not included in the cascade care. Additional work is needed to prevent HIV-associated infant mortality and improve virological suppression among infants on ART.

No conflict of interest
Abstract: O_02

Comprehensive Pediatric HIV care

Impact of the frequency of plasma viral load monitoring on treatment outcome among perinatally HIV-infected Asian children stable on first-line cART

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Introduction: Recommendations on the optimal frequency of plasma viral load (pVL) monitoring in HIV-infected children stable on combination antiretroviral therapy (cART) are inconsistent. This study aimed to determine the impact of annual versus semi-annual pVL testing on treatment outcomes in this population.

Methods: Perinatally HIV-infected children aged <18 years followed in the TREAT Asia Pediatric HIV Observational Database (n=16 sites; 6 countries) who were on first-line non-nucleoside reverse transcriptase inhibitor (NNRTI)-based cART with virologic suppression (two consecutive pVL <400 copies/ml >6 months apart) were included in the analysis. Children exposed to prior mono- or dual-therapy were excluded. The frequency of pVL monitoring (annual versus semi-annual) was determined at site-level based on the median rate of pVL measurement at each clinical site. The median rates of 0.75-1.5 and >1.5 pVL testing/child/year were classified as annual and semi-annual monitoring, respectively. Treatment failure was defined as virologic failure (two consecutive pVL >1000 copies/ml), change of antiretroviral drug class, or death. Baseline was the date of the second consecutive pVL <400 copies/ml. Kaplan Meier estimates and log-rank tests were performed to describe and compare the cumulative probability of treatment failure by monitoring frequency. Competing-risks regression models were used to identify independent predictors of treatment failure.

Results: Of 1220 eligible children from 10 clinical sites that performed at least annual pVL monitoring; 1042 (85%) from 6 sites had annual pVL monitoring, and 178 (15%) from 4 sites had semi-annual monitoring. The median age (IQR) was 9.2 (6.3-12.0) years, and 52% were female. Prior to baseline, 304 (25%) children ever had World Health Organization (WHO) clinical stage 4, and their nadir CD4 (IQR) was 9% (3-14%; n=1213). The median pVL at cART initiation (IQR) was 5.2 (4.8-5.7; n=529) log10 copies/ml. At baseline, 786 (64%) children were on nevirapine-based regimens; the median CD4 (IQR) was 26% (20-31%); and the median duration of cART use (IQR) was 1.6 (1.0-3.0) years. Overall, 258 (25%) with annual and 40 (23%) with semi-annual pVL monitoring developed treatment failure, corresponding to the incidence rates of 5.4 (95%CI: 4.8-6.1) and 4.3 (95%CI: 3.1-5.8) per 100 person-years follow-up, respectively. The cumulative probability of treatment failure did not differ between groups (log-rank P=0.27). In multivariate analyses, there was no association between annual pVL monitoring and treatment failure (adjusted hazard ratio [aHR]: 1.12; 95%CI: 0.80-1.59), but older age (aHR: 1.11; 95%CI: 1.07-1.14) and WHO clinical stage 4 prior to baseline (aHR: 1.43; 95%CI: 1.08-1.88) increased the risk, and longer duration of cART use at baseline (aHR: 0.85; 95%CI: 0.77-0.93) reduced the risk of treatment failure.

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Conclusions: Annual pVL monitoring was not associated with increased treatment failure compared to semi-annual monitoring in this observational cohort of perinatally HIV-infected children with pre-existing viral suppression on first-line NNRTI-based cART. For virally suppressed children, annual pVL testing may be sufficient to support treatment monitoring. Taking into consideration patient-level factors such as prior virologic status and current adherence behaviors when determining monitoring frequency may help to balance clinical needs and program costs.

No conflict of interest

Abstract: O_03

ARV treatment of Pediatric HIV infection

Virological response and resistance among HIV-infected children on first-line antiretroviral therapy without routine virological monitoring


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Background: Although WHO guidelines recommend routine viral load (VL) monitoring on antiretroviral therapy (ART), availability in low-income countries remains limited. We investigated long-term virological outcomes in HIV-infected children managed without VL.

Methods: In the ARROW trial, Ugandan/Zimbabwean children initiating ART were randomized to monitoring with/without 3-monthly CD4 measurements. Long-term, two-thirds received standard two nucleoside-reverse-transcriptase-inhibitor(NRTI)+non-NRTI(NNRTI) and the remainder received 3NRTIs. VL was assayed retrospectively on stored samples from all children at trial closure and from 316 children throughout the trial. Samples with VL >1000 copies/ml were genotyped.

Results: 1206 children initiated ART aged median 6.0 years (IQR 2.4,9.3) with median CD4% 12% (7%,17%). At trial closure, 1132(94%) children were alive and in follow-up having received median (range) 4.0 (3.3-5.0) years of ART; only 63(6%) had switched to
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second-line. VL was available for 1127 (99.6%). In cross-sectional analyses at trial closure, 559/753 (74%) 2NRTI+NNRTI maintenance vs. 194/374 (52%) 3NRTI maintenance were <80 copies/ml (p < 0.001); 605 (80%) vs. 244 (65%) were <1000 copies/ml respectively (p < 0.001). In 2NRTI+NNRTI maintenance, VL was <80 copies/ml in 284/378 (75%) versus 275/375 (73%) monitored with vs without CD4s respectively (p = 0.57); 308/378 (81%) versus 297/375 (79%) respectively were <1000 copies/ml (p = 0.43) (all children p = 0.78, p = 0.62 respectively). There was no difference between CD4 monitoring groups in intermediate/high-level resistance to NRTI/NNRTI (p > 0.2). Of 110 children with VL >1000 copies/ml and genotype on 2NRTI+NNRTI (vast majority on lamivudine+abacavir), only 17 (15%) had intermediate/high-level resistance to tenofovir and 10 (9%) to zidovudine. 8 (7%) children (5 monitored with CD4s, 3 without) had K65R. In a subset of 316 children with longitudinal VLs where resistance development could be investigated, blips ≥80 copies/ml (89% single; 11% double, all returning <80 copies/ml) were common, occurring in 93 (46%) 2NRTI+NNRTI vs 37 (35%) 3NRTI. 20 (10%) vs 39 (36%) children respectively experienced persistent low-level VL <5000 copies/ml (LLVL; geometric-mean 800 copies/ml) with no increase in VL over time during LLVL (p = 0.12). 28 (14%) vs 31 (29%) respectively experienced rebound ≥5000 copies/ml (geometric-mean 30,000 copies/ml); VL if anything decreased slightly over time following rebound (p = 0.04). In 12 on 2NRTI+NNRTI, a median 1 additional NRTI mutation accumulated over 2 years with ≥5000 copies/ml (p = 0.009). Over this time in rebound, only one child on 2NRTI+NNRTI developed intermediate-/high-level resistance to tenofovir and zidovudine. VL response was similar in CD4 monitoring groups throughout follow-up (p > 0.05); e.g. in the 305 in follow-up at week-144, those monitored with CD4s had 37% suppression/35% previous blips/11% pLLVL/17% rebound and those without 40%/34%/9%/17% (p = 0.94). Overall, 18% and 8% of single and confirmed VL measurements ≥1000 copies/ml, respectively, were immediately followed by a subsequent VL <1000 copies/ml. However, many VLs ≥1000 copies/ml were also ≥5000 copies/ml; more (35%) single VLs 1000-4999 copies/ml were immediately followed by a VL <1000 copies/ml.

Conclusion: Monitoring with/without CD4 did not impact VL failure or resistance in a large sub-Saharan African cohort of children. Nearly 1 in 10 confirmed values ≥1000 copies/ml returned to <1000 copies/ml. Despite absence of VL monitoring, only 14% on 2NRTI+NNRTI experienced rebound ≥5000 copies/ml. In rebound, genotypic resistance increased slightly over 2 years, suggesting switch to second-line ART should not be substantially delayed.

No conflict of interest
Abstract: O_04

Implementation research on PMTCT and pediatric treatment programs

Access to antiretroviral initiation among HIV-infected children aged 0-19 years in the International Epideimiologic Databases to Evaluate AIDS Global Network.

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Introduction: The attrition across the continuum of care of HIV-infected children from their HIV diagnosis to antiretroviral therapy (ART) initiation is not well known, but is crucial to understand how to reach the 90-90-90 target. We performed a global analysis of the pre-ART retention cascade of HIV-infected children from HIV diagnosis to antiretroviral therapy (ART) initiation within the iDea network.

Methods: We pooled data from cohorts of the iDea network in the Asia-Pacific, sub-Saharan Africa, and Latin America. We included all HIV-1 infected children, aged 0-19 years and ART-naive at enrolment into HIV programs from 2004 to 2014. We described the proportions of children initiating ART and the missed opportunities for ART initiation (death, loss to follow-up [LTFU]) since inclusion: program entry or date of confirmed HIV diagnosis if this occurred second. We computed the cumulative incidence functions (CIF) for ART initiation and analysed the determinants, accounting for death and LTFU as competing risks until 24 months. We classified children at inclusion according to the evolving WHO eligibility criteria of ART initiation.

Results: Among the 115,549 children included, 78,374 initiated ART (67.8%), 2.0% died, 4.5% were transferred-out, and 20.8% were LTFU before ART initiation. The 24-month CIF for ART initiation per region was 52.0% (95% Confidence Interval [CI]: 50.6-53.3) in Central-Africa, 57.8% (CI: 57.1-58.5) in East-Africa, 60.6% (CI: 59.5-61.7) in West-Africa, 66.7% (CI: 66.4-67.1) in Southern-Africa, 76.2% (CI: 74.8-77.6) in the Asia-Pacific, and 76.9% (CI: 74.4-79.2) in Latin-America. Median age at ART initiation varied across regions: 5 years in the Asia-Pacific and West-Africa, 7 years in East-Africa and Southern-Africa, 8 years (IQR: 3-16) in Latin-America, and 10 years (IQR: 5-15) in Central-Africa (p<0.01). Overall, 38% were eligible at inclusion of whom 75% were initiated on ART, but 10% were still alive and in follow-up but were not initiated on ART at database closure. Median CD4% at ART initiation varied from 10% in the Asia-Pacific, 13% in West-Africa, 14% in Central-Africa, East-Africa, and Southern-Africa, to 15% in Latin-America (p<0.01). Children aged 15-19 years and those aged <1 year had the lowest ART initiation rates compared to other ages, with an overall CI of ART initiation of 54.3% (95%CI:53.6%-55.0%) and 61.4% (95%CI:60.6%-62.1%), respectively. In the analysis of the determinants of ART initiation (adjusted by WHO eligibility criteria, period of inclusion, and regions), being a female, aged <10 years (worst outcome among those <1 year) and >15 years, becoming eligible during follow-up compared to eligibility at inclusion, and receiving care in a low- or low-middle income country were less likely to initiate ART.

Conclusions: Overall, 68% initiated ART, with a substantial risk of LTFU before ART initiation, which may also represent undocumented mortality. In 2014, many obstacles to ART initiation remain with substantial inequities. Females and those at the youngest and oldest ends of the paediatric age spectrum need more effective and targeted interventions to improve their access to ART initiation. There is an ethical priority to first treat all children who were eligible for ART before 2015 in reaching the 90% target.

No conflict of interest
Abstract: O_05

ARV treatment of Pediatric HIV infection

Switching to second-line antiretroviral therapy in HIV-infected children: a CIPHER cohort collaboration global analysis

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Background: Studies reporting time to switch from first to second-line antiretroviral therapy (ART) in children vary widely across settings, partly due to different definitions/methods used. We estimate time to switch to second-line ART globally.

Methods: Through the Collaborative Initiative for Paediatric HIV Education and Research (CIPHER), individual data on perinatally HIV-infected children (aged <10 years at entry to HIV care) from 12 cohort networks were pooled. Children aged <18 years when initiating combination ART (≥2 nucleoside reverse-transcriptase inhibitors (NRTI) plus non-NRTI (NNRTI) or boosted protease inhibitor (PI)) were included. Switch to second-line was defined as: (i) change of ≥1 NRTI plus either change in drug class (NNRTI to PI or vice versa) or PI change; (ii) change from single to dual PI; or (iii) addition of new drug class. A cause-specific hazard model assessed time to switch, with death and loss to follow-up (LTFU) as competing risks. Children were at risk from ART initiation until first episode of switch, last visit in paediatric care, or death.

Results: Among 95,194 children from 52 countries, <1% were from North America, 1% South America/Caribbean, 2% Europe/Russia, 6% South/South-East Asia, 18% South Africa and 72% from the rest of Sub-Saharan Africa. Half were male, calendar year of ART start ranged from 1996 to 2014. At ART start, the median [IQR] age was 3.7[1.6 – 6.8] years, median CD4% 15%[9-21%] and 42% had AIDS. 84,433 (89%) initiated ART with an NNRTI regimen (75% of which was nevirapine-based) and 10,761 (11%) a PI regimen (99% lopinavir-based). Regional variation was observed in median age (0.6-4.5 years) and CD4% (12-30%) at start of ART, and initial regimen (3% - 43% starting a PI). Median duration of follow-up from ART initiation was 26[9-51] months; 1% died, 26% were LTFU and 20% transferred out. LTFU ranged from 10% in North America to 29% in rest of Sub-Saharan Africa. Viral load monitoring after ART start was available in 6.8% in sub-Saharan Africa, 44% South/South-East Asia, 83% South Africa and >95% in Europe/Russia/North America. Overall 4266 (4.5%) switched to second-line ART, median time to switch was 33.8 [18.5, 55.1] months. By 1, 2 and 3 years after start of ART, 0.9% (95% CI 0.8-0.9%), 2.1% (2.0-2.2%) and 3.4% (3.3-3.5%) switched, respectively. The percentage switched by 3 years varied significantly across regions: 1.6% (1.5-1.7%) rest of Sub-Saharan Africa, 6.0% (4.6-7.8) South America/Caribbean, 6.7% (6.0-7.5%) South/South-East Asia, 7.1% (6.7-7.6%) South Africa, 11.7% (10.3-13.1%) Europe/Russia, 26.8% (20.6-33.3%) North America. Overall, the proportion switched was slightly higher in those starting a PI-based regimen: 3.1% (2.9-3.2%) NNRTI vs. 6.1% (5.6-6.6%) PI (log-rank p<0.0001), this difference was substantially more pronounced in North America and Europe/Russia. Lopinavir and nevirapine were the most common drug choices for second-line.

Conclusion: We estimate wide regional variations in proportion of children switching to second-line, with very low rates in sub-Saharan Africa, most likely due to limited paediatric ART options and viral load monitoring. High rates of transfer and loss to follow-up mean this estimate will be a lower bound of the true switch rate.

No conflict of interest
Abstract: O_06

Prevention of Mother-to-Child transmission

Raltegravir (RAL) Pharmacokinetics (PK) and Safety in HIV-1 Exposed Neonates at High Risk of Infection (IMPAACT P1110)


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Background: Safety and dosing information for antiretroviral drugs (ARVs) in neonates are limited. Raltegravir (RAL) has potential for use as prophylaxis to prevent mother to child transmission and as early intensive treatment of HIV-infected neonates. RAL is primarily metabolized by UGT1A1 enzyme. UGT enzyme activity is low at birth and increases exponentially over the first weeks to months of life. The objectives of IMPAACT P1110 study are to evaluate safety and pharmacokinetics of RAL and to determine the appropriate neonatal dose of RAL oral granules for suspension during the first 6 weeks of life.

Materials and Methods: IMPAACT P1110 is a phase 1 multicenter trial enrolling full-term HIV-1 exposed neonates at high risk of acquiring HIV-1-infection, with or without in utero RAL exposure. Study design includes two cohorts: cohort 1 infants receive 2 single RAL doses 1 week apart; cohort 2 infants receive daily RAL dosing for first 6 weeks of life. PK results from Cohort 1 (previously reported) were combined with that from older infants and children receiving daily dosing in a population PK model and simulations performed to develop a daily RAL dosing regimen to be evaluated in 20 infants in Cohort 2. The RAL dosing regimen under investigation in Cohort 2 for infants unexposed to RAL in utero is: 1.5 mg/kg daily starting within 48 hours of life through day 7; 3 mg/kg twice daily on days 8-28 of life; 6 mg/kg twice daily after 4 weeks of age. Four plasma samples were collected after the initial dose and on the increased dose between 15-18 days of life; sparse sampling was obtained when doses were changed. Samples were analyzed for RAL concentrations using a validated HPLC-MS-MS method. AUC was estimated after the first dose and for twice daily dose of 3 mg/kg using the trapezoidal method. Protocol exposure targets for each subject are AUC24_12-40 mgxh/L, AUC12_6-20 mgxh/L, Cmin> 33 ng/mL.

Results: PK results and 6 week safety data are available for the first 10 infants. After the first dose of 1.5 mg/kg, geometric mean RAL AUC24 was 38.9 mgxh/L (6/10 met target; range 18.6-78.3 mgxh/L). On 3 mg/kg twice daily the geometric mean for RAL AUC12 was 12.1 mgxh/L (7/10 met target; range 4.7-24.5 mgxh/L) and Cmin estimated to be 120.4 ng/mL. Sparse sampling confirmed that RAL plasma concentrations were within the expected range. There were no safety concerns associated with daily RAL administration based on safety data through 6 weeks of life.

Conclusions: Daily RAL was well tolerated in infants receiving this regimen during the first 6 weeks’ of life. AUC24 following the initial dose was slightly above the target range, but given the rapid increase in RAL metabolism over the first week of life, this exposure was considered acceptable. AUC24 and Cmin on day 15-18 were within the target range. The PK targets and the safety guidelines have been met for the first 10 RAL-unexposed infants in cohort 2. IMPAACT P1110 Cohort 2 enrollment is ongoing to reach our target of 20 PK evaluable infants.

Conflict of interest
Financial relationship(s): HT, AC, and BH are employees of Merck & Co. and may own stock and/or stock options in the company. The remaining authors have no conflicts of interest to disclose.
Abstract: O_07

Prevention of Mother-to-Child transmission

HIV PCR testing at birth in kwazulu natal, south africa – one year post introduction of the largest neonatal HIV testing programme.

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Background: South Africa's guidelines for early infant diagnosis (EID) of HIV have undergone a series of revisions since inception of the prevention of mother to child transmission (PMTCT) programme in 2002. Whereas implementation of routine HIV PCR testing at 6-weeks of age for all HIV-exposed infants has proven to be successful there remained concerns regarding delayed diagnosis and access to treatment for in utero infected infants. For this reason routine birth testing of all HIV-exposed infants was introduced into national guidelines in June 2015 in addition to testing at 10-weeks of age to identify intra-partum infection. KwaZulu Natal (KZN) officially implemented the new testing guidelines from April 2015. We describe uptake of birth testing and 10-week testing in KZN one year post implementation of the new guidelines and compare programmatic outcomes of current and preceding guidelines.

Materials & Methods: HIV PCR data was extracted from the National Health Laboratory Service Corporate Data Warehouse from April 2012 to March 2016. HIV PCR tests were categorized as follows: Birth test at age <7days; 6-week test at 7days-<2months of age and 10-week test at 7days-3months of age. Programmatic outcomes evaluated included % positivity rates (number of positive PCR results as a proportion of total number of PCR tests) and EID coverage calculated as number of PCR tests done over estimated number of HIV-exposed infants in KZN (calculated by multiplying provincial live births registered from Statistics South Africa by provincial maternal HIV seroprevalence) per fiscal year.

Results: The number of HIV-exposed infants born in KZN is estimated to be 6000 per month. During the fiscal year April 2014 to March 2015, an average of 5900 PCR tests were performed monthly at age 6-weeks amounting to a testing coverage of 95%. The positivity rate for this time period was 1.3%, a 0.2% decrease from the previous fiscal year when coverage was 85%. For the first year since the implementation of the new testing guidelines (fiscal year April 2015 to March 2016), an average of 4800 birth tests were performed per month, amounting to a birth testing coverage of 81% and intrauterine transmission rate of 0.8%. During this same time period, an average of 4675 10-week tests were performed per month amounting to 10-week coverage of 79%. The percentage positivity at 10-weeks could not be determined due to repeat testing being performed for confirmation of HIV status.

Conclusions: Findings suggest successful uptake of birth testing in KZN, scaling up to over 80% coverage in a matter of one year. Efforts should be directed at improving later testing at 10-weeks and linkage into care of PCR positive infants. As KZN's intrauterine transmission rate accounts for 60% of early infant transmission, the introduction of the new testing guidelines provide the opportunity for earlier initiation of ART in infected infants. However, the association between the introduction of birth testing and ART initiation and infant mortality rates remains to be determined.

No conflict of interest
Abstract: O_08

Comprehensive Pediatric HIV care

Paediatric HIV point of care testing: field evaluation of the performance of cepheid and alere qualitative HIV assays in a soweto academic hospital

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Introduction: In South Africa (SA) early infant diagnosis (EID) of HIV is conducted using molecular diagnostics at nine central laboratories in the National Health Laboratory Service (NHLS). Point-of-care (POC) EID technologies are becoming available that are simple to operate, do not require laboratory infrastructure and enable onsite molecular HIV diagnosis in infants in under two hours. However, the utility of these EID POC technologies in the SA context requires evaluation in clinical settings and experience with implementing the new technologies. The aim of this study is to evaluate the performance of two EID POC technologies in a busy hospital environment with 510 to 540 HIV-exposed, live births per month where neonates born by normal vaginal delivery are discharged at an average age of six hours in Johannesburg, SA.

Materials and methods: The study was conducted at Chris Hani Baragwanath Academic Hospital from 1 December 2015 to 1 April, 2016. Two POC technologies (Alere Q HIV-1/2 Detect and Cepheid GeneXpert HIV-1 Qual) were compared to the current standard of care in SA (HIV qualitative assay, Roche CAP/CTM v2). Laboratory testing was performed onsite in an accredited NHLS PCR laboratory. HIV-exposed neonates (at high risk of HIV transmission) were invited to join the study. To increase the rate of enrolment of HIV PCR-positive children, all children <18 months that were treatment naïve (excluding prophylaxis) and in whom an HIV PCR test was indicated, were eligible. EDTA anticoagulated whole blood specimens were collected during routine blood collection from patients whose parents provided consent. The specimens were stored at 4°C and run on both POC instruments within 72 hours of collection. Laboratory results, not POC results, were returned to patients.

Results: To date, there has been a high acceptability of HIV POC testing, with an enrolment rate of over 90% (109/120). Of 109 patients that were enrolled 54% were female. Results were concordant between the two POC platforms: thirty-three specimens tested positive and 76 tested negative, with a sensitivity of 97.06% (CI: 85.08% to 99.48%) and specificity of 98.68% (CI: 92.92% to 99.77%). All laboratory results concurred except for one neonate with a negative POC test who tested PCR indeterminate in the laboratory and on whom a repeat PCR has not been done to date. The median age of children testing positive was 84 days (IQR: 14-192 days) and negative was 1 day (IQR: 1-1 day). The error rate for the Cepheid instrument was 0.9% and for Alere was 7.7%.

Conclusions: The POC platforms have not yet missed an HIV-infected child and the interim results demonstrate excellent performance, however full sample size of 100 HIV PCR-positive and 100 HIV-PCR negative children is yet to be achieved. In our setting with large numbers of births and the NHLS PCR laboratory onsite, POC is potentially suitable for testing high-risk children who are discharged before the results are available to prevent loss to follow up.

No conflict of interest
Abstract: O_09

HIV infection and adolescents

The global epidemiology of perinatally HIV-infected adolescents: A CIPHER Global Cohort Collaboration analysis

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Background: The population of perinatally HIV-infected adolescents (PHA) continues to expand globally. This study aims to describe the geographic and temporal characteristics and outcomes of PHA.

Methods: Through the Collaborative Initiative for Pediatric HIV Education and Research (CIPHER) Global Cohort Collaboration, individual data were pooled from 12 cohort networks representing five regions: South America & Caribbean (4 countries), North America (1 country), Europe & Central Asia (14 countries), South & Southeast Asia (7 countries) and sub-Saharan Africa (24 countries). Included PHA entered care before age 10 years, a proxy for vertical HIV transmission, and were followed at least once beyond age 10 years. This analysis describes patient and treatment characteristics by region at first recorded visit, antiretroviral therapy (ART) start, start of adolescence (age 10 years) and at last follow-up. Outcomes of mortality, transfer out and loss to follow-up (LTFU) were analysed as competing risks.

Results: 37,468 PHA were included, 49.4% were male, 79% from sub-Saharan Africa, 8% from Europe & Central Asia, 8% from South & Southeast Asia, 3% from South America & Caribbean and 2% from North America. Median (interquartile range (IQR)) age at first recorded visit was 6.7 (4.4-8.4) years [range: median (IQR) range: 0.7 (0.3-2.1) North America to 7.1 (5.3-8.6) sub-Saharan Africa]. Median (IQR) follow-up during adolescence was 2.4 (1.0-4.4) years [range: 2.1 (0.9-3.8) sub-Saharan Africa to 6.4 (3.5-8.1) Europe & Central Asia]. 90% (33,620) of PHA received ART, 11.7% (3,917) started after age 10 years and 76% (28,651) were on ART at last visit. Median (IQR) WHO height-for-age Z-score (HAZ) at first recorded visit was -1.92 (-2.91; -0.97) [range: -2.37 (-3.29; -1.42) South & Southeast Asia to -0.75 (-1.60; 0.15) Europe & Central Asia]. Median (IQR) HAZ at last visit was -1.21 (-2.00; -0.36) [range: -1.76 (-2.58; 0.95) sub-Saharan Africa to -0.33 (-1.09; 0.43) North America]. There was little difference between HAZ in PHA on ART at last visit and not on ART (-1.59 (-2.44; -0.73) vs. -1.63 (-2.5; -0.72)). Median (IQR) CD4 count at first recorded visit was 429 (203-760) cells/µl [range: 253 (70-577) South & Southeast Asia to 1267 (777-2217) North America]. By last visit, median (IQR) CD4 count was 688 (465-947) cells/µl [range: 598 (377-860) South America & Caribbean to 748 (540-1003) South & Southeast Asia]. In the 30% of PHA on ART with an available HIV viral load at last visit, 75% were virologically suppressed. Reported mortality between age 10 and 15 years was 2.7% (95%CI 2.5-2.9) [range: 0.8% (95%CI 0.5-1.1) Europe & Central Asia to 4.4% (95%CI 3.1-6.1) South America & Caribbean]. 15.7% (95%CI 15.2-16.2) of PHA were transferred out [range: 1.9% (95%CI 1.1-3.0) North America to 19.7% (95%CI 19.0-20.3) sub-Saharan Africa] and 11.4% (10.9-11.8) were LTFU after age 10 years [range: 6.0% (95%CI 5.1-7.0) Europe & Central Asia to 13.3% (95%CI 12.7-13.8) sub-Saharan Africa].

Conclusion: The majority of PHA surviving into adolescence remained stunted despite receiving ART. Reported mortality of 2.7% is likely an underestimate in the presence of high LTFU.

No conflict of interest
Abstract

HIV infection and adolescents


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Background: In wealthy countries, many perinatally HIV-infected adolescents (PHA) transition from specialist pediatric clinics to adolescent/adult clinics during late adolescence. Transition may differ in sub-Saharan Africa, where pediatric HIV care is mostly provided in decentralized non-specialist primary care clinics. Children are either initiated on antiretroviral therapy (ART) in decentralized clinics or transferred from central facilities to decentralized clinics soon after ART initiation once they are stable on treatment. With increased decentralization and more primary care clinics providing pediatric ART, the proportion of children transferring to primary care facilities is increasing. We examined transfer patterns in PHA in Southern Africa.

Materials & Methods: We included presumed PHA (ART initiation at <9.5 years old without documented non-perinatal infection) with follow-up after 10 years of age at 12 leDewSA cohorts providing pediatric ART care from Malawi, South Africa, Zambia and Zimbabwe from 2000-2014. At 2 of these 12 cohorts, no children were recorded as transferred out and the 1660 PHA from these 2 cohorts were excluded from further analyses. We described characteristics at ART initiation, and at transfer or, in those remaining in care at their original site, at their last visit. We used Cox proportional hazards models to identify predictors of transfer.

Results: Among 3820 children included, 917 (24%) transferred out. The estimated probabilities of transfer by age 13 years varied widely between sites from 5.1% to 54.3%. Transfer was higher from specialist pediatric facilities compared to primary care facilities. Among the children who transferred out, 48% were female and at transfer the median (interquartile range [IQR]) age was 11.4 years (10.6-12.7); median (IQR) CD4 count was 779 cells/µl (569-1032); 82% of children had CD4 >500 cells/µl; 89% had HIV-RNA <400 copies/ml and 41% were stunted (height-for-age z-score < -2). When comparing these characteristics at transfer with characteristics at the last visit in those not transferred out, children remaining in care at the original site were older at their last visit with median (IQR) age of 12.1 years (10.9-13.8; p<0.001), had lower median (IQR) CD4 count of 725 cells/µl (518-950; p<0.001) and a smaller proportion had CD4 >500 cells/µl (77%; p=0.004) and HIV-RNA <400 copies/ml (73%; p<0.001), but a similar proportion were female (48%) and stunted (39%). After adjusting for site, PHA with the following characteristics were more likely to transfer during early adolescence: longer ART duration at 10 years (adjusted Hazard Ratio [aHR] 1.29 per additional year on ART, 95% Confidence Interval [CI]: 1.22-1.35) not severely immunodeficient at ART start (aHR 1.25; 95%CI: 1.03-1.52), CD4 >500 cells/µl at age 10

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Abstract: O_11

HIV infection and adolescents

High Retention and Viral Suppression Rates in a Dedicated Adolescent-Friendly HIV Clinic in South Africa

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Background: South Africa has the highest burden of HIV-infected youth in the world with an estimated 720,000 HIV-infected adolescents and young adults aged 15 to 24. Adolescents with chronic illness commonly struggle with poor adherence. Studies from North America, the United Kingdom, and Australia have documented high rates of mortality, loss to follow-up, and virologic failure among HIV-infected adolescents. To overcome these challenges, many HIV clinics have initiated adolescent-friendly services to assist with transitioning to adult care; however, outcomes in these adolescent clinics have not been described.

Methods: We performed a retrospective cohort analysis using medical records from 254 perinatally HIV-infected adolescents receiving antiretroviral therapy (ART) at a single site in KwaZulu-Natal, South Africa from April 2007 to November 2015. Adolescents could attend either: 1) Saturday teen clinic, with dedicated peer support and structured social activities, after 6 months on ART pending availability or remain in 2) standard weekday pediatric clinic. Enrollment in the teen clinic was based on availability of spaces. We analyzed records from all perinatally HIV-infected adolescents and young adults aged 13 to 24 attending the teen clinic or standard pediatric clinic. We performed a cross-sectional analysis comparing retention in care and viral suppression rates among adolescents attending each clinic. We used SAS version 9.4 to calculate descriptive statistics conduct univariable and multivariable logistic regression models.

years (aHR 1.30; 95%CI:1.01-1.6) and HIV-RNA <400 copies/ml at age 10 years (aHR 1.38; 95%CI:1.05-1.82).

Conclusion: Transfer patterns differ considerably between cohorts with overall about one quarter of children transferring during early adolescence. PHA were relatively well at transfer; more than 80% had CD4>500 cells/ul and were virologically controlled. Understanding transfer patterns and tracking outcomes after transfer is important to comprehensively evaluate PHA outcomes.

No conflict of interest
Results: Overall, the viral suppression rate among adolescents was 85% (196/231) and the retention rate was 89% (227/254) with retention outcomes in 99% of adolescents. We found significantly higher retention rates in adolescents attending the dedicated teen clinic (97%) versus adolescents in standard care (85%; p=0.005). Multivariable logistic regression adjusting for age at ART initiation, gender, pre-ART CD4, months on ART, and history of tuberculosis indicated higher retention rates in adolescents attending the teen clinic (97%) versus adolescents in standard care (85%; p=0.005). A similar multivariable logistic regression model adjusting for age at ART initiation, gender, pre-ART CD4, months on ART, and history of tuberculosis indicated higher viral suppression rates in adolescents attending the teen clinic (91%) versus the standard pediatric clinic (81%; p=0.048). A similar multivariable logistic regression model adjusting for age at ART initiation, gender, pre-ART CD4, months on ART, and history of tuberculosis indicated higher viral suppression rates in adolescents attending the teen clinic compared to standard clinic (OR = 9.6; p=0.004). In addition, we found higher viral suppression rates among adolescents attending the teen clinic (91%) versus the standard pediatric clinic (81%; p=0.048). A similar multivariable logistic regression model adjusting for age at ART initiation, gender, pre-ART CD4, months on ART, and history of tuberculosis indicated higher viral suppression rates in adolescents attending the teen clinic compared to standard clinic (OR = 9.6; p=0.004).

Conclusion: Despite lower pre-ART CD4 and older age at initiation, adolescents attending a dedicated Saturday teen clinic had higher retention in care and viral suppression rates compared to adolescents attending the standard pediatric clinic. Further studies are required to determine the factors that facilitate successful delivery of care among HIV-infected adolescents as they prepare to transition to adult care.

No conflict of interest

Abstract: O_12

Complications of HIV therapy

Decreased bone turnover in HIV-infected children on antiretroviral therapy

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Introduction: HIV-infected children have decreased bone mineral content (BMC). However, the relationship between chronic inflammation, bone remodeling, and BMC have not been well studied in the context of pediatric HIV.

Methods: 219 HIV-infected and 180 uninfected children enrolled in the CHANGES Bone Study in Johannesburg, South Africa. Whole body (WB) BMC was assessed by dual-energy X-ray absorptiometry. BMC Z-scores adjusted for sex, age, and height were generated. Bone formation and resorption markers, procollagen type 1 N-terminal propeptide (P1NP), and C-telopeptide (CTX), were measured as well as soluble CD14 (sCD14), a marker of monocyte and macrophage activation, proinflammatory cytokines IL-6 and TNF-α, and iPTH and 25(OH)D3.

Results: The 219 HIV-infected children (49% male) were younger than the 180 uninfected children (55% male) (6.36 vs. 7.12 years, p<0.01); 97% were Tanner 1 and mean 25(OH)D3 was 27.7 ng/ml. HIV-infected children were on treatment for a mean of 5.7 years and mean CD4% was 37%; 94% had viral suppression (HIV-1 RNA <400 copies/ml). Mean WB BMC Z-score was lower in HIV-infected than uninfected children (-0.95 vs. -0.79, p=0.05). CTX (1.72 vs. 2.05 ng/ml, p<0.01) and P1NP (584 vs 634 ng/ml, p<0.01) concentrations were lower in HIV-infected than uninfected children and remained lower after adjusting for sex, age, 25(OH)D3, and WB BMC. CTX and P1NP were positively correlated to each other (r=0.43, p<0.01). Although mean
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TNF-α was lower in HIV-infected compared to uninfected children (2.15 vs. 2.60 pg/ml, p=0<0.01), 98% had TNF-α levels in the normal range. Mean IL-6 was similar in HIV-infected and uninfected children (1.72 vs. 1.73 pg/ml, p=0.97). Mean sCD14 was higher in HIV-infected than uninfected children (1453 vs. 1195 ng/ml, p<0.01), even after adjustment for sex and age. However, the majority of all children (91.8% of HIV-infected group and 97.8% of HIV-uninfected group) had sCD14 <2300 ng/ml. CTX and P1NP correlated poorly with cytokines, sCD14 and WB BMC Z-scores (r<0.10).

Conclusions: In a group of HIV-infected children with viral suppression on antiretrovirals with low BMC, there was little evidence of immune activation. While formation and resorption do not appear uncoupled, bone turnover markers were decreased in HIV-infected children compared to uninfected children and were not correlated with markers of immune activation. These data suggest that in infected children with viral suppression, decreases in bone accrual may occur independently of immune activation mediated bone resorption. A better understanding of mechanisms of poor bone accrual in HIV-infected children is critical to the development of effective interventions for optimizing bone health during childhood.

No conflict of interest

Abstract: O_13

Prevention of Mother-to-Child transmission

Efficacy of the Amagugu intervention to increase maternal HIV disclosure to HIV-uninfected primary-school aged children in Southern Africa: A Randomised Controlled Trial.

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Introduction: Together with advances in HIV prevention and treatment, come longer-term challenges for the care and support of HIV-infected parents and their largely HIV-uninfected children. HIV-exposed children face many risks associated with parental ill health, hospitalisation, and death, often compounded by stigma and lack of adequate support. A major challenge these parents face is when, and how, to disclose their HIV status to their predominantly HIV-uninfected children. The Amagugu intervention targets maternal capacity to disclose and includes activities on disclosure, health care engagement and custody planning. An uncontrolled evaluation found the intervention increased disclosure, was feasible and acceptable. The primary aim of this research was to test the efficacy of the Amagugu intervention in a controlled study.

Materials and Methods: We completed an individually randomised, double blind, efficacy trial (2013-2015), follow-up to nine months (NCT01922882). We hypothesised that the six session Amagugu intervention, compared to a once-off clinic counselling session, would significantly increase maternal HIV disclosure to HIV-uninfected children aged 6-10 years, and lead to improvements in health care.
engagement, custody planning and the parent-child relationship. Participants were recruited from four primary health care clinics providing HIV treatment in rural KwaZulu-Natal, South Africa. We consecutively approached 634 women; 464 mothers met eligibility and were randomised (Intervention n=235; Standard of Care n=229), of whom 428 (92%) completed the 9-month endpoint assessment. Primary outcome was maternal HIV-disclosure (full, partial, none); secondary outcomes included: health care engagement (taking child on clinic visit); care and custody planning; quality of the parent-child relationship (Parenting Stress Index); maternal mental health (PHQ-9 Depression; GAD-7 Anxiety; MOS-36 Quality of life); child mental health (Child Behaviour Checklist) and family functioning (McMaster Family Assessment Device). Statistical analysis followed an intention to treat principle; we compared continuous variables using independent, two-sample t-tests and Wilcoxon-Mann-Whitney tests. We fitted logistic regression models, adjusting for covariates to compare the main outcomes. Kaplan-Meier estimates, log-rank tests and Cox proportional hazard models were used to analyse outcomes related to time to disclosure. Statistical analyses were performed using R version 3.2.

Results: The intervention led to an increase in any disclosure (aOR 9.61 [CI 5.43-16.99], p<0.001) and full disclosure using the words ‘HIV’ (aOR 3.99 [CI 2.7-5.86], p<0.001). Time to full disclosure was shorter in the Intervention vs Standard of Care arm (median 2.83 months [IQR 7.36] vs. 8.74 months [IQR 6.29] p<0.0001). More mothers in the intervention arm took their child to a clinic visit (aOR 31.47 [17.56-56.39], p<0.0001), discussed a care plan with their child (aOR 3.38 [1.58-7.19], p<0.002), and appointed a guardian (aOR 2.18 [1.23-3.83], p=0.007). There was a positive effect (borderline significance) on improving the quality of mother-child relationship in the intervention group at 9 month follow-up (p=0.054).

Conclusions and Relevance: This relatively low-intensity, lay-counsellor led, home-based intervention led to increased HIV disclosure to children, improvements in health care engagement and custody planning for the child. The intervention is easily adaptable to HIV-infected children, and our results demonstrate its efficacy and the potential for pre-adolescent HIV education and prevention.

No conflict of interest

Abstract: O_14

Implementation research on PMTCT and pediatric treatment programs

Comparing Point of Care to Laboratory HIV PCR testing at birth in a hospital setting in Johannesburg, South Africa

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Introduction: Universal birth testing of HIV-exposed neonates was introduced into South African guidelines mid-2015 and currently uses central laboratory-based HIV polymerase chain reaction (PCR) testing. Returning HIV test results is problematic because HIV-exposed neonates are discharged before results are available. Point of Care (POC) HIV testing allows results to be available prior to discharge retaining HIV-infected neonates in the Prevention of Mother to Child Transmission cascade for initiation of antiretroviral treatment (ART). This is the first description of POC testing implemented in the context of universal birth testing.

Methods: HIV-exposed neonates identified at delivery had blood sampled for laboratory-based HIV PCR testing (Roche COBAS® TaqMan® HIV-1 Qualitative Test V2). When staff capacity allowed, a sample for concurrent POC testing (Xpert® HIV-1 Qual [Cepheid]) was collected and performed by trained staff. POC testing coverage, performance and time to result receipt were compared to laboratory-based testing. Positive POC results prompted repeat sampling for confirmatory laboratory-based HIV testing and ART initiation. Telephonic tracking followed for all infected neonates discharged before a result was available.

No conflict of interest

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Results: Between October 2014 and February 2016, 3582 (94.6%) of the 3793 HIV-infected women delivering live births were interviewed. Mothers of 3561 (99.7%) neonates agreed to birth testing and laboratory-based testing was performed on 3490 (98.0%) and POC on 1914 (53.8%). Final HIV PCR laboratory results were available for 3485 neonates – 3434 (98.4%) negative, 48 (1.4%) positive and 3 (0.1%) indeterminate. Concurrent POC results were available for 1914 neonates of which 24 (1.3%) were positive. The POC test detected all HIV-infected neonates (sensitivity 100%), additionally 2 false positive results (specificity: 99.9% [95% CI: 99.7-100]; positive predictive value 92.3% [95% CI: 81-100]). In both cases the POC rerun result was negative. POC testing yielded 96 errors (5.0%), significantly more than laboratory-based testing (0.5%; p<0.0001). Of the POC errors, 92 were rerun with 87 negative results (94.6%) and 5 errors (5.4%). Thus the post-rerun error rate was 0.3%. Result return for HIV-uninfected neonates was significantly better with associated POC testing (93.5%) than with laboratory-based PCR alone (51.6%; p<0.0001) but was similar (>95%) for HIV-infected neonates, regardless of the testing performed. Of the 48 infected neonates, 47 (98%) initiated ART. Among those with a POC test, ART was initiated at a median of 1 day of age (IQR 1-2) compared to 6 days (IQR 5-10; p<0.0001) when POC testing was not available. Of the 47 infected neonates, 33 (89%) were tested at 4-14 weeks of age.

Conclusion: The Cepheid POC test identified 100% of HIV-infected neonates and repeating the test eliminated any false positives. Sampling enough blood to allow a rerun (an extra ±100ul) reduced the error rate significantly. POC HIV testing requires additional staff resources and a system to identify HIV-exposed neonates, test and provide results timeously. POC test results allowed earlier ART initiation, but return of results in our setting remained similar because we actively traced discharged HIV-infected neonates.

No conflict of interest

Abstract: O_15

Prevention of Mother-to-Child transmission

Does HIV DNA-PCR testing of HIV-exposed infants at birth reduce follow-up for routine testing at 4-14 weeks of age?

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Introduction: WHO guidelines recommend nucleic acid testing (HIV DNA-PCR) of HIV-exposed infants between 4–6 weeks of age. This should detect most in utero and intra-partum infections and is timed to coincide with routine immunization visits. However, there is significant attrition before 4-6 weeks and only 50% of all HIV-exposed infants were tested by the second month of age in 2014. Operationally, antiretroviral therapy (ART) initiation may be delayed in infected infants. Diagnostic HIV DNA-PCR testing of HIV-exposed infants at birth could improve early infant diagnostic (EID) yield; WHO is considering recommending routine or targeted nucleic acid testing at birth where feasible. A caveat is that a second HIV DNA-PCR will be required to detect late intra-partum and postnatal infections in addition to testing after cessation of breast-feeding. We examined whether receipt of a negative birth HIV DNA-PCR result decreased follow-up testing of infants at 4-14 weeks of age.

Materials and Methods: We included live infants born to HIV-infected women who received antenatal care (ANC) and/or delivered at a Midwife Obstetrics Unit and its referral centres in Cape Town, South Africa between February 2014 and March 2015. In August 2014 targeted birth HIV DNA-PCR testing was introduced for infants at 'high risk' for HIV transmission i.e. <3 months maternal ART, maternal viral load >1000 copies/ml, no ANC, infant <37 weeks gestation or birth weight <2kg. Using logistic regression we examined whether a negative birth result was associated with reduced follow-up for routine testing at 4-14...
weeks, adjusting for other predictors of testing at this time.

**Results:** Overall antenatal HIV prevalence was 14%. The cohort included 870 mother-infant dyads; 424 (49%) met ≥1 high risk criterion for transmission with 39% having a single high risk criterion, 9% having 2 criteria and 1% having ≥3 criteria. Only 18% of those with ≥1 high risk criterion received HIV DNA-PCR at birth. Overall vertical transmission was 1.2% by 14 weeks of age; 3.96% of birth tests were positive versus 0.31% at 4-14 weeks. Birth testing was significantly more likely with the following characteristics: seroconversion after first ANC visit, <3 months maternal ART, infant <37 weeks gestation or birth weight <2kg. In infants who were not tested at birth or who had a negative birth test, 74% underwent HIV DNA-PCR testing at 4-14 weeks of age. The following characteristics were associated with lower likelihood of infants being tested at 4-14 weeks: maternal age <35 years, no ANC, maternal seroconversion after first ANC visit, infant <37 weeks gestation and birth weight <2kg. In infants with negative birth test results were less likely to test again at 4-14 weeks (aOR 0.59; 95%CI: 0.37-0.93).

**Conclusion:** In this cohort, half of all HIV-exposed infants had ≥1 high risk criterion for HIV transmission, and nearly 4% of birth HIV DNA-PCR tests were positive. Receipt of a negative birth test result was associated with reduced follow-up testing. Strengthened follow-up systems are needed to ensure adequate EID coverage.

*No conflict of interest*
Results: Overall, 576 neonates underwent birth-testing (median gestational age at delivery (GA), 40wks, median birthweight, 2800grams). Among birth tests, there were 23 positive (4%), 2 equivocal and 551 negative results. Infants testing negative at birth were matched to 551 HEI who did not receive birth-testing (GA 39wks, birthweight 3140g). 73% of infants who underwent birth-testing had a subsequent routine EID test, compared to 85% of infants who did not receive birth-testing (OR,0.46; 95%CI,0.34-0.62). Routine EID testing also took place at a significantly older age in infants who had been tested at birth previously, compared to those who did not undergo birth-testing (mean age 60vs49 days, p<0.01). Positivity rates were similar for both groups: 2 (0.4%) infants who experienced birth-testing were subsequently identified positive compared to 3 (0.5%) who did not. The significant decrease in routine EID testing among children tested at birth persisted in multivariable analyses adjusting for maternal age, nadir CD4 cell count, ARV use during pregnancy, GA, infant sex, birthweight and infant feeding modality. Because low birthweight neonates were more likely to undergo birth-testing and may demise before routine EID testing, we conducted sensitivity analyses removing infants born low birthweight or premature; in this subgroup, the negative association between birth-testing and subsequent EID testing persisted (OR,0.41 95%CI,0.30-0.56).

Conclusions: These novel data suggest that neonates undergoing HIV testing at birth may be less likely to receive subsequent EID testing. In turn, implementation of birth-testing in SA has the potential to reduce population coverage of routine EID services. Birth-testing programmes must emphasize counselling mothers of birth-tested negative infants on the need for further HIV testing.

No conflict of interest
and outreach. Each infant received a virological EID test to determine infection status.

**Results:** A total of 117 infants were HIV-positive for an overall prevalence of 3.25%. The traditional EID entry point, EMTCT, had a prevalence of 3.84%, representing 19.6% of the HIV-infected infants identified. Fifty percent of the 117 identified HIV-positive infants were found in the nutrition wards, which had a prevalence of 9.83% (p<0.001 compared to EMTCT). Inpatient wards had a prevalence of 3.50% and yielded 17.9% of the infected infants identified. Immunization wards and outreach had the prevalence at less than 0.35%, and yielded 0.8% and 1.7% of the infected infants identified, respectively.

**Conclusions:** More effective identification of HIV-infected infants is critical to improve case-finding and initiate infants on life-saving ART. While EID testing should remain at EMTCT, strengthened, testing approaches should consider high HIV prevalence at nutrition and inpatient wards, which indicate that universal virological testing should be prioritized routinely at those entry points.

*No conflict of interest*

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**Abstract: O_18**

**Prevention of Mother-to-Child transmission**

**Maternal Triple Antiretrovirals (mART) and Infant Nevirapine (iNVP) Prophylaxis for the Prevention of Mother-to-Child Transmission (MTCT) of HIV during Breastfeeding (BF)**

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**Background:** Breastfeeding (BF) is crucial to reducing infant morbidity and mortality in developing countries but may result in HIV transmission if the mother is HIV-infected. Prior clinical trials showed that both mART and iNVP are effective in PMTCT of HIV. PROMISE is the first randomized trial designed to directly compare the efficacy and safety of these two strategies during extended BF.
Methods: PROMISE was conducted in sub-Saharan Africa (13 sites) and India (1 site). HIV-infected women with CD4+ counts >350 cells/mm3 (or > country-specific threshold for therapy if higher) and their HIV-uninfected newborns were randomized at 6-14 days to receive mART or iNVP. These regimens were continued until 18 months post-delivery unless there was cessation of BF, infant HIV infection, or development of toxicity. Kaplan-Meier (K-M) probabilities and incidence rates per 100 person-years were used in primary analyses of efficacy and safety.

Results: 2431 mother-infant pairs were enrolled between June 2011 and October 2014. Overall, women were asymptomatic (median CD4 count – 686 cells/mm3; 97% WHO clinical stage I) with median age of 26 years. Infant’s median gestational age and birthweight were 39 weeks and 2.9 kg, respectively. Maternal and infant baseline characteristics were comparable by study arm. Median duration of BF was 15 months and not significantly different by study arm (p=0.85). The K-M estimates of MTCT of HIV at ages 6, 9 and 12 months were 0.3% (95% CI 0.1-0.6), 0.5% (95% CI 0.2-0.8) and 0.6% (95% CI 0.4-1.1), respectively, and not significantly different between the two arms. Infant 12-month survival rate was extremely high (98.9%); and did not differ significantly by study arm. A total of 2416 mother-infant pairs were included in the safety analyses; 1211 in the mARV arm and 1205 in iNVP arm. The incidence rates (per 100 person-years) of maternal and infant safety endpoints did not differ significantly by study arm: (a) Composite of maternal Grade 3/4 signs and symptoms, Grade 2-4 laboratory events or maternal death (2 maternal deaths in the mART arm and 1 in the iNVP arm) was 14.8 (95% CI 12.7-17.3) in mARV and 14.6 (95% CI 12.5-16.9) in iNVP (p=0.99); (b) Composite severe maternal safety outcomes (same as in (a) but excludes Grade 2 laboratory events) was 5.1 (95% CI 4.3-6.1) in mARV and 5.6 (95% CI 4.8-6.6) in iNVP (p=0.61); (c) Composite of infant Grade 3/4 signs and symptoms, Grade 2-4 laboratory events or infant death was 44.1 (95% CI 39.2-49.5) in mARV and 43.5 (95% CI 38.7-48.8) in iNVP (p=0.95) and (d) Infant death (16 in mARV and 14 in iNVP arms) was 1.2 (95% CI 1.0-1.5) in mARV and 1.1 (95% CI 0.9-1.3) in iNVP (p=0.72).

Conclusions: Both mART and iNVP were safe, associated with very low postnatal MTCT rates during extended BF, and high infant survival rates. For mothers who either do not adhere to or tolerate ART, iNVP throughout BF offers a safe and effective PMTCT alternative during BF.

No conflict of interest
Abstract: O_19

Prevention of Mother-to-Child transmission

Outcomes of HIV exposed infants before and after implementing option B+ PMTCT guidelines in Kampala, Uganda: a retrospective cohort study

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Introduction: To assess the impact of Option B+ on outcomes of HIV-exposed infants (HEI), we compared the 18-month’s cumulative incidence of HIV infection, loss to follow-up (LTFU) and death in HEI before and after implementing Option B+. We also compared combination antiretroviral therapy (cART) initiation proportions among HIV-infected infants and determined factors associated with mother to child HIV transmission (MTCT) during Option B+.

Methods: We retrospectively analyzed routine data of HEI at Mulago Hospital in Kampala, Uganda. We compared estimated cumulative incidence of HIV infection, LTFU and death for HEI born from July 2010-June 2011 (Option A cohort) and July 2013-June 2014 (Option B+ cohort), accounting for competing risks. HIV infection was defined as having at least, one positive HIV DNA PCR test result anytime during the follow-up period or a positive HIV rapid test at 18 months of age. LTFU if there were three failed attempts to track them or if six months elapsed since their last clinic visit. We estimated the time to HIV infection and time to death from date of birth; and the time to LTFU from date of enrolment into care. We used Fisher's exact test to compare cART initiation proportions in HIV-infected infants in the two cohorts. Competing risks regression model by Fine and Gray (1999) was adopted to determine predictors of MTCT during Option B+.

Results: There were 2203 (Option A) and 1571 (Option B+) HEI enrolled at median age 6.4 and 6.3 weeks respectively. In both cohorts, about half of the HEI were boys and 98% received daily NVP. Eighty nine percent and 92% in Option A and Option B+ cohorts respectively were exclusively breastfed. In both cohorts, most mothers (98%) delivered in a health facility and 96% received ARVs for PMTCT. Among mother who received ARVs, 96% in Option B+ cohort received cART compared to 49% in Option B+ cohort. Other mothers in Option A cohort received AZT+3TC+sdNVP (16.4%), AZT+sdNVP (22%) and sdNVP (9.1%). The 18-month cumulative incidence of HIV infection were similarly low when comparing Option A to Option B cohorts, 5.1% (95% CI: 4.3%, 6.2%) Vs 4.3% (95% CI: 3.3%, 5.5%) respectively (p=0.2). LTFU were similar, 30.3% (95%CI: 28.4%, 32.3%) during option A Vs. 28.4% (95%CI: 26.2, 30.7) during Option B+ (p=0.06). Cumulative incidence death during Option A was 0.9 % (95% CI: 0.5%, 1.5%) Vs. 1.4% (95% CI: 0.8%, 2.2%) during Option B+ (p=0.3). cART initiation proportion in HIV infected infants was higher during Option B+ [88% (51/58) vs. 74% (72/97); p=0.04]. Mothers or infants not receiving ARVs for PMTCT were associated with MTCT, Adjusted Hazard Ratio: 16.3(95%CI: 7.6, 34.6; p<0.001) and 2.3(95%CI: 1.03, 4.95; p=0.04) respectively.

Conclusion: Outcomes of HIV-exposed infants at 18-months of life before and after implementing Option B+ were similar; however, the cART initiation in HIV-infected infants was better. Mothers or infants not receiving ARVs predicted MTCT during Option B+. LTFU remains high and should be addressed.

No conflict of interest
Abstract: O_20

Prevention of Mother-to-Child transmission

Impact of tenofovir-containing triple antiretroviral therapy (ART) on bone mineral density in HIV-infected breastfeeding women in sub-Saharan Africa


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Introduction: Both antiretroviral drug (ARV) use and lactation are known to temporarily decrease bone mineral density (BMD). To address concerns about the potential adverse impact on BMD of ARV prophylaxis taken during prolonged periods of breastfeeding, we evaluated the effect of postnatal ARV exposure on BMD among HIV-infected breastfeeding women enrolled in the bone and kidney health sub-study of the PROMISE trial – IMPAACT P1084s.

Material & Methods: IMPAACT P1084s was a sub-study that enrolled eligible mother-infant pairs from Zimbabwe, Uganda, South Africa and Malawi who had been randomised in the postpartum component of the PROMISE trial one week after delivery (6-14 days) to receive either maternal tenofovir-based triple ARV therapy (TDF-ART) or infant nevirapine prophylaxis (NVP) for prevention of postnatal transmission while breastfeeding. Maternal lumbar spine and hip BMD were measured using standard dual-energy x-ray absorptiometry (DXA) techniques soon after delivery and at 74 weeks postpartum by certified technicians on calibrated Hologic scanners. DXA scans were read centrally. Breastfeeding status was monitored throughout follow-up. We studied the effect of the postpartum randomization on percent change in BMD between delivery and week 74 at the lumbar spine (primary outcome) and hip in an intention-to-treat analysis with a t-test; mean and 95% confidence interval (CI) are presented.

Results: Four hundred women were enrolled in IMPAACT P1084s, having been randomized to maternal TDF-ART (202) and infant NVP (198). Among the 397 women included in this analysis (199 and 198, respectively), 373 (94%) completed follow-up and 24 (6%) prematurely discontinued before week 74 for similar reasons in each study arm. Baseline characteristics and duration of breastfeeding were comparable between the study arms: median (25th-75th percentile) age 26.5 years (23.3-30.0), BMI 24.7 kg/m² (22.3-28.0), HIV RNA level <400 copies/mL 39%, reported prior tobacco or alcohol use 21%, median time to cessation of breastfeeding 61 weeks. Lumbar spine BMD declined significantly more through week 74 in the maternal TDF-ART arm compared to the infant NVP arm; mean (95% CI) percent change -2.33% (-3.23, -1.42) versus -2.06% (-2.90, -1.23) versus +1.09% (0.11, 2.07) for a mean difference of -3.16% (-4.44, -1.87) (p-value<0.001). Similarly, hip BMD declined significantly more through week 74 in the maternal TDF-ART arm compared to the infant NVP arm: mean (95% CI) percent change -5.37% (-5.99, -4.76) versus -3.05% (-3.72, -2.38) for a mean difference of -2.33% (-3.23, -1.42) (p-value<0.001).

Conclusions: BMD decline between delivery and 74 weeks postpartum was significantly greater among HIV-infected breastfeeding women receiving TDF-ART compared with those assigned to infant NVP prophylaxis for prevention of postnatal transmission. This finding indicates a negative effect of maternal TDF-based ART use on BMD during extended lactation. Further study is needed to see if there is improvement in BMD following cessation of breastfeeding.

No conflict of interest
Abstract: 0_21

HIV infection and adolescents

Lung function in HIV infected South African adolescents on antiretroviral therapy: the Cape Town adolescent antiretroviral cohort

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Background: Respiratory disease is the commonest cause of illness in HIV-infected children in Sub-Saharan Africa. Lung function is a useful measure to delineate the spectrum of lung disease, but there is limited data on the spectrum and determinants of lung function in African HIV infected adolescents. Our study aimed to investigate lung function in South African HIV infected adolescents on antiretroviral therapy (ART) enrolled in a prospective cohort, the Cape Town Adolescent Anti-Retroviral Cohort (CTAAC).

Materials and methods: HIV-infected adolescents aged 9-14 years, with at least 6 months of ART and enrolled on CTAAC underwent lung function testing. Spirometry (pre and post bronchodilator), single breath carbon monoxide diffusion test, forced oscillation technique, nitrogen multiple breath wash out and six minute walk test were done at enrolment. Healthy HIV negative, age, sex and ethnically matched controls were also tested. Independent two sample t-test or Wilcoxon sum rank test was used to test differences between HIV infected and uninfected adolescents and multiple linear regression was used to adjust for age, gender and height for the observed differences.

Results: Five hundred and fifteen stable HIV-infected adolescents and 110 HIV negative controls were tested. The mean (SD) age was 12 (1.6) years; 52% were male. Median (IQR) duration of ART therapy was 7.6 (4.6-9.2) years and current CD4 was 714 (561-903) cells/mm³. HIV infected adolescents had lower lung function compared to HIV uninfected controls: forced expiratory volume in 1 sec (FEV₁) 1.60L vs 2.00L, p<0.001, FEV₁/FVC 89% vs 93%, p<0.001, transfer factor for carbon monoxide (TLCO) 16.6 vs 18.1mlCO/min/mmHg/L, p=0.048, respiratory system compliance 11.1 vs 13.5ml/cmH₂O,p=0.002 and functional residual capacity (FRC) 1.01L vs 1.16L, p=0.024. Resistance and lung clearance index (LCi) were significantly higher in HIV infected adolescents compared to HIV uninfected adolescents. These differences remained significant after correcting for age, size and gender. Seventy five (15%) HIV-infected children had a restrictive spirometric pattern, 44 (9%) had an obstructive pattern and 25 (4.9%) had a mixed pattern. Seventy five (15%) HIV infected and nine (8%) HIV uninfected controls had positive bronchodilator response, (p=0.058, 95%CI 0.01-0.13). There was no difference in distance walked in six minutes between HIV infected and uninfected adolescents.

Conclusion: African HIV infected adolescents on ART have reduced lung function compared to HIV uninfected adolescents, including decreased lung volumes, airflow and compliance and increased resistance and ventilation homogeneity. Further study of the determinants of lung function to identify possible intervention to optimise lung health is needed.

No conflict of interest
Abstract: O_22

Comprehensive Pediatric HIV care

Long term
Neurodevelopmental Outcomes on early limited or deferred continuous antiretroviral therapy: Evidence from the CHER trial

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Background: The Children with HIV Early Antiretroviral (CHER) trial showed that early limited antiretroviral therapy (ART) before 12 weeks of age reduces HIV morbidity and mortality and improves neurodevelopmental outcomes at a year of age, compared to deferred ART. The outcomes and impact of such a strategy on children is unknown. Here we report long-term neurodevelopmental outcomes among HIV+ children in CHER and HIV- controls.

Materials and methods: In the CHER trial, HIV+ infants <12 weeks of age with CD4%≥25% were randomised to: deferred ART (ART-Def), immediate ART for 40 weeks (ART-40W) or 96 weeks (ART-96W) with subsequent interruption until immunologic/clinical progression. The neurodevelopmental sub-study was conducted at 1 site (Cape Town) on CHER participants and age-matched HIV-exposed uninfected (HEU) and HIV-unexposed (HU) children. The Griffiths mental development scales (GMDS) were performed at ages 11, 21, 30, 42 and 60 months and the Beery-Buktenica tests for visual motor integration (VMI), visual perception (VP) and motor coordination (MC) at 60 months. Mixed model repeated measures ANOVA’s were used to compare GMDS scores between groups over the five assessments (group and time as fixed effects), and one-way ANOVA’s for Beery scores at 60 months.

Results: 28 ART-Def, 35 ART-40W and 33 ART-96W CHER children and 34 HEU and 39 HU controls were enrolled. ART was initiated at mean(SD) ages in months of 6.8(3.5) in ART-Def, 1.3(0.5) in ART-40W and 1.5(0.5) ART-96W. Among ART-40W, 29(83%) interrupted ART for median of 7.0 months [IQR 5.0-11.0] and among ART-96W 19(58%) interrupted for median of 8.0 months [IQR 7.0-36.0]. One participant in ART-40W and five in ART 96W were still off ART at 60 months. For ART-Def, ART40W and ART-96W at 60 months, HIV viral load was <400 in 92%, 97% and 94% and mean CD4% was 37%, 34% and 33% respectively. At 60 months 26(93%) ART-Def, 29(83%) ART-40W, 23(70%) ART-96W, 17(59%) HEU and 26(70%) HU were retained on study and assessed. Five additional HEU and 2 HU controls were enrolled at 60 months. GMDS scores over time were similar between the five groups in all subscales except for locomotor and general Griffiths. The difference between groups in these two scales was driven by a larger difference in early scores: mean locomotor quotients ranged between 89.5 - 105.9 at 11 months and 93.2- 98.7 at 60 months (interaction p=0.001); mean general Griffiths quotients ranged between100.2- 107.3 at 11 months and 81.8 - 84.7 at 60 months (interaction p=0.02). At 60 months, in each GMDS scale, the mean scores of the five groups were similar.

For the visual perceptual test at 60 months, there was a significant difference between groups with HIV+ scoring lowest (mean standard scores: 75.8 ART-Def, 79.8 ART-40W, 75.9 ART-96W, 84.4 HEU and 90.5 HU (p<0.01)), but VMI and MC were similar.

Conclusions: Similar neurodevelopmental outcomes at 5 years on the GMDS between HIV+ children on early limited therapy and uninfected controls is encouraging. The lower scores on Visual Perception in the HIV+ children may impact on childhood education outcomes and warrants further investigation.

No conflict of interest
Abstract: O_23

ARV treatment of Pediatric HIV infection

Neuropsychological performance in African HIV children in a multi-site ARV clinical trial is poorer than non-infected children


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Introduction: HIV-infected (HIV+) children are at neuropsychological risk, but few studies have evaluated this at multiple sites in resource-poor settings. We compared neuropsychological outcomes at baseline among HIV+, HIV-uninfected perinatally-exposed (HEU), and HIV-unexposed (HU) children at 6 sub-Saharan sites with language and cultural differences.

Methods: IMPAACT P1060 compared Nevirapine (NVP) versus Lopinavir/Ritonavir (LPVr)-initiated ART in HIV-infected children 6 to 35 months of age. P1104s enrolled these children at 5-11 years of age and evaluate their neuropsychological performance at 3 time points over 2 years, compared to age-matched HEU and HU controls. Evaluation tools include the Kaufman Assessment Battery for Children, 2nd edition (KABC-II) cognitive ability scales, computerized Tests of Variables of Attention (TOVA) of attention and impulsivity, the Bruininks-Oseretsky motor proficiency test, 2nd edition (BOT-2), and Behavior Rating Inventory of Executive Function (BRIEF) questionnaire (completed by parents). Caregiver depression and anxiety were also measured with the Hopkins Symptoms Checklist. Cohorts were compared using GEE least-squares means adjusted for site, child age and gender, and personal and social characteristics for child and caregiver. Exploratory HIV treatment-arm comparisons were made using Wilcoxon rank-sum tests.

Results: 611 (246 HIV, 183 HEU, 182 HU) of the 615 enrolled in P1060 at 6 sites (South Africa [3], Zimbabwe, Malawi, Uganda) were eligible for analysis. Mean age was 7.2 years, 48% male, 69% in school. 94% of caregivers were biological mothers, 32% had completed high school, 22% received social grants, 38% lived in urban areas, 29% judged family income as sufficient. Unadjusted and adjusted comparisons were consistent. The HIV+ cohort performed significantly worse than HEU and HU cohorts on KABC-II, TOVA, and BOT-2 overall performance ($P<0.05$), but not on the BRIEF. HU and HEU cohorts were comparable. Associations between test scores and caregiver socio-economic indicators as well as child school status, development and disability scores were observed. BRIEF scores were worse for children whose caregivers scored higher on depression and anxiety. In the HIV cohort, the NVP arm had lower median KABC-II Nonverbal Index scores (by 3 points, $P=0.05$) and BOT-2 standardized scores (by 1.5 points, $P=0.03$) than the LPVr arm (unadjusted intent-to-treat).

Conclusions: Significant cognitive deficits were documented for the HIV cohort across sites. Earlier HIV treatment, neuropsychological monitoring and rehabilitative interventions are needed. Testing for 2 more years will help evaluate whether ongoing effects of HIV infection and ART exposure will affect the developmental trajectory.

No conflict of interest
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Abstracts
Poster Presentations
Abstract: P_24

ARV treatment of Pediatric HIV infection

Improved adherence to antiretroviral treatment observed among children whose caregivers had positive beliefs in medicine


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Background: CHAPAS-3 trial investigated how the views of the child’s caregiver towards medicine affected the adherence of their child to fixed-dose combination ART.

Methods: 478 HIV-infected children aged one month to 13 years were randomized to one of three first-line ART regimens in Uganda and Zambia. Children were ART naïve (n=365) or ART experienced (n=113) at enrolment. We measured adherence to ART using medication event monitoring systems (MEMS) caps, and caregivers’ views towards all medicines and medicines currently prescribed using the Beliefs in Medicine Questionnaire (BMQ). MEMS caps data were collected during weeks 0-18 and 54-72. The BMQ was completed by caregivers at weeks 0, 6, 24, 48, 72 and 96. We used repeated measures linear regression models to investigate associations between MEMS adherence in weeks 0-18 and BMQ at weeks 0 and 6 (period 1), and MEMS adherence in weeks 54-72 and BMQ in week 48 (period 2).

Results: MEMS adherence and BMQ data were available from 271/365 (74%) ART naïve and 97/113 (86%) ART experienced children in period 1, and 235/335 (70%) naïve and 98/112 (88%) experienced children in period 2. We present results from the ART naïve group in period 1, similar results were observed in period 2, and also among ART experienced children. Caregivers belief in the necessity of ART was stronger on average than their concern, median (IQR) scores were 20.0 (19.3, 21.7) and 12.0 (10.7, 14.7) for necessity and concern respectively. The median (IQR) necessity-concern differential was 8.3 (6.7, 9.7). Adherence was good, as measured by MEMS, with median (IQR) 92% (84%,96%) doses taken. A significant positive association was observed between high necessity-concern score and high mems adherence, p=0.028 (β=0.236). A significant association was also seen among naïve children in period 2 (p<0.001) but not among ART experienced children.

Conclusions: Caregivers of HIV-infected children had a strong belief in the necessity of ART, outweighing their concerns about treatment. High levels of adherence to ART were associated with positive overall beliefs towards medicine. There is a need of emphasizing the necessity of treatment to caregivers, while addressing any concerns they may have about ART.

No conflict of interest

Abstract: P_25

ARV treatment of Pediatric HIV infection

Subtype A is not associated with poorer neurocognitive outcomes than subtype D in HIV-infected children receiving antiretroviral therapy

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Background: HIV subtype A was associated with poorer neurocognitive outcomes compared to HIV subtype D in a cohort of school aged HIV-infected Ugandan children who, with high CD4
counts, were not eligible for antiretroviral therapy (ART). With this study, we sought to determine whether subtype specific differences persisted among children receiving ART.

**Materials and Methods:** Children were recruited from PROMOTE-Pediatrics, a clinical trial in which children were randomized to receive either lopinavir (LPV) or non-nucleoside reverse transcriptase inhibitor (NNRTI) based ART (NCT00978068). Age at initiation of ART was 6 months to 6 years. HIV subtype and recombinant status were determined by PCR amplification and population sequencing of the pol region derived from PBMC DNA, followed by application of the REGA, RIP, and GARD algorithms. Children were assessed for general cognition, working memory, visual spatial processing and planning using the Kaufman Assessment Battery for Children (Second Edition), attention using the Test of Variables of Attention and motor skills using the Bruininks-Oseretsky Test of Motor Proficiency (Second Edition). The primary outcomes were general cognition, attention and motor skills. Home environment was assessed using the HOME scale, and nutritional status by the CDC norms. Age-adjusted Z scores from the tests were entered into a regression model controlling for sex, socioeconomic status score, HOME score, years of schooling, and ART treatment type.

**Results:** One hundred five children were tested, with median (interquartile) age of 7.05 years (6.30 – 8.44), CD4 count of 867.7 cells/mm$^3$ (416.0 – 1203.5), and duration on ART of 4.03 years (3.55 – 4.23). Thirty three (31.7%) children had HIV RNA < 400 c/ml. Fifty five (52.4%) received LPV-based ART and 50 (47.6%) received NNRTI-based ART. Seventy eight children had HIV subtype A and 27 had subtype D; children with subtype A and D had comparable baseline characteristics, except that those with Subtype A were more likely male (64.7% vs 35.3%, p = 0.02). There were no differences between subtype A and D in general cognition (estimated mean difference: 0.20; 95% CI: -0.11 to 0.50; p = 0.21), attention (0.18, 95% CI: -0.60 to 0.24, p = 0.41), motor skills (1.60, 95% CI: -0.84 to 4.04, p = 0.20) and in the secondary outcomes. Viral load and ART treatment type were not associated with any neurocognitive outcome.

**Conclusion:** Our results suggest that ART diminishes the neurocognitive disadvantage seen in treatment naïve HIV-infected children with subtype A. This is probably through viral load suppression and reduction of opportunistic infections which are associated with neurocognitive outcome.

No conflict of interest

**Abstract: P_26**

ARV treatment of Pediatric HIV infection

Acceptability and experiences of young people on weekend ART breaks - a qualitative study as part of the BREATHER trial

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**Background:** In a qualitative sub-study of the BREATHER trial, comparing virological control of Short Cycle Therapy (SCT) (5 days on: 2 days off) with Continuous EFV-based Therapy (CT) in young people (YP) with viral load <50c/ml, we examined adaptation, acceptability and experience of SCT in order to inform its potential impact and the design of any future rollout.

**Methods:** We interviewed 43 YP in the trial (38% total YP; age 11-22 years, who knew their HIV diagnosis and gave additional consent) at trial start and towards trial end in UK/Ireland (7), USA (10) and Uganda (26). Focus groups were held with 25 trial participants and interviews with 16 of their caregivers in the Ugandan site at the end of the trial.

**Results:** YP from both arms discussed initial anxieties about the impact of SCT on their health and adherence patterns, but these concerns decreased over the early months in the trial. At trial end, YP randomised to SCT reported an overall preference for SCT.
compared to their previous regimen. SCT was reported to reduce side-effects and the pressure to carry and remember medication, thus enabling more weekend activities. Across all sites, attitudes to SCT did not vary greatly by sex or country. YP from both arms reported frequent side effects. They also reported occasional missed doses throughout the course of the study which had been difficult to voice (despite having VL<50c/ml). Although participants liked SCT, they had concerns that peers who had problems adhering would also have difficulty managing SCT, with it potentially being disruptive, confusing, and leading to longer ‘slippages’.

Conclusion: Our findings indicate that SCT has the potential to encourage more candid discussions about missed doses and how treatment demands can be managed alongside YP’s other priorities. While participants described a broadly positive SCT experience, they also reported challenges adapting to SCT in the short term. To realise the potential of SCT (and mitigate possible risks) careful dissemination and communication post-trial is needed. SCT should be provided as part of a package of monitoring, support and education interventions over 3 months to allow adaptation.

No conflict of interest

Abstract: P_27

ARV treatment of Pediatric HIV infection

Investigating the status and barriers to scale-up of paediatric provider-initiated testing and counselling in malawi

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Introduction: Malawi’s paediatric HIV coverage at 49% lags significantly behind adult coverage at 67%, and an estimated 50,000 children living with HIV who are in need of antiretroviral therapy (ART) remain untreated. Identifying all HIV+ children and linking them to treatment is critical to achieving the UNAIDS 90-90-90 targets. Malawi has had a provider-initiated testing and counselling (PITC) policy since 2009; however, a large number of children remain undiagnosed. An assessment was conducted to review the performance and uptake of paediatric PITC, understand the quality of services provided, and identify barriers and potential solutions to increase uptake.

Material & Methods: A mixed methods assessment was conducted in 2015 at 38 facilities in six districts prioritized by high estimated paediatric treatment gaps. Quantitative data was collected through reviews of HIV testing and counselling (HTC) and admission registers from 2014 in outpatient, inpatient and nutrition wards. Qualitative data was compiled through surveys with HIV Service Providers (clinicians, HTC counsellors, EID and ART focal persons) about their experience with paediatric PITC and infant testing.

Results: Across all facilities, a median of 1.1% of children receiving outpatient or inpatient health services were tested via PITC, and a median of 6% of children tested positive. In facilities with inpatient wards, a median of 7% of admitted children were tested via PITC, with 10.4% testing positive. Paediatric testing efforts have been mainly focused on the exposed infant population through the PMTCT programme: among all children 12 months to 14 years tested via PITC, 55% were 12-24 months (4.0% yield) and 23% were 5-14 years (13.1% yield). The majority (66%) of clinicians believed they were not as effective at providing paediatric PITC as they could be, the top two reasons being lack of training (54%) and high workload (29%).

Conclusions: The assessment demonstrated that paediatric PITC uptake in Malawi is extremely low and needs to be strengthened to scale-up paediatric ART coverage and improve health outcomes. The assessment results informed the development of the 2016 HTS
guidelines, ensuring an adequate focus on paediatric case finding strategies, and will be used to inform the operationalization of HIV testing strategies.

No conflict of interest

Abstract: P_28

ARV treatment of Pediatric HIV infection

Incidence of antiretroviral drug discontinuations due to toxicity in children

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Introduction: Paediatric antiretroviral therapy (ART) programmes offer fewer antiretroviral options than are available for adults, particularly in resource-limited settings. Data regarding the long-term safety and durability of ART in children are thus important in order to optimise management and to forecast the future need for different antiretrovirals. We describe the incidence of and reasons for antiretroviral discontinuations in South African children and identify associations with treatment-limiting toxicities.

Materials and methods: We included children (<16 years at ART initiation) from two urban public sector ART clinics who initiated at least three antiretrovirals between 2004–2014 with at least one follow-up visit on ART. Both clinics treat patients according to South African national guidelines and collect routine clinical data and ART prescription records electronically. We described time from ART initiation to first toxicity-related antiretroviral discontinuation by Kaplan-Meier estimates. We identified factors associated with treatment-limiting toxicity using Cox regression.

Results: We included 3579 children with median follow-up duration of 41 months (interquartile range (IQR) 14 to 72). At ART initiation, median age and CD4 percent were 44 months (IQR 13 to 89) and 15% (IQR 9 to 21%), respectively. At 1, 3 and 5 years on ART, 95%, 72% and 26% of children respectively remained on their initial regimen. Discontinuations for treatment failure and toxicity were 1% each in year 1 and 4% each in year 2. By 5 years on ART, the most common reasons for discontinuations were toxicity (32%), treatment failure (18%), treatment simplification (5%), drug interactions (3%), and other or unspecified reasons (16%). The overall incidence of treatment-limiting toxicity was 13.4 per 1000 patient years (95% CI 11.3 to 16.0). Stavudine was the most frequently discontinued drug, with an incidence of 87 per 1000 person years (95% confidence interval (CI) 81.1 to 92.8), and abnormal fat distribution was the most common treatment limiting toxicity (465 of 483 patients (96%) with treatment limiting toxicity). Children on stavudine had a 30.8-fold (95% CI 4.3 to 220.2) higher risk of treatment-limiting toxicity compared to children on abacavir. Children ≥3 years old at ART initiation had a 1.8-fold (95% CI 1.4 to 2.4) higher risk of treatment-limiting toxicity compared to younger children.

Conclusions: The probability of treatment-limiting toxicity increased with longer ART duration. Stavudine was associated with the highest risk of treatment-limiting toxicity, supporting the World Health Organisation recommendation to replace stavudine with abacavir in paediatric first-line ART regimens. It is unclear why older children had a greater risk of treatment-limiting toxicity, but it might be due to the age-specific regimens used, or because toxicity such as lipodystrophy might be difficult to diagnose in younger children.

No conflict of interest
Abstract: P_30

ARV treatment of Pediatric HIV infection

HIV-infected children who initiated ART during infancy (early ART) have improved neurocognitive outcomes compared with late-treated children

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Background: HIV-infected children have high risk of learning and behavior difficulties at school-age. The long-term benefit of early antiretroviral treatment (infancy) for reducing these risks is unknown. Methods. Antiretroviral treatment (ART) was initiated with Kenyan HIV-infected infants at age <12 months (early-treated; 2007-2009) or at age 18-60 months (late-treated; 2004-2008). Neurocognitive assessments were completed at school-age and adolescence. Assessments included the Kaufman Assessment Battery for Children 2nd edition (cognitive ability, short-term memory, visual-spatial processing, planning, learning, and non-verbal), Test of Variables of Attention (attention), and Bruininck’s-Oseretsky Test of Motor Proficiency-2 (motor). Age-matched (to the early-treated group) HIV-exposed-uninfected (HEU) and HIV-unexposed-uninfected (HUU) children were also assessed. Scores were standardized using US norm data to allow cohort comparisons. Standardized scores were compared using multivariable linear regression analyses adjusted for caregiver years of education, to account for socioeconomic differences.

Results: At neurocognitive assessment, median ages were 6.7 years (HUU; N=63), 7.4 years (HEU; N=43), 6.9 years (HIV+ early-treated; N=54) and 13.4 years (HIV+ late-treated; N=24). Early and late-treated children initiated ART at a median 0.4 and 3.3 years of age, respectively. Mean scores in HUU children were 75.0 (cognitive), 83.3 (short-term memory), 73.4 (visual-spatial processing), 86.2 (learning), 71.3 (planning), 72.8 (non-verbal), 83.1 (attention), and 44.6 (motor). In multivariable analyses, compared with HUU children, HIV+ early-treated children had lower scores for short-term memory (adjusted mean difference, -5.15; P=0.015). Compared with HUU children, HIV+ late-treated children had significantly lower scores (adjusted mean differences, cognitive ability, -8.80; P=0.002; short-term memory -11.77; P<0.001; visual-spatial processing, -7.97; P=0.02; non-verbal, -9.36; P=0.004; motor, -9.48; P<0.001). Compared with early-treated children, late-treated children also had significantly lower scores (adjusted mean differences, short-term memory, -6.38; P=0.03; learning, -7.14; P=0.04, non-verbal, -6.76, P=0.02, and motor -7.13, P=0.001).

Conclusions: Children who had received ART by age one year had subtle short-term memory deficits compared with HUU. Children who initiated ART later had deficits in multiple domains including cognition, short-term memory, visual-spatial processing, learning and motor skills, compared with HUU or HIV+ early-treated children or both. Earlier ART appears to prevent broader neurodevelopmental compromise due to pediatric HIV infection.

No conflict of interest
Abstract

P_31

ARV treatment of Pediatric HIV infection

Concurrent influences of antiretroviral therapy duration and adherence on CD4 percent in HIV-infected Kenyan children

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Introduction: Adherence to antiretroviral therapy (ART) is essential for HIV suppression and for reduction of HIV-related morbidity and mortality, but how patterns of long-term ART adherence impact children’s immunologic outcomes over various time periods of treatment and child development in resource-limited settings are not well understood. We assessed the concurrent and interacting influences of ART duration and medication adherence on CD4 percentage (CD4%) among HIV-infected Kenyan children.

Materials & Methods: We enrolled HIV-infected Kenyan children ages 0-15 years for a prospective cohort study with intensive adherence monitoring. Participating children had moderate to severe clinical disease and were on first-line ART regimens with either a nevirapine or efavirenz backbone. Patients’ ART adherence was monitored by the Medication Event Monitoring Systems (MEMS®), which recorded the openings of medication bottles for 6 months. CD4% was determined at the end of the 6-month follow-up period. We performed semiparametric regression analysis to examine the effects of medication adherence and ART treatment duration on CD4%, while adjusting for the effects of age and BMI z-score. Unlike traditional linear regression, semi-parametric regression modelling is a new analytical method to measure nonlinear effects and interacting influences. Separate analyses were performed for boys and girls. The estimated mean CD4% at different combinations of medication adherence and treatment duration were presented as colored contour plots, with warmer color indicating higher CD4% level. The model was adjusted for the effects of age and for BMI Z-score on CD4%.

Results: We analyzed data from 200 children (109 girls). Mean age was 8.4 years (range 1.5–14.9). Mean CD4% at study enrollment was 26.0% (SD 10.7%). Participants had been on ART for an average of 2.3 years. Mean MEMS® adherence over the 6-month study period was 86.4% (SD 16.7% and range 2.8-100%). Both ART duration and current levels of adherence were significantly associated with CD4% measured at 6-month follow-up in boys and girls. Shorter treatment duration and greater adherence were independently associated with higher CD4% levels (all p values <0.011). Effect contour plots (not included) showed that the influence of adherence on CD4% attenuated with increased treatment duration: Suboptimal ART adherence generally resulted in poorer immunologic outcome in patients who had been treated for longer durations, whereas good ART adherence tended to have a greater effect on improving immunologic status in those who had been on treatment for relatively short durations. The effect patterns were generally consistent between boys and girls, but the treatment duration-related decline in adherence effect was much more pronounced in girls.

Conclusions: The analysis highlights the critical importance of sustaining ART adherence for children over the long-term. Not only does immunologic status tend to decrease over time, but the impact of poor adherence on CD4% appears to be even more significant the longer the child has been on ART. These findings have strong implications for the role of adherence support for children over a lifetime of HIV treatment and through transition into adolescence and adulthood.

No conflict of interest
Validation of Adherence Questionnaire Items for HIV-Infected Children and Adolescents in Thailand

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Introduction: Routine assessment of adherence to antiretroviral therapy (ART) is recommended standard of care, but there are few low-cost, validated adherence tools for use among HIV-infected children. Using previously validated adherence questionnaire items among HIV-infected children in Kenya, we tested item performance among a similarly-aged HIV-infected cohort in Thailand.

Materials & Methods: We conducted a validation study of a 10-item adherence questionnaire among a cohort of 100 HIV-infected children attending the HIV-NAT clinic in Bangkok, Thailand. The adherence questionnaire included items related to who gives the child medicines, disclosure status, adherence-related barriers, and missed and late medication-taking. Participants were followed for 6 months. The questionnaire was administered during routine clinical care encounters at baseline, 3 months, and 6 months. The questionnaire was administered in Thai by a clinic nurse to the child’s caregiver and to the child if he or she was responsible for medication-taking. Medication Event Monitoring System (MEMS) that record the time and date of medication bottle opening were used as external criterion for adherence. We conducted logistic regression analysis with repeated measures to validate questionnaire items by assessing the item’s association with dichotomized MEMS adherence (>90% doses taken). Odds ratios (OR) and 95% confidence intervals (95%CI) were calculated with an OR > 1.00 indicating a higher odds of adherence.

Results: Ninety-one children completed the study. Mean age was 13.1 years and 53% were female. Most children (51%) were responsible for taking their own medication. The most common type of caregiver for participants was the biological mother (35%). Median MEMS adherence improved slightly during the study; at month 3 it was 91.8% (IQR 63.6%, 98.8%) and at month 6 it was 93.4% (IQR, 70.6%, 98.8%; p=0.32). When the questionnaire was administered to the caregiver, the following items showed a significant association with MEMS adherence: sibling giving ART (OR 0.41, 95%CI 0.40-0.42); relative or non-family member giving ART (OR 1.45, 95%CI 1.15-1.83); problems keeping time with medication-taking (OR 0.92, 95%CI 0.86-0.98); problems getting the child to take ART (OR 0.87, 95%CI 0.85-0.89); missing at least one dose in the past 7 days (OR 0.92, 95%CI 0.88-0.95) or in the past 30 days (OR 0.98, 95%CI 0.97-0.99). When the questionnaire was administered to the child, the following items were significantly correlated with MEMS adherence: sibling giving ART (OR 0.41, 95%CI 0.40-0.42); relative or non-family member giving ART (OR 1.45, 95%CI 1.15-1.83); problems taking ART (OR 0.87, 95%CI 0.85-0.89); missing at least one dose in the past 7 days (OR 0.94, 95%CI 0.90-0.98); taking a dose at least one hour late in the past 7 days (OR 0.92, 95%CI 0.87-0.98); and, missing more than one dose in the past 30 days (OR 0.97, 95%CI 0.95-0.99).

Conclusions: Most items were significantly associated with MEMS and were consistent when the item was administered to the caregiver or child. The findings indicate good validity in the questionnaire’s ability to assess adherence to ART among a pediatric population in Thailand.

No conflict of interest
Abstract: P 33

ARV treatment of Pediatric HIV infection

Virological failure in south african children and adolescents: baseline characteristics and management strategies


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Abstract

Background: Treatment failure in HIV-infected children is difficult to manage in resource-limited settings, given limited availability of alternative drugs and concerns around adherence and developing viral resistance. We aimed to describe children with virologic failure (VF) managed with different treatment strategies using the International epidemiologic Databases to Evaluate AIDS Southern Africa (IeDEA-SA) collaborative cohort database.

Materials and Methods: We included all children from 8 IeDEA-SA sites, who initiated and remained on combination antiretroviral therapy (cART-defined as ≥ 3 drugs from ≥2 classes) for at least 6 months from April 2004-December 2012.

VF was defined as 2 consecutive viral loads (VL) >1000 copies/ml ≥1 month apart for 6 months on ART. After failure, children followed one of four treatment strategies:

1. Switch to new cART regimen based on guidelines or HIV resistance testing.
2. Continuing failing regimen with ≤1 same class drug substitution.
3. Switch to either lamivudine mono-therapy or other non-cART regimen (holding regimen).
4. Discontinue all antiretroviral drugs.

Multinomial logistic regression was used to compare characteristics of children placed on each strategy compared to switching to new cART.

Results: Among 7053 children, 1347 (19.1%) experienced VF at a median age of 6.4 years (interquartile range [IQR]: 2.9-11.1) and median duration on ART of 1.5 years (IQR 1.0-2.5).

Children with VF were more likely to be male (53% vs 50%, p=0.04) and exposed to drugs for prevention of mother-to-child transmission (PMTCT) (13% vs 10%; p=0.02) than those without VF. At ART initiation, children who developed VF had lower median baseline weight for age z-score [-2.13; IQR -3.22, -1.17] vs. -1.76; IQR -2.88,-0.83, p=<0.001) and median height for age z-score [-2.59; IQR -3.15,-1.59 vs. -2.27; IQR -3.24,-1.36, p=<0.001]; and were severely immune-suppressed according to WHO 2006 definition using CD4 percentage/absolute count (57% vs 53%, p=<0.001), compared to children without VF.

After VF 673/1347 (50%) children remained on their failing regimen, 443/1347 (33%) switched to new cART, 44/1347 (3%) switched to a holding regimen and 184/1347 (14%) stopped all ART. In adjusted analyses, compared to switching to new cART, predictors of remaining on a failing regimen were female gender (aOR 1.45, 95% CI 1.04-2.01, p=0.027), lower viral load at VF (aOR 0.76, 95% CI 0.61-0.93, p=0.01), being on a PI regimen at VF (aOR 20.60, 95% CI 12.44-34.10, p<0.0001), fewer

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years of follow-up after VF (aOR 0.73, 95% CI 0.61-0.87, p<0.0001), and receiving care from a primary care clinic compared to secondary/tertiary care (aOR 3.49, 95% CI 2.25-5.41, p<0.0001). Predictors of switching to a holding regimen (vs a new regimen) were longer ART duration before VF (aOR 1.98, 95% CI 1.15-3.40, p=0.014), and later year of ART start (OR 1.95, 95% CI 1.16-3.28, p=0.012).

Conclusions: Almost 20% of children in this cohort developed VF. These children had more advanced clinical and immunological HIV disease at ART initiation, and may be at risk of deterioration if VL suppression is not achieved on a new cART regimen. A number of factors are associated with treatment strategy decisions after failure, likely to influence outcomes.

No conflict of interest

Abstract: P_34

ARV treatment of Pediatric HIV infection

Outcomes in hiv-positive children on lamivudine monotherapy as a holding regimen in the iedea southern african cohorts

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Background: Treatment failure in HIV-infected children on antiretroviral therapy (ART) in resource-limited settings is a growing concern given poor access to new drugs and lack of targeted strategies to improve adherence. Lamivudine monotherapy (LM) is a holding regimen used whilst psychosocial barriers to adherence and medication availability are addressed. We aimed to investigate characteristics of children placed on LM and their outcomes.

Materials and Methods: We included children (age <16 years at ART start) from 5 South African iDEA-SA cohorts who received LM. Kaplan-Meier estimates and Cox-proportional hazards models were used to determine probability and predictors of immunological decline (ID), defined as a drop in CD4 below 500, or, in those who initiated LM with CD4<500, a drop in CD4 of >10%. Average CD4 trajectories were estimated using linear mixed-effects models.

Results: Of 232 children included in the study, 58% were male, median age at ART start was 7.4 years (interquartile range [IQR 3.3-10.0]), median CD4 and CD4% were 346.5 (IQR 185-604) and 12.6 (7.3-18.0) respectively. AT LM start median age was 12 years (IQR 7.2-14.6), median time on ART was 3.5 years (IQR 1.9-5.7), and median CD4 and CD4% were 601 (IQR 425-869) and 21.7 (IQR 16.4-28.0) respectively. Prior to LM, 75 (34%) had CD4<500, and 122 (53%) were on an efavirenz-based regimen. The median time on LM at study closure was 309 days (88.5-664), 173 (75%) had resumed ART, 43 (19%) remained in care on LM, 4 (2%) died whilst on LM, 9 (4%) transferred care and 3 (1%) were lost to follow-up. Of those on LM for >90 days, 44% (72/163) experienced ID; 21% (34/163) experienced a gain in CD4 of >10%. Among 102 patients on LM >6 months, the 6 month risk of ID was 23% (95% CI 17.7%; 30.4%). Predictors of ID included older age at ART initiation, those >9 years had a 3-fold higher risk of ID compared to those <2 years (aHR 4.4, 95% CI 2.1; 9.1); treatment interruption prior to LM start (aHR 1.9, 95% CI 1.1; 3.5); and CD4 at LM start, children with CD4>=1000 having 60% lower risk of ID compared to those with CD4<500 (aHR 0.4, 95% CI 0.2; 0.7). Being on a protease inhibitor-based regimen prior to LM was not associated with ID. Predicted CD4 decline at 6 months on LM was greater in those with a higher CD4 count at LM start, -40.2 cells/µL (95% CI -49.2; -31.2) in those with a CD4>=400 compared to -4.2 cells/µL (95% CI -23.6; 15.3) in those with CD4<400. Predicted CD4 decline at 6 months on LM was greater in those younger at ART start, -61.8
cells/µL (95% CI -78.2; -45.4) in those <2 years, compared to -41.5 cells/µL (95% CI -53.1; -29.8) in those >9 years.

Conclusions: Most children on LM experienced a drop in CD4, while less than half experienced ID. The clinical significance of this decline and outcomes after restarting suppressive ART warrant further investigation including comparison with those who interrupt treatment or remain on triple therapy.

No conflict of interest

Abstract: P_35

ARV treatment of Pediatric HIV infection

Does antiretroviral therapy before 12 weeks of age preserve neurometabolite levels at 7 years in HIV-infected children? – Evidence from the CHER trial

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Background: Starting antiretroviral therapy (ART) before 3 months of age yields good clinical, immunological and developmental outcomes. Long-term studies are necessary to understand the long-term impact of HIV and ART on brain development.

1H magnetic resonance spectroscopy (MRS) non-invasively measures localized brain metabolism providing information about biochemical aspects of brain maturation. N-Acetyl-Aspartate (NAA) is associated with neuronal integrity. Total creatine (Cr+PCr) is related to energy metabolism. Total choline (GPC+PCh) is associated with cellular density. Glutamate, Glu, is the most abundant excitatory neurotransmitter also an important molecule in synapse formation, dendrite pruning, cell migration, differentiation and death. Differences in metabolite levels in HIV-infected children may provide insight into the long-term effects of HIV infection and different early ART regimes. This study aims to explore the effects of HIV infection and early ART regimes on brain development by examining NAA, Cr+PCr, GPC+PCh and Glu levels in basal ganglia (BG), midfrontal gray matter (MFGM), and peririgonal white matter (PWM) in HIV-infected and HIV uninfected children at 7 years.

Materials & Methods: Subjects. Participants included HIV-infected and HIV uninfected 7-year old children from a multimodal longitudinal neuroimaging study. HIV-infected children were stratified into those starting ART at or before 12 weeks of age (Early-ART) or after 12 weeks (Late-ART). The control group comprised matched HIV uninfected (HU) and HIV-exposed, uninfected (HEU) children.

Neuroimaging. The protocol included a high-resolution T1-weighted acquisition and single voxel 1H-MRS in three brain regions (BG, MFGM, and PWM) performed on a3T Allegra MRI Scanner (Siemens, Erlangen, Germany) in Cape Town, South Africa. Absolute metabolite levels calculated with LCModel.

Statistics. The R-programming language was used to examine group differences. We used a linear regression model with age at scan, gender, ethnicity, metabolite standard deviation and signal-to-noise ratio as confounders.

Results: Fifty-six HIV-infected (13 Late-ART/43 Early-ART; 31 girls; mean age in years ± standard deviation: 7.2 ± 0.1; 7 Cape Coloured/49 Xhosa) and 45 HIV-uninfected children (27 HU/18 HEU; 20 girls; 7.2 ± 0.1; 9 Cape Coloured/36 Xhosa) were analyzed.

BG and PWM. No significant differences in mean metabolite levels were observed between groups.

Conclusions: Surprisingly we found no metabolite differences in the BG, a region highly vulnerable to HIV infection. Apart from glutamate in MFGM, we find no differences in metabolite levels at 7 years, suggesting healthy regional development among the HIV-infected children. The reduced mean glutamate level
observed in HIV-infected children is possibly a result of localized delayed maturation.

No conflict of interest

Abstract: P_36

ARV treatment of Pediatric HIV infection

Viral drug resistance in children taking once-versus twice-daily abacavir and lamivudine in African children in the ARROW trial


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Background: ART adherence is critical for successful HIV treatment outcomes. Once-daily dosing could improve adherence. In this analysis in the ARROW trial (NCT02028676, ISRCTN24791884) in Uganda and Zimbabwe, we compared development of viral resistance over 96 weeks in children randomised between once-daily vs twice-daily dosing of abacavir+lamivudine.

Methods: 669 children taking abacavir+lamivudine-containing first-line regimens twice-daily for >36 weeks (either with an NNRTI or as a 3NRTI regimen) were randomised to continue twice-daily versus move to once-daily abacavir+lamivudine (open-label) and followed for median 114 weeks (IQR 106-125). Viral load (VL) was assayed retrospectively on stored plasma samples at 0, 48 and 96 weeks after randomisation. Samples >1000 copies/ml were genotyped using in-house primers at the Joint Clinical Research Centre, Kampala, Uganda. HIV subtype was predicted using REGA v3.0, drug-resistance mutations defined using IAS-USA 2013, and drug susceptibility predicted using Stanford v7. Comparisons were made between randomized groups using chi-squared tests for categorical outcomes.

Results: VL was >1000 c/ml in 50/331 (15%) vs 64/335 (19%) children randomised to twice-daily vs once-daily abacavir+lamivudine at week 0 (p=0.17); 66/331 (20%) vs 68/330 (21%) respectively at week 48 (p=0.83) and 63/326 (19%) vs 72/331 (22%) respectively at week 96 (p=0.44). Genotypes were obtained in 105/114 (92%), 129/134 (96%) and 130/135 (96%) (p>0.3 comparing twice- vs once-daily). Overall 179 (49%) genotypes were subtype-A, 90 (25%) were subtype-C (including all Zimbabwean children) and 72 (20%) were subtype-D. Only 6 (6%), 4 (3%) and 4 (3%) children had no or at most low-level resistance to all NRTIs and NNRTIs at weeks 0, 48 and 96 respectively, suggesting non-adherence. There was no evidence of differences between twice-daily and once-daily groups in intermediate/high-level resistance to any NRTI, or in specific NRTI mutations, at any timepoint (p>0.15). Children had a median (IQR) 3 (2-3), 3 (2-4) and 3 (2-4) NRTI mutations at weeks 0, 48, and 96 respectively suggesting slow accumulation of additional mutations (p>0.3 comparing twice- vs once-daily). As expected, M184V/I mutations were common (>80%) in both groups. Only 6 (6%), 8 (6%) and 6 (5%) children had K65R mutations at weeks 0, 48 and 96 respectively (6/7/3 on abacavir+lamivudine+NNRTI, 0/1/3 on 3NRTI). Q151M was seen in one child on once-daily 3NRTIs at both week 48 and 96 (also with K65R at both timepoints). As expected, thymidine-analogue mutations (TAMs) were rarely seen in children on abacavir+lamivudine+NNRTI, but 74V mutations were observed in 56%/64%/70% and 115F in 56%/62%/68% at weeks 0/48/96 respectively. 74V and 115F were much less frequent in children receiving 3NRTIs (3%/3%/3% and 16%/20%/19% respectively; all p<0.001 vs abacavir+lamivudine+NNRTIs). Children receiving the current WHO preferred regimen of abacavir+lamivudine+NNRTI could use zidovudine or tenofovir as second-line NRTIs. In the subgroup of children randomised to abacavir+lamivudine twice- or once-daily with an NNRTI, intermediate or high-level resistance 0/48/96 weeks after randomisation was 15%/16%/8% for tenofovir and 0%/4%/2% for zidovudine.

Conclusion: Once-daily dosing of the WHO-preferred NRTI backbone abacavir+lamivudine...
was non-inferior to twice-daily dosing in terms of development of viral resistance. Both tenofovir and zidovudine are reasonable second-line NRTI options for children failing abacavir+lamivudine.

No conflict of interest

Abstract: P_37

ARV treatment of Pediatric HIV infection

Population Pharmacokinetics of Lopinavir/ritonavir in Severely Malnourished HIV-Infected Children: Early versus Delayed Initiation of Antiretroviral Treatment

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Introduction: In developing countries, malnutrition remains a common clinical syndrome at initial presentation in HIV-infected children thus requiring the initiation of antiretroviral treatment (ART) in a malnourished child. During nutritional recovery there are continuous shifts in oxidative stressors, lean body tissue, albumin levels, intestinal absorption, mitochondrial, hepatic and renal function and other changes potentially affecting the pharmacokinetics of antiretroviral drugs.¹ ² As part of the Malnutrition and Antiretroviral Timing in Children with HIV (MATCH) trial we described the population pharmacokinetics of lopinavir/ritonavir in severely malnourished HIV-infected pediatric patients, investigating the impact of early vs. delayed initiation of HAART on exposure to lopinavir and to identify covariates explaining pharmacokinetic variability in this population.

Methods: Pharmacokinetic data was obtained from the MATCH study, which is a prospective, randomized controlled interventional trial comparing immediate initiation of HAART to delayed initiation until recovery from the acute phase of severe malnutrition. Lopinavir/ritonavir doses were given as per WHO weight band dosage charts, twice daily as oral solution. Five lopinavir concentrations were measured on day 1 and five (+ pre-dose) concentrations were measured on day 14 post initiation of antiretroviral treatment. The population pharmacokinetics of lopinavir were identified using NONMEM v7.3. One- and two-compartment disposition models with first-order elimination were tested. Between subject (BSV) and between occasion variability (BOV) were estimated. Covariates screened to assess their influence on the pharmacokinetics of lopinavir included: early versus delayed HAART start, study day, weight, fat-free mass (FFM),³ age, cholesterol, triglyceride, anthropometrical measurements, and the combined effect of a rifampicin-containing anti-tuberculosis regimen and ritonavir super-boosted Lopinavir. Model evaluation was performed using prediction-corrected visual predictive checks (pcVPC) and bootstrap.

Results: 502 lopinavir concentrations were collected from 62 paediatric patients aged 0.1-3.9 years (median: 0.9 years), 105 of whom were receiving rifampin-based antituberculosis treatment concurrently with extra ritonavir (4-fold the usual dose). Lopinavir disposition was well described by a one-compartment model with first order elimination. Reduced adherence was identified for the non-study day observation (pre-dose sample), compared to day 1 and day 14 of the protocol. Neither randomisation to early or delayed ART, tuberculosis co-medications nor anthropometrical measurements explained pharmacokinetic variability. FFM (allometrically scaled) influenced clearance (CL) and volume of distribution (Vs). Parameter estimates (BOV (%CV)) were CL/F (L/h/5.6kg): 3.59 (136%), Vs/F (L/5.6kg): 12.0, ka (h⁻¹) 0.387 (60%), bioavailability (F) on non-study days was reduced to 28% compared to day 1 and day 14. BSV (%CV) on F was 68.6%. The proportional error component of RUV (%CV) was 39.3% for samples taken within the first 5 hours after the dose and 28.2% for all others.

Conclusions: FFM influenced the pharmacokinetics of lopinavir in severely malnourished HIV-infected pediatric patients. Lopinavir pharmacokinetics was not affected by the management of severe acute malnutrition or...
Abstract

Background: While studies have shown increased risk of clinical events among adults with poor immune response (PIR) despite viral suppression on antiretroviral therapy (ART) versus immune responders, there are scarce data in children. We assessed PIR prevalence, associated factors and clinical outcomes in children on suppressive ART in EPPICC, which includes cohorts from 16 European countries and Thailand.

Methods: Children aged<18 years at start of combination ART, with ≥1 year follow-up on ART, ≥1 viral load (VL) and ≥1 CD4 measurements were eligible. Viral suppression (VS) was defined as VL≤400copies/mL within 12-months of ART (<18-months for infants) and sustained VL≤400c/mL for ≥1 year (allow unconfirmed blips <10,000c/mL). PIR was defined as WHO immunological stages ‘advanced’ or ‘severe’ (CD4%<30 for age <12-months, CD4%<25 for 12-35 months, CD4%<20 for 35-59 months; CD4%<15 or CD4<350cells/mm³ for ≥5 years). Follow-up was censored at earliest of: confirmed VL>400c/mL, unconfirmed VL≥10,000c/mL or gap between VL measurements of ≥15 months. Factors associated with PIR at 1 year of VS were explored using logistic regression. Rates of clinical events (death/first CDC C event) occurring after 1 year of VS were compared with immune responders (none/mild immune stage).

Results: Of 3,488 children starting ART, 2,007 (58%) had sustained VS for ≥1 year and included in the analysis; 47% were male, 92% perinatally infected, 36%, 20% and 8% were from the UK/Ireland, Thailand and Ukraine, respectively. At ART start, median age was 6.4yrs [IQR 2.2-10.4]; CD4% 15% [8-23]; 15% and 55% were WHO advanced and severe immune stage, respectively. Median duration of follow-up after ART start was 6.2yrs [3.7-8.7]. PIR prevalence was 12%(212/1697) at 1 year of VS, reducing to 7%(93/1347) at 2 years and 4%(44/1100) at 3 years. Factors at ART initiation associated with PIR at 1 year of VS were: older age (adjusted odds ratio (aOR) (95%CI) 5-<10yrs aOR=1.7(1.0-2.7), 10-<15yrs aOR=1.8(1.1-3.1), ≥15yrs aOR=6.0(2.9-12.7) vs. <5yrs, p<0.001); worse immune stage (mild aOR=2.6(0.6-11.3), advanced aOR=7.2(2.1-25.1), severe aOR=13.2(4.1-42.8) vs. none, p<0.001); Thai cohort (aOR=2.3(1.5-3.5) vs Europe, p<0.001); non-perinatal HIV infection (aOR=2.6(1.5-4.7), p=0.001); lower VL (≤100,000 aOR=1.6(1.1-2.4) vs. >100,000, p=0.011), and earlier calendar year (1997-2003 aOR=1.3(0.8-2.3), 2004-2007 aOR=1.9(1.1-3.1) vs. 2008-2013, p=0.033). There were 3 deaths (2 HIV-related, 1 unknown) and 21 AIDS events after 1 year of VS, of which 2 and 5 were among PIR patients, respectively. The rate of deaths/AIDS was 0.94(0.45-1.97) per 100 person-years among PIR vs 0.30(0.19-0.48) among immune responders; rate ratio of 3.14(1.30-7.56). Growth was also poorer among PIRs with lower median change in height-for-age z-score by 1 year of VS as compared to immune responders (p=0.002), while there was no difference in rate of treatment change during VS (p=0.790).
Conclusions: Poor immune response in children on suppressive ART was relatively rare, but they experienced a three-fold increase in risk of AIDS/death during viral suppression as compared to immune responders. Strongest predictors of PIR include older age and worse immune status at ART start, supporting calls for immediate ART in all children. Those with PIR should continue to have CD4 monitoring even when VL monitoring is available.

No conflict of interest

Abstract: P_39

ARV treatment of Pediatric HIV infection

Virological response to first-line ART in children in the European Pregnancy and Paediatric HIV Cohort Collaboration (EPPICC)

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Background: Studies comparing efficacy of protease inhibitor (PI) and non-nucleoside reverse transcriptase inhibitor (NNRTI)-based initial ART regimens in children have shown inconsistent results. We investigated virological response (viral load (VL) <400 copies/ml) by 12 months in children from 19 cohorts across 16 European countries and Thailand.

Methods: The median(IQR) gap between VL measurements varied by calendar year and cohort. Therefore time of virological response was assumed to lie in the interval defined by the last VL ≥400 copies/ml and the first VL <400 copies/ml, rather than at a known time e.g. the midpoint. Multivariable stepwise interval-censored Cox regression models (backwards elimination, exit probability p=0.05) were used to identify factors associated with time to virological response from ART initiation (baseline). Follow-up was censored at the earliest of a gap between VL measurements of >15 months or last VL date. Missing baseline CD4 (18%) and VL (22%) measurements were multiply imputed.

Results: 2901 children initiating ART <18 years with a boosted PI or NNRTI plus ≥2 NRTI had ≥1 VL measurement available within the first 15 months of ART and baseline VL >400 copies/ml. 90% were perinatally infected, 53% female, with 33%, 14%, 35% and 18% from UK/Ireland, Russia/Ukraine, the rest of Europe and Thailand respectively. 34% of children initiated ART with a bPI-based regimen (93% lopinavir), 33% efavirenz+2NRTI, 28% nevirapine+2NRTI and 4% an NNRTI+3NRTI (94% nevirapine). 33% started an abacavir-containing regimen. At ART initiation, median age was 6.1 (1.6, 10.6) years, 12% had an AIDS diagnosis, 56% had VL ≤100,000 copies/ml and 46%, 25% and 19% had CD4% <15%, 15-24% and >25% respectively. Overall, an estimated 89% [95% CI: 88%, 90%] achieved virological response by 12 months. In multivariable analysis, the effect of initial ART regimen on time to suppression differed according to age at initiation (p=0.02). In those <3 years old, time to response was fastest in those starting a bPI-based regimen (aHR 1.20 [1.03,1.39], p=0.02). Time to response was significantly faster in those ≥3 years of age, but did not vary significantly by regimen (p=0.11). Higher CD4% (15-24%: aHR 1.10 [0.99,1.23], ≥25%: aHR 1.14 [1.01,1.29] vs <15%; p=0.07), lower VL (≤100,000 copies/ml: aHR 1.43 [1.29,1.59] vs >100,000 copies/ml: p<0.001), and use of abacavir (aHR 1.24 [1.12,1.38], p<0.001) were associated with faster time to virological response. Children in Russia and Ukraine had slower time to response (Russia/Ukraine: aHR 0.73 [0.64,0.84], UK/Ireland: aHR 1.20 [1.08,1.34], Thailand: aHR 1.17 [1.02,1.34] vs Rest of Europe; p<0.001) as did those starting a PI-based regimen (aHR 1.20 [1.08,1.34] vs <15%; p=0.07), lower VL (≤100,000 copies/ml: aHR 1.43 [1.29,1.59] vs >100,000 copies/ml: p<0.001), and use of abacavir (aHR 1.24 [1.12,1.38], p<0.001) were associated with faster time to virological response. Children in Russia and Ukraine had slower time to response (Russia/Ukraine: aHR 0.73 [0.64,0.84], UK/Ireland: aHR 1.20 [1.08,1.34], Thailand: aHR 1.17 [1.02,1.34] vs Rest of Europe; p<0.001) as did those with earlier calendar year of ART start (1997-2003: aHR 0.93 [0.83,1.03], ≥2008: aHR 1.09 [0.98,1.21] vs 2004-2007; p=0.03). There was no significant effect of gender, AIDS diagnosis, HCV, HBV or TB co-infection at ART start or mode of HIV infection. Complete case analysis (n=2061) gave very similar results.
Conclusion: Most children achieved virological response by 12 months. Response was faster in older children, with no difference between regimens; younger children responded fastest on a bPI-based regimen. Faster response in those with higher CD4% adds weight to recent recommendations for immediate ART initiation in all children irrespective of age/CD4 count.

No conflict of interest

Abstract: P_40

ARV treatment of Pediatric HIV infection

Does antiretroviral therapy before 12 weeks of age preserve neurometabolite levels at 9 years in HIV-infected children? Evidence from CHER trial

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Introduction: Starting antiretroviral therapy (ART) before 3 months of age yields good clinical, immunological and developmental outcomes. However, studies are needed to investigate the long-term impact of HIV and ART on brain development. ¹H magnetic resonance spectroscopy (MRS) noninvasively measures localized brain metabolism providing information about biochemical aspects of brain maturation. N-Acetyl-Aspartate (NAA) is associated with neuronal integrity. Total creatine (Cr+Pcr) relates to energy metabolism. Total choline (GPC+PCh) is associated with cellular density, inflammation and astrocytosis. Glutamate, Glu, is the most abundant excitatory neurotransmitter also an important molecule in synapse formation, dendrite pruning, cell migration, differentiation and death. Differences in metabolite levels in HIV-infected children may provide insight into the long-term effects of HIV infection and different early ART regimens. This study aims to explore the effects of HIV infection and early ART regimens on brain development by examining NAA, Cr+Pcr, GPCPCh and Glu levels in basal ganglia (BG), midfrontal gray matter (MFGM), and peritrigonal white matter (PWM) in HIV-infected and HIV uninfected children at 9 years.

Materials & Methods: Subjects. Participants included HIV-infected and HIV-uninfected 9-year old children from a multimodal longitudinal neuroimaging study. HIV-infected children were stratified into those starting ART before (Early-ART) or after 12 weeks (Late-ART). The control group comprised matched HIV uninfected (HU) and HIV-exposed, uninfected (HEU) children. Neuroimaging. The protocol included a high-resolution T1-weighted acquisition and single voxel ¹H-MRS in three brain regions (BG, MFGM, and PWM) performed on a 3T Skyra MRI Scanner (Siemens, Erlangen, Germany) in Cape Town, South Africa. Absolute metabolite levels were calculated with LCModel. Statistics: A linear regression model in R was used to examine group differences in metabolite levels, with age at scan, gender, ethnicity and signal-to-noise ratio as confounders.

Results: Sixty-two HIV-infected (16 Late-ART; 31 girls; mean age ± standard deviation: 9.3 ± 0.2; 8 Cape Coloured/54 Xhosa) and 33 HIV-uninfected children (18 HU/15 HEU; 16 girls; 9.7 ± 0.5; 7 Cape Coloured/26 Xhosa) were analysed. MFGM. Mean choline levels were significantly higher in HIV-infected compared to HIV-uninfected children (β=0.10, p = 0.009). Although there was no difference in mean choline level between early and late groups (β=-0.04, p=0.7), when compared to HIV uninfected children, the Early-ART group showed significantly higher mean choline (β= 0.11, p = 0.008). BG and PWM. No significant group differences in metabolite levels were observed.

Conclusions: Even though the BG is the region highly vulnerable to HIV infection, we find no differences in metabolite levels between HIV-infected and HIV-uninfected children. Elevated choline levels observed in the MFGM in the Early-ART group may indicate inflammation or an abnormal increase in astrocytes in HIV-infected children.

No conflict of interest
Abstract: P_41

ARV treatment of Pediatric HIV infection

Baseline drug resistance and viral suppression on antiretroviral therapy in HIV-infected children who failed prevention of mother-to-child-transmission programmes


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Introduction: Limited data exists from Southern Africa on baseline antiretroviral drug resistance and the impact thereof on HIV-1 infected children. We describe drug resistance mutations in children after failing prevention-of-mother-to-child-transmission (PMTCT) programmes, as well as factors associated with viral suppression on antiretroviral therapy (ART).

Methods: A prospective observational cohort study was conducted at the Paediatric HIV Clinic at Kalafong Hospital in Pretoria, South Africa. Children referred for ART initiation between July 2010 and March 2013 were enrolled. Data collection included demographic and anthropometric measurements, PMTCT history, ART regimes, HIV clinical staging and concomitant tuberculosis treatment. Blood specimens collected at enrolment and at monthly follow-up visits included CD4+ and CD8+ T-cell counts/percentages and HIV RNA plasma viral loads (VL). Baseline genotypic drug resistance testing was done. Drug resistance testing was additionally performed on dried blood spots using an oligonucleotide ligation assay (OLA), which can detect and quantify HIV-resistant subpopulations comprising ≥2% using probes optimized for HIV subtype C codons K103N, V106M, Y181C and G190A. Frequencies of drug resistance mutations were determined and associations with viral suppression identified.

Results: The study included 101 children (median age 9.7 months [IQR 4.3; 16.6]), with 84 children returning for follow-up visits and included for further analysis. Maternal PMTCT-interventions included triple-ART in 12.2%, while 51.9% received antenatal zidovudine and 73.4% nevirapine at delivery. The majority of children (91.6%) received nevirapine prophylaxis (median 14 days, IQR 1; 42 days), and protease-inhibitor (PI)-based ART was used as paediatric treatment regimens in 88.1%. The majority of children had advanced clinical disease (stages 3 or 4 disease in 73.8%), severe malnutrition (mean weight-for-age Z-score -1.98 (SD 1.59) and height-for-age Z-score -2.50 (1.72)), high baseline HIV VL (median 6.1 log10, IQR 5.4; 6.7) and frequent tuberculosis co-infection (44%). Two-thirds of children suppressed their VLs (<200 copies/ml) during the initial 12 months of ART. Slow viral suppression was associated with low weight-for-age (p=0.004); advanced clinical disease stage (p=0.008), tuberculosis co-treatment (p=0.0004) and lower CD4-quartiles at ART initiation (p=0.01). On genotyping non-nucleoside reverse transcriptase inhibitor (NNRTI) mutations were found at baseline in 53% (42/79) of all tested children, and 51% (32/63) among tested children included in the 12 month follow-up subset. The most common mutation were: K103KNR = 17.5%, V106AM = 4.8%, V179DT = 4.8%, Y181CY = 33.3% and G190ARS = 11.1%. On OLA results 41% of children had significant (≥20%) NNRTI resistance with regards to the 4 tested mutations, with an average concordance of 93.7 % compared to genotyping.

Conclusions: In South African children who failed HIV-prophylaxis, half the children presenting for ART had NNRTI-resistant HIV, emphasizing the need for PI-based ART initiation regimens. The need for early ART initiation before disease progression is evident, and tuberculosis co-infection is a major reason for slow viral suppression in children.

No conflict of interest
Abstract: P_42

ARV treatment of Pediatric HIV infection

HIV drug resistance mutations among newly diagnosed HIV-infected infants in Thailand

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Background: Prevention of mother-to-child transmission (PMTCT) of HIV has resulted in a dramatic reduce the risk of MTCT. However, the use of antiretroviral drugs for pre-partum in pregnant women and as prophylaxis in newborns can lead to selecting of HIV drug resistance (HIVDR) mutations in infected infants. The presence of HIVDR mutations in infants has important clinical implication since it can reduce the efficacy of first-line antiretroviral treatment. In Thailand, HIVDR genotyping testing in infected infants is not performed before initiation of therapy, although it has recommended by WHO. Thus, data on HIVDR mutations from the HIV-infected pediatric population especially infants younger than 18 months are limited. The objective of this study was to determine HIVDR mutations among newly diagnosed HIV-infected infants in Thailand.

Materials & Methods: Faculty of Associated Medical Sciences, Chiang Mai University is the reference center for early infant diagnosis (EID) using dried blood spot (DBS) by Real-time PCR to hospitals across Thailand since 2007. DBS samples were obtained from newly diagnosed HIV-infected infants less than 18 months of age from 2007 to 2014. The samples were analyzed for HIV drug resistance and subtypes through sequencing of the pol gene. HIV drug resistance was interpreted using the Stanford University HIV Drug Resistance Database. Subtype diversity was determined using REGA subtyping tool. Associations between occurrence of drug resistance mutations and infant or maternal factors were performed using STATA 10 (Stata Corporation, USA).

Results: Two hundred and eighty eight of 298 DBS samples (96.6%) were successfully amplified and sequenced. The median age of infants at blood draw was 2.3 months (IQR, 2-4.1). The most prevalent HIV-1 subtype was CRF01_AE (91.7%) followed by subtype B (8%) and C (0.3%). The resistance-associated mutations to nucleoside reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs), and protease inhibitors (PIs) were detected in 5.4%, 9.1%, and 1.6%, respectively. The most frequent mutations in reverse transcriptase gene were Y181C (n=7), K103N (n=4), whereas M46L (n=3) and V82A (n=1) were found in protease gene. Age, signs of HIV infection, maternal ARV treatment, and PMTCT exposure had no significant difference in the occurrence of HIV drug resistance mutations.

Conclusions: We report the data of HIVDR mutations among newly diagnosed HIV-infected infants younger than 18 months old in Thailand. Our results highlight the values of HIVDR testing for HIV-infected infants before initiation of therapy and the use of DBS specimens being tested for EID. These will help in planning protocols and policies related to antiretroviral management for the pediatric population in Thailand and other resource-limited countries.

No conflict of interest
Abstract: P_43

Comprehensive Pediatric HIV care


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Background: Despite the World Health Organization (WHO) regularly updating guidelines to allow earlier initiation of antiretroviral therapy (ART) in children, the proportion of HIV-infected children initiating ART in sub-Saharan Africa lags behind adults. The impacts of implementing increasingly less conservative ART guidelines on access to care and treatment initiation has not been described in Central Africa. We describe trend characteristics of children 0 – 12 years entering HIV care and initiating ART from 2004-2013 in Burundi, Democratic Republic of Congo, and Rwanda.

Methods: Data are from the Central Africa International Epidemiologic Databases to Evaluate AIDS (IeDEA) pediatric cohort of all children (n=5508) entering care. Measures included CD4 count, WHO clinical stage, age, and weight-for-age Z score (WAZ) using 2006 WHO standards, taken both at enrollment into HIV care and at ART initiation. Changes in the median or proportions of each measure by year of enrollment and at ART initiation were assessed to capture potential impacts of changing ART guidelines

Results: Median age at care enrollment was 77.2 months (interquartile range (IQR); 44.8, 110) in 2004-2005, decreasing progressively to 30.3 months (IQR 5.8, 86.6) in 2012+. The proportion of children 0-24 months increased from 12.7% in 2004-2005 to 46.7% in 2012+. Similar, though less pronounced trend was observed at ART initiation with median age decreasing from 83.0 months (IQR 49.8, 117) in 2004-2005 to 66.9 (IQR 24.3, 115) in 2012+. The proportion of children 0-24 months at ART initiation also increased from 9.6% in 2004-2005 to 24.2% in 2012+.

Conclusion: Changes in guidelines may have succeeded in increasing the number of children entering care and/or initiating ART earlier. Gaps remain and more needs to be done to reduce time between diagnosis, enrollment in care and ART initiation.

No conflict of interest

Abstract: P_44

Comprehensive Pediatric HIV care

Standardized Pediatric Expedited Encounters for ART Drugs Initiative (SPEEDI): description of an innovative pediatric ART delivery model in Tanzania

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Introduction: In resource limited settings (RLS), critical shortages of health care workers coupled with large patient volumes hinder the effective delivery of antiretroviral therapy (ART) services. In addition, frequent clinic visits create burdens on patients due to costs associated with transport and missed worked, driving high attrition rates. Innovative ART programs that reduce these burdens have been successfully piloted in adults, but to date, no such program has been described in children living with HIV. This abstract describes the Standardized
Pediatric Expedited Encounters for ART Drugs Initiative (SPEEDI) and examines its effectiveness in children on ART in Mbeya, Tanzania.

**Materials and Methods:** The SPEEDI program was implemented in January 2013 at the Baylor College of Medicine Tanzania Centre of Excellence (COE) in Mbeya, Tanzania. To qualify for a SPEEDI visit, the following criteria are met: 1) On ART for at least 4 months; 2) No medical or social complications, and no concerning lab results; 3) Good adherence to ART (95-105% via pill counts); and 4) Presence of a reliable caregiver. During a SPEEDI visit, patients are triaged for vital signs, anthropometrics, and pill counts. Patients/caregivers are given the option to see a doctor, and if deferred they will proceed directly to collect medications. The file is reviewed by a doctor to ensure the patient is appropriate for SPEEDI prior to writing prescriptions. SPEEDI patients are given a two month follow up visit, and alternate SPEEDI with routine visits that include physician examination.

Retrospective chart review of patients with at least one SPEEDI visit between 1st January 2013 and 31st December 2015 was performed. 'Good Outcome' included patients still active in care and those transferred out; 'Poor Outcome' included deaths and lost to follow up (LTFU). COE patients on ART between 1st March 2011 (when the COE opened) and 31 December 2012 (before the SPEEDI program started) were used as a comparison group.

**Results:** A total of 1164 pediatric ART patients utilized SPEEDI, totaling 3499 total SPEEDI visits. SPEEDI reached 51.3% (1164/2269) of the total pediatric ART patients and accounted for 7.9% (3499/44489) of all patient encounters during this time. The demographics of SPEEDI patients were: 52% (605/1164) female, median age of 9 years (range 1-18yr), and median time on ART prior to first SPEEDI of 21 months (range 4-130 months). 98.7% (1150/1164) of SPEEDI patients had good outcomes, and 1.2% had poor outcomes (14/1164). Prior to implementation of SPEEDI, the mortality rate of COE patients on ART was 2.8 deaths per 100 patient-years and LTFU was 3.0%. Mortality rate of the SPEEDI cohort was 0.37 deaths per 100 patient-years and LTFU was <0.1%.

**Conclusion:** SPEEDI was an effective, feasible way to delivery ART to children in a RLS, and led to good clinical outcomes. Potential benefits include better utilization of clinician’s time and skills, reduced wait times, patient satisfaction and increased retention, and need to be further explored. SPEEDI can serve as an ART delivery model for children that can be adapted and scaled up in other RLS.

**No conflict of interest**

**Abstract: P_45**

**Comprehensive Pediatric HIV care**

**An RCT study to evaluate the caregiving and neurodevelopmental benefits of a year-long training program for Ugandan preschool children affected by HIV**


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**Introduction:** Mediational intervention for sensitizing caregivers (MISC) has a structured training program to enable caregivers to improve their children’s cognitive and social development during daily casual interactions in the home. In our preliminary findings in Uganda, children of caregivers receiving MISC training biweekly for a year showed significantly greater gains on the Mullen Early Learning Scales Composite of g fluid intelligence, when compared to children whose caregivers received a standard health/nutrition education intervention. The MISC caregivers were also significantly less depressed, and their child mortality that year was significantly lower. These preliminary findings supported an RCT study of Mediational Intervention for Sensitizing Caregivers (MISC) was used to enable
Caregivers to enhance their child's cognitive and social development through daily interactions.

Methods: Caregivers of half of 120 perinatally HIV infected (PHIV) and 120 uninfected HIV-exposed (PHEU) preschool children had biweekly MISC training for one year, emphasizing practical strategies for cognitive enrichment of daily mother/child interactions. Treatment as usual (TAU) dyads received a health and nutrition curriculum. Children and caregivers were evaluated at baseline, 6 months, 1 year (conclusion of caregiver training), and finally a year after the completion of caregiver training. Children were tested with the Mullen Scales of Early Learning (MSEL), the Color-Object Association Test (COAT) for memory, the Early Childhood Vigilance Test (ECVT) for attention, and the Behavior Rating Inventory of Executive Function (BRIEF; caregiver responses about child). Caregivers completed a questionnaire of depression and anxiety as well as functionality in activities of daily living, psychosocial support, and means of coping with stress scales. Caldwell HOME scale and videos of caregiver/child interactions in the home scored for MISC interactions used to evaluate fidelity of MISC training at baseline, 6 months, 12 months, and 1 year post training.

Results: For both the PHIV and PHEU cohorts, MISC intervention arm children had significantly greater gains compared to controls on the Mullen Receptive Language Scale, with significant benefits persisting even a year following completion of training. MISC caregivers had better functionality through training and at one year follow-up, compared to control caregivers. For the MISC mothers, videotaped quality of caregiving was significantly related to the caregiver functionality and Mullen receptive language scores. Therefore, MISC benefits on language development were partially mediated by improvements in caregiver functionality. Quality of caregiving was also related to Mullen composite cognitive development, ECVT attention and to COAT working memory gains. These relationships were not evident for the TAU arm.

Conclusions: A year-long MISC caregiver training program lead to better child developmental outcomes for their HIV-affected children compared with treatment-as-usual health and nutritional education. Our RCT findings support the recent care for child development (CCD) global initiatives by WHO/UNICEF in promoting such programs as the most strategic means of addressing the needs of vulnerable and at-risk children globally in low-resource settings. MISC is an important evidence-based option for such programs because of its emphasis on enhancing CCD through culturally sensitive and appropriate, as well as practical and sustainable techniques and strategies during the course of daily interactions in the home.

No conflict of interest

Abstract: P_46

Comprehensive Pediatric HIV care

Viremia copy-years over the first 2 years predicts immunologic outcome in a pediatric HIV cohort in Jamaica


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Background: Viremia copy-years (VCY) is reported to be a better prognostic indicator of HIV disease progression than traditional cross-sectional viral loads. We examined the determinants and immunologic consequences of VCY in a pediatric HIV cohort in Kingston, Jamaica.

Methods: Analysis of longitudinal data from HIV-infected children followed at three sites in the Greater Kingston Metropolitan Region from the Pediatric and Perinatal HIV/AIDS Program (KPAIDS), Kingston, Jamaica. VCY was defined as the number of copies of HIV RNA/ml/year circulating in plasma and integrated over the number of years since HIV infection. Main outcome was changes in CD4 count and cumulative viral load measured as VCY was the explanatory variable. We analyzed the association between VCY and log-transformed CD4 count using linear mixed-
Abstract: P_47

Comprehensive Pediatric HIV care

Child growth according to maternal and child HIV status in Zimbabwe


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Introduction: Growth failure is a recognized complication of perinatal HIV infection, but the effects of HIV exposure or timing of HIV acquisition on growth are uncertain. Using an historical birth cohort from Zimbabwe, we compared growth in children by HIV infection or exposure status.

Materials and methods: 14,110 infants were enrolled in the ZVITAMBO trial in Harare, Zimbabwe before the availability of antiretroviral therapy or co-trimoxazole. Weight and height were recorded from birth through 12-24 months of age and expressed as Z-scores. Growth outcomes were compared between 5 categories of children: HIV-infected in utero (IU), intrapartum (IP) or postnatally (PN); HIV-exposed uninfected (HEU); and HIV-unexposed.

Results: Growth failure was common across all groups of children. Compared to HIV-unexposed children, IU, IP and PN-infected children had significantly lower length-for-age and weight-for-length Z-scores through 2 years of age. Timing of HIV acquisition was associated with the degree of growth failure, such that at 12 months, odds ratios for stunting were higher in IU infants (6.25, 95%CI 4.20, 9.31) and IP infants (4.76, 95%CI 3.58, 6.33) than PN infants (1.70, 95%CI 1.16, 2.47). Compared to HIV-unexposed infants, HEU infants had poorer linear and ponderal growth through 12 months of age. At 12 months, HEU infants had odds ratios for stunting of 1.23 (95%CI 1.08, 1.39) and wasting of 1.56 (95%CI 1.22, 2.00).

Conclusions: HIV status was associated with growth failure in early life. HIV-infected infants

Abstract

effects model while adjusting for demographic covariates. The within-sample variation was also accounted for through random-effects with unstructured correlation.

Results: The study included 230 children who had ≥2 viral load measurements from 2004 to 2014. Fifty-nine percent were female and 41% were male. Mode of transmission: mother-to-child transmission (MTCT), behavioral, and blood transfusion was 82%, 15%, and 1%, respectively. Age was significantly associated with the magnitude of VCY (p=4.0×10^{-55}). There was no statistical significant association between gender and VCY (p=0.28). VCY had a significant negative association with log-transformed CD4 count (p=2.5×10^{-20}) when age was adjusted for as a covariate. VCY calculated using first 2 years of available viral load measurements preceding a CD4 determination, removing the potential confounding effect of age, has statistically significant association with log-transformed CD4 count (p=1.1×10^{-14}).

Conclusions: Since decline in CD4 is the hallmark HIV disease progression, high VCY may increase all-cause HIV morbidity and mortality. VCY over the first 2 years (VCY_{2Y}) could serve as the ‘set-point’ and could predict CD4 trajectory. Thus VCY may be a good alternate to routine cross-sectional viral load in resource-limited settings as its determination could be less frequent.

No conflict of interest
had very high rates of stunting and wasting, particularly among those who acquired HIV before or around birth, highlighting the importance of early infant diagnosis. HEU infants had poorer linear and ponderal growth than HIV-unexposed infants over the first 12 months. Longitudinal growth should be assessed in contemporary cohorts to determine the prevalence of stunting and wasting in the current ART era.

No conflict of interest

Abstract: P_48

Comprehensive Pediatric HIV care

The effects of HIV exposure and timing of HIV infection on head growth in Zimbabwean children

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Introduction: Head growth may be impaired in infants with HIV exposure or infection. We describe the head growth of children according to maternal and child HIV infection status in Zimbabwe, before the availability of antiretroviral therapy.

Methods: We performed a retrospective, longitudinal analysis of head circumference data from 13,647 children in the ZVITAMBO trial, which was undertaken in Harare, Zimbabwe between 1997 and 2001. Head circumference was measured within 96 hours of birth, then at regular intervals through 24 months of age. Mean head circumference-for-age Z-scores (HCZ) and prevalence of microcephaly (HCZ < -2) were compared between HIV-unexposed children, HIV-exposed uninfected children (HEU), and children infected with HIV in utero (IU), intrapartum (IP), and postnatally (PN).

Results: HIV exposure and infection were associated with poor head growth. HEU children had significantly lower head circumferences than HIV-unexposed children through the first 12 months of life, although no statistically significant differences were identified in the second year of life. Children infected with HIV before birth (IU children) had poor head growth; 11.1% of IU children had microcephaly at birth, and mean HCZ continued to decline throughout the follow-up period. By 12 months, mean (95%CI) HCZ was -0.62 (-0.86, 0.39) in IU children and there was almost 8-fold higher odds of microcephaly compared to HIV-unexposed children (OR 7.84, 95%CI 4.34, 14.16). Head growth was also poor in IP infants, but, unlike IU children, the mean HCZ remained relatively stable throughout follow-up; by 12 months of age, mean (95% CI) HCZ was -0.43 (-0.60, -0.26) and there was 6.5-fold higher odds of microcephaly compared to HIV-unexposed children (OR 6.51, 95%CI 4.07, 10.42). Microcephaly was more common among IU and IP children than among HIV-uninfected children through 24-months. During the second year of life, mean HCZ in the PN group declined, and reached a similar mean to IP children by the end of the study period.

Conclusions: Compared to HIV-unexposed children, HEU children had poorer head growth until 12 months of age, and HIV-infected children had poorer head growth throughout the first 24 months of life. Timing of HIV acquisition was associated with head growth, with those infected before birth having particularly low head circumference. Correlations between head growth and neurodevelopment in the context of maternal/infant HIV infection will be helpful to determine the predictive value of routine head circumference measurement.

No conflict of interest
Abstract: P_49

Comprehensive Pediatric HIV care

Outcomes of children down referred after ART initiation at Dora Nginza Hospital, Eastern Cape, South Africa

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Background: Decentralization of HIV care for children has been recommended to improve pediatric outcomes by making treatment more accessible. We documented outcomes of children down referred from a large referral hospital in the Eastern Cape of South Africa after ART initiation and conducted community tracing to locate children who were lost to follow-up.

Methods and methods: We examined electronic medical records for all children 0-15 years who initiated ART at Dora Nginza Hospital (DNH) in Port Elizabeth, South Africa January 2004-September 2015 to identify those down referred to lower level health facilities to continue treatment. Medical records were then reviewed at 16 primary health care facilities to determine the proportion of children who attended care at assigned down-referral facilities (DRF) and outcomes following down referral including loss to follow-up (LTF), death (recorded in medical records) and documented transfer. LTF was defined as no recorded clinical visit or medication pick-up within the past 6 months. Community tracing was conducted for children currently ≤15 years with contact information who were LTF at DNH, LTF at DRF, and for children who never attended visits at assigned DRF. When located, caregivers were consented and interviewed.

Results: Among 1,583 children initiated on ART at Dora Nginza Hospital, 889 (56.2%) were down referred, 644 (72.4%) to one of the 16 DRF included in the study. 67 (9.6%) children were LTF while in care at DNH. Median age at ART initiation for down referred children was 4years (IQR:2-8), median age at down referral was 8years (IQR:5-11) and median time from ART initiation to down referral was 36months (IQR:20-49). 432 (67.3%) down referred children were found to have ever attended care at the assigned DRF; among these children, 84 (19.3%) were subsequently LTF, 2 (0.5%) died, 78 (17.9%) had a documented transfer to another health facility and 272 (76.4%) were still in care. 212 (32.9%) children never attended care at the assigned DRF. Community tracing was conducted for 120 children; 66 (55.0%) caregivers were located and reported that 4 (6.1%) children died, 2 (3.0%) were in care at the DRF, 51 (77.3%) were in care at another facility and 9 (13.6%) were not receiving routine care. Of the 62 children still alive, 45 (72.6%) were currently taking ART; reasons for stopping ART in 17 children included 6 (35.3%) children refusing medication, 3 (17.6%) caregivers not having time to pick-up ART and 2 (11.8%) caregivers not wanting child taking ART.

Conclusions: Among children down referred after initiating ART at a large referral hospital in South Africa, only two thirds ever attended care at referral facilities. Most children LTF who were found through community tracing were receiving care at another health facility however rates of death and disengagement from care were likely higher among the children not located through tracing. We also found that 27% of children traced in the community had stopped taking ART. Greater efforts are needed to ensure that referrals are completed and that children and caregivers are supported to remain on ART.

No conflict of interest
Abstract: P_50

Comprehensive Pediatric HIV care

KNOW YOUR CHILD’S HIV STATUS: An innovative approach to targeted pediatric case finding in Malawi

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Introduction: Despite Malawi’s progress in expanding HIV prevention, care and treatment services, the number of children on antiretroviral therapy (ART) remains low. Only 50% of children younger than 15 years of age with HIV were currently alive and on treatment as of December 2015. Strategies aimed at improving pediatric case finding and linkage to care are essential in closing this treatment gap and ensuring that all infected children benefit from care and treatment. EGPAAF’s Know Your Child’s HIV Status (KYCS) is an innovative approach for finding HIV-positive children, through targeted testing children of adult ART index clients to increase pediatric case finding with funding from CIFF and U.S. President’s Emergency Plan for AIDS Relief.

Methods: EGPAAF, in collaboration with the MOH, developed guidelines for the implementation of KYCS and identified a focal person for each of the six pilot health facilities. Adults receiving ART at these facilities were invited to bring their children for HIV testing on Saturdays. The testing was done by qualified HIV testing service (HTS) providers at facilities as per the national guidelines. In some facilities, where available, HTS providers also conducted point-of-care CD4 testing. Qualified clinical and nursing staff were available to enrol children who tested positive into care and treatment. The data was recorded by the data clerks in the standard MOH registers.

Results: During the four-month period of December 2015-March, 2016, of the 7,713 families that were booked, 7,660 families brought 8,784 children for testing, and 8,520 children under 15 years were tested. Of the children tested, 62.6% were aged 6-14 years, 37% were 1-5 years, and 0.4 % were 11 months or younger. A total of 182 (2%) HIV-positive children were identified. The majority (80%) of children identified as HIV-positive were aged 6-14 years. All (100%) of the newly identified HIV-positive children were enrolled into care and 75% were initiated on ART within two weeks of identification.

Conclusions: KYCS is feasible and highly acceptable among caregivers. However, the success of KYCS campaign is dependent on a multi-disciplinary team approach to include clinical and nursing facility staff, data clerks and HTS providers. In addition, availability of point-of-care technology for CD4 testing facilitates timely initiation of HIV-infected children on ART (though Test and Start is preferable and anticipated). The positivity rate is significant especially given the fact that most of the identified children were over six years of age and would not have been identified until they were sick, as they were no longer attending the under 5 clinic.

No conflict of interest

Abstract: P_51

Comprehensive Pediatric HIV care

Feasibility and yield of routine HIV testing and counselling through use of lay counselors in Lesotho health facilities

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Background: Improved case-finding strategies along with linkage to care and treatment are needed in Lesotho in order to meet UNAIDS 90-90-90 targets (90% with known status, 90% on ART, and 90% suppressed). Provider-initiated testing and counselling is a potential strategy, but increases workload in health facilities already challenged with limited human resources. We explored the feasibility of lay
Counsellors specifically trained in HIV testing and counselling (HTC) to provide routine testing in health facilities.

**Description:** In September 2015, Baylor College of Medicine Children’s Foundation-Lesotho through support from PEPFAR/CDC placed 50 lay counsellors in 39 public health facilities in the districts of Berea and Leribe to provide HTC. Patients were offered HTC if they 1) were never tested or 2) required retesting (last test >3 months ago and patient is either breastfeeding or sexually active). DNA PCR testing was available for children < 18 months. Patients found to be HIV positive were enrolled on the same day for HIV care and treatment. Patients who refused immediate enrolment or desired enrolment in another health facility were referred for patient follow-up.

**Lesson learned:** We analyzed routine program data for all clients who were tested from September to December 2015. During this period, 26,289 patients were tested, of whom 12,493 (48%) were children and adolescents (0-19 years). 5,591 (21%) had not been previously tested. HTC yield was 61 (0.8%), 90 (1.7%), and 1084 (7.9%) among patients 0-9, 10-19, and > 19 years, respectively. Among the 1235 patients who were tested positive for HIV, 1157 (94%) were enrolled into care on the same day. The relatively low HTC yield among children 0-9 years may be due to testing in a cohort with regular access to healthcare, and therefore, PMTCT services. HTC strategies in the community targeting exposed children may be needed for improved case-finding in this population.

**Conclusion/next steps:** Use of lay counsellors trained in HTC for routine testing at health facilities is feasible and a potential low-cost strategy for case-finding and linkage to HIV care and treatment. However, exploration of alternate strategies for children is needed.
follow-up was 5.6 (2.9, 8.7) years. There were 94 deaths and 174 first AIDS-defining events, of which 43 (46%) and 79 (45%) respectively occurred within 6 months of cART initiation. The crude mortality rate was 2.50 [95%CI 1.86, 3.37]/100 person-years (PY) in the ≤6 month period, and 0.27 [0.21, 0.36] thereafter. 60 (64%) (32 ≤6 months) deaths were from HIV-related infections, 18 (19%) (8) HIV-related non-infectious conditions, 12 (13%) (1) HIV-unrelated, and 4 (4%) (2) unknown. The rate of first AIDS-defining event was 0.88 [0.76, 1.02]/100PY, including 31 (18%) HIV encephalopathy, 29 (17%) tuberculosis and 25 (14%) HIV-wasting syndrome.

Significant baseline predictors of increased mortality >6 months of cART in multivariable analysis were: middle-income (Russia, Ukraine, Thailand) v. high-income country (high-income adjusted hazard ratio (aHR)=0.5 [0.3, 1.0], p=0.042); earlier calendar year at cART start (2004-2007 aHR=0.4 [0.2, 0.8], ≥2008 aHR=0.5 [0.2, 1.5] v. 1997-2003, p=0.037) and lower BMI-for-age z-score at cART start (>0 aHR=0.2 [0.1, 0.6], <-3 aHR=0.5 [0.2, 1.8] v. -3 to 0, p=0.070). Time-updated multivariable predictors were: lower or higher current age (<2 years aHR=3.7 [1.2, 10.8], 2-<5 years aHR=0.2 [0.1, 1.6], ≥14 years aHR=1.8 [0.9, 3.7] v. 5-<14 years, p=0.005); current WHO immunological stage severe (non-severe aHR=0.1 [0.1, 0.2] v. severe, p<0.001); lower current BMI-for-age z-score (>0 aHR=1.1 [0.4, 2.9], <-3 aHR=18.8 [6.9, 51.3] v. -3 to 0, p<0.001); and viral load ≤400c/ml (≤400 aHR=0.4 [0.2, 0.9] v. >400, p=0.068). Predictors for death ≤6 months (baseline only) and progression to AIDS (baseline and time-updated) were similar. 21 adolescents (≥14 years) died >6 months of cART (14 HIV-related infections, 3 HIV-related non-infectious conditions, 4 HIV-unrelated). Their median (IQR) ages at HIV diagnosis and cART initiation were 9.9 (8.5, 11.3) and 10.8 (8.7, 11.9) years respectively, and they took ART for a median of 6.2 (4.5, 7.6) years.

Conclusion: Almost half of deaths occurred ≤6 months of cART, after which current severe WHO immunological stage, low BMI-for-age z-score, and VL>400c/ml were the strongest predictors for mortality. The raised mortality risk in adolescents and in middle-income countries raises concern.

Conflict of interest

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Abstract: P_53

Comprehensive Pediatric HIV care

Outcomes of a cohort of ART-eligible children in Eastern Cape, South Africa

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Background: Data on virologic outcomes among children enrolled in routine HIV treatment programs in sub-Saharan Africa are limited. We examined viral suppression (VS) and death in a cohort of ART-eligible children followed at health facilities in the Eastern Cape Province of South Africa.

Methods: The PESS study enrolled HIV+ children 0-12 years of age who were identified as ART eligible by healthcare providers at 5 participating PEPFAR-supported health facilities, between 2012-2014. All children received routine HIV care and treatment services; data for the study were extracted from medical charts, including viral load (VL). Children attended quarterly study visits which included anthropometric measures and caregiver questionnaires. Time to VS amongst those starting treatment was measured from the day of ART initiation to the first VL <1000 and <50 copies/mL using competing risk estimators, with death as a competing risk. We also examined cumulative incidence of death using Kaplan-Meier estimators. Multivariable sub-distributional hazards models adjusted for age, viral load and weight-for-age z-score (WAZ) at enrollment examined characteristics associated with VS. Cox proportional hazards models were used to examine factors associated with death.

Results: Of the 397 children enrolled, 156 (39.3%) were <12 months, 127 (32%) were 1-5 years and 114 (28.7%) were 6-12 years. Median age at HIV diagnosis was 15 months
(IQR 3-52); 161 (40.6%) children were hospitalized at enrollment; and 138 (34.8%) currently had TB or had a history of TB. Median time on study was 22 months (IQR 14-24). Among all children at enrollment: median VL was 446,895 copies/mL (IQR 97,865-2,169,330) and 75.5% had a VL>100,000 copies; median CD4 count was 579 (IQR 314-1156); WAZ -1.8 (IQR: -3.1 to -0.4). Among children starting ART at 6, 12 and 24 months, the rates of viral suppression <1000 copies/mL were 48.7 (95% CI 43.3-54.0), 72.8 (95% CI 67.7-77.3) and 84.8 (95% CI 79.8-88.7) and <50 copies/mL were 33.4 (95% CI 28.4-38.4), 56.1 (95% CI 50.5-61.3) and 73.4 (95% CI 67.4-78.4). In multivariable models, only enrollment VL was associated with suppression. Cumulative incidence of death at 12 months among all children enrolled was 8.6 (95% CI 5.9-11.4) and 9.3 (95% CI 6.4-12.1) at 24 months; mortality after treatment initiation was lower, 2.4 (95% CI 1.1-4.5) at 12 months and 3.2 (95% CI 1.6-5.7) at 24 months. There were no enrollment factors significantly associated with death, however, starting ART was strongly protective against death (adjusted hazard ratio 0.01, 95% CI 0.01-0.04).

Conclusions: In this cohort of ART eligible children enrolled in routine HIV care, many had advanced disease status despite scale-up of HIV testing and treatment services for children in South Africa. Mortality was also high, particularly among children prior to ART initiation. Among the children who started treatment, a high proportion achieved VS <1000 copies/mL which is encouraging and is comparable with other cohorts from resource-limited settings. These findings highlight the urgent need to more effectively identify children with HIV and rapidly initiate them on ART in order to prevent mortality.

No conflict of interest

Abstract: P_54

Comprehensive Pediatric HIV care

Impact of Inpatient ART Initiation and Community Health Workers to Increase Post-Discharge Linkage, ART uptake, and Reduce Lost-to-Follow-up for HIV Infected in Malawi

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Introduction: With the recent recommendations from the World Health Organization for universal implementation of ‘test and treat’, uptake of this recommendation will be difficult for large referral hospitals in Sub-Saharan African due to poor post-discharge linkage-to-care. Kamuzu Central Hospital (KCH) is the largest referral hospital in Malawi with over 10,000 annual pediatric admissions and is considered a high burden, high yield site for HIV testing. Baylor College of Medicine- Children's Foundation Malawi (BCM-CFM) in a bid to reduce HIV morbidity among children, has successfully scaled up provider initiated testing and counseling (PITC) services with over 95% testing coverage at KCH and on average 40 infected children identified monthly. Though the PITC program is highly successful, antiretroviral (ART) initiation and post-discharge linkage to care have been a struggle. High rates of readmission for those who defaulted ART at the central hospital signify poor linkage and referral efforts. BCM-CFM developed a linkage to care and follow up program at KCH using the Community Health Workers (CHW) and linkage experts to address this gap as a model that can be used at large referral hospitals in Malawi and Sub-Saharan Africa.

Methods: Standard operating procedures on hospital follow-ups and linkage-to-care were developed including registers, five Community health workers, three community nurses, and
five linkage experts were hired to address linkage and LTFU at KCH. Data was reviewed retrospectively for Oct 2015-March 2016 from HTC, linkage, and LTFU registers at KCH and a descriptive analysis of the data was performed. Gaps noted were expanded through verbal interviews with nurse matrons, ward nurses, and registry clerks. Community health workers called or visited guardians 2 weeks and 2 months after discharge to follow up on linkage, ART initiation, and retention in care.

Results: 110 children were recruited from the wards for community linkage. Of the 110 children, 52 (47%) were initiated on ART on the wards of which 49 continued after discharge (94%). Of the remaining 58 children, 6 died prior to ART initiation (5%), 2 absconded, and 48 were discharged without initiating ART. Of the 48 discharged without ART initiation, only 20 (42%) went for follow-up at a community health center and were initiated on ART. The remaining 28 agreed to follow up and ART initiation only after home visits from the community health workers and community nurses who escorted the patients to the local clinics.

Conclusions: 'Test-and-treat' on inpatient wards versus community initiation and the use of community health workers can significantly reduce lost-to-follow-up and improve ART uptake for newly identified patients at large referral hospitals. The work of CHWs can also be minimized if ART initiation is done whilst the patient is in the ward. A universal policy on inpatient ART initiation needs to be developed before 'test-and-treat' rolls out with clear guidance and monitoring of linkage into the communities.

No conflict of interest

Abstract: P_55

Implementation research on PMTCT and pediatric treatment programs

Pediatric HIV disclosure intervention improves knowledge and clinical outcomes in HIV-infected children and adolescents in Namibia

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Introduction: In 2010, Namibia’s Ministry of Health and Social Services (MOHSS) developed and implemented a structured intervention to assist healthcare workers and parents/caregivers with HIV disclosure to children and adolescents. We conducted an evaluation of HIV-infected children and adolescents enrolled in care to assess impact of the intervention on child health outcomes and knowledge.

Material and Methods: Data was abstracted from electronic medical record databases and patient charts for HIV-infected children aged 7-15 years across 4 high-volume pediatric HIV clinics in Namibia. Disclosure rates, time to disclosure, and HIV knowledge in 314 children documented as participating in the disclosure intervention were described. Logistic regression was used to identify correlates of partial vs. complete disclosure. Paired t-tests were used to compare mean adherence percent and viral load before versus after enrollment among children who initiated the intervention in 2011.

Results: Among 314 children with documented participation in the disclosure intervention, 11% knew their HIV status at enrollment and 38% reached complete disclosure following enrollment. The average time to complete disclosure was 2.5 years (IQR: 1.2 – 2 years).
Among children who reported no or incorrect knowledge of why they take their medicine, 83% showed improved understanding after the intervention, defined as knowledge of HIV status or adopting intervention-specific language to discuss their medication use. Children who achieved complete disclosure were more likely to be older, have lower viral loads, and have been on ART longer. In comparisons before vs. 12-24 months after participating in the disclosure intervention, viral load decreased by 0.5 log copies/ml (N=53, p-value=0.006) while mean adherence scores increased by 7 percentage points (N=73, p-value=0.019) in children who had been on ART >18 months at enrollment and had pre and post enrollment measurements collected.

**Conclusion:** There is a need to improve pediatric HIV disclosure rates and experiences. This HIV disclosure intervention demonstrated improved viral suppression, adherence, and HIV knowledge and should be considered for translation to other settings.

**No conflict of interest**

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**Abstract: P_56**

Implementation research on PMTCT and pediatric treatment programs

**Improving Dried Blood Spot Transport Logistics for Early Infant Diagnosis (EID) in Nigeria: The SPEEiD Model**

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**Background:** WHO recommends that all children exposed to HIV be tested within four to six weeks of birth to ensure that all infected infants are initiated on treatment early. One major challenge with EID of HIV in Nigeria remains the absence of standardized logistic sample transfer systems, resulting in long turnarounds between date of sample collection and date of return results to the mother-baby pair. The USAID-funded ProACT project implemented by MSH pioneered a unique dried blood spot (DBS) transport model in Nigeria. Strengthening the Processes for Effective Early Infant Diagnosis of HIV (SPEEiD) model focuses on the transportation of dried blood spot (DBS) samples to regional PCR labs in partnership with the Nigerian Postal Service (NIPOST) utilizing its courier Express Mail Service (EMS). The NIPOST mail route has a network of over 900 post offices and 3,000 postal agencies spread across the country, ensuring coverage of most localities where HIV services are delivered. The objective of this study was to review the effect of utilizing an innovative DBS transport model in improving DBS transportation.

**Materials and Methods:** We carried out a retrospective analysis of logistic data from 177 samples transferred from 28 PMTCT sites using the SPEEiD model over a 12 month period from March 2013 to February 2014 in Kwara state, North Central Nigeria

**Results:** A review of the data showed a reduction in Turnaround Time (TAT) for return of results from 3-6 months to 3-4 weeks utilizing the SPEEiD Model. Results were received for 97% of samples (171/177) transported with this model, compared to 51% previously. The average cost of sample transfer was estimated at between $20-$40 per batch and remains comparatively less expensive to other models by at least 30%.

**Conclusions:** The MSH SPEEiD model remains an indigenous, cost effective, sustainable, and time sensitive sample transfer model which ensures that exposed infants are able to receive their EID test results quickly. This approach may be easily replicated by other partners within Nigeria and other similar resource limited setting with existing mail infrastructures. This model thus helps to provide a practical solution to DBS sample transfer, which remains one of the major challenges affecting early infant diagnosis of HIV in Nigeria.

**No conflict of interest**
Abstract: P _57

Implementation research on PMTCT and pediatric treatment programs

Active electronic surveillance of maternal HIV testing in the Prevention of Mother-to-Child Transmission continuum in South Africa – closing the gaps

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Introduction: Despite substantial reductions in vertically transmitted HIV in South Africa, elimination remains elusive due to persistent Prevention of Mother-to-Child Transmission (PMTCT) continuum coverage gaps, including incomplete maternal HIV testing. In Cape Town, the majority of pregnant women attend antenatal care (ANC) and deliver in a facility. At the time of this study the Western Cape PMTCT Guidelines recommended at least three maternal HIV tests: 1) at first presentation to ANC (± 20 weeks); 2) during the 3rd trimester (+32 weeks); and 3) during labour/immediately post-partum. We implemented an active surveillance system of the PMTCT continuum utilizing the existing electronic monitoring platform to examine coverage of maternal HIV testing using longitudinal individual patient data in Mitchells Plain Midwife Obstetrics Unit (MPMOU) in Cape Town.

Materials and Methods: All women who delivered at MPMOU between February 2014 and December 2015 were included. Separate routine paper-based antenatal, PMTCT and delivery registers were consolidated into a single electronic register (e-register) allowing identification of individual-level as well as facility-level coverage gaps. For each time-point at which an HIV test was indicated, we described the proportion of women who underwent testing, and the proportion identified as HIV-infected.

Results: Among the 3708 women included HIV prevalence was 14%. The median [IQR] age of HIV-infected women was higher (30[26-33] years) than HIV-uninfected women (26[22-30] years). Of the 61% of HIV-infected women who knew their status before the first antenatal visit, 68% were already on antiretroviral therapy (ART). Among women not previously known to be HIV-infected, 52% attended antenatal care before 28 weeks gestation and 94% tested for HIV; 65% had a visit between 28-40 weeks gestation of whom 81% were tested. Overall only 14% of all women were tested at labour/delivery. Among women never tested previously in pregnancy, 33% were tested during labour/delivery, versus 6% of women who had tested antenatally. Eighteen percent of women have no recorded HIV test at the facility. HIV prevalence was 6% among women tested for the first time in labour/delivery, but lower in HIV tests done at first ANC visit (4%) or in subsequent tests (1%).

Conclusion: 1. Although coverage with at least one HIV test for women presenting for antenatal care was high, repeat testing during follow-up and especially at delivery was low, even among those who were not tested antenatally. Since pregnant women with incident HIV infection and untreated HIV-infected women are at high risk of vertical transmission, peri-partum testing strategies should be strengthened.

2. More than 60% of HIV-infected women had been diagnosed before pregnancy and more than two thirds of these women were already on ART; adherence and viral load monitoring will become increasingly important to PMTCT programmes, as well as monitoring the long term outcomes of infants exposed to ART during early pregnancy.

No conflict of interest
Abstract: P_58

Implementation research on PMTCT and pediatric treatment programs

Infant Birth HIV Testing is Acceptable and Does Not Inhibit Return for 6-Week Testing

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Introduction: Initial HIV testing at age 4-6 weeks is recommended by WHO, capturing in-utero/intrapartum/early breastmilk transmission. However, in utero infection is associated with a rapid rise in mortality, as high as 20-30% by age 8-12 weeks, before most diagnostic tests return. HIV birth testing, identifying in-utero infection, has been proposed to allow earlier diagnosis and treatment, but there remain questions about feasibility and whether a negative birth test would inhibit mothers returning for the 6-week test, required to detect intrapartum/early breastmilk infection.

Materials & Methods: An ongoing observational cohort to evaluate PMTCT effectiveness was established in 13 health facilities in Lesotho. Pregnant women are enrolled and followed to 2 years postpartum. As part of this study, HIV birth testing was introduced at study sites. Dried blood spots were obtained at birth (birth to age 2 weeks) and sent to National Reference Laboratories in Maseru for DNA-PCR testing. Women delivering at home or other facilities were told to return to clinic for testing as soon as possible.

Results: 446 women enrolled in the study have delivered (all on ART during pregnancy); of these, complete data on birth testing was available for 438 (98.2%) deliveries. An HIV test at birth was performed on 350/438 (79.9%) of infants. Birth testing (by age 2 weeks) was less likely when women delivered at a non-study facility (OR 0.28, 95% CI 0.17-0.47, p=0.00) or delivered at home (OR 0.07, 95% CI 0.01-0.83, p=0.03) and more likely among mother who had disclosed their HIV status to a relative/friend (OR 1.86, 95% CI 1.15-3.01, p=0.01). Of 273 infants who had a birth test performed and were eligible for a 6-week test, 270 (98.9%) returned to have their 6-week HIV test performed; of 61 infants without a birth test eligible for a 6-week test, 59 (96.7%) had it performed.

Conclusion: Birth testing appeared acceptable to most women when offered, with lack of testing being associated with delivery at facilities without testing offered or delivery at home, as well as lack of disclosure. Performance of an HIV test at birth did not appear to reduce HIV testing at age 6 weeks.

No conflict of interest

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Abstract: P_59

Implementation research on PMTCT and pediatric treatment programs

Implementation of an active case management network to identify HIV-infected infants and accelerate the initiation of antiretroviral therapy, Thailand 2015


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Reviews in Antiviral Therapy & Infectious Diseases 2016_7
Background: Early initiation of antiretroviral therapy (ART) among HIV-infected infants can reduce HIV/AIDS associated morbidity and mortality. In Thailand in 2012, only 52% of HIV-infected infants received ART in the first year of life. We implemented a National Active Case Management (ACC) Network to promote early ART initiation in August 2014.

Methods: Thailand’s 2014 HIV Treatment Guidelines recommend that HIV-exposed infants have HIV PCR testing at birth, 1 and 2-4 months. When an HIV-infected infant (HIV PCR+) is identified, lab staff sends the result to the hospital. In addition, as part of the ACC, lab staff alert a regional case manager (CM) who contacts hospital staff to provide technical support, ensure prompt ART initiation, and support ART adherence among HIV-infected infants and mothers. We analyzed national data collected on HIV-infected infants by the ACC Network.

Results: During August 2014-December 2015, 101 infants had at least one positive HIV PCR. Mean age at first positive PCR was 93 days (range: 0-424) and 60 (59%) were female. Thirteen (13%) had a positive PCR result at birth; mean age 2.5 days (range: 0-8), and 88 (87%) had a positive result at other visits; mean age 106 days (range: 26-424). Among the 101 infants, 83 (82%) had received ART as of December 2015; 19 (23%) started ART before 2 months, 67 (81%) before 6 months, and 79 (95%) before one year of age. Among the 18 infants not receiving ART, 9 (50%) died, 6 (33%) lost to follow-up, and 3 (17%) were diagnosed HIV infection in December 2015. Mean age at ART initiation was 31 days (range: 15-52) for those HIV PCR positive at birth, and 129 days (range: 35-465) for those HIV PCR positive at other visits. The mean time from blood collection to notification of the CM until the infant started ART was 15 days (range: 0-140).

Conclusions: The ACC network has been successfully established and initial results suggest the Network is promoting early ART initiation. This Network may be adaptable to other settings.

No conflict of interest

Abstract: P_60

Implementation research on PMTCT and pediatric treatment programs

Implementation of dried blood spot HIV DNA PCR testing at birth among infants born to HIV-infected mothers in Thailand

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Background: Thailand’s National HIV Treatment and Care Guideline 2014 recommends HIV PCR testing using a dried blood spot (DBS) at birth for infants born to HIV-infected women. We report uptake and results of HIV PCR testing at birth.

Reviews in Antiviral Therapy & Infectious Diseases 2016_7
Abstract: HIV PCR testing is performed free of charge at two laboratories: the Department of Medical Sciences, Thailand Ministry of Public Health (DMSc) and Department of Medical Technology, Chiang Mai University (CMU). DNA is extracted (QIAGEN, DMsc and Chelex method, CMU) then amplified using real-time PCR (ABI 7300, DMsc and LightCycler 96 Real-Time PCR System, CMU). Infants at high risk for mother-to-child HIV transmission (MTCT) are defined as infants whose mothers had VL >50 copies/mL at gestational age >36 weeks or received HAART for <4 weeks prior to delivery. HIV PCR testing at birth data were compiled from the two labs and analyzed. We used National PMTCT Program data to estimate the number of infants born to HIV-infected mothers.

Results: An estimated 4,800 infants are born to HIV-infected mothers annually. From August 2014-December 2015, 3,024 HIV PCR at birth specimens were collected from infants at 538 hospitals. Uptake of HIV PCR testing increased from 33 specimens in August 2014 to 194 specimens in December 2015. Mean age at the time of collection was 2.4 (range 1-8) days. The median time from the lab receipt of the HIV PCR at birth until the result was reported was 5 days (range 1-24 days). There were a total of 13 (0.4%) positive HIV results and all 13 infections occurred among 852 high risk babies (1.5%; 95% CI: 0.8-2.6). Of 101 HIV-exposed infants diagnosed with HIV infection by HIV PCR during the reporting period (including infants diagnosed at visits after birth), 29 (28.7%) had an HIV PCR done at birth and 13 (44.8%) of these tested positive.

Conclusions: DBS HIV PCR testing of HIV-exposed infants at birth has been successfully implemented. All HIV infections diagnosed at birth occurred among infants at high risk of HIV infection. In resource-limited settings, DBS HIV PCR at birth is useful for detecting HIV infection among high MTCT risk infants.

No conflict of interest
questionnaires and VL testing conducted separately from either ART service.

**Results:** Between February and September 2015, 129 postpartum women were enrolled (mean age, 28 years; median nadir CD4 cell count, 400 cells/µL; median time postpartum, 10 days). After being offered the choice of postpartum ART services, 65% of women (n=84) opted for ACs and 35% (n=45) for PHC. There were no observed differences in demographic or clinical characteristics across women's choice. Reasons for choice included shorter wait times, ability to receive ART from lay counsellors and less frequent appointments among those choosing ACs; women opting for PHC cited proximity to their homes and/or routine infant health services and more frequent contact with clinicians. Among women choosing ACs, 64% were retained in ACs through 6 months postpartum; 14% never attended a club visit; 18% dropped out after at least one visit and 2% were referred from club back to PHC for clinical reasons. Of the women who chose ACs, 61% (n=51), 26% (n=22), and 13% (n=11) reported none, <1, and 1+ missed doses, on average, per 30 days on ART up to 6 months postpartum, respectively. In this group, 87% (n=73) had 6 month VL measure. Of these, 88% (n=64) and 92% (n=67) had VL<50 and <1000 copies/mL, respectively. Compared to women who were retained, women who disengaged from ACs were more likely to have VL≥50 (p=0.051) and VL≥1000 (p=0.001).

**Conclusions:** These data demonstrate that it is possible to refer HIV-infected women on ART in ACs in the immediate postpartum period. However ongoing retention in care remains a concern and further research is needed to evaluate long-term outcomes. ACs offer a potentially valuable model for differentiated ART care during the postpartum period in high-burden and resource-limited settings.

No conflict of interest

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**Abstract: P_62**

**Implementation research on PMTCT and pediatric treatment programs**

**Will low HIV re-test rates threaten the MTCT elimination agenda?: programmatic evidence from Zimbabwe**

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**Introduction:** Zimbabwe has an HIV prevalence of 16.1% among women in antenatal care and HIV is the leading cause of maternal death. Elimination of mother-to-child-transmission (MTCT) of HIV in Zimbabwe (<5%) will require effective identification and enhanced interventions among groups of HIV positive women at high risk of MTCT. Women who acquire incident HIV infection during pregnancy and breastfeeding are known to be at increased risk for vertical transmission. Accordingly, national guidelines in Zimbabwe recommend re-testing among all women with negative or unknown HIV status at first antenatal care (ANC) visit, 32 weeks gestation, labor and delivery (L&D), 6 weeks post-delivery and every 6 months until cessation of breastfeeding. Our objective was to determine recorded rates of HIV re-testing in Zimbabwe’s PMTCT program.

**Materials & Methods:** We utilized PMTCT program data from 824 health care facilities in 6 Provinces of Zimbabwe. Data used in this analysis comprised of routinely collected PMTCT program indicators, derived from multiple paper-based facility registers and reported in aggregate form on a monthly basis. We descriptively analyzed program data from September 2014 to December 2015 to determine number of women identified as eligible for HIV re-testing and HIV re-test rates among women testing negative at first antenatal care (ANC) visit. Data was entered into MS Excel and analysed using Stata V.13. Chi square tests were used to determine significance of differences in proportion of women re-tested for HIV in ANC, L&D and postnatal care (PNC) in PMTCT care settings.
Results: From Sept 2014-Dec 2015, among 245,816 women recorded at first ANC, HIV prevalence was 13.2% (n= 32,463). Among HIV positive women, just over half (51.1%; n=16,583) entered ANC with a known HIV positive status, with the remaining testing positive at first ANC visit. With a total of 213,353 women testing negative at first ANC (eligible for re-testing at 32 weeks), a total of 115,730 re-tests (54.2%) were recorded in ANC over the same period of interest. Compared to the number documented as eligible for re-testing, the proportion of women re-tested in Labor and Delivery were high (97.4%) while the re-test rate in postnatal care was low (54.8%), a highly significant difference $\chi^2(1, N = 179,668) = 2265.55$, $p < 0.001$.

Conclusions: While limited by our inability to document individual-level outcomes due to use of aggregate program data, our analysis documented low HIV re-test rates among pregnant and breastfeeding women in both antenatal and postnatal care in Zimbabwe. Failure to provide HIV re-testing as recommended will result in missed opportunities to identify incident HIV infections, known to increase risk of MTCT. Future research on supply- and demand-side barriers and implementation research on enhanced interventions to increase HIV re-testing in Zimbabwe’s PMTCT program should be supported as a national priority in the drive to eliminate pediatric HIV and keep mothers alive.

No conflict of interest

Abstract: P_63

Implementation research on PMTCT and pediatric treatment programs

Effective facilitated linkage to care among HIV+ children identified by a hybrid mobile testing program in rural East Africa


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Background: Less than half of HIV+ children in sub-Saharan Africa currently receive antiretroviral therapy (ART). Expanded testing programs have increased diagnoses, but a large portion of HIV+ children fail to establish care. Effective mechanisms that link HIV+ children from testing to treatment are needed.

Methods: Children in 16 rural Kenyan and Ugandan communities had HIV testing via a hybrid mobile strategy of community health campaigns followed by targeted home based testing [SEARCH HIV test-and-treat trial (NCT 01864603)]. HIV+ children aged 2-14 years and their caregivers were offered facilitated linkage that included redeemable transport vouchers upon arrival to clinic, telephone access to clinicians, and appointment reminders with outreach tracking of non-linkers. The proportion of HIV+ children not in care (=HIV RNA > 1000 copies/ml and no prior clinical record) that successfully linked (=attended ≥1 appointment during the following year) was calculated. Child and maternal characteristics were examined as predictors of linkage failure using multivariate logistic regression.
Results: Of 59,544 children tested, 621 (1%) were HIV+. Among these, 228 (37%) children were not previously in care, the median age (IQR) was 7 years (4-10); 159/228 (70%) had CD4>500, 61% were female, 157 lived in Kenya (69%) and 66/228 (29%) of caregivers reported not knowing the child’s HIV+ status. Overall 181/228 (79%) successfully linked to care within 1 year (Table), with 133(73%) attending their initial referral appointment.

<table>
<thead>
<tr>
<th>Linked</th>
<th>Attended initial appointment after referral at testing site</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>169 (74%)</td>
</tr>
<tr>
<td>Missed initial appointment but attended after outreach tracking</td>
<td>12 (5%)</td>
</tr>
<tr>
<td>Unlinked</td>
<td>Found in tracking, but didn’t go to clinic</td>
</tr>
<tr>
<td></td>
<td>30 (13%)</td>
</tr>
<tr>
<td>Reported to have died or moved</td>
<td>6 (3%)</td>
</tr>
<tr>
<td>Not found in tracking</td>
<td>11 (5%)</td>
</tr>
</tbody>
</table>

Table. Linkage outcomes of 228 HIV+ children not previously in care

Residence in Kenya (adjusted odds ratio [aOR]: 3.5, 95%CI: 1.2-10.4) and not having a mother herself on ART (aOR: 2.5, 95%CI: 1.2-5.0) was associated with non-linkage, while gender, age, CD4 count, test site, household wealth index, maternal marital status and maternal education were not.

Conclusion: This facilitated linkage-to-care program successfully linked 79% of HIV+ children to treatment programs, with most attending their initial referral appointment. Similar strategies that include linkage of HIV+ mothers could be employed by countries working towards universal testing and treatment of children.

No conflict of interest

Abstract: P_64

Implementation research on PMTCT and pediatric treatment programs

At birth point of care early infant diagnosis is accurate and feasible in primary health care facilities and enables earlier detection of higher numbers of HIV-positive infants

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Introduction: Global access to paediatric antiretroviral treatment is limited by poor access to early infant diagnosis (EID). Recent WHO guidelines recommend testing at birth to expand on the current testing algorithm around 4-6 weeks. Point-of-care (POC) testing may provide opportunities to operationalize near birth testing. We evaluated the accuracy, feasibility, and diagnostic yield of a nucleic acid POC test at birth in primary health clinics (PHC) in Mozambique.

Methods: Infants born to HIV-infected mothers delivering consecutively at six PHC maternity wards were tested by nurses using the Alere q POC EID technology within 24 hours of delivery. Dried blood spot specimens were collected simultaneously for testing on the Roche CAP/CTM laboratory EID technology. Enrolled newborns were then followed up after one month for testing on both POC and laboratory testing. Test operators were blinded to results of the other assay. Demographic and treatment data were collected for each mother-infant pair.

Results: A total of 1,361 HIV-exposed infants were successfully tested at birth using both technologies. Twenty-two infants tested HIV-positive using both assays at birth, for a POC test sensitivity and specificity of 100% (95% CI: 97.6-100).
of health worker - HIV diagnostic assistants (HDAs)- to focus on identifying HIV-positives and linking them to care and treatment.

Materials and Methods: EGPAF-Malawi subcontracted two local organizations to hire 140 HDAs to be assigned to 63 priority health facilities in seven districts. The HDAs were deployed between July and September 2015 after undergoing intensive HIV testing and counseling training including child counseling and DNA/PCR DBS collection and ongoing supervision. EGPAF reviewed routinely collected and aggregated HIV testing data from the Ministry of Health for the six-month period prior to and following the introduction of HDAs. EGPAF aimed to understand how testing levels and yield for children was affected by this intervention.

Results: Following the intervention, the number of children provided with HTS services more than doubled from 4251 in April-June to 9344 in July-September and to 15,655 in October – December 2015. The number of HIV-positive children identified increased from 249 in April – June to 484 in July – September and 561 in October – December 2015. A total of 205 (42%) HIV-positive children were initiated on ART in July – September 2015 period and 247 (44%) in October – December 2015 period.

Conclusion: The introduction of HDAs significantly increased both the number of children tested for HIV and the number of HIV-positive children identified in a short period of time. The availability of properly trained, dedicated cadres of lay health workers to provide HIV testing and counseling services can expedite the identification of HIV-infected children. We anticipate the number of children initiated on ART to increase with the implementation of Test and Start guidelines since at present only under five children are universally eligible for ART.

No conflict of interest
Abstract: P_66

Implementation research on PMTCT and pediatric treatment programs

Outcomes of Children Transferring Out of a Specialist Pediatric Clinic using Linkage to Laboratory Data

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Background: Maintaining children and adolescents on antiretroviral therapy (ART) across the continuum of HIV care is crucial to successful treatment programs. Decentralization of pediatric HIV care in resource-limited settings has expanded ART access. However, there is limited data on outcomes of children transferred from higher to lower level health facilities. We aimed to describe the outcomes of children who initiated ART at Red Cross War Memorial Children's Hospital (RCWMCH), a tertiary pediatric facility in the Western Cape Province (WCP) of South Africa, and were transferred to lower level facilities within the WCP.

Methods: We included ART-naïve HIV-infected children who started ART at <16 years old at RCWMCH from 2008-2011. Since 2007, a single unique patient identifier is used across all health services in WCP. The National Health Laboratory Service (NHLS) conducts all WCP public sector laboratory tests. We linked RCWMCH cohort data to NHLS data using the unique identifier to determine the proportion of children that successfully transferred to lower level facilities. Successful transfer was defined in two ways: a laboratory test performed by a lower level health facility (i) ≤18 months or (ii) ≤48 months after transfer date. The first interval corresponds to guideline recommendations for annual CD4/viral load monitoring; the second captures all children retained in care. We used logistic regression to identify characteristics associated with successful transfer. In children who successfully transferred, we compared CD4% at transfer and first visit post-transfer.

Results: The median age at ART initiation of 1127 children included was 5.6 months (interquartile range [IQR] 3.1-19.9); at ART initiation 85% had WHO stage III/IV disease and 57% were severely immunosuppressed. A total of 725 (64%) children were transferred; 69% (496) and 76% (541) successfully transferred within 18 and 48 months respectively. Since there is about 90% compliance with annual CD4/viral load monitoring guidelines, we estimate that up to 85% of children may have actually successfully transferred. Median time to successful transfer was 5.4 months (IQR 3.7-7.8). Among the 184 children (25%) who did not transfer successfully, 11% returned to RCWMCH. In patients who successfully transferred, median (IQR) CD4% increased between transfer and first visit post-transfer [25.1% (17.3-33.8%) vs 30.2% (22.9-36.6%), p<0.0001].

Virologically suppressed children and those on ART for 6-11.9 months (compared to shorter or longer durations) were more likely to successfully transfer (odds ratio (OR):1.69; 95% confidence interval (CI):1.19-2.4 and OR:1.76; 95%CI:1.09-2.83 respectively). However, neither variable was associated with successful transfer in multivariable analysis. Children with the transfer site recorded in the RCWMCH database were more likely to successfully transfer compared to children where no site was recorded in the database (OR:1.53; 95%CI:1.09-2.16, p<0.05).

Conclusion: The proportion of children remaining in HIV care by 48 months after transfer was at least 76% with the majority reaching the referral facility and undergoing a laboratory test within 18 months of transfer. In children who successfully transferred, CD4% improved after transfer. This suggests that pediatric ART decentralization is feasible with good outcomes, however outcomes in those who were lost after transfer need further investigation.

No conflict of interest
Implementation research on PMTCT and pediatric treatment programs

Pediatric First 2 90s: Assessment of HIV testing and linkage to care among infants and children in Zimbabwe

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Abstract: P_67

Implementation research on PMTCT and pediatric treatment programs

Pediatric First 2 90s: Assessment of HIV testing and linkage to care among infants and children in Zimbabwe

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Introduction: An estimated 12.3% of the 1,390,211 people living with HIV (PLHIV) in Zimbabwe are children aged 0-14 years. Reaching virtual elimination of pediatric HIV and ambitious 90-90-90 targets in Zimbabwe will require strengthening access to HIV testing and counseling (HTC) for children at all health care entry points and ensuring effective linkages to treatment and care for those testing HIV positive. The objective of our assessment was to establish current HIV test yields among children aged 0-14 years and documented linkage of those testing HIV positive to treatment and care from different health care entry points.

Materials & Methods: We selected 11 health facilities in Makoni and Mutare Districts of Manicaland Province using a modified probability proportional to size technique based on number of PLHIV accessing antiretroviral therapy (ART) over the previous year. In October 2015, we conducted a retrospective cohort analysis, tracing all individuals accessing HIV testing services from Jan-Mar 2015 through multiple facility-based registers. Available data for each patient entry aged 0-14 years was recording including age, gender, entry point for HIV testing, receipt of HIV test result, whether HIV test was first or repeat test and HIV test method employed. Among those testing HIV positive, linkage to care and treatment up to September 2015 was determined by patient identification in pre-ART and ART registers. De-identified data were entered into MExcel and analyzed descriptively using StataV12.

Results: Children aged 0-14 comprised 10.3% (392/3,816) of all HIV tests conducted at selected health facilities from Jan-March 2015. A general increasing trend of HIV positive test results was observed in children with increasing age. Infants less than 2 months tested in Early Infant Diagnosis (EID) had the lowest HIV test yield (1.9%) and children aged 5-9 years testing in diagnostic settings had highest test yield (10.6%). The overall positivity rate among children from 1 to <14 years was 7.3% (22/301), with the majority of HIV positive children (77.3%; n=17) having received HIV testing for the first time. Of concern, 28% (7/25) of girls aged 10-14 tested were documented as being HIV tested while receiving antenatal, postnatal or family planning services. Among all infants and children testing HIV positive (n=24), 79.1% (n=19) appeared in pre-ART registers, and 50% (n=12) in ART registers. Older children aged 5-9 (n=7) and 10-14 (n=3) had poorest linkage to ART, with the majority of those failing to link to care and treatment tested in diagnostic settings with no vital status or transfers documented.

Conclusions: We observed increasing HIV test yields and decreasing linkage to HIV care and treatment services among older children. The majority of children tested positive in diagnostic entry points, highlighting the potential value of routine HIV testing of all children presenting for inpatient and outpatient services in endemic countries such as Zimbabwe. Greater effort is required to ensure standard documentation procedures for entry codes, transfers and vital status outcomes among all children receiving HIV testing, care and treatment services.

No conflict of interest

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Implementation research on PMTCT and pediatric treatment programs

Estimation of timely EID and mortality among HIV-exposed infants in Mashonaland East Province, Zimbabwe: a sampling-based approach

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Introduction: In Zimbabwe, HIV prevalence among women in antenatal care (ANC) is 16.1%. While national estimates based on aggregate data indicate only 45% of HIV-exposed infants receive timely Early Infant Diagnosis (EID), determination of survival and timely access to EID is difficult due to documentation of health services received by HIV positive pregnant women and their exposed-infants in multiple, paper-based registers. Accordingly, the proportion of individual mother-infant pairs who uptake timely EID is not routinely reported. We conducted a population-based survey in which individual HIV infected mother-HIV exposed infant pairs were followed through registers to identify and trace a random sample of HIV positive women with no documented EID for their exposed infants to ascertain better estimates of timely EID completion.

Methods: A modified probability proportional to size schema was used to select 45 of 193 health facilities in Mashonaland East Province. Outcomes of all HIV positive mothers enrolled in ANC from Apr-12 to May-13 were traced through facility registers to determine documented uptake of EID for their HIV-exposed infant within three months of birth. A random sample of women with no documented uptake of EID was traced at household level to determine true outcomes using a structured, pre-tested questionnaire. We estimate cumulative incidence of timely EID and death by 3 months of age among the population of HIV-exposed infants. Data was entered into Open Data Kit (ODK) and analysed using StataV13.

Results: Among a population of 18,065 women attending ANC, 2,651 were HIV positive (14.7%); 31.2% (n=828) had documented uptake of EID within three months (95%CI: 29.5%-33.0%). From Mar-May15, we attempted household tracing of a random sample of 643/1,826 (35.3%) with no documented EID, with 256(39.8%) of those mothers successfully traced at household level. The majority of infants (76.9%; n=190) traced were reported to have had DNA PCR samples for EID, however only 38.4% (n=73) confirmed timely EID within 3 months of birth. We observed a high rate of HIV-exposed infant mortality (17.8%; 66/371) among infants for whom vital status outcomes could be ascertained and ‘my child died’ was the number one reason provided among the ‘no EID’ group. Weighted population estimates indicate cumulative incidence of infant death by 90 days at 3% (95%CI: 3.4% to 4.4%) and an annual infant mortality rate of 7.7% (95%CI: 4.7%-13.5%). Cumulative incidence of timely EID with death as a competing risk was 60% (95%CI: 58.7% to 61.3%).

Conclusion: Our findings indicate uptake of timely EID among HIV-exposed infants is currently underestimated, with sample-corrected cumulative incidence of timely EID 15% higher than reported national estimates. High, early mortality among HIV-exposed infants underscore need to identify HIV positive mother-HIV exposed infant pairs at high risk of adverse outcomes and loss to follow up. Discrepant rates of timely EID by data source indicate urgent need to strengthen health information systems. Sampling-based approaches are valuable tools for providing a better picture of PMTCT program effectiveness.

No conflict of interest
Abstract

Implementation research on PMTCT and pediatric treatment programs

Self-reported antenatal adherence to predict postnatal viral rebound among women initiating ART during pregnancy in Cape Town, South Africa: a prospective study

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Background: Maintaining postnatal viral suppression is critical to minimize risk of mother-to-child transmission (MTCT) through breastfeeding and ensure ongoing maternal health. Integrated antenatal care and antiretroviral therapy (ART) services have contributed to improved ART uptake and lower transmission rates. However, there are increasing concerns about adherence and transmission in the postnatal period. Identifying simple ways to identify women at risk of postnatal viraemia will have benefits for PMTCT programs and maternal health.

Methods: HIV+ women who initiated ART during pregnancy at a large primary care clinic with integrated antenatal and ART services were recruited and followed prospectively as part of the MCH-ART study in Cape Town, South Africa. Consenting women completed up to eight study visits from ART initiation through 12 months postpartum, including demographics, reported missed doses in the previous 30 days and viral load (VL) measurement. We investigated time to viral rebound >50 and >1000 copies/mL and the association between an aggregate antenatal adherence measure (self-reported missed ART doses from ART initiation through to delivery) and viral rebound among women who had VL ≤50 copies/mL at delivery.

Results: Of 471 women who were breastfeeding at delivery and enrolled into postpartum follow-up, 339 women had a VL ≤50 copies/mL at delivery and were included in this analysis (97% Xhosa speaking, median age 28, median 18 weeks on ART). Across study visits from ART initiation through delivery, 28% of women reported any missed ART doses, 16% reported one or more and 9% reported two or more missed doses/month on average. Using product limit methods, 98%, 87% and 68% of these women remained suppressed below 50 copies/mL at six weeks, six months and 12 months postpartum, respectively. At 12 months postpartum 79% of women remained suppressed below 1000 copies/mL. In a proportional hazards model adjusted for age, duration of antenatal ART and previous ART use, reporting one or more missed doses per 30 days on average during pregnancy was associated with a two-fold increase in the hazard of postnatal viral rebound >50 and >1000 copies/mL (adjusted hazard ratio [aHR] 2.31 and 2.64, respectively, both p<0.001). Previous ART use increased the hazard of viral rebound while increasing age and weeks on ART were protective. When stratified by age, the association between missed doses and viral rebound was stronger among women ≥25 years compared to younger women (aHR 2.49 and 2.18 respectively for VL>50 copies/mL; aHR 3.88 and 2.20 respectively for VL>1000 copies/mL).

Discussion: In this cohort of women who initiated ART in pregnancy and were suppressed at delivery, report of antenatal missed ART doses was predictive of postnatal viraemia. Self-reported antenatal missed doses, together with other routinely collected antenatal risk factors like younger age, time on ART and prior ART use, could be used to flag women at high risk of viral rebound after delivery. There is need for further research to explore how reported antenatal ART adherence could be used in low-resource routine care settings to target adherence interventions to the women most at risk.

No conflict of interest
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Implementation research on PMTCT and pediatric treatment programs

WHO HIV testing algorithm fails to identify substantial proportion of infants with HIV infection


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Background: The WHO HIV testing algorithm for infants at sick care visits involves HIV serologic testing followed by virologic testing if seropositive. Additionally, in PMTCT programs, HIV-exposed infant testing algorithms include virologic testing at 6 weeks, and serologic testing at 9 and 18 months. PCR testing is conducted on infants with positive HIV serology while seronegative infants receive repeat serotesting at future visits.

Materials & methods: Within a clinical trial (NCT02063880) conducted among critically ill, hospitalized children in 4 Kenyan hospitals, serologic and virologic tests on all HIV-exposed infants < 9 months were performed. Maternal and infant serologic tests (using Determine® or KHB® for first test and Unigold® or First response® for second test per Kenyan guidelines) were performed in tandem. Dry blood spots were collected and tested using HIV DNA PCR irrespective of serological test results to determine the proportion of infant infections missed by the WHO algorithm.

Results: Among 142 HIV-exposed infants < 9 months with both serologic and PCR testing, 44 (31%) were PCR positive. Among 50 seronegative infants 12 (24%) were PCR positive; among 82 seropositive infants 29 (35%) were PCR positive; among 10 serology indeterminate infants 3 (30%) were PCR positive. The research algorithm, which included PCR testing of seronegative infants, identified 38% more infant infections, compared to the WHO algorithm (44 vs 32 infections, respectively). Among the 12 serology negative, PCR positive infants, 7 (58%) were missed by PMTCT programs because their mothers reported testing HIV negative during pregnancy, likely representing acute infections during late pregnancy and postpartum; 2 (17%) infants of known HIV-infected mothers had tested negative earlier during infancy, likely representing breastfeeding transmissions; 2 (17%) infants were not previously tested despite known maternal HIV status; and 1 infant's mother was not tested for HIV in pregnancy.

Conclusions: The current WHO HIV testing algorithm for sick infants using serology for screening did not detect a substantial number of infants with HIV infections detected by PCR. Virologic testing of HIV-exposed infants presenting for sick visits, regardless of their serologic status, may be warranted to improve early detection and treatment of HIV.

No conflict of interest

Abstract: P_71

Implementation research on PMTCT and pediatric treatment programs

Low sensitivity of Xpert MTB/RIF on routine pulmonary samples from HIV-infected children in Soweto, South Africa

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Introduction: In December 2010, the WHO endorsed the Xpert MTB/RIF (Xpert) assay as the initial diagnostic test for simultaneous detection of Mycobacterium tuberculosis and...
Abstract

Resistance to rifampicin in adults with presumptive TB. In 2011, the WHO recommendation was extended to children, based on generalisation of data from adults. South Africa was the first country to replace smear microscopy by Xpert on a national scale. While the performance of Xpert has been studied in hospitalized children under research conditions, little is known about the assay’s performance at routine paediatric outpatient clinics. The aim of this study was to compare the yield of smear microscopy, culture and Xpert and determine the diagnostic performance of Xpert in HIV-infected children presenting with suspected TB at a routine care clinic.

Methods: HIV positive children (aged 0-14 years) seen at the Harriet Shezi pediatric HIV clinic in Johannesburg, South Africa, were eligible if the routine care physician requested a respiratory sample for assessment of TB. Induced sputum or spontaneous sputum samples were collected by routine clinical staff. Smear microscopy, culture and Xpert were performed on a single specimen. Specimens did not undergo any pre-processing and were analysed according to standard procedures at certified laboratories. Yield was defined as the percentage of positive results per specimen. Sensitivity and specificity was calculated using liquid culture as the gold standard. Differences between groups were evaluated using χ² tests.

Results: Between July 2011 and September 2013, 238 HIV-infected children were assessed by Xpert. Median age was 5.8 years, median CD4 count was 730 (Inter-quartile range IQR: 362-1322). Most children (153, 64%) were on ART for a median of 1.6 years (IQR: 0.4-2.9) at the time of sample collection but only 44% (n=67) were suppressed (viral load <400 copies /ml). The majority (142, 60%) of specimens collected were induced sputum specimens. Seven children were culture-positive, of which only 1 was Xpert positive, and none were smear microscopy positive. The yields of smear microscopy, culture and Xpert were 0%, 4.4% and 0.6%, respectively. Among the 238 sputum specimens, Xpert and culture results were available for 158 (66%). Sensitivity of Xpert was 14.3% (95% CI: 0.4-57.9), specificity 100% (95% CI: 97.6-100.0), positive predictive value 100% (2.5-100); and negative predictive value 96.2% (91.9-98.6).

Conclusions: At a routine pediatric outpatient HIV care clinic, the yield of all mycobacteriological assays (smear microscopy, Xpert and culture) in HIV-positive children with suspected TB was very low (<5%). Compared to culture, sensitivity of Xpert was low, but precision was poor given the low number of positive cases. Novel non-sputum based diagnostic assays, preferably assays that do not depend on the detection of mycobacteria, are needed for efficient diagnosis of TB in children presenting with symptoms of TB at outpatient clinics.

No conflict of interest

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Implementation research on PMTCT and pediatric treatment programs

Effect of alcohol consumption and psychosocial stressors on preterm and SGA births in HIV infected women in South Africa: a cohort study

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Background: As the use of antiretroviral therapy (ART) has greatly reduced mother to child transmission of HIV, the number of HIV exposed uninfected infants (HEU) is rapidly rising. A large number of HEU infants are born preterm and small-for-gestational-age (SGA), conditions which put children at higher risk of mortality, morbidity, poor growth and development. The high incidence of preterm and other poor birth outcomes is partially attributed to maternal HIV infection and ART use. Psychosocial stressors such as depression and stress, intimate partner violence (IPV) and alcohol use in pregnancy have been linked to preterm births and SGA in general populations. Though the prevalence of psychosocial stressors and alcohol abuse is high in many HIV infected (HIV+) populations, the role of these exposures on birth outcomes in this population is yet to be evaluated.
Materials & Methods: This prospective cohort study is part of a larger study of ART services for HIV+ pregnant/postpartum women in Cape Town, South Africa, the MCH-ART study. Participants included women initiating ART with efavirenz+emtricitibine+tenofovir during pregnancy. Using the intergrowth-21st standards, SGA was defined as birthweight <10th percentile for gestational age. Preterm birth was defined as birth <37 completed weeks. Alcohol consumption using the Alcohol Use Disorders Identification Test (AUDIT), depression using the Edinburgh Postnatal Depression Scale (EPDS), nonspecific psychological distress using the Kessler-10 scale and IPV using the WHO Violence Against Women tool were measured during the second trimester of pregnancy (median gestation at assessment, 5 months). Log binomial regression models were used to estimate the risk ratios (RR) and 95% confidence intervals of the effects of psychosocial stressors and alcohol on SGA and preterm.

Results: Of 571 mother-infant pairs, a quarter of the pregnant women (26%) reported moderate to heavy alcohol consumption in pre-conception and early pregnancy periods, 11% reported depressive symptoms, 7% reported nonspecific psychological stress and 15% reported experiencing physical or psychological violence. 14% of the infants were born preterm and 12% were SGA. Infants born to women reporting moderate to heavy drinking were twice (adjusted RR 2.00 [95% CI 1.13, 3.54]) more likely to be SGA compared to women reporting low alcohol intake in early pregnancy. Alcohol consumption did not have a significant effect on incidence of preterm birth. Moderate to severe depressive symptoms, non-specific stress, physical and psychological violence did not increase the risk of SGA or preterm birth significantly.

Conclusions: The observed lack of effect of mental health stressors on birth outcomes is possibly due to the high incidence of ART associated preterm birth, and homogeneity of potential mediators such as utilization of antenatal care and adherence to ART in our study population. Alcohol consumption during pregnancy increased risk of SGA substantially. In populations with a high prevalence of alcohol abuse, interventions focusing on reduction in periods before conception and early pregnancy may lower the incidence of SGA.

No conflict of interest
Methods: A retrospective review was done from October 1, 2015-March 30, 2016 of the admission, HIV Testing and Counseling (HTC), early-infant-diagnosis dried blood spot (DBS), and linkage registers at the Kamuzu Central Hospital inpatient pediatric ward. A descriptive analysis of the data was performed.

Results: During the above period, 6,958 children were admitted on the pediatric ward. 11,548 guardians and children were tested of which 4,761 were guardians and 6,787 were children admitted on the wards. Total testing coverage was 97.5% of pediatric admissions, 37% increase from the baseline of 60%. Of those tested, 462 total (108 males, 354) were found positive (4% testing yield), with 206 children (114 males, 92 females) newly identified, giving an inpatient testing yield of 3% (3-6% is the national average). Of the children found infected, 55 (27%) were 0-11 months, 128 (62%) were 1-9 years, and 23 (11%) were 10-14 years. Children over 14 years are not admitted to the pediatric wards.

Conclusion: A simple system such as the ‘sticker system’ can help improve testing coverage of high volume inpatient settings without increasing personnel in resource limited setting. Achieving universal testing coverage in high-burden, high volume inpatient sites is possible. Normal to high testing yields signify importance of inpatient testing for identifying children, especially for small babies where rates are still high despite preventing mother-to-child-transmission.

No conflict of interest

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Abstract: P_74

HIV infection and adolescents

Prevalence of acute and chronic malnutrition in adolescents living with HIV in Lilongwe, Malawi

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Introduction: Though the adverse effects of HIV on nutritional status are widely understood, there is a paucity of nutrition-related data for adolescents living with HIV (ALHIV). Most research, national programming and treatment interventions in Malawi focus on children under five and pregnant women. Baylor College of Medicine Abbott Fund Children’s Clinical Centre of Excellence Malawi (BCOE) has developed comprehensive programming for ALHIV throughout Malawi; however, nutritional needs are unmet in this population. Baseline data on the rates of malnutrition in ALHIV receiving care at BCOE were reviewed to help guide programming needs.

Material and Methods: Electronic medical records (EMR) at BCOE were reviewed between January to March 2015. Weight and height for all active adolescent patients aged 10-19 years living with HIV were reviewed, and z-scores for height-for-age and body mass index (BMI)-for-age were calculated. Definitions for wasting and stunting followed WHO guidelines: mild wasting between -2 and -1 z-score, moderate wasting and stunting between -3 and -2, and severe wasting and stunting below -3.

Results: 1172 adolescent patients had a visit during the evaluated time period (590 male, 582 female). 757 were younger teens aged 10-14 years, and 415 were older teens 15-19 years. 1095 (93%) had both height and weight recorded. Of those with complete data, 311 (28.4%) had mild wasting, 105 (9.7%) had moderate wasting, and 35 (3.1%) had severe wasting. 340 (31%) had moderate stunting, and 158 (14%) had severe stunting. Using logistic regression analysis, males had higher rates of
wasting (OR 2.29, 1.79-2.94), as did older teens (OR 1.32, 1.02-1.7). Males also had higher rates of stunting (OR 1.68, 1.32-2.14), as did younger teens (OR 1.35, 1.05-1.73). Males had higher risk of severe wasting (OR 2.88, 1.36-6.08) than moderate wasting (OR 2.47, 1.6-3.8) and mild wasting (OR 1.55, 1.21-2.06).

Conclusions: The prevalence of wasting and stunting is high in ALHIV, and was higher amongst males. Older teens are more affected by acute malnutrition, while younger teens are more affected by chronic malnutrition. Screening for malnutrition in ALHIV should be emphasized in national programming, and treatment programming tailored for ALHIV needs to be scaled up to prevent nutrition-related morbidity and mortality.

No conflict of interest

Abstract: P_75

HIV infection and adolescents

Beyond Clinical Trials: associations between ART regimens and reporting multiple medication side-effects among adolescents in South Africa

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Introduction: High rates of non-adherence to antiretroviral therapy (ART) ranging from 36% in the past week (Cluver et al., AIDS 2015) to 93% at two years (Nachega et al., JAIDS 2009) have been reported amongst treatment-initiated adolescents living with HIV in Sub-Saharan Africa. Side-effects are a vital characteristic of any prescribed regimen that can importantly influence non-adherence to medication—limiting long-term treatment success. Although drug trials (which often exclude or include too few children and have limited follow-up periods) have shown ART regimens to be associated with adverse events, pragmatic studies investigating ART-associated side-effects among adolescents in resource-limited settings are rare beyond clinical trial settings. This study examines cross-sectional associations between various types of ART and reporting multiple medication side-effects, conducted with the largest community-traced sample of HIV-positive adolescents at present.

Materials & Methods: The study traced, interviewed and included N=1059 ART-initiated adolescents aged 10-19 years attending 53 healthcare facilities in the Eastern Cape in 2014-15. Interviewed adolescents provided names and/or photographs of their current medication. A literature-based strategy was used to decide which measured symptoms to analyse as side-effects. The major outcome was computed to include adolescents reporting more than 3 side-effects in the past 6 months, hereafter called multiple medication side-effects. Potential confounders included age, gender, rural residence, overall health, food insecurity, lacking basic necessities, antibiotics/TB medication, pill burden, medication frequency, ART non-adherence, CD4 count <350 cells/mm³ and time on treatment. Multivariate logistic regression analyses—including all covariates simultaneously—followed by post-estimation computation of adjusted predicted probabilities for each ART were conducted in Stata 13.

Results: Prevalence of symptoms included in computing the outcome was: headache (77%), nausea/vomiting (44%), diarrhea (43%), tiredness (43%), skin rash (41%), stomach problems (41%), insomnia/bad dreams (35%), dizziness (34%), ear problems (34%), weight loss (28%), anxiety (3%). Nearly half (49%) of the adolescents were on Efavirenz-based regimens, Lamivudine (43%), Efavirenz (34%), Abacavir (31%), Abacavir + Lamivudine + Efavirenz (ABC+3TC+EFV) (22%), Tenofovir + Emtricitabine + Efavirenz (TDF+FTC+EFV) (15%), second line ART (12%), Lopinavir/Ritonavir (LPV/r) (11%), Zidovudine (6%), Stavudine (5%) and Tenofovir (4%). Prevalence of multiple medication side-effects was 58%. Compared with other ART, treatment with a fixed dose combination containing TDF+FTC+EFV was independently associated with multiple medication side-effects, OR=1.81 (95% CI 1.04-3.17). LPV/r co-formulation was significantly associated with a 47% reduction in
Conclusions: In this study of HIV+ ART-initiated South African adolescents, treatment with TDF+FTC+EFV increases the odds of reporting multiple medication side-effects by 81% independent of known and measured covariates whereas Lopinavir/Ritonavir co-formulation continues to be well-tolerated by adolescents independent of time on treatment. Increasing the proportion of HIV+ adolescents on combination therapy with Lopinavir/Ritonavir may improve adherence to ART, leading to better long-term treatment outcomes for adolescents.

No conflict of interest

Abstract: P_76

HIV infection and adolescents

Resilience in perinatally HIV-infected and perinatally HIV-exposed adolescents and young adults growing up in high risk environments

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Introduction: Globally, pediatric HIV is increasingly an adolescent and young adult (AYA) epidemic. Research with perinatally HIV-infected (PHIV+) AYA has prioritized identification of poor health and behavioral risk outcomes but understanding positive outcomes in spite of adversity is critical to informing evidence-based programs. Using data from a New York City longitudinal cohort study (CASAH) of PHIV+ and perinatally HIV-exposed but uninfected (PHIV-) youth, we examined psychosocial and health outcomes pertinent to understanding resilience.

Material and Methods: Data are from the most recent CASAH follow-up interview (2014-2015) with 135 PHIV+ and 86 PHIV- AYA to date who were originally recruited at ages 9-16 years (2003-2008). A psychosocial battery is administered every 12-18 months; PHIV+ youth viral load (VL) and CD4 are abstracted from medical records. Data on psychiatric disorders, sexual behavior, substance use disorders (SUD), young adult milestones were compared across HIV status and age groups. Descriptive statistics, and chi square and t-tests for comparing groups were used.

Results: Most participants were female (55%), African-American (67%), living in impoverished communities (100%); mean age was 22 years (range 15-28). There were no HIV-status differences in rates of psychiatric disorder (28%), SUD (27%), or past 3-month condomless sex (36%). Only a minority of PHIV+ AYA had a psychiatric disorder (29%) or SUD (25%). Most PHIV+ AYA aged > 19 years had achieved young adult milestones: 78% had graduated high school, 29% had taken college classes; 40% were working; 86% had ever had sex; 41% were in romantic relationships. Achieving milestones did not differ by HIV status. Among all PHIV+ AYA, most had positive health outcomes: CD4 >250 cells/mm³ (79%) and VL<1000 copies/ml (70%); 46% had VL<50 copies/ml. Older age was associated with CD4 <250 cells/mm³ ($X^2=7.01, df=2, p=.030$) and having a psychiatric disorder was associated with VL >1000 copies/ml ($X^2=4.29, df=1, p=.038$).

Conclusions: In one of the few ongoing US-based study with this population, we found that, despite significant biopsychosocial risks, many PHIV+ AYA have positive health and mental health outcomes and achieve AYA milestones comparable to PHIV- AYA and other vulnerable populations. Identification of the protective factors conferring this resilience can inform evidence-based practice for the millions of PHIV+ youth world-wide.

No conflict of interest
Abstract: P_77

HIV infection and adolescents

Resilience in Perinatal HIV+ Adolescents in South Africa

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Introduction: Increasing numbers of perinatally HIV infected (PHIV+) youth are surviving into adulthood with better access to ARV treatment. However, few studies specifically examine achievement of positive outcomes in the face of adversity (resilience) for PHIV+ youth. Social Action Theory (SAT) guides the organization of contextual, social and self-regulatory factors that facilitate health and wellbeing and provided the theoretical framework for this study of resilience in PHIV+ youth in South Africa.

Materials & Methods: Data are from youth and caregiver baseline interviews, simply pooled from a pilot and larger randomized control trial (RCT) of the VUKA Family program in KwaZulu-Natal, South Africa. The pilot RCT involved 66 children and their caregivers. The larger RCT included 111 child-caregiver dyads. The outcomes of interest are emotional and behavioral functioning, and pro-social behaviors. Other variables include socio-demographics, caregiver health and mental health, parent-child relationships, child coping and support, stigma, and youth self-esteem.

Results: Regression analyses adjusted for age, gender and study revealed significant associations at the contextual, social and self-regulation level. Lower total difficulties scores among children were associated with lower caregiver depression (β=-0.722, p=0.020) and use of wishful thinking (β=5.532, p=.009) as a way of coping. Less youth depression was associated with higher caregiver education (β=-0.399, p=0.010), greater caregiver supervision (β=-1.261, p=.012), more social support seeking (β=-0.453, p=.002), higher youth self-concept scores (β=-0.067, p<.001), lower levels of internal stigma (β=-0.608, p=.040) and the use of resignation as a coping mechanism (β=1.152, p=.041).

Conclusions: This study can inform evidence-based family interventions that also promote youth self-regulation skills to enhance the health and mental health of PHIV+ youth. Longitudinal studies with larger samples are required to determine pathways of causality.

No conflict of interest

Abstract: P_78

HIV infection and adolescents

Socio-demographic and behavioral predictors of poor virological control in HIV-infected adolescents

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Background: Maintaining good adherence to antiretroviral therapy (ART) is challenging for adolescents and can be influenced by several factors. Our study investigated sociodemographic and behavioral characteristics of with children (β=-0.722, p=0.020) and use of wishful thinking (β=5.532, p=.009) as a way of coping. Less youth depression was associated with higher caregiver education (β=-0.399, p=0.010), greater caregiver supervision (β=-1.261, p=.012), more social support seeking (β=-0.453, p=.002), higher youth self-concept scores (β=-0.067, p<.001), lower levels of internal stigma (β=-0.608, p=.040) and the use of resignation as a coping mechanism (β=1.152, p=.041).

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No conflict of interest

Abstract: P_78

HIV infection and adolescents

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Conclusions: This study can inform evidence-based family interventions that also promote youth self-regulation skills to enhance the health and mental health of PHIV+ youth. Longitudinal studies with larger samples are required to determine pathways of causality.

No conflict of interest
adolescents and their relationship to virologic control in a regional cohort in Asia.

**Materials and Methods:** HIV-infected adolescents aged 12-18 years were enrolled from 9 sites in Malaysia, Thailand, and Vietnam. An audio computer-assisted self-interview (ACASI) consisting of a maximum of 84 questions on demographic factors, adherence, sexual activity, and substance use, was used to collect data. HIV clinical and laboratory information was contributed from a parallel observational cohort study. Participants who completed the ACASI questionnaire and had HIV viral load (VL) results within 6 months of the ACASI visit were included in this analysis.

**Results:** Of 248 HIV-infected adolescents enrolled, 136 (42% male; median age 16 years) had available VL results and were included in this analysis. The majority (85%) were Thai, 13% were Malaysian, and 2% were Vietnamese. The median (interquartile range; IQR) duration of ART was 8 (6-12) years; the current CD4 was 663 (490-846) cells/mm$^3$, VL was 1.60 (1.10-2.55) log$_{10}$copies/ml, and 92 (68%) had virologic suppression (VL <50 copies/ml). Of those with poor virologic control (VL >50 copies/ml; N=44), 31 (70%) had virologic failure (VL >1000 copies/ml) and 21/44 (48%) reported adherence ≤80%. Compared to those with virologic suppression, more patients with poor virologic control were using protease inhibitor (PI)-based regimens (64% vs. 32%; p <0.001), and had lower CD4 levels (476 vs. 759 cells/mm$^3$; p <0.001). Although the proportions who ever tried alcohol (45% vs. 42%; p=0.74) or smoked cigarettes (23% vs. 15%, p=0.28) were similar, more adolescents with poor virologic control had ever used cannabis (11% vs. 2%; p=0.02) and reported initiating sexual activity (34% vs. 11%; p=0.001). Among all sexually active adolescents (n=25), 40% had their first sexual activity at age <15 years and less than half (47% vs. 40%; p=0.74) always used condoms. More adolescents with poor virologic control had >1 partner within the past 3 months (9% vs. 2%; p=0.09), had experienced symptoms associated with sexually transmitted infections (9% vs. 1%; p=0.04), and had ever been pregnant if female (25% vs. 8%; p=0.005). In a multivariate model, after adjusting for site, being on a PI-based regimen (odds ratio [OR] 5.64; 95%CI 2.19 – 14.54), reporting adherence ≤80% (OR 4.72; 95%CI 1.77-12.58), and ever having sexual intercourse (OR 6.43; 95%CI 2.01-20.53) were significantly associated with poor virologic control.

**Conclusions:** Poor adherence and being sexually active were independently associated with viremia and poor virologic control in this cohort of Asian adolescents. As one-third of those on PI-based regimens were on second-line regimens due to first-line ART failure, this represents a group who have continued to be at high risk of poor treatment outcomes. Appropriate psychosocial interventions that address behavioral risk reduction are needed alongside youth-appropriate adherence counseling in order to prevent poor health and social outcomes in adolescents.

No conflict of interest

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**Abstract: P_79**

**HIV infection and adolescents**

**Successful Integration of STD Screening into the Point-of-care HIV Screening of Adolescents**

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**Introduction:** Screening for sexually transmitted diseases (STD),including HIV, should be an integral part of the healthcare services provided to adolescents. Access and uptake of HIV and STD counseling and testing by adolescents are low in adult and pediatric healthcare settings globally. Located in the area of high prevalence of HIV and STDs in Washington, DC, Children’s National Health System (CNHS) operates successful pediatric Emergency Department (ED) HIV point-of-care testing (POCT) since 2009, and has screened >20,000 patients≥13 years of age. The screening for STDs, however, remained...
primarily symptom based. Between 2009-2013 high rates of STD prevalence have been reported among adolescents and young adults in Washington, DC with 69% of all chlamydia and 60% of all gonorrhea cases. In response to these high rates of STDs, CNHS expanded HIV POCT to incorporate STD screening in 2015. Here we describe the implementation of the integrated HIV and STD screening among adolescents in the pediatric ED setting.

Materials & Methods: With input from key stakeholders, we designed an algorithm to add opt-out urine PCR testing for gonorrhea (GC) and chlamydia (CT) into the existing workflow of the HIV POCT program screening all adolescents ≥13 years of age presenting to the pediatric ED. Since urine STD test results are not available as POCT, the screening program has established a thorough multidisciplinary follow-up mechanism for providing education, checking STD test results, notifying positive patients and linking positives to treatment. The addition of STD screening to HIV POCT provides adolescents with a more comprehensive sexual health assessment and allows positive patients to be linked to treatment, provides screening for partners and expands overall reproductive health counseling and education.

Results: Adolescents were approached for HIV plus STD screening using the universal opt-out algorithm for HIV POCT, with language about STD added to the HIV screening script. During the pilot period, from July-December 2015, the number of patients approached and tested for STDs steadily increased over time. Overall, ED staff approached 1146 adolescents for HIV and 581 for STD screening. Out of those approached, 631 (55%) patients were tested for HIV, and 279 (48%) were tested for STD, respectively. A small number of patients (n=21) were tested for STD only. ED staff initially reported being more comfortable approaching adolescents for HIV screening rather than STD screening at the beginning of the pilot period due to the reduced stigma associated with HIV screening occurring at the UMC ED as a result of the universal HIV screening program.

Conclusions: The integration of STD screening into the successful POCT HIV screening of adolescents has demonstrated good uptake by staff and patients in a pediatric ED during the pilot stage. While HIV POCT screening began with higher rates of acceptability, the uptake of the STD testing is increasing as a result of staff and patient support which allows for an integrated approach to addressing reproductive health needs of adolescents in pediatric healthcare settings within the community carrying the burden of both epidemics.

No conflict of interest

Abstract: P_80

HIV infection and adolescents

Predictors of adherence to antiretroviral therapy among adolescents with perinatal HIV in the AALPHI cohort in England

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Background: Perinatally HIV-infected (PHIV) young people are entering adulthood, often with complex clinical and psychosocial issues which may affect ART adherence. This is at a time when they are increasingly expected to self-manage their HIV care.

Methods: 296 PHIV aged 13-21 years were recruited into the AALPHI cohort in England from 2013-15. Baseline data included (via computer-assisted self-interview) short-term adherence (number of missed ART doses in last three days), anxiety/depression (HADS), health-related quality of life (PedsQL, not HIV-specific), ever use of drugs/alcohol, self-perception about having HIV (composite score of level of upset, worry, sadness, loneliness, concern about future health), and who they had told and who they can talk to about HIV.
Cognitive function tests assessed 6 domains with a summary (NPZ-6) z-score calculated. Logistic regression examined predictors of missing ≥1 ART dose in the last 3 days, adjusting a priori for gender, age at interview, born in the UK vs. abroad, and ethnicity.

**Results:** 261(88%) were on ART (94% once-daily) at recruitment. 111(43%) were male, 220(84%) black, median age was 16 years [IQR 15,18] and for 87(35%) one/both biological parents had died. 72(28%) had CDC Stage C; 78% viral load (VL)≤50 copies/ml. 242(93%) were in full-time education, 236(91%) lived with parents/carer, and 50(19%) had transferred to adult care. 17% and 5% had moderate/severe anxiety and depression respectively, and mean NPZ-6 score was -0.58(SD 0.86). 143(56%) reported having told no-one about their HIV status, 62(24%) had told 1-2 others, and 49(19%) ≥3 people. Overall 70(27%) reported missing ≥1 ART dose in the last 3 days, most often due to forgetting (68%) and being away from home (37%). Of those with VL≥50copies/mL, 51% reported missing doses, vs. 20% for those with VL<50. In multivariable analysis, anxiety/depression, NPZ-6, CDC C diagnosis, ever alcohol/drugs, having transferred to adult care, and the number of people the participant could talk to about HIV did not predict 3 day non-adherence. However those with decreased QoL (adjusted odds ratio (aOR)=1.1(95%CI 1.0,1.2) per 100 units decreased QoL, p=0.029), negative perceptions about having HIV (aOR=1.1(95%CI 1.0,1.2) per 5 units decreased (negative) score, p=0.043), and those ever smoking cigarettes (aOR=2.7(95%CI 1.3,5.7) vs. never smoked, p=0.010), had higher odds of 3 day non-adherence. Participants who had themselves told more people about their HIV diagnosis had higher odds of non-adherence (1-2 people aOR=1.6(95%CI 0.7,3.3), ≥3 people aOR=2.6(95%CI 1.1,5.9) vs. no one, p=0.075), with this trend being strengthened when QL was removed from the model (p=0.031). Decreased QL was associated with an increased number of people told: those who told no-one had a median QL score of 1800, vs. 1488 for 1-2 people, and 1475 for ≥3 people (p=0.011).

**Conclusions:** Over one in four PHIV reported poor adherence to ART in the previous three days. Cognitive function and anxiety/depression did not directly predict adherence but may act as moderators. The associations between telling more people about HIV, lower QL and greater non-adherence requires further exploration and may reflect young people coping less well and seeking additional support for their HIV and adherence problems.

*No conflict of interest*

**Abstract: P_81**

**HIV infection and adolescents**

**Sexual activity and risk behaviour among young people with and without perinatal HIV in the AALPHI cohort in England**

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**Background:** Children with perinatally acquired HIV (PHIV+) are reaching adolescence and adulthood and may initiate sexual activity with the potential to transmit HIV. Previous studies report PHIV+ young people having less sex than their HIV negative (HIV-) peers. Here we report findings for PHIV+ and HIV- young people from the AALPHI cohort in England.

**Methods:** 296 PHIV+ aged 13-21 years and 96 HIV- affected (96% siblings of PHIV+ or HIV+ mother) young people aged 13-23 years were recruited to the AALPHI cohort in 2013-15. Computer-assisted self-interview collected data on sexual activity (including type of sex, number of partners in last year and condom use), alcohol and recreational drug use, as well as self-perception about having HIV (level of upset, worry, sadness, loneliness, concern about future health) and ART adherence for PHIV+ only. NPZ-6 scores were calculated for cognitive function, and IDACI scores measured household deprivation. T-tests compared means, and χ² proportions; logistic regression examined predictors of ever having sex.
Results: 120(41%) PHIV+ and 31(32%) HIV- were male, 254(86%) and 70(73%) were black, and median age was 16[IQR 15,18] and 16[14,18] years respectively. 77(26%) PHIV+ had a previous CDC C diagnosis. 273(92%) PHIV+ and 87(91%) HIV- were in full-time education, for 101(36%) and 21(23%) one/both parents had died, 122(42%) and 43(46%) had ever drunk alcohol and 43(15%) and 26(29%) had ever taken recreational drugs. 90(31%) PHIV+ and 37(39%) HIV- had ever had sex; median number of partners in the last year was 3[1,6] and 4[1,6] respectively. 25(20%) of those reporting ever sex were <15 years of age at sexual initiation. 61(68%) PHIV+ and 14(38%) HIV- reported always using condoms (p=0.005). Of the 90 PHIV+ ever having sex, for 59(76%) the most recent viral load (within 6 months pre/post interview) was <400c/ml. Multivariable analysis identified older age (adjusted odds ratio (aOR)=1.55 (95%CI 1.36,1.77) per year increase, p<0.001), ever had alcohol (aOR=2.43 (95%CI 1.33,4.44), p=0.004) and recreational drugs (aOR=3.17 (95%CI 1.55,6.51), p=0.002) with ever having sex, but not HIV status (PHIV+ no CDC C aOR=0.73 (95%CI 0.37,1.44), PHIV+ with CDC C aOR=0.78 (95%CI 0.33,1.84) v HIV-, p=0.66). In multivariable analysis for PHIV+ only, age, alcohol and/or drugs were all associated with ever having sex (similar results to above), and also decreased age at HIV naming (aOR=1.26 (95%CI 1.08,1.48) per 1 year decrease, p=0.004) and feeling more upset about having HIV (aOR=1.17 (95%CI 1.04,1.30) per 1 unit increased (negative) score, p=0.007). For the 248 young people who had never had sex, the main reasons cited were not being ready yet (67%), fear of HIV transmission (29% overall; 35% of PHIV and 7% of HIV-), and religious beliefs (22%).

Conclusions: Levels of sexual activity were similar among PHIV+ and HIV- and comparable to national normative data (Natsal-3). Reported condom use was significantly higher in PHIV+ than HIV- in our study, and contrary to other studies which have found higher risky sexual behaviour in PHIV+; findings underline the need for increased sexual health education for both groups of young people.

No conflict of interest

Abstract: P_82

HIV infection and adolescents

Patients with perinatal HIV transitioning to adulthood in the UK: clinical outcomes in adult care

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Background: With improved survival, adolescents with perinatal HIV (PHIV) are transitioning from paediatric to adult care, but there are few published data on clinical outcomes post-transfer. We used linked data from patients in the national UK/Ireland CHIPS paediatric cohort and UK CHIC (representing approximately one-third of the national adult HIV population) to describe mortality and changes in immunological and virological status following transfer to adult care.

Methods: Patients participating in CHIPS aged ≥13 years by the end of 2013 were matched to the UK CHIC database. Median CD4 counts at 12 months (+/-6months) prior to leaving paediatric care and 12 months after starting adult care were compared as were the proportions with CD4<200c/mm3 or confirmed viremia (two consecutive VL>400c/mL within 6 months) in the 24 months prior to leaving paediatric care and after starting adult care. Wilcoxon matched-pairs signed-ranks and McNemar's tests compared medians and proportions respectively.

Results: Of 1,215 CHIPS patients aged ≥13 years, 271 (22%) were matched to a UK CHIC record, of whom 229 (85%) were documented in CHIPS as having transferred to adult care, 25 (9.2%) were reported as lost to follow-up in paediatric care and 17 (6.3%) reported as in follow-up in paediatric care (due to reporting time-lag i/in transition process). Of those matched, 146 (53%) were female, median age at last visit in paediatric care was 17
[interquartile range, IQR 16,18] and median age at last follow-up in adult care was 20 [19,23] years. The median duration of follow-up in paediatric care was 11.8 [6.6,15.5] years. The median gap between last paediatric care visit and first adult UK CHIC clinic visit was 2.4 [1.0,4.4] months (17 patients had a gap of ≥12 months), and median duration of follow-up in adult care was 2.9 [1.5,5.9] years, giving a median total duration of follow-up in HIV care of 15.4 [10.6,19.3] years. At last follow-up, 86 (32%) had a CDC C diagnosis, of whom 77 had their first CDC C event in paediatric care. At last visit in paediatric care, 200 (74%) were on ART, increasing to 228 (84%, p=0.001) at last follow-up in adult care. Median CD4 at 12 months before leaving paediatric care was 456c/mm³ [286,660] and 450/mm³ [271,669] at 12 months after starting adult care (p=0.37). In the 24 months before leaving paediatric care, 31% had ≥1 CD4 measurements <200c/mm³, increasing to 39% (p=0.014) in the 24 months period after starting adult care. Among those on ART for at least 6 months (n=181), 50% and 50% (p=1.00) had confirmed viremia in each of the two periods respectively. Seven (3%) patients died after transfer to adult care; age at death ranged from 18-23 years, and causes were advanced HIV (3), leukoencephalopathy (1), renal failure (1) and pulmonary tuberculosis (1) (missing for 1).

Conclusion: The proportion of PHIV on ART increased after transfer to adult care, although there was no change in the median CD4 count or the proportion with confirmed viremia on ART. Further analyses will explore predictors for immunological and virological status after transition.

No conflict of interest

Abstract: P_83
HIV infection and adolescents

The impact of HIV infection among children and their mothers on children’s behavior, cognitive and language development

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Background: The Asenze study investigated the effects of child and maternal HIV status (HIV affect) on the prevalence of behavioral problems among a population-based cohort of children 4-6 years old in an area of high HIV prevalence in Kwa-Zulu Natal, South Africa. Our findings showed that children infected with HIV had significantly lower scores on child behavior outcomes. In the present analyses we investigate whether HIV + children are more likely to have behavioral and developmental problems than HIV- children with HIV+ mothers, as well as whether HIV- children with HIV+ mothers are more likely to have behavioral and developmental problems than HIV- children with HIV- mothers.

Materials & Methods: HIV affect was categorized as (a) child and mother infected (n=62), (b) child not infected but mother infected (n=257), and (c) neither child nor mother infected (n=694). Children’s behavior was assessed using the Strengths and Difficulties Questionnaire (SDQ), a 25-item scale that assesses children on emotional symptoms, conduct problems, hyperactivity/inattention, peer relationship problems and prosocial behavior. Cognitive development was assessed using the Grover Counter Scale, a 5-section scale that assesses children’s recognition of shapes and colors, ability to reconstruct pattern, copying skills, and memory. Language development was assessed using the Reynell Developmental Language Scale, a two-scale

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questionnaire that assesses children's language comprehension and production. Using Chi Square analyses, we examined the influence of HIV affect on the child's total behavior scores using the UK cut-offs for a categorical measure of behavioral difficulties, and the prosocial subscale. We also assessed the influence of HIV affect on problematic language and cognitive development, defined as

**Results:** There was a high prevalence of behavioral (total) difficulties (42%) in the entire study population. HIV affect was significantly associated with behavioral difficulties ($p=0.002$). Prevalence among group a was 55%, prevalence among group b was 48% and prevalence among group c was 39%. The groups did not differ on prosocial scores. Problematic cognitive development was also prevalent (18%). HIV affect was significantly associated with problematic cognitive development ($p=0.018$). Prevalence among group a was 30%, prevalence among group b was 15% and prevalence among group c was 18%. Problematic language development was the least prevalent (7%). HIV affect was significantly associated with problematic cognitive development ($p=0.0001$). Prevalence among group a was 20%, prevalence among group b was 5% and prevalence among group c was 6%.

**Conclusions:** HIV+ children with HIV+ mothers had a higher prevalence of behavior difficulties and problematic cognitive and language development compared to HIV- children with HIV- mothers. However, our analyses did not support the hypothesis that HIV- children with HIV+ mothers were at an equal disadvantage in their behavior or development compared to children who were HIV+.

**No conflict of interest**

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**Abstract:** P_84

**HIV infection and adolescents**

**Social and emotional impairment in perinatally HIV-infected adolescents in Cape Town, South Africa**


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**Background:** There are growing numbers of perinatally-infected HIV positive (PHIV+) adolescents across Africa and widespread concern regarding the psychosocial well-being of this vulnerable group. However, few studies have investigated mental health in African PHIV+ adolescents, and fewer studies have included local comparator groups of HIV negative (HIV-) adolescents. We examined social/emotional impairment in PHIV+ and HIV- adolescents participating in the Cape Town Adolescent Antiretroviral Cohort (CTAAC).

**Materials & Methods:** This cross-sectional analysis from CTAAC included 474 PHIV+ adolescents (eligibility: ages 9-14 years, on ART for >6 months, disclosed about their HIV status and recruited from services across the city) and 103 HIV- controls drawn from comparable communities. With interviewer support, participants completed the Becks Youth Inventory (BYI-II) which consists of five subscales assessing Depression, Anxiety, Anger, Disruptive Behavior, and Self-Concept. Raw scores were standardized using age- and sex-
adjusted normative data. Wilcoxon rank sum tests (Mann Whitney tests) were used to compare scores between PHIV+ and HIV- adolescents; and linear regression was used to investigate variables associated with higher scores on each of the five sub-scale measures.

**Results :** The mean age was 12.5 years in PHIV+ adolescents and 12.3 years in HIV- controls, with 50% and 46% of participants male, respectively. The median age at ART initiation was 4.4 years [IQR, 2.0-7.6]. The reliability of the BYI-II was high across subscales (Cronbach's alphas, 0.86-0.91). Mean BYI-II sub-scale scores for PHIV+ vs HIV- groups were 40.6 vs 42.5 for depression (p=0.039); 42.3 vs 45.6 for anxiety (p=0.003); 37.1 vs 38.4 anger (p=0.107); 39.7 vs 40.4 for disruptive behavior (p=0.351); and 52.2 vs 52.1 (p=0.935) for self-concept. After adjusting for child age, gender and socioeconomic status, PHIV+ adolescents scored lower, on average, on sub-scales for depression (regression coefficient: -2.27; 95% CI: -4.11, -0.44), anxiety (regression coefficient: -4.05; 95% CI: -6.29, -1.82), and anger (regression coefficient: -1.87; 95% CI: -3.52, -0.22), compared with HIV- controls. There was little variation in sub-scale scores by age at ART initiation, but higher current grade in school was strongly predictive of poorer scores for children on the disruptive behavior sub-scale. When analyses were restricted to older children (ages 12-15), the associations between HIV-status and depression and anxiety persisted. Among PHIV+, after adjusting for age, sex, socioeconomic status and current CD4 cell count, current use of efavirenz was weakly associated with only the disruptive behavior sub-scale scores, and current use of protease inhibitors was not associated with any sub-scale scores.

**Conclusions:** Overall, PHIV+ adolescents do not appear to perform significantly worse than their HIV- counterparts across measures of social/emotional impairment in this setting. It is possible that PHIV+ adolescents receive more support via frequent health service contact compared to HIV- adolescents and that this may explain the observed associations. The absence of associations between clinical factors and BYI-II scores on PHIV+ adolescents suggests that social/emotional outcomes may be more influenced by social and economic contexts. These contexts, as well as the implications and consistency of these findings into adulthood, require ongoing attention.

*No conflict of interest*

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Abstract: P_85

**HIV infection and adolescents**

**Pregnancy and birth outcomes among women with perinatally versus sexually acquired HIV infection in Botswana**

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**Background:** The increasing availability of antiretroviral therapy (ART) for children living with HIV has resulted in their improved survival. A growing population of individuals with perinatally acquired HIV are now reaching childbearing age. Little is known about pregnancy and birth outcomes among women with perinatally acquired HIV (PHIV), particularly in resource-limited settings.

**Methods:** Data from an ongoing birth outcomes surveillance study at 8 government delivery sites in Botswana, representing ~50% of all births in the country, was used for this descriptive analysis. Pregnant women diagnosed with HIV before their 8th birthday were classified as having perinatally acquired HIV; all other women were considered to have been sexually infected. Birth outcomes included small for gestational age (SGA) (<10th percentile weight for gestational age (GA)), preterm delivery (PTD) (<37 weeks GA), and stillbirths (SB). Descriptive analyses were restricted to pregnant women within the same age range as those who were perinatally infected to ensure fair comparability.

**Results:** Among 10 066 HIV-infected women who delivered between 6 July 2014 and 26 April 2016 at surveillance sites, 9039 (90%) had known HIV diagnosis date, 44 (0.5%) were PHIV and 8995 (99.5%) SHIV. The median age for PHIV was 18 (range 15, 24) and 31 (range 15, 48) for SHIV women. The comparison group for this analysis included 1879 (21%) SHIV women between 15 and 24 years. The median age of diagnosis was 7 years for PHIV women (0 years, 30%; 1-3 years, 18%; 7-8 years, 52%)
and 21 years for SHIV women (9-15 years, 5%; 16-20 years, 43%; 21-24 years, 52%). PHIV women were more likely to be current students (32% vs. 9%), and more likely to be pregnant for the first time (93% vs. 48%). All PHIV women, versus 87% of SHIV women, had documentation of ARV use during pregnancy, and 91% of PHIV women had started ART before pregnancy. The most common ART regimen used during pregnancy by PHIV women was nevirapine/zidovudine/lamivudine (39%). Among SHIV women, 67% initiated ART during pregnancy and majority were on tenofovir/emtricitabine/efavirenz (77%). Prevalence of adverse birth outcomes were 21% SGA, 17% PTD and 0% SB for PHIV women, and for SHIV women 15% SGA, 22% PTD and 2% SB.

Conclusions: This is the first population-based description of pregnant perinatally HIV-infected women in sub-Saharan Africa, and represents a first step towards understanding the unique reproductive and perinatal health care needs of this new and growing population in a resource-limited setting.

No conflict of interest

Abstract: P_86

HIV infection and adolescents

T2 Transition Training: Transferring Economic, Psychosocial, and Self-care Skills Needed for Young Adults Living with HIV in Malawi for Successful Transition into Adulthood

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Introduction: In Sub-Saharan Africa, there is a large gap in age-appropriate medical and non-medical services for perinatally-infected young adults living with HIV. HIV-specific adolescent programming often lacks the tools necessary for adolescents to successfully transition into adulthood. During this crucial transition period, psychosocial support is often withdrawn and older adolescents are pushed directly into adult care. Baylor College of Medicine-Children's Foundation Malawi (BCM-CFM) runs a network of adolescent and psychosocial programs called 'Teen Clubs' across Malawi with over 800 adolescents living with HIV (ALHIV) at the center in Lilongwe. With no suitable psychosocial services for young adults, Teen Clubs are becoming overcrowded. The Transition Training (T²) program was developed to equip young adults (18-24 years) living with HIV with life skills to gain financial security and social enfranchisement, and to strengthen medical and non-medical self-care skills. Participants selected from local 'Teen Club' graduate pools enroll in a 6-week program meeting twice weekly. Sessions are divided between economic empowerment and healthy positive living. All participants design career goals, cover letters, CVs, partake in mock interviews, and create email addresses.

Methods: Unstructured follow-up interviews were conducted for 100 participants who completed the program between January 2013 and December 2015 as a routine part of the program. 25 females answered additional questions regarding sexual reproductive health. Retrospective chart reviews were also conducted for 70 graduates who follow up at the Baylor College of Medicine Centre of Excellence (COE) from January 2013 to December 2015.

Results: From January 2013-December 2015, BCM-CFM conducted four T² sessions with 105 graduates (54 males, 51 females). Average age at enrollment was 20 years. Of the 100 interviewed: 27% re-enrolled in secondary school (19 male, 7 females), 3% enrolled in university (2 female, 1 male), 14% found employment (10 males, 4 females), 5% secured internships (2 males, 3 girls), 36% are ALHIV program mentors, 12% enrolled in a computer training program. 24% disclosed their HIV status to a friend or partner (15 males, 9 females). Of the 25 females interviewed, 18 (72%) are sexually active and of whom 15(85%) use condom regularly, 8 (32%) use long-acting contraception. Of the 70 of graduates followed at the COE, 83% had good adherence (95-105% by pill count at last visit) compared to adolescent adherence of 81%, and clinic adherence of 79%. 43 had viral loads drawn
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since participation, 37 (86%) were suppressed (<150 copies detected) compared to adolescent and clinic suppression rates of 77%. Of the 70, 64 (91%) are retained in care, 3 transferred out, 1 died (pill dumping), and 1 is lost-to-follow-up.

**Conclusion:** Transition programs such as T<sup>2</sup> focusing on self-empowerment, sexual and reproductive health, social enfranchisement, career development, and HIV self care are paramount for aiding young adults living with HIV with transitioning to adulthood. Transition programs are also crucial for decompressing crowded adolescent programs, and program graduates become a resourceful pool of mentors for younger ALHIV, increasing long-term sustainability of such programs. Transition programs can contribute to improved anti-retroviral therapy adherence, viral suppression, and retention in care in this age group.

*No conflict of interest*

**Abstract: P_87**

**HIV infection and adolescents**

**Addressing Psychosocial Needs and Care/Treatment Delivery Gaps for Adolescents Living With HIV (ALHIV) Using Technology: The Teen Support Line (TSL) Experience In Malawi**

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**Introduction:** Though a cornerstone for improving physical and mental health outcomes, quality psychosocial services are sparse across Sub-Saharan Africa and very limited for ALHIV. Regional networks of youth-friendly-services are forming to increase access to care, however distance to health centers and transport costs are major barriers to accessing services. The Teen Support Line (TSL) bridges these service gaps giving ALHIV in Malawi 24-hour access to HIV-specific information, psychosocial support, and linkage to care centers through a free cellular hotline service. Teens can call, flash, or SMS the hotline. Call-takers provide counseling, information, referrals, follow-ups, and healthcare-center linkages. Because the number is shared only with ALHIV, callers do not need to disclose their status verbally to the call-takers. A clinician, social worker, and counselor are on-call for immediate response to emergent issues. Regional feedback is provided monthly to districts. Healthcare providers and community mentors share The Teen Support Line number with adolescents after receiving full disclosure of HIV status in pediatric ART clinics. The number is included in the Ministry of Health disclosure material and flip charts. The number is also shared through the network of 'Teen Clubs' across Malawi for ALHIV.

**Methods:** From March 2013 to March-2016, the hotline number was shared with 3126 ALHIV using the existing 'Teen Club' network and targeted TSL launches across Malawi. Call-takers complete M&E forms eliciting caller demographics, topics, pre-and-post caller feelings/presence of mind and call details. Data was collected from the call-taker M&E forms from March 2013-March 2016 and a retrospective review and descriptive analysis of results was done.

**Results:** During the period under review the TSL hotline received a total 876 calls. 46% (400) callers were female and 56% (486) male. 50% (438) were aged between 12-15 years, 34% (297) were 16-19 years. 33% (291) used their own phone and 43% (381) used a guardian's phone. 33.3% (292) of the calls were made within peak call time of 4-9 pm. 18% (160) were first-time callers and 40% (346) were returning callers.15% (135) of the callers were referred for depressive symptoms. 12% (107) of calls required follow-up. At the call conclusion, 87% (763) felt better about their situation and 78% (686) indicated that they had learned something from the call. Most common call topics were: Teen club/clinic appointment information (29%), ART and adherence (19%), stigma/discrimination (11%), caretaker issues (10%), and sexual reproductive health (9%).

**Conclusions:** ALHIV reached through targeted activities are using the TSL hotline as their trusted source of information. An ALHIV-specific hotline can provide psychosocial
services lacking at health-centers and reduce distance as an overriding constraint in providing case-specific counseling. ALHIV-specific hotlines should be considered as an adjunct to care in countries burdened with adolescent-focused delivery gaps. However, the success of such hotlines is dependent on safeguarding the privacy and confidentiality of ALHIV, and well trained call takers.

No conflict of interest

Abstract: P_88

HIV infection and adolescents

Human Papillomavirus Infection Among Perinatally HIV-infected And HIV-uninfected Male Adolescents In Thailand

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Introduction: Human papillomavirus (HPV) is the most common cause of anogenital cancers in men. HIV infection increases the risk of persistent HPV infection and long-term complications. Data on the prevalence of HPV infection and factors associated with HPV infection among male adolescents with perinatal HIV infection (paHIV) are limited.

Materials and methods: A cross-sectional study was conducted in paHIV and HIV-uninfected Thai male adolescents, matched in a 1:1 ratio by age and lifetime number of sexual partners (i.e., ≤3 or >3). None had received an HPV vaccine. We studied the prevalence of HPV infection by genotype, anatomical site of infection, type of sexual relationship, and other factors associated with HPV infection. HPV infection was detected by polymerase chain reaction. Factors associated with HPV infection, including demographic, clinical, behavioral, and sexual risk characteristics were determined by univariate and multivariate analyses using logistic regression methods.

Results: A total of 49 paHIV and 47 HIV-uninfected male adolescents were enrolled from referral centers in Bangkok. The median (IQR) age was 18 (17 – 20) years. The median (IQR) lifetime number of partners was 4 (2-10). A total of 18 adolescents were MSM (12% of paHIV and 26% of HIV-uninfected adolescents; P=0.12). Among the paHIV, the median (IQR) CD4 cell count was 573 (434 – 747) cells/mm³, and 69% had an HIV RNA load <40 copies/mL. paHIV males were more likely to always use a condom with insertive vaginal intercourse during the past 6 months than HIV-uninfected adolescents (41% vs. 9%, P=0.001).

The prevalence of any HPV infection was 61% in paHIV and 49% in HIV-uninfected adolescents (P=0.23). Among HPV-infected participants, 55% were infected with any high-risk HPV type, and 28% were infected with vaccine containing types, HPV-16 and/or HPV-18. The most common high-risk HPV type was HPV-59. The prevalence of high-risk HPV infection was 33% in paHIV and 28% in HIV-uninfected adolescents (P=0.59). None of the HIV-uninfected group were infected with HPV-16. The overall rate of HPV detection was 77% at the penis and 40% at the anus. Any HPV types in paHIV males and controls were detected in 49% vs. 36% of penile samples (P=0.21), 37% vs.28% of scrotal samples (P=0.34), 24% vs. 19% of anal samples (P=0.53) and 16% vs. 2% of oral samples (P=0.02). High-risk HPV types were found in 24% vs. 19% of penile samples (P=0.53), 10% vs. 15% of scrotal samples (P=0.49), 14% vs. 9% of anal samples (P=0.38), and 4% vs. 0% of oral samples (P=0.50) among paHIV males and controls.

In multivariate models, reporting symptoms of a sexually transmitted infection (STI; P=0.04) was associated with any HPV infection, and factors associated with high-risk HPV infection were smoking (P=0.01) and report of experiencing STI symptoms (P=0.004).
Conclusions: Over half of sexually active, paHIV Thai male adolescents had detectable HPV infection, which was comparable to uninfected controls. In all, smoking and report of experiencing STI symptoms were independently associated with high-risk HPV type infection.

No conflict of interest

Abstract: P_89

Prevention of Mother-to-Child transmission

Increased Mortality Risk among Formula Fed HIV-Exposed Uninfected Infants in Socioeconomically Challenged Households – Findings from the Mpepu Study

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Introduction: A South African observational study, conducted when policy promoted HIV-infected maternal infant feeding choice based upon formula feeding acceptability, feasibility, affordability, sustainability, and safety, identified > 3-fold increased mortality risk among HIV-exposed formula fed infants in households without piped water, electricity, or gas for fuel, compared with breastfed infants. We sought to determine the applicability of these findings in Botswana, where the prevention of mother-to-child HIV transmission program promotes exclusive formula feeding for all HIV-exposed uninfected (HEU) infants.

Materials and Methods: Demographic and health outcomes data from the Mpepu study, a Botswana-based randomized double-blinded clinical trial investigating prophylactic cotrimoxazole as a means of reducing mortality among HEU infants, were used to quantify differences in the combined end point of hospitalizations and mortality between breastfed and formula fed HEU infants residing in households without piped water, electricity, or gas for a fuel source. Per Botswana guidelines, infant feeding was according to maternal choice, with free formula provided by the Botswana government for mothers choosing to formula feed.

Results: A total of 680 (21%) of 3,164 Mpepu enrolled infants resided in households without piped water, electricity or gas for fuel source, 552 (81%) formula fed and 128 (19%) breastfed. Formula fed infants experienced a higher prevalence of hospitalization or death in the first six months of life (10.0% versus 3.9%; p = 0.04). In multivariate analysis including infant feeding practice and randomized treatment, formula feeding was associated with increased odds of hospitalization or death in the first six months of life (aOR 2.73; 95% CI 1.07-6.96; p=0.04), but there was no benefit of Cotrimoxazole prophylaxis (aOR 0.97; 95% CI 0.57-1.65; p=0.91).

Conclusions: Formula fed HEU infants residing in socioeconomically challenged households in Botswana experienced significantly higher hospitalizations or mortality through 6 months, supporting the South African study’s generalizability. Infants in our population were confirmed HIV-uninfected, and morbidity and mortality rates were low in the cohort as a whole, highlighting the excess risk associated with formula feeding even in regions of Africa where formula feeding may currently be considered a safe option.

No conflict of interest
Abstract: P_90

Prevention of Mother-to-Child transmission

Pregnancy Outcomes of Perinatally vs. non-Perinatally HIV-infected Pregnant Women in the U.S.: Results from PHACS SMARTT and IMPAACT P1025


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Background: The success of antiretroviral therapy (ART) has resulted in perinatally HIV-infected (PHIV) youth reaching reproductive age. Pregnancy outcomes of PHIV women compared to women acquiring HIV non-perinatally (nPHIV) are poorly defined.

Methods: We compared birth weight (BW) and preterm delivery (PTD) outcomes of PHIV versus nPHIV pregnant women enrolled in the PHACS Surveillance Monitoring for ART Toxicities Study (SMARTT) or IMPAACT P1025 protocol. Women were 13-30 years old. Infants were HIV-uninfected singleton liveborns. Maternal PHIV status was identified by self-report, medical record review, or HIV infection documented within 5 years of birth. BW z-scores (BWZ) and small-for-gestational-age (SGA) were calculated using U.S. standards. Mixed effects models were applied to assess the association of maternal PHIV status with infant BWZ; log binomial models using generalized estimating equations were fit for PTD (delivery at <37 weeks) and SGA outcomes.

Results: From 1998-2013, 2,270 HIV-infected pregnant women delivered 2,692 newborns (270 born to PHIV and 2,422 to nPHIV women). Compared to nPHIV women, PHIV women were younger (mean age 21 vs. 25 years, p<0.01) and less often Black (55% vs. 67%, p<0.01). PHIV women were more likely to have a CD4 count <200 cells/mm³ during pregnancy (19% vs. 11%, p=0.01), delivery HIV RNA level >400 copies/mL (28% vs. 23%, p<0.01), receipt of ≥3-class ART during pregnancy (23% vs. 2%, p<0.01), and pre-pregnancy body mass index (BMI) <18.5 kg/m² (6% vs. 3%, p<0.01). PHIV were less likely to report tobacco (14% vs. 20%, p=0.01) and substance use (1.7% vs. 3.3%, p<0.01) during pregnancy. After adjustment, BWZ was 0.13 lower in infants of PHIV vs. nPHIV women (adjusted mean: -0.46 vs. -0.33, p=0.03). Black race, tobacco and substance use in pregnancy, and maternal pre-pregnancy BMI <18.5 kg/m² were also significantly associated with lower infant BWZ. No associations between maternal PHIV status and PTD or SGA were observed.

Conclusions: Infants of PHIV versus nPHIV women may be at greater risk for lower BW, although the absolute difference was small. Future studies are warranted to understand mechanisms by which the intrauterine environment of PHIV women may affect fetal growth.

No conflict of interest
Abstract: P_91

Prevention of Mother-to-Child transmission

HIV viral load monitoring in HIV-infected pregnant women established on antiretroviral therapy in Cape Town, South Africa.

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Introduction: Use of viral load (VL) monitoring is increasing across Africa however there are few insights into VL monitoring strategies during pregnancy. We describe public sector VL monitoring practices in a cohort of HIV-infected pregnant women established on antiretroviral therapy (ART) in Cape Town, South Africa. Annual VL monitoring has been routine in this setting since 2010, with two consecutive VL results >1000 copies/mL used to diagnose virologic failure, and VL testing indicated at least once during pregnancy to monitor mother-to-child transmission (MTCT) risk.

Methods: We enrolled consecutive pregnant women on ART for at least 4 months and making their first visit to a primary care antenatal clinic between March 2013 and June 2014. All women received a research ultrasound to determine gestation and estimated date of conception, and then used laboratory systems to follow-up routine VL testing practices from 15 months before the estimated date of conception to 6 weeks after delivery.

Results: Among 538 women the median age was 31 years and the median duration of ART use was 31 months [IQR, 17-59 months]. In the 15 months before the estimated date of conception, 64% (n=327) had at least one VL test done in routine adult ART services, and 9% of these results (n=28) were >1000 copies/mL. During the pregnancy, 81% (n=437) of women had at least one VL test done and 12% (n=53) of these results were >1000 copies/mL. Pregnant women with elevated VL were more likely to report missed ART doses in pregnancy (p=0.036) and be on a PI-based regimen (p=0.054). Among women with VL ≥1000 copies/mL during pregnancy, 62% (n=33) had a repeat VL test done at a median of 4 months after the initial test (IQR 2-5 months) and 48% of women (n=16) had a VL ≥1000 copies/mL on this second test suggesting virologic failure.

Conclusions: While coverage of VL monitoring appears high in this setting, VL testing during pregnancy occurs less frequently. A substantial fraction of women with elevated VL in pregnancy are never retested, and the time to retesting appears unusually long for some women, presenting potential missed opportunities to reduce MTCT risk. With increasing numbers of HIV positive women using ART, greater attention is needed to design and implement effective strategies for VL monitoring in pregnancy.

No conflict of interest
Abstract

Prevention of Mother-to-Child transmission

Neurodevelopment of Ugandan and Malawian PROMISE exposed and unexposed uninfected children at 12 and 24 months of age

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Introduction: HIV exposed uninfected children (HEU) in Africa are developmentally at-risk both from the effects of HIV disease on the mother and fetus during gestation, and from pre- and postnatal (breast feeding) exposure to anti-retroviral treatments (ARTs). This study compares neurodevelopmental outcomes of co-enrolled PROMISE Malawian and Ugandan children, to age and gender-matched HIV uninfected unexposed (HUU) community controls.

Methods: 188 Malawian (Blantyre) and 208 Ugandan (Kampala) HEU infants followed at two research sites were tested with the Mullen Scales of Early Learning (MSEL) at 12 months of age, along with 179 Malawian and 194 Ugandan age- and gender-matched HUU children. At 24 months 214 Malawian and 219 Ugandan HEU children were tested, along with 202 Malawian and 213 Ugandan HUU children. Least-squared means for standardized scores were compared by exposure group (HUU, HEU) and by country site (Uganda, Malawi) for 12 and 24 months using the linear mixed models with interaction effects of time, site and HIV exposure status.

Results: In a repeated-measure (12 & 24 months) mixed models, HUU children had higher MSEL composite cognitive ability scores than the HEU cohort for the Malawian children at 12 months (group mean HUU vs HEU, 98 vs 94, p=0.01) and for the Ugandan children at 24 months (group mean HUU vs HEU, 90 vs 86, p <0.01)). This composite difference of ~1/2 SD (normative) is clinically meaningful in terms of developmental delay. Significant MSEL differences also favoring HUU were obtained for Visual Reception at 12 mos in Malawi (group mean 51 vs 49, p<0.01), and 24 mos in Uganda, group mean 41 vs 39, p=0.01); in Uganda for Fine Motor at 12 months (group mean 51 vs 48, p<0.01) and 24 months (group mean 46 vs 42, p<0.01); as well as Expressive Language at 24 mos, (group mean 43 vs 41, p=0.01). Receptive Language between-cohort differences were not significant for HUU and HEU groups in either country site. In a separate analysis comparing the combined HEU/HUU Ugandan and Malawian cohorts on MSEL scores, scores were generally significantly higher for the Malawian children on Visual Reception and Expressive Language; while the Ugandan children scored higher on Fine Motor and Receptive Language.

Conclusions: HEU children on NVP prophylaxis or with maternal ART exposure in Uganda and Malawi were at greater overall neurodevelopmental risk than a matched cohort of HUU children, even though the HEU children received monthly medical and nutritional monitoring and support through their follow up in the IMPAACT PROMISE study. MSEL test performance differences between study sites may be developmental differences, or they may be partly due to contextual differences in adaptation and administration of the MSEL.

No conflict of interest
Abstract: P_93

Prevention of Mother-to-Child transmission

Is it successful?: Review on cascade of prevention of mother-to-child transmission of HIV services in Myanmar

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Introduction: Prevention of mother-to-child transmission (PMTCT) services are the key factors in improving maternal and child health related to HIV. In Myanmar, systematic evaluation of PMTCT services implementation has not done yet. Therefore, a study was conducted to determine the situation of cascade of PMTCT services implemented in Myanmar.

Material and Methods: Mixed method design was applied which includes secondary data review and prospective data collection using qualitative research methods. Records of HIV positive pregnant women from PMTCT sites in all regions of Myanmar during 2012 to 2014 were compiled, reviewed and analyzed to determine the situation of cascade of PMTCT services. In-depth interviews (IDIs) were also conducted with health care providers and HIV positive mothers.

Results: A total of 3,372 records of HIV positive pregnant women were included in the assessment. Nearly 59% (1985/3372) of HIV infected pregnant women received anti-retroviral (ARV) drugs for PMTCT according to the records. Among them, majority (85.6%, 1699/1985) received ARV during antenatal period. One third of HIV positive mothers (33%, 1114/3372) delivered their babies as normal vaginal delivery while 38.5% (1297/3372) were not recorded. Just over 47% (1589/3372) of children have received Nevirapine for prevention of transmission and 26% (890/3372) have provided Cotrimoxazole. Exclusive breast feeding was practiced by 30% (1003/3372) of women and 27.4% (924/3372) did not breast fed their babies. Among those who have delivered, 27% (469/1739) of the children received PCR test for early infant diagnosis (EID) of which 13.4% (63/469) were detected as HIV positive. One-fourth (25.1%, 436/1739) completed antibody test and 12.6% (55/436) were identified as HIV positive. Weakness in integration with routine antenatal care services, problem of loss to follow up, limited human resource, over workload of midwives, weakness in monitoring and supervision, low education status of community at rural area, stigma and discrimination and frequent change in reporting format were mentioned as the challenges of PMTCT services.

Conclusion: Gaps were identified in each step of PMTCT services. Ways and means to overcome the challenges in provision of services should be elicited for successful implementation of PMTCT. Strengthening of integration with routine AN care services is recommended.

No conflict of interest

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Prevention of Mother-to-Child transmission

Prevalence and determinants of unplanned pregnancy in HIV-infected and uninfected pregnant women seeking antenatal care in Cape Town, South Africa

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Background: Prevention of unplanned pregnancy is a crucial aspect of preventing mother-to-child HIV transmission (PMTCT).
However, we have little understanding of how HIV status and antiretroviral therapy (ART) may modify pregnancy planning. There are few data on pregnancy planning in HIV-infected (HIV+) South African women, and no comparative data with HIV-uninfected (HIV-) women.

**Methods:** We conducted a cross-sectional study of 2105 pregnant women (1512 HIV+; 593 HIV-) ages 18-44 making their first antenatal clinic visit at a primary-level health care facility in Gugulethu, Cape Town. All women completed structured questionnaires including the London Measure of Unplanned Pregnancy (LMUP); a 6-item scale that categorises pregnancies into planned, ambivalent and unplanned. Analyses examined LMUP results across 4 groups of participants: HIV+ established on ART; known HIV+ but not currently on ART; newly diagnosed HIV+; and HIV-.

**Results:** Overall, the mean age was 29 years, 43% of women were married/cohabiting and 20% were nulliparous. The LMUP performed well across all groups (Cronbach’s α=0.84). Levels of unplanned pregnancy were higher in HIV+ versus HIV- women (50% vs 33%, \(p<0.001\)); and highest in women not on ART (Figure 1). Overall, 69% of women reported contraceptive use in the year before pregnancy; this was strongly associated with unplanned pregnancy (\(p<0.001\)). Compared to HIV- women, HIV+ women had significantly higher odds of unplanned pregnancy, even after adjusting for age, parity and cohabiting status. The odds were greatest among women newly-diagnosed with HIV and previously diagnosed but not on ART (OR: 1.61; 95% CI: 1.17-2.23 and OR: 2.04; 95% CI: 1.44-2.89, respectively). Increased parity and age <24 years were also associated with unplanned pregnancy (OR 3.42; 95% CI: 2.13-5.47 and OR 2.05; 95% CI: 1.34-3.16 respectively).

**Conclusions:** These data indicate high levels of unplanned pregnancy in a high HIV prevalence setting, highlighting missed opportunities for PMTCT through improved family planning services.

No conflict of interest
or maternal self-reported positive) were invited for facility-based follow-up at 3, 6, 9, 12, 15 and 18 months. At each follow-up visit, caregivers were interviewed and infants were tested for HIV infection. Analysis was weighted for sample ascertainment, population live births, consent to follow-up (if eligible) and loss to follow-up.

Results: Analysis of 9120 iDBS at 4-8 weeks revealed 33.1% infant HIV exposure (95% Confidence Interval, 31.8-34.3%) and 2.6% (2.0-3.2) MTCT. HIV-exposed infants were followed up at 18 months with retention rate of 71%. Cumulative MTCT and ‘MTCT-or-death’ by 3, 6, 9, 12, 15, months was 2.7% (2.6-12.6) and 2.8% (2.6-19); 3.5% (3.1-4.4) and 4.2% (3.5-5.4); 3.7% (3.2-4.6) and 5.1% (4.4-6.2); 3.9% (3.4-4.7) and 5.7% (5.0-6.8); 4.1% (3.5-4.8) and 6.0% (5.2-7.0), and at 18 months, 4.3% (3.7-5.0) and 6.2% (5.5-7.3) respectively. 81% of MTCT and 67% of ‘MTCT-or-death’ occurred by 6 months postpartum. Maternal receipt of CD4-cell-count result and not breastfeeding protected against MTCT (Adjusted hazard ratio HRa, 0.3 [0.2-0.6], and 0.3, [ 0.07-0.9], respectively). Mixed feeding and infant nevirapine did not significantly increase MTCT-or-death (HRa 1.4 [0.8-2.4] and 2.1 [0.8-5.4], respectively).Having a refrigerator significantly protected against MTCT-or-death (HRa 0.5 [0.3-1.0], respectively).

Conclusions: The first 6 months postpartum is a critical period for following up HIV-exposed infants and providing regular HIV testing.

No conflict of interest

Abstract: P_96

Prevention of Mother-to-Child transmission

Adherence and viral suppression in pregnant women already on ART when entering antenatal care in Cape Town, South Africa

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Background: Prevention of mother-to-child transmission (PMTCT) services have previously focussed on HIV+ women who are newly initiating antiretroviral therapy (ART) in pregnancy. However, increasing numbers of women are already on ART when entering antenatal care. Despite the growing size of this population, there are few data on their ART adherence and HIV viral suppression. We examined self-reported non-adherence, non-suppressed viral load (VL), and factors associated with each among HIV+ pregnant women already on ART when entering PMTCT services in Cape Town, South Africa.

Methods: We recruited HIV+ women entering PMTCT services at a large primary care clinic for the MCH-ART study. This analysis focussed on women on ART ≥4 months. At enrolment, self-report measures of concerns about taking ART during the perinatal period (Cronbach’s α: 0.77), adherence self-efficacy (α: 0.93) and ART adherence were administered; VL testing (Abbott RealTime HIV-1) was conducted. We used multivariable logistic regression to explore factors associated with non-adherence (defined as missed ART doses on ≥2 days during the preceding 30 days) and with non-suppressed VL (VL >1,000 copies/mL).

Results: Among 482 women (mean age: 31.2 years; mean duration of ART use: 3.4 years), 22% reported any missed ART dose in the
preceding 30 days; 15% reported non-adherence; and 20% and 12% had VL >50 and >1,000 copies/mL, respectively. Non-adherence was strongly associated with non-suppressed VL (OR: 2.68; 95% CI: 1.41-5.11). Adjusting for age, non-adherence was associated with single marital status (OR: 1.80; 95% CI: 1.03-3.15), unintended pregnancy (OR: 1.75; 95% CI: 0.99-3.08) and greater concern about taking ART (OR: 1.40; 95% CI: 1.09-1.82); higher adherence self-efficacy was associated with a reduced odds of non-adherence (OR: 0.47; 95% CI: 0.26-0.82). In adjusted analyses, non-suppressed VL was associated with report of previous discontinuation of ART (OR: 6.59; 95% CI: 2.93-14.79), greater concern about taking ART (OR: 1.38; 95% CI: 1.03-1.85) and unintended pregnancy (OR: 1.92; 95% CI: 1.02-3.64).

**Discussion:** Among HIV+ pregnant women entering PMTCT on ART, substantial levels of non-adherence and non-suppressed VL were observed. Tools for identifying women entering antenatal care already on ART with adherence difficulties and elevated VL are needed to target counselling interventions and adherence monitoring.

No conflict of interest

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**Abstract:** P_97

**Prevention of Mother-to-Child transmission**

**Multimodal neuroimaging differences related to HIV/ART exposure in 7-year-old South African children**

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**Introduction:** A result of the high success of PMTCT programs in South Africa is a burgeoning population of HIV-exposed, uninfected (HEU) children. The long-term effects of exposure to ART/HIV in utero are still relatively unknown, and multimodal magnetic resonance imaging (MRI) neuroimaging studies can quantify the possible long-term effects of ART/HIV exposure on neurodevelopment. We present significant group differences between measures of brain structure, function and metabolism in a cohort of HEU and HIV uninfected (HU) children at age 7.

**Methods:** Fifty-one 7-year-old children were scanned (23 Female; mean age ± sd: 7.2 ± 0.1; 23 HEU; 9 Cape Coloured/42 Xhosa) as part of an on-going longitudinal study on a Siemens 3T Allegra Scanner (Siemens, Erlangen, Germany) in Cape Town, South Africa. HEU children were exposed to treatment for PMTCT. The protocol included structural MRI, single voxel 1H magnetic resonance spectroscopy (MRS) in the midfrontal gray matter (MFGM), diffusion tensor imaging (DTI), and resting state functional MRI (RS–FMRI). Specific exclusion criteria was applied to each modality to ensure quality data. Statistical analyses included gender and ethnicity confounds.
Results: Group comparisons between HEU and HU children were performed. Compared to HU children, we found that HEU children had significantly:

1. Higher local gyrification indices (LGIs) \((p < \) ) in the left precuneus region,
2. Higher mean choline levels \((p = 0.02)\) and lower mean NAA/Creatine ratios \((p = 0.05)\),
3. Higher mean connectivity \((p < 0.05)\) from seeds within the default mode, executive control, motor, salience networks, and
4. Higher FA \((p < 0.0005)\) and lower MD \((p < 0.0001)\) in bilateral corticospinal tract clusters.

Conclusions: We found significant differences between HEU and HU children across all neuroimaging modalities. These results suggest differences in maturation throughout the brain related to HIV/ART exposure - involving cortical folding, localized metabolism, numerous functional networks, and white matter microstructure properties.

No conflict of interest

Abstract: P_98

Prevention of Mother-to-Child transmission

NRTI backbones and pregnancy outcomes: results from a European cohort collaboration

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Introduction: Data on safety of contemporary antiretroviral therapy (ART) regimens in pregnancy are essential to inform clinical guidelines. Combination ART has been associated with increased risk of preterm delivery (PTD), with risk potentially differing by regimen. Our aim was to investigate whether specific NRTI backbones are associated with risk of adverse pregnancy outcomes within a pan-European cohort collaboration.

Material & Methods: Pregnancies conceived off treatment, with initiation of a single cART regimen (defined as ≥3 antiretroviral drugs started within 7 days including ≥2 NRTIs), which ended in a singleton live birth in 2008-2014 were included. Pregnancies with <2 weeks ART or at a site with <10 eligible pregnancies were excluded. 7257 pregnancies from 8 countries and 7 cohorts were included. Associations between NRTI backbone and PTD (<37 completed gestation weeks) and small-for-gestational-age (SGA, sex-specific US standards) were investigated with Poisson regression models with robust estimates, adjusted for potential confounders.

Results: 45% (3260) of pregnancies were from UK/Ireland and 43% (3144) from Ukraine. Median maternal age was 29 years [IQR 25,33], maternal injecting drug use (IDU) prevalence was 5% (302/5916) and median first antenatal CD4 count was 395 cells/mm³ [IQR 260, 559]. LPV/r+ZDV+3TC was received by 63% (n=4571), LPV/r+3TC+ABC and LPV/r+TDF+FTC/3TC by 6% each (n=464, n=457), and TDF+FTC/3TC with another PI by 6% (n=461); NNRTI-based cART was received in 7% (n=523) pregnancies overall. The MTCT rate was 1.17% [95%CI 0.90-1.51]. Overall, 10.0% (722/7192) deliveries were preterm and 20.9% (1483/7090) infants were SGA.

In a complete case analysis of 5353 pregnancies adjusting for calendar year, country of delivery, parity, maternal IDU, CD4 count, maternal age, NRTI backbone and third agent, PTD was not associated with NRTI backbone (AIRR 0.99 [95%CI 0.74-1.34] for 3TC+ABC, AIRR 1.06 [0.83-1.36] for TDF+FTC/3TC, AIRR 0.75 [0.46-1.23] for other NRTI backbones, with ZDV+3TC as reference category), or third agent (AIRR 1.28 [0.98-1.68] for LPV/r, AIRR 1.06 [0.72-1.56] for NNRTI, AIRR 1.28 [0.75-2.20] for PI+NNRTI /Integrase /Fusion /only NRTIs, all vs. other PI). Overall, PTD was associated with maternal IDU (AIRR 1.98 [1.51-2.60], maternal age 30-39 vs. 21-29 years (AIRR 1.21 [1.01-1.43]) and CD4 <200 cells/mm³ vs. ≥350 cells/mm³ (AIRR 1.30 [1.04-1.64]). In a restricted analysis among 4011 pregnancies with LPV/r, there was no association between NRTI backbone and PTD.

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In a model for SGA including antenatal ART duration and infant sex plus the factors in PTD model (N=4648), NRTI backbone was not associated with SGA risk (AIRR 0.85 [0.68-1.05] for 3TC+ABC, AIRR 0.87 [0.71-1.06] for TDF+FTC/3TC and AIRR 1.02 [0.73-1.43] for other NRTI, all vs. ZDV+3TC). Infants exposed to LPV/r in-utero were more likely to be SGA (AIRR 1.25 [1.01-1.56] \(p=0.043\) vs other PI); this association remained in analysis restricted to uninfected infants. Other risk factors were maternal IDU (AIRR 1.45 [1.19-1.76]), primiparity (AIRR 1.19 [1.01-1.40] vs ≥2 previous births) and infant male sex (AIRR 1.14 [1.02-1.27]).

**Conclusion:** In this study of women starting cART in pregnancy, no association between NRTI backbone and PTD or SGA was found, but SGA was more common among infants exposed to LPV/r.

No conflict of interest

**Abstract: P_99**

**Prevention of Mother-to-Child transmission**

**Co-occurring syndemic factors during pregnancy and association with non-suppressed viral load at delivery among HIV-infected women in Cape Town, South Africa**

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**Background:** Adverse psychological and social factors may be prevalent among HIV-infected pregnant women, with well-documented harmful effects. However, there are few data exploring the co-occurrence of these factors during pregnancy and the syndemic effect on HIV-related outcomes. We examined the co-occurrence of unintended pregnancy and depression, intimate partner violence (IPV) and hazardous alcohol use during pregnancy; and explored associations with non-suppressed viral load (VL) at delivery among pregnant women initiating lifelong antiretroviral therapy (ART) in Cape Town, South Africa.

**Materials & Methods:** ART-eligible women were recruited as part of the MCH-ART study at their first antenatal visit, and were prospectively followed through pregnancy to an early postpartum visit. Measures of depression (Edinburgh Postnatal Depression Scale; EPDS), IPV (World Health Organization Violence Against Women questionnaire), and hazardous alcohol use (Alcohol Use Disorders Identification Test – Consumption; AUDIT-C) were administered, and VL testing (Abbott RealTime HIV-1) was conducted. A psychosocial risk score was calculated by summing the presence (vs absence) of each individual risk factor, using standardized cut-off scores for each scale. We used linear regression to explore associations with psychosocial risk scores; and logistic regression to explore associations between psychosocial risk scores and non-suppressed VL (VL ≥1000 copies/mL) within 30 days of delivery.

**Results:** Among 543 women (mean age: 28.2 years), 70% reported unintended pregnancy, 11% reported antenatal depression, 10% reported hazardous alcohol use and 6% reported IPV. These factors were highly associated with each other, and women reported experiencing a total of 0 (25%), 1 (56%), 2 (15%) and 3 (4%) risk factors, respectively. After adjustment for age and timing of HIV diagnosis, a higher psychosocial risk score was observed among women reporting single marital status (\(p<0.001\)) and lower socioeconomic status (SES; \(p=0.002\)). A higher risk score was strongly associated with later gestation when entering antenatal care (\(p<0.001\)), higher VL prior to ART initiation (\(p=0.003\)) and reduced time on ART at delivery (\(p=0.001\)), independent of demographic characteristics. At delivery, VL ≥50 and ≥1000 copies/mL was observed in 24% and 7% of women, respectively. After adjustment for age, marital status, SES and timing of HIV diagnosis, a higher risk score was associated with an increased odds of VL ≥1000 copies/mL at delivery.
delivery (adjusted odds ratio: 2.22; 95% CI: 1.44-3.43; p<0.001); consistent results were observed when VL ≥50 copies/mL was examined. These associations appear to be mediated by higher VL prior to ART initiation and later gestation when entering antenatal care, and consequent reduced time on ART at delivery.

Conclusions: Adverse psychological and social factors during pregnancy are prevalent in this population, and frequently co-occur. A higher psychosocial burden appears to be associated with an increased odds of non-suppressed VL at delivery, with this association explained by later gestation when entering antenatal care and higher VL prior to ART initiation. These novel data suggest that interventions to reduce additive psychosocial risk are urgently needed in this context, and further research should explore how these syndemic factors interact to mutually enhance poor outcomes.

No conflict of interest

Abstract: P_100

Prevention of Mother-to-Child transmission

Breastfeeding cessation, maternal adherence to antiretroviral therapy and HIV viremia in the early postpartum period: a prospective cohort study

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Background: Current World Health Organization prevention of mother-to-child HIV transmission (PMTCT) recommendations promote lifelong universal maternal antiretroviral (ART, 'Option B+') in pregnant and breastfeeding women; in most resource-limited settings, women on ART should exclusively breastfeed for 6 months, with continuation through 12 months. However, both maternal adherence to ART and recommended breastfeeding practices may be hampered by factors such as maternal health-related behavior, illness, and socio-economic challenges. In combination, non-adherence to maternal ART and suboptimal infant feeding practices may limit the potential child health benefits of Option B+, but data on these interrelationships are few. We investigated the association between infant breastfeeding practices and maternal ART use in Cape Town, South Africa.

Materials & Methods: As part of a larger study of ART services for HIV+ women and their children [the Maternal-Child Health-Antiretroviral Therapy (MCH-ART) study], a cohort of women initiating ART during pregnancy at a primary care clinic were followed through 12 months postpartum with their breastfeeding infants. Maternal ART adherence (30-day maternal recall of missed doses) and viral load (VL) testing (Abbot Realtime HIV-1 assay) were collected at study visits separate from routine health services. For this analysis, suboptimal maternal ART use was defined and analyzed separately as (a) at least one VL >400 copies/ml ('viremia') close to delivery, at 6 weeks and/or 3 months postpartum; and (b) >1 missed ART dose in preceding month, averaged over all follow-up time. Proportional hazards models were used to examine associations between suboptimal maternal ART use and breastfeeding duration, adjusting for maternal and child characteristics with results presented as adjusted hazard ratios (aHR) with 95% Confidence Intervals (CI).

Results: Four-hundred and forty-six women [median age 28 years; interquartile range (IQR) 25-32; 18% primigravida; median nadir CD4 cell count 354 cells/μL] were followed a median of 52 weeks postpartum. Median duration of any breastfeeding was 29.4 weeks (IQR 9.4-52) and of exclusive breastfeeding, 9.8 weeks (IQR 3.8-23.9). Overall, 15% of the cohort experienced at least one VL >400 copies/mL; 17% reported missing at least one ART dose/30 days. Women with viremia on ART breastfed for significantly
shorter periods of time (median, 16 weeks) compared to women who remained virologically suppressed (median, 32 weeks; aHR 1.68, 95%CI:1.18-2.40). In addition, breastfeeding cessation occurred earlier among women who missed an average of >1 ART dose/month (median, 16 weeks vs. 32 weeks; aHR 1.59, 95% CI (1.11-2.27]). Results were similar for duration of exclusive breastfeeding. Adjusting for viremia, breastfeeding cessation was significantly associated with maternal employment (aHR 1.57, 95%CI:1.21-2.05), hazardous postpartum drinking (aHR 1.69, 95% CI:1.13-2.54), higher baseline CD4 cell count (≥ vs < 350 cells/µL; aHR 1.34, 95%CI:1.03-1.74); and marginally with postpartum depression (aHR 1.80, 95%CI:0.98-3.30).

Conclusions: These novel data suggest that HIV+ women with evidence of suboptimal ART use may also be more likely to stop breastfeeding early. While further research is needed to understand the relationship between maternal ART adherence and breastfeeding, these data point to the potential need for postpartum interventions that integrate the maternal and child health aspects of Option B+ services.

No conflict of interest

Abstract: P_101

Prevention of Mother-to-Child transmission

Missed Diagnostic Opportunities within South Africa’s Early Infant Diagnosis Programme, 2010 – 2015

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Introduction: Specimens submitted for HIV PCR testing that require but do not yield a positive or negative result represent missed diagnostic opportunities (MDOs) within the laboratory. As South Africa prepares for the elimination of mother to child transmission (EMTCT), knowledge of performance of testing, including specimen rejection, is critical. We describe, enumerate and characterize, for the first time, MDOs in South Africa’s HIV infant diagnosis programme from 2010 – 2015.

Materials & Methods: All specimens registered for HIV PCR testing within the National Health Laboratory Service (NHLS) from 01 January 2010 to 31 December 2015 that did not receive either a positive or negative result were extracted from the NHLS Corporate Data Warehouse (CDW). Descriptive analysis was performed on the collated laboratory data which were coded and categorized into four groups according to the rejection text on the laboratory information system (LIS), namely: healthcare worker error, laboratory error, non-coded error, and no result required.

Results: A total of 2180611 specimens were registered for HIV PCR testing from 2010 to 2015 of which 136030 (6.2%) received neither a positive or negative result. Healthcare worker error comprised 42194 specimens (31%), laboratory error 34061 (25%), non-coded error 50222 (37%), and no result required 9553 (7%), leaving a total of 126477 MDOs. As a proportion of total HIV PCR specimens registered, MDOs represent 5.8% of tests within the EID programme from 2010 to 2015, with the total number of MDOs per year remaining fairly constant but proportionally decreasing from 21079 specimens (7.1%) in 2010 to 21382 specimens (4.4%) in 2015.

Of the 76255 MDOs associated with a rejection code, healthcare worker error represented 55.0% and laboratory error 45.0%. Healthcare worker error comprised specimens with insufficient volume (49.5%), clerical error (22.2%), poor quality specimens (17.5%), and incorrect specimen type (10.8%). Although insufficient specimen volume has been the principal reason for healthcare worker error since 2012, this number has reduced since 2013 but there have been simultaneous increases in clerical error and poor quality specimens.

Laboratory error comprised pre-analytical error (18.5%), which included specimens lost in transit (13.7% of total lab error), and analytical error (81.5%) which was further divided into indeterminate (49.9%), invalid (23.4%), and non-specific analytical laboratory errors (8.2%). The percentage of indeterminate results as a proportion of detected specimens (positives and indeterminates) has remained constant at around 17% per annum since 2011 with no
marked monthly changes seen since the introduction of universal birth testing in the national guidelines in June 2015.

Conclusions: Missed diagnostic opportunities account for >17000 specimens per annum since 2010 (4.4-7.4% of all registered HIV PCR specimens), with healthcare worker error comprising more than half of MDOs associated with a rejection code. The wastage of resources and delayed diagnosis associated with MDOs need to be addressed as South Africa works towards EMTCT. Data from the NHLS CDW provides the opportunity for surveillance and quality improvement within the EID programme, although uniform laboratory practice should be re-enforced including the adoption of national standard operating procedures encompassing pre-analytical and analytical specimen rejection.

No conflict of interest

Abstract: P_102

Prevention of Mother-to-Child transmission

Low acceptance of early antiretroviral therapy (ART) among post-partum women in 14 countries across the globe

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Introduction: Beginning in 2011, the PROMISE trials enrolled 5398 asymptomatic HIV-infected pregnant women who did not meet local criteria for antiretroviral treatment (ART). At enrolment, women were randomly assigned different antiretroviral strategies to assess vertical transmission during pregnancy and post-delivery, infant safety, and maternal health. In June 2015 the START study results were announced, demonstrating that early ART initiation regardless of CD4 count reduces the risk of HIV disease progression. The PROMISE study team rapidly informed active participants of these results and strongly recommended that
women not receiving ART immediately initiate treatment to optimise their own health. In November 2015 an independent data and safety monitoring board recommended beginning the process of summarizing and publishing results of this ongoing study. We summarize PROMISE participants’ responses to these recommendations and their reasons given to either accept or decline the offer of early ART.

Material & Methods: A mixed methods approach was used to gather both qualitative and quantitative responses from PROMISE participants who received the START information. PROMISE study staff actively contacted participants to return to the clinic. At clinic visits, staff delivered START results, utilising a structured script in a language chosen by the participant and assessing comprehension. Women not on ART were advised to accept the offer to initiate ART, during a client-centred counselling session. The information-giving and counselling sessions were documented in real time by staff completing closed and open-ended questions on a data form. Women selected their primary reason for accepting or rejecting the offer of early ART from a set of closed options. We report the uptake of early ART and the primary reasons in support of their decisions among PROMISE participants.

Results: Of the 4513 PROMISE active participants, 4192 (93%) underwent the standardised information-giving and counselling session. These women had been in follow-up for a mean of 2.8 years (range 8 months – 6 years). There were 1483 women not on ART (35%) who were advised to initiate ART. The offer was accepted by 984 women (66%) but 499 (34%) declined. Acceptance rates by country varied from 37-100%. The primary reasons given for declining ART were wanting more time to consider (40%) and feeling well and knowing CD4 count was high (18%), with a minority expressing concerns about potential side effects of ART (8%). The primary reasons given for accepting early ART were concern about health (45%) and because of the recommendation given by the protocol team (36%).

Conclusions: These data from a large sample recruited across a wide variety of settings demonstrate that a substantial number of women were not willing to initiate early ART after a single counselling session. Despite prior exposure to intense ART education and HIV monitoring within a highly-resourced clinical trial setting, more than one third of women still needed more time to consider the offer to start early ART for their own health. This finding is of importance to ART programme implementers as they develop communication materials for the test-and-treat strategy.

No conflict of interest

Abstract: P_103

Prevention of Mother-to-Child transmission

Impact of maternal antiretroviral therapy (ART) versus infant nevirapine prophylaxis on somatic growth of breastfeeding infants in the PROMISE trial

Introduction: To address concerns about the potential adverse impact of antiretroviral (ARV) exposure on infant growth and bone
mineralization, we evaluated the effect of postnatal ARV exposure on somatic growth of HIV-exposed uninfected breastfed infants (HEUs) in sub-Saharan Africa and India.

Material & Methods: The postpartum component of the multi-site PROMISE trial randomised eligible mother-infant pairs 6-14 days after delivery to maternal triple ART or infant nevirapine prophylaxis (NVP) for prevention of vertical transmission while breastfeeding (maternal CD4 count above local limit for ART initiation and infant >=2000g). ARV exposure in utero was by prior randomization to three groups; tenofovir-based triple ART (11.9%), zidovudine-based triple ART (41.3%), or zidovudine alone (41.5%); and 128 late presenters enrolled in labour or after delivery had no in utero ARV exposure (not randomized) (5.3%). Growth parameters were measured using standard methods at birth and age 10, 26, 74 and 104 weeks. Infant feeding method and HIV status were monitored throughout follow-up. We studied the effect of the postpartum randomization on infants’ growth using an intention-to-treat approach and World Health Organisation z-scores for length-for-age (LAZ, primary outcome), weight-for-age (WAZ) and head circumference-for-age (HCAZ) at birth, age 26 weeks (primary time point) and 74 weeks. Student T-tests were used to evaluate LAZ, WAZ and HCAZ; mean and 95% confidence interval (CI) are presented. The primary outcome was further analysed by ARV exposure in utero in linear regression models.

Results: The 2444 infants born to 2431 mothers were randomized to maternal triple ART (1227) or infant NVP (1217) and followed through a median of 104 weeks of age. The maternal triple ART regimen contained tenofovir/emtricitabine (98%) plus lopinavir/ritonavir. Ten percent of infants (236) prematurely discontinued study follow-up, 38 due to death (2%). Maternal and infant baseline characteristics were comparable between study arms (median birthweight 2900g; gestational age 39 weeks; maternal age 26.6 years; postpartum CD4 count 686 cells/mm$^3$). At week 26 the mean LAZ was -0.93 (95% CI -1.02, -0.83) in the maternal triple ART arm and -0.86 (-0.95, -0.77) in the infant NVP arm. There was no significant difference between the arms for LAZ at week 26 (mean difference -0.07 (95%CI -0.20, 0.06), p-value=0.30), or WAZ (mean difference -0.07 (95%CI -0.20, 0.06), p-value=0.30) and HCAZ (mean difference -0.08 (95%CI -0.19, 0.02), p-value=0.13). There was no significant evidence that the postpartum randomization treatment effect on LAZ at week 26 differed by the four in utero ARV exposure groups (p-value=0.56). Similarly, there was no significant difference between the arms for length-, weight- or head circumference z-score outcomes at week 74 (p-value>= 0.18).

Conclusions: Growth outcomes in breastfed HEUs through age 74 weeks did not differ significantly between infants who received NVP prophylaxis and those whose mothers received predominantly tenofovir-containing triple ART.

No conflict of interest

Abstract: P_104
Prevention of Mother-to-Child transmission
Impact of Maternal Sero-conversion during Pregnancy and Breast Feeding on Vertical Transmission and Implications for Preventing Mother-to-Child Transmission in Malawi

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Introduction: Due to the success of Option B+ and preventing-mother-to-child-transmission (PMTCT) cascades, Malawi has seen a significant drop in mother-to-child-transmission over the past 3 years (40% to less than 5%). The number of new infections identified amongst infants on inpatient wards however remains high (25% of new pediatric infections). Pregnant women in Malawi who present for care are tested at the first antenatal clinic (ANC) visit, those infected are referred for antiretroviral therapy (ART), those who are negative receive counseling on high-risk behavior and not routinely retested. Malawi has a known 4% false-positive rate for ANC testing. Though
previously thought negligible, a disproportionately high number of infected infants/children are being identified whose mothers tested negative at ANC, suggesting maternal sero-conversion during pregnancy/breast-feeding is occurring and contributing to new infections amongst infants/breast-feeding children.

**Methods:** A retrospective chart review was done of the HIV Testing and Counseling (HTC), early-infant-diagnosis dried blood spot (DBS), and linkage registers at the Kamuzu Central Hospital inpatient pediatric ward from January 1, 2016-March 30, 2016. Data was collected from all mother-child pairs who received HTC testing. Data on mother's ANC testing was collected for those with children under 36-months and/or still breast-feeding at the time of testing including confirmation of ANC testing results in the mother's passbook. Exposed infants received same day DBS-testing using a point-of-care machine. A descriptive analysis of the data was performed.

**Results:** 2745 mother/child pairs were tested during the above period of which 160 mothers (5.8%) and 118 children (4%) were found to have positive rapid tests. Of the 160 mothers found newly positive, 20 have documented negative rapid tests from ANC within the past 3 years (12.5%). Of those 20 mothers with newly positive rapid tests, 17 children (85%) were confirmed infected with either DBS (<12 months) or rapid test (>12 months), 14% of all children found infected. 10/20 were found with presumed-severe-HIV-Disease (PSHD) (7 DBS positive, 3 DBS negative) and 10 were found in the nutritional rehabilitation unit with severe acute malnutrition (all rapid test positive). Mean age at admission was 14-months (6.8 months for PSHD, 19-months for SAM). 2/17 (12%) children died during the admission, (average inpatient mortality for newly-infected children is 7%), 11 were initiated on ART during the hospital admission, 3 initiated on ART post-discharge, and 1 absconded.

**Conclusion:** The phenomenon of maternal sero-conversion during late pregnancy and/or while breast-feeding is real and associated with high rates of vertical transmission and infant mortality. Though false negative tests during ANC are likely, they are not accounting for all the seroconverted results. Traditional PMTCT cascades that promote testing only at the first ANC visit will miss mothers who seroconvert. Due to the associated mortality, catching the children on inpatient wards when they present sick is not enough. PMTCT cascades need to consider universal retesting of negative pregnant women on labour wards and breast-feeding mothers at the 9-month vaccine visit. Further investigations are needed to classify high-risk behaviors of the mothers and their partners during late pregnancy and while breast-feeding that are contributing to the new infections.

**No conflict of interest**
was used to estimate risk in infant HIV infection attributable to maternal, delivery, and infant interventions.

**Results:** 9935 infants of HIV positive mothers were evaluated by the EID programme from September 2009 to December 2014. The median age at first infant PCR test was 6 weeks (IQR 4-12) and this declined over the period of the programme (20wks (2010) to 4.5wks (2014) trend \( p<0.001 \)). 61.5% of mothers were reported to have received antiretrovirals during pregnancy, 59.3% of deliveries were in hospital; 90.4% vaginal. During the period, the proportion of infants issued with antiretroviral prophylaxis after birth rose from 57.0% (2010) to 78.5% (2014, trend \( p<0.001 \)).

Overall, 4.3% [299/7032] of infants tested under 8 weeks were PCR positive versus 11.4% [259/2275] at 8-32 weeks and 29.6% [186/628] at >32 weeks. Crude and adjusted risk factors for positive PCR before 8 weeks are shown in table 1. Absolute transmission risk was 11.7% [95%CI 9.8-14.0] for mother-pairs where neither received antiretrovirals, and 2.1%[95%CI 1.7-2.6] for mother-pairs who both received antiretrovirals. This suggests the programme averts 63.2% of expected transmission at current Option B+ coverage, but could avert a further 18.8% if comprehensively adopted.

**Conclusions:** The Haitian EID programme is effective and meets international targets for the elimination of MTC in a challenging context. Further research is needed to understand the origins of missed opportunities for maternal and infant intervention.

*No conflict of interest*

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**Abstract: P_106**

**Prevention of Mother-to-Child transmission**

**Setting a new frontier for elimination of mother to child transmission of HIV: Identifying the new priority countries**

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**Background:** Mother to child transmission of HIV infection remains a major public health concern in sub-Saharan Africa despite the notable scale up of HIV care and treatment services especially with the advent of the Global Plan towards the elimination of new HIV infections among children and keeping their mothers alive. Priority countries targeted by Global Plan on average are yet to meet most of the set goals and therefore requiring the need to re-define the goals and objectives of the elimination interventions. This study is to evaluate the status of the Global Plan programme and refine the definition of priority countries in relation to their performance prior to 2015.

**Methods:** The mid-point estimates for the 2015 Global Progress Report was used to analyses the trend from 2009 to 2015. A special assessment tool with the scale of 0-2 was used in determining the performance of different countries based on different prong targets and goal such as: a) Percentage reduction in the number of new HIV infections among children aged 0–14 years (2009-2015); b) Final mother-to-child transmission rate; c) Antiretroviral therapy coverage among children (aged 0–14 years); d) Percentage of infants born to women living with HIV receiving a virological test within two months of birth; and e) Proportion of HIV-positive pregnant women receiving lifelong antiretroviral therapy. A total score of 0-1 was termed poor performance, score of 2-3 was described as average and 4- and above was termed a good performance.
**Abstract**

**Results:** Among the priority countries, Angola, Burundi, Cameroun, Chad, Cote d’Ivoire, Democratic Republic of Congo, Ghana and Nigeria were rated as having poor performance with low scores in relation to various prong targets and goal that were evaluated. South Africa, Botswana, Swaziland, Uganda, Tanzania, Namibia and Mozambique performed very well. These seven countries made the greatest progress in reducing new infections. About half of the priority countries achieved the goal of reduction of 50% or more by the end of 2014. However countries like Nigeria still have very high numbers of new infections among children and women in reproductive age group. There was a very low performance in terms of paediatric antiretroviral coverage in most of the priority countries.

**Conclusion:** The eight countries that performed below expectation by failing to reach almost all the set targets should be redefined as the new priority countries and most of the efforts towards the elimination initiatives should be targeted at these countries. Increased funding are needed from multinational organisations, local funding agencies and increased budgetary allocation by various Governments. These agencies must work hand in hand with the Governments of these countries by investing in infrastructures and human resources, and ensuring judicious use of the fund. The health system policies in these countries should also be revisited and adapted to suit the reality on ground. There should also be increased collaboration among the countries that are doing well and the poor performers.

*No conflict of interest*

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**Abstract: P_107**

**Coinfections in HIV infected children**

**Long-term maintenance of undetectable viral is associated with better response to immunization among HIV vertically-infected children, in Rio de Janeiro, Brazil**

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**Background:** Immunization guidelines use CD4 cell count and/or percent as the main criterion to immunize HIV infected children. The impact of undetectable viral load in children with high CD4 cell counts at immunization has not been evaluated. The aim of this is study was to compare the immune response after two doses (12-18 month interval between doses) of *Neisseria meningitidis* C conjugate vaccine (C Polysaccharide/CRM197) at dose (10 μg/0.5 ml) among individuals who were able to maintain undetectable viral load (UVL) through study follow up (at least 12 months) or not (non-UVL).

**Methods:** HIV vertically-infected patients, aged 2-18 years old, with CD4+ cell count>15% or >350 cells/mm³ without active infection were immunized. One month after the second dose, post-immunization protective antibody titer, defined as a serum bactericidal assay(SBA) titer ≥ 1:4 (with human complement), was evaluated. Children were classified as responders (SBA≥1:4) or otherwise non-responders SBA (<1:4). Abivariate analysis was performed, and variables with p-value < 0.15 were independently evaluated through logistic regression analysis.

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*No conflict of interest*
Results: 124 children using cART (defined as three ARTs, from at least two different classes) before the study initiation were enrolled: 62 (50%) were able to maintain UVL through the follow up. The median of study follow up was 13.1 and 13.3 months for UVL and non-UVL groups, respectively, p=0.11. At the study entry, the median of cART duration was 6.2 years for UVL and 6.4 for non-UVL, p=0.71. 57 (92%) and 41 (66%) were able to present immune response to the vaccine (responders) in the UVL and the non-UVL groups, respectively p< 0.01. The median age was 12.5 years for the non-responders group and 13 for the responders, p=0.14. 53 (57%) were female in the responders group and 13 (50%) in non-responders, p=0.52. Among the non-responders the median of the CD4 cells percent was 26% in the non-responders group and 29% in the responders, p< 0.01. Factors associated with protective antibody concentration were: maintenance of UVL through study (OR=5.1, 95%CI=1.7-14.9) and higher CD4 cells percent at study entry (OR=1.1, 95%CI=1.0-1.2)

Conclusion: UVL was an associated with response to vaccination independent of CD4 cell percent and should be considered when planning immunization of HIV infected children.

No conflict of interest

Abstract: P_108

Coinfections in HIV infected children

Neuroradiological findings and outcome in HIV infected children and adolescents: a case series analysis

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Background: Newlands clinic is one of the major HIV treatment centers in Harare, Zimbabwe looking after children and adults. Approximately 1923 patients below the age of 24 years have ever been registered at Newlands clinic, which has been operational since 1 February 2004. The cohort of children managed has been largely consistent and has patient who have been followed up over 12 years by the same health care providers. Located in a country with a high prevalence of HIV in a low resource economy, it provides a rich environment to study the natural history of HIV related disease complications and their outcomes. Neurological manifestations and particularly cerebrovascular disease occurring in the pediatric population have been described. This analysis presents one of the largest number of pediatric patients followed up at the same health institution.

Materials & Methods: This was a retrospective case series analysis. Using the Newlands clinic electronic medical record system Epoch; Files of patients in the age group 1-19 years who were registered in the period 1 February 2004-31 December 2015 were searched. Those with a recorded diagnosis related to stroke were retrieved and analyzed for the following: Demographic data, presenting symptoms and signs, investigations carried out particularly neuro-radiological tests and findings, Clinical state of patient on subsequent visits after initial presentation described as outcome within the period under review. The data was exported into excel and analyzed using stata. It was presented as tables and case summaries.

Results: 14 patients had a recorded diagnosis suggestive of stroke in the period 2004-2015. 3/14 were male. The mean CD4 count was 259. 10 patients were already on ARVs. Hemiparesis was the main presenting sign in all the patients. 6/14 patients had CD4 below 200. 11/14 had neuro-radiological imaging consisting CT, MRI and/or CT angiography. Findings on neuro-radiological imaging were: 6/11 vasculitis with no evidence of another infective cause, 1/11 vasculitis with toxoplasmosis, 1/11 vasculitis with PML, 1/11 PML, 1/11 cerebritis and encephalopathy, 1/11 vasculopathy with aneurysmal dilatation of the middle cerebellar arteries. 8/14 deceased in the period under review; 5/8 died within 2 years of event. There was recorded progression of condition in all patients. In the 6/14 alive; 1/6 developed seizures in 3 years, 1 transferred out, 1/6 developed encephalopathy and HAND, 3/6 have motor related disability.

Conclusions: Vasculitis was a common neuro-radiological imaging finding in patients with a stroke diagnosis in this analysis. The clinical outcome of this group of stroke patients was poor, with a greater proportion dying within the first 3 years of stroke related complications.

No conflict of interest
Abstract: P_109

Coinfections in HIV infected children

Malaria and HIV in Ugandan children hospitalized for acute febrile illness

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Background: Dual infection with HIV and malaria fuels the spread of both diseases in sub-Saharan Africa. Implications for diagnosis and management among children hospitalized with fever in areas where both pathogens co-circulate deserve further study.

Methods: A prospective cohort study was conducted among children (2mo-5yr) hospitalized with acute febrile illness at the Jinja Regional Referral Hospital, Uganda, who presented between 15 February, 2012 and 29 August, 2013.

Results: Of 2085 children, 78 (3.7%) were seropositive for HIV. Of these, 39/78 had detectable HIV RNA (median 69,000, IQR 6,500 to 740,000 copies/mL). Overall, 43 infants and children were HIV-infected (seropositive beyond 24mo and/or HIV RNA-positive), and 24 infants were HIV-exposed, uninfected (seropositive, HIV RNA negative, <24mo). 986/2085 (47%) had a diagnosis of P. falciparum (highly specific parasitologic criteria: rapid test positive for both HRP2 and pLDH antigen, and positive thick blood smear). HIV-malaria co-infection was found in 8 patients. The rate of co-infection was lower than expected, under the null hypothesis that infections are independent: malaria prevalence 8/43 (19%) among patients with HIV vs 978/2038 (49%) among patients without HIV, OR 0.25 (95%CI 0.11-0.54), p=0.0001. One co-infected patient died (12%) compared to 23/978 (2.4%) deaths among HIV uninfected patients with malaria (p=0.18). HIV infection was associated with higher mortality among patients with non-malarial febrile illness (7/25 (28%) vs 26/470 (5.5%), OR 6.6 (95%CI 2.5-17), p=0.0006).

Conclusions: The proportion of febrile illness requiring hospital admission attributable to malaria was lower among HIV-infected than HIV-uninfected children. This may be explained by relatively increased susceptibility to pathogens other than malaria among HIV infected children.

No conflict of interest
Abstract

Coinfections in HIV infected children

Tuberculosis in HIV-infected children in Europe, Thailand and Brazil: paediatric TB:HIV EuroCoord study

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Abstract: P_110

Tuberculosis in HIV-infected children in Europe, Thailand and Brazil: paediatric TB:HIV EuroCoord study

Background: Tuberculosis (TB) is the major cause of mortality and morbidity in HIV-infected children. Diagnosis is difficult and successful TB-treatment outcomes vary across settings from 69% to 88%. Contemporary data are scarce in high and middle-income settings.

Methods: Fifteen cohorts/sites participated. HIV-infected children aged <16 years diagnosed with TB in 2011-2013 were included and followed-up for 2 years. Treatment outcomes were categorised as favourable: cured and treatment completed; or unfavourable: treatment not completed, recurrence, death, and not known. TB incidence per 100,000 person-years (PY) was calculated. Characteristics were compared by TB outcome using Fisher’s exact test for categorical variables and Wilcoxon’s rank-sum test for continuous variables. Adjusted analyses were not possible due to the small sample size.

Results: Of 4,265 children, 127 (3%) were diagnosed with TB: 1%, 3%, 5% and 8% in Western Europe, Eastern Europe (EE), Thailand and Brazil respectively. Estimated TB incidence rates were 239, 982, 1633 and 2551 per 100,000PY respectively. Median age at TB diagnosis was 6.8 (IQR 3.0-11.5) years. 63 (52%) had advanced/severe WHO immunological stage. Children in EE were younger (p=0.005), in Thailand they were more immunocompromised (none/mild vs advanced/severe WHO immunological stage; p<0.0001), and in Brazil more children reached HIV CDC stage C prior to TB diagnosis (p=0.0003). 48 (38%) diagnoses were bacteriologically-confirmed.

TB preventive treatment was used in 23% (23/102) of those diagnosed with TB after HIV.

Of 67 children not on ART, 93% initiated/restarted ART at a median 1.8 (0.8, 3.9) months after TB diagnosis; 94% achieved VL<400 c/ml within 12 months. Of 60 children on ART, TB was diagnosed at median 29.7 (IQR 6.1-55.0) months after ART initiation, and 51% had VL ≤400 c/ml at TB diagnosis. Seven participants had TB-IRIS at a median of 2.3 (IQR 1.1-8.8) months after ART initiation.

Nine children had drug-resistant TB, 8 from EE. 10% (12/118) of children with suspected drug-resistant TB were treated without rifamycins. Streptomycin was used in 25 children (23/102) of those diagnosed with TB after HIV. Of 67 children not on ART, 93% initiated/restarted ART at a median 1.8 (0.8, 3.9) months after TB diagnosis; 94% achieved VL<400 c/ml within 12 months. Of 60 children on ART, TB was diagnosed at median 29.7 (IQR 6.1-55.0) months after ART initiation, and 51% had VL ≤400 c/ml at TB diagnosis. Seven participants had TB-IRIS at a median of 2.3 (IQR 1.1-8.8) months after ART initiation.

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Nineteen children had unfavourable TB outcomes (4 died, 5 did not complete treatment, 1 recurrent TB, 1 unknown outcome). In unadjusted analysis, children from Brazil, not virologically suppressed on ART and with a previous CDC stage C event had a significantly

Keywords: Tuberculosis, HIV, children, Europe, Thailand, Brazil, HIV-infection, treatment, outcomes.

Conclusions: The EuroCoord study provides important evidence on TB in HIV-infected children in Europe, Thailand and Brazil. Further studies are needed to understand factors associated with successful treatment and prevention of TB in HIV-infected children.
increased risk of an unfavourable TB outcome (p<0.05).

Conclusion: TB incidence is higher in HIV-infected children compared to the general population from the same countries. Universal ART initiation and scale-up of preventive treatment would reduce missed opportunities to prevent TB. Some prescribing practices in EE, including widespread use of streptomycin and adding less than three second-line drugs in the setting with high MDR-TB, are sub-optimal and should be addressed. Despite differences in management, most children had good outcomes.

Conflict of interest
Financial relationship(s): The European Union Seventh Framework Programme (FP7/2007-2013) under EuroCoord (grant #260694, www.eurocoord.net) PENTA Foundation

Abstract: P_111

Complications of HIV therapy

Anthropometric measures at 12 and 24 months of age among ‘HIV and prophylactic ARV drug’ perinatal exposed and unexposed children in Malawi and Uganda

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Background: Previous studies based on European and North American cohorts suggest that perinatal exposures to maternal HIV and prophylactic antiretroviral (ARV) drugs are associated with negative childhood growth. However, evidence based on breastfeeding populations with prolonged HIV and ARV exposures is limited. This study compares anthropometric measures at 12 and 24 months of age among ‘HIV and ARV perinatal exposed but HIV uninfected’ (HEU) children to measures among ‘HIV uninfected and unexposed’ (HUU) controls.

Materials and Methods: A prospective cohort study was enrolled from 09/2013-10/2014 at two sites in Blantyre, Malawi and Kampala, Uganda. HEU children were co-enrolled from the PROMISE prevention of mother-to-child transmission ARV randomized trial, and age- and gender-matched to HUU controls from child-well clinics. Group comparisons by exposure (HEU vs. HUU) and by site of WHO standardized age- and gender-based Z scores for weight (WAZ), length (LAZ) and head circumference (HCAZ) at 12 and 24 months of age were performed using mixed effects models that generalize classical analysis of repeated measures. Least square means by exposure and site at 12 and 24 months of age were compared. Proportions of children below clinically meaningful standard deviation (SD) cut-offs (WAZ<-1, LAZ<-2, HCAZ<0) were analyzed using generalized mixed models with logit link function and binomial error distribution appropriate for the repeated measures of binary data.

Results: Sample size at 12 and 24 months of age, was 367 and 417 children in Malawi; and 407 and 434 in Uganda, respectively, with 52% and 51% HEU in Malawi and Uganda, respectively. Lower anthropometric group mean Z scores (HEU versus HUU) were observed among Ugandan children at 12 months of age: WAZ (-0.19 vs. 0.44, p=0.02); LAZ (-1.31 vs. -0.94, p<0.01) but not for HCAZ (0.44 vs. 0.44, p=0.96); and at 24 months of age: WAZ (-0.40 vs. -0.11, p<0.01); LAZ (-1.46 vs. -1.08, p<0.01) and HCAZ (0.31 vs. 0.57, p=0.01). No significant differences were noted between Malawian HEU and HUU groups at either 12 or 24 months. In Uganda, a similar trend was observed with higher odds of lower anthropometric measures observed among HEU versus HUU based on Z score cut-offs: Odds Ratio (95% Confidence Interval) at 12 months for LAZ was 2.66(1.57, 4.49) and at 24 months, for WAZ was 1.72(1.05, 2.81); LAZ was 1.83(1.19, 2.83) and HCAZ was 1.56(1.05, 2.33).
Conclusion: These data indicate that in Uganda but not Malawi, perinatal exposures to both HIV and ARVs were associated with lowered growth parameters at 12 and 24 months of age compared to non HIV non ARV exposed children. The reasons for the differences in growth findings between Uganda and Malawi are unknown. Longer term follow-up through 60 months of age is ongoing.

Abstract: P_112

Complications of HIV therapy

Long-term lipodystrophy outcomes in stavudine-treated children randomised to remain on stavudine or switch to abacavir

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Introduction: Stavudine has been phased out of HIV treatment recommendations owing to toxicity concerns. We conducted a randomised trial (2010-2012 during the phase-out) among 213 HIV-infected children aged 3-5 years who had initiated stavudine-containing ART regimens and had no lipodystrophy at entry. Children were randomised to either switch to an abacavir-containing regimen or to remain on their stavudine-containing regimen. In addition, ART regimens included lamivudine and ritonavir/lopinavir or efavirenz. Here we report long-term follow-up beyond the initial one year period of the original trial.

Methods: In 2013 we enrolled children from the trial into an observational cohort study at Rahima Moosa Mother and Child Hospital, Johannesburg, South Africa. Clinical management followed routine practices. Six-monthly study visits comprised standardised clinical assessments to determine if features of lipoatrophy (sunken cheeks, temporal wasting, skinny limbs, wasted buttocks) or lipohypertrophy (increased abdominal girth, dorsal cervical enlargement, breast enlargement) were present. Children were categorised as having definite lipodystrophy if ≥2 features were present and possible lipodystrophy if 1 feature was present. Standardised skinfolds and circumferences were measured.

Results: Of 106 children randomised to remain on stavudine, 81 (76.4%) were enrolled in the cohort study and 54 (66.7%) were still on stavudine at entry. Of 107 children randomised to switch to abacavir, 87 (81.3%) were enrolled and 81 (93%) were still on abacavir. Mean age at entry into the cohort study was 6.2 years (SD 1.5); children had been on ART for an average of 5.4 years (SD 1.3) and were on average 2.0 years (SD 0.7) post-randomisation. Children still on stavudine at entry were more likely to be diagnosed with definite or possible lipodystrophy during follow-up to 48 months after randomisation than children on abacavir (65.6 vs 48.5%, p=0.048). This association, when more stringent criteria were used (i.e. definite lipodystrophy diagnosis confirmed at the subsequent visit), remained: 28.0% vs. 16.8% in the stavudine vs. abacavir groups, respectively, p=0.09. Sunken cheeks (33.3%) and skinny limbs (63.9%) were the most common features of lipodystrophy in the stavudine group. On average, the proportion of leg skinfolds out of total skinfolds during long-term follow-up was 1% higher in the abacavir compared to the stavudine group (p=0.04), indicating less lipodystrophy. At the completion of the original trial, 17 children initially randomised to remain on stavudine had developed lipodystrophy and were switched to abacavir. 13 of these children were enrolled in the cohort study an average of 1.5 years after switching to abacavir (SD 0.9). During subsequent follow-up, lipodystrophy in 10/13 improved or resolved – three remained with persisting lipodystrophy more than 3 years after switching to abacavir.

Conclusion: Long-term stavudine use increased the likelihood of being diagnosed with lipodystrophy, but the condition also developed among children previously treated with stavudine and switched to abacavir. Despite changing children to a stavudine-free regimen, alterations in body shape may still occur and/or persist in a modest proportion.

No conflict of interest
Abstract: P_113

Complications of HIV therapy

Location of white matter microstructural abnormalities in children with HIV and bilateral lower limb spasticity compared to spastic CP: a DTI study


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Background: The clinical presentation of children with bilateral lower limb (BLL) spasticity due to HIV encephalopathy (HIVE) shows similarities to children with BLL spasticity and Cerebral Palsy (CP). However, as the etiology is different, there may be structural and microstructural differences on magnetic resonance imaging (MRI) of the central nervous system between these children. The aim of this study was to determine i) the regions involved and microstructural integrity of connecting white matter tracts based on Diffusion Tensor Imaging (DTI) of the brain and spine in children with BLL due to HIVE and CP; and ii) relationships between the involved DTI clusters and functional (upper and lower limb) status.

Materials & Methods: In this cross-sectional study, 41 children with BLL spasticity were recruited from children’s hospitals and special schools in Cape Town. Twenty-seven children were diagnosed with HIVE (mean age: 8.7±2.2 years, 11boys) and 15 with CP (mean age: 8.7±2.1 years, 9boys). DTI images were acquired on a 1.5 Tesla Phillips scanner, located at Red Cross Memorial Children’s Hospital. All data were preprocessed using TORTOISE, the relevant maps of DTI scalar parameters (FA, MD) were generated, and were coregistered to an MNI pediatric template using AFNI. Voxelwise comparisons were performed in FSL-randomise to identify clusters showing significant differences between groups. To control for Type I error, cluster size correction at \( p<0.01 \) was performed using AFNI-AlphaSim. Functional status was defined by Manual Ability Classification System (MACS) and Purdue Peg Board scores for upper limb function, and Gross Motor Function Classification System (GMFCS) and Gross Motor Function Measure (GMFM) scores for gross motor (lower limb) function. Mean DTI parameters in each cluster determined by voxelwise comparisons were correlated to the functional measurements using Pearson’s correlation, with \( p<0.05 \) defined as significant.

Results: Based on the DTI, voxelwise analyses revealed lower FA and higher MD in R corticospinal tract (R-CST) in children with HIVE. Conversely, lower FA and higher MD were found in 3 regions—right anterior right thalamic radiation (R-ATR), body of corpus callosum (BCC) and splenium of corpus callosum (SCC)—in children with CP compared to children with HIVE. Higher MD in Left (L) ATR and L superior longitudinal fasciculus (L-SLF) were also seen in children with CP. Mean FAs and MDs in R-ATR, BCC, SCC, L-ATR and L-SLF clusters were significantly correlated with MACS (except for L-ATR) and Purdue Peg Board scores of non-pereferred hand. However, no significant correlations were found with (lower limb) gross motor function scores.

Conclusions: This study demonstrates that despite similar clinical features of BLL spasticity, there are clear differences in white matter tract involvement in these two conditions. The finding of impaired white matter microstructural integrity in the corticospinal tract in these children with HIVE is in keeping with the location of white matter abnormalities reported in other cohorts of HIV infected children without BLL spasticity as part of their clinical phenotype. This suggests that the HIV virus itself does play a direct role in the aetiology of this severe physical manifestation of HIVE.

No conflict of interest
Abstract: P_114

Complications of HIV therapy

Gyrification differences in 7 year old HIV-infected children starting ART before or after 12 weeks of age

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Introduction: Early antiretroviral therapy (ART) has been found to improve outcomes for HIV-infected infants, however, long-term effects on brain development require further investigation. This study used magnetic resonance imaging (MRI) to measure cortical thickness, gyrification – measure of cortical folding - and subcortical brain volumes in 7-year-old vertically-infected children who started ART either before or after 12 weeks of age.

Methods: Participants were 61 HIV-infected Xhosa children (28 boys, age 7.21 ± 0.12 years) from the Children with HIV early Antiretroviral (CHER) trial and 43 uninfected controls (25 boys, age 7.23 ± 0.16 years, 20 HIV-exposed uninfected: HEU, 23 HIV-unexposed uninfected: HUU). 46 started time-limited ART before 12 weeks of age (Early-ART) while 15 started after 12 weeks of age (Late-ART). MRI scans were obtained following protocols approved by the Faculty of Health Sciences Human Research Ethics Committees of Universities of Cape Town and Stellenbosch. Viral loads were suppressed at time of scan. FreeSurfer software v5.1.0 was used to perform automated segmentation and reconstruction. Whole-brain cortical thickness and gyrification, as well as regional brain volumes, were compared between Late-ART and Early-ART children and to HEU and HUU children using a general linear model.

Results: There were no differences in cortical thickness or regional brain volumes between Late-ART and Early-ART children. However, Late-ART children had significantly greater gyrification than Early-ART children in a large bilateral medial frontal region, even after controlling for duration of ART interruption. There was a positive association between age at ART initiation and gyrification in similar regions. Late-ART children also showed greater frontal gyrification than controls, while Early-ART children had less gyrification than controls. Further, Late-ART children showed significantly greater frontal gyrification than HEU children, but not HUU children.

Conclusion: Gyral formation in childhood is sensitive to time of ART initiation. ART started before 12 weeks, irrespective of interruption, may impact the development of cortical folding during an early critical period, compared to delayed treatment. Increased gyrification observed in Late-ART children relative to controls may be due to inclusion of HIV-exposed controls, or may reflect an abnormal increase, as has previously been associated with certain neurodevelopmental disorders. Further neuropsychological tests will help clarify the effects of less cortical folding on cognitive sphere of Early-ART children and whether this is due to HIV or early ART.

No conflict of interest
Abstract: P_115

Complications of HIV therapy

Peripheral neuropathy among HIV-infected children on fixed-dose antiretroviral therapy in Zambia and Uganda: the CHAPAS-3 randomised clinical trial

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Background: Peripheral neuropathy (PN) is common in HIV infection and is a well-recognised adverse effect of some antiretrovirals and of isoniazid prophylaxis. We conducted PN assessment using a clinical tool among children on antiretroviral therapy (ART) in the open-label Zambian/Ugandan CHAPAS-3 Trial.

Methods: CHAPAS 3 recruited and randomised 478 HIV-infected children who were previously untreated (ART naive) or on stavudine for more than 2 years (ART experienced) to zidovudine/stavudine/abacavir with lamivudine and nevirapine or efavirenz as fixed dose or single, dispersible solid formulations. Blinded assessments of PN were performed at week 96 (earlier if starting isoniazid prophylaxis) and again at either 144 weeks or at trial exit. Symptoms of PN were assessed using a 6-point neuropathy symptom score (NSS) based on symptoms of gait unsteadiness, pain, numbness and foot discomfort. Clinical signs were measured on a 10-point neuropathy disability score (NDS) which used ankle reflex, temperature, vibration and pin-prick perception. PN was defined as presence of one or more symptom (NSS ≥1) and/or presence of 2 or more signs (NSD score≥2).

Results: A total of 375 children were evaluated for PN initially between weeks 84-96, and a second assessment between weeks 96-144. At baseline (week 0), the median CD4% was 21.3(15.8-31.5), mean (SD) weight-for-age z-score (WAZ) of -1.7(-1.4) and 130(34%) vs 122(33%) vs 123 (33%) randomised to zidovudine/stavudine/abacavir respectively. The median (IQR) age at initial PN assessment was 5.9(4.1-7.8) years. Thirty five percent (35%) were receiving isoniazid prophylaxis at the time of initial assessment. Symptoms of neuropathy were reported by 2.7%(10/375) at initial and 0.5%(2/166) at the second assessment. The most common symptoms reported were pain, pinprick sensation and numbness. Presence of signs of PN were detected in 5.9%(22/375) at initial and 1.8%(4/166) at second assessment. The most frequent abnormalities elicited were diminished ankle reflexes, vibration and pinprick perception. Of the 166 children that completed both assessments, the prevalence of clinical PN decreased from 10.2%(95% CI: 5.6, 14.9) to 2.4%(95% CI: 0.1, 4.8) between the first and second assessment. Use of stavudine (0.27), isoniazid (p=0.34), and low WAZ (p=0.32) were not associated with presence of clinical PN.

Conclusion: The study shows that prevalence of PN in these children who had been taking nucleoside reverse transcriptase inhibitors based regimens reduced over time on ART and was not associated with stavudine or isoniazid use. Assessment of neuropathy in younger HIV-infected children on ART is feasible using clinical tools.

No conflict of interest
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Abstracts
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Abstract: A_116

ARV treatment of Pediatric HIV infection

Treatment outcomes & need for third line ARVs among HIV-infected children less than 15 years on second line antiretroviral therapy in Uganda

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Background: Third-line ART (Anti-Retroviral Therapy) needs across high HIV burden countries in Africa, especially for growing populations of children and adolescents on ART, are largely unknown. With no prior nationwide assessment of second-line ART treatment failure rates on record, we conducted this study to establish treatment outcomes of children less than 15 years of age who have ever been initiated on second-line ART, the need for third-line pediatric anti-retroviral drugs (ARVs) and factors associated with failure on second-line ARV’s. At the time of the study, Uganda had not yet operationalized routine viral load testing, so WHO clinical staging and CD4 count were used to determine failure.

Methods: The study was conducted in October-November 2014. It was a retrospective review of records of HIV-infected children under 15 years of age who have ever been initiated on second-line ART. Children aged less than 15 years who were active in care were studied to determine the need for third-line regimens. The assessment was conducted in 60 purposively selected public and private health facilities in all regions in the country. Facilities with at least 10 children active on second-line ARVs based on data from DHIS2 (District Health Information System) for July-September 2014 were selected.

Results: A total of 1,438 children on second line ART was included, and 56% of them were male. Most (63%) of the patients had prior exposure to ART through the PMTCT program. Overall, 1,282 (89%) of the children were alive and on treatment, 4% were transferred out, 3% were dead, and 3% were lost to follow up. Of the 1,282 children, 208 (16 %) were failing on treatment using WHO clinical staging and CD4 count. The main factor associated with failure was being older than 5 years, the risk was 19 times greater in these children compared to the under 5’s. Other factors included; drug interruption while on second line ART and being on ART for more than 5 years.

Conclusions: Screening for possible failure on second-line ART should be intensified among older children and adolescents. Further study should be conducted where viral load is used to determine treatment failure.

No conflict of interest

Abstract: A_117

ARV treatment of Pediatric HIV infection

Anthropometric z-score improvement following initiation of first line ART among HIV infected under five children: implications for follow up

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Introduction: Antiretroviral therapy (ART) is a lifesaving intervention for HIV infected children. Despite advances to optimize the care and treatment, there is a need for optimization and measurement of effect of ART for young children. The current study tried to assess the
pattern of anthropometric Z-score improvement following initiation of first-line ART for under-five children and the relationship between anthropometric Z-score improvement and immunologic recovery.

Methods: We included under-five children who were on first-line ART at five major hospitals in Addis Ababa, Ethiopia. We measured their anthropometry at follow up and retrieved anthropometric and clinical information at ART initiation from records. Z-scores for each of the anthropometric indices were calculated using ENA for SMART 2011 software. CD4 percentage at initiation and follow up was retrieved from the records. Clinical information including CD4 count, opportunistic infections, nutritional history and nutritional assessment were also recorded. Linear regression was used to assess the correlation between time on ART and anthropometric Z-score improvement and also to assess the relationship between anthropometric Z-score improvement and immunologic recovery. Logistic regression was used to assess the independent predictors of anthropometric Z-score improvement.

Results: The mean age of the participants was 3.99 (SD=1.06) years. More than half (52.48%) were female. The median duration on follow up was 1.88 (SD=0.93) years. There was a significant improvement in all anthropometric Z-scores at any follow up after initiation of first-line ART (underweight at any visit; 39.5% Vs 16.5%, stunting at any visit; 71.3% vs 62.9% and wasting at any visit; 16.3%vs 1.0%; p-value<0.0001). There was an inverse relationship between improvement in weight for age Z-score (WAZ) and time on ART (R^2= 0.04; F (1, 158); p=0.013). Height for age Z-score (HAZ) both at the time of ART initiation and follow up has a positive linear relationship with CD4 percentage at follow up (Coef. = 1.92; R^2= 0.05; p-value=0.002). CD4 percentage more than 35% was found to be an independent predictor of improvement in WAZ at any follow up visit (AOR=0.28, 95% CI: 0.14-0.59).

Conclusion: There was a significant improvement in all anthropometric Z-score at any follow-up after initiation of first-line ART among under-five children. HAZ was positively related with immunologic recovery on follow up. The findings indicate that anthropometric Z-scores could be taken as proxy indicators of immunologic recovery for under-five children.

No conflict of interest
reservoir was determined by the measure of HIV blood cell associated total DNA.

**Results:** The children studied had a median of 9.8 years of age (IQR = 7.0 - 13.1) at time of inclusion. In median, they had started HAART at 3.3 years of age (IQR = 1.9 - 7) and were on HAART for the past 5.4 years (IQR = 3.5 - 7). The median level of total HIV DNA was 445 copies/10^6 cells (IQR = 187 - 914), the median anti-gp41 antibodies activity was 0.29 UA (IQR = 0.18 - 0.75). A low activity of anti-gp41 antibodies was associated with a younger age of treatment instauration (p = 0.01). No correlation was found between anti-gp41 antibodies and DNA HIV (p = 0.17). The 9 children having an HIV DNA under the threshold (< 66 copies/10^6 cells) tended to have a lower anti-gp41 antibodies activity versus children with an HIV DNA > 66 copies/10^6 cells (p = 0.11). Overall, eight seroreversions were identified (negative ELISA Architect) in which 2 children had an HIV DNA under the threshold (1 detectable and 1 undetectable) with a low anti-gp41 antibodies activity.

**Conclusions:** In conclusion, the results of this study show that HIV-1 global seroreversion and low anti-gp41 activity in vertically HIV-infected children with early initiation of HAART is a common phenomenon that should be considered for proof-of-concept studies aiming to cure children. This study may be helpful to identify candidates with low viral reservoir and low antibodies level for future trials aiming reduce or control HIV reservoir in order to limit children HAART duration.

*No conflict of interest*

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**Abstract: A_119**

**ARV treatment of Pediatric HIV infection**

**It’s as easy as ABC: Efficacy of Abacavir versus Stavudine containing regimens in South African children**

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**Introduction:** Paediatric antiretroviral therapy (ART) guidelines recommend initiating ART with abacavir (ABC) instead of stavudine (d4T) to avoid complications. However, there is concern that ABC efficacy is poorer than d4T in South African children. We compared treatment outcomes with ABC vs. d4T in a cohort of HIV-1 infected South African children 6 and 12 months after ART initiation.

**Materials and Methods:** We performed a matched-case control cohort study using programmatic data from a paediatric ART site in Soweto. Children on ABC/d4T who had initiated ART at age <3 years with a regimen including lamivudine and lopinavir/ritonavir and had at least one 6 or 12 month viral load result were eligible. All ABC cases identified were matched for age at ART initiation and gender (in a 1:2 ratio) to eligible d4T controls. The period of evaluation was between 5 Nov 2010 to 28 May 2013 for ABC and 25 Aug 2005 and 6 Sep 2011 for d4T.

Outcome variables were virological failure (VF) defined as viral load >400cp/mL, mortality, immunological failure defined as CD4 percentage <20%, and anthropometry: weight-for-age (WAZ), height-for-age (HAZ), weight-for-length (WLZ) and body mass index (BMIz) z-scores. Categorical and continuous measures were compared by chi-square and Kruskal-Wallis tests respectively.

**Results:** We identified 57 eligible ABC cases and selected 114 matched d4T controls. Overall, 57% were females and 89% started treatment.
at age <1 year. The median age at ART initiation was 3 months.

Pre-ART, there was no difference in median viral load (ABC log_{10} 5.77 vs. d4T log_{10} 5.88; p=0.69) or CD4 percentage (ABC 25.3% vs. d4T 24.6%; p=0.80), however the d4T group had a larger proportion with a baseline viral load of >500,000 cp/mL (ABC 52% vs. d4T 81%; p<0.001). The ABC group had higher median WAZ (ABC -1.15 vs. d4T -1.88; p<0.001); WLZ (ABC 0.28 vs. d4T -0.5; p<0.001=0.0002); and BMIZ (ABC -0.23 vs. d4T-1.20; p<0.001) whereas the difference in HAZ was not significant (-1.43 vs. -2.20; p=0.05).

There was no significant difference in the proportion with VF at 6 months (ABC 46% vs. d4T 33%; p=0.13) and 12 months (ABC 33% vs. d4T 28%, p=0.53) post-ART initiation. The proportion of children who died over 12 months was 3.5% in the ABC and 7.9% in the d4T group (p=0.27). Similarly, the rates of immunological failure were comparable (9% vs. 11%; p=0.78 at 6 months and 10% vs. 7%; p=0.54 at 12 months) and there was no difference in the median WAZ, HAZ, WLZ and BMIZ at 6 and 12 months post-ART.

Adherence of <90% was observed in 5% of patients on ABC compared to 14% on d4T (p=0.10). Adherence to lamivudine and lopinavir/ritonavir was similar in both groups.

Conclusion: We found no difference in virological, immunological or clinical efficacy between ABC and d4T in young children in Soweto with good adherence. The similarity of the anthropometric measures at 6 and 12 months showed a rapid growth recovery in the d4T recipients.

No conflict of interest

Abstract: A_120

ARV treatment of Pediatric HIV infection

Adherence Measurement and Support Services for HIV-infected Children and Adolescents Followed in Global Sites of the IeDEA Consortium

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Introduction: Sustaining adherence to antiretroviral therapy (ART) is central to successful long-term HIV care for children and adolescents. We do not know the most effective strategies to improve adherence in resource-limited settings or the services currently available. We sought to describe how global HIV care programs measure and support pediatric ART adherence.

Materials and Methods: Using a web-based survey (REDCap), we assessed adherence measurement, support services, and relevant pediatric care system characteristics at sites caring for pediatric patients in 6 global regions of the International Epidemiologic Databases to Evaluate AIDS (IeDEA) consortium.
Results: Clinical staff from 180 pediatric sites in 45 countries completed the adherence survey between June 2014-March 2015. Sites were in Asia (n=16 sites; 4,357 children), Central and South America (n=7; 1,746 children), Central Africa (n=18; 906 children), East Africa (n=33; 12,218 children), Southern Africa (n=95; 45,641 children), and West Africa (n=11; 8,932 children). Most sites managed both adults and children (82%). Clinician adherence assessment (used at 87% of sites) and pharmacy refills (86% of sites) were the most common adherence measurement methods used globally. Other common methods were structured recall items (one recall item, any report time period) (77%) and targeted HIV viral loads used when clinicians were concerned about adherence (75%). Instruments with multiple adherence question items were used in 61% of sites, and few sites used validated measures. Pill counts were used in 40% of sites. Only 12 global sites (7%) used drug levels and 4 sites (2%) used electronic dose monitoring. The percentage of sites in a region using routine viral load monitoring to assess adherence ranged from 79-13%. All sites used at least one measure. Available adherence support services varied widely across sites, with counseling most common and few sites using SMS reminders.

Conclusions: Global pediatric HIV care services routinely measure adherence, but few use objective or validated measures. General support services are available, but more targeted adherence support for children and adolescents may not be present. Investigating the impact and cost-effectiveness of adherence interventions remains a global priority and regional priorities can be guided by this comprehensive global picture of adherence-related measurement and support.

No conflict of interest
Results: Among 69 infants, the median age at study entry was 3.8 months. At entry (prior to ART), median plasma HIV RNA level was 6.55 log_{10} copies/ml, median CD4% was 18, and median WAZ was -2.20. At baseline, mean sCD14 was 3,421ng/ml, sCD163: 1,385ng/ml and neopterin: 11.7ng/ml. At 6-months post-ART, sCD14 increased (mean, 4,114ng/ml; paired t-test, p=0.08); sCD163 decreased (mean 1,088; p<0.001), and neopterin decreased (mean 7.01; p=0.04). Infants with higher sCD14 at entry had significantly higher plasma HIV RNA (6.42 vs 6.95 log_{10} copies/ml; t-test, p=0.02). Infants with high baseline neopterin had significantly lower CD4 percentages (24% vs. 17%, t-test, p=0.003). Adjusted for WAZ at entry, infants with higher entry sCD163 achieved earlier sitting (1.1 months earlier (95% confidence interval (CI) 0.3, 2.0 months); p=0.009), but had no differences in age at walking or speech. Infants with elevated sCD163 at 6 months achieved later speech (1.5 months later (95% CI, -0.1, 3.1 months)), and this difference was most notable in infants with plasma HIV RNA <1000 copies/ml at 6 months (3.4 months later; 95% CI, 0.9, 5.9 months; p=0.01). Infants with elevated vs non-elevated sCD14 or neopterin at 6-months had comparable ages at walking and speech.

Conclusion: Infants with high sCD163 at entry had earlier sitting whereas infants with elevated 6-month post ART sCD163 was associated with later speech. Prior to ART, elevated sCD163 may be protective or may reflect later timing of HIV acquisition or less severe HIV disease. Following initiation of ART, infants with elevated sCD163 may have neurocompromise in spite of suppressive ART.
The HIV-infected children's average age was 7.45 years, 54.4% were girls. The children's WHO HIV disease stage was stage 4 in 49.4% and stage 3 in 40.5%.

**Conclusion:** The caregivers are generally young, Black African females and the biological mothers of the HIV-infected children. The majority were HIV+, unemployed and lacked financial stability. The fathers were primarily absent and not supportive. Our data suggest a need for support on several levels to assist the caregivers in performing their caring role of HIV+ children.

No conflict of interest

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**Abstract: A_123**

**Comprehensive Pediatric HIV care**

**Healthcare Transition Practices across the Baylor College of Medicine International Pediatric AIDS Initiative (BIPAI) Network of Pediatric HIV Clinics**

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**Background:** The Baylor College of Medicine International Pediatric AIDS Initiative (BIPAI) network has provided care to over 250,000 HIV-infected and -exposed children and youth resulting in a large number of youth that will transition from pediatric- to adult-model care.

The purpose of this study is to describe the characteristics and current healthcare transition practices of BIPAI clinics in order to assess transition-related needs and identify ways to improve the transition process.

**Methods:** Seven of eight African BIPAI sites responded to a 40-item survey: Gaborone, Botswana; Maseru, Lesotho; Lilongwe, Malawi; Mbabane, Swaziland; Mbeya, Tanzania; Mwanza, Tanzania; and Houston, Texas, USA. The survey elicited information about clinic staffing, patient demographics, current healthcare transition-related activities, and perceived barriers to youth healthcare transition.

**Results:** Demographics: A total of 16,453 active patients were enrolled at the 7 sites, ranging from 127 to 5320 patients per site; 53% were female, 3066 (18.6%) were adolescents (15-19 years), and 2801 (17%) were youth older than 20 years of age. Almost all patients were perinatally infected. **Clinic Structure:** Each clinic described a multidisciplinary model of care including medical and psychosocial services as well as significant additional support services for adolescent and young adult patients including support groups, nutritional support, camps, and life skills education. **Transitioning:** A total of 263 patients were transferred from BIPAI clinics in the past year. The number of patients transitioned ranged from 5 to 87 patients per site. Reasons for transferring patients included age, pregnancy and changes in residence, school and/or work location. **Barriers to Transitioning:** Few adolescents and youth patients had been transitioned from the BIPAI site. Clinic respondents cited concerns regarding transition-readiness of patients and the lack of support services outside of the pediatric clinic as potential barriers to healthcare transition.

**Conclusions:** Across the BIPAI network there is a significant and rapidly increasing number of patients to transition to adult-model care. Few patients transitioned and the number of patients transitioned varied widely by site due in part to concerns about patient readiness and the potential loss of services available in the pediatric clinic. Improving patient readiness and active linkage to community support services may reduce resistance to transition. A systematic evaluation and improvement of the transition process at each site and follow-up of those who have transitioned is recommended.

No conflict of interest

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Abstract: A_124

Comprehensive Pediatric HIV care

Neurodevelopmental status of pre-school children receiving cART

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Introduction: HIV is known to cause neurodevelopmental complications in infants and young children. The impact of HIV on the development of pre-school age children has not been as well investigated.

Method: This study was conducted at an urban HIV clinic in Johannesburg, South Africa using a sample of convenience. Sixty eight medically stable children infected with HIV between the ages of three and five years were assessed using the Griffiths Scales of Mental Development (GSMD). Children were excluded from the study if they had severe HIV encephalopathy which made it impossible for them to participate in the items on the GSMD.

Results: The mean age of initiating cART was 8.1 months. The majority of the children were virologically suppressed and did not present with wasting or stunting. Severe global developmental delay (z scores<-2SD) was detected in 55.88% of children. Developmental facets related to speech, cognition and perception were the most severely affected. Personal social development was the least affected with only 13.4% of the children demonstrating severe delay.

Conclusion: Despite having early access to cART, children infected with HIV are still at risk of severe developmental delay across a number of developmental facets. Very early initiation of cART may help alleviate this problem. All pre-school children infected with HIV should have routine developmental screening.

No conflict of interest

Abstract: A_125

Comprehensive Pediatric HIV care

Trends in global pediatric HIV programmatic capacity among sites of the InternationalEpidemiologic Databases to Evaluate AIDS (IeDEA) consortium

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Introduction: Global pediatric HIV care sites push to expand access to care and implement recommended guidelines. We sought to describe trends in site capacity and comprehensiveness of services among global pediatric HIV care programs between 2009 and 2014.

Materials and Methods: In 2009, we assessed available services at sites caring for pediatric patients in 6 global regions of the International Epidemiologic Database to Evaluate AIDS (IeDEA) consortium. Between September 2014 and January 2015, we repeated this assessment, using a web-based survey across IeDEA regions. The surveys asked about facility characteristics and capacity to deliver WHO-recommended pediatric HIV prevention, care, and treatment services. We created a measure of comprehensiveness of available pediatric care services based on the WHO's current 9 categories of essential services (ART adherence, Nutrition, PMTCT, CD4 and HIV Viral Load Testing, TB Screening, HIV Counseling and Testing, CO-trimoxazole, Immunizations, and Outreach.) In the subset of sites with data from both 2009 and 2014, we evaluated trends in service delivery capacity.
Abstract

Comprehensive Pediatric HIV care

Evaluation of the growth of young children born to HIV-infected mothers in western Kenya

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Introduction: Understanding growth patterns and associated factors for children born to HIV-infected mothers is critical for reducing morbidity and mortality. This study evaluated anthropometrics and factors associated with underweight and wasted status for children born to HIV-infected mother in western Kenya, including a comparison of anthropometrics between those who are HIV-infected and HIV-exposed, uninfected (HEU).

Materials & Methods: Retrospective chart review was performed using data collected prospectively and stored in the electronic medical record system of Academic Model Providing Access to Healthcare. Data were obtained from children under the age of 5 years between January 2011-September 2014. Summary statistics were performed on demographics and anthropometrics. Logistic regression analysis was used to identify correlates of underweight and wasted status. A resampling method was used to compare the areas under the fitted growth curves to compare males/females and HIV-infected/HEU. P-values were calculated from the empirical distribution of the test statistic under the null hypothesis of no differences between two z-score curves.

Results: Data from 13,925 children born to HIV-infected mothers were included. 51.7% (n=7197) female, 2.67% (n=3731) double orphans, 69.2% (n=9639) HEU, 14.75% (n=2054) HIV-infected, and 16.0% (n=2232) without confirmatory HIV testing during study

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Results: Clinical staff from 172 pediatric sites in 45 countries completed the 2014-2015 site survey. The available services in 2014 varied across regions and sites overall; only 40% of sites provided HIV counseling and testing, whereas 99% offered adherence counseling. In 2014, almost all sites offered PMTCT services (96%), co-trimoxazole prophylaxis (97%) and outreach services (95%) More than two thirds of pediatric sites also offered TB screening and immunization services. Although there was significant increase in all WHO essential services available to children across the regions between 2009 and 2014, for the 38 sites with data from both 2009 and 2014, nutrition-related services and CD4 and viral load testing increased the most, by 57% (11% to 68%) and 50% (3% to 53%) respectively between 2009 and 2014. Overall, 35% of sites (n=61) offered comprehensive services (8-9 essential services out of 9), while 55% (n=94) offered 5-7 essential services and 10% (n=17) offered only 3-5. In the 2014 survey, the median comprehensiveness score across all of the sites was 7.0 (IQR 6.0-8.0), a significant increase from the median of 6.0 (IQR 4.2-6.0) in 2009 (p<0.001), and the magnitude of change varied by region (p<0.01). The two WHO essential services with most varied provision across global regions were 1) HIV counseling and testing and 2) both CD4 and HIV viral load testing.

Conclusions: This global survey demonstrates significant gains in the comprehensiveness of services available for HIV-infected children worldwide, while identifying gaps to target resources.

No conflict of interest
period. Mean age at HIV diagnosis was 2.04±1.53 years. Mean weight-for-age Z score (WFAZ) was -0.68 ±1.45. 32.8% (n=4561) WFAZ -2 to -3 (moderately underweight) and 14.4% (n=2014) WFAZ <-3 (severely underweight) during the study period. Mean height-for-age Z score (HFAZ) was -1.38±1.92. 46.7% (n=6506) HFAZ -2 to -3 (moderately stunted) and 25.0% (n=3488) HFAZ <-3 (severely stunted). Mean weight-for-height Z score (WFHZ) was 0.35±2.09. 17.5% (n=3044) WFHZ -2 to -3 (moderately wasted) and 13.1% (n=2295) WFHZ < -3 (severely wasted).

When comparing z-score by age between HIV-infected and HEU children, a statistically significant difference was found for HFAZ (p-value=0.000), WFAZ (p-value=0.000), WFHZ (p-value=0.000). When comparing z-scores by age between male and female children, a difference was found for HFAZ (p-value=0.028). For those with a HIV-infected sibling, the HIV-infected children in this study were more likely to have WFAZ<-2 (OR: 1.167; 95%CI: 1.042-1.307), while HEU were less likely (OR:0.932; 95%CI: 0.970-0.998). HEU were more likely to have WFAZ<-2 if they were orphaned (OR 1.189; 95%CI: 1.001-1.413) and enrolled in clinic at a later age (OR 3.212; 95%CI: 3.012-3.425), with each year of delayed enrollment increasing risk of WFAZ<-2 by 17% (OR:1.167; p-value<0.001). HEU were more likely to have WFHZ <-2 if they were enrolled in clinic at a later age (OR: 1.502; 95%CI: 1.328-1.697). There were no significant correlations between HIV-infected children’s WFHZ and orphan status, age of clinic enrollment, and presence of an HIV-infected sibling.

Conclusions: Children born to HIV-infected mothers in western Kenya have greater degrees of underweight, stunting, and wasting than the general Kenyan population. Children who are HIV-infected and HEU differ in their anthropometrics, with HIV-infected children having overall lower z-score anthropometrics. Late enrollment in clinic increases the risk for HEU children to experience wasting and underweight status. HEU is a unique pediatric population who warrants further investigation of their growth and development.

No conflict of interest

Abstract: A_127

Implementation research on PMTCT and pediatric treatment programs

Transition Care of the Youth from Adolescents’ to Adults’ ART Clinic: Lessons from Uganda. A Qualitative Study

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Background: Antiretroviral therapy (ART) and improved care have enhanced survival of HIV-infected infants into adolescents and young adults in many settings including Uganda. Nsambya Home Care (NHC) is a specialized HIV/TB Department of St. Francis Hospital Nsambya, in Kampala, Uganda. In 2011, NHC initiated Youths’ Transition Care Counselling to prepare youths living with HIV and their caregivers for transfer of care to a user fee applying adults’ ART clinic. We aimed to explore challenges, barriers and enabling factors associated with the process.

Methodology: We conducted a general qualitative descriptive study to examine enabling factors, barriers and challenges to the transfer of the youth from the adolescents’ clinic to the adults’ ART clinic at NHC. The study covered 12 months (September 2014-August 2015), and the participants included all youths living with HIV aged 17-28 years, attending the adolescents’ clinic over the study period. We used semi-structured face-to-face and telephone interviews to collect data that was complemented by chart reviews. Data was analysed using techniques from thematic and framework analysis. The Uganda National Council for Science and Technology approved the study, and we obtained informed consents for the interviews.

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Results: We studied 132 youths; mean age 20.1 (range 17-28 years), the majority were female (60.6%), on ART (96%), education level above primary (66%). Sixty-five percent accepted a transfer from the adolescents’ to the adults’ clinic, but only 12% eventually transferred to the adults’ clinic. Even though 85% were paying user fees, just 35% were earning incomes.

Enabling factors: included perceptions of maturity, having financial security and other support structures, and feeling in a safe and secure environment (e.g. same clinic or staffs and peer support networks).

Barriers and Challenges: comprised of financial insecurity, no support structures, user fees, stigma from adults and unfavourable adults’ clinic appointments. Others were breaking up of peer support networks and emotional and psychological unpreparedness.

Conclusion: Organized transfer of the youth from adolescents’ to adults’ ART clinics is an added health system challenge in Uganda. Our findings provide vital considerations for securing a smooth transition care for this population.

No conflict of interest

Abstract: A_128

Implementation research on PMTCT and pediatric treatment programs

Assessment of Knowledge of Pediatric HIV Care and Treatment among Health Workers in Southeastern Malawi

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Introduction: 2.6 million children under 15 are living with HIV globally, but 1.8 million lack access to lifesaving treatment. To close the treatment gap and provide quality care, well-trained health workers (HCW) are needed. Focused mentorship can equip HCWs to diagnose HIV in children and administer quality care, but there is a paucity of research on specific mentorship needs. Our objective was to assess self-perceived and objective knowledge of pediatric HIV topics (PMTCT/EID, diagnosis, HIV-related diseases, staging, treatment/monitoring) among HCW caring for HIV-infected patients in Southeastern Malawi.

Methods: We provided a self-administered anonymous survey to HCWs in six districts (catchment area 1.9 million) within Malawi's Southeast Zone. Perceived knowledge was assessed using a standard four-point Likert scale (1-beginner, 2-somewhat knowledgeable, 3-knowledgeable, 4-expert) and objective knowledge measured using multiple-choice problem-based scenarios based on 2014 Malawi Ministry of Health ART-PMTCT guidelines defining expected standard knowledge. The survey was piloted, refined, and administered over a 6-month period. Data was entered into an MSAccess database and summarized by descriptive statistics (mean, sd, frequency, percentage). Spearman correlation coefficient was calculated to assess correlation between objective and perceived knowledge using summarized scores by topic.
Results: 292 HCW from 66 facilities participated. Mean(SD) age was 32.9(10.1) years, 56.9% were female, 32.9% were clinicians (Medical/Clinical Officers and Medical Assistants) and 66.4% nurses. Most providers (79.1%) had treated patients with HIV in the previous month. Mean(SD) self-assessed knowledge score was 2.79 (0.66). Mean(SD) objective score was 71.9%(6.4%). Scores were highest in EID/PMTCT (81%) and poor in pediatric TB(47%). Treatment/monitoring and staging were also suboptimal. Overall perceived and objective knowledge were positively correlated(p< 0.0001).

Conclusions: HCW in Malawi have knowledge deficits in pediatric HIV, with notable gaps in tuberculosis, treatment/monitoring, and staging. Focused attention to these areas may improve quality care for HIV-infected children. The correlation between perceived and objective knowledge suggests that self-assessment may be an appropriate surrogate for objective assessment in setting training priorities.

No conflict of interest

Abstract: A_129
Implementation research on PMTCT and pediatric treatment programs

Burnout and self-reported patient care amongst health care workers providing HIV care in Malawi

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Background: Since 2002 there has been a >100-fold increase in the number of persons accessing antiretroviral treatment, without a concomitant increase in healthcare workers (HCWs) providing HIV care. Burnout is a syndrome of emotional exhaustion (EE), depersonalization (DP), and a sense of low personal accomplishment (PA). Burnout amongst HCWs may have a negative impact on services. The aim of this study was to determine the prevalence of burnout amongst HCWs in Malawi and explore its relationship to self-reported patient care practices.

Methods: Cross-sectional study amongst HCWs providing HIV care in 66 facilities, across 6 high HIV prevalence districts in southeastern Malawi. Burnout was measured using the Maslach Burnout Inventory and defined as scores in the mid-high range on the EE or DP subscales. Nine questions developed for this study assessed self-reported patient care practices and attitudes. Surveys were administered anonymously. Data was summarized by descriptive statistics (mean, SD, frequency). Chi-square test was used to test the association between burnout and any self-reported suboptimal patient care practice/attitude.

Results: Among 292 HCWs (mean (SD) age 33 (10) years, 57% female, 56% married) 56% met criterion for burnout. In the three dimensions of burnout, 47% reported moderate-high EE, 28% moderate-high DP. Participants reported several suboptimal patient care practices including making mistakes in treatment not due to lack of knowledge/experience (51%), shouting at patients (41%), and not performing diagnostic tests due to a desire to finish up quickly (34%). Compared with non–burned-out HCWs burned-out HCWs were significantly more likely to self-report any suboptimal patient care practice/attitude (93% vs. 81%; P=0.001).

Conclusion: Burnout was common among HCWs providing HIV care and was associated with self-reported suboptimal patient care practices/attitudes. Additional research is needed to identify factors that contribute to or protect against burnout to inform the development of strategies to reduce burnout.

No conflict of interest
Abstract: A_130

Implementation research on PMTCT and pediatric treatment programs

Healthcare worker experiences with Option B+ for prevention of mother-to-child HIV transmission in Swaziland: Findings from a two-year follow-up study

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Introduction: Since 2013, prevention of mother-to-child transmission (PMTCT) across sub-Saharan Africa has rapidly shifted towards Option B+, an approach in which all HIV+ pregnant and breastfeeding women initiate lifelong antiretroviral therapy (ART) independent of CD4+ count. As of October 2015, 95% of Global Plan priority countries have nationally endorsed Option B+, including the Kingdom of Swaziland. Healthcare workers (HCW) are critical to the successful implementation of Option B+, yet little is known about acceptability of Option B+ among HCWs, particularly over time.

Methods: Ten health facilities in the Manzini and Lubombo regions of Swaziland transitioned from Option A to Option B+ between 2013 and 2014 as part of the Safe Generations study examining PMTCT retention. Fifty HCWs (5 per facility) completed questionnaires assessing feasibility and acceptability: (1) prior to transitioning to Option B+, (2) two months post-transition, and (3) approximately 2 years post-transition. This analysis describes HCW perceptions and experiences two years after transitioning to Option B+.

Results: Participants in the final survey included nurses/nurse midwives (54%), mentor mothers/peer counselors (32%), and expert clients (10%). Overall, two years after transition, 80% reported that Option B+ was easy, noting that Option B+ was particularly easy to explain and coordinate, and that immediate ART initiation reduced delays from tests or labs. Additionally, HCWs reported ease of patient follow-up (58%), documentation (56%), and counseling (50%) under Option B+.

Compared to two months post-transition, after two years fewer HCWs reported barriers to care such as an inadequate appointment systems, lack of supplies, overcrowded clinics, long wait times, attitudes of healthcare workers, overworked staff, lack of counseling support, concerns about confidentiality, or clients not believing they have HIV. Only 4% of HCWs cited lack of coordination between services (requiring women to visit multiple service points) as a barrier to PMTCT uptake two years after transitioning compared to 40% at two months post-transition, suggesting increased integration of services over time. However, HCWs consistently reported increased workloads since Option B+ implementation, with more work reported by 62% of HCW at two years post-transition and 68% at two months post-transition. Over half (56%) of HCWs at two years post-transition reported that same-day ART initiation reported that same-day ART initiation under Option B+ introduced a barrier for patients who may be hesitant to start treatment, citing issues related to disclosure/partner consultation and/or reluctance to initiate lifelong treatment. However, fewer HCWs (14%) reported that it was common for women to refuse to initiate ART on the same day as diagnosis two years post-transition compared to two months (32%). Additionally, 28% of HCWs noted that retention and adherence under Option B+ was difficult at two years post-transition.

Conclusions: As Swaziland rolled out Option B+ nationally, findings demonstrate that HCWs view Option B+ as an acceptable and feasible PMTCT approach. Further strengthening of the healthcare system may be necessary to alleviate worker burden and to ensure effective monitoring of client retention and adherence. HCW perceptions and experiences with Option B+ should be considered more broadly as countries implement Option B+ and consider universal treatment for all HIV+ individuals.

No conflict of interest
Abstract: A_131

Implementation research on PMTCT and pediatric treatment programs

Comparison between HIV viral load testing using dried blood spots samples in children on ART in Mozambique

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Introduction: The World Health Organization 2013 guidelines, recommends the use of viral load (VL) as the preferred approach for HIV treatment monitoring. Current challenges involve the need to overcome the limitation imposed by traditional VL tests, which demand the use of plasma samples. In Mozambique, efforts are being made to make HIV viral load testing routinely available to all patients on ART aiming to eradicate vertical transmission of HIV and pediatric ART monitoring. Dried blood spots collected by finger stick (FS-DBS) can be an alternative to plasma VL as there is no need for complex processing and cold chain, thus reducing cost and making VL monitoring feasible in contexts with scarce resources. FS-DBS is widely used for early infant diagnosis and has shown to be effective for HIV drug resistance (HIVDR) genotyping; however, the utility of DBS for VL monitoring may be undermined by lower specificities seen at VL below 5000 copies/ml in different studies when compared to the plasma gold standard methodologies because of cell-associated viral nucleic acid. In this study, we compared the performance of HIV VL testing using DBS as an alternative to the plasma for VL testing for children on ART.

Materials and Methods: The study took place in six urban and peri-urban health care facilities in Maputo, Mozambique, providing pediatric ART services. Children under 15 years old, on ART > 12 months were enrolled. Plasma samples were prepared from venous blood. DBS were prepared by lay health care workers, who used finger-sticks to collect blood in micro-EDTA tubes and spotted DBS (FS-DBS) with transfer pipette with 75 μL of blood per spot and cards dried overnight. Plasma VL was performed at the Mozambican HIV reference laboratory using COBAS Amplitrep/Cobas (CAP/CTM) HIV-1 test, v2.0 (Roche, Basel, Switzerland), following manufactures instructions. DBS VL was tested on NucliSENS EasyQ HIV-1 test, v2.0 (Biomerieux, France) at the Laboratory of Hospital Geral Jose Macamo, Mozambique, following manufactures instructions. Statistical analysis was performed using SAS 9.3 and STATA 13.

Results: In total 723 children aged bellow 15 years old were enrolled and paired plasma and finger-prick DBS were available for 84 children. Higher sensitivity was observed at 500 - 1000 copies/ml (77.0%) and it tended to decrease with increasing viral load threshold (54% at 5000 copies/ml). Conversely, specificity was seen to increase with increasing threshold (0.81 to 1.00 from 500 to 5000 copies/ml).

Conclusions: The BioMérieux NucliSENS EasyQ HIV-1 v2.0 showed excellent values for specificity at 3000 and 5000 copies/ml compared to plasma values from Roche Cobas TaqMan HIV-1 v2.0. However, the DBS VL at 1000 copies/mL threshold showed the best values for sensitivity (77.0%) and negative predictive value (0.88; p<0.05).

No conflict of interest
Abstract: A_132

HIV infection and adolescents

Transitioning HIV-Infected Children into Adult Care - Voices of Jamaican Adolescents and their Healthcare Providers

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Introduction: Successful public access to antiretroviral therapy in resource-limited settings (RLS) has resulted in survival of HIV perinatally-infected children into adulthood. However, there are few studies or guidelines on transition of care in RLS, where 90% of HIV-infected children reside. We aimed to characterize the current landscape of the transfer process of HIV-infected adolescents from the perspectives of both the adolescents and providers in one such RLS, Jamaica.

Material and Methods: We conducted in-depth semi-structured interviews of 18 HIV-infected adolescents in pediatric care at the University Hospital of the West Indies and 21 health care providers from various clinical sites across Jamaica. We audiotaped, and transcribed verbatim the interviews, then organized, and coded transcripts using the software ATLAS.ti. We analyzed the data using the grounded theory approach.

Results: Five themes emerged: 1. Adolescent patients articulated psychosocial benefits associated with pediatric care. Pediatric clinics were like families who provided care-taking and developmental support in addition to HIV care. 2. Both adolescent patients and pediatric providers felt the quality of care adolescents received in the pediatric clinic was better than it would be in the adult setting. 3. Given the social significance of pediatrics clinics in participants' lives, alongside the concerns regarding adult care, there was rootedness in the pediatric clinic and apprehension about transfer to the adult clinic. 4. In the face of the national policy of transfer to adult care at 13, no formalized national structures or services for adolescents, and the challenges HIV-infected adolescents experience, some physicians sought to bridge the gap between childhood and adulthood by providing adolescent-centered services for their HIV-infected clients. 5. Narratives speak to the transfer as a critical juncture in adolescents' care and a transition as holistic process, an element of which is the transfer.

Conclusions: We conclude that a formal, culturally, and developmentally appropriate process of transition is necessary to manage the fear and apprehension both providers and adolescent patients experience when confronted with the transfer from pediatric to adult care.

No conflict of interest

Abstract: A_133

HIV infection and adolescents

Assessment of the Utilization of Culturally-Sensitive Disclosure Counseling Tools for HIV-infected Adolescents and Caregivers in Western Kenya

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Introduction: Disclosure of HIV status to children is a key aspect of their disease management; however, structured counseling resources to support disclosure are limited. Our objective was to evaluate the usage of culturally
adapted tools for disclosure counseling with children and caregivers in Kenya and identify critical themes in disclosure counseling.

Methods: We evaluated disclosure counseling sessions offered as part of a 2-year, clinic-based intervention to support HIV disclosure for Kenyan children aged 10-15 years and their caregivers within the Academic Model Providing Access to Healthcare (AMPATH). Child, caregiver, and family counseling were offered at four HIV clinics. Disclosure counselors created individualized counseling plans for participants and documented disclosure status and psychosocial issues on a structured counseling encounter form. Counselors had access to culturally adapted resources (e.g. disclosure video narratives, HIV educational pamphlets) created from previous qualitative work with this cohort. To evaluate implementation of these resources and identify critical themes related to disclosure and child behavioral outcomes, we used thematic analysis of the counseling encounter notes, with progressive coding and constant comparison. Themes were coded and triangulated among multiple reviewers.

Results: Counselors documented 349 counseling encounters related to 122 children, using disclosure videos (127), HIV information books (128), and pamphlets (19). For caregivers of non-disclosed participants, common themes included disclosure preparedness and adherence management. Videos were most often used with caregivers to overcome disclosure barriers (e.g. child not ready, fear child’s reaction) and initiate the disclosure process, particularly for children suspecting their status. Two themes arose related to post-disclosure in children: positive functioning (e.g. mild demeanor, accepting of HIV status) and poor functioning (e.g. worsened adherence, personalized HIV stigma). For ‘poor functioning’ children, counselors used HIV information books and videos, encouraging children to understand and accept their HIV status. Counselors noted improved child adherence and psychosocial issues (e.g. stigma reduction, acceptance of status) after using the tools.

Conclusion: Culturally-adapted disclosure tools were used by disclosure counselors to mitigate disclosure barriers with non-disclosed caregivers and improve post-disclosure functioning. Understanding the content of typical disclosure counseling sessions provides input for the design of future disclosure counseling interventions and for counseling implementation.

No conflict of interest

Abstract: A_134

HIV infection and adolescents

Creating Contextualized Films Through Community Engagement to Address HIV-Stigma in Western Kenya.

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Introduction: HIV-related stigma (HIV-stigma) impacts HIV-infected adolescents’ psychosocial development and how they navigate their social surroundings. We sought to better understand the experiences of HIV-infected adolescents in western Kenya with HIV-stigma and to subsequently develop culturally sensitive films to reflect those experiences.

Methods: A US and Kenyan collaborative team conducted a qualitative study investigating the social and cultural impact of HIV-stigma on adolescents living with HIV. Our participatory research strategy included focus group discussions with HIV-infected adolescents and with caregivers of children with HIV, followed by in-depth interviews with participants, including HIV-infected adolescents and various community members in Eldoret, a mid-sized town in western Kenya (e.g. shop owners, pastors, teachers). Interviews, conducted in Kiswahili or English, were translated and transcribed. Applied thematic analysis was used to identify themes reflecting the lived experience of stigma. A participatory advisory
board, comprised of research investigators, HIV disclosure counselors, and HIV-infected adolescents, drew upon these culturally contextualized themes to create narrative scripts for films focused on HIV-stigma.

**Results:** The participatory advisory board generated 4 film narratives from the in-depth interview transcripts. Major themes of HIV-stigma included enacted stigma from neighbors, school children, and caregivers. The in-depth interviews from community members (e.g. shop keepers, pastors, and teachers) emphasized enacted examples of HIV-stigma from community social systems, including public ridicule, shaming, and shunning for families and adolescents living with HIV. HIV-infected adolescents shared personal narratives of perceived HIV-stigma in school and college environments, and experiences of enacted stigma from caregivers and family members. Filming and producing the films was conducted in July 2015, followed by post-production editing. Using local Kenyan actors in partnership with Moi University, the collaborative team created four film narratives that showcase the experience of HIV-stigma from the perspective of HIV-infected adolescent main characters.

**Conclusion:** Using a context-focused methodology and community participatory approach, we developed four unique films showcasing the impact of HIV-stigma in western Kenya. With planned use in clinical, counseling, and community-based settings, these films could mitigate the impact of HIV-stigma and serve as tools to encourage dialogue and openness about HIV.

*No conflict of interest*

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**Abstract: A_135**

**Title:** HIV infection and adolescents

**Diversity in adolescent HIV care services in the public sector in Cape Town, South Africa**

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**Introduction:** Appropriate HIV care and treatment services tailored for infected adolescents are widely discussed, but with few insights into varying models of care in high-burden settings. We investigated the routine public sector services provided to children enrolled in the Cape Town Adolescent Antiretroviral Cohort (CTAAC).

**Methods:** CTAAC enrolled perinatally-infected adolescents aged 9-14 years and on ART for ≥6 months at 7 public sector facilities. We administered a questionnaire on local standards of care to each facility providing routine care, including tertiary, secondary and primary care clinics.

**Results:** 515 adolescents were enrolled at 2 tertiary hospitals (1 of which is a paediatric hospital), one secondary level hospital and 4 community based primary level clinics. At these sites, adolescents are seen mainly by generalist clinicians who manage adults and children. Adolescents had a ‘named’ clinician and counselor at only two sites. At these two sites counsellors had received specific training on adolescent issues. All sites cared for 50 to ≥100 adolescents. Most sites dedicated one day a week to adolescents. Only one site offered ‘adolescent friendly times’ (late afternoon and Saturday mornings). Four sites could refer to the single dedicated
adolescent ward should hospitalization be needed. Most sites offered family planning and sexually transmitted infection counselling; however mental health services were available on site at only four facilities. One site offered substance abuse counselling on site. Six sites offered annual influenza vaccine while only two sites offered catch-up EPI vaccines and checked hepatitis B immunity routinely. Routine checking of HPV vaccination (implemented via school programs as part of EPI) was not undertaken. Only one site had a formal ‘in house’ guideline on transitioning adolescents to adult care. Reasons given for timing of transition were mostly related to age cut offs, varying between 13 up to 22 years. Other reasons cited were: ‘after school completion’, ‘after return from circumcision in the bush’, ‘adolescent or caregiver requested’, ‘defaulted clinic attendance’ or ‘became pregnant’.

Conclusions: There is a large variation in types of care available to adolescents in this setting. The most comprehensive services are available at tertiary and secondary facilities rather than at primary care. Only one facility had formal guidelines on transitioning adolescents to adult care despite large number of adolescents at these facilities. There is a need for adolescent mental health services, vaccination guidelines and formal transition guidelines.

No conflict of interest

Abstract: A_136

HIV infection and adolescents

The Adolescent and Young Adult HIV Continuum of Care in South Africa: The Cresting Wave

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Background: South Africa has the most HIV infections of any country in the world, yet little is known about the adolescent and young adult continuum of care from HIV diagnosis through viral suppression.

Methods: We conducted a systematic review of published literature and conference proceedings containing South African cohorts and epidemiological data reporting primary data for youth (15 to 24 years of age) at each stage of the HIV continuum of care (i.e., diagnosis, treatment, retention, viral suppression) and conducted a meta-analysis for retention in care and viral suppression.

Results: Among the estimated 867,283 HIV-infected youth from 15 to 24 years old in South Africa, 14% access antiretroviral therapy. We reviewed 119 published articles and 1,255 conference abstracts. We found 13 observational cohorts with primary South African retention or viral suppression data for adolescents aged 15 to 24. Based on our meta-analysis approximately 83% of the adolescents and young adults in South Africa receiving antiretroviral therapy are retained in care for at least 1 year and approximately 81% are virally suppressed with less than 400 copies/ml. Overall, we estimate that 10% of HIV-infected youth in South Africa are virally suppressed.

Conclusion: Retention and viral suppression rates are high among HIV-infected adolescents and young adults in South Africa; however, only a small percentage are virally suppressed, largely due to low numbers of adolescents and young adults accessing ART. Efforts are needed to engage more adolescents and young adults into care and increase ART initiation in this population.

No conflict of interest
Abstract: A_137

HIV infection and adolescents

How do young people living with HIV feel on antiretroviral therapy?: The need to address side-effects and treatment disengagement

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Background: Poor adherence and treatment disengagement are of great concern, especially among adolescents. Recent research with young people (YP) highlights a scarcity of opportunities to share their perspectives on the impact of HIV and antiretroviral therapy (ART) on their lives. In addition, their time in clinical care and on treatment significantly shape the meanings they attach to both HIV and ART. Yet there remains limited research about the psychosocial effects of treatment- and HIV-related symptoms on YP’s health, well-being and adherence behaviours.

Methods: A longitudinal qualitative study embedded within a randomised controlled trial (BREATHER) testing the safety of a treatment interruption intervention (Short Cycle Therapy (SCT)). We repeatedly interviewed 43 YP throughout the trial (38% total YP; age 11-22 years, who knew their HIV diagnosis and gave additional consent) in UK/Ireland (7), USA (10) and Uganda (26). Focus groups with 25 trial participants and interviews with 16 of their caregivers were also held in the Ugandan site at the end of the trial. The qualitative study explored YP’s experiences of the BREATHER trial as well as broader issues of ART adherence.

Results: Treatment side-effects and physical symptoms were not a specific focus of our study, yet they emerge as central to how participants spoke about their condition. Views about pills and toxicity, fear of future illness (particularly from non-adherence), neuro-cognitive difficulties, anxiety and hunger, were all notable features of participants’ narratives. Interviews with caregivers further suggest the centrality of the physical dimension of HIV and ART for the YP in their care (e.g. specific diets, weight gain or loss, drug toxicity, issues with concentration) and the way in which feelings about ART might affect YP’s adherence.

Conclusion: The physical dimension of HIV and ART for YP living with HIV and particularly for adolescents, remains poorly understood. Further evidence, including our study findings, can help us illuminate how clinical understandings of HIV and ART interplay with community and personal narratives and how these might shape health and adherence behaviours. In the future, this may inform ways to engage and support YP in relation to how they feel about their health and bodies.

No conflict of interest

Abstract: A_138

HIV infection and adolescents

Are they disclosed?: Situation of HIV status disclosure among adolescents in Myanmar

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Background: Disclosing HIV status to vertically HIV infected adolescents is crucial for preventing further transmission of HIV, maintaining drug adherence, and preventing possible unsafe reproductive behavior. However, little is known about the situation of HIV status disclosure among these adolescents in Myanmar. Therefore, the study was conducted with the objective of identifying disclosure related information among HIV infected adolescents.
**Methods:** A community-based cross-sectional exploratory study was conducted in 2015 by applying face-to-face interviews with adolescents using a structured questionnaire. Moreover, focus group discussions (FGDs) and in-depth interviews (IDIs) with the guardians, providers and focal persons.

**Results:** Total of 66 adolescents aged were 10-16 years with the mean age of 12.5±2.0. About 44% of adolescents were double orphans and 32% were single orphans. Nearly 82% were currently attending school and over 16% of the children were dropped out from the school. Of all adolescents, 81.8% knew their HIV status in which over 42% of the children were disclosed by health staffs. During FGDs, about half of the guardians stated that they have not disclosed HIV status to their children properly. They just let them know that they have an illness which needs daily medication for their survival. One third of adolescents have not received any counseling. At the time of disclosure, half of the children did not express their emotional responses. Over half of the adolescents have not discussed about HIV some of them have discussed with their guardians on transmission of HIV (16.7%), HIV virus (40.9%) and treatment of HIV (19.7%). As regards to reproductive health information, 18.4%, 7.7%, 6.2%, and 4.6% of adolescents received discussion about sexually transmitted diseases, puberty changes, pregnancy and reproductive organs respectively. Most guardians revealed that they rarely discussed about reproductive health with their children although they know that it is important for their future reproductive life.

**Conclusions:** Proper and comprehensive disclosure counseling is needed for vertically HIV infected adolescents. Awareness raising activities for guardians on advantages of disclosure counseling and provision of RH information to all infected adolescents are also recommended.

No conflict of interest

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**Abstract: A_139**

**HIV infection and adolescents**

“I always wanted a big family because I lost mine”: A qualitative analysis of parenting perspectives among young parents with perinatally-acquired HIV

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**Introduction:** Globally, children with perinatally-acquired HIV (PHIV) are now living into young adulthood and having children of their own. Little is known about the parenting perspectives of youth who may have experienced family disruption due to loss/illness of biological parents. This research explores the perceptions of adolescents and young adults (AYA) living with PHIV as they transition into parenthood.

**Materials and Methods:** We conducted hour-long, semi-structured, audio recorded interviews with a purposive sample of 16 AYA parents with PHIV who were current or former patients at two U.S. pediatric/adolescent infectious diseases clinics. Participants were asked about their childhood family structure, rewards/challenges of parenting, and anticipated future fertility desires/intentions. Analysis of the transcribed interviews was guided by grounded theory identifying key common themes across the interviews.

**Results:** Mean age of participants was 22 years. The majority were black (7) or Hispanic (4) and female (14). Four AYA were raised by biological mothers, five by foster/adoptive parents and the others by relatives. Participants had a range of 1-3 children (mean=1.4), one of whom was HIV-positive. Participants expressed many normative parenting rewards/challenges such as the joy of their child’s smile and financial concerns. Unique themes associated with HIV infection included a concern about not “being
there for their child due to sickness and worries that their child may experience HIV-related discrimination. Among those parents who intended to have another child, many were motivated by a strong desire to create a family of their own as a way to deal with HIV-related losses and stigma. Finally, participants also noted the positive role played by pediatric and adolescent medical providers, even if they had transitioned to adult care. Participants reported the importance of emotional support offered by providers as well as concrete social services available in that care setting.

Conclusions: AYA with PHIV who have children experience many of the same issues as other young parents. However, they also have HIV-specific experiences that influence their parenting such as illness, discrimination, and childhood parental loss that may intensify their fertility desires. The positive impact providers have throughout the childhood of a youth with PHIV childhood must be recognized and capitalized upon.

No conflict of interest

Abstract: A_140

HIV infection and adolescents

Barriers to and Factors associated with Adherence to Antiretroviral Therapy (ART) Adherence in Adolescents Living with HIV (ALHIV) based on self-report in Malawi

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Objective: Adolescents and young adults account for >40% of new HIV infections, with HIV-related deaths amongst adolescents increasing by 50% from 2005-2012. Adherence to ART is critical to control viral replication and preserve health, however, there is a paucity of research on treatment adherence amongst the growing population of adolescents living with HIV/AIDS (ALHIV) in Sub-Saharan Africa. Our objective was to examine levels of self-reported ART adherence, barriers to adherence and factors associated with non-adherence amongst ALHIV in Malawi.

Methods: Convenience sample from a cross-sectional study of ALHIV (12-18years) attending the two largest HIV clinics in central and southeastern Malawi. Participants self-reported missed doses (past week/month), barriers to adherence, and completed questionnaires on past traumatic events/stressors, disclosure, depression, substance use, treatment self-efficacy, and social support. Biomedical data was retrieved from existing medical records. Multivariate logistic regression (MVLR) was performed to identify factors independently associated with self-reported ART adherence (7 day recall).

Results: The mean(SD) age was 14.5(2) years and 290(56%) were female. Of the 519 participants, 153(30%) reported having missed ART doses within the past week, and 234(45%) in the past month. Commonly reported barriers to adherence included forgetting (39%), travel from home (14%), busy doing other things (11%), feeling depressed/overwhelmed (6%), not having enough food to eat (4%), running out of medicine (4%), and fear of stigma. Factors found to be significantly associated with missing a dose in the past week in the MVLR analysis were drinking alcohol in the past month (OR 4.78 95% [1.34-17.0]), missing a clinic appointment in the past 6 months, witnessed or experienced violence in the home, and poor treatment self-efficacy. Sex and age were not found to be associated with adherence.

Conclusions: Poor adherence is a major issue for ALHIV, compromising treatment outcomes and leading to early death. In our study, a very high proportion of ALHIV reported missing ART doses. Forgetting to take ART and travel from home were the most commonly self-reported barriers. Alcohol use and poor treatment self-efficacy were associated with worse adherence. Programs specifically tailored to address those
challenges most pertinent to ALHIV may help improve adherence to ART.

No conflict of interest

Abstract: A_141

HIV infection and adolescents

Disclosure of HIV status to HIV-infected adolescents in Togo and Côte d’Ivoire


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Introduction: Adolescents living with HIV face numerous challenges for themselves, their families and health care providers. Studies have described that few of them were aware of their HIV status while this awareness is of high importance for adherence to antiretroviral therapy and prevention of secondary HIV transmission. COHADO is a cohort of HIV-infected adolescents conducted in Côte d’Ivoire and Togo, aiming to document prospectively issues specific to HIV-infected adolescents within the West African International epidemiologic Database to Evaluate AIDS (IeDEA) Collaboration. The objectives of the present analysis were to estimate the frequency of adolescents aware of their HIV status at enrolment and identify their associated characteristics.

Material and methods: COHADO includes adolescents infected with HIV from birth, aged 10-19 years, followed-up in the Yopougon teaching hospital in Abidjan and in the Sylvanus Olympio Teaching Hospital in Lomé, and who agreed, with their caregivers, to participate. The cohort was approved by the Ethic Committees of Côte d’Ivoire and Togo. Specific case record forms were used by health care workers during routine care every six months. All children with completed data at enrolment were included in this analysis. Prevalence of adolescents aware of their HIV status was estimated with its 95% confidence interval (CI). Logistical regression was used to identify associated characteristics.

Results: From January to October 2015, 210 children were enrolled. Of 203 adolescents with completed data, 53.2% were from Abidjan, 54.2 %, were female, 97.5 %, on antiretroviral treatment, 96.6% were schooled and 43.3% had theirs two parents alive. In Abidjan, median age was 14.0 years (Inter-quartile range [IQR]: 12.4; 15.5), median height-for-age z-score (HAZ) -1.2 (IQR: -1.9; -0.3), and median CD4 count 540 cell/mm$^3$ (IQR: 314-753). In Lomé the baseline characteristics were lower: median age was 13.0 years (IQR: 11.1; 15.3) (p<0.01), median HAZ, -2.1 (IQR: -2.7; -1.1) (p<0.01), and median CD4 count 474 cell/mm$^3$ (IQR: 265-751) (p=0.49). The frequency of adolescents aware of their HIV status at enrolment was 42.4 % (95%CI: 35.5; 49.2): 54.4% in Cote d’Ivoire and 25.3% in Togo (p<0.01), for a median period of 12 months (IQR: 6-21) and 33 months (IQR: 11-58), respectively. Adherence to antiretroviral therapy was good (>95% drugs taken in the four past days) in 71% of adolescents and similar according to disclosure status (p=0.69). Among the 11 adolescents (5%) who reported to have already had a sexual relationship, 82% were aware of their HIV status. Among disclosed children, caregivers were involved in 52% of the events and disclosure had been prepared in 70%. Among adolescents who did not know their HIV status, parents had refused disclosure to their child in 27% in Lomé and in 91% in Abidjan. Ivorian site (OR=4.7, 95%CI: 1.7-13.2) and age>15 (OR=19.5, 95%CI: 7.8-48.8) were independently associated with disclosed HIV status.

Conclusion: Only ¼ of the adolescents knew their HIV status in Lomé and slightly more than half in Abidjan. Younger age was associated with lower frequency of disclosure but also site-related characteristics. We need to tailor context-specific interventions to help the disclosure process in adolescents.

No conflict of interest
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HIV infection and adolescents

Models of support for disclosure of HIV status to HIV-infected children and adolescents in resource-limited settings

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Introduction: Disclosure of HIV status to HIV-infected children and adolescents is a major care challenges. We describe current policies and available interventions to support disclosure of HIV status, in paediatric HIV care settings in resource-limited settings within the International Epidemiologic Databases to Evaluate AIDS (IeDEA) consortium.

Materials and Methods: An online site assessment survey was conducted across the sites caring for children within 6 global regions of the IeDEA collaboration. A standardized questionnaire was constructed and administered to the sites through the REDCap platform within a survey about adherence and support services for children and adolescents. The disclosure survey results were analysed.

Results: From June 2014 to March 2015, 180 sites in 31 countries completed the online survey: 53% were from Southern Africa; 57% were urban; 43% were health centers, 25% were district hospitals and 32% were regional, or university hospitals; and 86% were clinics where providers care for both adults and children. The clinics cared for a median of 162 children each (inter quartile range [IQR]=81-351) in the past 12 months. Respondents were mainly paediatricians (62%). Almost all the sites (98%) reported offering disclosure counselling services. Disclosure counselling was most often provided by counsellors (87%), but also by nurses (77%), physicians (74%), social workers (68%) or other clinicians (65%). It was offered to both caregivers and children in 92% of the 177 sites. Disclosure resources and procedures varied across regions: specific staff training on counselling for disclosure was done in 72% to 96% of sites, a protocol for disclosure of HIV status to children was available in 14% to 71% of sites, and HIV disclosure status was collected routinely in 50% to 91%. Caregivers were involved in the disclosure process in 71% to 100 of the sites. Among the 53 sites (29%) with a formal disclosure protocol, 32 designed it locally and 21 borrowed/adapted from various external sources. Among the 143 sites (79%) routinely collecting disclosure status, the main collection method was through asking the caregiver and child (85%). Collection of disclosure status was done every three months in 63% of these sites and 71% stored disclosure status data electronically (88% of the sites with electronic disclosure data were from Southern and Eastern Africa). According to respondents’ estimates, the median percentage of HIV-infected adolescents who knew they were infected by age 14 was 80% (IQR=75%-80%).

Conclusion: The majority of the sites reported offering disclosure counselling services, but educational and social support resources and capacities for data collection varied across regions. Paediatric HIV care sites worldwide still need specific staff training, development and implementation of guidelines for HIV disclosure and standardized data collection on this key issue for the long-term care and research of HIV-infected youth.

No conflict of interest
Abstract: A_143

HIV infection and adolescents

Diverse Antiretroviral Histories & current health status among Perinatally-Infected South African Adolescents

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Background: The number of perinatally HIV-infected (HIV+) children and adolescents using antiretroviral therapy (ART) has increased rapidly across southern Africa in the past decade. Access to antiretroviral agents (ARVs) has changed radically over this time but there are few insights into the clinical histories of this group and how this relates to current health status.

Materials & Methods: The Cape Town Adolescent Antiretroviral Cohort (CTAAC) recruited perinatally-infected adolescents ages 9-14 years on ART for at least 6 months from public sector HIV services (either community-based primary care clinics or hospital-based paediatric outpatient services) across Cape Town, South Africa. At enrolment all individuals underwent structured clinical examination with phlebotomy for viral load (VL; Abbot RealTime HIV-1) and CD4 cell count (Beckman Coulter); medical history was abstracted from routine public sector records. Age-period-cohort (APC) analyses examined ART histories and cumulative number of ARVs used by age, duration of ART use and calendar time.

Results: Among 515 adolescents (mean age, 12.0 years; 49% female; median CD4 cell count, 712 cells/μL [IQR 556-959]), the median age at ART initiation and duration of ART use was 4.3 years [IQR, 2.0-7.5] and 7.7 years [IQR, 4.6-9.2], respectively. Overall, 24% of adolescents started ART before 2 years of age; 30% of children had a previous pneumonia admission and 61% had a history of TB treatment. Marked APC effects were evident in ART histories, with a group of older children who had limited access to ART during the period 1999-2003 with late ART initiation, followed by initiation at progressively younger ages from 2004. Protease Inhibitor use (predominantly lopinavir/ritonavir) increased gradually over time, and a rapid shift in the most commonly used nucleoside reverse transcriptase inhibitors from d4T to abacavir during 2010-2012 is evident. At the time of enrolment, the mean cumulative number of ARVs used was 4.4 (range, 3-8) with the total number of ARVs a linear function of time on treatment (p<0.001); 25% of children remained on their initial ART regimen and another 38% had undergone only single drug substitution. VL was >50 and >1000 copies/mL in 23% and 13% of adolescents, respectively. VL>1000 copies/mL was significantly more common in children exposed to higher numbers of drugs over time (p=0.008), children with a shorter total duration of ART use (p=0.007), and among males (p=0.015), independent of current age.

Conclusions: Despite limited antiretroviral options available in this setting, South African perinatally-infected adolescents have complex clinical and treatment histories shaped by changing HIV and ART policies over time that are reflected in current health status. The diversity of this growing patient population is likely to present unique clinical questions and challenges to care in the coming years.

No conflict of interest
Abstract: A_144

HIV infection and adolescents

Tablet-Based Resources for Disclosure Counseling for HIV-Infected Adolescents and their Families in Kenya: A Pilot Study of Perspectives from Providers

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Introduction: Overwhelmed, undertrained medical staff working in resource-limited settings need efficient resources to help support families during the process of HIV disclosure to children. This study evaluated providers’ perceptions of using tablet computers for disclosure-related counseling with HIV-infected children and their caregivers in western Kenya. Additionally, it assessed for changes in provider comfort, ability, and knowledge of HIV disclosure.

Materials & Methods: This study used a mixed-methods design at three large, rural HIV clinics in western Kenya (Bumala, Busia, and Port Victoria) within Academic Model Providing Access to Healthcare (AMPATH). Healthcare providers involved with pediatric disclosure were recruited. Initial interviews focused on understanding current disclosure practices and barriers. Tablets containing disclosure-related resources were distributed. Resources included short narrative videos created in this context to highlight issues relevant to child HIV disclosure. Self-reported use was tracked with five monthly surveys, followed by repeat interviews. Interviews were transcribed and coded using a grounded theory approach to identify key themes. Survey data were analyzed using Wilcoxon signed ranks test, Fisher’s Exact Test, and Kruskal-Wallis.

Results: 21 healthcare providers participated (8 clinical officers, 5 nurses, 8 social support staff). The proportion of participants, in regards to gender and clinical roles, was similar among each of the clinics (p-values 1.00 and 0.654, respectively). Most believed caregivers should disclose their children’s status to them, with healthcare providers offering encouragement and answering children’s questions. Major perceived barriers for caregivers to disclose were lack of parental HIV knowledge and stigma. Surveys indicated tablets were used during 75% or more of clinic encounters by 67% (14/21) of providers one month after tablet distribution, and 85% (18/21) at the end of the study. Provider comfort with disclosure increased significantly between the first and third surveys (p-value=0.039). This increased comfort persistent during the study period (p-value 0.024 between 1\(^{st}\) and 4\(^{th}\) survey, p-value of 0.027 between 1\(^{st}\) and 5\(^{th}\) survey). Although it did not reach statistical significance, males seem to indicate that the tablet was more helpful in their discussion of HIV disclosure counseling compared to females (p-value=0.051). At follow-up, all (n=21) providers reported tablets improved clinic disclosure process. Many (n=16) reported child participation and adherence improved and children increasingly attended clinic specifically to watch tablet disclosure videos. Providers reported caregivers and children began initiating dialogue about critical issues such as medication adherence after watching the disclosure videos. Additionally, all (n=21) reported reviewing materials during their free time, in particular outside of work, to increase their own knowledge and comfort with disclosure. No technical issues were reported.

Conclusions: Provider comfort with HIV disclosure increased significantly during the duration of this study. Providers expressed that the tablets had made a positive impact on their clinic and helped them navigate the disclosure process. Tablet computers with culturally relevant resources for disclosure are an acceptable and potentially effective resource to help providers support families with disclosure.

No conflict of interest
Abstract

**HIV infection and adolescents**

**Skinfold thicknesses and body fat percentage do not predict lipid abnormalities in perinatally-infected HIV+ adolescents on ART**

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**Background:** Chronic HIV infection and antiretroviral therapy (ART) are both associated with serum lipid abnormalities in HIV+ children. Skin fold thickness (SFT) measures and body fat percentages may be used as a screening tool for lipid abnormalities, but there are scant data from HIV+ African adolescents. We investigated the associations between SFT and serum lipid levels in perinatally HIV-infected (PHIV+) adolescents and HIV- controls in the Cape Town Adolescent Antiretroviral Cohort (CTAAC) in Cape Town, South Africa.

**Methods:** PHIV+ adolescents ages 9-14 years on ART for at least 6 months and HIV- controls underwent clinical examination including Tanner staging and assessment of lipodystrophy; measurements were taken of the biceps, triceps, subscapular and suprailiac SFT on the right side by trained clinical personnel; and head, mid-upper arm, waist, hip and thigh circumferences were also measured. Fasting total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and triglycerides (TG) were collected. The Slaughter equation was used to estimate percent body fat and this with SFT measures were standardised using age- and sex-adjusted norms from National Health and Nutrition Examination Survey (NHANES). Spearman’s correlations were calculated between SFT measures (including body fat percentage) and serum lipids, with linear regression to adjust for covariation by age, sex, puberty onset and current ART regimen.

**Results:** Among 515 PHIV+ adolescents (median age, 12 years; 49% female; median age at ART initiation, 4.3 years, IQR 2.0-7.6) and 110 HIV- controls (median age, 11.7 years; 55% female), Z-scores for SFT measures were lower than reference norms and in PHIV+ compared to controls across all age groupings. The median percent body fat Z-score was -0.7 [IQR, -1.6-0.0] in PHIV+ vs -0.1 [IQR, -0.8-0.4] in HIV- controls (p<0.001). Delayed onset of puberty in PHIV+ adolescents attenuated most observed differences in SFT measures when compared to HIV- controls. Mean TC (4.2 vs 3.8 mmol/L, p<0.001), LDL-C (2.2 vs 2.0 mmol/L, p=0.040), and TG (1.0 vs 0.7 mmol/L, p=0.001) were higher in PHIV+ adolescents vs HIV- controls. Pre-pubescent PHIV+ participants had higher TC and LDL levels compared to those who had initiated puberty. Overall, SFT measures correlated weakly with elevated lipid values, although slightly higher correlations were observed in children currently using d4T (8% of adolescents) and/or protease inhibitors (37% of adolescents). Among PHIV+ adolescents, no SFT measure or combination thereof, including estimated body fat percentage, was consistently associated with lipid abnormalities independent of age, sex, puberty status and current ART regimen; these results were consistent when restricted to adolescents with or without evidence of lipodystrophy.

**Conclusion:** Lower SFT and body fat observed in PHIV+ adolescents could largely be attributed to delayed puberty. SFT measurements or estimated body fat percentage are not useful for predicting serum lipid abnormalities.

Conflict of interest

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Abstract: A_146

HIV infection and adolescents

Adolescent HIV testing: perceived quality, HIV knowledge, and intent to retest


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Background: Adolescents are the only demographic group globally in which HIV incidence and mortality are increasing. Improving the quality of voluntary counseling and testing (VCT) services may promote better adolescent testing habits, curb transmission, and promote timely treatment.

Materials & Methods: All adolescents and youth ages 14-24 years tested for HIV at Kenyatta National Hospital VCT services in Nairobi, Kenya, were invited to complete an anonymous, self-administered exit survey measuring demographics, HIV status, reasons for testing, perceived quality, HIV knowledge, and intent to retest. Questions about HIV knowledge were adapted from the DHS AIDS Indicator Survey. Cofactors for knowledge and intent to retest were determined using univariate and multivariate relative risk regression (generalized linear model with binary family and log link).

Results: Among 227 adolescents, the average age was 21 (IQR: 19-23) and average number of years of education was 17 (IQR: 12-19). Two percent of adolescents reported testing HIV positive, 95% reported testing HIV negative and 3% did not report results. One third (32%) of adolescents were testing for HIV for the first time. Perceived quality of testing services was high (mean 4.5 on 5 point scale). HIV knowledge was low with 25% accurately identifying routes of transmission and 49% accurately identifying prevention measures. Among those with inaccurate knowledge of prevention, the most frequent inaccuracy was assuming that 'open mouth kissing' transmitted HIV (92%). Among those with inaccurate knowledge of HIV prevention, the most frequent inaccuracies were not identifying having one faithful, uninfected partner (53%) or abstaining from sex (68%) as ways to prevent HIV acquisition.

In univariate analyses, older age and higher years of education were associated with greater likelihood of accurate prevention knowledge (one year increase RR: 1.07, 95%CI: 1.00-1.14, p=0.04; RR: 1.05, 95%CI: 1.01-1.10, p=0.02, respectively). Multivariate analysis was not attempted because of collinearity of age and years of education. In univariate analyses, higher education was associated with greater likelihood of accurate transmission knowledge (one year increase RR: 1.09, 95%CI: 1.01-1.17, p=0.03), and there was a trend towards an association between first time testing and lower likelihood of accurate transmission knowledge (RR: 0.51, 95% CI: 0.24-1.07, p=0.08). In multivariate analyses including education and first time testing for HIV, education was no longer associated with increased likelihood of accurate transmission knowledge (RR: 0.53, 95% CI: 0.25-1.12, p=0.1).

Conclusion: Perceived quality of HIV testing and intent to retest were high at this urban referral hospital. Improving knowledge of HIV transmission and prevention is an opportunity to further improve the quality of testing services.

No conflict of interest
Abstract: A_147

HIV infection and adolescents

Continuous Quality Improvement (CQI) intervention improved adolescent HIV knowledge and intent to retest at a youth counseling center in Kenya

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Background: Adolescents in sub-Saharan Africa have high HIV incidence and are the only age group in which HIV-related mortality is increasing. Improving the quality of the HIV testing experience may increase linkage to care among HIV-infected adolescents and facilitate prevention behaviors and regular testing patterns among HIV-uninfected adolescents.

Materials & Methods: Following a baseline data collection period, a continuous quality improvement (CQI) intervention was introduced at 2 HIV testing clinics within Kenyatta National Hospital in Nairobi, Kenya: general voluntary counseling at testing (VCT) and Youth Centre. Healthcare worker teams were trained in CQI methodology and met weekly to plan and evaluate tested micro-changes using a plan-do-study-act approach, informed by a team-generated key driver diagram. Primary outcomes were adolescent satisfaction with the test experience (5-point likert scale), intent to retest within a year (5-point likert scale), and full and accurate knowledge of HIV prevention and HIV transmission (both binary outcomes). Data were analyzed using an interrupted time series analysis with Prais-Winston regression (linear regression with first order autocorrelation).

Results: There were 176 adolescents (111 in Youth Center and 65 in VCT) during the 6 weeks of baseline data and 565 (371 in Youth Center and 194 in VCT) during the 18 weeks of intervention. The micro-change concepts tested by the 3 teams focused on adolescent satisfaction (through creating a welcoming, youth-friendly atmosphere) and communicating modes of HIV prevention and transmission (through checklists and/or ‘teach back’ techniques).

The CQI intervention was associated with an increase in the proportion of adolescents with accurate knowledge of HIV transmission in both sites: absolute 58 percentage point increase in Youth Center (p<0.001) and absolute 33 percentage point increase in VCT (p=0.008). The intervention was showed a trend towards an increase in the proportion of adolescents with accurate knowledge of HIV prevention in VCT (absolute 25 percentage point increase, p=0.057), but not Youth Center (p=0.21). The intervention was also associated with a trend towards greater likelihood of retesting within a year in Youth Center (0.44 point greater likelihood, p=0.067, at Youth Center), but not in VCT (p=0.24, high baseline and remained high during intervention). In both clinics, the intervention was not associated with changes in satisfaction, which was high during baseline and remained high during the intervention period (overall average score: 4.5/5 satisfaction, p>0.4 for all comparisons).

Conclusions: The CQI intervention improved adolescent knowledge of HIV transmission, and showed trends with knowledge of prevention and intent to retest. CQI was highly acceptable to front line health care workers and did not decrease adolescent satisfaction, which remained high during the intervention period. CQI may be a simple intervention to improve the quality of adolescent-friendly services in resource-limited settings.

No conflict of interest
Abstract: A_148

HIV infection and adolescents

Evaluating Impact of Group Therapy Based Intervention on Anti-Retroviral Therapy (ART) Adherence Amongst Adolescents Living with HIV (ALHIV) in Malawi

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Introduction: Adolescents living with HIV (ALHIV) experience psychological and emotional distress which negatively impacts their adherence to anti-retroviral therapy (ART) and overall physical and mental health. A review of individual counseling sessions offered at the Baylor College of Medicine Center of Excellence in Malawi from September 2013-March 2014 showed that despite individual counseling, many of the teens still experienced persistent poor adherence. To improve treatment and prevention of psychosocial problems in ALHIV, group therapy was introduced in April 2014 focusing on the common psychosocial issues.

Methods: 20 adolescents aged between 11 to 15 years with poor adherence for over three month were enrolled using cluster random sampling in April and July 2014 and 27 adolescents attending boarding school were enrolled in December 2014 and July 2015. The 20 adolescents attended 6 sessions and those at boarding school attended 3 sessions. Group discussions were used to identify common psychosocial issues that contributed to poor adherence. Rationale emotive behavioral approaches were used to address issues. Retrospective chart review of participants was done evaluating adherence 1 year after participation (6 month review for the July 2015 participants) evaluating ART adherence and a descriptive analysis of the data was performed.

Results: From the group discussions, participants self identified the following contributing factors to poor adherence: 15% religious influences (3 participants), 55% classroom issues including stigma (11 participants), 20% parental issues (4 participants), 10% issues related to sense of belonging (2 participants). For the teens in boarding school participants identified the following contributing factors of poor adherence: 63% reported fear of stigma (17 participants), 63% fear of being seen taking ART due to sleeping arrangements (17 participants), 37% due to lack of lockable cupboards for ART (10 participants), and 88% identified lack of trust in school staff (24 participants). Following the group counseling at 1 year, 18 out of 20 adolescents have excellent adherence to ART (90%) defined as 95-105% adherence by pill count. Adherence for 12 out of 20 adolescents improved from the sessions alone (60%), adherence for the remaining 6 adolescents improved after two and three supportive individual counseling sessions (30%). However only 20 out of 27 adolescents in boarding school have excellent adherence (74%). Due to distance of the boarding schools from clinic, these teens are not able to attend individual counseling.

Conclusions: Group counseling has proven effective in addressing psychological issues affecting ALHIV and improving adherence and should be considered for ALHIV who have persistent poor adherence. More attention is needed to address barriers to good adherence at boarding school that are out of the adolescents’ control including training teachers, head masters, and school prefects in ways to support ALHIV and ART adherence without increasing school based stigma and discrimination.

No conflict of interest
Abstract: A_149

HIV infection and adolescents

Transitioning adolescents with HIV – the Zimbabwean perspective

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Introduction: In high resource settings, transitioning care is widely promoted as a strategy to address the multi-faceted needs of adolescents with HIV moving from paediatric to adult services. Yet as the majority of adolescents with HIV worldwide live in low resource settings and attend primary health care facilities where there is no distinction between paediatric and adult services, initiatives to support transitional care for adolescents with HIV should therefore focus on primary health care facilities.

Methods: Between 2013 and 2015, a government-led capacity strengthening programme was implemented for health care workers across all provinces of Zimbabwe, aimed at strengthening their competencies to provide quality services which are responsive to the individualised, evolving needs of adolescents and young people with HIV. This involved a combination of residential training, facility-level mentorship, provision of counselling tools as well as the establishment and integration of community initiatives including adolescent review days, support groups and peer counsellor teams, known as Community Adolescent Treatment Supporters (CATS).

Results: A total of 1955 health care workers (HCWs) from primary health care facilities were trained and mentored, with the number and geographical coverage expanding each year (90 in 2013, 605 in 2014 and 1260 in 2015). Health care workers demonstrated improved awareness, skills and confidence to adapt their care to the specific needs of adolescents within their general clinics. In addition to improved counselling skills, health care workers were then supported to establish adolescent support groups (n = 66), clinic review days on Saturdays so that adolescents do not need to miss school and the integration of 125 HIV positive peer counsellors known as Community Adolescent Treatment Supporters (CATS). CATS were mentored by health facility primary counsellors and were active in providing facility based counselling as well as follow up through home visits. Robust referral pathways and case management processes were also established to ensure the linkage between health and social protection services. Adolescent-led information, education and communications materials were also disseminated to all districts across the country. HCWs describe improved linkage, retention, adherence and mental health outcomes in the adolescents they are providing services for. They also described a high regard and acceptance of CATS and the role of community initiatives in enhancing the care they are able to provide as young people transition into adulthood.

Conclusions: In Zimbabwe, the majority of adolescents are transitioning from childhood to adulthood within the same health facility. Training and mentorship for HCWs in those facilities is therefore essential so that they can transition their care accordingly. This approach should continue to be scaled up. Evidence is required of the impact on outcomes across the HIV care cascade as young people transition into adulthood.

No conflict of interest
Abstract: A_150

Prevention of Mother-to-Child transmission

Maternal HIV Status and Reported Child Mortality – Findings from the Mpepu Study, Botswana

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Introduction: Women living with HIV face health and social challenges, particularly in resource-constrained settings. We sought to describe the experience of HIV-infected women in Botswana with under-5 mortality among their previous live-born infant.

Materials and Methods: Women enrolling in the latter period of the Mpepu study, a randomized trial of extended cotrimoxazole versus placebo prophylaxis among HIV-exposed uninfected infants, were surveyed with baseline questions about obstetric history, feeding practices, and survival of previous children. Responses from women with one prior pregnancy who reported knowing their HIV-status in the prior pregnancy just prior to their current child were analyzed.

Results: Of 3,334 enrolled HIV-infected women, 1,146 (34%) multiparous women completed a baseline survey of whom 1,123 (97%) reported knowing their HIV-status in the prior pregnancy. A total of 290 (25%) had one prior pregnancy, of whom 136 (47%) indicated that they were HIV-infected at that time, while 154 (53%) reported being HIV-uninfected during the prior pregnancy. Median age (p=0.21), education (p=0.80), and income (p=0.90) of the women did not differ by reported HIV-status in the prior pregnancy. Death of their first born child before age 5 was experienced by 11 (8.1%) women who reported being HIV-infected during the pregnancy compared with 6 (3.9%) by women who reported being HIV-uninfected during the prior pregnancy (p=0.14). Almost all women who reported being HIV-infected in the prior pregnancy (87%) formula fed their infants, while 91% of those reporting being HIV-uninfected breastfed their infant. This pattern is in keeping with Botswana's national Prevention of Mother-to-Child HIV Transmission programming.

Conclusions: Among women who had one prior pregnancy and reported knowing their HIV status in the prior pregnancy, there was a trend for higher child mortality among those known to be HIV-infected during their prior pregnancy. While this analysis precludes determination of the cause of higher under-5 mortality (e.g. infant HIV infection, replacement feeding, or other factors), our findings highlight the high risk of child mortality that HIV-infected women experience. This underscores the importance of optimizing interventions to improve the health of HIV-exposed children, and provide appropriate counseling and support for HIV-infected women.

No conflict of interest

Abstract: A_151

Prevention of Mother-to-Child transmission

Optimizing PMTCT service Uptake through community involvement in Enugu state, Nigeria

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**Background:** Nigeria ranked high among countries with the highest global Mother To Child Transmission (MTCT) burden. Despite this fact, only 8% of identified HIV positive pregnant women were offered Anti-retroviral (ARV) prophylaxis due to missed opportunities and inadequate access to services. The poor access to Prevention of Mother To Child Transmission (PMTCT) services greatly affect the population living in the rural areas due to high stigma levels, illiteracy and abject poverty.

**Materials & Methods:** Community leaders in targeted communities of South-East Nigeria were partnered with to identify mobile HIV Testing and Counseling team who were equipped to mobilize pregnant women to access PMTCT services in health facilities within their communities, provide HIV Counseling and Testing (HCT) services to pregnant women within the community as well as provide escort services to identified HIV positive pregnant women to the rural HIV clinics in January 2014. The rural HIV Testing and Counseling team were also supported to track and return back to care HIV positive pregnant women previously identified, but not on ARV Prophylaxis. Excel and Statistical Package for the Social Sciences SPSS packages were used to compare quarterly PMTCT services uptake at the community health facilities between Oct-Dec, 2013 (Pre-intervention) and subsequent quarters in 2014 (Post-intervention).

**Results:** The number of pregnant women who came for first time antenatal visit were 2,426 (pre-intervention period: Oct-Dec, 2013); 3,573 (Jan-Mar, 2014); 3,269 (Apr-Jun, 2014); 7,981 (Jul-Sep, 2014); and 7,111 (Oct-Dec, 2014) respectively. Thus, 2,426 (pre-intervention period) accounted for only 9.96% of the total 24,360 new ANC clients who visited the rural facilities during the review period. The number of pregnant women who were counseled, tested for HIV and received results were 2,785 (Oct-Dec, 2013); 6,627 (Jan-Mar, 2014); 8,905 (Apr-Jun, 2014); 23,889 (Jul-Sep, 2014); and 7,455 (Oct-Dec, 2014) respectively. Similarly, more HIV positive pregnant women (37- Oct-Dec, 2013; 58- Jan-Mar, 2014, 56- Apr-Jun, 2014, 87- Jul-Sep, 2014, 104- Oct-Dec, 2014) were identified and placed on ARV prophylaxis in the post intervention period. There were increased hospital deliveries (466- Oct-Dec, 2013; 808- Jan-Mar, 2014, 868- Apr-Jun, 2014, 796- Jul-Sep, 2014, 699- Oct-Dec, 2014) in rural communities during the post intervention period.

**Conclusions:** Strategically engaging community in the implementation of the HIV program resulted in the observed increase in the number of women accessing Ante Natal Clinic (ANC)/PMTCT services at the community health facilities.

**No conflict of interest**

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**Abstract: A_152**

**Prevention of Mother-to-Child transmission**

**Scaling up early infant diagnosis (EID) services in Nigeria through EID mentor approach**

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**Introduction:** Ninety five percent (95%) of pediatric HIV infection in Nigeria occurs during pregnancy, child birth, or through breast feeding. One of the challenges with scaling up pediatric HIV treatment in Nigeria is the inability to make pediatric diagnosis early due to poor health workers skills on pediatric diagnosis, lack of access to the modern diagnostic technologies including polymerase Chain Reaction (PCR) assays and delays in returning results of Early Infant Diagnosis (EID) form reference labs. Majority of the PMTCT sites in Nigeria are located in the rural areas. A review of the rural Standalone Prevention of Mother To Child Transmission of HIV (sapMTCT) sites at 209 health facilities in South East Nigeria showed that none of the staff at the standalone PMTCT (saPMTCT) sites demonstrated the ability to provide EID services and so onsite DBS sample collection was a challenge. HIV Exposed Infants (HEIs) caregivers were either referred from the
rural Primary Health Centres (PHCs) to the closest Comprehensive Care and Treatment (CCT) facility for DBS sample collection, drying, packaging and transportation. This arrangement was characterized by incomplete referrals and high cost for the HEIs Caregivers.

**Materials & Methods:** 'EID Mentor' Approach (EMA), which involves the use of live HEIs to provide hands-on mentoring on EID, including DBS sample collection, drying, packaging and transportation, to facility staff during micro cluster (a micro cluster consists of 2-3 nearby health facilities) meetings and routine facility visits was introduced to the rural health facilities in January, 2014. These health care workers (HCWs) then became EID Mentors (EMs) that further developed the capacities of their colleagues in nearby supported facilities. EMs phone directories were developed and shared with several nearby health facilities to support timely Dry Blood Specimen (DBS) collection; enabling the EMs to mentor staff of facilities that called them while collecting the DBS. These newly trained HCWs subsequently became EMs also and train others. A retrospective data collation of two targeted indicators from the supported health facilities at 6 months before- and 6 months after- the intervention was conducted. The data were reviewed and analyzed using Microsoft Excel and Statistical Package for the Social Sciences (SPSS) soft wares.

**Results:** The percentage of eligible HEIs at standalone PMTCT that accessed EID services increased from 24% (pre-intervention) to 81% at 6 months post-intervention (p < 0.05). Only 13% of health care workers in selected health facilities demonstrated the ability for EID services before the intervention, this increased to 87% at 6 months post intervention.

**Conclusions:** The introduction of EMA demonstrated the value of using empowered HCWs as mentors to their colleagues in ensuring that children born to HIV infected women readily access EID services, especially in the rural areas at no extra cost to both the caregivers and HIV project.

No conflict of interest
Conclusions: Despite access to ART, stigma remained a feature in descriptions of disclosure, particularly in relation to partner disclosure. For women who tacitly disclosed, they either intentionally undermined the fear of being ‘known’ as HIV positive, or else did not feel this stigma. The juxtaposition of tacit disclosure with ongoing stigma suggests an evolution of the epidemic in contexts of relatively good ART access, perhaps signalling normalisation and destigmatization. In this context, the strong promotion of disclosure by HIV-related services may unintentionally thwart attempts to continue the destigmatization of HIV status.

No conflict of interest

Abstract: A_154

Prevention of Mother-to-Child transmission

The Pediatric Infectious Event Tool for Research (PIET-R): a new tool to grade infectious morbidity

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Introduction: In the Mother Infant Health Study (MIHS) of infectious morbidity in HIV exposed and unexposed infants, infectious event outcome definitions were required that were: 1) relevant to local disease profiles, 2) easily applied without special investigations or expert opinion, 3) able to discriminate severity amongst non-life threatening hospitalizations. Existing clinical trial research and infectious disease surveillance definitions did not meet these needs. For the PIET-R, World Health Organisation Integrated Management of Childhood Illnesses (IMCI) and South African pediatric clinical management algorithms were adapted to include case-definitions of common childhood illnesses including respiratory tract, diarrheal, mucocutaneous and invasive bacterial infections. Severity grading (mild-moderate or severe) was defined according to IMCI or clinical management criteria for hospitalization. HIV exposure information was removed from the standardized abstraction form to reduce bias.

Methods: The PIET-R was evaluated using two approaches. A) Cross-sectional validation study of 50 non-MIHS hospitalizations to test reliability (inter-observer agreement measured by prevalence-adjusted-bias-adjusted-kappa [PABAK]) and validity (sensitivity, specificity) of diarrhea and lower respiratory tract infection (LRTI) definitions. The treating pediatrician assigned a gold standard diagnosis for each hospitalization using all available information and diagnostic tests. Chart abstractions and classification of hospitalization events were then performed by a second pediatrician, general practitioner and registered nurse using the PIET-R. Reliability was interpreted according to the lower bound 95% confidence interval for PABAK as slight (0.21-0.40), fair (0.41-0.60), good (0.61-0.80), very good (0.81-0.92), excellent (0.93-1.00) agreement. B) Application of the PIET-R in the MIHS. Two abstractors (a medical student and registered nurse) conducted chart abstractions for all hospitalized infants in the MIHS. Two pediatricians, blinded to HIV exposure, used the abstraction form to independently classify and grade hospitalization events according to the PIET-R and Division of AIDS (DAIDS) Adverse Event Grading Table.

Results: A) In the cross-sectional validation study (n=50), 28 events were assigned a gold standard diagnosis of diarrhea (26 severe) and 26 LRTI (19 severe). Inter-observer agreement was fair to very good for ‘all diarrhea’, ‘all LRTI’ and ‘severe LRTI’ but was slight for ‘severe diarrhea’. Sensitivity was >80% for ‘all diarrhea’, ‘all LRTI’ and ‘severe LRTI’ and 54-77% for ‘severe diarrhea’. Positive predictive value was >80% for all classifications. Specificity and negative predictive value were >80% for ‘all diarrhea’ and ‘all LRTI’. Insufficient numbers of negative severe events precluded evaluation of specificity and negative predictive value for severe classifications. B) In the MIHS, 12.1% (32/264) of infants (age 0-12 months) were hospitalized at least once. For 50 infectious events: 24 (48%) were LRTI, 17 (34%) diarrhea, 9 (18%) other events. Thirty-six (72%) events were severe according to PIET-R and 100% (50/50) were assigned DAIDS grade 3. Observed agreement between the two
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Pediatricians was 94% (47/50) for type of event and 100% (50/50) for severity.

Conclusion: Clinical management case-definitions without special investigations can be reliably used for infectious disease research outcome classification. The PIET-R definitions were appropriate for the local disease profile and the grading identified a difference in severity not seen with DAIDS grading.

No conflict of interest

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Prevention of Mother-to-Child transmission

Utilization of prevention of mother-to-child transmission of HIV services by adolescent and young mothers in mulago hospital, Uganda

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Introduction: Over 90% of HIV infection in children occurs through mother to child transmission (MTCT) of HIV. In order to eliminate Paediatric HIV infection, World Health Organization (WHO) recommends prevention of mother to child transmission (PMTCT) Option B plus (lifelong antiretroviral therapy for all pregnant and breastfeeding women living with HIV regardless of CD4 count or WHO clinical stage). In Uganda, 25% of girls have had a pregnancy by the age of 18 years. Moreover, adolescents have been noted to have poor utilization of health services. Adolescent and young mothers are therefore a vulnerable population which contributes significantly to shaping the future course of the HIV epidemic. However little is known about utilization of PMTCT services in this group. We therefore aimed to describe the utilization of PMTCT services by adolescents and young mothers attending Mulago National Referral Hospital, and to explore the factors that affect the optimal utilization of PMTCT services by these mothers.

Methods: This was an analytical and descriptive cross sectional study of 418 adolescent and young mothers, using quantitative and qualitative methods of data collection. Optimal utilization of PMTCT was defined as being up to date with utilization of PMTCT services for reported HIV status. An interviewer-administered questionnaire was used to obtain information on maternal socio-demographic characteristics, HIV/AIDS and PMTCT-related knowledge, PMTCT utilization, and factors influencing utilization of PMTCT services. Twenty in-depth interviews with selected adolescent and young mothers, and nine key informant interviews with health workers at the hospital were conducted to obtain an in-depth understanding of the context and factors influencing utilization of PMTCT services. The overall proportion of participants who optimally utilized PMTCT services was determined using descriptive statistics. The factors associated with optimal utilization of PMTCT services were determined by logistic regression. Data analysis was with STATA version 12. Qualitative data was analyzed manually using the content thematic approach.

Results: The median age of the mothers was 22 years (IQR 15-24 years). Of the 418 participants, 65 (15.5%) were HIV positive. Only 30% (126/418) of the participants had optimally utilized PMTCT services. Utilization of PMTCT services was better among HIV positive mothers, with 83% (54/65) having utilized the services optimally, compared to only 20% (72/353) of the HIV negative mothers (p-value 0.001). Significant losses and delays occurred throughout the PMTCT cascade. The major reported factors motivating adolescent and young mothers to utilize PMTCT services included: the benefits of knowing ones HIV status, and the health of the unborn child. Stigma was the commonest reported barrier to adolescent and young mothers’ utilization of PMTCT services.

Conclusion: Utilization of PMTCT services by adolescent and young mothers at 30% was low, especially among HIV negative mothers. Reported positive HIV status was significantly associated with optimal utilization of PMTCT services. The benefits of knowing ones HIV status, and the health of the unborn child, were the major factors motivating adolescent and young mothers to utilize PMTCT services, while stigma was a key demotivating factor.

No conflict of interest
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Prevention of Mother-to-Child transmission

Timing of presentation for antenatal care among HIV-infected women in Cape Town, South Africa

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Background: As with other maternal health interventions, effective prevention of mother-to-child transmission (PMTCT) benefits from early presentation to antenatal care (ANC). However, delayed presentation is common in South Africa. We examined the timing of ANC presentation and associated risk factors in HIV-infected (HIV+) women.

Methods: As part of a larger study of maternal HIV care and treatment, we enrolled consecutive HIV+ women making their first ANC visit at a primary care facility in Cape Town, South Africa. All women underwent research ultrasonography for pregnancy dating and completed a structured questionnaire. We analysed factors associated with presentation in tertiles of < 17, 17-24, and 25+ weeks' gestation; logistic regression was used to examine independent predictors of presentation >25 (late) versus ≤24 (early) weeks gestation.

Results: Among 1518 women, median gestational age at booking, was 21 weeks, median age was 29 years, with 40% presenting during the third trimester. Lower socioeconomic status, not being married/cohabiting and having an unplanned pregnancy increased the odds of booking late. (Table 1). Being newly HIV diagnosed in the current pregnancy was strongly associated with later booking gestation, but among women previously diagnosed, antiretroviral therapy (ART) use was not associated with booking time. In multiple logistic regression, having an unplanned pregnancy, being unemployed and having no PMTCT history were predictors of late booking (aOR 0.55; 95% CI: 0.41-0.74, aOR 0.60; 95% CI: 0.44-0.80, aOR 1.68; 95% CI: 1.18-2.39, respectively).

Conclusions: Despite the availability of effective interventions, late ANC presentation remains a significant barrier to the success of PMTCT programs. These results will assist in strengthening existing interventions to ensure maximum duration of ART use during pregnancy, particularly in those newly diagnosed, who may be particularly vulnerable. There is opportunity for improved integration of HIV and reproductive care services to ensure women test regularly and access ANC services as early as possible.

No conflict of interest

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Prevention of Mother-to-Child transmission

Childbearing intentions and family planning uptake in HIV+ women on antiretroviral therapy (ART) in the postpartum period

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Background: There are growing concerns about the childbearing intentions and family planning (FP) needs of women on ART, yet little is known about these issues in HIV+ women during the postpartum period. We examined childbearing intentions and FP uptake among...
HIV+ women during the first year postpartum in Cape Town, South Africa.

**Methods:** We followed 471 women on ART from delivery through 12 months postpartum between June 2013-June 2015. In up to 5 interviews conducted separately from routine health services, women reported on FP use and childbearing intentions; the latter was recorded using a 4-point scale measuring perceived future desires, categorised as (i) unsure, (ii) definitely do not want to become pregnant in the future, (iii) may want to become pregnant in the future, (iv) definitely do want to become pregnant in the next 12 months.

**Results:** In this population (median age, 29; 42% married/cohabiting), childbearing intentions remained stable throughout the postpartum period: across visits, 90-92% of women were unsure or definitely did not want to become pregnant in the future (Figure 1). Desire to become pregnant in the next 12 months was reported in < 2% of women consistently over time. In contrast, the proportion of women not using FP increased, from 4% to 17% by 12 months postpartum; these increases were driven by discontinuation of injectables. Use of implants and intrauterine devices (IUDs) increased over time (14-19%). Among women at 12 months postpartum who were unsure or definitely did not want to become pregnant in the future, 18% were not using FP.

**Conclusions:** Non-use of FP increases over the postpartum period among HIV+ women. Discontinuation of injectables contributes to non-use. While further research into the determinants of childbearing intentions and FP use are needed in this population, long-acting methods suitable for women using ART, such as the IUD require ongoing programmatic support.

*No conflict of interest*

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**Prevention of Mother-to-Child transmission**

**Reducing mother to child transmission of HIV through a multi-faceted strategy: the Ugandan experience**

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**Background:** In an endeavour to reduce mother to child transmission (MTCT) of HIV to less than 5%, Uganda adopted the following guidelines: (i) provision of lifelong ART to all HIV-infected pregnant and lactating mothers irrespective of CD4 count or clinical stage (Option B+); (ii) special precautions during delivery; (iii) provision of ARVs (NVP) to HIV-exposed infants from birth to 6 weeks postpartum and (iv) exclusive breastfeeding up to 6 months postpartum. We examined adherence to the eMTCT interventions among HIV-infected mothers and determined MTCT rate at 6 weeks postpartum.

**Materials and Methods:** We performed a retrospective cohort analysis of data abstracted from health facility records of 2,169 pregnant or lactating mothers and their babies enrolled on Option B+ between January and March 2013 in a representative sample of 145 health facilities in 24 districts of central region of Uganda. We measured compliance to the eMTCT guidelines. The MTCT rates were determined using survival analysis and factors associated with HIV transmission were evaluated using Cox proportional hazard modelling.

**Results:** The median follow-up time for the mothers and their babies was 20.2 months (IQR, 4.2-22.5) and 9.0 months (IQR 2.6-13.6), respectively. Median age of the mothers at ART enrolment was 25 years (IQR, 22-29) while that of the infants at enrolment into HIV care was 1.5 months (IQR 1.5-2.0). Nearly all mothers (97.0%) were initiated on Tenofovir/Lamivudine/Efavirenz regimen. Median CD4 count at ART initiation was 524 cells/µl (IQR, 343-737). 82.1% of the mothers...
had supervised deliveries during which special precautions were undertaken. 83.0% of the infants received daily NVP from birth to 6 weeks postpartum and 84.0 of the infants were exclusively breastfed for the first 6 months of life. The rate of infection per month, based on the 1st PCR was 3.2/100 person months (95% CI 2.4-4.3). Poor adherence to ARVs by mothers (adjusted Hazard Ratio (aHR) 1.89 (95% CI 1.30-2.73) and a baby receiving no ARVs (aHR 1.22 (95% CI 1.03-1.45) were associated with increased risk of MTCT of HIV.

Conclusion: These findings suggest that compliance to the eMTCT guidelines is high and the strategies adopted are effective in reducing MTCT of HIV to less than 5%. Poor maternal adherence to drugs and failure to provide babies with ARVs increase the risk of transmission.

No conflict of interest

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Prevention of Mother-to-Child transmission

Association of gestational age measures in HIV-infected pregnant women

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Introduction: PMTCT with ART from early pregnancy has successfully reduced the number of infected children globally, but prolonged ART exposure may be associated with increased adverse pregnancy outcomes including prematurity, low birthweight and/or small for gestational age deliveries. Accurate gestational age (GA) assessment is of critical importance for the correct diagnosis of these adverse outcomes, particularly in high HIV prevalence areas, where ultrasonography is usually unavailable and GA assessment is routinely based on clinical assessment including dating the last menstrual period (LMP) and measurement of symphysis-fundal height (SFH). However, LMP-based GA may be unreliable with recall issues and use of injectable hormonal contraception (with lack of, or irregular, periods after cessation), while SFH-based GA assessment is difficult in women early in pregnancy (<12 weeks) and in women with high BMI. We describe GA estimation methods in an ongoing prospective observational study: ‘Prematurity Immunology in HIV-infected Mothers and their Infants Study’ (PIMS)

Methods: From April 2015 to March 2016, pregnant women regardless of HIV status at first antenatal care (ANC) visit at the Gugulethu Midwife Obstetric Unit were enrolled in PIMS. Women clinically assessed (LMP and/or SFH) during routine ANC to be ≤24 weeks gestation were referred for research ultrasound scan (US) for pregnancy dating. Gestation at first ANC visit based on routinely collected LMP and SFH measurements were compared to US-based gestation to inform understanding of under- or over estimation of duration of pregnancy.

Results: To date, 1200 women had at least one GA measurement. Of these (median age 28 years, 25% nulliparous, 32% HIV-infected), 91% (n=1087) had a LMP-based GA, 59% (n=712) a SFH-based GA and 60% (n=720) an US-based GA; 26% (n=313) had a GA based on all three methods. Estimated median (IQR) LMP-based GA was 17 weeks (12-23), SFH-based 23 weeks (19-27) and US-based 15 weeks (12-20). SFH-based GA was strongly correlated with US-based GA (r=0.86); correlations between LMP-based GA and US-based GA (r=0.69) and between LMP-based GA and SFH-based GA (r=0.68) were moderate. Estimated concordance (<7 days difference) with US GA estimates was 18% (107 of 587 GA estimates with both measurements) for LMP and 33% (n=118) for SFH. LMP underestimated the US GA by ≥7 days, in 274 cases (47%), and overestimated in 206 cases (35%). Percentages of under- and overestimation for SFH were 20% (n=118) for SFH. LMP underestimated the US GA by ≥7 days, in 274 cases (47%), and overestimated in 206 cases (35%). Percentages of under- and overestimation for SFH were 20% (n=74) and 47% (n=169) respectively. Compared to US-based GA, being nulliparous and obese (BMI > 29) was associated with a decreased risk of underestimation by LMP: aRR=0.43 (95%CI 0.24, 0.79) and aRR=0.57 (95%CI 0.31, 1.05) respectively.
Conclusion: Before 24 weeks of pregnancy, estimated GA on the basis of SFH appears to be more accurate than reported LMP assessments of GA. This suggests that SFH estimation is a more accurate estimation tool in high HIV prevalence areas in the absence of ultrasound facilities.

No conflict of interest

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Nursing Education for an AIDS-Free Generation: Evaluating an Option B+ E-Learning Module

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Introduction: Task-shifting from doctors to nurses is increasingly recommended in sub-Saharan Africa for scale-up of antiretroviral therapy (ART) to prevent of mother-to-child transmission (PMTCT) according to the Option B+ approach, yet nursing schools lack resources to adequately prepare graduates for an expanded scope of practice. In 2015, ICAP and the Center for Teaching and Learning at Columbia University, with funding from the United States President’s Emergency Plan for AIDS Relief thorough the Heath Resources and Services Administration, launched and evaluated an Option B+ e-learning module for nursing students.

Methods: A purposive sample of nursing students from eight schools in Lesotho, Zambia, and Malawi participated in the study. Adapting Kirkpatrick’s model for evaluating training, quantitative and qualitative data were collected to assess outcomes at three levels: 1) Satisfaction with training was measured via an online post-training survey; 2) Knowledge gained through training was measured via an online pre-post multiple choice test; and 3) Clinical practice was measured via a survey of self-report post-training. Quantitative data underwent descriptive statistical analysis and qualitative data were analyzed for recurring themes.

Results: A total of 220 students completed the module and evaluation. 91% indicated satisfaction with the training, specifically with relevance of content and delivery methods. Students reported challenges with limited internet access, faculty support, and hands-on clinical experience. Students’ knowledge of HIV care and treatment for PMTCT using Option B+ increased by 13% from pre- (68%) to post-test (81%). Following completion of the module, 57% indicated they were prepared to prescribe ART to HIV-infected pregnant or breastfeeding women in clinical practice.

Conclusion: Completion of the Option B+ e-learning module resulted in high levels of user satisfaction, increased knowledge, and preparation for clinical practice among nursing students. Together with faculty support and clinical experience, e-learning may enable schools to better prepare graduates for an expanded scope of practice. Lessons learned will inform development of a new e-learning module in pediatric HIV care and treatment. Preparing competent nursing students for an expanded scope of practice is critical to scale-up HIV care and treatment for PMTCT and achieve an AIDS-free generation.

No conflict of interest
Abstract: A_161

Prevention of Mother-to-Child transmission

HIV counselling and testing among sub-Saharan African pregnant women: Geographical variations and the hotspots

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Background: Knowing the level of HIV counselling and testing (HCT) utilisation among pregnant women in high burden countries is important for measuring the performance of the prevention of mother-to-child transmission of HIV programmes. Knowledge of HIV status of pregnant women is important in making critical clinical decisions during pregnancy, labour, delivery and breastfeeding periods. The purpose of this study was to examine the extent of regional, national disparities of HCT, geographical variation and to identify the 'hotspot areas of low performance' in sub-Saharan Africa.

Methods: The study used data from the population-based Demographic and Health Survey (DHS) from different 32 countries in sub-Saharan Africa within the time frame of 2009 - 2015. The participants were women aged 15-49 who gave birth in the two years preceding the survey. They were counselled, tested for HIV during antenatal care and obtained the results. Descriptive statistics and spatial scan were used to map hotspot areas of low uptake of HCT by pregnant women. Kruskal-Wallis test was also used in the analysis.

Results: The pregnant women who were counselled, tested for HIV during antenatal care and obtained the results ranged from 6.9% in Madagascar to 94.5% in Rwanda. Zambia, Kenya, Namibia and Rwanda had >90% utilisation while five of the countries had <20% performance. On average, the countries of West African, Central/East African and Southern African sub-regions recorded 40.8%, 54.1% and 72.5% respectively. Among the 32 countries, 16 had various regional hotspots of poor performance. On sub-national level, Anosy region of Madagascar had the lowest performance at 1.6% while Embu region of Kenya recorded 100%. There was no significant differences among the three sub-regions, p=0.108.

Conclusions: There is a wide variation in the level of HCT utilisation among pregnant women in sub-Saharan Africa. The outcome of this study showed that there are many pregnant women with unknown HIV status in many African countries thereby impeding the efforts to eliminate mother to child transmission of HIV. Statistical and geospatial monitoring approaches contribute to better understanding for identification of poor performing areas for HCT utilisation among pregnant women in sub-Saharan Africa.

No conflict of interest

Abstract: A_162

Complications of HIV therapy

HIV-1 subtype C resistance patterns in children on antiretrovirals with viral loads >1000 copies/ml in the Ekurhuleni east district, South Africa

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Introduction: South Africa currently has one of the largest antiretroviral programmes in the world with an estimated 144 742 of the 460 000 HIV infected children on combination antiretroviral treatment (ART). Monitoring drug resistance patterns in a resource-poor setting like South Africa is essential as there are limited drug treatment options available for children. The aim of this study was to characterise the frequency and patterns of acquired HIV-1 subtype C drug resistance in HIV positive children with virological failure from the Ekurhuleni East sub-district.

Material & Methods: A retrospective secondary data analysis of genotypic and phenotypic data collected prospectively as part
of screening for the open label, multicenter, multiple-dose pharmacokinetic, safety and efficacy trial of Maraviroc in combination with optimized background therapy for the treatment of antiretroviral-experienced CCR5-tropic HIV-1 infected children 2-18 years of age (A4001031) trial. Children were considered eligible for this trial if they had a viral load >1000 copies/ml with >6 months ART exposure including at least two antiretroviral classes. R5 tropic children were included in the trial and X4 tropic as well as children with dual/mixed tropism were excluded from the trial. All patients who received tropism screening for this study were included in the data analysis, regardless of tropism results. The PhenoSense GT assay was used. The prevalence and frequency of mutations were analysed in conjunction with selected clinical and demographic data.

Results: A total of 70 children were successfully genotyped; 57 on first line NNRTI regimens, four on first line PI regimens and nine on second line PI regimens at the time of genotyping. Of the 70 patients genotyped 61,4% had mixed wild type and mutant mutations. 95,7% had at least one mutation. The M184V mutation occurred in 80% of patients. The second most common mutation was K103N/R/S and was found in 62,9% of patients. 33 (47,1%) patients had at least one thymidine analogue mutation (TAM), 16 (22,9%) had only one TAM, four (5,7%) had two TAMs and 13 (18,6%) had three or more TAMs. There were no children with two major PI mutations in this cohort but four children had one major PI mutation each. Only two children had complete resistance to lopinavir/ritonavir (LPV/r) and none had intermediate resistance.

Conclusion: Results were largely in keeping with similar studies from other parts of South Africa. Of concern is the high percentage of mutations in this urban primary health care setting compared to tertiary hospitals in South Africa. The high frequency of mutations in the Ekurhuleni East district may in part be explained by poor adherence and delayed intervention or referral of patients with virological failure to tertiary settings. Possible solutions include stricter monitoring and earlier referral to secondary or tertiary care or, alternatively, initial secondary or tertiary management of all HIV positive children with down referral of patients who are stable on therapy.

No conflict of interest
Abstract

The Joint model has allowed to assess the risk of death, depending both on the WAZ value and WAZ slope over time. Two periods of follow-up were distinguished: the first two years on ART, with clinical and immunological parameters improving markedly for all children, and the 2-5 years period after ART initiation, with most of the survivors being at a more stable HIV disease progression. Adjustment variables were sex, age, severity of immunodeficiency for age, and severity of malnutrition at ART initiation.

Results: Overall, in the first two years of ART, 3606 children were included and contributed to 23804 weight measurements. Among them, 54% were boys, 57% were underweight and 31% were severely immunodeficient at ART initiation; during this period, 306 (8.5%) deceased and weight evolved significantly, especially for the youngest children and those severely underweight at ART initiation. The joint model showed that a low WAZ value within the first two years of ART was associated with a higher risk of death, adjusted on WAZ slope and covariables (aHR=2.35, CI95%=2.07-2.65). Younger age and severe immunodeficiency at ART initiation were also associated with a higher risk of death. In the 2-5 years period after ART initiation, 26/2071 (1.2%) children deceased, while there was no more weight evolution, a low WAZ value was still the main factor associated with a higher risk of death (aHR=3.60, CI95%=2.43-5.33).

Conclusion: Children who experienced weight deficiency during follow-up on ART were at high risk of death, whatever their duration on ART. Using a joint modeling approach, weight evolution on ART could be view as a predictor of death. Other adverse events such as CD4 drop or viral rebound could be investigated in further analyses. Moreover, patterns of anthropometric indicators evolution could be also identified with a latent-class joint modeling approach. Monitoring routinely these growth patterns among ART-treated children is needed to identify early those at higher risk of death, and improve their care in resource-limited settings.

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Complications of HIV therapy

Static or progressive? A one year follow up of gross motor and upper limb function in children with bilateral lower limb spasticity due to HIV encephalopathy

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Background: HIV encephalopathy (HIVE) is the most common neurological manifestation of HIV in children and bilateral lower limb (BLL) spasticity often forms part of an HIVE diagnosis. Furthermore, it was recently noted that some children with HIVE and BLL spasticity also have significant limitations in upper limb motor function. At present, it is unclear whether physical impairments associated with HIVE are static or progressive. As a result, it is unclear whether children with HIVE and BLL spasticity should receive surgical interventions for secondary abnormalities related to HIVE and BLL spasticity. Therefore, the aim of the current study was to investigate the change in (i) gross motor function and (ii) upper limb motor function over a one year period in children with bilateral lower limb spasticity due to HIVE.

Materials and Methods: Twenty children with BLL spasticity due to HIVE were recruited at Red Cross War Memorial Children’s Hospital and Tygerberg Hospital in Cape Town, South Africa. The group consisted of 8 boys and 12 girls with a mean age of 8y10mo (range 5y5mo-12y8mo) and Gross Motor Function Classification System level of I (n=6), II (n=6) and III (n=8). Gross motor function was assessed using the 88-item Gross Motor Function Measure (GMFM) and upper limb motor function using the Purdue Pegboard with both assessments conducted at baseline and
one year later. Change in the 'Standing' domain, 'Walking, Running and Jumping' domain and total GMFM score along with change in the 'Preferred hand', 'Non-preferred hand' and 'Both hands' Purdue Pegboard tasks were compared between the baseline and follow-up assessment using a Wilcoxon matched pairs test.

Results: There was a significant improvement in the 'Walking, Running and Jumping' domain of the GMFM (mean ±SD 56±29% vs. 60±31%, p=0.04) as well as in total GMFM score (83±12% vs. 84±13%, p=0.05) with no significant change in the 'Standing' domain (70±23% vs. 72±24%, p=0.37). Purdue pegboard scores showed no significant change in the tasks involving the preferred hand, non-preferred hand and both hands (-2.7±1.4 vs. -3.0±1.5, -2.2±1.4 vs. -2.6±1.5 and -3.0±1.4 vs. -2.9±1.4, p≥0.10).

Conclusions: The current findings suggest that there was no deterioration in the gross motor function of children with HIVE and BLL spasticity over a one year period. There were, in fact, statistically significant improvements in some GMFM outcomes although the clinical significance of these changes requires further investigation. The study also showed no apparent deterioration in the ability to perform simple activities with the upper limbs. These observations constitute important preliminary insight into the natural history of HIVE and BLL spasticity and may help to inform larger studies, with longer periods of follow-up, along with the future development of evidence-based treatment guidelines.

No conflict of interest

Abstract: A_165

Complications of HIV therapy

Investigating the neurocognitive status of children with HIV encephalopathy and spastic diplegia

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Introduction: In prenatally infected children, Human Immunodeficiency Virus (HIV) is particularly damaging because it invades and impairs the developing Central Nervous System (CNS) early after infection. This impairment of CNS function may leave children with a range of cognitive, behavioural and motor deficits. The most common clinical presentation of HIV-related CNS problems among children is HIV encephalopathy (HIVE). Although the introduction of Highly Active Antiretroviral Treatment has reduced the incidence of HIVE and associated neurodevelopmental outcomes somewhat, there are still residual deficits that occur. One of the frequently observed residual motor impairments in children is spastic diplegia. However, little is known about the physical impairment of spastic diplegia associated with HIVE. Clinically, spastic diplegia secondary to HIVE seems to present similarly to children with spastic diplegia cerebral palsy (CP), but there is no previous research comparing the neurocognitive profiles of these two groups.

Material & Methods: This study forms part of a larger study investigating the aetiology and natural history of spastic diplegia in children with HIVE. In 2014, we investigated the neurocognitive functioning of children with HIVE spastic diplegia as compared to children with spastic diplegic CP in 36 children (n = 24 HIVE, n = 12 CP, participants). In 2015, we followed up on the children who participated in the 2014 study, exploring within- and between-group changes one year later. Neurocognitive data from 35 children (n = 22 HIVE participants, n = 13 CP participants) were explored and
compared in this follow-up study. We conducted ANOVAs and a paired sample t-test to assess between- and within-group differences, respectively, and a MRA to control for significant between-group demographic differences.

**Results:** In 2014, we found no significant between-group differences between the HIVE and CP groups, with the exception of verbal IQ (VIQ). The children in the CP group obtained a significantly higher VIQ than the HIVE group. However, significant between-group differences in participants’ home language largely accounted for this outcome. In 2015, we found no significant between-group differences, with VIQ only tending towards significance at this time. Within group change showed significantly lower VIQ and Full Scale IQ for HIVE group from time 1 to time 2, with significant increases in verbal recognition memory at time 2.

**Conclusions:** Although between group differences in language confounds between-group VIQ differences in CP and HIVE groups, the within-group change in the HIVE group suggests that this domain requires specific further investigation in the HIVE group. Neurocognitive functioning in children with HIVE and spastic diplegia and children with spastic diplegic CP appears to be similar and may be facilitated by biological damage as a result of the injury caused by each condition to the developing brain. Consideration should be made of the demographic and socioeconomic factors that may be powerful mediators in terms of neurocognitive outcomes.

**Conflict of interest**

Financial relationship(s): I received a CIPHER Grant/scholarship for participating and collecting data in the study.
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