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Abstracts

Oral Presentations
Abstract 1

Comparing Conventional to Point-of-Care (POC) Early Infant Diagnosis (EID): Pre and post intervention data from a multi-country evaluation

Bianchi F1, Nzima V2, Chadambuka A3, Mataka A4, Machekano R1, Sacks E1, Bailey R6, Alban R1, Lemaire J5, Cohn J5

1Elizabeth Glaser Pediatric AIDS Foundation, 2Elizabeth Glaser Pediatric AIDS Foundation, 3Elizabeth Glaser Pediatric AIDS Foundation, 4Elizabeth Glaser Pediatric AIDS Foundation, 5Elizabeth Glaser Pediatric AIDS Foundation

Background: Survival of HIV-infected infants depends on a robust early infant diagnosis (EID) system. Currently, too few HIV-exposed infants (HEI) receive timely EID. Integration of point-of-care (POC) or near-POC molecular EID testing into a country’s existing laboratory network could improve turnaround time (TAT) of result return and ART initiation. In 2016, the Elizabeth Glaser Pediatric AIDS Foundation (EGPAF) began a phased scale-up of POC EID, with the goal of reaching 1755 sites across nine African countries by 2018. This is the first multi-country evaluation of routine POC EID usage, as compared to conventional POC.

Methods: Using a pre-post intervention design, key clinical and service delivery outcomes were compared in 3 intervention countries (Cameroon, Lesotho, and Zimbabwe). Pre-intervention data were retrospectively collected from facility registers from a sub-set of sites in each country beginning at least three months before the time of data extraction. Data from any HEI who did not receive a result three months or more after sample collection was censored. Data extracted from clinic-level sources included percent of results returned to HEI caregiver, TAT from sample collection to result return, percent of HIV-infected infants initiation on ART and time to ART initiation. Intervention data were collected prospectively in sites using POC using an EID testing request form.

Results: Pre-intervention data were collected for 1082 infants in 37 sites. 67% of test results were received by caregivers. The median turnaround time was 34 days from sample collection with a range of 0-432 days. Only 58% of infants diagnosed with HIV had been initiated on treatment. POC EID implementation began in December 2016; as of April 2017, 1436 tests have been conducted on 1393 children in 18 testing and 33 spoke sites, in the three countries. 99% of tests results had reached caregivers; 71% of results had reached the caregiver on the same day while 93% received their results in 7 days or less. The median turnaround time between sample collection and POC EID test results received was 0 days with a range of 0-59 days. 89% of HIV-Infected infants were initiated on treatment and the median turnaround time from receipt of result to ART initiation was 0 days, with a range of 0-58 days. Using the Global Fund’s estimates of total costs of ownership for conventional and POC EID systems, cost per test result received ranged from $21.64-$27.61 USD for conventional and $21.21-$32.83 USD for POC.

Conclusions: Early prospective findings from three diverse country contexts show considerable improvements in percent of results received, TAT from sample collection to result return and a greater percentage of HIV-infected infants started on ART. Initial data from routine, real-world use of POC EID show that the introduction of POC or near-POC technologies into the conventional EID system results is improving patient-level outcomes and may reduce HIV-related pediatric morbidity and mortality. Cost per test result returned suggests that POC is cost effective.
Abstract 2

Virological dynamics in HIV-infected infants following very early antiretroviral treatment

Strehau R1, Shiau S1,2,3, Technau K1, Patel F1, Conradi M1, Burke M1, Sherman G1,4, Coovadia A1, Aldrovandi G5, Tiemessen C4, Abrams E1,6,7, Kuhn L1,2,3

1Empilweni Services and Research Unit, Department Of Paediatrics and Child Health, Wits University, 2Gertrude H. Sergievsky Center, College of Physicians and Surgeons, Columbia University, 3Department of Epidemiology, Mailman School of Public Health, Columbia University, 4Centre for HIV and STIs, National Institute for Communicable Diseases and Faculty of Health Sciences, Wits University, 5David Geffen School of Medicine at UCLA, Mattel Children’s Hospital, 6ICAP and Department of Epidemiology, Mailman School of Public Health, Columbia University, 7Department of Pediatrics, College of Physicians and Surgeons, Columbia University

Background: Antiretroviral treatment (ART) of primary HIV infection in adults and infants has raised the hope that very early ART may alter HIV pathogenesis and lead to HIV remission in at least some individuals. However, data to support this hypothesis are limited. Rapid viral load decline after ART initiation is presumed to be a necessary first step along the pathway by which treatment of primary infection may lead to remission.

Methods: For the past 2.5 years, HIV PCR testing has been offered for all HIV-exposed newborns at Rahima Moosa Mother and Child Hospital in Johannesburg, South Africa. Standard HIV PCR tests are done at the national state laboratory. On weekdays when staff capacity permits, point-of-care HIV PCR tests (Xpert® HIV-1 Qual) are concurrently done. All infants with positive PCR results are actively traced for confirmatory testing and engagement in care. ART is initiated as soon as possible with nevirapine, lamivudine and zidovudine with substitution of lopinavir/ritonavir for nevirapine at 42 weeks post-menstrual age or later. Plasma HIV RNA is measured at frequent intervals using Roche COBAS® AmpliPrep/COBAS® TaqMan® HIV-1 with a lower detection limit (LDL) of 20 copies/ml, and qualitative diagnostic HIV PCR tests are repeated. We compared virological response over the first year of life among infants initiating ART within 48 hours of birth and those initiating after 48 hours but within 7 days of birth.

Results: Through September 2016, we enrolled 75 birth-identified HIV-infected infants into clinical trial protocols to track their virological response to ART. Thirty-three of these infants started ART <48 hours after birth, 22 started >48 hours to 7 days, and 20 started 8 or more days after birth. Of those starting at <48 hours, 3 died in the first months of life and 3 had refused follow-up. The probability of achieving HIV RNA level <20 copies/ml was similar between those who started <48 hours compared to those who started >48h-7 days by 12 months (73.3 vs. 66.2%, p=0.79) and the proportion sustaining LDL through 12 months or the last visit was also similar: 40.0% if <48 hours and 40.9% if >48h-7 days. Negative diagnostic HIV PCR tests (some transient) were observed during follow-up in 16.7% <48 hours and 13.6% if >48h-7 days. There was a trend towards the probability of achieving “target not detected” by 12 months being greater in those who started <48 hours compared to those who started >48h-7 days (70.9 vs. 40.3%, p=0.061).

Conclusions: There are only subtle differences in virological response to early ART between those treated <48 hours and those treated slightly later. Clinical and social factors are associated with the timing of ART initiation and ongoing adherence, and complicate interpretation. Standard virological markers used to track response to ART appear to be inadequate to discern whether or not ART initiated within the first 48 hours of life is any more likely to influence the likelihood of remission than ART initiated within the first week.
Abstract 3


Iyun V1, Technau K2, Eley B3, Rabie H4, Boullé A1,5, Fatti G6, Tanser F2,3, Wood RP, Fairlie L10, Davies M1

1Centre for Infectious Disease Epidemiology and Research (CIDER), University Of Cape Town, 2Rahima Moosa Mother and Child Hospital, University of the Witwatersrand, 3 Red Cross War Memorial Children's Hospital and Department of Paediatrics, University of Cape Town, 4Tygerberg Academic Hospital and Department of Paediatrics, University of Stellenbosch, 5Khayelitsha ART Programme and Department of Health Impact Assessment, Western Cape Department of Health, 6Khetimpilo, Africa Centre for Population Health, 7Faculty of Health Sciences, University of KwaZulu Natal, 8Gugulethu ART Programme and Desmond Tutu HIV Centre, University of Cape Town, 9Faculty of Health Sciences, Wits Reproductive Health and HIV Research Institute, University of the Witwatersrand

Background: The context of HIV prevention and treatment for children in South Africa has significantly improved; Immediate antiretroviral therapy (ART) was expanded to children younger than 12, 24 and 60 months (WHO Paediatric ART guidelines in 2008, 2010 and 2013 respectively), there is widespread ART coverage for pregnant and breastfeeding women (Option B+, 2013), regimens for prevention of mother-to-child transmission have been improved, and, more recently there is a shift toward birth early infant diagnosis (EID) and early infant ART (Birth EID, 2015). However, there is limited data that describes the impact of these changes on characteristics of infants starting ART in resource-limited settings. We describe the trends in characteristic and outcomes of children initiating ART in the context of changing paediatric HIV testing and treatment guidelines in South Africa.

Method: We conducted a retrospective cohort analysis using data from eight cohorts within the IeDEA-SA collaboration. All HIV-infected children initiating combination ART at <3 months old, from 2006 – 2016 were included. We described changes in characteristics of children starting ART as well as mortality, loss to follow-up (LTFU (last visit date >6 months before site database closure)) and transfer out by 12 months on ART. Three time periods; 2006-2009, 2010-2012 and 2013 onwards (2013+) were utilized to show the trends in infant characteristics at ART initiation.

Results: Among 1380 infants, the median age at ART initiation was 62 (interquartile range (IQR) 37-79) days; median time on ART was 13.6 (IQR 4.0-34.5) months. The median age at ART start decreased from 67 (IQR 53-81) days in 2006-2009 to 48 (IQR 9-74) days in 2013+ (p<0.001). Similarly, there was a moderate decline in median log viral load from 5.9 (IQR 5.4- 6.4) in 2006-2009 to 5.4 (IQR 3.9-6.3) in 2013+ (p<0.001). The median absolute CD4 count increased progressively from 888 (IQR 380-1703) in 2006-2009 to 1526 (IQR 659-2231) in 2013+ (p<0.001). Among infants with data on WHO disease staging (n=865), 84% (n=299) started ART with WHO disease stage 3/4 in 2006-2009 compared to 39% (n=279) from 2013 onwards (p<0.001). After 1 year on ART, 11% (median age 68 days (IQR 55-75)) and 4% (median age 60 days (IQR 25-83)) of children died in 2006-2009 and 2013+ respectively (p<0.001). There was marked trend in LTFU and transfer out: LTFU increased from 7% in 2006-2009 to 21% in 2013+ (p=0.002) and transfer out declined from 20% in 2006-2009 to 12% in 2013+ (p<0.001).

Conclusion: The changing context of HIV prevention, testing and treatment for infants has allowed children to start ART earlier and with less progressive disease and associated declines in mortality; however mortality and LTFU in infants starting ART remains unacceptably high. In view of the scale up of birth PCR testing in South Africa, a significant proportion of children still start ART with advanced disease. There is a need for a more focused and innovative approach towards early infant HIV testing, follow-up, as well as linkage to and early care on ART.
Abstract 4

Age-stratified rates of mortality and key clinical events in youth aged 0-24 years in the multiregional IeDEA network

Desmonde S1, Neillan A2, Malaste K3, Yiannoustos G4, Musick B5, Patten G6, Duda S7, Kariminia A8, Edmonds A9, Wools-Kaloustian K10, Ciaramello A11, Davies M12, Leroy V13, on behalf of the IeDEA global cohort consortium

1Inserm U1027, University Toulouse 3, 2Massachusetts General Hospital, 3Harvard Medical School, 4Inserm U1219, Université de Bordeaux, 5School of Medicine, Indiana University, 6School of Public Health and Family Medicine, Faculty of Health Sciences, University of Cape Town, 7Vanderbilt University Medical Center, 8The Kirby Institute, 9Department of Epidemiology, Gillings School of Global Public Health, The University of North Carolina at Chapel Hill

Background: Few data from programmatic settings exist about risks of mortality and morbidity for youth living with HIV. We describe age-stratified crude incidence rates (IRs) of mortality and first occurrence of key clinical events among HIV-infected children and youth aged 0-24 years before and after antiretroviral therapy (ART) initiation in the IeDEA multiregional collaboration, including sub-Saharan Africa, Asia-Pacific, and Latin America.

Methods: HIV1-infected, ART-naïve individuals enrolled at <24 years of age with ≥1 CD4% (<5y) or CD4 cell count (≥5y) during follow-up were included. We estimated IRs of mortality and first occurrence of key clinical events among HIV-infected children and youth aged 0-24 years before and after antiretroviral therapy (ART) initiation in the IeDEA multiregional collaboration, including sub-Saharan Africa, Asia-Pacific, and Latin America. Mortality and first occurrence of key clinical events were censored at death, loss to follow-up (LTFU: last clinical contact >6 months if off ART or >3 months if on ART), or database closure, whichever occurred first.

Results: Overall, 208,962 children and youth were included, of whom 67,688 (32.4%) were enrolled <10y and 141,274 (67.6%) were enrolled ≥10y. Among the 173,425 with "pre-ART" follow-up, 67.5% initiated ART, 1.8% died, and 26.8% were LTFU. Among the 152,588 with "post-ART" follow-up, 5.1% died and 51.1% were LTFU at study closure. The overall pre-ART mortality IR among children aged <10y at inclusion was 2.48/100PY (95%CI:2.36-2.61), and was highest among children aged <2y (8.60/100PY, 95%CI:7.99-9.26). Pre-ART mortality IR was significantly lower in those ≥10y at inclusion: 1.57/100 PY (95%CI:1.50-1.66). Overall post-ART mortality IR was (1.36/100 PY, 95%CI:1.33-1.39). At centers with available clinical data, the overall IRs of pre-ART WHO-3 and WHO-4 events were 9.64/100PY (95%CI:9.40-9.89) and 4.28/100PY (95%CI:4.12-4.44); these were highest among children <2y (WHO-3: 34.6/100PY, 95%CI:32.57-36.78, WHO-4: 11.3/100PY, 95%CI:10.22-12.52). Post-ART WHO-3 and WHO-4 event IRs dropped in all age groups: overall IRs were 1.71/100PY (95%CI:1.64-1.78) and 0.70/100PY (95%CI:0.68-0.73), respectively. As observed in the pre-ART period, IRs in the post-ART period were highest among those <2y. Among those who accessed care ≥10y, we observed significantly higher pre-ART mortality IRs compared to those who accessed care <10y (1.58/100 PY, 95%CI:1.50-1.66 and 0.95/100 PY, 95%CI:0.78-1.17). Post-ART mortality IRs followed the same pattern (1.49/100 PY, 95%CI:1.45-1.54 compared to 0.79/100 PY, 95%CI:0.73-0.85). We observed the same trends for both pre- and post-ART WHO-3 and WHO-4 event IRs.

Conclusion: Age-stratified IRs of mortality and WHO-3 and WHO-4 events were lower after ART initiation. IRs were highest among children <2y, underscoring the importance of prioritizing access to early HIV diagnosis and care. Furthermore, among adolescents and young adults aged 10-24y, pre- and post-ART mortality and WHO-3 and WHO-4 IRs were highest among those enrolled ≥10y. High rates of LTFU may also be due to under-ascertainment of mortality. The scale-up of adolescent-focused HIV services remains critical in both populations.
Abstract 5

Incidence of virological failure to first-line ART among children in Europe and Thailand

Goodall R1, Chiappini E2, Klimentait T3, Ngo-Giang-Huong N4, Thorne C5, Turkova A1, Judd A1, on behalf of the European Pregnancy and Paediatric HIV Cohort Collaboration (EPPICC)

1MRC Clinical Trials Unit at UCL, 2University of Florence, 3University of Basel, 4MI 174 PHPT/Faculty of Medical Sciences, Chiang Mai University, 5UCL Great Ormond Street Institute of Child Health

Background: Previous analyses reported that 89% of children initiating combination antiretroviral therapy (cART) achieved virological suppression (VS) by 12-months. We consider the durability of this response in the EPPICC cohort.

Methods: Children <18 years with viral load (VL) >400c/ml, initiating cART (boosted PI or NNRTI plus >2 NRTI) with VL measurements available both before 15 months and after 12 months of cART were included. Time to virological failure (VF) was defined as the earliest of: confirmed virological rebound >400c/ml following VS, unconfirmed rebound >400c/ml following VS, with a change in ART or death within 6 months of rebound, or VL >400c/ml after 12 months without previous VS. Follow-up was censored at the earliest of time of VF, last VL date or gap in VL measurement of >15 months. Multivariable stepwise Cox regression models (backwards elimination, exit probability p=0.05) identified factors associated with VF.

Results: 90% of 2636 children were perinatally infected, 53% female, with 34%, 12%, 35% and 18% from UK/Ireland, Russia/Ukraine, rest of Europe and Thailand respectively. 33% initiated ART with a PI-based regimen (93% lopinavir/r), 34% efavirenz-based and 33% nevirapine-based ART. 32% started an abacavir-containing regimen. At ART initiation, children had median [IQR] age 6.3[1.7,10.6] years, CD4% 15[8,23]% and log10VL 5.1[4.5,5.7]c/ml. Median follow-up was 4.4[2.2,7.7] years. 748 children had VF (62% and 6% had confirmed/unconfirmed rebound, 32% had no VS by 12 months). Overall cumulative probability of VF (95% CI) at 3, 5 and 7 years after cART start were 25(23-27)%, 31(29-33)% and 37(35-39)% respectively. In multivariable analysis, compared to a bPI-based regimen, there was no difference in risk of VF for children initiating on an EFV-based regimen (aHR 0.97(0.79, 1.21)), but risk was higher for children starting NVP-based ART (aHR 1.27(1.03, 1.56); overall p=0.02). Risk of failure was increased for infants and older children (<1yr: aHR 1.44(1.11, 1.87), 1-<3yrs: aHR 1.18(0.88, 1.58), 6-<11yrs: aHR 1.33(1.05, 1.67), ≥11yrs: aHR 1.61(1.25, 2.08) vs 3-6yrs; p=0.003) and earlier calendar year of ART initiation (1997-2003: aHR 1.56(1.32, 1.84), ≥2008: aHR 0.99(0.80, 1.22) vs 2004-2007; p<0.001). Risk was reduced in children initiating on abacavir (aHR 0.77(0.64, 0.92); p=0.004). Additionally children in Russia/Ukraine and UK/Ireland had higher VF risk compared to those elsewhere in Europe, and children in Thailand had lower risk (Russia/Ukraine: aHR 1.54(1.13, 2.09), UK/Ireland: aHR 1.33(1.10, 1.61), Thailand: aHR 0.69(0.54, 0.88) vs Rest of Europe; p<0.001). There was no significant effect of gender, mode of infection, AIDS diagnosis, VL, CD4%, HCV, HBV or TB co-infection at ART start on risk of VF.

Conclusion: We found similar failure rates to those reported in horizontally-infected young adults in Europe. Infants and teenagers were at higher risk of VF, possibly related to difficulties with dose adjustment in infants and poorer adherence in adolescents; these groups should be targeted in clinic for additional support. Lower failure rates in Thailand could be related to high use of fixed-dose combinations; higher failure rates in Russia/Ukraine may be partly explained by rationing of VL tests with preferential use in children who are of clinical concern.
Abstract 6

Multi-month prescription of antiretroviral therapy and its feasibility - experiences from the Baylor International Pediatric AIDS initiative (BIPAI) in six Southern African countries

Wanless R1, Kim M2, Ahmed S2, Anzel A3, Golin R2, Abrams E4, Chidah N5, Damba D6, Dlamini S7, Mhango J2, Mokhali M8, Chodota M9, Kayabu A10

1Baylor International Pediatric AIDS Initiative, 2Baylor International Pediatric AIDS Initiative, Children’s Clinical Center of Excellence, 3United States Agency for International Development, 4International Center for AIDS Care and Treatment Programs, Mailman School of Public Health, Columbia University, 5Baylor International Pediatric AIDS Initiative, Children’s Clinical Center of Excellence, 6Baylor International Pediatric AIDS Initiative, Children’s Clinical Center of Excellence, 7Baylor International Pediatric AIDS Initiative, Children’s Clinical Center of Excellence, 8Baylor International Pediatric AIDS Initiative, Children’s Clinical Center of Excellence, 9Baylor International Pediatric AIDS Initiative, Children’s Clinical Center of Excellence, 10Baylor International Pediatric AIDS Initiative, Children’s Clinical Center of Excellence

Background: To improve antiretroviral coverage (ART) and help reach the 90-90-90 treatment targets, differentiated approaches to care are necessary, including reduced frequency of clinic visits for stable patients. Given the paucity of data regarding the impact of differentiated care models on pediatric outcomes, BIPAI conducted a retrospective analysis of clinical outcomes, comparing monthly (MS) with multi-monthly (MMS) ART prescription schedules for children and adolescents in Botswana, Lesotho, Swaziland, Malawi, Uganda and Tanzania.

Methods: MMS was introduced in each country in line with national policy. Patients were transferred to MMS when clinically stable and ART adherent, after 6-9 months of monthly prescriptions. For analysis patients were allocated to the MMS group after three consecutive visits at intervals of greater than 56 days. Adherence, lost-to-follow up rates, CD4 counts and viral load were compared between MS and MMS patients by two-sample tests for binomial proportions. Mortality was compared by log rank test. To avoid bias against the MS groups, deaths in the first 6 months of MS therapy were excluded, given the known, high early rates of mortality. To avoid immortal time bias, MMS patients contributed person-time to the MS group between ART initiation and the start of MMS. The analysis was conducted according to an IRP approved protocol.

Results: There were 11,421 MS and 18,137 MMS patients aged between 0 and 19 years. Comparison of clinical outcomes gave the following results. MMS patients had statistically lower mortality at 0.4 deaths per 100 patient years compared with 2.9 for MS patients (p < 0.0001) and lower lost-to-follow up rates: 1.8% for MMS vs. 7.1% for MS (p < 0.0002). 78.5% of MMS patients had average ART adherence rates between 95% and 105% compared with 68.7% among MS patients (p < 0.0002). Response to ART assessed by CD4 counts and viral load measurements was superior in MMS patients. 92.8% of MMS patients had CD4 counts greater than 350 among patients more than 5 years of age or > 25 % among patients under 5 years of age (p < 0.0002). Viral load was undetectable in 78.9% of MMS patients compared to 63.3% of MS patients (p < 0.0002).

Conclusions: This study, representing data from six African countries, provides reassurance that patients 0-19 years of age who are clinically stable and ART adherent, can do well with reduced clinical visits via MMS. The consequent reduction in visits can yield additional benefits by decreasing the burden on health systems and patient time.
Abstract 7

Structured and Culturally-Relevant Disclosure Intervention Improves Pediatric HIV Disclosure in Ghana: The SANKOFA Experience

Paintsil E1, Kyriakides T1, Antwi S2, Renner L3, Lartey M3, Catlin A4, Gan G1, Reynolds N1

1Yale University, 2Komfo Anokye Teaching Hospital, 3University of Ghana Medical School, 4Purdue University

Background: Millions of perinatally HIV-infected children now have access to life-saving antiretroviral therapy (ART) and are expected to live into adulthood. Expanded access to ART is not, in and of itself, sufficient for these expectations to be fully realized. Changes in other inter-related elements of pediatric care such as informing the child that he/she has HIV in a timely, age-appropriate manner are also needed. Despite compelling evidence supporting the merits of informing children of their HIV status, there has been little emphasis on equipping the child’s caregiver with information and skills to promote disclosure, particularly, when the caregiver faces a variety of socio-cultural barriers and is reluctant to do so. We previously reported that the disclosure rate among HIV-infected children was 21%. About 75% of HIV-infected children in sub-Saharan Africa are not aware of their status. We hypothesized that a theory-guided, structured and culturally-relevant disclosure intervention would lead to an increase in HIV disclosure rate at 48 weeks.

Methods: HIV-infected children aged 7 to 18 years and their caregivers were enrolled to the Pediatric HIV disclosure intervention trial (“Sankofa”) from two sites (Komfo-Anokye Teaching Hospital–intervention arm and Korle-Bu Teaching Hospital – control arm) in Ghana (NCT01701635). The intervention contains two key elements to target well-documented, modifiable barriers to promote disclosure. The first component is use of an adherence and disclosure specialist (ADDS) model where a designated clinic staff member familiar with the socio-cultural norms of the community was trained to assist families go through the process of disclosure (i.e., pre-disclosure, disclosure, and post-disclosure phases). The second component is disclosure as a process whereby the ADDS guides the intervention sessions to the Information, Motivation and Behavioral Skills needs of the caregiver and the neurocognitive development of the child. Outcome measures (collected over 48 weeks) post-randomization included rate of disclosure (primary) and health outcomes of the children (virologic, immunologic, psychosocial, and behavioral) and the caregiver (psychosocial) (secondary).

Results: 433 (206 from the intervention site and 227 from the control site) child-caregiver dyads were enrolled between January 2013 to June 2016. 52% of the children participants were male, mean age 9.82 (±2.28) years; over 95% in school; and the majority (84%) were infected by mother-to-child transmission. In preliminary analyses, a statistically significant step-wise increase in the rate of disclosure was observed in the treatment group at all study time points (12, 24, 36, and 48 weeks) (p<0.001). The rate of disclosure at 48 weeks was 52.4% in the treatment group and 16.4% in the control group (p<0.001). Thus compared to study participants in the control group, study participants in the treatment group were 5.6 times more likely to have been disclosed by week 48 (95% CL, 3.5, 8.9).

Conclusion: A structured, culturally-relevant, and personalized disclosure intervention dramatically increased the Pediatric HIV disclosure rate in Ghana. The intervention was administered by HIV clinic staff who were given extra training. This cost-effective intervention can be easily scaled-up in Ghana. Additional analyses will allow us to further assess health benefits and predictors of disclosure.
Abstract 8

Growth evolution and stunting among HIV-infected adolescents in the multiregional IeDEA cohort consortium

Jesson J1, Schomaker M2, Malateste K3, Kumara Wati D4, Kariminia A5, Sylla M6, Kouadio K7, Sawry S8,9, Vinikoor M10

1Inserm U1027, Université Paul Sabatier Toulouse 3, 2School of Public Health and Family Medicine, Faculty of Health Sciences, University of Cape Town, 3Inserm U1219, Bordeaux Population Health Center, Université de Bordeaux, 4Sanglah Hospital, 5The Kirby Institute, UNSW, 6Hôpital Gabriel Touré, 7CIRBA, Hamlet Shezi Clinic, Chris Hani Baragwanath Hospital, 8Faculty of Health Sciences, Wits Reproductive Health and HIV Research Institute, University of the Witwatersrand, 9Centre for Infectious Disease Research in Zambia

Background: HIV-infected adolescents face many challenges worldwide. One of them is stunting, which is difficult to resolve in the long-term, especially for perinatally-infected adolescents (PHA). However, no large-scale estimates of stunting are available for this population. We assessed the prevalence of stunting and growth evolution among adolescents enrolled in the IeDEA consortium.

Methods: Data from Asia-Pacific [AP], Southern Africa [SA], and West Africa [WA] were compiled. All HIV-infected patients enrolled from 2003, with follow-up while aged 10-19 years, with at least one height measurement available, were included. If no information was recorded on the HIV infection mode, children who entered care at 10 years or younger were considered PHA, and those who entered later behaviourally-infected (BHA) and PHA. Growth was described using Height-for-Age Z-score (HAZ), according to the WHO Child Growth Standards. Prevalence of stunting (HAZ<−2 SD) and its associated factors at age 10 and 15 years were studied using logistic regressions. Correlates of growth evolution between ages 10-19 years were studied using a linear mixed model, with an unstructured variance-covariance matrix, random intercept, slope for time, and a spline term at 14 years. Analyses were adjusted by regions, sex, infection mode, age at ART initiation, CD4 cell count and viral load.

Results: Overall, 18 276 adolescents were included (20% AP, 64% SA, 16% WA). PHA were 64% of the cohort, 55% were female, 97% received ART (15% before age 5 years, 35% 5-10 years, 50% after 10 years). At 10 years of age (N=8878), 38% were stunted (42% AP, 39% SA, 26% WA), with higher odds for girls (adjusted odds ration [aOR]=1.23, 95% confidence interval [CI]=1.13-1.35), those initiated on ART after 5 years of age compared to those initiated before (aOR=1.89, 95%CI=1.70-2.10), and those with CD4 cell count <250 compared to ≥500 cells/ml at 10 years (aOR=1.67, 95%CI =1.44-1.93). At 15 years of age (N=6514), 43% were stunted (36% AP, 48% SA, 37% WA), with higher odds for boys (aOR=2.67, 95%CI =2.40-2.96) and those who entered care after age 10 years (aOR=1.43, 95%CI =1.23-1.66). Growth between ages 10-19 years evolved in a bimodal way: a decrease of HAZ from ages 10 to 14 years (mean per year: -0.04, standard error [SE] 0.00), which was more pronounced for boys and WA children; then an increase until 19 years (mean per year: +0.13, SE 0.00), which was higher for girls. Children initiated on ART after 5 years of age had significant increases in HAZ after 15 years of age, reaching similar HAZ values by age 19 years as children initiated on ART earlier, for whom mean HAZ was stable, ≥-2 SD, throughout adolescence.

Conclusions: Prevalence of stunting was high among HIV-infected adolescents. PHA who presented to care before 10 years of age had less stunting than those presenting between 10 and 15 years of age, suggesting the majority of patients in the latter group are actually PHA. A growth spurt appeared at 14 years of age, suggesting a delayed onset of puberty different according to gender, but reasonable growth thereafter.
Abstract 9

Structural brain changes and associations in perinatally infected younger adolescents in CTAAC

Hoare J1, Fouche J1, Phillips N1, Jaska J1, Myer L1, Zar H1, Stein D1

1University Of Cape Town

Background: Adolescents perinatally infected with HIV carry a significant risk of neurocognitive impairment, yet the corresponding structural brain changes of perinatally acquired infection is poorly understood.

Methods: Two hundred and four adolescents with perinatally acquired HIV (median age 10 years; median duration of ART 9 months; median CD4 953) and 44 uninfected matched controls aged 9 to 11 years were enrolled within the Cape Town Adolescent Antiretroviral Cohort (CTAAC). Both groups completed diffusion tensor imaging (DTI) and structural brain magnetic resonance imaging (MRI) to determine fractional anisotropy (FA), mean diffusivity (MD), axial diffusivity (AD), radial diffusivity (RD), gray and white matter volumes, total white matter volume, total gray matter volume, cortical thickness and cortical surface area. Total gray matter volume, total white matter volume, cortical surface area, cortical thickness, whole brain FA and whole brain MD were correlated with current CD4 counts, viral load, age of initiation of antiretroviral therapy, current efavirenz use, general intellectual functioning, Becks Youth Inventories, Child Motivation Scale and the Child Behavior Checklist total competence within the HIV infected group.

Results: HIV infected adolescents had significant FA decreases, indicating damaged neuronal microstructure and increased MD, suggestive of inflammation. HIV infected adolescents had significant decreases in gray matter volume in the postcentral gyrus, cortical surface area in the precentral gyrus and the pericalcarine gyrus, decreased gyrification of the inferior temporal and right lateral occipital gyri. Within the HIV infected group, there were significant associations of greater total gray and white matter volume with better intellectual functioning and the Becks self-concept subscale. Higher viral loads were associated with reduced cortical thickness. Lower whole brain FA, a marker of damaged neuronal microstructure, was associated with higher scores on the Becks anger and disruptive behavior subscales. Higher whole brain MD, a marker of inflammation was associated with poor functional competence, apathy and current efavirenz use.

Conclusions: The pattern of damaged neuronal microstructure, smaller gray matter volumes, and reduced cortical surface area and decreased gyrification, suggests abnormal neurodevelopment in perinatally infected younger adolescents. Longitudinal neuroimaging studies of this cohort are needed to determine the impact of HIV on brain remodeling typically seen in later adolescence.
Abstract 10

Pregnancy and Neonatal Outcomes following Prenatal Exposure to Dolutegravir

Thorne C, Favarato G1, Peters H1, Soriano-Aranedes T2, Floridia M, Colbers A4, Goetghebuer T5, Ragone L6, Burger D4, Poznia A7, Giaquinto C8, Aebi-Popp K9, Vannappagari V6, European Pregnancy and Paediatric Cohort Collaboration (EPPICC)

1 UCL Great Ormond Street Institute of Child Health, Faculty of Population Health Sciences, 2 Hospital Vall d’Hebron, 3 Istituto Superiore di Sanita, 4 Radboud University Nijmegen Medical Centre, 5 Hopital Saint-Pierre, 6 ViiV Healthcare, 7 Chelsea and Westminster Hospital, 8 University of Padova, 9 Bern University Hospital

Background: Dolutegravir (DTG) is an integrase strand inhibitor approved for the treatment of HIV in adults and adolescents since 2013. There is minimal information on use of DTG in pregnant women. Our aim was to assess maternal and fetal outcomes following DTG use during pregnancy in real-world European settings.

Methods: A retrospective analysis of individual patient data prospectively collected in observational studies of pregnant women living with HIV and their infants within the European Pregnancy and Paediatric HIV Cohort Collaboration was conducted. All women with any prenatal exposure to DTG and reported to studies by September 2016 were included.

Results: A total of 81 pregnancies in 81 women were identified. Median maternal age at conception was 33.1 years (interquartile range [IQR], 26.7-37.1 years), and 44/81 (54.3%) born in sub-Saharan Africa. Most (62/74, 83.8%, 7 unknown acquisition) women had heterosexual acquisition of HIV, 9 women were vertically infected and 3 had injecting drug use acquisition. Most women had been diagnosed with HIV before conception (70/75, 6 unknown), 48 conceived whilst on any ART and 28 conceived on a DTG-based regimen. There were two twin pregnancies (all live births). Pregnancy outcomes were known for 64 pregnancies (1 moved to another country before delivery, 16 continuing): 61 ended in live births (29 with 1st trimester DTG exposure), 1 in stillbirth (without 1st trimester DTG exposure), 1 in termination (with 1st trimester DTG exposure) and 1 in spontaneous abortion (with 1st trimester DTG exposure). The remaining results relate to the 63 delivered live born infants (including 2 twin pairs) and 1 stillborn infant (i.e. a total of 62 pregnancies). Median first prenatal CD4 count was 525 cells/mm3 (IQR, 323-660) and 338 cells/mm3 (218-591) in pregnancies with earliest DTG exposure in 1st trimester and 2nd/3rd trimester respectively (missing, 4). Among 60 singleton infants, preterm delivery before 37 weeks gestation occurred in 7.4% (2/27) of pregnancies with 1st trimester DTG exposure and 27.3% (9/33) of those with earliest DTG exposure in the 2nd/3rd trimester; low birth weight (<2500g) was reported in 32.0% (8/25) and 39.4% (13/33) for these groups respectively, with no babies weighing <1500g. Congenital abnormalities were reported in 6.9% (2/29, 2 missing) livebirths with 1st trimester DTG exposure (in one child, patent foramen ovale and in the other, bilateral hexadactyly of hands [familial] and hypospadias); in the 32 livebirths with earliest DTG in the 2nd/3rd trimester, one case of ankyloglossia was reported.

Conclusions: Although this is the largest study to date of DTG use in pregnancy in Europe, small numbers preclude firm conclusions regarding its safety and further prospective monitoring is required.
Abstract 11

Intensification of antiretroviral treatment with raltegravir for late-presenting HIV-infected pregnant women

Thepnarong N1,2, Puthanakit T1,2, Chaithongwongwatthana S2,3, Anugulruengkitt S1,2, Anunsittichai O1, Theerawit T2, Ubolyam S4, Pancharoen C1,2, Phanuphak P5

1Department of Pediatrics, Faculty of Medicine, Chulalongkorn University, 2Research Unit in Pediatric Infectious Diseases and Vaccines, Faculty of Medicine, Chulalongkorn University, 3Department of Obstetrics and Gynecology, Faculty of Medicine, Chulalongkorn University, 4HIV-NAT Research Laboratory, 5Thai Red Cross AIDS Research Centre

Background: The risk of HIV vertical transmission from HIV-infected pregnant women who initiated antiretroviral therapy (ART) during late pregnancy is up to 6-10%. Raltegravir, HIV integrase inhibitor, has rapid viral reduction and could be benefit in this setting. This study is aimed to describe HIV vertical transmission rate from pregnant women who received raltegravir intensification ART during late pregnancy.

Materials & Methods: A prospective cohort study was conducted at the Thai Red Cross AIDS Research Centre. Inclusion criteria were HIV-infected pregnant women with high-risk of HIV vertical transmission defined as (1) initiating ART at gestational age (GA) >32 weeks or (2) receiving ART but yet having HIV-RNA >1,000 copies/ml at GA 32-38 weeks. Pregnant women received standard 3-drug ART regimen plus raltegravir 400 mg twice daily until delivery and then were continued on 3-drug ART after delivery. Plasma HIV-RNA was performed prior to initiating raltegravir and at delivery. HIV status of infant was determined by HIV-DNA PCR at birth, 1, 2 and 4 months. HIV-infected infant was defined by 2 positive tests of HIV DNA PCR. HIV-uninfected infant was defined by > 2 negative HIV DNA PCR test; "definitely HIV-uninfected" if negative at 4 months of age and "presumptively HIV-uninfected" if negative at 2 months of age. Infants who did not have HIV DNA PCR test at 2 months of age were defined as undetermined HIV status.

Results: From January 2016 to March 2017, 73 pregnant women were enrolled; 58 (80%) initiated ART at GA ≥ 32 weeks. Median CD4 count and HIV RNA prior to initiate raltegravir were 386 cell/mm3 (IQR 212-569) and 3.8 log10 copies/ml (IQR 3.3-4.3), respectively. Combinations of ART were 56% EFV-based, 40% LPV/r-based. Median GA at the time of initiating raltegravir was 35 weeks (IQR 33-37). By the end of December 2016, 56 pregnant women were enrolled. There were 58 infants born by these 56 pregnant women (including 2 set of twins). Median time of taking raltegravir was 23 days (IQR 8-34). HIV RNA at the time of delivery was available in 53 (95%) pregnant women. The proportion of pregnant women who had plasma HIV-RNA <50 and <1,000 copies/ml at time of delivery were 47% and 81%, respectively. Twenty-three (40%) infants were delivered by cesarean section. Median GA at birth was 38 weeks (IQR 38-39) with 5 (9%) preterms (GA <37 weeks) and 9 (16%) birthweight < 2500 gm. 55 (95%) had HIV DNA test at birth, and all tests were negative. HIV status of infant were 36 (62%) HIV uninfected, 15 (26%) presumptively uninfected. Seven infants (12%) had undetermined HIV status (all negative DNA PCR at birth and 4 negative DNA PCR at 1 month). HIV perinatal transmission rate was 0% (95% CI 0-6).

Conclusions: No HIV vertical transmission occurred among high-risk HIV pregnant women who received raltegravir intensification ART. This strategy should be considered in late presenting HIV-infected pregnant women who have high-risk of HIV vertical transmission.
Abstract 12

Is Tenofovir Use in Pregnancy Associated with Preterm Delivery? A Canadian Perinatal HIV Surveillance Program Analysis

Brophy J1, Lee T2, Bitun A3, Kakkar F4, Singer J2, Alimenti A5, Money D5, Vaudry W6, Samson L1, Sauvé L5

1Children’s Hospital Of Eastern Ontario, 2CIHR Canadian HIV Trials Network, 3The Hospital for Sick Children, 4CHU Ste-Justine, 5BC Women’s Hospital, 6Stollery Children’s Hospital

Background: Tenofovir-based cART was associated with significantly higher rates of very preterm delivery and infant death in the recently published PROMISE trial (which compared outcomes from women treated with zidovudine/single-dose nevirapine, zidovudine/lamivudine/lopinavir-ritonavir or tenofovir/lamivudine/lopinavir-ritonavir). We assessed rates of preterm delivery according to cART components in the Canadian Perinatal HIV Surveillance Program (CPHSP).

Methods: Data collected annually from 22 pediatric and HIV centres participating in the CPHSP were reviewed for 1997-2015, including: rates of preterm (<37weeks) delivery, antiretroviral choice, maternal demographics and clinical parameters.

Results: Among 2816 cART-treated mother-infant pairs from 1997-2015, 1732 (61.5%) received zidovudine, 575 received abacavir (20.4%) and 501 received tenofovir (17.8%). Tenofovir use in pregnancy began in 2004 (0.75% of pregnancies) and increased every year since to 54.1% in 2015; conversely, zidovudine use decreased from 100% in 1997 to 14.7% in 2015. The overall preterm delivery rate was 16.0%, with a significantly higher rate in mothers treated with tenofovir versus not (19.4% vs 15.2%, Chi-square p=0.022). No other significant differences were found comparing mothers treated vs not treated with abacavir (15.9% vs 16.0%), zidovudine (16.6% vs 15.3%), protease inhibitors (PIs, 15.9% vs 16.0%), non-nucleoside reverse transcriptase inhibitors (NNRTIs, 16.2% vs 15.0%) or integrase inhibitors (INSTIs, 16.0% vs 13.8%). There was no difference in proportion of preterm delivery among women exposed to tenofovir with versus without a PI (19.3% vs. 19.5%), NNRTI (18.0% vs 19.6%) or INSTI (17.8% vs 19.3%). Other significant predictors of preterm delivery included: race/ethnicity (Indigenous 26.9% vs White 17.2% vs Black 13.0%, p<0.0001), maternal risk factor (IVDU 27.6% vs sexual 13.8% vs other 12.1%, p<0.0001), and viral load (VL) closest to delivery (detectable 24.7% vs undetectable 15.5%, p=0.0001), but not once-daily combinations or trimester of cART start.

Multivariate analysis (restricted to 2006-2015 when VL data was more complete) revealed tenofovir (p=0.0209) and zidovudine use (p=0.0187), IVDU (p=0.0086), and detectable VL (p=0.0145) as predictive of preterm birth.

Conclusions: In Canada, preterm delivery risk was higher amongst mothers treated with tenofovir, amongst other factors. Allowing for biases of observational cohort studies, this finding warrants further investigation to determine the safest antiretroviral treatment in pregnancy.
Abstract 13

Hepatotoxicity in HIV+ Postpartum Women Initiating Efavirenz-Containing Regimens

Bhattacharya D1, Gupta A2, Tiemey C3, Huang S3, Peters M4, Chipato T5, Martinson F6, Dula D7, Chaktoura N8, Klingman K5, Gnanashanmugam D5, Currier J1, Fowler M2

1University Of California-los Angeles, 2Johns Hopkins University, 3Harvard University, 4University of California-San Francisco, 5National Institutes of Health, 6University of Zimbabwe, 7University of North Carolina-Chapel Hill, 8College of Medicine-Johns Hopkins Research Project

Background: Recently hepatotoxicity in HIV+ pregnant African women initiating efavirenz (EFV), was reported. We assessed the incidence and association of hepatotoxicity i.e. liver enzyme elevation (LEE) in postpartum (PP) women initiating EFV in the PROMISE study.

Methods: In PROMISE 1077BF/FF, HIV+ antiretroviral treatment (ART) naïve pregnant women with CD4>350 and ALT< 2.5 ULN were assigned to antepartum (AP) and PP ART strategies to assess HIV vertical transmission, safety, and maternal disease progression. Sites participated between 4/2011-9/2016. In July 2015, based on the START study, participants were recommended to initiate ART, including EFV. LEE was defined as grade 2 (2.6 - 5.0), grade 3 (5.1 - 10.0), or grade 4 (> 10.0) x ULN ALT elevation. Cox proportional hazards models (ratio (HR), 95% confidence interval (CI)) were run for each covariate and entered in a multivariable model. Covariates included age, BMI, ALT, prior ALT elevation, HBsAg, ART regimen prior to EFV, CD4, country, EFV initiation date, time from delivery to EFV initiation, receipt of EFV prior to delivery, NRTI in regimen, and AP and PP randomized assignments.

Results: Among 3575 women, 2318 (65%) initiated EFV, 2267 (98%) PP. At EFV initiation median age was 29.2 yrs and median CD4 was 625, 62% were not on ARVs, 3% had prior ALT elevation and HBsAg+ was 4% (82/2318). After EFV, 7.3% (170/2318) and 2.5% (59/2318) had ≥grade 2 and > grade 3 LEE PP, respectively; with an incidence of > 3 LEE of 2.2 (95% CI 1.9-2.5) per 100-person years. Most were asymptomatic. In multivariable analysis, older age but not CD4 or HBsAg, was significantly associated with increased risk of grade 3/4 LEE PP after EFV initiation (HR per 5 years 1.35 CI (1.06-1.71) and per 50 cells higher 1.04 (0.986,1.086)), other covariates p> 0.14. Events occurred between 1-132 wks PP: 2 maternal deaths associated with LEE occurred at 16 and 25 weeks after EFV-ART.

Conclusions: Greater than 7% of PP women initiating EFV had grade 2 or greater LEE. Late-occurring and asymptomatic hepatotoxicity after EFV occurred. The risk of hepatotoxicity underscores the importance of laboratory monitoring for maternal LEE in ART treatment/PMTCT programs.
Abstract 14

Asymptomatic Hematologic Toxicity Associated with Very Early Combination Antiretroviral Therapy (cART) in In Utero HIV-infected Infants

Chadwick E1, Tierney C2, Coletti A3, Cotton M4, Ruel T5, Reding C6, Zimmer B6, Qian M7, Jean-Philippe P8, Hazra R8, Jackson C9, Spector S10, Capparelli E11, Mirochnick M11, Purdue L1, Costello D12, Jennings C13, Luzuriaga K14, Perlowski C15, Bwakura-Dangarembizi M16, Naidoo K16, Persaud D17, Byson Y16, for the IMPAACT P1115 Study Team19

1Northwestern Univ Feinberg School Of Medicine, 2Harvard T.H. Chan School of Public Health, 3FHI 360, 4KID-CRU, Stellenbosch University, 5University of California, San Francisco, 6Frontier Science Technology and Research Foundation, Inc., 7National Institutes of Health/NIAID/DAIDS, 8Eunice Kennedy Shriver National Institute of Child Health and Human Development/NIH, 9Baylor/Texas Children’s Hospital, 10UC San Diego School of Medicine, 11Boston University School of Medicine, 12UCLA, 13Rush Medical College, 14University of Massachusetts Medical School, 15University of Zimbabwe College of Health Sciences, 16Nelson R. Mandela School of Medicine, Univ of KwaZulu-Natal, 17Johns Hopkins University School of Medicine, 18David Geffen School of Medicine, UCLA, 19IMPAACT Network

Background: In the ongoing IMPAACT P1115 study, cART comprised of zidovudine, lamivudine, and nevirapine is initiated within 48 hours of birth to high-risk HIV-exposed neonates. Routine safety monitoring led us to investigate the rate of asymptomatic hematologic toxicity (HT) [low hemoglobin (Hgb) and/or low absolute neutrophil count (ANC)] among in utero exposed and infected infants.

Materials & Methods: Infants enrolled in P1115 are monitored with complete blood count and differential at entry and every 2-4 weeks on study. In utero infection (IN) status (+HIV PCR <48 hours age) is determined by 2 weeks of age. All infants initiate cART within 48 hours of birth, dosed to achieve therapeutic levels; infants identified as uninfected in utero (UN) receive 7-14 days of cART before switching to standard HIV prophylaxis and are followed until 2 weeks of age or until HT is ≤Grade 1 using the 2004 DAIDS toxicity table.

Results: Between 1/23/15 and 2/28/17, 255 infants from 11 countries (9 US, 208 from 7 African countries, 4 Thailand, 23 Brazil, 11 Haiti) were enrolled at a median of 1 day of age (95th%ile 2 days, range 1-9). 236/255 (92%) were born to untreated mothers and 30/255 (12%) were <37 weeks gestation at birth. Thirty (12%) were IN and received cART for a median of 13.9 weeks while 225 (88%) UN received a median of 1.2 weeks of cART. 29/255 (11%) experienced ≥Grade 3 HT assessed as at least possibly related to cART; all infants were clinically asymptomatic. 16/225 (7%) UN and 13/30 (43%) IN experienced HT. Among HT infants, the median time to onset of low Hgb and ANC was 16 (IQR 15-26) and 18 (IQR 15-28) days from birth for UN and for IN, 21 (IQR 18-45) and 40 (18-46) days from birth, respectively. 79% (15/19) of ANC toxicities were in Zimbabwean infants, who comprised 33% (84/255) of enrolled infants. Among 13 IN with ≥Grade 3 HT at least possibly related, substituting abacavir (10) or stavudine (2) for zidovudine led to improvement to ≤Grade 2 Hgb or ANC in a median of 20 and 22 days, respectively. Neonatal sepsis and/or congenital syphilis occurred equally among 5 IN with (3) or without (2) HT. There were no deaths among IN through median of 23 weeks of follow up.

Conclusion: High grade asymptomatic cART related hematologic toxicity is frequent in in utero HIV-infected infants initiated on cART in the first 48 hours of life, exacerbating the normal nadir of Hgb in the first 6 weeks of life. Early switch from zidovudine to abacavir might be a reasonable strategy to avoid HT in early treated infants. Compared with historically high mortality rates of untreated HT in early treated infants, the favorable clinical course seen in very early treated HIV infected infants in P1115 to date supports further study of very early treatment despite high-grade asymptomatic hematologic toxicity.
Abstract 15

The population effect of HIV exposure in HIV-uninfected children on infant mortality in Botswana and South Africa

Slogrove A1,2, Johnson L1, Powis K3,4,5

1Centre for Infectious Disease Epidemiology and Research, University Of Cape Town, 2Department of Paediatrics & Child Health, Stellenbosch University, 3Department of Immunology and Infectious Diseases, Harvard T.H. Chan School of Public Health, 4Department of Internal Medicine and Paediatrics, Massachusetts General Hospital, 5Botswana Harvard AIDS Institute Partnership

Introduction: With declining maternal-child HIV transmission but stagnant HIV prevalence in pregnant women, the population of HIV-exposed uninfected (HEU) infants accounts for >20% of the infant population in Botswana and South Africa. HEU infants are at greater risk for mortality and morbidity than HIV-unexposed (HU) infants, with these trends persisting despite maternal antiretroviral therapy and uptake of safer breastfeeding. We therefore aimed to quantify the population effect of excess HEU infant mortality in Botswana and South Africa.

Methods: Population attributable fractions (PAF) for infant mortality in the first year of life due to HIV-exposure in HIV-uninfected infants were estimated for Botswana and South Africa for the year 2013 using standard formulae and the following assumptions: 1. Prevalence of infant HIV exposure, 26% in Botswana and 23% in South Africa; 2. Rate of perinatal HIV transmission, 3% in both countries; 3. In HEU compared to HU infants, relative risk (RR) for mortality of 1.8 [95% confidence interval (CI) 1.2; 2.8]. To calculate the excess infant deaths due to HIV-exposure per 1000 HIV-uninfected infants, the PAF was applied to the 2013 UNICEF infant mortality rate [lower bound; upper bound] estimates for Botswana (36.4 [22.2; 56.7] per 1000) and South Africa (35.3 [29.1; 42.7] per 1000) after removing the proportion of infant mortality occurring in HIV-infected infants, assumed to be 8% in both countries. Additionally, a South African demographic model was used to estimate the proportion of all South African infant mortality due to excess mortality in HEU infants from 1990-2015 as HIV-exposure prevalence and the proportion of infant deaths due to HIV changed over time.

Results: The PAF [lower bound; upper bound] of infant mortality due to HIV-exposure in HIV-uninfected infants in 2013 was 16.8% [2.5; 31.2] in Botswana and 15.1% [2.2; 28.2] in South Africa. Excess infant deaths due to HIV-exposure were estimated to be 5.6 [0.5; 16.6] per 1000 HIV-uninfected infants in Botswana and 4.9 [0.6; 11.2] per 1000 HIV-uninfected infants in South Africa. According to the South African demographic model, the proportion of all South African infant mortality due to excess mortality in HEU infants increased from 0.4% in 1990 to 13.8% in 2015.

Conclusion: With the high prevalence of infant HIV-exposure in Botswana and South Africa, at a population level the excess mortality in HEU compared to HU infants may account for 15% of all infant mortality in HIV-uninfected children and may be increasing the infant mortality rate by 5 deaths per 1000 infants. At these rates, excess mortality in HEU infants is accounting for a greater proportion of mortality than infant HIV-infection itself. This threatens achievement of optimal health and well-being of HEU infants despite tremendous efforts to avoid HIV-infection in this population and furthermore hampers achievement of Sustainable Development Goal targets for under-5 mortality in high HIV-burden countries. Strategies to identify the HEU child population within national and global child mortality monitoring systems are urgently needed along with prioritization of research aimed at understanding pathways to and mitigators of excess mortality in this population.
Abstract 16

Developmental outcomes of breastfed, HIV-exposed uninfected and breastfed, HIV-unexposed children in the context of universal maternal antiretroviral therapy: a prospective cohort


1University Of Cape Town, 2Department Paediatric Neurodevelopment, University of Cape Town, 3Red Cross War Memorial Children’s Hospital, 4Centre for Infectious Diseases Epidemiology & Research, School of Public Health & Family Medicine, 5ICAP, Columbia University, Mailman School of Public Health, 6College of Physicians and Surgeons, Columbia University

Background: Perinatal exposure to maternal HIV and triple-drug antiretroviral therapy (ART) may impact early childhood development. However, little is known about the developmental outcomes of breastfed, HIV-exposed uninfected children (HEU) born under current recommendations of universal ART, and few studies have included appropriate HIV-unexposed (HU) comparators. We examined developmental outcomes among breastfed HEU and HU children from a peri-urban community in Cape Town, South Africa.

Materials & Methods: HIV-infected (HIV+) women initiating universal, lifelong ART (efavirenz-emtricitabine-tenofovir) under “Option B+” policies, and a comparison group of HIV-uninfected (HIV-) women were enrolled during pregnancy and followed through delivery; breastfeeding mother-infant pairs were then followed for up to 18 months postpartum. Developmental assessments were conducted at 12 months of age with Bayley Scales of Infant Development (BSID-III; age corrected for gestation at delivery) excluding those with HIV-infection, congenital defects, cerebral palsy or born at <28 weeks gestation. BSID-III composite cognitive and motor scores (mean 100, SD 15) were categorized to indicate “some” (<85) and “no” (≥85) delay for logistic regression analysis. Potential third variables included preterm birth (<37 weeks); small-for-gestational-age (SGA, birthweight<10th centile); gender; breastfeeding duration and maternal psychosocial/economic factors including intimate partner violence (IPV) and risky drinking, measured during pregnancy with standardized tools.

Results: Assessments were completed on 505 children (HEU, n=202; HU, n=303), median age 13 months (interquartile range, IQR 12–14). Compared to HIV- women, HIV+ women (pre-ART median CD4 cell count 352 cells/mm3) had lower levels of secondary education (27% vs 48%, p<0.0001) and employment (37% vs 47%, 0.02); were more likely to report risky drinking (16% vs 5%, p<0.0001), IPV (21% vs 8%, p<0.0001) or breastfeed for <9 months (55% vs. 41%, p=0.001). Prevalence of prematurity was similar between HEU and HU (13% vs 9%, p=0.12). Overall, mean(SD) scores of HEU approximated those of HU [cognitive, 101(15.4) vs. 101.1(12.4), p=0.76; motor 98.9(15.8) vs. 98.2(12.1), p=0.59]. However, a larger proportion of HEU demonstrated cognitive delay [10% vs. 5%; odds ratio (OR) 2.19, 95% CI 1.07–4.48] and/or motor delay (9% vs 6%; OR 1.97, 95% CI 0.95–4.10), compared to HU. There was also evidence of interaction between HIV-exposure and prematurity; while both term HEU (OR 2.14, 95%CI 0.95–4.84) and preterm HU (OR 3.15, 95%CI 0.82-12.11) had higher risks for cognitive delay than term HU, preterm HEU were at highest risk (OR 5.76, 95%CI 1.83-18.12). Similar results were observed for motor delay with ORs (vs term HU): 1.48 (95% CI 0.59-3.72); 4.82 (95%CI 1.40-16.6) and 13.25 (95% CI 4.60-38.16) for term HEU, preterm HU and preterm HEU, respectively. Associations persisted after adjusting for maternal age, education, employment, housing, IPV, risky drinking and breastfeeding. In addition, motor delay was associated with IPV (aOR 2.98, 95% CI 1.14–7.77) and informal housing (aOR 2.89, 95% CI 1.21–6.91).

Conclusions: Among breastfed children within the same community, perinatal HIV/ART-exposure was associated with increased risks of cognitive and motor delay. Infants born both preterm and HEU appear to be at particularly high risk for developmental delay, a novel finding which warrants further investigation.
Abstract 17

Inequality in outcomes for adolescents living with perinatally-acquired HIV in sub-Saharan Africa: a Collaborative Initiative for Paediatric HIV Education and Research (CIPHER) cohort collaboration analysis

Slogrove A¹, Yotebieng M². The CIPHER Cohort Collaboration Adolescent Project Team³

¹Centre for Infectious Disease Epidemiology and Research, University Of Cape Town, ²College of Public Health, Ohio State University, ³Collaborative Initiative for Paediatric HIV Education and Research (CIPHER) of the International AIDS Society

Background: Eighty percent of adolescents living with perinatally- and behaviourally-acquired HIV live in sub-Saharan Africa (SSA), a continent with marked economic inequality. Extending our previous global description of adolescents living with perinatally-acquired HIV (APH), this analysis aimed to describe APH outcomes in SSA by country income group (CIG).

Methods: Through the CIPHER cohort collaboration, individual retrospective data from 7 networks and 25 countries representing SSA were included. APH were included if they entered care at age <10 years (as a proxy for perinatally-acquired HIV), and had follow-up at age >10 years. World Bank CIG classification for median year of first visit was used. Cumulative incidence functions were calculated by competing risks analysis for mortality, transfer-out and loss-to-follow-up. Mortality was compared across CIG by Cox proportional hazards models with multiple imputation for missing values.

Results: 30,296 APH were included, 50.9% were female; 75.7% resident in low income countries (LIC), 4.6% in lower-middle income countries (LMIC) and 19.8% in upper-middle income countries (UMIC). 19,352 (64%) were born ≥2000. In UMIC 9/11 (82%) cohorts were ART treatment-only cohorts compared to 12/40 (30%) in LIC and 1/5 (20%) in LMIC. Median [interquartile range (IQR)] age at antiretroviral therapy (ART) start was 8.1 [6.3; 9.5], 7.8 [6.2; 9.3] and 7.3 [5.2; 8.9] years in LIC, LMIC and UMIC respectively. Median age at last follow-up was 12.1 [10.9; 13.8] years, with no difference between CIG. Amongst APH starting ART, a greater proportion started at age >10 years in LIC (14.3%) compared to LMIC (11.7%) and UMIC (6.6%). Individual CD4 count improved between ART start and last visit in all CIG; the largest median (95% CI) change occurred in LMIC (463 [440; 486] cells/µl) compared to LIC (295 [286; 303] cells/µl) and UMIC (353 [338; 367] cells/µl). Median height-for-age z-score (HAZ) at ART start was <2 in all CIG and improved by last visit in LIC (mean (95% CI) HAZ-change 0.16 (0.14; 0.18)) and LMIC (0.44 (0.40; 0.49)) but not LMIC (0.04 (-0.10; 0.02)). Cumulative incidence (95% CI) for mortality between age 10-15 years was lowest in UMIC (1.1% (0.8; 1.4)) compared to LIC (3.5% (3.1; 3.8)) and LMIC (3.9% (2.7; 5.4)). Loss-to-follow-up was highest in UMIC (14.0% (12.9; 15.3)) compared to LIC (13.1% (12.4; 13.8)) and LMIC (8.3% (6.3; 10.6)). Adjusted for gender, birth cohort, ever on ART and baseline characteristics (first visit age, CD4, HAZ), the adjusted hazard ratios (95% CI) for mortality in APH in LIC and LMIC in reference to UMIC were 2.50 (1.85; 3.37) and 2.96 (1.90; 4.61) respectively. There was little change in relative mortality hazards when restricted only to APH who ever received ART (adjusted hazard ratio (95% CI) LIC: 2.67 (1.94; 3.67); LMIC: 3.07 (95% CI 1.91; 4.95))

Conclusion: Despite starting ART later in childhood, improvements in CD4 count and height were observed in the majority of APH surviving to adolescence. Mortality rates are likely under-estimated. However, results highlight probable inequality in mortality and access to ART according to CIG in SSA.
Abstract 18

Attrition and treatment outcomes among perinatally and behaviourally HIV-infected adolescents and youths in Thai National AIDS program

Teeraananchai S1,2, Puthanakit T1,3,4, Chaivoot S5, Kiertiburanakul S6, Chokephaibulkit K7, Kerr S1,2, Bhakeechoep S8, Teeraratkul A4, Law M9, Ruxungham K1,3

1HIV-NAT Research Collaboration, 2Kirby InstituteUniversity of New South Wales, 3Department of Pediatrics, Faculty of Medicine, Chulalongkorn University, 4Research Unit in Pediatric Infectious Diseases and Vaccines, Chulalongkorn University, 5The HIV/AIDS, Tuberculosis and Infectious Diseases Program, National Health Security Office (NHSCO), 6Department of Medicine, Faculty of Medicine Ramathibodi Hospital, Mahidol University, 7Department of Pediatrics, Faculty of Medicine Siriraj Hospital, Mahidol University, 8Thailand MOPH - U.S. CDC Collaboration, 9Department of Medicine, Faculty of Medicine, Chulalongkorn University

Background: Successful prevention of mother-to-child transmission (PMTCT) programs has reduced the number of children infected with HIV. Many of those who were perinatally-infected during the early epidemic in Thailand are now adolescents, but youth aged 15-19 years infected by behavioural transmission currently account for a large number of new infections. HIV-infected adolescent and youth by any transmission routes are at risk of poor treatment outcomes due to adherence and psychosocial factors. This study aimed to describe attrition and treatment failure among behaviourally HIV-infected youths (BIY) and perinatally HIV-infected young adolescents (PIY) who initiated antiretroviral treatment (ART) in the National AIDS program (NAP).

Materials & Methods: We studied HIV-infected youth aged 10-24 years who initiated ART from 2008-2013 through the NAP. This was done using the National Health Security Office (NHSCO) database by linkage with the National Death Registry. Attrition outcomes analysed using Cox regression were mortality and LTFU after ART initiation. LTFU was defined as not having of two consecutive CD4 testing or not active in care ≥ 12 months, irrespective of whether or not patients later returned. Logistic regression was used to assess predictors of treatment failure, a composite endpoint of viral load ≥ 1,000 copies/mL (VF) or a regimen major class switch (NNRTI to PI or PI to NNRTI) and/or death/LTFU for those who did not have viral load (VL) measurements, one year after ART initiation. We assessed youth initiating ART: BIY aged 15-19 years (BIY1) and BIY aged 20-24 (BIY2) were compared against PIY aged 10-14 years as a reference group.

Results: Of 11,954 patients, 9,909 (83%) were BIY. A higher proportion of BIY were female (54% vs 58%; P=<0.001), and median interquartile range (IQR) at ART initiation was higher (190 (53-330) vs 154 (39-307) cells/mm3; P=0.001). Mortality rates were not significantly different among PIY (2.54, 95%Confidence interval (CI) 2.22-2.92 per 100 person-year (PY)), BIY1(3.12 (95%CI 2.74-3.56/100PY)) and BIY2 (2.91, 95%CI 2.66-3.17/100PY; P = 0.46). Compared to PIY with a crude LTFU rate of 2.89 (95%CI 2.54 – 3.29/100PY; P=<0.001), LTFU was significantly higher in BIY1 (13.87 (95%CI 12.98-14.82/100PY) and BIY2 9.49 (95%CI 9.02-9.99/100PY)). This increased risk of LTFU in BIY (adjusted hazard ratio (aHR) 2.91 (95%CI 2.49-3.40) BIY1 and aHR 2.67 (95%CI 2.30-3.10) BIY2; P=<0.001) was also evident in a multivariate Cox model adjusting for sex, calendar year of ART initiation, first regimen, baseline CD4 and region. We also found that after adjusting for sex, year of ART initiation, first regimen, baseline CD4 and region, the odds of treatment failure one year after initiating ART were significantly higher in BIY1 (adjusted odd ratio (aOR) 1.45 , 95%CI 1.26-1.66) and BIY2 (1.22, 95%CI 1.08-1.38; P=<0.001) compared to PIY.

Conclusions: BIY aged 15-19 years and 20-24 years had comparable mortality, but a higher risk of treatment failure and higher LTFU rates compared to PIY. BIY, with higher median CD4 counts at ART initiation were more likely to be LTFU and this would potentially lead to HIV transmission. The Thai NAP should target interventions to adolescents to improve treatment outcomes.
Abstract 19

**What constitutes adolescent-friendly health services? Clinic characteristics that attenuate internalised HIV stigma among adolescents living with HIV**

**Pantelic M.**, Cluver L.1,2

1University Of Oxford, 2University of Cape Town

**Background:** Southern Africa is home to 2 million adolescents living with HIV. These youth are dying at alarming rates, as healthcare providers struggle to retain them in care. The World Health Organisation recommends ‘adolescent-friendly health services’ for governments to better meet the specialised needs of this high-risk population. However little is known about what specific health services matter for adolescents living with HIV. Qualitative data suggest that barriers to treatment access and adverse interactions with healthcare providers evoke a profound fear of judgement and HIV-related shame among adolescents. This study quantitatively tested associations between hypothesised ‘adolescent-friendly’ clinic indicators and internalized HIV stigma among adolescents living with HIV.

**Materials and Methods:** Total population sampling of HIV-positive adolescents (aged 10-19) who had ever initiated anti-retroviral treatment in 53 public health facilities in the Eastern Cape, South Africa was used. 90.1% of eligible HIV-positive adolescents were interviewed (n=1060, 55% female, mean age = 13.8, 21% living in rural locations and 67% perinatally infected). Internalized HIV stigma was measured via the adolescents living with HIV stigma scale (ALHIV-SS). Potential adolescent-friendly clinic indicators were: 1) accessibility: medication stock outs, travel costs and time, missing school and clinic area safety; and 2) clinic experiences: staff availability, attitude and knowledge, waiting time, and data confidentiality. Analyses were conducted in 3 stages using Stata 14. First, interviewed participants and those who were not interviewed were compared on known socio-demographic characteristics (age, gender and urban/rural household location). Second, we tested associations between each hypothesised adolescent-friendly clinic indicator and internalized HIV stigma. Hosmer and Lemeshow’s sequential approach was followed: the first model included all potential covariates and adolescent friendly clinic indicators; the second model retained covariates and clinic factors significant at p < .1; and the final model included only covariates and clinic factors significant at p < .05. Third, a marginal effects model tested for additive effects of combined adolescent friendly clinic characteristics.

**Results:** No differences were observed between adolescents who were interviewed and those who were not. Prevalence of internalized HIV stigma was 26.5%. Three key ‘adolescent-friendly’ characteristics emerged. Adolescents who went to well-stocked clinics (AOR=.392, 95%CI: .226, .680); who didn’t miss school excessively for clinic appointments (AOR=.638, 95%CI: .472, .862); and who didn’t get scolded by healthcare providers (AOR=.534, 95%CI: .378, .755) had significantly lower odds of internalizing HIV stigma. The marginal effects model suggested strong additive effects between these three factors. Adolescents going to clinics with none of these three ‘adolescent-friendly’ characteristics were more than three times as likely to experience internalized HIV stigma than adolescents going to ‘adolescent-friendly’ clinics (60.8% compared to 17.6%). No other significant associations were found.

**Conclusions:** Findings suggest that positive healthcare experiences can act as a buffer against HIV-related shame among adolescents living with HIV. In particular, clinics that are well stocked, offer appointments outside of school hours and have supportive staff are most likely to be accepted by HIV-positive adolescents. Importantly, these findings highlight the potential of health systems approaches to stigma reduction among HIV-positive adolescents.
Abstract 20

Experiences of transition to adult care and readiness to self-manage care in young people with perinatal HIV in England

Le Prevost M1, Thompson L1, Foster C2, Rowson K1, Sturgeon K1, Brice S1, Gibb D1, Judd A1, on behalf of the Adolescents and Adults Living with Perinatal HIV (AALPHI) Steering Committee

1University College London, 2Imperial College Healthcare NHS Trust

Background: There are few data on young people's own experiences of transition from paediatric to adult care or readiness to self-manage care. We describe transition experiences in the AALPHI cohort of young people with perinatal HIV in England.

Methods: 120 young people with perinatal HIV aged 13-21 years were asked about transition experiences, including their rating of adult care compared to paediatric care, and their readiness to self-manage their HIV care, during AALPHI interviews in 2016-7. A minority with significant cognitive impairment, who were carer-dependent, were not included, and those who were included were broadly representative of the wider UK perinatal HIV cohort. Descriptive statistics summarised data, and chi2 tests compared proportions.

Results: Of 38 (32%) in paediatric care (median age 16 years [IQR 16,17]), 34 (89%) reported that transition discussions had begun, at median age 15 years [15,16]. Of 82 in adult care (median age 20 years [18,22]), 58 (71%) reported direct transfer from the paediatric to adult clinic (at median age 17 years [16,18]), and 19 (23%) shared care transfer (at median age 16 years [15,17]) (6% missing transfer type) with a median of three [2,4] shared paediatric/adult appointments. 19% moved hospital when transitioning to adult care; 85% (70/82) went to a designated young adult service. The majority rated adult care as better or no different to paediatric care for services and support offered, with only 12% rating the adult clinic environment as worse than paediatrics, and likewise 10% for the times of adult clinics, 10% flexibility of appointment times, 9% for responsibility the participant had, 9% how well the service met their needs, 8% for advice about educational needs, 8% support given, 6% for understanding of YPs' needs and 5% for the staff members. Those in adult care were more likely than those in paediatric care to report self-management for appointments (82% vs 47% respectively, p=0.001), making their own travel arrangements to clinic (93% vs 63%, p<0.001), and informing the clinic when an ART prescription was need (93% vs 62%, p<0.001). However knowledge of ART was similar, with half or less in each group being able to name their ART drugs (49% vs 38%, p=0.374), or know their most recent CD4 and viral load values (40% vs 37%, p=0.680), and around 65% in each group being able to name possible side effects of their ART. A high proportion in each group knew how many pills they took each day (98% vs 92%, p=0.130) and 95% in both groups could tell their doctor how their health had been. There was no association between knowing how many pills taken or naming ART drugs and 3 day adherence.

Conclusions: Transition discussions occurred prior to transfer to adult care, following good practice guidelines. The proportion reporting direct transfer was higher than expected given recommendation for a period of shared care across transition. Adult care was considered better than paediatric care by many patients, although further education around ART and its potential side effects, CD4 and viral load knowledge is required.
9th International Workshop on HIV Pediatrics

21 – 22 July 2017, Paris, France

Abstracts

Poster Presentations
Abstract 21

Setting global research priorities in paediatric & adolescent HIV: testing, treatment, service delivery, care and support

Vicari M, Armstrong A, Irvine C, Schaaf D, Penazzato M

1International Aids Society, 2Independent Consultant, 3HIV Department, World Health Organization

Background: Accelerated action is required to reach super-fast track targets endorsed by the global community. However, evidence gaps on how to best diagnose and treat children and adolescents living with HIV persist. Diminishing resources for future clinical and operational research require targeted efforts to maximize impact. To support this, a global research prioritization exercise was undertaken by WHO and CIPHER.

Materials & Methods: The Child Health and Nutrition Research Initiative (CHNRI) methodology, a well-established approach for setting health research priorities, was adapted and used. Five phases were carried out in parallel for children and adolescents: 1. an expert working group was established to better define the scope of the exercise; 2. an online survey to collect research questions was disseminated using snowballing and targeted dissemination to reach a broad range of stakeholders; 3. thematic coding and analysis of questions submitted was undertaken; 4. respondents were invited to score the collated lists of research questions against pre-defined criteria (answerability, impact, implementation, and equity); 5. the outcome of the CHNRI process was then reviewed by an expert group charged to identify 5 priority themes among the top 10 ranked questions in each topic area (testing, treatment, and service delivery). This was considered in the context of existing policies, systematic reviews, recently published research, and planned and ongoing research.

Results: Over 1,500 research questions were submitted by 375 individuals (36% researchers) from 71 countries across all WHO regions (51% from the African region). Collation and analysis of these produced an overall list of 52 and 62 questions (12-32 questions per topic), for children and adolescents respectively. These were then scored by 48% of respondents who contributed to the final prioritization according the CHNRI methodology. The final 5 themes identified in each area by the end of the exercise address the following. Testing: strategies and interventions to improve access, uptake and linkage to care and factors that affect success, with novel diagnostic tools and entry points beyond ANC highlighted for children; consent, self-testing and safe, acceptable strategies for key populations were highlighted for adolescents; Treatment: strategies and interventions to improve adherence, short- and long term outcomes as well as prevention and management of co-infections were prioritized for both populations; optimal drugs and formulations and early treatment were highlighted for children while novel drug delivery systems and optimal ART sequencing were included for adolescents. Service delivery: strategies or interventions to improve access, uptake and retention in care, including psychosocial and family support, were prioritized for both populations. Approaches to HIV disclosure and reduction of stigma and discrimination were prioritized for children while improving sexual and reproductive health outcomes were highlighted for adolescents.

Conclusions: This is the largest CHNRI exercise ever undertaken in HIV, reaching a very broad set of stakeholders globally. The results of this process provide guidance to researchers and donors, given the current need and research landscape, with the aim of focusing future research in paediatric and adolescent HIV on questions with the highest impact for clinical, policy and programmatic decision making.
Abstract 22

Implementation of a health information system to improve uptake of HIV early infant diagnosis (EID) in HIV-exposed infants and birth Hepatitis immunization coverage in HBV-exposed infants in Abidjan, Cote d'Ivoire: the DEPISTNEO project

Desmonde S1, Amorissani-Folquet M2, Amani-Bossé C1, Lennaud S1, Karcher S1, Lohoues-Kouacou M1, Bengali M1, Inwoley A3, Ahoba I3, Leroy V1

1Inserm U1027, 2PACCI programme, 3Department of Pediatrics, University Hospital of Cocody, *MEREVA, Inserm UMR 1219, University of Bordeaux, 4Department of Hepatology, University Hospital of Cocody, 6Center for Diagnostics and Research on HIV and other infectious diseases (CeDReS), 7National AIDS&STD Control Program

Introduction: Early infant diagnosis (EID) coverage is insufficient in Abidjan, partially due to poor linkage between birth and 6-week EID. We implemented a novel routine screening strategy that combines rapid diagnostic testing for both maternal HIV and HBV exposure in newborns at time of birth linked to a computer-based health information system (HIS) that tracks from birth HIV/HBV-exposed mother-infant pairs through the continuum of postnatal care in Abidjan, Côte d'Ivoire.

Methods: All mother-infant pairs who give maternal consent in the five participating maternity clinics are included. At birth, all mothers are HIV-tested and those infected who are unaware of their HIV-status are offered a second opportunity to be enrolled in HIV-care. All those HIV-infected receive PMTCT. Additionally, rapid HBV-testing is offered; HBs-Ag-exposed newborns receive immunization at birth. All livebirths are recorded in the HIS; HIV-exposed and HBV-exposed infants are tracked through the continuum of care. Each step of the EID and immunization cascades (6-10-14 Weeks) is recorded in the HIS. Weekly reports alert social workers who trace families in case of a missed visit to re-schedule. HIV-exposed infants are followed-up until definite diagnosis after breastfeeding cessation.

Results: Between 08/2016-04/2017, 6,572 mothers gave birth. Acceptability of maternal HBV testing reached 95.2%. HBV prevalence was 6.8% (95% Confidence Interval (95%CI): 6.2%-7.4%). Among the 434 HBV-exposed children, 419 (96.5%) were immunized at birth. Maternal HIV testing coverage at time of birth was 99%; maternal HIV prevalence was 3.9% (95%CI: 3.5%-4.4%). Of those HIV-infected, 62.4% were already on combined ART. Among the 237 HIV-exposed live-born infants, 172 had reached follow-up >6 weeks at database closeout date: 58.1% (95%CI: 50.8%-65.5%) had a DBS for virological testing by 6 weeks. After HIS alerts, 6-week virological testing coverage reached 61.6% (95%CI: 54.4%-68.9%). Among the 106 children HIV-tested, further follow-up was available for 92 children (86.8%): 34 DBS (32%) results were returned to the clinics after a median time of 50 days since testing (interquartile range (IQR): 35-70), of which 32 (94%) were subsequently returned to families after a median time of 2 days (IQR: 1-13). Among the 34 infants with available results, three came back positive yielding to a 6-week incidence rate of HIV among HIV-exposed infants of 8.8% (95%CI: 0-18.3%). All three were initiated on ART after a median time of 21 days since result-return to the clinic but on the day the result was communicated to the family. Among the 643 children exposed to HIV (+/HBV), 462 (71.9%) had at 6-week follow-up. The 6-week immunization coverage was estimated 64.5% (95%CI:60.1%-68.8%). After HIS alert this reached 69.7% (95%CI: 65.5%-73.9%). Among those HIV-exposed, 6-week immunization coverage was estimated 61.6% (95%CI:54.4%-68.9%) and reached 65.1% (95%CI: 62.1%-64.0%) after HIS alerts.

Conclusion: Maternal HIV and HBV rapid diagnostic testing at birth is both feasible and acceptable. HBV immunization coverage at birth was high while the 6-week immunization coverage among HBV or HIV-exposed infants remained insufficient. EID uptake was 58% and improved by the HIS compared to 2015 Ivorian national reports. However, result turnaround time remains high and efforts remain...
Abstract 23

The clinical impact and cost-effectiveness of incorporating point-of-care (POC) assays into early infant HIV diagnosis (EID) programs at 6 weeks of age in Zimbabwe: A model-based analysis

Frank S1,2, Cohn J3,4, Dunning L5, Sacks E6, Walensky R1,2,7, Mukherjee S6, Turunga E3, Freedberg K1,2,7, Ciaranello A1,2

1Massachusetts General Hospital, Medical Practice Evaluation Center, 2Massachusetts General Hospital, Division of General Internal Medicine, 3Elizabeth Glaser Pediatric AIDS Foundation, 4University of Pennsylvania, Division of Infectious Disease, 5University of Cape Town, Division of Epidemiology and Biostatistics, School of Public Health & Family Medicine, 6Elizabeth Glaser Pediatric AIDS Foundation, 7Massachusetts General Hospital, Division of Infectious Disease

Background: Many EID programs use laboratory-based total nucleic acid (conventional) assays. New POC EID assays are costlier, but may increase access to testing and shorten time to result-return and ART initiation.

Materials & Methods: We used the CEPAC-Pediatric model to examine the clinical benefits, costs, and cost-effectiveness of using POC EID assays at 6 weeks of age in Zimbabwe. We simulated two EID strategies: conventional and POC. Positive results led to ART initiation; ART was stopped if a confirmatory assay of the same type and a third conventional assay (all sent pre-ART) were negative. Modeled assays differed in sensitivity (conventional: 100%; POC: 96.9%), specificity (conventional: 98.8%; POC: 100%), time and probability of result-return (conventional: 1-month delay, 71%; POC: immediate, 97%), and cost (conventional: $15; POC: $21). Model outcomes included monthly survival, life expectancy (LE), and average lifetime per-person cost, reported separately for 1) HIV-infected infants and 2) all HIV-exposed infants. The second cohort of all HIV-exposed infants included both HIV-infected and HIV-uninfected infants. We calculated incremental cost-effectiveness ratios (ICERs) using discounted (3%/year) costs and LE for all HIV-exposed infants, defining ICERS ≤$930/life-year saved (Zimbabwe per-capita GDP) as cost-effective.

Results: With conventional EID, projected undiscounted LE was 24.95y (HIV-infected infants) and 60.16y (all HIV-exposed infants), at a lifetime cost of $1,050/HIV-exposed infant. POC EID improved projected undiscounted LE (HIV-infected: 26.58y, HIV-exposed: 60.27y) at $1,120/infant, and increased survival by 4.5% in months 1-2 of life. The ICER of POC vs. conventional was $730/life-year saved (LYS). Holding conventional EID characteristics constant, this ICER remained <$930/LYS if POC assay specificity was >95% or POC assay sensitivity was >85%. Large improvements in conventional assay result-return were needed to offset the slightly lower sensitivity of the POC assay. Even if conventional assay result-return probability improves to 80%, POC assays with sensitivity >90% will remain cost-effective. If conventional assay result-return probability further improves to 90%, POC assays with sensitivity >96% will remain cost-effective. Results were robust to plausible variations in assay cost, probability of linkage to ART, and probability of POC result-return.

Conclusions: POC assays for HIV-exposed infants improve survival and life expectancy and are cost-effective compared to conventional assays. EID programs in Zimbabwe should replace conventional testing with POC assays.
Abstract 24

A Quality Improvement Collaborative (QIC) to improve HIV Exposed Infant (HEI) Early Infant Diagnosis (EID) testing at 17 health facilities in Center and Littoral Regions in Cameroon

Dougherty G1, Abena T2, Abesselo J2, Bilo R2, Biyaga T3, Ebogo M2, Jed S2, Kakanou Z2, Mayer M5, Madevu-Matson C1, Nitsana N2, Tsioria F1, Walker L1, Rabkin M1

1ICAP at Columbia University, 2ICAP Cameroon, 3Ministry of Health, 4U.S. Health Resources and Services Administration, 5Centers for Disease Control and Prevention Cameroon

Background: Cameroon’s EID coverage is suboptimal and DNA PCR testing turnaround times (TAT) are much longer than the national standard of 2 to 4 weeks. Timely HEI EID is necessary to identify and treat HIV-infected infants, and expanding pediatric ART initiation services is a MoH Cameroon national priority. Despite roll out of national policies, guidelines and training, EID implementation has not been consistently implemented with facilities experiencing frequent process and system breakdowns, significant referral lab delays, staffing shortages and poor documentation of services leading to preventable infant mortality.

Materials and Methods: In October 2016, ICAP in partnership with MoH Cameroon, HRSA and CDC Cameroon, designed and implemented a QIC to catalyze improvements in EID testing and reduce testing TAT at 17 health facilities in Center and Littoral Regions, two high-HIV prevalence regions. Each QIC facility team had two aims: (1) to improve EID testing from baseline to > 50% of HEI tested with results shared with caregiver within 12 months of sample collection (testing coverage), and (2) to reduce the average time of test to results shared with the caregiver to under 6 weeks (42 days) (TAT reduction). Following site selection, aim statement development, and indicator selection, each facility established a QI team. ICAP provided baseline training to 53 HCW’s on QI methods and tools, and conducted monthly supportive supervision visits. Each QI team worked to: identify contextually appropriate interventions conduct rapid iterative tests of change using plan-do-study-act (PDSA) cycles; collect monthly aggregate data using District Health Information System (DHIS2); and analyze progress using standardized run charts. ICAP convened 3 quarterly meetings where teams compared progress and experiences, and a final “harvest” meeting to synthesize lessons learned and identify effective interventions.

Results: QI teams tested 118 interventions over 12 months including: improvements in staff and client education, staffing patterns, workflow, commodity management, documentation, test kit management, and referrals. At baseline only 14% of HEI were tested and had results shared with caregiver and an average of 100 days from the time of testing to results being shared with the caregiver. After 12 months of the QIC intervention HEI testing coverage rose to 77% and average TAT reduced to 42 days in Jan 2017. Overall, the second aim was reached during the project’s last 4 months with an average TAT of 38 days. Sixteen out of the 17 facility teams reached testing coverage > 50% and on average it took 2.6 months to achieve. All 17 teams succeeded in reaching TAT ≤ 42 days.

Conclusions: Bridging the stubborn “know-do gap” is one of the greatest challenges facing HIV programs. QIC methodology improved HEI EID services (what we know works) by helping facilities to generate local innovations to ensure that EID is put into practice consistently (what we do). In addition to building QI capacity and improving targeted outcomes, the EID QIC resulted in a “change package” of successful initiatives tested by facility QI teams that will be widely disseminated within Cameroon.
Abstract 25

Implementation of point-of-care (POC) HIV viral load (VL) monitoring during antenatal care at a primary care clinic in Cape Town, South Africa

Dunning L1,2, Ndlovu L1,2, Hsiao N3, Myer L1,2

1University of Cape Town, Division of Epidemiology & Biostatistics, 2University of Cape Town, Centre for Infectious Diseases Epidemiology & Research, 3National Health Laboratory Services & University of Cape Town, Division of Medical Virology

Background: POC VL testing could increase access to virologic monitoring and help improve viral suppression on antiretroviral therapy (ART). However, limited data is available on the use of POC VL monitoring during pregnancy, the acceptability of the device to patients and what implementation challenges may exist in field settings.

Methods: We conducted an implementation science study using the Alere q POC device (input 25µL whole blood; results available in approximately 55 minutes) at a large public sector primary care facility. POC VL testing was conducted for pregnant women initiating ART or requiring routine VL monitoring. As part of the implementation, possible benefits of receiving a POC result were explained to patients; POC results were returned if patients chose to wait. Analysis examined performance of POC using whole blood samples by comparing it to laboratory-based plasma testing, the rate of errors and successful result-return, acceptability to patients and impact of POC VL monitoring on patients' HIV knowledge (determined using a standardized 8-item scale).

Results: Overall 356 tests were completed between January-November 2016. POC tests were completed as a baseline assessment of VL for 103 women initiating ART and in addition to laboratory-based testing for 253 women undergoing a routine VL. Correlation between POC and laboratory-based testing was r=0.51 but improved at high levels of VL ≥10,000 copies/ml (r=0.89). Error results were displayed for 5% of tests (n=18) and 3 machine breakdowns occurred meaning 43 eligible participants did not receive a POC test. POC results were returned to 78% of women; rates of result return did not vary by age, VL result, time on ART, education, mode of transport, gravidity or time of diagnosis. HIV knowledge improved for 62% of women who received a baseline POC (mean score 5.4 vs 6.1, p=0.005) and was significantly higher at time of VL testing than those who did not receive a baseline POC test (mean score; 5.6 p=0.007)

Conclusions: POC VL monitoring appears feasible in a busy primary care, resource limited setting. Most women who received a POC test waited for their result, allowing healthcare providers to act immediately during a high-risk window for mother-to-child transmission of HIV. POC VL testing during pregnancy has potential to improve adherence but further research is required to facilitate the adoption of this technology in low-resource settings.

Abstract 26

Expanding Access to Early Infant Diagnosis through Integration with Immunization Services in Rwenzori region, Uganda

Bitimwine H1, Musiime F1, Ajuna P1, Lutaaya A1, Kekitiinwa A1

1Baylor College of Medicine Children's Foundation-Uganda

Background: Although HIV exposed infants are supposed to receive DPT1 immunization and first HIV DNA PCR test at 6 weeks of age, in Uganda DPT1 coverage is much higher than EID coverage at 2 months (99% and 35% respectively). The high DPT1 coverage presents an opportunity to improve EID coverage at 2 months through integration of immunization and EID services. We determined whether integrating early infant diagnosis into immunization services would increase EID coverage at 2 months in seven districts of Rwenzori region in Uganda.
Method: Our intervention had two components: 1) Between July-December 2016, we conducted a 2 day site-based training of immunization service providers at 83 health facilities on pro-active identification and referral of HIV exposed infants. The trainings were followed with a one- day mentorship visits to the site within 14 days after training. 2) After October 2016, we rolled out the use of ‘appointment’ stickers alongside the trainings and mentorships. The stickers were placed on the child health card or mother’s passport for every infant less than 18 months at immunization service point. The purpose of the sticker was to prompt health workers to determine HIV exposure status of the infants at the immunization service point and to alert health workers on infants whose HIV exposure status had been already determined. The sticker had a caregiver and health worker section. The caregiver section contained the date of next appointment and location where (i.e. immunization point for unexposed infants or mother-baby care point for HIV exposed infants) the child should receive a service at the next visit. While the health worker section had a request to determine the infant’s HIV exposure status and the date the exposure status was determined.

We abstracted consolidated data from the District Health Information system and summarized the EID coverage at 2 months for the period in quarter before the intervention (April-June 2016) and after the intervention (July- October 2016, October-December 2016 and January-March 2017) in the four districts. EID coverage at 2 months obtained was compared for the period before and after the intervention in the four districts using ANOVA. For the three districts, EID coverage at 2 months for the period in quarter before the intervention (October-December 2016) and after the intervention (January-March 2017) were compared.

Results: Following the interventions to integrate EID & immunization, the EID coverage at 2 months steadily increased over a nine months period in the four districts from 31% to 48% with a statistically significant in the second and third quarter after the intervention. We also observed a near twofold increase in EID uptake from 29% to 42% over one quarter (p < 0.05) following later scale up of the EID/Immunization integration interventions to the rest of the three districts.

Conclusion: Integration of EID into immunization services following capacity building for immunization workers and HTS providers at immunization service points and the use of ‘appointment’ stickers enhanced EID coverage at 2 months in Rwenzori region, Uganda.

Abstract 27

Financial incentives to increase pediatric HIV testing in Kenya: A pilot randomized trial

Niuguna F1,2, Wagner A2, Neary J3, Bosire R1, Babigumira J1, Levin C2, Maleche-Obirimo E3, Wamalwa D1, John-Stewart G2, Slyker J3

1Kenyataa National Hospital, 2Department of Epidemiology, University of Washington, 3Department of Global Health, University of Washington, 4Centre for Public Health Research, Kenya Medical Research Institute, 5Department of Pediatrics and Child Health, University of Nairobi, 6Departments of Epidemiology, Global Health, Medicine & Pediatrics, University of Washington

Background: Starting antiretroviral therapy (ART) prior to onset of symptomatic disease improves survival, neuro-development, and reduces risk of opportunistic infections in HIV-infected children. However, pediatric HIV diagnosis is often delayed due to parental reluctance to test and financial barriers. Systematically offering pediatric testing to HIV-infected parents typically results in low uptake, suggesting the need for additional interventions. We conducted a pilot study to assess acceptability and feasibility of financial incentives to increase pediatric testing, and to identify the optimal range of incentive values in preparation for a larger randomized trial.

Materials and Methods: Between September-December 2016, we recruited female HIV-infected caregivers at Kisumu County Hospital, Kenya, who had children of unknown HIV status aged 0-12 years, and randomized them to receive $5, $10 or, $15 conditional on completing child testing within 2 months. We attempted to screen every female adult receiving care at the site. To determine the optimal incentive range for an efficacy trial, we compared proportion who completed child
testing between study arms, and additionally assessed preferences for incentive format (cash, goods, services).

Results: Of 1,991 female caregivers screened, 71 (4%) had children of unknown status age 0-12 years, 1,250 (63%) had tested all their children, 506 (25%) had children of unknown status but aged >12, 163 (8%) had no children, and 1 caregiver declined to give information. Of 71 eligible, 60 (85%) were randomized with equal allocation between arms. The most common reason for non-randomization was not being the primary caregiver (10%). Forty-four caregivers (73%) tested children in the 2-month window; 15 (75%), 14 (70%) and 15 (75%) in the $5, $10, $15 arms, respectively. There was no difference in testing rates across arms (p>0.99). Overall uptake was substantially and significantly higher than in a recent cohort at the same location with similar procedures but no financial incentive (72% vs. 14%, p<0.001).

A total of 55 children were tested, with median age of 9 years (IQR 5, 11), and 1 (1.8%) was HIV positive. Median time to testing was 6 (IQR: 1, 20) days and did not differ between arms (p=0.97). Financial incentives were highly-motivating; 35 (81%) said the incentive motivated them to test or to test earlier. Thirteen (30%) perceived their children were HIV positive before testing, but all of these tested negative. Eighteen (42%) caregivers previously avoided seeking care for their children during minor illnesses for fear of HIV testing, and 27 (61%) reported they were more likely to seek care after learning the child’s status.

Most people found cash acceptable (36%), some would have preferred household and agricultural goods (23%), health services or food vouchers (9%) and 30% had no specific preferences. Almost half of the incentives (45%) were delivered by mobile phone money transfer.

Conclusion: Cash incentives were acceptable, and motivated pediatric HIV testing. The similarity between testing rates in the 3 arms warrants evaluation of lower incentive values; a larger efficacy trial with incentive values of $0, $1.25, $2.50, $5, and $10 began in January 2017 and will enroll 800 caregivers.

Abstract 28


Okoko N1, Mocello A2, Kadima J1, Lewis Kulzer J2, Nyanaro G1, Blat C2, Guze M2, Bukusi E1, Cohen C2, Abuogi L3, Shade S2

1Kenya Medical Research Institute (KEMRI); Family AIDS Care and Education Services (FACES), 2Department of Obstetrics, Gynecology and Reproductive Sciences, University of California, San Francisco, CA, USA, 3Department of Pediatrics, University of Colorado, Aurora, CO, USA

Introduction: Despite declining new infections, pediatric HIV remains significant, with 150,000 new infections annually and 1.8 million children (<15 years old) living with HIV globally. We examined whether activities under the Accelerating Children’s HIV/AIDS Treatment (ACT) initiative increased testing and identification of children with HIV.

Methods: Family AIDS Care and Education Services (FACES) implemented activities under the ACT initiative in 144 health facilities in western Kenya between October 2015 and September 2016. Interventions targeting pediatric testing included: provision of HIV-testing counselors; renovation/allocation of space for HIV testing and counseling (HTC space); use of a Family Information Table (FIT) and FIT chart audits; community outreach testing; and text message reminders for HIV-exposed infants. We compared the number of children tested monthly and the number of HIV-positive children between intervention and control sites using negative binomial generalized estimating equations. Analyses adjusted for repeated measures, geographic location, health facility tier, and test kit stock-outs.

Results: Mean number of children tested monthly increased across all age groups: from 2.8 to 7.2 (p<.0001) in infants <18 months; from 44.8 to 142.0 (p<.0001) in children 18 months to 9 years; and from 30.1 to 123.3 (p<.0001) in adolescents 10-14 years.
Identification of HIV-positive children increased: 0.06 to 0.37 (per month per facility; p<.0001) in infants; 0.34 to 0.62 (p=.002) in children; and 0.17 to 0.26 (p=.03) in adolescents. Use of the FIT was significantly associated with increased HIV testing in infants, incidence rate ratio (IRR)=2.89 (95% confidence interval [CI]=1.53,5.49; p<0.001) and identification of HIV-positive infants, IRR=8.71 (95% CI=1.45,52.4; p<0.02). Among children, FIT chart audits were significantly associated with increased testing, IRR=2.15 (95% CI=1.36,3.40; p<0.001). Among adolescents, HTC space was significantly associated with increased HIV testing, IRR=1.45 (95% CI=1.09,1.93; p<0.01).

Conclusions: Targeted testing of family members of HIV-positive adults increased both testing and identification of HIV-positive children. Our findings suggest that the one-time investment in improving HTC space may be an effective approach for increasing HIV-testing among adolescents in this context. Significant increases in number of children tested resulted in only a modest number of new children identified with HIV, highlighting the need for multiple testing approaches.

Abstract 29
Provider-initiated testing and counseling: Is it still high yield?
Yield of routine HIV testing in pediatric and adult inpatient wards in central and southern Malawi

Simon K1,2, Montandon M1,2, Kim M1,2, Wetzel E1,2, Sabelli R1,2, Beyene T1,2, Kavuta E1, Chikoti C1, Namachapa K3, Kazembe P1,2, Ahmed S1,2
1Baylor College Of Medicine Children’s Foundation Malawi, 2Baylor International Pediatric AIDS Initiative at Texas Children’s Hospital, Baylor College of Medicine, 3Malawi Ministry of Health, Department of HIV/AIDS

Background: Routine HIV testing at health facilities (known as provider-initiated testing and counseling, or PITC) is recommended at presumed high yield service delivery points such as inpatient wards, yet limited recent data exist on testing yield in settings like Malawi with mature Option B+ and active HIV case finding programs. We evaluated inpatient PITC yield at three hospitals in central and southern Malawi.

Materials & Methods: Data on PITC in inpatient wards (adult, pediatric, and pediatric nutritional rehabilitation units (NRU) were collected from July-Dec 2016 (Salima) and Oct-Dec 2016 (Balaka and Mangochi) using a dedicated PITC register. Per national guidelines, patients one year of age and older underwent rapid antibody testing to determine HIV status; mothers of infants less than one year of age (or if unavailable, infants) underwent rapid testing to determine HIV exposure. Patients were offered testing if they had never been tested for HIV, tested negative >3 months ago, or had no documentation of prior testing. HIV status (known or newly ascertained) and testing outcomes for patients one year of age or older were analyzed to determine ward HIV prevalence and testing yield.

Ward prevalence was defined as the total of known and new HIV infected patients out of the total number of patients >1 year of age who had their status ascertained. Testing yield was defined as the total number of newly identified HIV infected patients out of the total number of patients over 1 year of age who were tested.

Results: Of 7664 inpatients (3526 pediatric, 4064 adult, 74 NRU) admitted during the evaluation period, 6266 (82%) were assessed for testing eligibility. Of those assessed, 4742 (76%) either did not have documented HIV status (including those never tested) or tested negative >3 months ago and were offered testing. Refusal rate was 1.6%.

Ward prevalence was highest in the NRU (25.5%, 13/51) followed by adult inpatient wards (23.7%, 787/3327) and lowest in the pediatric inpatient ward (3.5%, 75/2118). Testing yield was notably lower than ward prevalence, at 12.5% (4/32) in the NRU, 4.8% (102/2141) in adult inpatient ward, and 1.1% (19/1799) in pediatric inpatient ward. The majority of HIV-positive inpatients knew their HIV status prior to admission (87% of HIV+ inpatients in adult wards, 75% in pediatric wards, 69% in NRU). Inpatient ward HIV prevalence was higher than national population HIV prevalence (1.6% among 0-14y and 10.6% among 15-64y) (Malawi Population-based HIV Impact Assessment 2016). Yield of
new HIV testing among inpatients (excluding NRU) was lower than population prevalence.

**Conclusions:** PITC remains an important approach for HIV case finding and is critical for prompt treatment initiation, however in the setting of Option B+ and active HIV case finding, yield may be decreasing. Additional data on PITC yield in other settings and identification of novel high-yield case finding strategies are needed.

**Abstract 30**

**Use and safety of tenofovir disoproxil fumarate (TDF) in children and adolescents with HIV in paediatric cohorts in the European Union**


1MRC Clinical Trials Unit at University College London, 2Paediatric Infectious Diseases, Department of Paediatrics, Hospital 12 de Octubre, Universidad Complutense, 3Victor Babes” Hospital for Infectious and Tropical Diseases, 4University of Florence, 5Hospital St Pierre, 6Paediatric Infectious Disease Unit, Hospital Sant Joan de Déu, Barcelona University, 7Dept. of Paediatrics, University Hospital Frankfurt, Goethe University, 8Dept. of Children’s Infectious Diseases, Medical University of Warsaw, 9Paediatric Department, Infectious Diseases and Immundeficiency Unit, Centro Hospitalar do Porto, 10Dept. of Paediatrics Karolinska Institutet and Karolinska University Hospital, 11Dept. of Paediatric Haematology, Immunology, and Infectious Diseases, Emma Children’s Hospital, Academic Medical Centre, University of Amsterdam, 12Dutch HIV Monitoring Foundation, 13Paediatric department, Hospital de Santa Maria/CHLN, 14UCL Institute of Child Health, University College London, 15Dept. Paediatrics, University of Copenhagen Hvidovre Hospital, 16Paediatric European Network for the Treatment of AIDS (PENTA)

**Background:** Surveillance for mid- to long-term antiretroviral therapy (ART) toxicity in children is important to inform treatment guidelines. Tenofovir disoproxil fumarate (TDF) is recommended as a preferred first-line agent in children aged ≥12 years and as an alternative first-line agent in children ≥3 years. We report characteristics of children on TDF in Europe and incidence of adverse events (AEs).

**Methods:** Patient-level data were pooled from 12 cohorts in EPPICC. All HIV-infected children who were both <18 years of age at TDF initiation and who were taking TDF on or after 22/11/2012 (the Viread® European Medical Agency approval date) were included. Patients were followed-up until 31/12/2015. Rates of Division of AIDS (DAIDS) grade 1/2/3 laboratory AEs per 100 person-years (100py) were estimated for 13 biomarkers including serum creatinine, calcium, phosphate and alkaline phosphatase (ALP). Clinical AEs and reasons for discontinuation were described.

**Results:** Of 825 patients on TDF, most were from the UK/Ireland (48%), Spain (21%) and the Netherlands (6%). Median age at TDF start was 12.7 years [IQR 10.5-14.5]; five (0.6%) patients were <2 years at TDF start (off-label use). Forty-nine percent (404/825) were male. At TDF start, 18% (150/825) were ART-naive, 62% (515/825) had 1-3 prior ART regimens and 19% (160/825) had ≥4 prior regimens. Thirty-five percent (285/825) of patients initiated TDF on Viread®, while 65% received TDF-containing fixed-dose combination (FDC): Truvada (37%); Atripla (25%); Eviplera (3%); Stribild (0.5%). The majority (86% (452/524)) of those with weight/dose data available were prescribed a dose consistent with Viread® licensing recommendations for weight/age. Fifty percent (409/825) initiated TDF with a non-nucleotide reverse transcriptase inhibitor, and 41% (337/825) with a protease inhibitor. Median duration on TDF at last follow-up was 3.4 [IQR 1.8-5.6] years.

For those on a TDF dose consistent with the Viread® licensed dose, the rate of DAIDS grade 1 laboratory events per 100py (95% CI) were: creatinine 1.1 (0.0-2.4); phosphate 6.4 (3.2-9.6); calcium 3.4 (1.1-5.8) and alkaline phosphatase 32.6 (24.7-40.5). The highest rates/100py of DAIDS grade ≥3 were observed for lipase (6.5; 0.0-18.9), phosphate (2.6; 0.5-4.6) and total bilirubin (2.0; 0.3-3.8), with lower rates for creatinine (0.4; 0.0-1.1) and calcium (0.4; 0.0-1.2).

Eight serious clinical AEs were reported as causally associated with TDF (five low vitamin D3 tests, two abnormal DEXA scans and an ophthalmic toxicity) six of which occurred in patients concurrently taking a PI. Four of
these AEs resolved, all without TDF discontinuation. Overall 10% (82/825) of patients had discontinued TDF by last follow-up, of which 18% (15/82) were due to toxicity (33% (5/15) of which were renal toxicity). Thirteen percent (11/82) discontinued due to patient’s preference, 12% (10/82) due to availability of more effective treatment and 12% due to non-compliance.

Conclusion: TDF is increasingly used within the EPPICC cohorts, largely as part of an FDC. TDF appears well tolerated with low rates of DAIDS grade ≥3 renal/bone events. Few children experienced serious AEs causally related to TDF, but of those that did most were related to renal/bone abnormalities and half resolved. Discontinuation of TDF was relatively low.

Abstract 31
Population pharmacokinetics and safety of nevirapine in high risk HIV-exposed infants

Anugulruengkit S1,2, Suntarattiwong P1, Ounchanum P1, Srimompotong L1, Jantarabenjakul W1,2, Sophonphan J3, Tawon Y4, Cressey T5,8,9, Punnahtinanon S1, Pancharoen C1,2, Puthanakit T1,2, on behalf of CIPHER_AEPEP study team

1Department of Pediatrics, Faculty of Medicine, Chulalongkorn University, 2Research Unit in Pediatric Infectious Diseases and Vaccines, Faculty of Medicine, Chulalongkorn University, 3Department of Pediatrics, Faculty of Medicine, Queen Sirikit National Institute of Child Health, 4Chiang Rai Prachanukroh Hospital, 5Khon Kaen Hospital, 7The HIV Netherlands Australia Thailand Research Collaboration (HIV-NAT), the Thai Red Cross AIDS Research Centre, 8Program for HIV Prevention and Treatment, Department of Medical Technology, Faculty of Associated Medical Sciences (IRD/174), Chiang Mai University, 9Harvard T.H. Chan School of Public Health, 3Department of Molecular & Clinical Pharmacology, University of Liverpool

Background: A six-week triple antiretroviral prophylaxis combination of zidovudine (ZDV)/lamivudine (3TC)/nevirapine (NVP) is recommended to prevent HIV transmission for high risk HIV-exposed neonates in Thailand. Pharmacokinetics and safety data of this regimen in infants initiating NVP at 4 mg/kg at birth are limited. We describe the pharmacokinetics of NVP and safety in infants receiving this triple drug prophylaxis regimen.

Materials & Methods: This is an ongoing prospective cohort study among non-breastfed HIV-exposed infants in Thailand. Neonates with high risk of HIV transmission were defined as born to mothers with a HIV RNA >50 copies/mL prior to delivery or maternal antiretroviral treatment (ART) <12 weeks. Neonates received AZT (4 mg/kg) and 3TC (2 mg/kg) twice daily, plus NVP (4 mg/kg/dose) once daily, for 6 weeks. Neonates with standard risk of HIV transmission, who received 4-weeks ZDV prophylaxis, were enrolled as a comparison group for adverse events. Plasma samples were collected within 6 hours after the first and/or second dose of NVP and randomly at 5, 14, 28 days of life. NVP concentrations were determined using a validated liquid chromatography-triple quadrupole mass spectrometry assay. Target NVP trough concentration (C24) for prophylaxis was >0.1 mg/L. Infant NVP population PK parameters were estimated using a non-linear mixed-effects model and NVP C24 were predicted at each time point. Laboratory tests were performed to monitor potential adverse events including complete blood count, aspartate transaminase (AST), alanine transaminase (ALT) at birth, 1, 2 and 4 months of age. Adverse events (AE) were graded according to DAIDS toxicity table 2014.

Results: From October 2015 to February 2017, 157 HIV-exposed infants were enrolled (62 high-risk and 95 standard-risk). In this PK analysis, NVP concentrations were available from 36 infants (102 plasma samples). Among these infants, 19 (51% were male), median (IQR) gestational age were 38 (36-39) weeks and birth weight 2.8 (2.5-3.1) kg. Regarding maternal ART for the high risk infants, 31 (86%) mothers received ART; NRTI-backbone AZT/3TC (29%) or tenofovir/emtricitabine (71%) in combination with efavirenz (53%) or lopinavir/ritonavir (31%) or raltegravir (3%). Median (IQR) NVP dose at age 14 days was 3.9 (3.7-4.7) mg/kg and at 28 days was 3.2 (3.0-3.6) mg/kg. All predicted NVP C24 were >0.1 mg/L. Median (IQR) NVP C24 was 2.0 (1.7-2.6) mg/L at day 1 (n=13), 2.3 (2.0-2.8) at day 2 (n=36), 3.0 (2.1-3.7) at day 5 (n=22), 1.9 (1.2-2.3) at day 14 (n=13) and 0.7 (0.5-1.1) mg/L at day 28 (n=18). Maternal EFV treatment did not influence infant NVP pharmacokinetics. Among 157 HIV-exposed infants, there was no statistically significant difference in AE rates
between triple and AZT prophylaxis; all grade anemia (45.2% vs 39.2%), grade 3-4 anemia (3.5% vs 4.2%), all grade neutropenia (6.5% vs 6.0%), grade 3-4 neutropenia (2.0% vs 0.9%), grade 1 elevated AST (1.0% vs 1.2%), and grade 1 elevated ALT (2.5% vs 3.7%).

Conclusions: Triple antiretroviral prophylaxis for high risk HIV-exposed neonates with AZT/3TC/NVP appears to be safe and initiating NVP at 4 mg/kg/day maintains concentrations above the prophylactic target during the first 4 weeks of life.

Abstract 32
Safety and efficacy of E/C/F/TAF in virologically suppressed, HIV-infected children through 48 weeks


1Children’s National Health System, The George Washington University, 2Joint Clinical Research Centre, 3Khon Kaen University, 4Miller Children’s Hospital, 5St. Jude Children’s Research Hospital, 6Gilead Sciences

Background: Currently, no once-daily single-tablet regimen (STR) is approved for use in HIV-infected children <12 years of age. Elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (EVG/COBI/FTC/TAF; E/C/F/TAF) is a once-daily integrase inhibitor (INSTI)-based STR approved for use in adults and adolescents ≥12 years of age weighing ≥35 kg. We report safety and efficacy data of using E/C/F/TAF in virologically suppressed children (weighing ≥25 kg) through Week 48. We have previously reported PK parameters showing exposures of all analytes within the safe and efficacious range of those observed in adults.

Methods: This study is a prospective, single-arm, open-label, 2-part, 48-week clinical trial to evaluate the PK, safety and efficacy of switching to the current formulation of E/C/F/TAF (150/150/200/10 mg) administered once-daily in virologically suppressed children (6 to <12 years) weighing ≥25 kg. Adverse events (AE), laboratory tests, including HIV-1 RNA, were assessed. Bone mineral density (BMD) was measured by dual-energy X-ray absorptiometry.

Results: We enrolled 23 children; median age 10 y (range 8-11 y), median weight 31 kg (25.5-58.2 kg), 61% female, 78% Black, median CD4 count 969 cells/μL. All (100%) maintained HIV-1 RNA <50 c/mL at Week 48. No participant had a serious AE or AE leading to study drug discontinuation. Estimated GFR (Schwartz formula) decreased at Week 4 and remained stable (median change at Week 48: -1.5 mL/min/1.73 m2), consistent with inhibition of renal tubular creatinine (Cr) secretion by COBI, as previously seen in the adult population. Median % change in BMD at Week 48 was +4.3% for spine and +3.7% for total body less head (TBH). At Week 48, BMD decreases of ≥4% occurred in 1 participant for spine and 1 for TBH. Median change in BMD height-age Z-score was +0.04 for spine and +0.02 for TBH. One participant, without a spine or TBH BMD decrease from baseline, had a trauma-related bone fracture that was considered as unrelated to study drugs.

Conclusion: In HIV-infected children weighing at least 25 kg, the currently available formulation of E/C/F/TAF was well tolerated and safe as reflected by sustained virologic suppression and a persistent favorable renal and bone safety profile out to Week 48. These findings support the safety and efficacy of E/C/F/TAF as the first once-daily INSTI-based STR in children weighing ≥25 kg.

Abstract 33
Longer-term Safety of Maraviroc in Pediatric Patients with R5 HIV – Follow-up Data from Study A4001031


1University of Padova, 2Sefako Makgatho Health Sciences University, 3Siriraj Hospital, Mahidol University, 4Instituto de Infectologia Emilio Ribas, 5Lakeview Hospital, 6Medical Centre, 7Pfizer Inc, 8The Research Network, 9Gilead Sciences, 10Pfizer Inc.
Background: Study A4001031 evaluated the pharmacokinetics (PK), safety and efficacy of maraviroc (MVC) in treatment-experienced (TE) pediatric patients with R5 HIV. Week 48 data demonstrated that MVC exposures achieved were in the same ranges as those seen in adults. MVC was safe and well-tolerated with a similar safety profile and efficacy compared to adults. Based on this data MVC was recently approved in the USA (with doses based on body weight and concomitant medication) for the treatment of children (2-18 years) with R5 HIV. Safety and efficacy data from the longer-term post Week 48 follow-up of patients remaining in study are described.

Methods: This open-label, age-stratified, non-comparative, multicenter study of MVC plus optimized background therapy (OBT) had a primary endpoint analysis conducted at Week 48, but is continuing to 5 years to assess long-term safety. Patients were enrolled into one of four age/formulation cohorts and received twice daily doses of MVC, selected based on body surface area and adjusted for potential interactions with OBT.

Results: One-hundred and three participants were enrolled, of whom 52% were female. The majority (68.9%) were black, with 15.5% White and 10.7% Asian. As of 19 February 2016, all patients remaining in study (n=65) have reached 96 weeks, and 18 have reached the 5 year endpoint. Fifty participants discontinued from treatment, with insufficient clinical response (n=32) being the main reason for discontinuation. Of patients remaining in study, 52/65 (80%) and 47/55 (85%) had HIV-1 RNA <48 copies/mL at Weeks 96 and 144, respectively, compared to 49/72 (68%) at Week 48. CD4 cell count increases (absolute and percentage) were maintained after Week 48. Three participants discontinued due to adverse events (AEs). AEs occurring in >10% (diarrhoea, vomiting, pyrexia, bronchitis, upper respiratory tract infection and cough) are common in this population. The frequency and nature of AEs remained similar to what was seen at Week 48, and consistent with MVC’s safety profile in adults.

Conclusions: Long-term follow-up data from study A4001031 confirmed the safety and tolerability of MVC in pediatric patients with no new safety concerns observed. Virologic responses were maintained in the majority of patients remaining in study.

Abstract 34
High dose of efavirenz (25 mg/kg) in children under 3 years old

Pressiat C1, Amorissani-Folquet M2, Yonaba C3, Tréluyer J4, Dahourou D5,6,7, Eboua F, Blanche S3,8, Mea-Assande V8, Bouazza N, Foissac F, Malaste K3, Ouedraogo S9, Lui G1, Leroy V10, Hirt D1,4

1Paris Descartes University, EA 7323, 2Pediatric Department, Centre Hospitalier Universitaire de Cocody, 3Pediatric Department, Centre Hospitalier Universitaire Yalgado Ouedraogo, 4Clinical Pharmacology Department, AP-HP, Paris Centre Hospital Group, 5MONOD Project, ANRS 12206, Centre de Recherche Internationale pour la Santé, 6Centre Muraz, 7Insem, Unité U1219, Université Bordeaux, 8Pediatric Department, Centre Hospitalier Universitaire de Yopougon, 9Immunology Hematology Pediatric Unit, AP-HP, Necker Hospital, 10PACCI Programme, Site ANRS, MONOD Project, 11Department of Paediatrics, CHU Charles de Gaulle, Université de Ouagadougou, 12Insem, Unité U1027, Université Paul Sabatier de Toulouse 3

Background: The MONOD ANRS 12206 trial was designated to assess simplification of a successful LPV-based antiretroviral treatment in young HIV-infected children using efavirenz (25 mg/kg/day) to preserve the protease inhibitors class before the age of 3. In this sub-study, EFV concentrations were measured to check the consistency of a 25 mg/kg EFV dose and to compare it with the 2016 FDA recommended dose.

Methods: Fifty-two children underwent blood sampling for pharmacokinetic study at 6-month and 12-month after switching to EFV. We applied a Bayesian approach to derive EFV pharmacokinetic parameters using the NONMEM nonlinear mixed-effect modeling program. The proportion of mid interval concentrations (C12h) in the EFV therapeutic pharmacokinetic thresholds (1-4 mg/L) was assessed according to different dose regimens (25 mg/kg in the MONOD study versus the 2016 FDA recommended dose).

Results: With both 25 mg/kg/day or 2016 FDA recommended EFV dose, simulations show that the majority of C12h were within the therapeutic ranges (62.6% vs 62.8%). However, there were more children underexposed with the 2016 FDA
recommended dose: 11.6% vs. 1.2%. Conversely, there were more concentrations above the threshold of toxicity with a 25 mg/kg dose (36.2% vs. 25.6%) with C12h up to 15 mg/L. Only one child/52 was switched back to LPV because of persistent sleeping disorders, but was within therapeutic ranges.

**Conclusions:** A high EFV dose of 25 mg/kg per day in children under 3 years old achieved satisfactory therapeutic effective levels. However, the 2016 FDA recommended EFV dose appeared to provide more acceptable therapeutic safe profiles.

**Abstract 35**

**Safety of Etravirine (ETR) in young people with HIV: Patient characteristics, adverse events and discontinuation**

Lyons A1, Collins I1, Chappell E1, Tostevin A1, Thompson L1, Ramos-Amador J1, Rojo Conejo P2, Dobrokov K3, Ene L3, Galli L4, Goethgebuer T4, Jourdain G5,6,7, Noguer-Julian A4,5, Königs C6, Kosararaka P7, Lumbiganon P7, Marczynska M7,8, Marques L9, Naver L10, Okhonskaia L10, Prata F10, Puthanakit T11, Rudin C12, Thorne C12, Valerius N12, Gibb D12, Giaquinto C13, Judd A1, On behalf of the The European Pregnancy and Paediatric HIV Cohort Collaboration (EPPICC) study group in EuroCoord

1MRC Clinical Trials Unit at UCL, 2Paediatric Infectious Diseases, Department of Paediatrics, Hospital 12 de Octubre, Universidad Complutense, 3The Republican Hospital of Infectious Diseases of the Ministry of Health of Russia, Federal Centre for the Prevention and Treatment of HIV infection in Pregnant Women and Children, “Victor Babes” Hospital for Infectious and Tropical Diseases, 4University of Florence, 5Hospital St Pierre, 7 Institut de Recherche pour le Développement (IRD) (UMI 174-PHPT), 6Harvard T.H. Chan School of Public Health, 8Faculty of Associated Medical Sciences, Chiang Mai University, 9Paediatric Infectious Disease Unit, Hospital Sant Joan de Déu, Barcelona University, 10Dept. of Paediatrics, University Hospital Frankfurt, Goethe University, 12Srinagarind Hospital, Khon Kaen University, 13Department of Children’s Infectious Diseases, Medical University of Warsaw, 14Paediatric Department, Infectious Diseases and Immunodeficiency Unit, Centro Hospitalar do Porto, 15Dept. of Paediatrics Karolinska Institutet and Karolinska University Hospital, 16Paediatric department, Hospital de Santa Maria/CHLN, 17The HIV Netherlands Australia Thailand Research Collaboration (HIV-NAT), the Thai Red Cross AIDS Research Center, 18University

**Methods:** Patients aged <18 years at start of ETR were eligible. Sixteen EPPICC paediatric HIV cohorts from twelve European countries and Thailand provided individual patient data (characteristics, adverse events (AEs) and reasons for discontinuation) until 31/12/2015. Rates of Division of AIDS (DAIDS) grade 1/2≥3 laboratory AEs were estimated for thirteen biomarkers and details of clinical AEs were recorded.

**Results:** Of 151 patients on ETR most were from Spain (41%), Italy (17%) and Thailand (16%). The majority of patients were male 54% (82/151) and the median age was 14.4 years [12.3-15.6] at ETR start (four patients were <6 years). The median calendar year at start of ETR was 2010 [2008-2012]. Amongst the 108 with weight and dose data available 82% (89/108) initiated ETR on a licensed dose, 10% (11/108) an unlicensed dose, and 7% (8/108) on an off-label dose. Four were ART naïve at ETR start but the majority were highly treatment experienced with 56% (85/151) having received ≥8 ART drugs previously. The median age at ART initiation was 1.8 years [IQR 0.5-4.6] and the median duration on ART prior to ETR start was 11.2 years [7.7-13.3]. Most patients started ETR combined with a PI (75% (113/151)). Median time on ETR at last follow-up was 30.1 months [12.4-55.2]. Median HIV viral load (VL) at ETR start was 2.6 [1.7-4.0] log copies/mL and declined to 1.7 [1.3-2.2] log copies/mL at 12 months post ETR start; the proportion with VL <400 copies/mL increased from 43% (65/151) to 68% (75/110), respectively. Median CD4 cell count was 476 [276-714] cells/µL at ETR start and 611 [445-824] cells/µL at 12 months post ETR start. Grade ≥3 AEs occurred infrequently and rates were low (<3 per 100 person-years) across all dosing groups for all biomarkers.
Five clinical AEs were considered causally related to ETR, all cutaneous and in the licensed group. Of these, two were considered serious or life threatening (both were reported as hypersensitivity reactions/exfoliative dermatitis/Stevens Johnson syndrome/toxic epidermal necrosis). Both patients discontinued ETR at the time of AE diagnosis and the events subsequently resolved. Two patients experienced a non-serious rash/erythema that resolved (one stopped ETR) and one patient experienced generalised hypersensitivity/urticaria, which resolved after discontinuation.

Overall 33% (50/151) of patients discontinued ETR of which 20% (10/50) stopped due to treatment failure and 18% (9/50) due to safety concerns, most commonly due to hypersensitivity reactions (44% (4/9)).

Conclusions: ETR use is relatively uncommon in our largely European paediatric cohort. Most patients were highly treatment experienced. The majority achieved viral suppression at 12 months after ETR start. Rates of DAIDS grade ≥3 adverse laboratory events were low. There were two severe clinical AEs, both of which resolved after discontinuation of ETR. One in three children had discontinued ETR by last follow-up.

Abstract 36

Maraviroc pharmacokinetics and dose recommendations in CCR5-tropic HIV-1 infected children aged 2 to <18 years


1Pfizer, 2Pfizer Inc, 3Pfizer Inc, 4ViiV Healthcare

Background: Maraviroc (MVC) is a CCR5-antagonist approved to treat adults infected with CCR5-tropic HIV-1 in combination with other antiretroviral therapy. Study A4001031 was conducted to evaluate the pharmacokinetics (PK), safety and efficacy of MVC in treatment-experienced (TE) pediatric subjects which informed MVC dose recommendations in this population.

Materials & Methods: Children aged 2 to <18 years received optimized background therapy and MVC tablet or oral solution twice-daily (BID) according to body surface area (BSA) and concomitant medications (i.e., presence of CYP3A inhibitors and/or inducers). Intensive and sparse MVC PK up to Week 48 were determined in subjects to assess dose or modify dose in stage-1 (dose-finding), if required, to achieve an average MVC concentration (Cavg) ≥100 ng/mL. Weight-based doses were determined using modeling and simulation and standard PK analyses.

Results: 97 evaluable subjects were treated with MVC with/without food (including 50 subjects who participated in stage-1). Of the total subjects, 85 received MVC with a potent CYP3A inhibitor, 10 received MVC with non-interacting drugs, and 2 received MVC with a potent CYP3A inducer (without potent CYP3A inhibitors); 50 were female and 47 were male. The age and weight range was 2 to 17 years and 10.2 to 69.8 kg, respectively. Observed and model-based MVC PK were utilized to determine various weight (kg)-bands from protocol BSA-dosing scenarios. MVC PK in children based on body weight (kg)-bands and concomitant medication fell within the ranges observed in adults on approved doses. Children receiving non-interacting drugs required greater mg/kg MVC dose compared to adults to achieve target exposures; however, MVC dose should not exceed the recommended adult dose. Regulatory approval in US was achieved for children ≥30 kg receiving non-interacting concomitant medications and for children 10 kg to ≥40 kg receiving concomitant CYP3A inhibitors (with/without CYP3A inducers).

MVC dose differs based on weight and concomitant medications. For children ≥30 kg receiving non-interacting concomitant medications, MVC 300 mg BID (adult dose) is recommended. For children receiving concomitant CYP3A inhibitors, MVC dose by weight bands are: 10 to <20 kg-MVC 50 mg BID, 20 to <30 kg-MVC 75 mg BID, 30 to <40 kg-MVC 100 mg BID, and >40 kg-MVC 150 mg BID (adult dose). EU approval is pending and submissions in other regions are planned. Insufficient PK data are available to make dose recommendations for children receiving MVC in combination with potent CYP3A inducers (without CYP3A inhibitors).
Conclusions: MVC exposure in children based on MVC dose by body weight and concomitant medication were similar to those observed in adults at approved doses and serves as the basis for MVC tablet and oral solution dose recommendations in children 2 to <18 years weighing ≥10kg.

Abstract 37

Crushing of Raltegravir (RAL) chewable tablets for administration in infants and young children

Teppler H, Thompson K, Chain A, Mathe M, Nachman S, Clarke D

Background: There are a limited number of antiretroviral formulations suitable for treatment of HIV-1 infected young children. Raltegravir is the only integrase inhibitor approved for use in children as young as 4 weeks of age. Current options for children using weight-based dosing at ~ 6mg/kg twice daily include raltegravir chewable tablets (25mg, 100mg scored) in children ≥10kg and oral granules for suspension for infants and toddlers ≥4 weeks and ≥3kg. The granules for oral suspension require careful measurement for both reconstitution and dosing, and clean potable water. We explored whether (1) crushing the raltegravir chewable tablets could be used instead of the granules for oral suspension in young infants and toddlers ≥4 weeks and ≥3kg. The granules for oral suspension require careful measurement for both reconstitution and dosing, and clean potable water. We explored whether (1) crushing the raltegravir chewable tablets could be used instead of the granules for oral suspension in young children, and (2) if the use of multiple tablets would meet established pharmacokinetic (PK) targets for safety and efficacy.

Methods: Stability: One 25mg chewable tablet was dispersed by agitation for 10-15 minutes in 5mL of each of the following: tap water, sterile water, apple juice, and breast milk at room temperature. Two sets of samples were prepared for analysis by reverse phase HPLC to assess stability: 1) immediate analysis, 2) after 30 minutes (lower limit for detection of potential degradation products is 0.02%).

Modeling: Dosing simulations were performed in NONMEM using a population PK model that described data† for raltegravir chewable tablets and established PK targets for trough concentration C12 >75μM (>33 ng/mL), AUC0-12 14-45 μM*hr (6-20 mg*h/L), Cmax <19.63 μM (8724 ng/mL). Appropriate dosing regimens were explored for children ≥ 4 weeks of age using pediatric weight bands established by WHO from 3 to 24.9kg. In this model, weight is a significant covariate. Various twice daily (BID) dosing regimens were simulated to best meet the PK targets.

Results: Stability: After crushing in 5 mL of liquid, raltegravir chewable tablets demonstrated adequate stability for 30 minutes with each vehicle. Initial vs 30 minute results were: sterile water (102.5%-103.5%), tap water (99.5%-99.0%), apple juice (95.5%-97.0%), and breast milk (96.4%-97.3%). Degradates were below 0.02% in each vehicle. Modeling: Modeling and simulation indicated that PK targets, for subjects in the WHO weight bands between 3–25kg, are achieved by administering BID doses in increments of 25 mg as available in the raltegravir chewable tablets. The doses successfully modeled in each weight band are: 3–5.9kg [25 mg (1X25mg tablet)]; 6-9.9kg [50mg (2X25mg tablets)]; 10-13.9kg [75 mg (3X25mg tablets)]; 14-19.9kg [100 mg (1X100mg tablet)]; 20-24.9kg [150 mg (1.5X100mg tablet)]. These in vitro and in silico data indicate that crushing the chewable tablet is feasible and predict that chewable tablets administered after crushing to children as young as 4 weeks and weighing at least 3 kg can be expected to produce drug exposures associated with safety and efficacy.

Conclusion: Raltegravir chewable tablets can be prepared by wetting, crushing with spoon, and stirring until dispersed in water, apple juice, or breast milk for simple administration to younger children following WHO weight bands. Once crushed, in vitro data suggest this will result in therapeutic plasma levels; however, there are no efficacy/safety data to support this use.
Abstract 38

Medication Adherence, Quality of Life and Psychosocial Status in Children with HIV

Sari N

1Harapan Kita Women and Children Hospital

Background: Adherence to antiretroviral therapy is crucial to the success of HIV treatment. Children living with HIV infection showed various health characteristic, stressful life events, and life chaos as well as unannounced pil counts to determine prospective medication adherence and medical record chart abstractions for HIV viral load. The relationship between quality of life and compliance is complex and merits careful study. Monitoring quality of life and psychosocial status may be one of the best ways of improving adherence treatment.

Objective: We describe antiretroviral adherence, quality of life and psychosocial status in children living with HIV.

Methods: A cross-sectional analysis was conducted that examined the ART adherence and psychosocial status in children with HIV based on caregiver report. We performed Medication Adherence Questionnaire, Pediatric Quality of Life Inventory (PedsQLTM) and Pediatric Symptom Checklist (PSC-17) in children with HIV.

Results: In last 10 years there are 100 patients who referred to pediatric HIV clinic, 15 patients were died and 23 were referred to another hospital because of distance reason. A total of 62 subjects, 33 were girls and the rest were boys. Medication adherence in the patients showed average score 7 (medium adherence) based on Medication Adherence Questionnaire. The average score of PedsQL presented 91.56. Average score of physical functioning was 90.60, average score of emotional functioning was 96.04 and average score of social functioning was 95.41. The PSC-17 examination showed average score of internalization was 0.7, average score of externalization was 1.16 and average score of attention was 0.91.

Conclusion: The medication adherence and quality of life of patients in this study were good and there was no psychosocial impact detected in this study. Monitoring quality of life and psychosocial status will contribute to improve medication adherence in children with HIV.

Abstract 39

Retention and viral suppression of patients enrolled in family ART adherence clubs in Cape Town, South Africa

Tsondai P, Wilkinson L1,2, Henwood R2, Ullauri A1, Cassidy T2, Tutu S3, Davies M1

1Centre for Infectious Diseases Epidemiology and Research, School of Public Health and Family Medicine, University Of Cape Town, 2Medecins Sans Frontiéres, Khayelitsha, 3Department of Health, Provincial Government of the Western Cape

Background: Design and implementation of differentiated antiretroviral therapy (ART) delivery models are important for children as well as adults. Since 2011, HIV positive children (stable on ART) and their caregivers (stable or not on ART) were offered the option to enrol in family ART adherence clubs (FCs) - a healthcare worker managed group model of ART delivery for families with five visits per year. In addition to ART refills, participants also receive child disclosure support. Patients that require more frequent adherence or clinical follow-up (including when the patient’s viral load is >400 copies/mL) are referred back to clinician-led individual care. We describe retention and viral suppression outcomes of patients enrolled in FCs.

Materials & Methods: We conducted a retrospective cohort analysis of children and caregivers on ART enrolled in FCs between March 2011 and December 2014. We digitized patient registers and linked patients to laboratory and service access data to validate retention and virologic outcomes. Using Kaplan-Meier methods, we estimated the outcomes: retention, loss to follow up (LTFU), transfers (TFO), mortality and viral load completion and suppression (≤400 copies/mL).
LTFU was defined as having no FC or clinic contact between January and June 2015.

**Results:** 163 children and 84 caregivers on ART were included in this analysis, contributing 733 person-years of follow-up (88% in FC, median 3.7 years). The proportion of follow-up time spent by children and caregivers in the FC model rather than routine care was 84.2% (Interquartile range (IQR), 76.5-90.4) and 95.6% (IQR, 90.1-99.9) respectively. At enrolment, 45% of children were female, median age 8.7 (IQR, 6.3-11.1) years, median time on ART 5.0 (IQR, 3.1-6.4) years; and 95% of caregivers were female, median age 37.7 (IQR, 33.5-41.8) years, median time on ART 4.5 (IQR, 2.8-6.1) years. Over the study period 1 (0.4%) patient died, 11 (4.5%) transferred care and 39 (15.8%) were LTFU. Cumulatively retention among the children decreased from 93.7% (95% confidence interval (CI), 88.7-96.6) at 12 months to 86.1% (95% CI, 79.5-90.8) at 36 months; and among the caregivers from 93.9% (95% CI, 85.9-97.4) at 12 months to 89.7% (95% CI, 80.4-94.8) at 36 months. After 36 months, 86.2% (95% CI, 78.3-92.1) of children and 94.9% (95% CI, 83.6-99.4) of caregivers were virally suppressed, with viral load completion in 98% and 89% of patients respectively.

**Conclusions:** The FC model ensured simplified, family-centred HIV care and ART refill access for children and their caregivers stable on ART, supporting high rates of retention and viral suppression. These findings provide evidence that differentiated ART delivery models can safely be provided to stable children and family-centred management is feasible within such group models.

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**Abstract 40**

**Use of Digital Gaming and Wisepill Dispenser Technology to Measure Adherence among HIV-infected Adolescents and Young Adults**

**Griffith C1, Castel A2, Greenberg D3, Elienberger N4, Lewis B5, Hussein N1, Howard T2, Rakhmanina N2,5**

1Children’s National Health System, 2George Washington University, 3Media Rez, 4Howard University, 5Elizabeth Glaser Pediatric AIDS Foundation

**Background:** There is an unmet need for effective interventions to improve adherence to antiretroviral treatment (ART) among HIV-infected adolescents and young adults (AYAs). Interventions that utilize user-friendly gaming with motivational components have shown promise for behavior change in AYAs. Currently, the data on the role of gaming and real-time medication adherence monitoring of ART adherence remain limited. This study examined the uptake of interactive smartphone based games interlinked with a medication-monitoring device (Wisepill dispenser) among a cohort of HIV-infected AYAs on ART.

**Materials & Methods:** Participants were recruited from the Special Immunology clinic at Children’s National Health System in Washington, D.C. HIV-infected AYAs ages 13-24 years on ART for at least six months with suboptimal ART adherence (defined as most recent detectable HIV viral load (VL)) were eligible. Participant VLs were measured at baseline and at three-month follow up. VL changes at three-month follow up were defined as a log change (log10 increase/decrease). Participants were provided with smartphones containing three digital games with varying levels of difficulty and a Wisepill dispenser, for which openings were linked to in-game incentives, for a three-month period. Gameplay data, including the number of levels completed, were extracted from the phones and Wisepill dispenser openings were tracked using wireless technology. Descriptive statistics were used for data analysis.

**Results:** Twenty-four participants (mean age=18 years; 12M/12F) were recruited; 20 (10M/10F) completed the 3-month follow up;
13 participants (6M/7F) contributed both gameplay and Wisepill data; data from 12 participants (4M/8F) were included in VL analysis, due to loss-to-follow-up (n=4) and lack of laboratory follow up (n=5). All participants were prescribed a once per day ART regimen. Participants opened their Wisepill dispensers only 24% of the time based on the prescribed ART frequency (273 actual/1155 prescribed openings). On time Wisepill dispenser openings (± one hour of self-reported daily medication ingestion times) were observed only 8% of the time (91 actual/1155 prescribed openings). Over two-thirds (69%; n=9) of participants decreased their Wisepill openings during the study period. Available game data showed overall little gameplay (mean level of completion=12%; range=0-34%). There were no differences in amount of gameplay by age; however, females showed slightly higher completion compared to males (14% vs. 12%). Among the three games, higher degrees of game difficulty were associated with lower degrees of completion. Less than half of participants (42%) with VL data (n=5; 3M/2F) had a VL decrease; 25% (n=3; 3F) experienced a VL increase; 33% (n=4; 1M/3F) showed no VL change during the intervention.

Conclusions: Although a real-time, electronic ART adherence monitoring system interlinked with smartphone gaming was technically feasible, we observed low uptake of this technology among this cohort of HIV-infected AYAs with suboptimal ART adherence. While the trend of decreased VL was observed, it was likely not related to gaming. Future tailoring of the digital game designs may help improve acceptance of the study intervention. Data from ongoing exit surveys will be used to modify gaming and adherence monitoring design.

Abstract 41

Early initiation of antiretroviral treatment is associated with less HIV DNA in peripheral blood among HIV-infected children suppressed on treatment

**Paximadis M**, Shiau S1,2, Da Costa Dias B1, Loubser S3, Strehlau R1, Patel F4, Coovadia A1, Puren A1, Abrams E2,5, Kuhn L2,3, Tiemessen C1

1Centre for HIV and STIs, National Institute For Communicable Diseases and Faculty of Health Sciences, University of the Witwatersrand; 2Gertrude H. Sergievsky Center, College of Physicians and Surgeons, Columbia University, 3Department of Epidemiology, Mailman School of Public Health, Columbia University, 4Empilweni Services and Research Unit, Rahima Moosa Mother and Child Hospital, Department of Paediatrics and Child Health, Faculty of Health Sciences, University of the Witwatersrand, 5ICAP, Mailman School of Public Health, Columbia University and Department of Pediatrics, College of Physicians & Surgeons, Columbia University

Background: Early initiation of antiretroviral therapy (ART) in infants, in the days, weeks, months soon after birth, is hypothesized to favorably influence the size of the viral reservoir. Here we investigated whether HIV DNA levels in peripheral blood were associated with age at ART initiation in HIV-infected children suppressed after four years on therapy.

Materials & Methods: As part of clinical trials at Rahima Moosa Mother and Child Hospital in Johannesburg, South Africa, HIV-infected infants and young children coming to clinical attention and initiating lopinavir/ritonavir-based ART were enrolled and followed. From this cohort, we selected 66 infants who had started ART 0-3 months, 62 infants who started 4-6 months and 21 infants who started 7-14 months. At the time of measurement, all children had undetectable HIV RNA levels on standard assays and had been treated for an average of 4.3 years. Genomic DNA extracted from buffy coat was tested with an in-house semi-nested real-time PCR assay to quantitate HIV total DNA. This is a hydrolysis probe-based assay designed to target the HIV-1 subtype C reverse transcriptase gene. In addition, plasma was screened for HIV
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antibodies using an enzyme immunoassay (EIA) (GenescreenTM HIV1/2 version 2; Bio-Rad). Wilcoxon-rank sum tests were used to test for differences in HIV DNA levels between groups.

Results: Median HIV DNA levels were lower in the children who started ART 0-3 months (34 copies/106 cells; Interquartile range [IQR]: 12 to 68) compared to those who started 4-6 months (84 copies/106cells; IQR: 30 to 169; p=0.0005) or 7-14 months (82 copies/106cells; IQR: 20 to 63; p=0.04). Further stratification within infants who started 0-3 months, revealed a gradient of the lowest HIV DNA levels in the 20 infants who initiated under 2 months (25 copies/106 cells; IQR: 10 to 93) compared to the 21 who initiated during month 2 (50 copies/106 cells; IQR: 28 to 93; p=0.025) or the 25 who initiated during month 3 (38 copies/106 cells; IQR: 10 to 65; p=0.27). Among the 20 infants who initiated under 2 months, the mean age at ART initiation was 51 days and the youngest 24 days. Too few children had initiated ART within the first month of life to examine this group separately. In the group initiating ART 0-3 months, median HIV DNA levels were not significantly lower in the children who were non-reactive for HIV antibodies (31 copies/106 cells; IQR: 10 to 93; p=0.70). There was no discernable effect of duration of ART on HIV DNA levels but heterogeneity was limited.

Conclusions: Initiation of ART at 3 months or younger was associated with lower concentrations of HIV DNA in peripheral blood than initiation of ART 4-14 months of age among HIV-infected children suppressed on ART for more than four years. Lowest HIV DNA levels were among those who initiated ART under 2 months of age.

Abstract 42

Altered Phenotype of T Follicular Helper and B Cells in HIV-1-Infected Infants in the Context of Very Early Antiretroviral Treatment

Shalekoff S1, Loubser S1, Da Costa Dias B1, Strehlau R2, Patel F2, Technau K3, Sherman G1,2, Coovadia A2, Abrams E1, Kuhn L5, Tiemessen C1

1CHIYSTI, NICD and Faculty of Health Sciences, University of the Witwatersrand, 2Empilweni Services and Research Unit, Rahima Moosa Mother and Child Hospital, Department of Paediatrics and Child Health, Faculty of Health Sciences, University of the Witwatersrand, 3Department of Paediatrics and Child Health, 4ICAP, Mailman School of Public Health, Department of Pediatrics, College of Physicians & Surgeons, Department of Epidemiology, Mailman School of Public Health, Columbia University, 5Gertrude H. Sergievsky Center, College of Physicians and Surgeons, Department of Epidemiology, Mailman School of Public Health, Columbia University

Background: Circulating T follicular helper cells (Tfh) are important in the development of memory B cells. Here we characterized the development of these cells in relation to naïve-memory B cell subsets, in very early life analyzing the impact of HIV-1 infection with early antiretroviral treatment (ART) on these subsets.

Methods: The percentage and phenotype of Tfh and B cells were analyzed in blood of 24 HIV-1 infected and 18 HIV-1 exposed uninfected (EU) infants at birth, four and 12 weeks. HIV-1 infected infants were started on ART within 48 hours of birth and were divided into three groups based on their virologic response to ART over the first year of life. Good responders achieved and sustained viral suppression below the detection threshold of the assay (<20 copies/ml), normal responders achieved and sustained HIV-1 RNA between 20 and 400 copies/ml, and poor responders either did not achieve this threshold or rebounded. Peripheral blood Tfh cells were defined as CD27+CD45RA-CXCR5+ CD4 T cells and were further divided into Th1 (CXCR3+CCR6-), Th2 (CXCR3-CCR6-) and Th17 (CXCR3-CCR6+) Tfh subsets. B cell phenotypes were defined as naïve
(CD21+CD27-), tissue-like memory (CD21-CD27-), resting memory (CD21+CD27+) and activated memory (CD21-CD27+) cells.

**Results:** The percentage of Tfh cells was higher in HIV-1-infected compared to EU infants at birth (P=0.001). Further, subdividing Tfh cells into Th1, Th2 and Th17 subsets revealed a higher percentage in the HIV-infected infants of Th1 at birth (P=0.001), 4 weeks (P<0.001) and 12 weeks (P=0.003), with concomitant lower percentage of Th2 at birth (P<0.001) and 12 weeks (P=0.015) and decreased percentage of Th17 at 4 weeks (P<0.001) and 12 weeks (P<0.001) compared to EU infants. There were no significant differences in Tfh cell percentage within the HIV-1-infected group by ART response. In contrast, poor responders had a lower percentage of naïve B cells at birth than normal responders (P=0.005) and at 12 weeks than EU (P=0.022). Further, poor ART responders had a higher percentage of tissue-like memory cells than EU (P=0.047) and a higher percentage of activated memory cells than EU (P<0.001) and normal responders (P=0.012) at 12 weeks. Interestingly, normal responders had a lower percentage of resting memory B cells at birth (P=0.002) than other groups and 4 weeks (P=0.012) than EU. No significant difference in the B cell subsets was observed between the EU and good responders.

**Conclusions:** We observed a reduction in proportions of naïve B cell subsets with a corresponding increase in proportions of tissue-like memory and activated memory B cell subsets in very early treated infants who did not achieve virological control. However, the Tfh cells from the HIV-1-infected infants, regardless of whether they responded well to ART or not, showed an increased proportion of Th1 cells (that lack capacity to help B cells produce immunoglobulin) and a decreased proportion of Th17 and Th2 cells (that induce naïve B cells to produce antibody). Thus, there is dysregulation of Tfh and B cell subsets in HIV-infected infants in early life even with very early initiation of ART.

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**Abstract 43**

**Factors associated with HIV DNA levels in children starting ART early in infancy**


1MRC Clinical Trials Unit at UCL, 2Department of Pediatrics, Hospital 12 de Octubre, 3University Department of Pediatrics, Unit of Immune and Infectious Diseases, Children’s Hospital Bambino Gesù, 4UCL GOS Institute of Child Health, 5UCL/UCLH NIHR Biomedical Research Centre, 6University of Padova, 7Imperial College healthcare NHS trust, 8Biobank, Hospital Universitario Gregorio Marañón, 9Hospital Sant Joan de Deu, 10Pediatrics Infectious Diseases Unit, Hospital Universitario Gregorio Marañón, 11Pediatrics Infectious Diseases Unit, Hospital Universitario La Paz, 12Department of Women and Child Health, University of Padova

**Background:** A major obstacle to curing HIV infection is persistence of virus as integrated proviral DNA in long-lived cells even after many years of suppressive ART. Future strategies aimed at achieving ART-free HIV remission are likely to target individuals with low levels of HIV-1 DNA who are likely to have started ART early. We investigated factors associated with HIV-1 DNA levels in children starting ART early in infancy.

**Methods:** 51 children with perinatal HIV aged <6 months at start of standard combination ART were included from 5 cohorts (CHIPS, MADRID, CORISPE-CAT, PADOVA, ROME). Factors associated with log10 Total HIV-1 DNA levels were investigated using linear regression. Regression diagnostics were examined to ensure that all model assumptions were met, particularly normality of residuals further tested using the Shapiro-Wilk test. All HIV DNA measurements were done after viral suppression (≥2 consecutive VL<50) and before viral failure (≥2 consecutive VL≥400). The median [IQR] time since suppression to DNA determination was 6.3 [2.8,8.2] years.
Results: A total of 55% of children were female and, 16%, 31% and 53% were from UK/Ireland, Spain and Italy, respectively. 10% had an AIDS diagnosis at the time of ART initiation; the initial ART regimen included NNRTI-based regimen (49%), PI-based regimen (31%) and other (20%). At ART initiation, median [IQR] age was 2.3 [1.2,4.1] months, CD4% 37% [24%,45%], CD4 count 1495 [507,3420], CD8% 28% [18%,35%], total lymphocyte count 5730 [2430,7277] and log10VL 5.4 [4.4,5.9] copies/ml. Data missingness ranged from 20% to 39%. The median [IQR] age at HIV DNA determination was 7.3 [4.2,10.9] years and log10 Total HIV-1 DNA level was 1.9 [0.7,2.4]. Following viral suppression, 49% of children experienced ≥1 blips (single VL 50-400 preceded and followed by VL<50), 33% had ≥1 spikes (single VL≥400 preceded and followed by VL<400) and 20% had suboptimal viral response (≥2 consecutive VL 50-400).

Adjusting for age at DNA measurement and cohort effect, a month increase in age at ART start was associated with a 18% increase (p=0.0019) in Total HIV-1 DNA. Suboptimal viral response (Ref: no suboptimal response) after viral suppression was also associated with a 60% increase (p=0.0411) in Total HIV-1 DNA levels. There was no significant effect of other factors investigated including gender, AIDS diagnosis, blips, spikes, baseline log10VL, CD4% and CD8%.

Conclusion: In this retrospective study, we found that lower Total HIV-1 DNA was associated with earlier age at ART initiation and absence of suboptimal viral response. Our findings strongly support the recent recommendations for early ART initiation in children. However, further confirmation of results and evaluation of additional relevant factors will be required in larger prospective independent studies.

Abstract 44
Nonreactivity of HIV antibody tests and seroreversion among children initiating early antiretroviral therapy

Puthanakit T1,2,3, de Souza M4, Ubolyam S1, Akapirat S5, Pinyakarn S6, Suntarattiwong P7, Kosalaraksa P8, Chokephaibulkit K9, Jupimai T1, Ananworanich J4

1HIV-NAT, Thai Red Cross AIDS Research Centre, 2Department of Pediatrics, Faculty of Medicine, Chulalongkorn University, 3Research Unit in Pediatric Infectious Diseases and Vaccines, Chulalongkorn University, 4SEARCH, The Thai Red Cross AIDS Research Centre, 5Armed Forces Research Institute of Medical Sciences (AFRIMS), 6U.S. Military HIV Research Program Henry M. Jackson Foundation for the Advancement of Military Medicine, 7Queen Sirikit National Institute of Child Health, 8Department of Pediatrics, Faculty of Medicine, Srinagarind Hospital, Khon Kaen University, 9Department of Pediatrics, Faculty of Medicine, Siriraj Hospital, Mahidol University

Background: Early antiretroviral therapy (ART) can affect antibody responses to HIV infection in children. We aimed to assess the frequency of seronegativity and seroreversion of commercial HIV diagnostic assays widely used in Thailand among children initiating treatment within 6 months of life.

Methods: This is a prospective study of early ART treated HIV-infected children to characterize the latent HIV reservoir in Thai children. HIV infection was determined by at least 2 positive HIV DNA PCR tests. ART was initiated at < 6 months of age. HIV antibody tests were performed after at least 1 year of treatment. Participants who initiated ART after September 2014 have HIV antibody tests annually. HIV antibody tests (generation[G]; test antigens) were: Avioq HIV-1 Microelisa (2ndG; viral lysate), Genscreen HIV-1/2 (3rdG;gp160,p24), ARCHITECT HIV Ag/Ab Combo (4thG;gp41) and two rapid assays: SD Bioline HIV-1/2 (gp41, p24), Alere Determine HIV-1/2 (gp41). Factors associated with seronegativity to the 4thG test were analysed using logistic regression.

Results: The study included 76 children with median age of 16 weeks at ART initiation, duration of ART 2.3 years (IQR 1.1-4.6 years)
and 92% had plasma HIV RNA < 40 copies/ml. There were 37 children (49%) who started ART before 3 months of age and 48 children (63%) who received ART for > 2 years. The proportion of children with seronegative HIV antibody by the different tests were 2ndG-IA (20%), 3rdG-IA (24%) 4thG-IA(47%), rapid test SD Bioline (57%) and Alere Determine (65%). ART initiation at < 3 months of age was associated with 4thG non-reactivity (OR 5.3,95% CI 2.0-14.1). Nine of 48 children (19%) who received ART for >2 years were non-reactive to all 5 tests. Seven children had follow-up HIV antibody tests in 2 consecutive years at median ages of 15 (IQR15-20) and 28 (IQR27-30) months, respectively. Seroreversion to non-reactivity during the 2nd year of ART was observed to at least one of the five tests in 4 out of 7 children (57%), with 2 children showing seroreversion on more than one platform.

Conclusions: HIV seronegativity is observed in up to two-thirds of children who initiated ART early, particularly within the first 3 months of life. HIV rapid assays have the highest rate of seronegative results. Seroreversion may relate to waning of passive maternal antibody or low antigenic stimulation to mount infant antibody response. This will impact the interpretation of HIV serologic tests in the context of early ART scale up in young infants.

Abstract 45

Localization of infection in neonatal rhesus macaques after oral viral challenge

Taylor R1, McRaven M1, Matias E1, Gupta S1, Marie D1, Klotnik Halavaty K1, Allen E1, Lakhasics S1, Ruprecht R2, Hope T1

1Northwestern University, 2Texas Biomedical Research Institute & SNPRC

Background: HIV+ mothers who are not on antiretroviral therapy have up to a 40% chance of passing HIV onto their children, resulting in 150,000-200,000 cases of mother-to-child HIV transmission every year. Pediatric HIV transmission occurs most commonly through breast milk. The site of viral entry in breastfed infants is unknown. The overall goal of our study is to identify which tissues in the oral mucosa and gastrointestinal (GI) tract are susceptible to viral infection and to identify the initial viral target cells. Mothers also transfer antibodies during breastfeeding. Studies examining Dengue Virus suggest non-neutralizing antibodies may enhance viral transmission. We hypothesized that the passive transfer of non-neutralizing antibodies will enhance viral transmission.

Materials and Methods: Neonatal rhesus macaques (< 1 week) were orally challenged with a non-replicating reporter virus (LICh) or a mixture of LICh and replication-competent virus SHIV1157ipd3N4, which encodes HIV Clade C envelope four times per day. Animals were sacrificed and tissues were harvested at 53 and 96 hours after initial challenge. Tissues were examined for foci of LICh transduced cells by luciferase activity using an In Vivo Imaging System (IVIS). Tissues were then analyzed by nested PCR to identify viral DNA and microscopy to phenotype target cells. Serum viral loads were measured by QiaAmp Viral RNA Mini-Kit. Two additional animals were given 600ug/ml non-neutralizing IgG at the same time as oral challenge with LICh and SHIV1157ipd3N4 to examine possible effects of passively transferred non-neutralizing IgG through breast milk.

Results: Initial experiments challenging animals with LICh alone validated that our viral vector can be used to identify virally transduced cells after oral challenge. Because the LICh vector cannot replicate, any mCherry+ were transduced by the challenge inoculum. At 53 and 96 hours, we identified foci of LICh transduced cells in the oral mucosa and upper GI tract by IVIS in the animals challenged with a mixture of LICh and SHIV1157ipd3N4. Additionally, mCherry DNA was found in the tongue and transformation zone of the stomach. Nested PCR for gag DNA demonstrated that replicative SHIV1157ipd3N4 infection had spread to the esophagus and stomach at 53 hours. At 96 hours, viral dissemination was more widespread; gag DNA was found throughout the oral cavity, esophagus, stomach, spleen, liver, and gut. SHIV1157ipd3N4 infected cells were detected in the neck lymph node, stomach, and spleen at 96 hours by microscopy. Infected T cells were identified in the spleen and large intestine by colocalization of gag and CD3 staining. Infected macaques had an average viral load of 156,533 ± 135,936 copies/ml. Non-
neutralizing IgG treatment reduced the viral load at least 10-fold (5,271 ± 7,398 copies/ml).

**Conclusions:** These results at 96 hours and previous work suggest that immune cells within the oral cavity, esophagus, and transformation zone to the stomach are susceptible to viral transduction. Additionally, our data reveal that the entire GI tract is highly susceptible to replicative viral infection. Preliminary studies suggest non-neutralizing IgG may slow replicative viral dissemination rather than enhance it.

**Abstract 46**

**Predictors of HIV reservoir size in peripheral blood of perinatally HIV-infected children: preliminary results from EPIC4 (Early Pediatric Initiation, Canada Child Cure Cohort Study)**

Bitnun A1, Kakkar F2, Brophy J1, Samson L3, Hawkes M4, Read S1, Ransy D5, Sandstrom P1, Kim J1, Lavigne C5, Lavoie S5, Wender P6, Soudeyns H2

1The Hospital for Sick Children, 2CHU Ste-Justine, 3Children’s Hospital of Eastern Ontario, 4Stollery Children’s Hospital, 5National HIV & Retrovirology Laboratories, Public Health Agency of Canada, 6Department of Chemistry, Stanford University

**Background:** EPIC4 is a multicenter Canadian study investigating the impact of early initiation of combination antiretroviral therapy (cART) on HIV reservoirs and HIV-specific immune responses in perinatally infected children. Preliminary results on predictors of HIV reservoir size are described.

**Methods:** Cross-sectional analysis of children enrolled in EPIC4 with sustained virologic suppression (SVS) after initiation of their first cART regimen; children with intermittent virologic blips were included if SVS was subsequently achieved without cART regimen change. HIV reservoir size estimated by measuring viral load in cell culture supernatants following stimulation of CD4+ T-cells with a synthetic prostratin analog. HIV serologic responses were quantified using the Architect HIV-1/2 Ag/Ab combination screening test, expressed as signal-to-cutoff value (S/CO).

**Results:** Twenty-nine children with median age 10.7 years (range 4.2-18.4 years) were included; 62% were female. Median age at cART initiation was 1.3 years (range 1 day – 16 yrs), age at SVS was 2.4 years (range 89 days – 17.6 years), and duration of SVS was 6.5 years (91 days – 14.5 years). Median reservoir size (copies/10^6 CD4 T-cells) was significantly lower for children initiated on cART prior to 6 months of age (n=10) compared to those started later (n=19) (median 3.4 copies/10^6 CD4 T-cells [IQR 0, 48.1] vs. 67.4 copies/10^6 CD4 T-cells [IQR 30.3, 287.3]; p=0.02). Five children had no detectable virus, three of whom initiated cART within 72 hours of birth. Reservoir size correlated directly with age at cART initiation (Spearman correlation, p<0.01) and age at virologic suppression (p=0.04) and inversely with proportion of life on cART (p=0.02); all correlations were more robust in analysis restricted to those without virologic blips (n=23; p<0.01). The magnitude of HIV serologic response (n=20) correlated directly with age at cART initiation and age at virologic suppression and inversely with proportion of life on cART and proportion of life with SVS (all p<0.01).

**Conclusions:** In perinatally HIV-infected children, earlier initiation of cART is associated with reduced HIV reservoir size in peripheral blood as estimated by the prostratin stimulation assay. Other potential predictors of reservoir size include age and duration of SVS, and magnitude of HIV-specific humoral immune response.
Abstract 47

Impact of low-level viremia on virologic failure among treatment-experienced HIV-infected Asian children

Sudjaritruk T1,2, Teeraananchai S2, Karimnia A1, Laphra K4, Kumparasamy N5, Fong M6, Hansudewwachakul R2, Puthanakit T4, Ly P4, Nallusamy R10, Sohn A11, Sirisanthana V4

1Department of Pediatrics, Faculty of Medicine, Chiang Mai University, 2Research Institute for Health Sciences, Chiang Mai University, 3The Kirby Institute, UNSW Australia, 4Department of Pediatrics, Faculty of Medicine, Siriraj Hospital, Mahidol University, 5YRG CARE Medical Centre, CART CRS, 6Hospital Likas, 7Chiangrai Prachanukroh Hospital, 8Department of Pediatrics, Faculty of Medicine and Research unit in Pediatric Infectious Diseases, Chulalongkorn University, 9National Centre for HIV/AIDS, Dermatology and STDs and University of Health Sciences, 10Penang Hospital, 11TREAT Asia/amfAR – The Foundation for AIDS Research

Background: The primary goal of combination antiretroviral therapy (cART) is to prevent HIV-associated morbidity and mortality, and improve quality of life among people living with HIV. Although complete virologic suppression is recommended, a number of patients experience transient rebounds of viremia (low-level viremia, LLV) during the course of treatment. The impact of LLV on the risk of subsequent virologic failure (VF) is controversial. This study aimed to determine the association of LLV with VF among treatment-experienced HIV-infected Asian children.

Methods: HIV-infected children (age <18 years) followed in the TREAT Asia Pediatric HIV Observational Database of IeDEA Asia-Pacific who were on cART for at least 12 months and had a documented history of virologic suppression, defined as two consecutive plasma viral loads (pVL) <50 copies/mL, were included. LLV was defined as a pVL of 50-1000 copies/mL, and VF as a single pVL >1000 copies/mL. Children who were started cART with mono or dual therapy, had a history of treatment interruption >14 days, or from sites with pVL lower limits of detection other than 50 copies/mL were excluded. Baseline was the time of the second pVL <50 copies/mL. Median values are provided with interquartile ranges. Cox proportional hazard models were used to assess the association of LLV and VF. Covariates with a P <0.1 in a univariable model were included in the multivariable analysis.

Results: Of 508 eligible children, 229 (45%) were male, with a median age of 9.6 (7.0-12.3) years. At cART initiation, approximately half of children (46%) had World Health Organization clinical stage 3 and 4. The median CD4 percentage was 9% (2-15%) and pVL was 5.1 (4.8-5.5) log10 copies/mL. At baseline, almost all (96.5%) were on non-nucleoside reverse transcriptase inhibitor-based cART, of which 67% were nevirapine-based, for a median duration of 1.4 (1.3-1.8) years. The median baseline CD4 percentage was 25% (20-30%) and CD4 T-cell count was 661 (480-889) cells/mm3. The median weight- and height-for-age z-scores were -1.3 (-1.9 to 0.4) and -1.6 (-2.5 to 0.8), respectively. Over a median follow-up time of 6.0 (3.1-8.9) years, 86 children (16.9%) experienced LLV, of whom 32 (37.2%) had ≥2 LLV episodes. Overall, 115 children (22.6%) had VF, corresponding to a rate of 3.7 (95% confidence interval [CI]: 3.1-4.5) per 100 person-years of follow-up (PYFU). VF was higher among children with prior LLV compared with those without (5.5 vs. 3.3 per 100 PYFU; P = 0.02). In the multivariable analysis, experiencing LLV (adjusted hazard ratio [aHR]: 1.6; 95% CI: 1.1-2.4), age ≥12 years at baseline (age ≥15 years, aHR: 2.3; 95% CI: 1.1-4.9, and age 12-15 years, aHR: 1.7; 95% CI: 1.1-2.7), and baseline CD4 percentage <25% (aHR: 1.8; 95% CI: 1.2-2.7) were associated with subsequent VF.

Conclusions: LLV was associated with subsequent VF among our treatment-experienced HIV-infected Asian children. Where resources are available, more frequent pVL monitoring for earlier detection of VF could facilitate the optimal management of children with LLV.
Abstract 48

Population level assessment of HIV+ Ugandan/Kenyan children who remained viremic in the SEARCH test-and-treat study, which achieved 90-90-90 coverage of adults

Ruel T1, Ayieko J2, Owaraganise A3, Mwangwa F3, Kaur M4, Liegler T1, Brown L1, Black D1, Jain V1, Cohen C1, Bukusi E3, Charlebois E1, Clark T1, Kwarisiima D, Petersen M5, Havlir D1, Kamya M3

1University Of California, San Francisco, 2Kenya Medical Research Institute, 3Infectious Diseases Research Collaboration, 4Makerere University Joint AIDS Program, 5University of California, Berkeley, 6Makerere University College of Health Sciences

Background: With 81% population-level virologic suppression among adults in rural Kenyan and Ugandan communities, the SEARCH HIV test-and-treat study (NCT01864603) achieved the UNAIDS 90-90-90 target. However, among children aged 2-14 years, the probability of viral suppression at 2 years was only 62%. We sought to describe the characteristics of viremic children and identify population-level predictors of viremia.

Methods: All HIV+ children (age 2-14) in 16 SEARCH Study intervention communities were offered ART in a streamlined model of care. Viral loads (VLs) were measured during annual community health campaigns and at clinic visits. We assessed children aged 2-14 years with ≥1 VL measured from May 2013-November 2016. Predictors of viremia (most recent VL>500 copies/ml), including demographic characteristics, HIV care status (never linked to care, linked to care but lost to follow-up [no visit in prior ≥9 months], or active/in care), household wealth index, and presence of an HIV+ mother with suppressed VL in the household using multivariable logistic regression.

Results: Overall, 700/739 (95%) HIV+ children had ≥1 VL measured. Children were 55% female, with 42% aged 2-6, 32% aged 7-10, and 26% aged 11-14 years. Among 262/700 (37%) viremic children, care-status varied: 43 (16%) had never linked to care, 54 (21%) linked but were lost to follow-up, and 165 (63%) were in care. Children aged 11-14 (aOR 2.45 [1.58-3.78]) and 2-6 years (aOR 1.90 [1.28-2.82]) had greater likelihood of viremia than 7-10 year-olds. Top household wealth quintile (vs. lowest) was associated with greater viremia (aOR 1.78 [1.00-3.15], while having a virally suppressed HIV+ mother predicted lower risk (aOR 0.69 [0.49-0.98]).

Conclusions: Children continue to suffer lower population-level viral suppression rates than adults in the era of rapidly expanding universal ART. Although new interventions to improve linkage and retention in care are needed, most viremic children are already in care. This emphasizes the crucial need for interventions focused on ART adherence and management of HIV drug resistance that are tailored to local systems, and that target specific age groups (e.g. younger/middle/older aged children). Interventions to better harness the support that HIV-positive family members can provide to children are also urgently needed.

Abstract 49

Epigenetic dysregulation of the major histocompatibility complex region in HIV-infected children on antiretroviral therapy

Shiau S1,2, Strehlau R2, Wang S1, Violari A1, Terry M1, Patel F1, Abrams E1,2, Liberty A3, Arpadi S1,2, Coovadia A2, Kuhn L1,2

1Columbia University, 2University of the Witwatersrand, Rahima Moosa Mother and Child Hospital, Empilweni Services and Research Unit, 3University of the Witwatersrand, Chris Hani Baragwanath Hospital, Perinatal HIV Research Unit

Background: Recent data in adults suggest HIV infection and antiretroviral therapy (ART) affect the host epigenome. However, epigenetic dysregulation in children with HIV has not been reported. We performed an epigenome-wide association study (EWAS) to identify differential DNA methylation patterns between treated HIV-infected and HIV-uninfected South African children.
Methods: Genome-wide DNA methylation was profiled using the Illumina HumanMethylation450 BeadChip array in whole blood from 120 HIV-infected children (46% male) and 60 age-matched HIV-uninfected children (50% male) aged 4–9 years (mean 6.4 years) in Johannesburg, South Africa. HIV-infected children were initiated on ART <2 years of age and were all suppressed <400 copies/mL on a lopinavir/ritonavir-based regimen when methylation was assessed. Pre-processing was performed with the R/Bioconductor RnBeads package. Differentially methylated CpG sites (DMCs) were selected (R package limma) if they had a False Discovery Rate q-value<0.05 and |Δβ|>0.05, where Δβ is the mean methylation difference between groups. Differentially methylated regions (DMRs) were selected (R package DMRcate) if they had a Stouffer p-value<0.05, maximum |Δβ|>0.05, and contained ≥2 CpG sites. Analyses were adjusted for age, sex, and estimated cell type proportions (R package minfi).

Results: 370,683 CpG sites and 179 samples were suitable for analysis after pre-processing. 1,309 DMCs were selected, including 1,271 hyper-methylated and 38 hypo-methylated in HIV-infected children. The top hyper-methylated DMC was located in the promoter region of the NLRC5 gene on chromosome 16 which regulates major histocompatibility complex (MHC) class I molecule expression. Many additional sites were associated with genes on the extended MHC region on chromosome 6, including TRIM27, HLA-DQB2, PSMB8, TAP1, PSMB9, BRD2, C6orf11, RGL2, and TAPBP. The selection of 315 DMRs also identified genes located in this region, including TRIM27, HLA-F, GTF2H4, VARS2L, HCG22, C6orf15, PSORS1C1, POU5F1, PSORS1C3, LY6G5C, C6orf29, AGER, NOTCH4, HLA-DQB2, TAP2, PSMB8, TAP1, PSMB9, and COL11A2.

Conclusions: We found extensive DNA methylation dysregulation in treated HIV-infected children compared to age-matched uninfected children. Many of these methylation changes were on genes involved in adaptive immunity. These results provide novel insights into biologic pathways affected by HIV.

Abstract 50
What should we do when HIV-positive children fail first-line combination anti-retroviral therapy (cART)? – a comparison of 4 ART management strategies


1Centre for Infectious Disease Research, School of Public Health and Family Medicine, University Of Cape Town, 2Wits Reproductive Health and HIV Institute, University of the Witwatersrand, 3Tygerberg Academic Hospital, University of Stellenbosch, 4Rahima Moosa Mother and Child Hospital, University of the Witwatersrand, 5Red Cross Children’s Hospital and School of Child and Adolescent Health, University of Cape Town, 6Wellcome Trust Africa Centre for Population Health, University of KwaZulu-Natal, 7Desmond Tutu HIV Centre Institute for Infectious Disease & Molecular Medicine, University of Cape Town, 8McCord Hospital, 9Stellenbosch University and Tygerberg Childrens’ Hospital, Department of Paediatrics and Child Health Division of Paediatric Infectious Diseases, 10Stellenbosch University and National Health Laboratory Service, Division of Medical Virology Faculty of Medicine and Health Sciences, 11Tulane University, School of Medicine, 12Harvard School of Public Health, Department of Epidemiology, Centre for Biostatistics in AIDS Research (CBAR), 13University of Bern, Institute of Social and Preventive Medicine (ISPM)

Background: Virologic failure (VF) in HIV-infected children is difficult to manage in resource-limited settings, given limited availability of alternative drugs and concerns around adherence and the development of viral resistance. We aimed to evaluate four management strategies for children following their first episode of VF by comparing their immunologic and virologic outcomes.

Materials & Methods: Children (age <16 years at cART start) with VF, defined as having ≥2 consecutive unsuppressed viral loads (>1000 copies/ml) ≥1 month apart ≥6 months on cART (at least 3 anti-retroviral drugs from at least 2 drug classes), were followed from their first episode of VF, starting from their second unsuppressed viral load
Children from 8 leDEA-SA cohorts initiating ART between 2004-2010, with recorded CD4% at VF, and with ≥1 subsequent CD4% were included. Children with VF followed one of four management strategies: 1) Continuing on their failing regimen with at most 1 same-class drug substitution; 2) Switching to a new cART regimen based on guidelines or resistance testing; 3) Switching to a holding regimen, either lamivudine monotherapy or other non-cART regimen; 4) Discontinuing all anti-retrovirals. We compared the effect of management strategy choice, relative to strategy 1, on both the 52-week change in CD4% and log₁₀VL from VF, using the inverse probability weighting of a marginal structural linear model.

Results: We included 982 patients with 54168 weeks of follow-up, of which 73.5% was spent on strategy 1, 23.8% on strategy 2, 1.0% on strategy 3 and 1.8% on strategy 4. All patients started on strategy 1, 564 remained on strategy 1, 328 switched to strategy 2, 25 to strategy 3 and 65 to strategy 4. Relative to strategy 1, those switched to strategy 2 had a predicted gain in CD4% of 1.5% (95% CI 0.1 - 2.7) and a decline in log₁₀VL of -1.4 (95% CI -2.0, -0.8) 52 weeks after VF, whereas those switched to strategy 3 or strategy 4 had predicted declines in CD4% of -4.5% (95% CI -10.0, 1.0) and -5.0% (95% CI -14.3, 4.3) respectively, and predicted gains in log₁₀VL of 0.2 (95% CI -3.6, 4.1) and 0.8 (95% CI -0.6, 2.1).

When restricting the database to those on non-nucleoside transcriptase inhibitor (NNRTI)-based first-line, compared to the main analysis we found similar CD4% outcomes in those switching to strategy 2 (1.3%, 95% CI 0.1, 2.5) or strategy 3 (-5.9%, 95% CI -12.8, 1.0), but larger declines for those switched to strategy 4 (-18.0%, 95% CI -33.4, -2.7). Virologic outcomes were similar for all three strategies: strategy 2: -1.4, (95% CI -2.1, -0.8), strategy 3: 0.5, (95% CI -2.5, 3.5), strategy 4: -0.8, (95% CI -2.9, 1.4).

Conclusions: Switching to a new cART regimen resulted in improved immunologic and virologic outcomes when compared with remaining on a failing regimen, whilst switching to a holding regimen or interrupting treatment showed declines in immune response. The results provide useful guidance for the management of children failing treatment, especially those on NNRTI-based first-line regimens, where switching to a robust second-line regimen is possible.

Abstract 51
CD4 recovery following antiretroviral treatment interruptions in HIV-positive children and adolescents in Europe and Thailand

Galli L†, Crichton S†, Buzzoni C†, Goetghebuer T†, Noguera-Julian A†, Jourdain G‡, Judd A*, Klein N*, Mellado M*, Rudin C*, Spoulou V*, Goodall P*, on behalf of the European Pregnancy and Paediatric HIV Cohort Collaboration (EPPICC)

1MRC Clinical Trials Unit at UCL, 2Department of Health Sciences, University of Florence, 3Clinical and Descriptive Epidemiology Unit, Cancer Prevention and Research Institute, 4Hospital St Pierre, 5M 174 PHPT/Faculty of Medical Sciences, Chiang Mai University, 6UCL Great Ormond Street Institute of Child Health, 7La Paz Hospital, 8Hospital Sant Juan de Deu, 9University of Basel, 10Aghia Sophia Children's Hospital, National and Kapodistrian University of Athens School of Medicine

Background: Trials in adults found increased risk of AIDS/non-AIDS events following planned treatment interruptions (TI). Conversely, studies in children found no evidence of similar risk and describe good immunological recovery following antiretroviral therapy (ART) restart. TI are common, particularly in adolescents, but their impact has not been well described. We explore factors associated with CD4% reconstitution following TI in children/adolescents in EPPICC.

Materials and Methods: HIV-infected children on cART (>3 drugs from >2 classes) for >6 months before a TI of >30 days while aged <18 years were included. CD4% in the 24 months after restart of ART (r-ART) following first TI was modelled using random-effects asymptotic regression. Models explored the effect of characteristics (sex, age at cART initiation, age at TI, length of TI, year of r-ART, no clinic visit during TI, new class at r-ART) on estimated CD4% at r-ART and 24 months later (24m), and rate of change of CD4%. Subgroup analyses were conducted: (i) in those ART
 naïve at cART initiation, (ii) in those with nadir CD4% prior to cART and during TI, and viral load (VL) at TI.

Results: Of 779 children with ≥1 TI, 34%, 17% and 17% were from UK/Ireland, Italy and France respectively; 53.8% were female, 92.8% perinatally infected, 48% naïve at cART initiation. Commonest reason for TI was patient's decision/non-compliance (48.7%). At time of TI, 54% took PI-based and 32% NNRTI-based cART; 55% started a new class at r-ART. Median[IQR] length of first TI was 9.0[3.5-22.5] months, median year of r-ART 2006(2003-2009); 199(25.5%) had ≥2 TI. At first TI, median age was 11.8[7.1-14.6] years, mean(stdandard deviation) CD4% 27.3%(11.0). In regression analysis, mean CD4% at r-ART was 19.2%(95%CI 18.3,20.1), and 27.1%(26.2,27.9) by 24m, with half the recovery in the first six months.

In multivariable analysis, CD4% was 4(2.5)% higher in females, and highest in children aged <3yrs, at both r-ART and 24m (all p<0.001). The difference between the youngest(<3yrs) and oldest(>10yrs) age groups was greater at 24m [10.7(7.8,13.6)%] than r-ART [7.3(4.1,10.5)%]. TI of 3-<6 months length [3-<6mths: ]-2.7(-4.9,-0.4)% vs 6<-24mths: -1.3(-3.3,0.7), 24mths: -0.7(-3.0,1.7)% vs 1-3mths: p=0.03] and those with r-ART before 2000 (<2000: -5.8(-9.3,-2.4)% vs 2005-2010: 0.3(-1.5,2.0)%, >2010: 0.7(-1.5,3.8)% vs 2000-2004; p=0.001) were associated with lower CD4% at 24m. No characteristics were associated with speed of reconstitution.

In children ART naïve at cART initiation (n=374) sex and age at TI predicted CD4% at r-ART and 24m; also those starting a new class had lower CD4% at r-ART [-3.1(-5.2,-1.1)%; p=0.003]. Among those with nadir CD4% and VL history (n=365), higher nadir CD4% at both cART initiation and during TI were associated with higher CD4% at r-ART; younger age at TI, more recent year of r-ART, undetectable VL at TI and higher nadir CD4% during TI were associated with higher CD4% at 24m. Undetectable VL and higher nadir CD4% during TI were associated with faster CD4% recovery.

Conclusions: TI were more likely in children >10 years. The best recovery was in females, younger children, those re-starting ART in later years, and children having a short TI.

Abstract 52

EnPRISE national survey reveals the alarming percentage of resistance to first-line ARV therapies among HIV+ children outside Dakar (Senegal)

Kebe K1, Cissé M3, Laborde G1, Philippe M4, DRAME A1, DIOP H1, DIOP K2, Niass E2, Have N4, Vidal N5, Thiam S4, WADE A2, Peeters M1, Taveme B7, Toure Kane C1

1LBV, IRESSEF, 2 Ministère de la Santé, 3 CRCF, Site ANRS Sénégal, Expertise France, 4 PACCI Abidjan Côte d’Ivoire ; IRD UMI 233 ; U 1175 INSERM, 5 CNLS, 6 RNP +, 7 IRD UMI 233 ; U 1175 INSERM

Background: Since 2001, scaling-up and free access to antiretroviral treatment (ART) were adopted in Senegal and expanded to rural areas. Although all children infected with HIV have access to ART, the efficacy of their treatment was studied in Dakar only. The EnPRISE project, funded by Expertise France, aimed to assess the virological status of children infected with HIV throughout the country’s decentralized facilities in order to improve access to quality care.

Materials and Methods: A cross-cutting epidemiological and virological study was conducted in the country, covering 13 of the country’s 14 regions, not including Dakar, between March and June 2015. Socio-demographic and clinical data, combined with a blood sample on blotting paper, were collected for children from 72 treatment sites. Samples were conveyed by public transportation, with the help of the RNP+ association network. A viral load (VL) assay was performed for each child. Resistance genotyping was carried out when VL>1000 copies/mL by Le Dantec bacteriological virology laboratory in Dakar and the IRD virology laboratory (UMI 233) in Montpellier (France), following the ANRS protocol.

Results: Of the 851 identified children, 666 (80%) participated in the study. Sex ratio was 1.03, and the average age was 8 years. 40% of children were orphans for one parent and 15% for both parents. In average, only the half of the siblings were tested for HIV in each home unit. Most of the children (96%) were
infected with HIV-1, and 90% of them were on ART, primarily with the AZT+3TC+NVP first-line therapeutic regimen. The median duration of follow-up was 21 months [min: 0–max: 129]. Almost two-thirds (64%) of the children were experiencing virologic failure (VF), with a median VL = 10 000 copies/mL. The factors associated with VF were male sex, follow-up by a generalist rather than a specialist, and treatment interruptions. Genotypic resistance testing was successful for 304 (95%) patients on VF. From them, 86.5% carried drug resistance mutations (DRM) to at least one antiretroviral molecule. As expected the most prevalent DRM affected nevirapine (96%), efavirenz (90%) and 3TC/FTC (74%). Moreover 73% of these children had either no effective ART or had only a single effective drug in their current regimen. Cross-resistance to new NNRTIs ETR or RPV was observed for half of the patients, and to abacavir for 62% of them.

Conclusions: We observed high levels of virologic failure and of multidrug resistance among children followed-up in decentralized settings in Senegal. Increased access to VL testing to enable early diagnosis and treatment of virologic failures, adjusting therapies and strengthening adherence are urgently needed to achieve the WHO 90-90-90 goals.

Abstract 53

AIDS-defining events and deaths in HIV-infected children and adolescents on antiretrovirals: a 14-year study in Thailand

Traisathit P1,2, Delory T3, Ngo-Giang-Huon N4,5, Somsamai P6, Techakunakorn P7, Theansavettrakul S8, Kanjanavanit S9, Mekmullica J10, Ngampiyaskul C11, Na-Rajsima S12, Lallemant M4,5, Cressey T6,7,12, Jourdain G2,4,5, Collins I13, Le Coeur S2,4,5,15

1Department of Statistics, Faculty of Science, Chiang Mai University, 2Institut de recherche pour le développement (IRD) UMI 174-PHPT, 3APHP, Service de maladies infectieuses et tropicales, hôpital Saint Louis, 4Department of Medical Technology, Faculty of Associated Medical Science, Chiang Mai University, 5Harvard T.H. Chan School of Public Health, 6Lampang Hospital, 7Phayao Provincial Hospital, 8Phan Hospital, 9Nakomping Hospital, 10Bhumibol Adulyadej Hospital, 11Prapokklao Hospital, 12Mahasarakam Hospital, 13Department of Molecular & Clinical Pharmacology, University of Liverpool, 14MRC Clinical Trials Unit, Institute of Clinical Trials & Methodology, University College London, 15Institut national d'études démographiques

Background: Data are scarce on the long-term clinical outcomes of perinatally HIV-infected children receiving antiretroviral therapy (ART) in low/middle-income countries, during the transition period into adolescence. Our objectives were to assess the incidence of mortality before ("early") and after ("late") 6-month of ART and the factors associated with the risk late AIDS-defining-events or deaths.

Materials and Methods: Study population was composed of perinatally HIV-infected children (≤18 years) initiated on ART within the prospective observational pediatric HIV cohort study in Thailand, the PHPT-cohort (NCT00433030). Clinical visits were scheduled at ART initiation, at 2 weeks, 1, 3 and 6 months, and then every 6 months thereafter. CD4 and virology testing was performed at start of ART and every 6 months thereafter. HIV-genotyping was performed in case of virological failure using the Agence Nationale de Recherches sur le SIDA (ANRS) in-house technique. The study outcome was composite and defined as "late" new/recurring AIDS-defining-event or death.

To determine factors associated with the outcome, we used Fine-Gray competing risk regression models accounting for loss-to-follow-up (LTFU) as competing events, and taking into account time-updated variables.

Results: Over the 14-year study period, 619 children ≤18 years initiated ART within the cohort. Overall, 53 (9%) children died during follow-up, 144 (23%) were LTFU and 152 (25%) voluntarily withdrew. The incidence (95%CI) of "early" mortality was 99 (95%CI, 69-142) per 1000-Person-year of follow-up (PYFU) and incidence of "late" mortality was 6 (95%CI, 4-9) per 1000-PYFU. 553 children (45% male) were included in the analysis of factors associated with the outcome ("late" new/recurring AIDS-defining-event or death). At ART initiation, their median age was 6.4 years, CD4% 8.2% and HIV-RNA 5.1 log10 copies/mL. A total of 38 (7%) children met the outcome after median time of 3.3 years (1.3 to
Abstract 54

Longitudinal cluster analysis of viral suppression during 25 months on antiretroviral therapy, adherence, and factors associated in young West-African children, in the MONOD ANRS 12206 cohort

Dahourou D,1,2 Benghezal M,1 Amorissani-Folquet M,1 Yonaba C,1 Malatête K,1 Toni T,1 Ouédraogo P,1 Desmonde S,4 Amani-Bossé C,1 Chaix M10,1 Devaux C11, Leroy V,1 for the MONOD ANRS 12206 Study Group

1Centre Muraz, 2Inserm U1219, Bordeaux School of Public Health, Université de Bordeaux, 3MONOD Project, ANRS 12206, Centre de Recherche Internationale pour la Santé, 4Inserm UMR1027, Université Paul Sabatier Toulouse 3, 5Service de pédiatrie, CHU de Cocody, 6Service de pédiatrie, CHU Charles de Gaulle, 7Laboratoire du CeDReS, 8Laboratoire du CHU Charles de Gaulle, 9Programme PACCI, Site ANRS, Projet Monod, 10Laboratoire de virologie, Hôpital Saint Louis, 11Laboratoire de rétrovirologie, Luxembourg Institute of Health

Background: Good adherence is crucial for achieving viral load suppression on antiretroviral therapy. The long term viral load suppression on antiretroviral therapy is specifically challenging in children. We described the dynamic of the virological response over 25 months among children ART-treated before the age of two in West-Africa, and investigated its association with adherence.

Methods: Between 5/2011 and 2/2013, all HIV-1-infected children confirmed, <2 years were initiated on an initial LPV/r based-ART cohort for 12 months before being enrolled at 13-month for those in VS in a randomized simplification trial, assessing an additional 12-month LPV/r vs EFV-based ART, in Ouagadougou, Burkina Faso, and Abidjan, Côte d’Ivoire. Adherence to ART was assessed at each scheduled monthly visit, using a 4-day recall of missed doses questionnaire to the caregiver and respect of medical appointments. Viral load (Biocentric) were measured three-monthly. Virological success was defined as HIV RNA < 500 copies/mL. We used a clusterwise linear regression (R package kmicov) to adjust the logarithm of viral load on the visit timing, 4-day recall of missed ART and delay between the theoretical visit and the effective visit to cluster our study population.

Results: Among the 156 children enrolled, 63% were from Abidjan; 53% were females, 67% have had access to tap water at home, and mother was their main caregiver (81%). After 25 months on ART, 13 (8%) children had died (9/13 deaths occurred within the first three months on ART), six were lost-to-follow-up or withdrew (4%). Virological success was achieved in 71%, 78%, 77% and 74% of children followed-up at six, 12, 19 and 25 months respectively. We identified four different longitudinal profiles of viral load response over 25 months: 66% had a good profile, with consistent virological success; 9% had a consistent longitudinal virological failure profile; 16% had an initial virological failure profile, then were virologically suppressed beyond 19 months; 9% had a “boom and bust” profile ending with virological failure. The good profile was characterized in children having more often access to tap water, females, and in those with the smallest number of missed ART doses, and days of delay to the appointed visits. In the virological failure profile, the caregiver was less often the mother and the...
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Viral Suppression and Associated Factors Among Children and Adolescents on Antiretroviral Therapy in sub-Saharan Africa: A Systematic Review

Nakawesi J1, Cunningham C2

1Mildmay Uganda, 2University College Cork

Background: Although the number of children receiving Antiretroviral Therapy (ART) in low- and middle-income countries has more than doubled from 2009 to 2013, children and adolescents experience unique challenges to sustained treatment adherence. This affects their ability to optimally suppress the virus. The systematic review was undertaken to determine factors that are associated with viral suppression rates among children and adolescents on antiretroviral therapy in sub-Saharan Africa.

Methods: Literature from four databases PubMed, EMBASE, MedLine and Cochrane Database of Systematic Reviews, using detailed search strategies and reference list cross-checking was reviewed. The review included Cohort, cross-sectional and randomized controlled trials from sub-Saharan Africa that were published in peer reviewed journals in the last 5 years and reported data on viral suppression and factors associated with it among HIV positive children and adolescents on antiretroviral therapy. Titles, abstracts and full articles were assessed using data extraction forms and standardized critical appraisal tools for study quality. The reviewer scrutinized and synthesized the data, using a narrative text approach to provide a descriptive narrative summary based on the research questions.

Results: The viral suppression rates at 6 months varied from 25% to 91% and from 55.6% to 89% at 12 months. Factors that were associated with viral suppression included early initiation of ART, Protease Inhibitor based regimen for the younger children, community based adherence support and assessment of medication using medication return. Factors associated with poor virological outcomes included the use of Nevirapine and Abacavir based regimen, presence of anaemia and adolescent age.

Conclusion: Viral suppression among children and adolescents with HIV in sub-Saharan Africa is still suboptimal. Countries in sub-Saharan Africa should hasten provision of Lopinavir/ritonavir based ART for children less than 3 years and continue early provision of ART for better outcomes. Countries should also scale up community based adherence support and all clinics should assess adherence using medication return as it is a cost effective method. There is a need for proactive follow up and monitoring of children on Abacavir based ART to document their outcomes and a larger study to evaluate the effects of anaemia on viral suppression.

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Predictors of attrition in Kenya pediatric HIV treatment program, 2004-2010

Nganga L1, Waruru A1, Onchiri P5, Ng'eno B5, Mukui P7, Inwani P1, Gichangi A4, Katana A1, Young P7, Ackers M6

1Division of Global HIV & TB, US Centers for Disease Control and Prevention, 2National AIDS & STI Control Program, Ministry of Health, 3University of Nairobi/Kenyatta National Hospital, 4Jhpiego, 5Division of Global HIV & TB, US Centers for Disease Control and Prevention, 6Seattle Children’s Research Institute

Objective: In the last decade, HIV care programs have expanded rapidly leading to improved access to life-saving antiretroviral therapy (ART) for many HIV-infected people, average number of missed doses and visit delays were significantly highest.

Conclusions: Different virological profiles can be identified in young HIV-infected children. Interventions targeting children at risk for treatment failure to support sustained adherence will be helpful in optimizing virological success.
including children. However, maintaining optimal child retention in care remains challenging. We investigated attrition among children enrolled in the national HIV program to inform interventions to improve retention in care.

Methods: We conducted a retrospective medical chart review of HIV-infected children aged < 15 years who enrolled in public HIV care and treatment facilities in Kenya between November 1, 2004, and March 31, 2010. We defined lost to follow up (LTFU) as no contact > 90 days after last scheduled visit. We estimated cumulative probabilities and incidence rates of attrition and assessed independent cofactors of attrition using Kaplan-Meier curves and multivariate Cox regression. All sample estimates were weighted to represent children enrolled at each site during the study period.

Results: Charts from 7,699 HIV-infected children who enrolled in care at 50 clinics were analyzed. Median age at enrollment was 2 years (IQR: 1-6). Overall, 27% of the children were LTFU, and 4.6% died, giving an overall attrition of 31.6%. Cumulative attrition rose sharply at 6, 12, 24, and 36 months to 14%, 19%, 25% and 29%; and then increased minimally at 48, 60, 72, and 84 months to 31%, 34% 36% and 38% respectively. The overall attrition rate was 100.9 children per 1000 person-years (95% CI: 95.8–106.4), and higher for < 2 years old [133.7 (95% CI: 124.4-143.8)] and 10-15 years old [103.1 (95% CI: 84.9-125.9)]. Baseline factors associated with attrition included: advanced or severe immunosuppression [adjusted Hazard Ratio (aHR)=1.3; 95% CI: 1.05-1.52] compared to no immunosuppression; advancing WHO stage disease I [aHR=1.29 (95% CI: 1.12-1.48)]; II [aHR=1.50 (95% CI: 1.31-1.72)] and IV [aHR=2.22 (95% CI: 1.78-2.77)] compared to stage I; and history of opportunistic infections [aHR=1.53 (95% CI: 1.36-1.72)]. Factors associated with attrition during follow-up included: not being on ART [aHR=5.72 (95% CI: 5.18-6.30)]; non-enrollment in a support group [aHR=5.04 (95% CI 3.64-6.98)]; low CD4 of 0 to 200 cells/mm3 [aHR=4.24 (95% CI: 3.60-5.00)] or >200 to 350 cells/mm3 [aHR=2.26 (95% CI: 1.83-2.79)] compared to >350 cells/mm3, hospitalization [aHR=1.24 (95% CI: 1.10-1.40)] and malnutrition [aHR=1.26 (95% CI: 1.11-1.42)].

Conclusion: Pediatric attrition after seven years was associated with advanced HIV disease, not receiving ART, non-enrollment in a support group, hospitalization and malnutrition. Reaching UNAIDS 90-90-90 goals will require early diagnosis and linkage to care and timely ART initiation necessitating targeted interventions to improve retention of HIV-infected children.

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Risk and warning signs for loss to follow-up in a cohort of HIV-infected children on antiretroviral therapy in Thailand

Kawilapat S1,2, Salvadori N1, Ngo-Giang-Huong N1,2,4, Lerodi C1, Ngampiyaskul C1, Kanjanavanit S2, Layangool P2, Lertpienthum N1, Hanpintisak S1, Puangsombat A10, Akarathum N1, Le Coeur S1,3, Lallemant M1,3,4, Traisathit P3, Jouardin G1,3,4

1UMI 174-PHPT, Faculty of Associated Medical Sciences, Chiang Mai University, 2Biostatistics and Applied Statistics Laboratory, Department of Statistics, Faculty of Science, Chiang Mai University, 3Institut de recherche pour le développement (IRD), UMI 174-PHPT, 4Harvard T H Chan School of Public Health, 5Prapokklao Hospital, 6Nakomping Hospital, 7Bhumibol Adulyadej Hospital, 8Buddhachinaraj Hospital, 9Regional Health Promotion Centre 6, 10Samutprakarn Hospital, 1Sanpatong Hospital

Background: Detecting signs associated with an increased risk of loss to follow-up (LTFU) may help maximize the effectiveness of antiretroviral therapy (ART) programs. Adolescence is a well-known factor contributing to the risk of LTFU but other information collected during follow-up may help clinicians focus on children at higher risk.

Methods: We used demographics and clinical data collected at ART initiation (baseline), 2 weeks, 1 month, 3 and 6 months, and every 6 months thereafter in children participating in the PHPT multicenter pediatric cohort in Thailand between January 1, 1999 and December 31, 2014. Children who did not come for follow-up >9 months after their last appointment were considered as LTFU. Discontinuation of ART was considered if >7
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days. Baseline and time-updated variables associated with LTFU were identified using Fine and Gray competing risk regression models accounting for deaths and referrals to other clinics as competing events. We adjusted for characteristics of the Thai program: calendar years of enrollment (quartiles: before 2003, 2003-2004, 2005-2006 and after) and regions in Thailand (northern and others). Missing values of time-updated variables were imputed using linear interpolation within 1 year before and after the missing visit.

Results: 832 children (445 female, 53%) were included in the analysis. Baseline median age was 7.2 years (IQR 3.1-10.0); 67 (9%) were living in orphanage and 508 (61%) in northern Thailand. 255 (34%) had HIV-RNA load >400 copies/mL at 5 years after initiation and 99 (12%) discontinued ART at least once. Median follow-up was 8.2 years (4.1-10.3): 184 (22%) were LTFU (observed cumulative risk of LTFU: 7.6% at 5 years and 29.5% at 10 years). The estimated cumulative incidence of LTFU (considering 184 children referred elsewhere and 72 deaths as competing) was 6.9% (95% CI 5.3-8.7%) at 5 years and 22.8% (19.8-26.0%) at 10 years. In the multivariable analysis, factors associated with a higher risk of LTFU were: not living in orphanage (p=0.006); and, as time-updated, age ≥13 years (p<0.001), HIV-RNA load >400 copies/mL (p=0.001), and previous ART transient discontinuation (p=0.001).

Conclusions: Transient discontinuation of ART at any time during the follow-up should draw clinicians’ attention to prevent definitive LTFU.

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The cascade of care for children with HIV in the UK and Ireland in 2015

Collins I1, Chappell E1, Peters H2, Francis K3, Thorne C2, Judd A1

1MRC Clinical Trials Unit at UCL, 2Population, Policy & Practice Programme, UCL Great Ormond Street Institute of Child Health, UCL

Introduction: The cascade of care is commonly used to assess responsiveness and functioning of HIV healthcare systems, with the UNAIDS 90-90-90 target aiming to help end the HIV epidemic. Increasing data are available for adults but studies of children remain limited. We used data from the UK/Ireland national paediatric HIV cohort (NSHPC and CHIPS) to assess the cascade in 2015.

Methods: All children aged<16 years diagnosed with HIV in the UK/Ireland are reported to NSHPC, then followed longitudinally in CHIPS. Patients aged<21 years and not known to have died, left the country, transferred to adult care or been lost-to-follow-up by 01/01/2015 were included. We describe: (i) the proportion in active HIV care (defined as ≥1 record of a clinic visit, CD4, viral load (VL) or ART change) during 2015; (ii) the proportion of those in active care on ART during 2015; (iii) of those on ART, the proportion virally suppressed (defined as ≥1 VL≤200 copies/mL) during 2015; and (iv) of those on ART, the proportion with good immune status (WHO immunological stage none/mild, defined as ≥1 CD4>30% for age <1 year, CD4>25% for 1-3 years, CD4>20% for 3-5 years, CD4>350 cells/mm3 for ≥5 years) during 2015. Results of the cascade are presented overall, and by age on 01/01/2015.

Results: Of 968 children meeting the inclusion criteria, 902 (93%) were in active HIV care, of whom 93% (839/902) were on ART. Of those on ART, 94% (769/821 with VL available) were suppressed and 97% (787/812 with CD4 available) had good immune status, corresponding to 79% (769/968) and 81% (787/968) of those in the total population, respectively.

Of the 63 in care but not on ART in 2015, 8% (5/63) had taken ART previously (2 on structured treatment interruption, 1 non-compliant, 2 other reasons). Of 839 children on ART, 99 (12%) spent >30 days in 2015 on a non-cART regimen (mono-/dual-therapy, or triple-therapy with an unboosted PI/3-NRTIs without abacavir), of whom 63 were on a mono PI or PI+1-NRTI.

The proportion of patients aged <5, 5-<10, 10-<15 and ≥15 years at the start of 2015 was 4%, 16%, 41% and 40% respectively. The proportion reaching each stage of the cascade was ≥90% across all age groups, however
patients ≥15 years were less likely to be in active care (90% vs. 96%, p<0.001), virologically suppressed (90% vs. 97%, p=0.001), or have good immune status (94% vs. 99%, p=0.001) compared to those aged 10-<15 years (although there was no difference in the proportion on ART, p=0.291). Of the total population, the proportion achieving viral suppression/good immune status was 80%/86% for those <5 years, 79%/84% for those 5-<10 years, 85%/86% for those 10-<15 years and 74%/75% for those ≥15 years.

Conclusion: Children in the UK/Ireland were meeting the second and third stages of the 90-90-90 targets in 2015, though we were unable to assess the first stage. Findings are comparable to those in adults in the UK. There were some variations by age group, those aged ≥15 years had slightly poorer outcomes than younger children (though still ≥90%).

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Pediatric HIV Care and Treatment Continuum in Zambia – The SmartCare Experience (2006 – 2015)

Munthali G¹, Ismail S³, Kimanga D²

¹Ministry Of Health Zambia, ²Elizabeth Glaser Pediatric AIDS Foundation, ³Elizabeth Glaser Pediatric AIDS Foundation.

Background: The UNAIDS “90-90-90” agenda sets a clear roadmap towards ending the HIV/AIDS epidemic. Whilst significant strides have been reported from adults in different settings, much less is known about progress in the pediatric HIV care and treatment continuum in resource-limited settings, including Zambia, which reports an estimated 100,000 children living with HIV infection in the year 2016. Good quality surveillance systems are critical to lay the groundwork for monitoring implementation of the “90-90-90” agenda and providing evidence-based programmatic feedback to inform intervention strategies.

Objectives: To describe the pediatric HIV care and treatment continuum in Zambia using routinely collected population level surveillance data.

Methods: A retrospective longitudinal analysis of data collected in SmartCare, an MoH-supported electronic health records (EHR) platform, from 532 public health facilities covering 87 districts from all the 10 provinces in Zambia, was done. Sociodemographic, clinical and laboratory data amongst HIV-infected children (<15 years old) enrolled for care between 2006 and 2015 was included. Basic descriptive and time to event analyses were done to describe the study population, treatment initiation, retention (at 24 months) and virologic suppression (viral load <1000 copies/ml).

Results: An estimated 169,251 HIV infected children were cumulatively enrolled into care (median age, 3.0 [IQR: 0.9 – 7.8] years; >2.0 years, n=99,410 [58.7%]). Of these (n=44,964 [26.6%]) were subsequently initiated on ART (>2 years, n=32,496 [32.7%]). Of those on ART, majority (91.6%) were initiated within 24 months of enrolment into care. After ART initiation 56.6% were retained at 24 months (>2 years, 60.4%). Overall, an estimated 1,120 viral load tests were reported. The median time from ART initiation to viral load monitoring was 29.5 (IQR: 17.1 – 45.6) months. Of these, 563 (50.3%) had achieved virologic suppression.

Conclusions: Data from the SmartCare for the period under review, show impressive efforts at identifying and linking HIV-infected children to care. However, a leaky cascade of care and treatment remains a challenge, including low treatment coverage, poor retention and sub-optimal virologic suppression. Further analysis and targeted efforts are needed to strengthen the pediatric HIV program in Zambia. On the other hand, this analysis confirms the unique potential of EHR platforms, to track HIV care and treatment and identify challenges for informed targeted interventions in Zambia.
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Retention trends over 10 years in children initiating antiretroviral therapy in the Zambia national HIV programme

Mubiana-Mbewe M1, Ismail S2, Machekeano R2, Mwila A3, Dziuban E4, Ellerbrock T4, Moyo C5, Munthali G5, Zulu I4

1Centre For Infectious Disease Research In Zambia, 2Elizabeth Glaser Pediatric AIDS Foundation, 3Centers for Disease Control and Prevention,, 4Centers for Disease Control and Prevention, 5Ministry of Health

Background: Zambia performed a National Antiretroviral Therapy (ART) Programme Outcomes and Impact Evaluation (NAPOIE) to describe patient retention and clinical and immunologic outcomes in a 10-year period. We describe retention (defined as patients alive and on treatment) and associated factors, for paediatric patients aged less than 15 years using data from NAPOIE.

Methods: We abstracted patient-level data from files of a sample of patients initiated on antiretroviral therapy between January 1, 2004, and December 31, 2014, at 40 randomly selected health facilities, and described demographic and baseline clinical characteristics of the study population using frequencies and percentages for categorical variables and means (SD) and/or medians (interquartile ranges) for continuous variables. We estimated the proportions of HIV-infected patients alive and on ART at 6, 12, and 24 months after initiating therapy and associated 95% confidence intervals, using survey-weighted methods, and explored factors potentially associated with retention. Ethical approval for this evaluation was obtained from the Chesapeake Institutional Review Board in the United States of America and the, University of Zambia Biomedical Research Ethics Committee.

Results: We analysed data from 1913 paediatric patients aged 14 years and younger. The median age at ART initiation was 6.2 years with 12% of the children initiated on ART before 1 year. 44% of children were classified in WHO stage 3 or 4. Children aged 5-14 years had significantly better retention over the follow-up period compared to children under 5 years (61% versus 54%, p=0.005). Similarly, retention rates at 6, 12, and 24 months were significantly better in those aged 5-14 years compared to those under 5 years. Having an uncle as the treatment supporter was significantly associated with retention in care compared with the biological mother as the treatment supporter (OR= 8.6; 95%CI=[2.3-32.4]). Children in WHO stage 4 (OR=0.5, 95%CI=[0.2-0.9]) were less likely to be retained in care compared to children in WHO stage 1.

Conclusion: In this national evaluation of the ART programme in Zambia, retention of paediatric patients in care was relatively low at 57%. We found that younger children and those starting ART with more advanced disease tended to have poorer retention. It is important to invest in strategies to improve retention as we expand access to treatment at an earlier age and implement the test and start strategy.

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Impacts of vitamin D and calcium supplementation on bone mineral density among perinatally HIV-infected adolescents: A 48-week randomized clinical trial

Sudjaritruk T1,2, Aupribul L2, Bunupuradah T3, Kanjanavanit S4, Chotecharoenthan T5, Taeparoenkul S2, Ounchanum P5, Suntarattiwong P5, Puthanakit T7,8

1Department of Pediatrics, Faculty of Medicine, Chiang Mai University, 2Research Institute for Health Sciences, Chiang Mai University, 3HIV-NAT, The Thai Red Cross AIDS Research Centre, 4Nakornping Hospital, 5Chiangrai Prachanukroh Hospital, 6Queen Sirikit National Institute of Child Health, 7Department of Pediatrics, Faculty of Medicine, Chulalongkorn University, 8Research Unit in Pediatric Infectious Diseases and Vaccines, Chulalongkorn University

Background: Adverse bone health is an important long-term, non-AIDS-related complication among people living with HIV (PLHIV). Reduced bone mineral accrual during adolescence is critical since it may result in low
adult peak bone mass, and thereby increase the risks of low bone mineral density (BMD), osteoporosis, and bone fragility later in life. This study aimed to determine the impacts of vitamin D and calcium (VitD/Ca) supplementation on BMD and bone metabolism among perinatally HIV-infected Thai adolescents.

**Methods:** An ongoing, randomized, open-label clinical trial has been conducted in Thailand. HIV-infected adolescents aged 10-20 years who were stable on antiretroviral treatment (ART), defined as plasma HIV RNA <400 copies/ml, were randomly assigned to receive either “high-dose” VitD/Ca (3200 IU/1.2 g daily) or “normal-dose” VitD/Ca (400 IU/1.2 g daily) supplementation for 48 weeks. Lumbar spine BMD and bone metabolism-related markers were evaluated at baseline and 48 weeks. BMD was measured by dual-energy X-ray absorptiometry, of which z-score ≤2 was defined as low BMD. Bone metabolism-related markers included 25-hydroxyvitamin D (25OHD), intact parathyroid hormone (iPTH), alkaline phosphatase (ALP), C-terminal telopeptide (CTX; bone resorption marker), and procollagen type I amino-terminal propeptide (PINP; bone formation marker). An interim analysis, stratified by baseline BMD z-score ≤2 (low BMD) vs. >-2 (normal BMD), was performed using the intention-to-treat analysis. Wilcoxon signed rank tests was conducted to evaluate the within-treatment group changes from baseline in outcomes over the study period.

**Results:** Between April 2015 and October 2016, 166 adolescents (83 for each group) were enrolled. Eighty-seven adolescents (52%) were female. The median age and ART duration (interquartile range [IQR]) were 16.0 (14.4-17.7) and 10.0 (7.0-12.3) years, respectively. The median baseline BMD z-score (IQR) was -1.5 (-2.3 to -0.3), and 67 adolescents (40%) had low BMD. Overall adherence to VitD/Ca supplementation was 80%. Among adolescents with low baseline BMD, there were significant increases in BMD z-scores at week 48 in those receiving “high-dose” (+0.74; P <0.001) and “normal-dose” supplementation (+0.49; P = 0.02). Among adolescents with normal baseline BMD, there were no significant changes in BMD z-scores at week 48, regardless of treatment group (“high-dose”: +0.10; P = 0.16; “normal-dose”: -0.07; P = 0.69). Additionally, in adolescents with low and normal baseline BMD, there were significant increase in 25OHD, and decreases in iPTH, ALP, CTX, and PINP levels at week 48 compared with baseline in both treatment groups (P <0.05).

**Conclusions:** With the preliminary results, BMD z-scores were significantly increased in our HIV-infected adolescents with low baseline BMD who received VitD/Ca supplementation over 48-week follow-up, with a trend of greater improvement among those receiving high-dose vitamin D supplementation. A prospective study with longer follow-up is warranted to confirm our findings.

**Abstract 62**

**Does HIV-Related Vascular Disease Gradually Improve with Accumulating Time on ART? Data from CHER**

**Innes S, Cotton M, Otwombe K, Laughton B, Browne S**

1 Family Infectious Diseases Clinical Research Unit (FAM-CRU), Stellenbosch University & Tygerberg Children's Hospital, 2 Perinatal HIV Research Unit (PHRU), Faculty of Health Sciences, University of the Witwatersrand and Baragwanath Hospital, 3 Department of Medicine, Division of Infectious Diseases, University of California San Diego, 4 Antiviral Research Centre, University of California San Diego

**Background:** Cross-sectional data suggests increased prevalence of vascular disease in HIV+ children on antiretroviral therapy (ART) after adjusting for traditional atherosclerosis risk factors, associated with advanced HIV disease and with ART, particularly lopinavir/ritonavir (LPVr). Whether very early ART will prevent HIV-related premature vascular disease is unknown. Additionally, no longitudinal pediatric PWV data are available for children on suppressive ART. Aorto-femoral pulse wave velocity (PWV) is a sophisticated and sensitive measure of elevated arterial wall stiffness, typically due to atherosclerosis or subclinical arteritis. Reduced arterial wall elasticity leads to faster propagation of the arterial pulse wave. PWV elevations strongly predict subsequent cardiovascular events in asymptomatic adults.
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**Methods:** Baseline, 1- and 2-year follow-up PWV measurements were performed in perinatally-HIV-infected primary-school-age children who initiated LPVr + zidovudine + lamivudine very early in infancy with minimal HIV disease and normal CD4 counts in a well-resourced trial setting (CHER); and in HIV-uninfected controls (HIV-exposed uninfected, HEU, and HIV-unexposed, HU) from the same communities and socio-economic background. Changes in raw PWV, height-based PWV Z-scores (PWVZ-ht) and age-based PWV Z-scores (PWVZ-age) were compared by ANOVA followed by pairwise T-test and adjusted using multivariable regression for body mass index, fasted glucose, total and low density lipoprotein cholesterol, triglycerides and serum cotinine.

**Results:** 84 HIV+ (median age 7.7 [IQR: 7.6-8.5] years) who initiated ART at median 9 (7–12) weeks of age, with cumulative time on ART of median 7.1 (6.7–7.5) years and normal CD4 counts. 51 uninfected (20 HEU; 31 HU) of median age 8.5 (IQR: 7.8-8.7) years, with similar anthropometric Z-scores between groups (p>0.10). Baseline PWV metrics in both HIV+ and HEU were higher than HU and this difference persisted in HIV+ after adjustment (p≤0.04 for all). At 1-year follow-up, both PWVZ-ht and PWVZ-age (unadjusted) had improved in HIV+ and HEU (p≤0.004), whereas HU remained unchanged. At 2-year follow-up, both PWVZ-ht and PWVZ-age had further improved substantially in HIV+ (p<0.0001) and moderately in HEU (p≤0.05), whereas HU remained unchanged.

**Conclusions:** Children who initiate ART very early in life are not spared from premature vascular hardening. Early PWV abnormalities gradually improve with accumulating time on ART. Interestingly, early-onset PWV elevations in HEU also appear to wane with time.

**Abstract 63**

**Endothelial dysfunction in HIV-infected children**

**Dirajal-fargo S**, **Sattar A**, **Funderburg N**, **A McComsey G**

1 University Hospitals Cleveland Medical Center, 2 Case Western Reserve University, 3 Ohio State University College of Medicine

**Background:** A majority of AIDS related mortality is now attributable to cardiovascular disease. As HIV infected youths are aging, it is becoming imperative to evaluate children and adolescents’ cardiovascular disease risk. Changes in the endothelium are one of the earliest alterations of the vessel wall which occurs prior to atherosclerosis. Endothelial dysfunction can be measured by peripheral arterial tonometry (endoPAT). A lower reactive hyperemic index (RHI) detected by endoPAT has been associated with higher risk of cardiac events. This study evaluates early endothelial dysfunction as measured by endoPAT in HIV infected youths and uninfected controls.

**Methods:** HIV infected youths (both congenitally and behaviorally infected) on stable antiretroviral therapy with HIV-1 RNA <1,000 copies/mL and HIV-uninfected controls were included. We measured endothelial function using endoPAT, and markers of systemic inflammation, monocyte activation, and gut integrity. T tests and Chi Square tests were used to compare markers by HIV status. Spearman correlations were used to explore relationships between endothelial function measures, HIV related risk factors, metabolic parameters and inflammation. Regression analyses were used to compare markers between groups after adjusting for demographic variables.

**Results:** Overall, 119 participants were enrolled [71 HIV positive (53 behaviorally infected and 18 congenitally infected) and 48 HIV negative controls]. Overall, 71 % were men; 77% African Americans and median age was 22 years old. Congenitally infected participants had higher median CD4 count when compared to behaviorally infected participants (860 vs 710; p=0.01) and longer cumulative ART duration (140 month vs 29 months respectively, p<0.01) but a similar.
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proportion of viral load < 50 copies/mL (72% vs 77% respectively, p = 0.24). Congenitally infected participants had higher total cholesterol, LDL, triglycerides and insulin resistance (as measured by the homeostatic model assessment) when compared to behaviorally infected youths and uninfected controls (p ≤ 0.04). Reactive hyperemic index (RHI) was lower in congenitally infected participants compared to behaviorally infected youths and uninfected controls. Median (interquartile range) RHI level in congenitally infected group was 1.34 (1.20, 1.42), in the behaviorally infected group was 1.52 (1.34, 1.75) and in the control group was 1.52 (1.27, 1.80) (p < 0.01). Results were unchanged when only virally suppressed patients were included in the analysis. Soluble CD14, a marker of immune activation, intestinal fatty acid-binding protein, a marker of gut integrity and soluble vascular cell adhesion molecule, a marker of vascular dysfunction, were different among the 3 groups (p ≤ 0.01). RHI correlated with age and protease inhibitor duration (p ≤ 0.01), but not with gut integrity or monocyte activation markers.

Conclusions: This is the first study to report on endothelial dysfunction as measured by peripheral arterial tonometry in HIV-infected youth. Higher levels of endothelial dysfunction and immune activation were found in youth congenitally infected with HIV when compared to behaviorally infected youth and uninfected controls. These results suggest that measuring endothelial dysfunction in this population is feasible and that congenitally infected children may be at higher risk of future cardiovascular disease. Longitudinal studies are crucial to determine these risks and to understand the contributing factors in this population.

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Prevalence and associated factors of asymptomatic peripheral arterial disease among perinatally HIV-infected Thai adolescents

Sudjaritruk T1,2, Aurpibul L2, Anugulreungkit S3,4, Chotecharoentanan T2, Thamsala S2, Thummalangka R2, Taejaroenkul S2, Rerkasem K2,6, Puthanakit T2,4,5

1Department of Pediatrics, Faculty of Medicine, Chiang Mai University, 2Research Institute for Health Sciences, Chiang Mai University, 3Department of Pediatrics, Faculty of Medicine, Chulalongkorn University, 4Research Unit in Pediatric Infectious Diseases and Vaccines, Chulalongkorn University, 5HIV-NAT, The Thai Red Cross AIDS Research Centre, 6Department of Surgery, Faculty of Medicine, Chiang Mai University

Background: Peripheral arterial disease (PAD) is a frequent manifestation of atherosclerosis and associated with an increased risk of cardiovascular disease, a growing concern in the management of HIV-infected patients. The information regarding PAD in HIV-infected adolescents, particularly in resource-limited countries, are scarce. This study aimed to assess the prevalence and associated factors of asymptomatic PAD among perinatally HIV-infected adolescents.

Methods: A multicenter, cross-sectional study was conducted in Thailand. Perinatally HIV-infected adolescents aged 10-25 years who received antiretroviral therapy (ART) for ≥12 months, and age- and sex-matched healthy controls were enrolled, in the ratio of 3:1. Ankle-brachial index (ABI) measurement was performed at rest and post-exercise (after 20 squats) for both extremities. Asymptomatic PAD was defined as a rest ABI ≤ 0.9, or a post-exercise ABI decreased ≥ 0.15 or ≥ 20%. Systemic hypertension (HT) was defined as systolic or diastolic blood pressure ≥ 130 or ≥ 85 mmHg, respectively. Metabolic parameters, including lipid profiles (cholesterol, low-density lipoprotein-cholesterol [LDL-C], high-density lipoprotein-cholesterol [HDL-C], and triglyceride [TG]), fasting plasma glucose, and insulin levels were measured. Median values are provided with interquartile ranges. Linear regression analysis was performed to identify
Factors associated with low ABI among HIV-infected adolescents.

**Results:** Between January and March 2017, 150 HIV-infected and 50 healthy adolescents, with a median age of 18.0 (14.7-20.5) years, were enrolled. One-hundred adolescents (50%) were female, and 31 (16%) were overweight. Systemic HT was identified in 14 adolescents (7%), all except one were isolated systolic HT. Among HIV-infected adolescents, 62 (41%) had World Health Organization (WHO) clinical stage 3 before ART initiation. At enrollment, the median ART duration was 12.8 (9.2-14.2) years, current CD4 T-cell was 28% (24-32%), and 82% had HIV RNA <50 copies/mL. Compared with healthy controls, HIV-infected adolescents had higher proportion of dyslipidemia (TG ≥150 mg/dL: 26% vs. 8%, and HDL-C <40 mg/dL: 25% vs. 6%; P <0.01), and insulin resistance (the homeostasis model assessment of insulin resistance >3.16; 30% vs. 8%; P <0.01). Based on ABI measurement at rest, asymptomatic PAD in any extremities was identified in 20 adolescents (10.0%; 95% confidence interval [CI]: 6.2-15.0%), of whom 17 (11.3%; 95% CI: 6.7-17.5%) were HIV-infected, and 3 (6.0%; 95% CI: 1.3-16.6%) were healthy adolescents (P = 0.28). Asymptomatic PAD in both extremities was documented in 7 adolescents, all were HIV-infected, corresponding to a prevalence of 3.5% (95% CI: 1.4-7.1%). Additionally, focused on post-exercise ABI measurement, asymptomatic PAD in both extremities were noted in only 3 adolescents (1.5%; 95% CI: 0.3-4.3%); 2 were HIV-infected, and 1 was healthy adolescents (P = 0.74). In the multivariable analysis among HIV-infected adolescents, female sex (adjusted mean difference: -0.04; 95% CI: -0.08 to -0.01) and WHO clinical stage 3-4 prior to ART initiation (adjusted mean difference: -0.04; 95% CI: -0.06 to -0.01) were associated with low ABI.

**Conclusions:** Asymptomatic PAD was relatively uncommon among our perinatally HIV-infected Thai adolescents. Serial ABI measurements among adolescents with PAD to monitor the progression of disease should be considered.

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**Abstract 65**

**Non-sexual transmission of HPV infection among HIV-infected adolescent girls prior to HPV Immunization in Côte d’Ivoire**

Tchounouga B1,2, Eboua F3, Amorissani-Folquet M4, Kouadio K5, Garigue f, Leroy V5, Dabis F6, Jaquet A2

1PACCI Research Center, 2University of Bordeaux, ISPED, Centre INSERM U1219, 3Service de Pédiatrie, Centre Hospitalier Universitaire de Yopougon, 4Service de Pédiatrie, Centre Hospitalier Universitaire de Cocody, 5Centre Intégré de Recherches Biocliniques d’Abidjan, 6CHU Bordeaux, Laboratoire de Virologie, 7Université de Toulouse, Centre INSERM U1027

**Background:** HIV is a major co-factor associated with the acquisition and persistence of Human Papilloma Virus (HPV) that lead to cervical cancer. However, there is limited data on the prevalence and distribution of HPV infection in the key population of HIV-infected adolescent female. This study aimed to describe the HPV prevalence and correlates among perinatally HIV-infected adolescent females eligible to HPV vaccination.

**Methods:** A cross-sectional study was conducted from April to June 2016, in the four major pediatric HIV clinics of Abidjan, Côte d’Ivoire. Prior to the administration of HPV immunization, all HIV-infected girls aged 11-15 years were proposed to participate to the study. A dedicated questionnaire was administered to assess sexual activity and gynecological hygiene practices in all participating girls, followed by a gynecological examination and a systematic vaginal swab collection. HPV genotype identification was performed using the AnyplexTMII HPV28 Detection (Seegene). A logistic regression analysis was used to identify factors associated with the presence of HPV infection.

**Results:** A total of 250 HIV-infected girls were included, with a median age of 13 years [IQR 11-14]. Among them, 237 (94.8%) were on antiretroviral treatment and their median CD4 count and viral load at enrolment were 660 [IQR 439-914] cells/mm3 and 2.0 log10 copies/mm3, respectively. Menstrual activity was reported by 111 (44.4%) participants and...
the frequent practice (1/day) of vaginal toilet was reported by 75 (30%) of them, with a median initiation age of 12 [IQR 10-13]. Sexual activity was reported by 12 (4.8%) participants, and ascertained by gynecological examination in 19 (7.8%) of them. The HPV prevalence was 3.6% (95%CI 1.6-6.7) with 77.8% of oncogenic HPV detected. HPV infection was significantly associated to the practice of vaginal toilet (OR=8.3; 95%CI [1.6-41.4]; p=0.009). No significant association was reported between HPV infection and sexual activity (OR=3.0; 95%CI [0.3-30.3]; p=0.346).

Conclusions: Prevalent HPV infections were identified in this population of HIV-infected girls eligible to HPV vaccination and were associated to vaginal toilet. Genital hygiene practices and sexual education should be promoted in HIV-infected young females, to prevent the acquisition of oncogenic HPV in this high-risk population.

Abstract 66

Spirometric Results in Malawian HIV-Infected Youth with and without Chronic Lung Disease

Lloyd S1,2, Mirkovic K2, Freeland D2, Modi S1, Singer D3, Ahmad N1,2, Akelo H1, Alexander H1, Chipungu G1, Gonzalez-Martinez C1,2, Gupta S1, Gutreuter S1, Hatcher C1, Hrapcak S1, Kabaghe C1, Koumans E1, McKenney A1, Murowa M1, O'Hare B1,12, Phiri S1, Taylor N1,13, Teleka A1, van Oosterhout J1,4, Wendel K1,14

1Centers for Disease Control and Prevention (CDC), Center for Global Health (CGH), Division of Global HIV and TB (DGHT), 2CDC/National Institute for Occupational Safety and Health/Respiratory Health Division, Surveillance Branch, 3Centers for Disease Control and Prevention (CDC)-Malawi, Center for Global Health (CGH), Division of Global HIV and TB (DGHT), 4Epidemic Intelligence Service Officer (EISO), CDC, 5Dignitas International, 6College of Medicine, University of Malawi, 7Baylor College of Medicine Children’s Clinical Center of Excellence, 8Ministry of Health, 9Lighthouse, Lilongwe Trust Clinic, 10CDC, Division of Scientific Education and Professional Development (DSEPD), Epidemiology Workforce Branch (EWB), New York State Department of Health, Bureau of Communicable Disease Control, 11Liverpool School of Tropical Medicine/Malawi Liverpool University

Background: Chronic lung disease (CLD) has been recognized as a serious complication among HIV-infected children and adolescents in several high HIV-prevalence African countries but the underlying pathology remains uncertain. Spirometry is one objective modality that can complement more subjective clinical symptoms when evaluating HIV-infected youth for CLD.

Methods: All HIV-infected 5-14 year old children attending seven outpatient HIV clinics in Malawi were eligible; exclusion criteria were unconfirmed HIV status, too ill to participate, self-reported pregnancy, and no informed consent/assent. CLD cases were defined as children with (1) chronic cough (>4 weeks) and self-reported breathlessness or (2) one of the previous symptoms and at least one of the following signs: hypoxia (resting oxygen saturation ≤92%), resting tachypnea (respiratory rate ≥24/minute), or finger clubbing. Spirometry was performed according to the American Thoracic Society guidelines and spirometric reference values [i.e., forced expiratory volume in 1 second (FEV1), forced vital capacity (FVC), and FEV1/FVC] from the Global Lung Initiative equations were used for comparison. The best FEV1 and FVC values from 3 high-quality traces (quality-control grade A or B) were included for analysis. Results of FEV1, FVC, and FEV1/FVC are reported as residual standard deviations (SD) below the mean (z-scores). Participants with an FEV1 and FEV1/FVC ratio less than the lower limit of normal (LLN) were classified as having an obstructive pattern and when FVC was less than LLN and FEV1/FVC was not, a reduced FVC pattern was documented. The LLN (1.64 SD below the mean) was defined as the 5th centile of the reference population. Continuous data are presented as median and interquartile range (IQR); Wilcoxon rank sum and chi square tests were used to assess statistical significance (defined as p-values ≤0.05).

Results: We enrolled 615 children, 582 (94.6%) attempted spirometry maneuvers, 397
(68.2%) produced evaluable tracings and 258 (65.0%) of these were grade A or B; 36 (14.0%) were CLD cases. Overall median FEV1, FVC, and FEV1/FVC z-scores were -0.47 (IQR: -1.29-0.33), -0.28 (IQR: -1.07-0.39), and -0.31 (IQR: -1.00-0.33), respectively. Median FEV1 z-scores for participants with CLD were significantly different from those without CLD [-0.91 (IQR: -1.69-0.06) vs. -0.45 (IQR: -1.15-0.37); p-value=0.05]. Median FVC and FEV1/FVC z-scores were not statistically significantly different between CLD and non-CLD cases, respectively [FVC: -0.41 (IQR: -1.50-0.17) vs. -0.27 (IQR: -1.00-0.47); p-value=0.19; FEV1/FVC: -0.44 (IQR: -1.39-0.02) vs. -0.26 (IQR: -0.91-0.35); p-value=0.07]. There was no statistically significant difference between the percentage of CLD and non-CLD cases whose tracings showed obstructive or reduced FVC patterns, respectively (obstructive: 8.3% vs. 3.6%; p-value=0.19 and reduced FVC: 13.9% vs. 12.2%; p-value=0.77).

Conclusions: CLD cases had lower FEV1 z-scores than those without CLD, suggesting a role for airflow limitation in the pathophysiology. A higher percentage of those diagnosed with CLD showed an obstructive pattern on spirometry, although this was not statistically different from those without CLD. Approximately 13% of HIV-infected youth, irrespective of CLD status, demonstrated reduced FVC patterns on spirometry. These findings are consistent with previous studies indicating HIV-associated CLD represents a spectrum of obstructive and restrictive lung diseases among HIV-infected youth.

Abstract 67

High Prevalence but Low Correlation of Spirometric and Chest CT Abnormalities Among HIV+ Adolescents In Nairobi, Kenya

Attia E1, Maleche Obimbo E2, Zhong D3, West T1,4,4, Cagle A3, Kiptinness C4, McGrath C5, Sakr S6, Njiru C6, Kicska G4, Crothers K1, Chung M6

1Division of Pulmonary and Critical Care Medicine, University Of Washington, 2Department of Paediatrics and Child Health, University of Nairobi, 3University of Washington, 4International Respiratory and Severe Illness Center, University of Washington, 5Coptic Hope Center for Infectious Diseases, Coptic Hospital, 6Department of Global Health, University of Washington

Background: Despite frequent chronic respiratory symptoms among HIV+ adolescents in Africa, chronic lung disease (CLD) in this population remains poorly understood. Spirometry and chest imaging can provide complementary functional and anatomic CLD characterization. We explored how these modalities relate to each other, hypothesizing that obstructed spirometry and CT findings consistent with small airways disease were common.

Materials & Methods: We performed a cross-sectional study of 50 perinatally-infected HIV+ adolescents from the Coptic Hope Center for Infectious Diseases in Nairobi. Demographic, anthropometric, respiratory symptom, exposure, and HIV-related data were obtained. Subjects underwent spirometry and high-resolution chest CT. Abnormal spirometry patterns included: obstructed (post-bronchodilator FEV1/FVC≥0.7 + FVC<80% predicted). CTs were interpreted by a radiologist blinded to clinical data. We determined correlations between spirometry and CT abnormalities and with clinical characteristics.

Results: Mean age was 13 (SD 3) years, 56% were male, 11% had wasting, 84% were exposed to indoor biofuel and 34% to cigarette smoke. Median CD4 was 672 cells/µL (IQR 406-870); 94% were on ART; 31% had WHO HIV Stage 3/4. Forty (80%) had ≥1 respiratory symptom: 21 had cough, 28 phlegm, 14 breathlessness. Of 47 with acceptable spirometry, 25 (51%) had abnormal spirometry patterns: 16 (34%) obstructed, 7 (15%) restricted. Overall, 39 (78%) had CT abnormalities: 24 (48%) had mosaic attenuation, 10 (20%) bronchial wall thickening, 8 (16%) micronodules, 4 (8%) bronchiectasis. Obstructed spirometry correlated with mosaic attenuation (r=0.6, p=0.02); there were no other significant correlations between spirometry and CT. WHO Stage 3/4 correlated with obstructed spirometry (r=0.3, p=0.01). Wasting correlated
with the restricted spirometry pattern \( r=0.4, p=0.01 \), bronchiectasis \( r=0.7, p=0.03 \), and micronodules \( r=0.6, p=0.03 \). Cough weakly correlated with the restricted pattern \( r=0.2, p=0.048 \). We detected no other correlations between symptoms, CD4, pulmonary infections, and biofuel/cigarette exposure with abnormal spirometry or CT.

**Conclusions:** The prevalence of abnormal spirometry and CTs is high among perinatally-infected HIV+ adolescents, despite preserved CD4. Obstructed spirometry was correlated with mosaic attenuation, consistent with small airways disease. We did not detect correlations between spirometry and other patterns, potentially due to small sample size.

**Abstract 68**

**Understanding mental health difficulties and associated psychosocial outcomes in HIV positive adolescents visiting the HIV clinic in Kenyatta National Hospital, Kenya**

**Gaitho D**\(^1\), Nduati R\(^1\), Kumar M\(^1\), Wamalwa D\(^1\)

\(^1\)University Of Nairobi / Kenyatta National Hospital

**Background:** Kenya is among six countries worldwide that contributes about half of the deaths due to AIDS related illnesses among adolescents which is the leading cause of mortality among this age group. Adolescents living with HIV face numerous challenges; key among them being HIV status disclosure, stigma & discrimination and adherence to medication. Tracking psychosocial adversities and behavioral outcomes in young people living with HIV provides unique insight into developing curative and preventative interventions and allow us to rethink pathways to various services and outreach implementation gaps.

**Methods:** We conducted a descriptive survey among 270 HIV positive adolescents aged 10 – 19 years to determine psychosocial challenges using the HEADSS assessment tool covering Home environment, Education, Activity & exercise, Drugs use, Sexuality functioning and suicide / depression. Depression was further assessed using a PHQ 9 scale. The study was conducted between August and December 2016 among adolescents enrolled into the Comprehensive care clinic (HIV clinic) at Kenyatta National Hospital, Nairobi.

**Results:** We enrolled 270 adolescents. The mean age of our sample was 14.75 years (SD=2.65) and 53.7% were males. Nearly all of the participants (99.6%) were in school, 18.5% \((n=50)\) had experienced bullying, 18.1% \((n=49)\) reported dropping school performance, 33.7% \((n=91)\) had repeated a class, 31.5% \((n=85)\) had changed school in the last 2 years, and 44.1% \((n=119)\) reported being sent away from school due to lack of fees. Another, 12.6% \((n=34)\) reported missing meals in the preceding 2 weeks and 29.6% \((n=80)\) were not involved in extracurricular activities. Of those adolescents who were 12 years and above 13.6% \((n=31)\) reported having had a sexual encounter of whom 69% \((n=20)\) did not consistently use a condom. Depressive symptoms were found in 52.6% \((n=142)\) of the study participants.

On univariate analysis, factors found to be associated with depression included the older adolescent aged 15-19 years \((x^2 (1, 270) =14.80; P<0.001)\), having repeated a class \((x^2 (1,270) = 3.67; P = 0.018)\), being sent away from school due to lack of fees \((x^2 (1,270) = 7.85; P=0.005)\) and ever missing a meal in the preceding 2 weeks \((x^2 (1,270) = 6.84; P=0.009)\). On multivariate analysis of association between PHQ-9 scores and other variables being of ages 15-19 years and missing meals due to food insecurity had odds of 2.88 \((CI 1.72 – 4.82)\) and 2.62 \((CI 1.09 – 6.28)\) respectively of developing depression.

**Conclusion:** One in every two adolescents living with HIV and attending the KNH clinic is suffering from depression. Older age and lack of food security were independent risk factors for depression.
Abstract 69

Neurodevelopment in Young Children Born to HIV-infected Mothers: A Meta-analysis

McHenry M1,2, McAteer C1, Oyungu E3, Bosma C1, Mpofu P4, Deathe A1, Ayaya S2,3, Vreeman R1,2,3

1Indiana University School Of Medicine, Pediatrics, 2Academic Model Providing Access to Healthcare (AMPATH), 3Moi University, College of Health Sciences, Department of Child Health and Paediatrics, 4Indiana University School of Medicine, Biostatistics

Background: Perinatal HIV infection has negative effects of early childhood development. However, for the growing population of HIV-exposed, uninfected children, the impact of HIV-exposure is less clear. Understanding the effects of HIV-exposure on early child development is critical, as interventions are most effective in this young age group. The objective of this study was to systematically review and meta-analyze the degree of cognitive and physical impairments in young children (< 8 years) who are HIV-infected (HIV+); HIV-exposed, uninfected (HEU); and HIV-unexposed children (HIV-).

Materials and Methods: On July 12, 2016, we systematically searched 3 electronic bibliographic databases: OVID Medline, PsychINFO, and EMBASE; as well as the Cochrane Collaborative Database, Google Scholar, and bibliographies of pertinent articles. Study inclusion criteria was as follows: having 2 of 3 populations of interest (HIV+, HEU, HIV-), participant age < 8 years old, using a standardized developmental assessment tool, and having a primary outcome of development. Exclusion criteria included: having a significant confounding variable in study population (e.g. haemophilia, CMV) and intervention-focused studies. Titles, abstracts, and full texts were assessed independently by 2 reviewers. Data from included studies were extracted by 2 independent reviewers and then cross-checked by an additional reviewer. Network meta-analysis was performed on studies using Mental Development Index (MDI) and the Psychomotor Development Index (PDI) from the Bayley Scales of Infant and Toddler Development (BSID). For studies using BSID-3rd edition, the cognitive score replaced the MDI. A Bayesian approach was used, adjusting for quality of the assessment, edition of the assessment, and antiretroviral treatment (ART) exposure.

Results: Searched yielded 10,451 unique titles. Out of 222 critically reviewed full-text articles, 47 met inclusion criteria for the systematic review and 12 of those were included in the meta-analysis. Results from the meta-analysis represented 354 HIV+, 1141 HEU, and 173 HIV- children for MDI and 352, 1140, and 173 for PDI, from six different countries. The meta-analysis indicated that HIV+ children have much lower MDI and PDI scores compared with both HEU and HIV-children (MDI: mean difference -10.4 and -17.3 with 95% credible intervals (CI) of [-15.4, -5.1] and [-25.7, -9.1], respectively) (PDI: mean difference -15.2 and -23.6, 95%CI [-22.0, -8.4] and [-34.3, -12.8], respectively). HEU children had lower MDI and PDI scores compared with HIV-, but these differences were not as large (MDI: mean difference -7.0, 95%CI [-15.1, 1.4]) (PDI: mean difference -8.4, 95%CI [-19.3, 1.9]). The 32 studies not included in the meta-analysis were evaluated qualitatively, showing a wide range of rates for cognitive and physical delays in the three populations. Significant group differences were commonly seen in developmental domains tested, with HIV+ faring worse.

Conclusions: This is the first meta-analysis comparing domains of early childhood development between HIV+, HEU, and HIV-. HIV+ children had much worse mental and psychomotor outcomes, even when controlling for ART, compared to HEU and HIV-children. HEU children appeared to have worse outcomes compared to HIV- children although differences were small. Increased attention must be given to HIV+ and HEU children to ensure they may reach their full developmental potential.
Abstract 70

Caregiver training to enhance neurodevelopment in HIV-exposed children. Results from a cluster randomized trial in Uganda.


1Department of Psychiatry, Michigan State University, 2Departments of Psychiatry and Statistics and Probability, Michigan State University, 3Department of Mental Health, Johns Hopkins Bloomberg School of Public Health, 4Makerere University

Background: HIV-exposed but uninfected infants are at increased risk for developmental and behavioral problems through the cumulative effect of HIV-related factors (viral and ART exposure in utero) and environmental factors (poverty, trauma) common across Sub-Saharan Africa. Caregivers can play an important role, through quality caregiving, in mitigating the negative effect of these stressors. We report on the effect of a caregiver intervention designed to enhance quality of caregiving on child neuropsychological outcomes.

Materials and Methods: 221 rural HIV-exposed but uninfected (HEU) child (2 to 3 years old) and caregiver dyads in 18 geographic clusters in Tororo District, Uganda were randomized by cluster to receive biweekly individualized sessions of either Mediation Intervention for Sensitizing Caregivers (MISC) training that emphasized quality of caregiving interactions for cognitive stimulation, or Uganda Community Based Association for Child Welfare program that delivered (UCOBAC) health and nutrition training. Children were evaluated at baseline, six months, one year (training conclusion), and one-year post-training with the Mullen Scales of Early Learning (MSEL), and the Behavior Rating Inventory of Executive Function (BRIEF-parent). The Caldwell HOME assessment was completed by observers to gauge caregiving quality after training.

Results: MISC resulted in significantly better HOME caregiving compared to UCOBAC mid-intervention with an adjusted mean difference (Mean adj. Diff.) of 2.34 (95% CI: 1.54, 3.15, p<0.01), post intervention (Mean adj. Diff=2.43, 95% CI: 1.61, 3.25, p<0.01) and at one year follow-up (Mean adj. Diff=2.07, 95% CI: 1.23, 2.90, p<0.01). MISC caregivers reported more problems on the BRIEF for their child at one-year post-training follow-up only (p<0.01). HOME caregiving quality was significantly correlated with MSEL composite (total cognitive) performance one-year post training for both the MISC and the UCOBAC trial arms.

Conclusions: Even though MISC demonstrated an advantage of improving caregiving quality, it did not produce better child cognitive outcomes compared to health and nutrition training. Results suggest that both healthy nutrition and cognitive stimulation coupled with nutritional supplementation are vital for early child development and should be integrated programmatically for HIV-exposed children.

Abstract 71

Neurocognitive outcome at the age of 4 to 9 in HIV-infected, -exposed or -naïve Cameroonian children from the ANRS Pediacam study: a cross-sectional study (PediacamDev- ANRS 12322)

DeBeaudrap P, Tejokem M, Diavolana Koecher D, Pasquier E, Germainaud D, Leroy V, Bodeau Livinec P, Warszawski J, Faye A

1Institut De Recherche Pour Le Développement (IRD), 2Centre Pasteur du Cameroun, 3Médecins Sans Frontières, 4Assistance Publique - Hôpitaux de Paris, 5Institut National de la Santé et de la Recherche Médicale (INSERM)

Background: Despite improved access to combined antiretroviral therapy (cART), studies have shown significant cognitive impairments in perinatally HIV-infected children. However, neurodevelopmental outcomes are poorly explored in children starting cART early during their first year of life or in HIV-exposed uninfected children, and factors related to the
child life environment have not been sufficiently considered. The PediacamDev study (ANRS12322) performed a comprehensive sensorial and neuro-cognitive evaluation of 4 to 9 years-old HIV-infected and HIV-uninfected (HIV-exposed and unexposed) children included before the age of 6 months in a prospective cohort in Cameroon (Pediacam - ANRS12140/12225).

Methods: Between 2007 and 2010, 210 HIV-infected (HI) children initiated on cART before one-year of age, 205 HIV-exposed uninfected (HEU) and 196 HIV-unexposed uninfected (HUU) infants were included in the Pediacam cohort. Of them, 338 children (127 HI, 101 HEU and 110 HUU) aged between 4- and 9-years participated in this cross-sectional evaluation. Cognitive development was assessed using the learning, sequential procession, planning, simultaneous processing, mental processing and the non-verbal indexes of the Kaufman Assessment Battery (KABC-2). Children environmental factors considered in the analysis were household income, quality of the home environment (Home Observatory Measurement of Environment [Home]), maternal education level and maternal anxiety and depression (HAD questionnaire).

Results: All HI children received cART with a median age at initiation of 4.4 months (IQR: 3.3–5.9). Sex ratio was similar between groups (p=0.5) but HI-children were slightly older than uninfected children (+4 months, p<0.001). The proportion of children living in unfavorable environment was highest among HI-children, followed by HEU-children and lowest among HUU-children: higher proportion of deprived household (p<0.001), lower maternal education level (p<0.001) and lower quality of the home environment (p<0.001). Compared to HUU-children, HI-children had significantly lower KABC-2 scores in all domains. Differences adjusted for age, gender, spoken language at home and interviewer identity were: -12.4 [-16.0 to -8.9] for learning index; -12.2 [-16.2 to -8.2] for sequential index; -13.6 [-18.7 to -8.4] for planning index; -11.3 [-14.6 to -7.9] for simultaneous index; -11.7 [-15.2 to -8.3] for non-verbal index; and -16.9 [-20.7 to -13.0] mental processing index. Although smaller, these differences remained also significant when adding adjustment for environmental factors: Learning index: -5.4 [-9.5 to -1.4]; sequential index: -7.1 [-11.7 to -2.4]; planning index: -5.9 [-12.1 to 0.4]; simultaneous index: -6.3 [-10.3 to -2.3], non-verbal index: -3.9 [-7.8 to 0.0] and MPI: -8.7 [- 13.1 to -4.3]. Age at ART initiation <4 months was associated with higher mental processing (+6.0 [0.78 to 11.3]) and sequential (+9.1 [2.9 to 15.2]) indexes. By contrast, in analysis adjusted for environmental factors, scores of HEU-children were not significantly different from those of HUU-children (all p-values>0.1).

Conclusion: Despite early cART initiation, living with HIV infection since birth is associated with poorer neurocognitive scores in childhood even after adjusting for various environmental factors. These results emphasizes the importance of maintaining and reinforcing efforts for the prevention of mother-to-child HIV transmission as well as the need of providing early developmental interventions infants diagnosed with HIV infection.

Abstract 72
Mental health and Suicidality in perinatally HIV-infected adolescents

Buckley J1, Otowome K1, Joyce C1, Hlongwane K1, Violari A1

1Perinatal HIV Research Unit, 2Chris Hani Baragwanath Academic Hospital

Background: Literature suggests a higher prevalence of mental health disorders in HIV-infected individuals. Difficult life circumstances as well as the HIV infection may predispose perinatally HIV-infected adolescents to mental illness. However, irrespective of HIV infection, adolescence is when mental health disorders can manifest for the first time. Therefore, an appropriate comparison group is important to provide context. This study investigates the prevalence of mental illness in HIV-infected adolescents and compares it to HIV-uninfected adolescents from a similar socioeconomic background.

Materials and methods: Between October 2016 and April 2017, HIV-infected adolescents aged 13-19, from Soweto, South Africa, were recruited from a treatment programme, while controls of the same age were recruited from the community. HIV status of the uninfected
participants was confirmed at study entry. The self-administered Patient Health Questionnaire for Adolescents (PHQ-A), Child Post Traumatic Stress Disorder (PTSD) Checklist and Millon Adolescent Clinical Inventory (MACI) tools assessed mental health and personality components. ART adherence was assessed using the Morisky Medication Adherence Scale (MMAS) and pharmacy records. Socio-demographic and virological data were also collected. Descriptive measures including medians and interquartile ranges (IQR) were determined for all variables and compared between groups using the Kruskal-Wallis non-parametric test and logistic regression.

Results: A total of 162 adolescents (50% HIV-infected, 61% female) with a median age of 16 years (IQR: 15-18) were enrolled. 20% of all adolescents had a depressive disorder, 19% in the HIV-infected versus 20% in the uninfected group. Overall, 35% had had suicidal ideation in the preceding two week period, with a higher proportion within the HIV-infected group (42% vs. 28%, p=0.07). All participants with suicidality were reviewed by a psychiatrist and two HIV-infected participants were referred for immediate psychiatric admission. The rest were not actively suicidal at that time and were managed with psychiatric, psychological and social support. A substance abuse/dependence diagnosis was made in 5% of the total population. Overall 22% percent were diagnosed with PTSD symptoms and the prevalence was similar in both groups (23% HIV-infected vs 22% HIV-uninfected). HIV-infected participants had a higher median score in negative personality patterns, relative to HIV-uninfected: Introversive (Median: 68 vs. 60, p=0.015), Avoidant (Median: 64 vs. 58, p=0.07) and Depressive (Median: 68 vs. 63, p=0.038). The odds of suicidality (OR: 1.8, 95% CI: 0.95-3.51; p=0.07) and pessimistic personality patterns (OR: 2.4, 95% CI: 1.1-5.4; p=0.028) were higher in the HIV-infected adolescents relative to the HIV-uninfected. Using the MMAS, no participants scored in the high range for adherence. Interestingly however, 77% had high drug adherence measured from pharmacy returns.

Conclusions: These findings show a high prevalence of depressive disorders, suicidality and PTSD symptoms across both groups of adolescents. The odds of suicidality and pessimistic personality patterns were higher in the HIV-infected population. Further analysis is ongoing to examine the relationship between mental illness and ART adherence and provide suggestions for adherence interventions. Incorporating simpler mental health screening in the care of HIV-infected adolescents will improve detection and treatment of common mental health disorders which may enhance ART adherence and improve long-term outcomes.

Abstract 73
Neurodevelopmental and Behavioral Outcomes in Early Treated HIV-Infected Young Children

Jantarabenjakul W1,2, Srisamer J, Theerawit T3, Sophonphan J1, Chanchaiya W4, Veeravigom M1, Puthanakit T1,2, Anatavoranich J1,2, Jahanshad N1, Thompson P5, Malee K6, Pancharoen C1,2, on behalf of CIPHER-DOET study

1Department of Pediatrics, Faculty of Medicine, Chulalongkorn University, 2Research Unit in Pediatric Infectious Diseases and Vaccines, Faculty of Medicine, Chulalongkorn University, 3The HIV Netherlands Australia Thailand Research Collaboration (HIV-NAT), Thai Red Cross AIDS Research Center, 4SEARCH, The Thai Red Cross AIDS Research Center (TRCARC), 5Henry M. Jackson Foundation for the Advancement of Military Medicine, 6Imaging Genetics Center, Stevens Neuroimaging and Informatics Institute, Keck School of Medicine of USC, 7Ann & Robert H. Lurie Children’s Hospital of Chicago, Northwestern University Feinberg School of Medicine

Background: Antiretroviral therapy (ART) is urgently initiated among HIV-infected infants to reduce mortality. However, data regarding neurodevelopmental outcomes among children with early ART initiation are limited. This study compares neurodevelopmental and behavioral outcomes among children with perinatally-acquired HIV infection (PHIV) who initiated ART within 12 months of life and perinatally HIV-exposed uninfected children (PHEU).

Materials & Methods: This is an observational study of children aged 12-56 months, born to HIV-positive mothers. PHIV children with 2 positive HIV DNA PCR tests, classified as early ART initiation if ART commenced within 3 months of life, and late ART initiation if ART...
began between 3 and 12 months. Age-matched PHEU children had negative HIV DNA PCR at age > 4 months or anti-HIV negative at age > 12 months. Neurodevelopmental outcomes were assessed with the Mullen Scale of Early Learning (MSEL); behavioral outcomes were evaluated through parent report on the Child Behavioral Checklist (CBCL). Primary caregivers were interviewed for social history and parenting style. Primary outcome is rate of global developmental impairment, defined by MSEL Early Learning Composite (ELC) Score of < 70. Factors associated with global developmental impairment were analyzed by logistic regression model. Prevalence of significant behavioral problems among PHIV and PHEU children were compared by ANOVA.

**Results:** From November 2016 to April 2017, 95 children were enrolled (13 early ART PHIV, 11 late ART PHIV, 71 PHEU children). Median (IQR) age was 28 (24-32) months. Median (IQR) age at ART initiation was 2.2 (1.6-2.7) months among early ART and 5.5 (4.2-6.3) months among late ART. 17/24 (71%) had undetectable HIV-RNA at the time of assessment. There were no differences in primary caregiver type, education, and income between PHIV and PHEU. Prevalence of global developmental impairment (ELC <70) was 8% in early ART, 45% in late ART and 10% in PHEU, p=0.005. Children with later ART achieved significantly lower scores than PHEU children on the ELC and in multiple developmental domains, including gross motor, fine motor, visual reception and expressive language. No significant composite or domain score differences were observed between children with early ART and PHEU children. Factors associated with global developmental impairment by univariate logistic regression were Z-score height for age < -1.5 (OR 4.55), HIV infection (OR =3.1), preterm (34-37 weeks) (OR =3.2), and permissive parenting style (OR =2.4), p<0.05. However, only Z-score height for age was statistically associated (aOR 4.61, p=0.03) in multivariate analysis. No significant group differences were observed in CBCL internalizing, externalizing or total behavioral problems. Among individual behavioral problems, anxious/depressed mood was reported more often regarding children with late ART initiation (45% in late ART, 23% in early ART and 10 % in PHEU, p=0.008).

**Conclusion:** Early initiation of ART appears to mitigate HIV-related global developmental impairment and behavioral problems among young children with PHIV. However, children with later ART initiation remain at risk for lower developmental functioning in multiple domains compared to PHEU children. Ongoing follow-up is essential to confirm the developmental efficacy of early ART among children with PHIV.

**Abstract 74**

Neurodevelopmental effects of type of antepartum and postpartum PMTCT ARV exposure on Ugandan and Malawian PROMISE HIV-exposed uninfected children at 12, 24, and 48 months of age

Boivin M1,2, Wambuzi Ogwang L3, Kawalazira R4, Maliwichi-Senganimalunje L5, Sikorski A1, Familiar-Lopez E, Kuteesa A2, Nykato M3, Mutebe A6, Makiteni M7, Mallewa M7, Aizire J1, Taha T7, Ruizier-Escudero H1, Fowler M8

1Michigan State University, 2University of Michigan, 3Makerere University - Johns Hopkins University, 4Malawi College of Medicine - Johns Hopkins University, 5University of Malawi - Chancellor's College, 6Global Health Uganda, 7Johns Hopkins University Bloomberg School of Public Health, 8Johns Hopkins University Medical Institute

**Background:** Despite WHO guidelines recommending antepartum and postpartum (if breast feeding) Triple-ARV for the prevention of mother-to-child transmission (PMTCT) of HIV, neurodevelopmental risk to infants for such exposure is unknown. Over 80% of children in the Promoting Maternal and Infant Survival Everywhere (PROMISE) Blantyre Malawi (N=188) and Kampala Uganda (N=208) study sites (2 of 14 sites) who were HIV-exposed but uninfected (birth weight above 2000 grams) were enrolled between 9 and 12 months of age for assessment of neurodevelopmental outcomes in response to the ARV trial arms for both antepartum and postpartum PMTCT.
Methods: At 12, 24, and 48 months of age, the Mullen Scales of Early Learning (MSEL) was used to evaluate children on the basis of the following treatment arms. During pregnancy, HIV-infected mothers were randomized to Triple-ARV prophylaxis (3TC-ZDV/LPV-RTV; MSEL available for N=178 or FTC-TDF/LPV-RTV; N=37) or Zidovudine (ZDV; N=178). Most of these mother/newborn dyads were then randomized postpartum to either maternal Triple-ARV (MSEL available for N=186) or infant Nevirapine (NVP; N=186), continuing on their trial arm regimen throughout breast feeding.

Results: Antepartum ARV regimen did not differ significantly on MSEL composite cognitive ability at age 12 months (p=0.89), but did at 24 months (p=0.02), with FTC-TDF/LPV-RTV exposed children doing significantly more poorly than Zidovudine. MSEL expressive language differences were not significantly different among treatment arms at 12 (p=0.84) or 24 (p=0.27) months, but were at 48 months (p=0.03), with antepartum 3TC-ZDV/LPV-RTV doing more poorly. Antepartum trial arms did not differ significantly for the MSEL gross motor, fine motor, visual reception, or receptive language scales at any of the three assessment points. Postpartum treatment arm did not differ significantly on any of the MSEL measures. For antepartum by postpartum treatment arm interaction effects, antepartum FTC-TDF/LPV-RTV followed by postpartum maternal triple ARV produced the worst, and ZDV followed by infant Nevirapine produced the best mean MSEL composite cognitive performance scores at 24 months (p<0.01).

Conclusions: These findings support the need for continued neurodevelopmental monitoring of HEU African children throughout early childhood so as to more conclusively assess the neurodevelopmental risk of both antepartum and postpartum (during breast feeding) triple-ARV exposure.

Abstract 75

Children and HIV in Nigeria: Prevalence, patterns and correlates of emotional and behavioral comorbidity

Adejumo O1, Malee K2, Hunter S3, Oladokun R4, Brown B4, Omigbodun O1,5, Ogunniyi A6, Robertson K7, Taiwo B8

1Centre For Child And Adolescent Mental Health, University of Ibadan, 2Department of Psychiatry and Behavioral Sciences, Feinberg School of Medicine, Northwestern University, 3Department of Psychiatry and Behavioral Neuroscience, Biological Sciences Division, Pritzker School of Medicine, The University of Chicago, 4Department of Paediatrics, College of Medicine, University of Ibadan, 5Department of Psychiatry, College of Medicine, University of Ibadan, 6Department of Neurology, College of Medicine, University of Ibadan, 7Department of Neurology, University of North Carolina, 8Division of Infectious Diseases, Center for Global Health, Feinberg School of Medicine, Northwestern University

Background: With effective treatment, children with perinatally acquired HIV are reaching adolescence and adulthood in increasing numbers. Emotional and behavioural problems (EBPs) are observed among children and adolescents with perinatally-acquired HIV infection (pHIV youth) across cultures. We characterized EBPs and their correlates in a cohort of pHIV youth in South-West Nigeria, in comparison to a non-infected, unexposed (HUU) group.

Materials and Methods: Data were collected from 102 pHIV and 101 HUU at entry into the Ibadan Cohort Study on NEUROAIDS in Children (ICONIC), a longitudinal cohort (aged 8 to 15 years) at the University College Hospital, Ibadan, South-West Nigeria. The pHIV and HUU groups had similar age and socioeconomic status, and resided in two communities within Ibadan. EBPs, defined as borderline and/or clinically significant problems on the caregiver-reported Child Behavior Checklist (CBCL) were assessed using age- and gender-standardized norms from the CBCL multicultural supplement. Clinical and sociodemographic variables were obtained using a structured parent interview and patient records, and caregiver depression was assessed using the Centre for Epidemiological Studies Depression Scale Revised (CESD-R).
CBCL problem and syndrome scale mean scores were compared using independent t tests, and univariate and multivariate analyses of EBP correlates were conducted with logistic regression.

Results: Among paHIV youth, 10.8% had EBPs in the borderline or clinical range, compared to 3.9% of comparison youth (p=0.014). Significant differences were detected in the Attention problems and Aggressive Behaviour subscales (7.8% vs 1.0%, p=0.001) and (12.7% vs 2.0%, p< 0.001) for paHIV and HUU respectively. Compared to paHIV youth between 8 and 11 years (N=76/102), more of those above 11 years (N=26/102) had Social Problems (19.2% vs 3.9%; p=0.024) and Thought Problems (15.4% vs 2.6%; p=0.036). Among biomedical and psychosocial variables, caregiver depression only was associated with CBCL Total Problem Scores in the borderline and clinical range for paHIV youth (OR 1.1, 95% CI 1.02-1.14; p=0.013).

Conclusions: EBPs, especially externalizing problems, are more prevalent among paHIV than HUU children in Nigeria and are associated with caregiver depression. With ongoing access to combination antiretroviral therapy, paHIV children in Nigeria require comprehensive health care, early diagnosis of existing EBPs, and family focused, evidence-informed mental health treatment and prevention programmes.

Abstract 76

Impact of caregiver depression symptoms over time on child neurocognitive development among infants of mixed HIV status in Uganda

Ruiseñor-Escudero H1, Familiar I1, Sikorski A12, McIvor-Murray S2, Boivin M1, Nakasujja N4, Opoka R5, Bass J6

1Department of Psychiatry, Michigan State University, 2Department of Statistics and Probability, Michigan State University, 3Mental Health Department, Johns Hopkins Bloomberg School of Public Health, 4Department of Psychiatry, Makerere University College of Health Sciences, 5Department of Pediatrics, Makerere University College of Health Sciences

Background: Depressive symptoms are frequent among HIV+ women, negatively impacting their health and possibly that of their young children through diminished caregiving. We aimed to evaluate how severity of depression symptoms in HIV+ Ugandan women is related to neurocognitive development of their young children.

Methods: Data come from 149 HIV+ women receiving a year-long, health and nutrition curriculum in Eastern Uganda developed by the Community Based Association for Child Welfare. Each woman was the primary caregiver of a 2-5 year old child who was living with HIV or HIV exposed but uninfected (HEU). We assessed changes in depression symptoms over time using the Hopkins Symptom Checklist-25 (HSCL) at 4 time points: baseline, 6-, 12-, and 24-months after initiating the curriculum. Severity of depressive symptoms at each time point was categorized as high or low based on established cut-off. Children were assessed at the same time points with the Mullen Scales of Early Learning (MSEL) and the Color-Object Association Test (COAT) for memory. In longitudinal analysis, linear mixed effects models related four repeated measures child scores in the MSEL and COAT domains to high/low categories of symptoms of depression as a time-varying covariate, while adjusting for child’s HIV status, age, gender, caregiver’s age, and wealth index.

Results: Women were on average 33 years old, 80% had at least some education, and 71% were married. During follow-up, 56% of women had high symptoms of depression at two or more time points. Prevalence of severe depression increased from 22% to 43% between the 12- and 24-month follow-ups. In the longitudinal analysis high depression symptomatology was associated with lower Visual Reception (β=- 1.65, standard error 0.84, p=.05) and lower immediate recall scores on the COAT (β=- 1.10, standard error 0.56, p=.05).

Conclusions: Our findings are suggestive that caregiver depression symptoms can have a negative impact on infant neurodevelopment, particularly in processing and memory domains. More than half of the sample experienced high depression symptomatology during the 24-month follow-up. Results support the view of program guidance for HIV-affected children towards family-oriented care with
emphasis on caregiver’s well-being and improving their abilities to provide for the child as tenants for optimal child development.

Abstract 77

Postpartum transfer of HIV-infected women initiating antiretroviral therapy (ART) during pregnancy in an integrated antenatal care (ANC)/ART service in Cape Town, South Africa: a cohort study

Phillips T1,2, Brittain K1,2, Zerbe A3, McIntyre J4,5, Petro G5, Abrams E6,7, Myer L1,2

1Division of Epidemiology & Biostatistics, University Of Cape Town, 2Centre for Infectious Diseases Epidemiology & Research, University of Cape Town, 3ICAP, Columbia University, 4Anova Health Institute, 5Department of Obstetrics & Gynaecology, 6College of Physicians & Surgeons, Columbia University

Background: Integrated ANC/ART services are commonplace in high-burden settings and require transfer to general ART care postpartum. Given the challenges in engaging postpartum women on ART, we examined how postpartum transfer of ART services influenced engagement in general ART care.

Methods: Consecutive HIV-infected pregnant women initiating ART in an integrated, public-sector ANC/ART service were followed from ART initiation through 20 months postpartum in the MCH-ART study. Referral from ANC/ART services occurred 0-13 months postpartum, with women referred to their nearest general ART clinic. Data on ART initiation and ANC/ART visits were abstracted from routine records, with time in ANC/ART clinic measured from ART start date to date of postpartum referral to general ART clinics. Electronic ART pharmacy refill (PR) was obtained through 20 months postpartum from all ART services in the Western Cape Province. Analyses used product-limit methods and Poisson models to evaluate predictors of successful transfer to ART care (defined as PR ≤3 months post-transfer).

Results: Among 486 women included, the median age was 28 years and median time in the integrated ANC/ART clinic before transfer was 276 days. Overall, 54% of women successfully transferred. Increased time in the integrated ANC/ART clinic was strongly associated with successful transfer (Figure, p< 0.001). After adjusting for age, gestation at ART initiation, relationship status, timing of HIV diagnosis and design effect, each additional month in the integrated ANC/ART clinic increased the likelihood of successful transfer by 7% (RR and 95%CI: 1.07 [1.04-1.10]). Women with >6 months in the ANC/ART clinic were 1.52 and 1.28 times more likely to transfer successfully than women in the ANC/ART clinic < 3 and 3-6 months (RR and 95%CI: 1.52 [1.07-2.16] and 1.28 [1.04-1.57], respectively).

Conclusions: While successful postpartum transfer appears low, raising concerns about disengagement from care after delivery, these data suggest that increasing total time in integrated ANC/ART services could be an important determinant of successful transfer.

Abstract 78

Real-world use of newly authorised antiretrovirals in pregnancy in the UK/Ireland and available safety data

Rasi V1, Thorne C1, Peters H1, Sconza R1, Francis K1

1UCL- Institute of Child Health

Background: In the UK and Ireland, the mother-to-child-transmission rate is <0.4%, reflecting a high proportion of women conceiving whilst receiving antiretroviral therapy (ART) (60% in 2012-14) and earlier start of ART in women untreated at conception. Data on safety and pregnancy outcomes in women taking newly authorised antiretrovirals are limited as pregnant women are excluded from registrational trials. Regulatory entities such as the EMA have specific pharmaco-
vigilance activities to assess risk of exposure in pregnancy and lactation, including the inverted black triangle (▼) label given to products requiring additional monitoring due to being new to market or with limited data on long-term use.

**Materials and methods:** Data on three newly registered drugs from different classes, Rilpivirine (RPV), a NNRTI, Dolutegravir (DTG), an INSTI, and Cobicistat (COBI), a booster, were assessed using two main data sources: the EMA public database (the European Public Assessment Reports and the Summary of Product Characteristics) for safety information, and the National Study of HIV in Pregnancy and Childhood (NSHPC), a comprehensive population-based surveillance study on all HIV-positive pregnant women seen for care in the UK and Ireland. Data on pregnancies reported to the NSHPC with estimated date of delivery (EDD) from 1st January 2013 to 31st March 2017 were included.

**Results:** EMA data showed the three drugs to have very different warnings and recommendations. For RPV as Edurant or Eviplera (RPV/FTC/TDF) recommendations are “not to use” while pregnant despite no preclinical findings of specific hazard. The black triangle label applies to both DTG as Tivicay or Triumeq (ABC/3TC) and COBI as Tybost or Stribild (EVG/COBI/FTC/TDF). DTG can cross the placenta while COBI shows some reproductive toxicity, therefore recommendations are to use these “only if clinical condition request it”. For the “real-life” data from the NSHPC: of 4831 pregnancies included, 343 (7%) were exposed to one of the three drugs: 33 (0.7%) to COBI-boosted regimen, 198 (4%) to a RPV-based regimen and 112 (2%) to a DTG combination. Of the 343 pregnancies, 240 (70%) were conceived on these drugs and for 97 (28%) there was antenatal initiation. Of 4526 pregnancies reported with EDD from 2013 to 2016, those conceived on RPV-combinations increased >10-fold (from 0.5% in 2013 to 5.6% in 2016). Between 2015 and 2016, the proportion of pregnancies conceived on DTG-combinations increased from 0.3% to 3.3%. Among the total 343 pregnancies, there were 241 livebirths (156 [65%] exposed from conception), 24 spontaneous abortions, 2 ectopic pregnancies, 7 terminations (3 with birth defects), 2 stillbirths, 3 pregnancies lost-to-follow-up and 63 pregnancies continuing to term. There were 4 (1.7%) birth defects reported among the livebirths.

**Conclusions:** Linking EMA recommendations with the NSHPC real world data shows the potential to improve some of the safety recommendations based on clinical findings. This is in line with regulators’ recent course of action of merging information from post-authorisation phase studies with real world use, in order to assure patients and clinicians that benefits outweigh risks, whilst offering patients the most effective and safe treatment options.

**Abstract 79**

**Stillbirth in HIV-infected women delivering in UK/Ireland between 2007 and 2015**

Favarato G1, Sconza R1, Peters H1, Horn A1, Francis K1, Bailey H1, Tookey P1, Thorne C1, on behalf of the UK/Ireland National Study of HIV in Pregnancy and Childhood (NSHPC)

1UCL Great Ormond Street Institute of Child Health

**Background:** Stillbirth (SB) has multifactorial and incompletely understood causes. We previously reported that HIV-infected women delivering in the UK/Ireland had higher SB rates than the general population, at 1.1% in 1990-2006. Our aim is to assess the updated SB rate and associated risk factors in HIV-infected women.

**Materials & Methods:** The NSHPC conducts comprehensive active surveillance on all HIV-positive pregnant women seen for care in the UK and Ireland, via named respondents in maternity units. We analysed data from singleton deliveries in 2007-2015 reported up to December 2016 and defined a SB as a baby delivered at ≥24 gestational weeks (GW) and reported as a stillbirth by the respondent. We performed multivariable Poisson regression with random effect to account for repeated pregnancies in the same mother to investigate whether maternal age, country of origin, delivery year, injecting drug use (IDU) history, parity, first antenatal CD4 count ≤350cells/µL, antenatal ART regimen and late antenatal
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Results: There were 10,316 singleton pregnancies delivered at ≥24GW in 8069 mothers; 75.4% of mothers were born in Sub-Saharan Africa (SSA); 49.4% pregnancies (4915) were conceived on ART. The most common antenatal ART regimens were PI/r (5454, 55.0%) and NNRTI-based (2427, 24.5%); specific regimen was unknown in 4.6% pregnancies. MTCT was reported in 43 (0.4%) cases. There were 89 (0.9%) SB. Compared to live births (LB) SB were more likely to be male (39/67 [58.2%] vs 5164/10290 [50.2%]), delivered pre-term (median 33 [IQR 27-37] GW vs 39 [IQR 38-40] GW) and to be SGA (34/62 [54.8%] % vs 2208/9982 [21.1%]). Among the 61/89(68.5%) SB and 10000/10316 (96.9%) LB with data on congenital abnormalities, 9/61 (14.8%) and 285/10000 (2.9%) had congenital abnormalities respectively. Multivariate analysis suggested significant risk factors associated with SB were antenatal CD4 count ≤350 cells/µL (IRR 1.73, 95%CI 1.05, 2.86), mother being primiparous (IRR 1.85, 95%CI 1.10, 3.12), older (IRR for age>36 years vs age<28 years: 4.12, 95%CI 1.49, 11.35) and originating from SSA (IRR for SSA vs Europe/Western Countries: 3.26, 95%CI 1.07, 9.95) or other world region (IRR for Other vs Europe/Western Countries: 5.59, 95%CI 1.46, 21.48). Type of antenatal ART regimen, conceiving on ART, delivery year, IDU history and late antenatal booking were not significantly associated with SB.

Conclusions: Despite continued declines in MTCT rates over this period (2007-2015) and increases in the proportion of women conceiving on ART and delivering with suppressed viral load, the SB rate (0.9%) did not decline and remained consistently higher in HIV-positive women than in the general population (0.5% in England/Wales for the same period). Limitations included lack of data on some important risk factors for SB (e.g. maternal BMI, socio-economic status, smoking), missing data for some SB infants and limited ability to classify SB as antepartum or intrapartum. To further understand the circumstances and risk factors for SB in HIV-infected women, the NSHPC plans to undertake an audit of pregnancies ending in SB (following established methodology used in an ongoing audit of cases in which MTCT occurred).

Abstract 80

The Immunological basis of preterm delivery in HIV infection: an exploration of systemic immune activation

Short C1, Quinlan R1, Shattock R1, Bennett P1, Taylor G1, on behalf of the London HIV Pregnancy Research Group (LHPRG)

1 Imperial College London

Background: We hypothesise that elevated rates of preterm delivery (PTD) observed in HIV-infected pregnant mothers, are likely to be driven by changes in immunological tolerance of the feta-placental unit, reflected by high levels of systemic immune activation. This study sought to characterise immunological profiles of HIV uninfected and infected mothers throughout gestation, compare by timing and class of combination antiretroviral therapy (cART) and to explore correlations with gestational age at delivery.

Materials & Methods: A multi-site, prospective, observational study of HIV-infected and uninfected mothers. Exclusion criteria: CD4 count <350 cells/µL, multiple or in-vitro fertilisation pregnancy, injecting drug use. PBMCs were isolated at 5 time points (14-21, 22-25, 26-31, 32-37, ≥38 weeks). Flow cytometry was performed for T-cell surface markers: CD4, CD8, HLA-DR and CD25. Median (IQR) were calculated for each lymphocyte sub-population and compared by group using Mann-Whitney U test. Spearman’s correlation coefficient was used to evaluate correlations with gestational age at delivery.

Results: Since November 2013 31 HIV uninfected and 63 HIV-1 infected pregnant women were recruited. Of the latter, 23 received Protease Inhibitor (PI)-based cART, 5 of whom initiated cART in the second trimester and 40 received non-PI cART, 7 of who initiated cART in the second trimester (3ABC/3TC/ZDV, 2RAL/FTC/TDF, 2DOL/ABC/3TC).

Preterm Delivery. Eight HIV-infected women (13%) and two uninfected (7%) delivered <37weeks. Of the HIV-infected mothers: four had preterm prelabour rupture of membranes
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Adverse pregnancy outcomes among HIV-positive pregnant women receiving antiretroviral therapy in Kenya: early results from a cluster randomized behavioral intervention study.

Abuogi L1, Helova A2, Owuor K3, Bukusi E3, Odeny T3,4, Onono M3, Turan J2

1Department of Pediatrics, University of Colorado Denver, 2Department of Health Care Policy and Organization, School of Public Health, University of Alabama at Birmingham, 3Kenya Medical Research Institute, The Research Care and Training Program, Center for Microbiology Research, 4Department of Epidemiology, University of Washington

Introduction: The scale up of life-long antiretroviral treatment (ART) for all pregnant and breastfeeding women living with HIV (WLWH) has the potential to facilitate elimination of mother-to-child transmission (MTCT) and improve the health of WLWH. However, there are growing concerns about adverse pregnancy outcomes (APO) for women on ART.

Methods: A total of 537 pregnant WLWH enrolled in the Mother-Infant Visit Adherence and Treatment Engagement (MOTIVATE) study in three high HIV prevalence counties in southwestern Kenya between January 2015 to March 2017 were included. Baseline perinatal mortality in the region is 28 per 1000 births. This study is a cluster-randomized trial with a 2X2 factorial design testing the impact of community mentors, text messages, both interventions, or standard of care on retention in care and antiretroviral treatment (ART) adherence among HIV-positive pregnant/postpartum women. Per Kenya national guidelines viral load of <1000 copies/ml is considered virally suppressed. Women with an adverse pregnancy outcome (miscarriage, stillbirth, neonatal death, infant death, preterm delivery, or low birth weight) by March 31, 2017 were compared with women with live birth at least 30 days postpartum without adverse outcomes using univariate and multivariate analysis. Logistic regression analysis was conducted accounting for

(PPROM) and four were induced two for intra-uterine growth restriction (IUGR) and two for fetal distress. One uninfected woman had PPROM and the second was induced for IUGR.

T-cell activation. Median baseline CD4+ cell count, cells/mm3 (%), was lower in HIV-1 infected pregnant women than uninfected pregnant women 611 (IQR 495-710) (36%) v 941 (IQR 863-1147) (50%), p<0.0001. There was no difference in baseline CD8+(%) cell count between infected and uninfected women (669 (IQR 525-871) (40%) v 603 (IQR 440-760)(30%), p=0.16). Median CD4/CD8 ratio was lower across gestation in HIV-1 infected mothers compared to uninfected (1.0 (IQR 0.9-1.2) v 1.8 (IQR 1.4-2.2), p<0.0001). Median baseline CD8+HLADR+ was 26% (IQR 16-35) in HIV-1 infected women compared to 14% (IQR 8-20), p=0.001 in uninfected women. Activated CD8+ cells (%HLA-DR+) were ≥1.5 fold higher in HIV-infected women across gestation, p<0.01.

Mothers who initiated cART post-conception had lower CD4/CD8 ratios throughout pregnancy 0.52 (IQR 0.44-0.99) compared with those who conceived on cART 1.04 (IQR 0.76-1.22),p<0.0001 and higher frequency of activated CD8 cells (HLADR+) 34% (IQR 25-44) v 24% (IQR 15-33), p<0.0001. No significant differences were observed by PI-exposure pre and post-conception. CD8+ activation was higher in women conceiving on PI-cART compared to non PI-cART (27% (IQR 19-33) v 21% (IQR13-33), p=0.036).

Gestational age at delivery correlated positively with CD4/CD8 ratio (r=0.235, p<0.0001) and inversely with total CD8 (r= -0.195, p=0.001), CD8% (r=-0.261, p<0.0001 and %CD8+HLADR+ Tcells (r=-0.141,p=0.02).

Conclusions: High levels of systemic T-cell activation are observed in HIV-infected mothers especially untreated, persist despite pre-conception cART, particularly in those conceiving on PI-cART. The correlation with gestational age at delivery suggests underlying immune dysregulation contributes to excess PTD observed with HIV infection.
clustering by site using generalized estimating equations.

Results: Among 537 HIV-positive pregnant women median age 28.8 years (IQR 24.8 – 32.8), 199 women (37.1%) experienced an adverse pregnancy outcome. Of these events, 33 (16.0%) were fatal, including stillbirths, miscarriages, and neonatal or infant deaths. The perinatal mortality rate was 47.4 per 1000 live births. Additionally, there were 155 preterm deliveries and 18 low birth weight infants. Most women (96%) were on non-nucleoside based ART with 91% of these on tenofovir-based regimens versus 9% on zidovudine. A total of 436 (79.4%) of women were diagnosed with HIV prior to pregnancy and median months on ART was 28.7 (IQR 14.5 - 49.7). In bivariate analysis, neither starting ART pre- vs post-conception, ART regimen, nor time on ART was associated with APO. Of 351 women with viral load available, 324 (92.3%) had < 1000 copies/ml. Women with baseline viral load >1000 copies/ml had higher rates of APO as compared to women with <1000 copies/ml, but this was not statistically significant. After adjusting for woman’s age, parity, hemoglobin, viral load there were trends towards increased odds of APO for every year increase in age (adjusted odds ratio (aOR) 1.02, 95% confidence interval (95% CI) 0.97, 1.07) and a potential protective effect of higher levels of hemoglobin (aOR 0.96, 95% CI 0.92, 1.00).

Conclusions: Pregnant women on ART in this region experience high rates of perinatal mortality, as well as preterm births and low birth weight infants. Enhanced surveillance among cohorts of pregnant women on ART and interventions to reduce adverse pregnancy outcomes in this population are needed.

Abstract 82

In-utero ART exposure and birth and early growth outcomes amongst HIV exposed uninfected infants attending immunization services: Results from national PMTCT surveillance, South Africa

Ramokolo V1,6, Goga A1,2, Lombard C3, Doherty T1,4, Jackson D1,5, Engebretsen I6

1Health Systems Research Unit, South African Medical Research Council, 2Department of Paediatrics and Child Health, Kalafong Hospital, University of Pretoria, 3Biostatistics Unit, South African Medical Research Council, 4School of Public Health, University of the Western Cape, 5UNICEF, 6Department of Global Public Health and Primary Health Care Centre for International health, University of Bergen

Background: Conflicting results have been reported on the effect of maternal antiretroviral treatment (ART) use in pregnancy on birth outcomes in resource-limited settings. We studied the effect of infant in-utero HIV and ART exposure on preterm delivery (PTD), low birth weight (LBW) and small-for-gestational age (SGA) at birth, and underweight-for-age (UFA) at six weeks postpartum.

Methods: We studied 6179 HIV unexposed (HUU) and 2599 HIV exposed uninfected (HEU) infants in a national facility-based cross-sectional survey, the South Africa Prevention of Mother to Child Transmission Evaluation study, which was conducted between October 2012 and May 2013. HEU infants were stratified into three antiretroviral (ARV) drug exposure groups: (i) maternal ART further subdivided by timing of initiation, (ii) maternal antenatal Zidovudine (ZDV) as prophylaxis, (iii) None: no ARV use. Outcomes included preterm delivery (PTD), low birth weight (LBW), small-for-gestational age (SGA) and underweight-for-age (UFA) at six weeks postpartum. Multivariable logistic regression was used to assess the effect of HIV and ARV exposure on these outcomes.

Results: Multivariable regression demonstrated higher odds of PTD (adjusted
odds ratio [AOR], 1.2; 95%CI, 1.0, 1.5) p=0.03, LBW (1.6; 1.3, 1.9) p<0.001, SGA (1.3; 1.1, 1.6) p<0.01, and underweight (1.4; 1.2, 1.7) p=0.001 in HEU than HUU infants. In the analysis of HEU infants, those in the None group or those whose mothers initiated ART pre-conceptually had almost twice the odds of PTD, (1.8; 1.2, 3.0 [p=0.02]) and (1.7; 1.1, 2.5 [p=0.02]) respectively, than infants whose mothers started ART post-conceptually.

Conclusions: HIV exposure was significantly associated with increased PTD, LBW, SGA and underweight. Among HEU infants, pre-conception initiation of ART and untreated maternal HIV infection were associated with increased risk of PTD but not LBW, SGA and underweight.

Abstract 83

Methods of gestational age assessment influence the observed association between ART exposure and preterm delivery: a prospective study in Cape Town, South Africa

Malaba T1,2, Newell M3, Madlala H1,2, Perez A1,2, Gray C4, Myer L1,2

1Division Of Epidemiology and Biostatistics, School of Public Health and Family Medicine, University of Cape Town, 2Centre for Infectious Disease Epidemiology & Research, School of Public Health and Family Medicine, University of Cape Town, 3Faculty of Medicine, University of Southampton, 4Division of Immunology, Institute of Infectious Disease Medicine, University of Cape Town

Background: The association between antenatal ART and preterm delivery (PTD) in HIV+ women is controversial and has not been reliably quantified. Measuring gestational age (GA) is challenging in resource-limited settings; different methods could explain heterogeneous findings. We examined impact of GA estimation methods on observed PTD deliveries rates, by maternal ART.

Materials & Methods: Between April 2015 and October 2016 we enrolled consecutive women regardless of HIV status seeking antenatal care at a large primary care antenatal clinic in Cape Town, South Africa into the The Prematurity Immunology in HIV-infected Mothers and their infants Study (PIMS). As part of routine antenatal services, public sector midwives estimated GA by last menstrual period (LMP) and symphysis-fundal height (SFH); separately, obstetric ultrasound was performed by a research sonographer blinded to midwife GA assessment if clinical GA was <24w. Analyses compared GA estimated by ultrasound, SFH and LMP; the association between HIV/ART status and PTD was examined by GA assessment method using multivariable logistic regression.

Results: Of 1060 women in the cohort who have delivered at the time of analysis (median age 28y; 46% HIV+ of whom 48% initiated ART pre-conception vs 52% initiated during pregnancy), 82% had LMP-based GA, 71% SFH-based GA, 58% ultrasound-based GA and 54% (n=576) had GA based on ultrasound and at least one other method. At first ANC visit, estimated median (IQR) GA was 18w (12-23w) by LMP, 23w (18-28w) by SFH and 17w (13-21w) by ultrasound. Overall PTD <37w was observed in 41% by LMP, 27% by SFH and 12% by ultrasound. In 1037 live singleton births (mean birthweight 3124g; 10% SGA <10th centile), PTD risk was doubled for HIV-infected compared to HIV-uninfected women for ultrasound-based GA (OR=2.01, 95%CI=1.15-3.51); but for LMP/SFH-based GA the association was not significant. These differences between GA assessment methods persisted after adjustment for age, parity, height and previous PTD; PTD risk did not vary by ART initiation timing for any GA method.

Conclusion: Our results suggest that findings for an association between HIV/ART and PTD are substantially influenced by GA assessment method. With growing scientific interest in this association, future research efforts should seek to standardize optimal measures of gestation.
Abstract 84

Longer-term health outcomes of HIV-exposed and HIV-unexposed children and their mothers enrolled in the 2012-13 national six week South African PMTCT Evaluation

Chirinda W1, Singh Y1, Ramraj T1, Ngandu N1, Noveve N1, Maduna V2, Vundli V1, Bhardwaj S2, Goga A1,3

1South African Medical Research Council, 2United Nations Children’s Fund (UNICEF), 3Department of Paediatrics, University of Pretoria

Introduction: The number of HIV-exposed, uninfected (HEU) infants is expected to increase, as more HIV infected pregnant women gain access to antiretroviral treatment (ART) to prevent mother-to-child transmission (MTCT) and for improving their own health. This study aimed to document the longer-term health and survival outcomes, after 18 months, amongst HIV exposed and HIV unexposed infants, enrolled in a nationally representative PMTCT effectiveness study, and determine factors associated with these outcomes.

Methods: A cross sectional telephonic survey of a national cohort of mothers and babies who participated in the 2012-14 South African Prevention of Mother-To-Child Transmission Evaluation (SAPMTCTE) was conducted. This cohort consisted of 2644 (94% of eligible) HIV exposed uninfected infants who were enrolled at six weeks (baseline) for follow up until 18 months between October 2012 and September 2014. A comparison group of HIV unexposed infants were identified from participants enrolled in the baseline 2012-13 national six week cross sectional SAPMTCTE (n=6843) which occurred between October 2012 and May 2013. Sample size (n=768 per arm) was calculated to compare longer-term outcomes amongst HIV exposed and unexposed infants. Ten trained data collectors conduct telephonic interviews with participants between January and May 2016. All information was self-reported. Descriptive statistics were used to summarize the data. Outcomes amongst HIV exposed and HIV unexposed infants were compared using chi-square tests or Fishers Exact tests for categorical variables and Kruskal-Wallis tests for continuous variables.

Logistic regression was used to evaluate the association between maternal and child health and survival outcomes and background risk factors and PMTCT services.

Results: We interviewed a randomly selected sample of caregivers of 811 HIV exposed and 970 HIV unexposed children, with mean age 3.5 years postpartum. Twelve (75%) and 4 (25%) (p=0.017) maternal deaths were reported for HIV exposed and HIV unexposed children, respectively, between February 2013 and April 2016. In total 43 children were reported to have died since baseline through March 2016, of which 26 (60.5%) were HIV exposed and 17 (39.5%) were HIV unexposed (p=0.047). 21 (3.0 %) children were reported to be HIV positive, and of these 18 (85.7%) were reported to be on ART. Among the HIV infected 89 (78.8%) had ever been diagnosed with TB compared to 24 (21.2%) among HIV uninfected (p<0.001). Surprisingly, HIV exposed children were less likely to have experienced recent morbid events (adjusted Odds Ratio aOR 0.46; 95%CI: 0.35-0.59) and hospitalization (aOR 0.51; 95%CI 0.30-0.86), after adjusting for maternal age survival status and education, and duration of breastfeeding.

Conclusion: Though ascertainment bias is likely, our longer-term follow-up results of a randomly selected sample drawn from a nationally representative sample, demonstrate adverse health and survival outcomes among HIV exposed infants compared with HIV unexposed, and HIV infected mothers compared with uninfected. Linkages to care, and good quality, regular postnatal care amongst HIV infected mothers should be prioritized.
Abstract 85

Near Real-Time Tracking of PMTCT Gaps in Three Districts of KwaZulu Natal Province, South Africa

Moyo F1,2, Haeri Mazanderani A1, Bhardwaj S3, Mhlongo O2, Kufa-Chakezha T1, Ng'oma K4, Smith B2, Sherman G1,2

1 Centre for HIV & STIs, National Institute for Communicable Diseases, 2 Department of Paediatrics and Child Health, University of the Witwatersrand, 3 UNICEF, 4 Department of Health, Province of KwaZulu Natal

Background: Over the past decade South Africa has seen significant reduction in early infant transmission of HIV from >20% to <2%. Progress is likely on account of increased access to effective maternal combination antiretroviral therapy (cART) and infant prophylactic regimens within the prevention of mother-to-child transmission (PMTCT) programme. Understanding PMTCT gaps that continue to fuel transmission rates will fast-track the last mile to eMTCT of HIV and mobile health technologies hold the key to rapidly identifying gaps for intervention.

We describe findings from an operational follow-up study that investigated in near real-time, PMTCT gaps among HIV-infected infants aged <18 months in three districts of KwaZulu-Natal Province.

Methods: Between May and September 2016, PMTCT co-ordinators from eThekwini, uMgungundlovu and uMkhanyakude districts received daily email notifications of all HIV PCR-positive results in their district, including patient identifying details and the name of the health facility from which the sample originated. Co-ordinators reviewed facility records for each infant to answer five questions structured to identify potential gaps in PMTCT care (relating to maternal age, timing of maternal HIV diagnosis, maternal treatment history, maternal viral load and infant prophylaxis). De-identified data was submitted via cellphone short-message-service (SMS) using Rapid Pro technology, exported and analyzed in STATA 14.

Results: A total of 400 infants in the three districts tested HIV PCR-positive for the first time during the five month period and 367 (91.8%) had data for analysis. 258 (70.3%) were identified from eThekwini, 58 (15.8%) from uMgungundlovu and 51 (13.9%) from uMkhanyakude. Data was received within a median of 12.5 days (interquartile range [IQR]: 6-23) with delays attributed to technological failures and/or poor record keeping at facility level. Median maternal age was 25 years (IQR 22-30) with no significant difference in PMTCT gaps observed between 48 teenage (15-19 years) mothers and 293 older (20-34 years) mothers. 220 (60.0%) mothers were first diagnosed prior to conception or at their first antenatal clinic (ANC) visit; 14 (3.8%) at a later ANC visit and 127 (34.6%) at or after delivery.

137 (37.3%) women transmitted despite receiving >12 weeks of cART with almost half diagnosed prior to conception. 257 (70.0%) women had no viral load (VL) result documented, despite 62 (24.1%) being on cART for >12 weeks. Amongst 110 women with a documented VL, 75 (68.2%) had received cART for >12 weeks with only 35 (46.7%) virologically suppressed. Low risk infant prophylaxis was given to 30/65 infants born to women with VL >1000 copies per millilitre (cpml). No statistically significant differences in PMTCT gaps were observed between the three districts.

Limitations include a lack of PMTCT gap data for HIV-exposed, uninfected mother-infant pairs and being confined to five questions.

Conclusion: Two thirds of the mothers who transmitted HIV to their infants did so despite receiving PMTCT services. This highlights the need to improve services during ANC as well as preventing maternal infections postpartum. The focus of maternal PMTCT care needs to shift towards VL monitoring. We intend using improved technology to streamline data collection and reporting towards eMTCT.
Abstract 86

Vertical HIV infections in the cART era: Data from The European Pregnancy and Paediatric Cohort Collaboration

Peters H1, Chiappini E2, Favarato G1, Gingaras C3, Kahlert C4, Latsycheva I5, Malyuta R6, Prieto L7, Rosenberg V8, Soriano-Arandes A9, Thorne C1, for the The European Pregnancy and Paediatric Cohort Collaboration (EPPICC)

1Population, Policy & Practice Programme, UCL GOS Institute Of Child Health, 2Meyer University Hospital, Florence University, 3Victor Babes Hospital, HIV Department, 4Children’s Hospital of Eastern Switzerland, 5Republican Hospital of Infectious Diseases, 6Perinatal Prevention of AIDS Initiative, 7Hospital Universitario de Getafe, 8Irkutsk HIV Centre, 9Hospital Universitari Vall d’Hebron

Background: WHO criteria for elimination of mother-to-child transmission of HIV (MTCT) include ≤50 new paediatric infections per 100,000 live births and a transmission rate of <2% in non-breastfeeding populations. We aim to describe the circumstances around vertical HIV transmissions that have occurred despite application of prevention of MTCT (PMTCT) interventions in 2002-2015.

Materials & Methods: EPPICC is a collaboration of HIV observational studies in pregnancy and childhood. Nine cohorts across 14 European countries provided individual patient-data on pregnant women diagnosed with HIV before/during pregnancy and their infants delivered 01/01/2002-30/04/2015. Data were provided in standardised formats based on the HIV Collaboration Data Exchange Protocol. Live-born infants with known infection status and exposure to antenatal and/or intrapartum and/or neonatal prophylaxis/treatment were included; for Ukraine, infants delivered pre-2009 were excluded due to widespread use of Option A prior to 2009. Late ART start was defined as >28 weeks gestation.

Results: There were 323 eligible vertically infected infants, 53% (172/323) born in Western/Central Europe and 151/323 in Eastern Europe. Maternal ethnicity was available for 266/323; two-thirds (173/266) were white, and 30% (80/266) Black African. Median maternal age at delivery was 28 years (IQR:24-32). Mode of maternal HIV acquisition was available for 264/323; 68% (180/264) acquired HIV heterosexually and 21% (55/264) through injecting drug use (IDU). 35% (112/323) of mothers were diagnosed before pregnancy and 65% (211/323) in pregnancy/at delivery. Among the latter timing was available for 153/211; 41% (62/153) diagnosed in third trimester, including 34/62 diagnosed ≤7 days before/at delivery.

Among women diagnosed before pregnancy only 13% (15/112) conceived on ART, 49% (55/112) started ART antenatally (15/55 started late) and the remaining 38% (42/112) received no antenatal ART (16/42 had intrapartum prophylaxis). Of women diagnosed in pregnancy, 59% (124/211) started ART antenatally, of whom 48% (60/124) started late and 41% (87/211) received no antenatal ART (26/87 had intrapartum prophylaxis). Overall, 59% (190/323) mothers had ≥1 antenatal VL available, only 16% (31/190) had VL <50c/ml at any point, 16/31 near delivery (<30days).

Over half of deliveries (172/319) were vaginal, 32% (102/319) elective caesarean sections (CS) and 14% (45/319) emergency CS. Overall, 23% (72/310) were born <37 weeks. Among infants, 7% (23/319) received no neonatal prophylaxis, 42% (133/319) combination (≥2 drugs) prophylaxis, 3 sdNVP only, 150 ZDV only (10 other/unknown type) and 4 unknown. 27% (88/323) of infants were tested within a week of birth, but 25 not until >6 months of age. Five babies were known to have died. Overall 18 infants were known to have breastfed. Timing of infant transmission could be estimated in 71/323 (22%) cases only; 42 were in utero, 18 intrapartum, 18 intrapartum/postnatal and 2 postnatal.

Conclusions: Missed opportunities for PMTCT were apparent, particularly as one-third of infants had mothers diagnosed prior to conception. Among women diagnosed antenatally, late diagnosis and late start or lack of ART were common. These findings may reflect problems with access to/engagement with HIV and/or antenatal care (of note, one-fifth were IDU). Use of elective CS was low, but two-fifths of infants received combination neonatal prophylaxis.
Abstract 87

No mother to child HIV transmission during the first six months post-delivery from mothers with viral load <1000 copies/ml: Findings from an Impact Evaluation of Option B+ plus Program, Zimbabwe, 2016

Dinh T1, Balachandra S2, Mushavi A3, Tippett Barr B3, Shambira G4, Nyakura J4, Munemo E5, Mugurungi O6, Broyles L1

1US. Centers For Disease Control And Prevention, Center for Global Health, Division of Global HIV/TB, 2U.S. Centers for Disease Control and Prevention, Center for Global Health, Division of Global HIV/TB, 3AIDS & TB Department, Ministry of Health & Child Care of Zimbabwe, 4University of Zimbabwe/Department of Community Health, 5National Microbiology Reference Laboratory of Zimbabwe

Background: Preventing mother-to-child HIV transmission (MTCT) depends on timing of antiretroviral treatment (ART) initiation and subsequent viral load (VL) suppression (<1000 copies/ml). We determined whether pre-conception ART initiation and VL monitoring have the potential to eliminate MTCT (eMTCT) in an Option B-plus program.

Methods: We used data collected from an ongoing 18-month, prospective observational cohort of a nationally-representative sample of 8792 mothers and their 4–12 week-old infants. Multistage sampling was used to recruit participants from 151 immunization clinics, February to May 2016. We conducted HIV rapid testing on mothers who were known HIV-negative or unknown status. For HIV-infected women, maternal dried-blood-spot samples underwent VL testing (Biomerieux NucliSENS Easy Mag and NucliSENS Easy Q platform, dynamic range, 182-10000000 copies/ml), and their infants had dried-blood-spot samples tested for HIV DNA PCR. We examined early MTCT at six weeks (range, 4–12 weeks) and the cumulative risk of late MTCT at six months (range, 5–7 months) post-delivery according to timing of ART initiation and maternal VL at six weeks postpartum. Findings were adjusted for study design and non-responses; when zero events were observed, Wilson-score confidence intervals (CI) are reported.

Results: Nationally, maternal HIV prevalence at 6 weeks post-delivery was 26.8% (95% CI: 24.6% - 29.0%). VL suppression was 80.8% (95% CI: 76.9% - 98.0%) in all HIV-positive mothers. ART was initiated pre-conception in 37.0% (95% CI: 33.6% - 40.3%), during pregnancy in 41.4% (95% CI: 38.1% - 44.8%), and within 3 months after delivery in 2.5% (1.5% - 3.5%). In these groups, VL <1000 copies/ml was found in 84.8% (95% CI: 81.7% - 87.9%), 81% (95% CI: 78.7% - 84.6%), and 76.3% (95% CI: 66.2% - 86.4%), respectively. Of mothers with VL <1000 copies/ml, early MTCT risk was 0.4% (0.1% - 0.8%) among mothers starting ART during pregnancy, and 0.0% (95% CI: 0.0% - 0.6%) among mothers starting pre-conception; late MTCT risk during 6 months post-delivery was 0.0% (95% CI: 0.0% - 0.3%). Of mothers with VL ≥1000 copies/ml, early MTCT risk was 7.6% (95% CI: 5.0% - 10.2%) and late MTCT was 3.2% (95% CI: 0.0% - 6.6%).

Conclusions: Achieving MTCT of <0.4% prenatally and zero during the first six months post-delivery is possible among HIV-positive mothers with VL<1000 copies/ml at six weeks postpartum. Initiating ART pre-conception maximizes the chances of VL suppression. VL monitoring during pregnancy and six weeks postpartum has the potential to eMTCT.

Abstract 88

Shifting dynamics of HIV transmission timing among infants in the era of option B+ and implications for infant testing

Tiam A1, Kassaye S1, Macheke R2, Gill M3, Tukei V4, Mokone M5, Mohale S6, Makhohlis A6, Letsie M7, Tsietso M8, Seipati P9, Isavwa A5, Guay L1,6

1Elizabeth Glaser Pediatric Aids Foundation, 2University of Bergen, 3George Town University, 4Elizabeth Glaser Pediatric AIDS Foundation, 5Ministry of Health, 6George Washington University

Background: Universal antiretroviral treatment (ART) for HIV-positive pregnant women is anticipated to significantly reduce mother-to-child HIV transmission (MTCT). The World
Health Organization recommends infant HIV testing at 4-6 weeks to capture in-utero/intrapartum/early breastfeeding transmission. In-utero infection is associated with high mortality of 20-30% by age 8-12 weeks. We conducted an implementation research study to determine the relative yield of HIV birth testing.

Methods: HIV-positive and negative pregnant women were enrolled in an observational cohort to evaluate effectiveness of universal maternal ART within 13 health facilities in Lesotho following introduction of Option B+. HIV birth testing (DNA PCR within two weeks of birth) was introduced at study sites in addition to routine six-week infant testing, per national guidelines. Dried blood spots were collected at birth for PCR testing (Roche CAP/CTM HIV v2) followed by routine six-week testing. Data were analyzed to identify HIV transmission rates at birth and six weeks.

Results: Among 602 women (median age, 29 years; median gestational age at first ANC visit, 24 weeks), 427/602 (70%) of their infants were tested at birth, 497/602 (83%) were tested at 6 weeks, and 363/422 (86%) of infants uninfected at birth were retested at 6 weeks. In utero HIV infection with positive birth PCR occurred in 5/427 (1.2%) infants. An additional 2 infants, one with a prior negative birth test and a second without a prior birth test tested positive at 6 weeks, for a cumulative MTCT incidence of 1.25% (95%CI: 0.5%-2.6%). The 6-week MTCT rate was 1/211 (0.5%) among women who initiated ART before pregnancy compared to 6/331 (1.8%) among women who started ART during pregnancy. Maternal HIV RNA levels were associated with transmission: median HIV RNA was 1.27 log10 copies/mL among non-transmitting women versus 5.03 log10 copies/mL among transmitting women.

Conclusion: Universal antenatal maternal ART resulted in very low 6-week MTCT (<1.5%); MTCT rates were lowest with pre-pregnancy ART initiation. Among infants, in contrast to pre-ART era, where ~30% of infections occurred in utero, most infections (5/7; 71%) were identified at birth, suggesting that introduction of birth testing, if accompanied by rapid infant ART initiation, could significantly impact the health of infected infants.

Abstract 89

Challenges in HIV Diagnosis in Pregnant and Breastfeeding Women in Zimbabwe: Limitations of Self-reported Positive Status and Dried Blood Spot Viral Load Results

Balachandra S1, Dinh T2, Mushavi A1, Tippett Barr B1, Shambira G1, Nyakura J1, Munemo E1, Mugrungi O1, Parekh B1, Broyles L2

1U.S. Centers for Disease Control and Prevention, Center for Global Health, Division of Global HIV/TB, 2U.S. Centers for Disease Control and Prevention, Center for Global Health, Division of Global HIV/TB, AIDS & TB Department, Ministry of Health & Child Care of Zimbabwe, 3University of Zimbabwe/Department of Community Health, 4National Microbiology Reference Laboratory of Zimbabwe

Background: Zimbabwe implemented Option B-plus nationwide in December 2014; accordingly all HIV-infected pregnant and breastfeeding women receive life-long antiretroviral treatment. The country also started rolling out HIV viral load (VL) testing using dried-blood-spots (DBS) in 2016. Ambiguity about an individual’s HIV status has serious implications for both the individual and the national program. We quantified the prevalence of 1) incorrect self-report of HIV-positive status and 2) undetectable VL at HIV diagnosis in mothers at 4-12 weeks postpartum.

Methods: We used baseline data collected for an ongoing 18-month facility-based prospective observational cohort of a nationally-representative sample of mothers and their 4–12 week-old infants. A multistage stratified cluster sampling design was used to select 151 immunization clinics across 10 provinces of Zimbabwe. Participants were recruited consecutively during a fixed three-month period concurrently at all study clinics, February to May 2016. We conducted HIV rapid testing (serial testing algorithm) on mothers reporting HIV status as unknown, negative, or positive with no documentation of antiretroviral drugs (ARV) use. DBS specimens were collected from HIV-positive mothers for VL testing (Biomerieux NucliSENS Easy Mag and NucliSENS Easy Q platform, dynamic range, 182–10000000 copies/ml). If a newly
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diagnosed HIV-positive mother had an undetectable VL result, the same DBS card was tested for HIV-antibodies using supplemental Geenius HIV-1/2 assay (Bio-Rad) to exclude false positive rapid test results and HIV-2 infection. All percentages and confidence intervals (CI) were weighted and accounted for study design and non-responses.

Results: Preliminarily, of 8792 participating mothers, 341 those mothers reporting HIV-positive status without documented ARV use of confirmed HIV-negative by HIV rapid testing at baseline. Of those mothers who were confirmed as positive, 42.4% (95% CI 35.6%-49.3%) had undetectable VL. Of 5498 mothers reporting HIV-negative status, 0.7% (95% CI 0.4%-0.9%) were confirmed as positive, of whom 10.7% (95% CI 0.0%-22.9%) had undetectable VL. Of 124 mothers with unknown status, 10.9% (95% CI 3.8%-17.9%) were identified as positive, of whom 11.2% (95% CI 0.0%-33.2%) had undetectable VL.

Conclusions: A high proportion of discrepancies between self-reported and laboratory confirmed HIV status underscore the importance of re-testing before ART initiation, consistent with 2015 WHO guidelines. DBS VL testing is not considered as a diagnostic assay; therefore should not be used to confirm HIV-positive status. These data further indicate this reality because of the high proportion of undetectable VL results among confirmed HIV-positive ART naïve mothers.

Abstract 90

Prevention of Mother-to-Child Transmission of HIV in an Urban Area of the USA: Are We Doing Too Much?


†Children’s National Medical Center, ‡The George Washington University, 2Elizabeth Glaser Pediatric AIDS Foundation

Background: In the last decade, the annual rate of infants born with HIV in the USA continued to decrease leading to several important updates in the national prevention of mother-to-child transmission (MTCT) guidelines allowing for vaginal delivery with an HIV viral load <1000 copies/mL, reserving the use of intravenous zidovudine during labor to women with an unknown or non-suppressed viral load, and reducing the duration of postpartum zidovudine prophylaxis for infants with low risk HIV exposure. Special Immunology Services (SIS) at Children’s National Medical Center serves the majority (>95%) of perinatally HIV-exposed infants (HEIs) in the high HIV prevalence (2%) metropolitan Washington, DC area, USA. The study aimed to analyze the current approaches to and outcomes of prevention of MTCT in the DC area.

Materials & Methods: This was a retrospective cohort analysis of SIS HEIs referred for HIV testing, care and treatment. We collected maternal demographics, ART during pregnancy and delivery, HIV viral load (VL) pre-delivery and delivery type; infant data included post-partum ART prophylaxis and final HIV status. De-identified data were obtained from our program referral database. Descriptive statistics were used for analysis.

Results: Data were abstracted from 279 records of 328 HEIs referred to SIS during 2013-2015. Mean maternal age was 30 years (range 15-48) and 93% (n=260) were Black. The majority (96%; n=268) received ART during pregnancy. The most frequently used backbone was fixed dose combination (FDC) of zidovudine+lamivudine (34%; n=91) and emricitabine+tenofovir (42%; n=112), with lopinavir/ritonavir (35%; n=94), and atazanavir/ritonavir (35%; n=93). A small proportion of mothers took novel ART including rilpivirine (9%; n=24), dolutegravir (0.4%; n=1) and raltegravir (4%; n=11). A majority (72%; n=202) of mothers received intravenous zidovudine during labor and 99% (n=275) of infants received zidovudine prophylaxis postpartum. Only 15% (n=43) of mothers were considered high-risk based on high (>1000 copies/mL) or unknown pre-delivery VL; 14 HEIs (33%) received triple (zidovudine/nevirapine/lamivudine) and 11 HEIs (26%) dual ART (zidovudine/nevirapine) prophylaxis. More than half of all deliveries (57%; n=159) were conducted via C-section; 117 (74%) of which occurred in low-risk
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Can the UNAIDS “90-90-90” Targets be Applied to Option B-plus Women and Provide Adequate Information to Reach the WHO’s Criteria for Validation of Elimination of Mother-to-Child HIV Transmission?

Tippett Barr B1, Mushavi A2, Balachandra S3, Shambira G4, Nyakura J5, Munemo E6, Mugurungi O2, Modi S6, Broyles L1, Dinh T1

1U.S. Centers for Disease Control and Prevention, Center for Global Health, Division of Global HIV/TB, 2AIDS & TB Department, Ministry of Health & Child Care of Zimbabwe, 3University of Zimbabwe/Department of Community Health, 4National Microbiology Reference Laboratory of Zimbabwe, 5U.S. Centers for Disease Control and Prevention, Center for Global Health, Division of Global HIV/AIDS

Background: Prevention of mother-to-child HIV transmission (MTCT) programs have historically used WHO “95-95-95” elimination of MTCT (eMTCT) process indicators; however, these indicators do not directly align with broader UNAIDS “90-90-90” targets for HIV epidemic control and do not include viral load suppression (VL<1000 copies/ml) to monitor the impact of Option B-plus on MTCT. We explored the utility of the UNAIDS goals for pregnant women (PW) and the WHO process indicators to monitor evolution toward eMTCT in Zimbabwe.

Methods: We analyzed data collected from a nationally-representative sample of 8,792 mothers and their 4–12 week-old infants for an ongoing 18-month prospective cohort. A multistage stratified cluster sampling design was used to select 151 immunization clinics across 10 provinces of Zimbabwe. Participants were recruited consecutively during a fixed three-month period concurrently at all study clinics, February to May 2016. We conducted HIV rapid testing on mothers with known HIV-negative or unknown HIV status. For HIV-infected women, maternal dried-blood-spots (DBS) samples underwent quantitative VL testing (Biomerieux NucliSENS Easy Mag and NucliSENS Easy Q platform, dynamic range, 182–10000000 copies/ml), and their infants had DBS samples tested for HIV DNA. All percentages and confidence intervals (CI) were weighted and accounted for study design and non-responses.

Results: Preliminarily, the overall early MTCT measured at 4–12 weeks post-delivery was 1.9% (95% CI: 1.3%–2.4%). Reviewing the WHO eMTCT indicators, Zimbabwe achieved 97.4% of PW attending ≥ one antenatal care visit, 97.5% of PW with known HIV status, and 81.1% of HIV-positive mothers on antiretroviral treatment (ART). Early MTCT among mothers on ART was 1.4% (95% CI 0.9%–1.9%) vs. 3.9% (95% CI: 2.1%–5.7%) among those not on ART. Regarding the UNAIDS 90-90-90 targets, 99.3% of HIV-positive PW knew their status, 82.1% of these received ART during pregnancy, and 82.9% of mothers on ART were virally suppressed at 4-12 weeks postpartum. Early MTCT among mothers with VL<1,000 copies/ml was 0.4% (95% CI: 0.1%–0.8%) compared to 6.2% (95% CI: 3.4%–8.9%) among mothers with VL ≥1,000 copies/ml.

Conclusions: Zimbabwe has achieved “97-97-81” towards the WHO “95-95-95” eMTCT progress indicators, and “99-82-83” on the UNAIDS ‘90-90-90’ targets in PW. The early MTCT was 0.4% among virally suppressed
women highlighting the importance of monitoring VL suppression in PW. These findings suggest that Global eMTCT progress indicators should be updated to include VL suppression, and the UNAIDS indicators should be maximized in their application for eMTCT validation.

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Long-term developmental outcomes and in utero antiretroviral exposure in HIV-exposed uninfected (HEU) children born to mothers living with HIV in British Columbia (BC), Canada

Piske M1, Budd M1, Qiu A2, Maan E3, Sauve L2,3, Alimenti A2,3, Forbes J2,3, Janssen P4,5, Côté H1,5

1Department of Pathology and Laboratory Medicine, UBC, 2Oak Tree Clinic, BC Women’s Hospital and Health Centre, 3Department of Population and Public Health, UBC, 4School of Population and Public Health, UBC, 5Women’s Health Research Institute

Background: Over 1.4 million children worldwide and more than 200 children in Canada are born annually to mothers living with HIV, and an increasing proportion are exposed to ARVs in utero during early development. Concerns exist on potentially adverse immunological, neurodevelopmental and mitochondrial effects from long-term ARV treatment; however, sociodemographic factors and adverse childhood experiences may also be involved. We previously reported a concerning prevalence of autism spectrum disorder in HEUs within the CARMA cohort. Here, we aimed to compare frequencies of neurodevelopmental disorders among HEU children born in BC and examine possible associations with exposure to maternal ARVs.

Materials & Methods: Data on 446 HEU children and 1323 HIV-unexposed uninfected (HUU) children (matched ~1:3 for age, sex and geocode) born between 1990 and 2012 were collected by Population Data BC from several data holdings including the BC Ministry of Health’s Medical Services Plan (ICD9/ICD9-CM), Perinatal Services BC, and ARV treatment information housed at Oak Tree Clinic. Association between ARV treatment in utero and developmental disorders were tested via a chi-squared test for independence with a two-tailed probability value. Calculated probability values for disorder-specific relative risks were two-tailed and obtained from the z-statistic in a standard normal distribution.

Results: One or more of the following developmental disorders: autism spectrum disorder, disturbance of emotions, hyperkinetic syndrome, developmental delay, intellectual disability, and/or epilepsy were diagnosed in 30% of our HEU cohort, compared to 13% in the matched HUU cohort (p<0.0001). Of 369 HEUs with any ARV exposure in utero, 101 (27.4%) had a disorder: a significantly lower proportion (p<0.01) than expected assuming no association between in utero ARV exposure and developmental disorders. Compared to HUUs, HEU children had higher relative risks of autism spectrum disorder (RR=2.97, p=0.02), disturbance of emotions (RR=2.76, p<0.0001), hyperkinetic syndrome (RR=2.97, p<0.0001), and developmental delay (RR=3.08, p<0.0001), but no increased risk of medical conditions such as asthma (RR=1.01, p=0.89) or neoplasms (RR=0.68, p=0.06). The HEU cohort showed higher proportions of exposure to maternal smoking (p<0.0001) and alcohol consumption (p<0.0001) during pregnancy.

Conclusions: Our data suggest a possible reassuring association between ARV exposure in utero and neurodevelopmental disorders within our HEU cohort. HEU children in BC however, appear to still be at a nearly three-fold higher risk for several neurodevelopmental disorders compared to matched HUUs. Our results therefore highlight the need for careful developmental monitoring and access to early interventions to optimize neurodevelopment for at-risk HEUs.
Abstract 93

Lower Dried Blood Spot Mitochondrial DNA (mtDNA) levels at birth in HIV-Exposed Uninfected (HEU) infants exposed to Ritonavir-boosted PI ART in utero compared to HEUs born to ART-naïve mothers

Ajaykumar A1,2, Gadawska I1, Kakkar F3,4, Boucoiran I3,5, Soudeyns H4,6, Alimenti A7, Forbes J1, Côté H1,2, and the CIHR Team in Cellular Aging and HIV Comorbidities in Women and Children (CARMA)

1Department of Pathology and Laboratory Medicine, University Of British Columbia, 2Centre for Blood Research, 3Centre Maternel et Infantile sur le SIDA (CMIS), CHU Sainte-Justine, 4Department of Pediatrics, Université de Montréal, 5Department of Obstetrics and Gynecology, Université de Montréal, 6Department of Microbiology, Infectiology and Immunology, Université de Montréal, 7Department of Pediatrics, British Columbia Women’s Hospital and Health Centre, University of British Columbia

Background: Treatment with zidovudine in pregnancy during the mid-1990’s, followed by the introduction of dual/triple antiretroviral therapy (ART) has drastically reduced mother-to-child HIV transmission. As they cross the placenta, antiretrovirals could affect cellular processes in developing fetuses. Some antiretrovirals can inhibit mitochondrial polymerase-γ, induce oxidative stress, and/or affect mitophagy; all these may result in mitochondrial alterations/dysfunction which can be reflected by compensatory changes in mtDNA content. Our objective was to investigate the impact of in utero ART exposure on infant blood mtDNA content at birth in two cohorts of HEU and HIV-unexposed uninfected (HUU) infants.

Methods: mtDNA content was measured via monochrome multiplex-qPCR in dried blood spots collected 0-5 days after birth from 104 HEU infants enrolled in the CMIS Mother-Child Cohort, and 68 HEU and 17 HUU infants in the CARMA Cohort. Non-parametric tests were used to evaluate univariate associations between mtDNA content and the following infant factors: infant sex, birth weight, gestational age at birth, ethnicity, as well as maternal factors: preterm delivery (<37w gestation), maternal age at delivery, Hepatitis B/C co-infection status, smoking during pregnancy, illicit drug use during pregnancy, viral load closest to delivery (detectable vs. undetectable), duration of ART during pregnancy and ART drug burden during pregnancy (mono- vs. dual- vs. triple vs. ART naïve). Factors that stood out in univariate analyses (p<0.1) were included in multivariable analyses.

Results: Among the 172 HEU infants, 46 were exposed to maternal AZT monotherapy in utero, 21 to AZT+3TC, 78 to triple therapy (n=66 2NRTIs+ritonavir-boosted PI, n=12 AZT+3TC+NFV) and the remaining 27 were born to ART-naïve mothers. In a multivariable analysis of all participants (n=189) that included gestational age (GA), infant sex and maternal ART during pregnancy, higher mtDNA content was associated with lower GA (p=0.002) and being HEUs born to untreated (p=0.006), mono- (p=0.047), dual- (p<0.001) and ritonavir-sparing triple therapy (p=0.026) treated mothers (ref. HUU). In a similar model among HEUs only, infants exposed to ritonavir-boosted PI ART had 23% lower mtDNA content (p=0.008) compared to ART-unexposed HEUs. In sensitivity analyses restricted to infants born at term, GA was no longer significantly associated with mtDNA content among all (n=166, p=0.06) or HEU (n=150, p=0.07), respectively.

Conclusions: Our results suggest that infant blood mtDNA content at birth is related to both maternal HIV and ART during pregnancy. Increase in mtDNA among HEUs born to untreated, mono- and dual-NRTI treated mothers compared to HUUs may reflect compensatory mitochondrial proliferation in response to stresses. Ritonavir-boosted PI regimens appear to lower mtDNA content, possibly through failure to compensate, or increased oxidative stress and mitophagy leading to mitochondria elimination.
Abstract 94

Determining the viral load threshold for initiating triple drug combination prophylaxis in newborns: The Canadian Perinatal HIV Surveillance Program 2001-2015

Kakkar F1, Lee T2, Brophy J3, Alimenti A4, Vaudry W5, Singer J1,6, Money D4, Sauve L4, Bitnun A7, Canadian Perinatal HIV Surveillance Program C7

1University Of Montreal, Sainte-Justine Hospital Center, 2Canadian HIV Trials Network, 3University of Ottawa, Children's Hospital of Eastern Ontario, 4University of British Columbia, Women's and Children's Hospital, 5University of Alberta, Stollery Children's Hospital, 6University of British Columbia, School of Public Health, 7University of Toronto, The Hospital for Sick Children, 8Public Health Agency of Canada

Background: Recent guidelines for the prevention of perinatal HIV infection distinguish between newborns at “standard” vs. “high” risk of infection, with recommendations for combination antiretroviral therapy (cART) in situations where maternal viral load (VL) is detectable prior to delivery. However, there is no consensus on the maternal VL threshold at which cART should be recommended. Practice in Canada varies by center. The objective of this study is to describe the use of cART as neonatal prophylaxis at low levels of maternal viremia within the Canadian Perinatal HIV Surveillance Program (CPHSP) database.

Methods: CPHSP is an observational surveillance database, which collects data annually from 22 sites across Canada on HIV infected mothers and their infants. These data include antiretroviral therapy (ART) use in pregnancy, intrapartum and in the neonate. This project was restricted to infants born in Canada between 2001 and 2015 whose HIV status was finalized according to standard criteria. Combination ART was defined as the use of 3 or more drugs in any combination.

Results: Of 2096 mother-infant pairs with available maternal VL at the time of or just prior to delivery, 1740 mothers had a VL<50 copies/mL, 229 VL between 50-1000 copies/mL, and 127 VL>1000 copies/mL. Among women with VL<50 copies/mL the transmission risk was 0.23% (4/1740); this increased to 0.87% (2/229) among women with VL>1000 copies/mL. Combination ART was used in 3.9% (68/1740) of infants born to mothers with VL<50 copies/mL, 17.5% (40/229) of infants born to mothers 50-1000 copies/mL, and 56% (71/127) of infants born to mothers >1000 copies/mL. Of the 17 HIV infected infants, 5 were infected in utero (test positive within 48 hours of birth); for the remaining 12 timing of infection was not clear (test not done at birth, or first positive result after 48hrs). Fourteen of the 17 infected infants, 5 of whom were confirmed in utero infections, had received triple drug prophylaxis.

Conclusions: While risk of perinatal HIV transmission was 4-fold higher among infants born to mothers with VL 50-1000 copies/ml vs. <50 copies/ml at the time of delivery, only 17.5% of infants this group were prescribed triple drug neonatal prophylaxis. Given the higher risk of transmission in this group, and the benefits of early treatment initiation for those infected in utero, these results suggest that triple drug cART may be of benefit in all infants born to mothers with detectable viremia including those with viral loads of 50-1000 copies/mL at or near delivery.
Abstract 95

The cost-effectiveness of integrating maternal ART into maternal & child health (MCH) services during the postpartum period in South Africa

Dugdale C1,2,3, Phillips T4,5, Myer L4,5, Hyle E1,2,6, Brittain K4,5, Cunnama L7, Zerbe A8, Abrams E8,9, Ciaranello A1,2, And the MCH-ART Trial Team

Abstract withdrawn due to IAS co-submission regulations
Abstract 96

Role of Support Persons in Adolescents and Young Adults Voluntary Counseling and Testing for HIV

Neary J1, Wagner A2, Mugo C3, Maingi Mutiti P4, Bukusi D5, John-Stewart G1,2,3, Wamalwa D3, Kohler P2,6,7, Slyker J1,2

1Department of Epidemiology, University of Washington, 2Department of Global Health, University of Washington, 3Department of Paediatrics and Child Health, University of Nairobi, 4VCT and HIV Prevention Unit/Youth Centre, Kenyatta National Hospital, 5School of Medicine, University of Washington, 6Department of Psychosocial and Community Health, 7International Training and Education Center for Health

Background: HIV incidence and mortality are high in adolescents and young adults (AYA), but testing rates remain low. Understanding how support persons influence HIV testing decisions of AYA may improve the uptake and quality of testing.

Methods: AYA aged 14-24 seeking HIV testing at a large urban referral hospital in Nairobi, Kenya completed a post-test survey which assessed the role of support persons in HIV testing. Correlates were evaluated using chi-square tests and multivariate relative risk regression.

Results: Among 1,062 AYA, median age was 21 (IQR: 19-23); 306 (29%) were adolescents (14-19 years), and 756 (71%) were young adults (20-24 years). Overall, 12.4% reported their decision to test was influenced by a parent, 20% by a partner, and 22% by a peer. Young adults were more likely than adolescents to be influenced to test by partners (23% vs 12%, p<0.001), and less likely by parents (7% vs 27%, p<0.001), health care workers (11% vs 16%, p=0.048), or counselors (9% vs 19%, p<0.001).

Half of AYA were accompanied for HIV testing (10% with parent, 11% partner, 23% peer, 4% others, and 2% with multiple types of support persons). Support persons were involved in various steps of the HIV testing process: 57% were present for pre-test counseling, 64% for finger prick/blood draw, 33% in disclosure of results, and 33% for post-test counseling.

Young adults were more likely than adolescents to present for VCT alone (58% vs 32%, p<0.001) or with a partner (12% vs 7%, p<0.001), and less likely to present with a parent (2% vs 31%, p<0.001). Similar proportions of adolescents and young adults came with a peer or in a group (p>0.05).

Correlates of presenting with a support person included: younger age (RR=1.63 [95%CI=1.37-1.94]), female sex (aRR=1.45 [95%CI=1.21-1.73]), and school enrollment (RR=1.43 [95%CI=1.07-1.92]). Accompanied and unaccompanied AYA had similar HIV transmission and prevention knowledge and similar proportions previously tested for STI (p>0.05).

Conclusion: Support persons play an important role in Kenyan AYA’s HIV testing experience; however, support person involvement may vary with age. Leveraging AYA support persons may provide interventional opportunities to enhance the uptake and quality of HIV testing for this population.

Abstract 97

Plasma IL-6 Levels in Youths with Perinatal HIV Infection - The ANRS EP38 IMMIP Study

Warszawski J2, Rouzioux C3,4, Scott-Algara D5, Montange T1, Le Chenadec J6, Avettand-Fenoel V5,6, Viard J1,6, Dollfus C6, Blacnhe S, Buseyne F7

1Institut Pasteur, 2INSERM, 3AP-HP, 4Université Paris Descartes

Background: Adolescents and young adults who were infected with HIV-1 during the perinatal period constitute a particular population. For those patients born at the beginning of the epidemic, the immune system developed in the presence of active HIV replication followed by periods of treatment-induced viral control of variable length. Inflammation has become a major concern in long-term HIV infection. Here, we assess
whether inflammation is associated with HIV disease history in these youths.

**Patients and methods:** The ANRS-EP38-IMMIP study included youths who acquired HIV during the perinatal period and who were living in France. The present analysis was focused on the 57 patients with undetectable plasma HIV RNA at the time of the study: the median (interquartile range) age was 18 (16-19) years, CD4 T-cell count 642 (522-949) cells/µl and duration of HIV RNA < 500 copies/ml 4.1 (1.6-6.3) years. Plasma IL-6 was assayed by Quantikine ELISA (R&D systems). CD4 T cells were phenotyped by flow cell cytometry. Linear regression was used for univariate and multivariate analysis of log10 transformed IL-6 concentrations.

**Results:** The median plasma IL-6 concentration was 1.03 pg/ml (IQR: 0.76-1.43). Higher IL-6 levels were associated with a previous CDC stage C event (Estimate [95% confidence intervals]: 0.22[0.01;0.42], P=0.04), a lower CD4 T cell % nadir over the last 10 years (-0.18[-0.29;-0.07] per percent, P=0.001) and a higher HIV RNA zenith before first HAART (0.27[0.80;4.56] per log10 HIV RNA copies/ml, P=0.005). Multivariate analysis confirmed these associations. IL-6 levels were negatively associated with expression of the high affinity IL-7 receptor (CD127) on both naive and memory CD4 T cells (adjusted estimate per 10 percent: - 0.20[-0.30;-0.10], P=0.0003 and -0.23[-0.37;-0.09], P=0.002, respectively), but not with the naive or recent thymic emigrant CD4 T-cell percentages. IL-6 levels were not associated with sex, ethnicity, current CD4 T-cell counts, blood HIV DNA levels, duration of severe immunosuppression, cumulative viremia, or duration of viral suppression.

**Conclusions:** In youths with long-term HIV infection and suppressed viral replication, inflammation, quantified by IL-6 concentrations, was associated the extreme HIV-RNA and CD4 levels over the last decade. Inflammation may negatively affect IL-7-dependent CD4 T-cell homeostasis, either directly through the action of cytokines on CD127 expression or indirectly through stimulation of TCR-dependent proliferation.

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**Abstract 98**

**Self-rated ability to take antiretroviral therapy among HIV-positive young people in Ukraine**


1University College London (UCL) Great Ormond Street Institute of Child Health, UCL, 2Shupyk National Medical Academy of Postgraduate Education, 3Perinatal Prevention of AIDS Initiative, 4MRC Clinical Trials Unit at University College London (UCL), Institute of Clinical Trials and Methodology, UCL, 5The Public Health Center of the Ministry of Health of Ukraine, 6Institute of Epidemiology and Infectious Diseases of NAMS

**Background:** Ukraine’s population of HIV-positive young people includes those with behaviourally-acquired infection (BHV), and an ageing cohort with perinatally-acquired HIV (PHIV). Data from other settings suggest poorer adherence to ART in youth vs. adults. It is unclear how attitudes towards taking ART may differ between BHV and PHIV youth in Ukraine, with possible implications for adherence.

**Materials & Methods:** 104 PHIV and 100 BHIV 13-25 year olds attending for routine care at Odessa and Kiev HIV/AIDS centres completed an anonymous tablet-based survey including the Hospital Anxiety and Depression Scale (HADS), Rosenberg Self-Esteem Scale (RSES), Minneapolis-Manchester Quality of Life Instrument (MMQL), HIV Stigma Scale (short version, composite of disclosure, negative self-image and public attitudes subscales; range 7-28) and Belief about Medicines Questionnaire ART version (BMQ-ART). Among 162 on ART, factors associated with self-rated ability (categorised as “high” (excellent/very good) vs. “lower” (good/fair/poor/very poor)) to take ART as prescribed (SRA-ART) were explored using chi-square/Fisher’s exact and Wilcoxon-Mann-Whitney rank sum tests; Poisson regression models were fitted with robust estimates due to high outcome prevalence.
Results: 97 PHIV and 65 BHIV were currently on ART; median age 15.6 [IQR 14.0, 17.2] and 23.1 [21.6, 24.5] years, 56% (54) and 26% (17) male, respectively. 53% in each group (50/94, 34/64) had high SRA-ART, and the rest lower SRA-ART (poor/very poor only selected by only 1% (1/94) and 2% (1/63) respectively). Among 84 BHIV and PHIV with high SRA-ART, 5% (4/83) reported a missed dose in last 3 days and 5% (4/82) reported two consecutive days with no ART in last month vs. 19% (14/74) and 16% (12/73) with lower SRA-ART (p = 0.010 and p = 0.032 respectively). High SRA-ART was associated with greater belief in need for medication (BMQ-ART necessity scale median 33 [30.38] vs 31 [28.34], p = 0.002) and lower concern about taking ART (BMQ-ART concern scale median 27 [23.5, 30] vs 29 [26.5, 33.5], p = 0.001). 65% (37/57) on once-daily ART had high SRA-ART vs 49% (42/86) on twice-daily and 33% (5/15) on three-times daily dosing (p = 0.046). High SRA-ART was also associated with higher self-esteem (RSES score 21 [19-24] vs 19.5 [18-21] with lower SRA-ART, p = 0.001) and overall better quality of life as measured by MMQL, driven by physical functioning and outlook sub-scales (p = 0.003 and p = 0.013). There was no association between SRA-ART and age (p = 0.73); HAD depression (p = 0.146), HIV Stigma Scale (p = 0.076) or sex (p = 0.12).

In a multivariable model, more frequent dosing remained associated with lower likelihood of high SRA-ART (APR 0.70 95% CI 0.51, 0.96 for twice-daily, APR 0.47 95% CI 0.20, 1.08 for three times daily vs. once-daily dosing) and higher RSES score with increased likelihood of high SRA-ART (APR 1.05 95% CI 1.01, 1.10 per 1 point). MMQL physical functioning domain was not associated with SRA-ART (p = 0.15); neither were a priori factors sex (p = 0.45), age (p = 0.70), mode of HIV acquisition (p = 0.93).

Conclusions: PHIV and BHIV young people’s self-rated ability to take ART was very similar, with no difference detected by age or sex in adjusted analysis. Adherence may be supported by once daily dosing and interventions which address ART-related concerns and perceived necessity of ART and increase self-esteem.

Abstract 99

Can adolescents and youth in Kenya afford free HIV testing services? A cost analysis


1University Of Washington, 2University of Nairobi, 3Kenyatta National Hospital

Background: Voluntary HIV testing among adolescents is critical to curb transmission and limit morbidity and mortality. Although HIV testing is free, other costs to adolescents may be barriers.

Methods: Adolescents and young adults (AYA) ages 14-24 who completed voluntary HIV testing and counseling (VCT) at a public hospital in Nairobi, Kenya were recruited. Direct non-medical costs (transportation, childcare, and food), indirect costs (missed income), and lost school time were collected. Per capita GDP ($115USD/mo) was used as a proxy for wages for unpaid work. Median and interquartile ranges (IQR) presented for participants with non-zero costs.

Results: Among 189 AYA, the median age was 20 (IQR: 18-22); 79 (42%) were 14-19 and 108 (56%) were 20-24; 122 (65%) were female. A majority had begun or completed university or polytechnical training (60%).

One hundred twenty-one (64%) reported non-zero costs; 118 (62%) had direct non-medical costs, 19 (10%) had indirect costs. Among those with non-zero costs, the median total cost was $1.98. Among those with non-zero costs, the median direct non-medical costs were $1.78 (IQR: $0.69-2.97) and median indirect costs were $7.97 ($5.01-10.50).

Food and transport were the largest components of direct costs: 79 (42%) paid for food or drink (median: $1.98 [IQR: $0.99-1.98]). Among the 125 AYA with transportation costs, 98 (52%) paid for their own transportation (median: $0.59 [IQR: $0.40-0.99]); 27 (14%) had transportation paid by another person. Among the 93 AYA who were accompanied, 20 (11%) paid transportation for their support person (median: $0.50 [IQR: $0.17-1.00]).
$0.30-0.79]) and 73 (39%) were accompanied but did not pay the other person’s transportation costs. Most AYA (62%) took the bus, 34% walked, and 4% drove or were driven in cars or motorbikes. Few (3 (2%)) had any childcare costs.

Few AYA (25 (13%)) had any paying job; 24 (13%) had a salaried job and 15 (8%) also had a non-salaried (casual labor) job. Eighty-six (46%) did unpaid work and 40 (21%) worked regularly on a farm. Income received from another source, like family or a partner, was uncommon (11 (6%)). The median monthly income from salaried jobs was $148.51 (IQR: $54.46-247.52) and from non-salaried jobs was $49.50 (IQR: $15.84-99.01). The monthly amount from other sources of income was $27.23 (IQR: $7.43-54.46). Nineteen (10%) AYA missed a half or full day of work and 78 (42%) missed a half or full day of school to get HTS. Overall, 13% of adolescents had any income; 52% reported no income but incurred direct costs; 35% reported no income and no direct costs.

In sex-stratified analyses, males were more likely to have direct and indirect cost than females (78% vs 53%, 15% vs 7%, respectively). They had similar sources of income, but males were more likely to have a salaried job (15% vs 10%). Males were more likely to pay for their transport than females (63% vs 45%).

Conclusions: The costs of HIV testing may influence adolescent care seeking and HIV detection. Interventions to address cost of seeking HIV testing and time away from school should be considered.

Abstract 100

Growth among HIV-infected adolescents in the paediatric IeDEA West African collaboration: evolution and association with death or loss-to-follow-up

Jessica J1, Koumakpai S2, Amorissani-Folquet M3, Desmonde S3, Sy H4, Malateste K5, Kouéta P5, NGbeche S5, Ephevi-Ga A6, Dikpo P6, Kouadio K6, Renner L11, Eboua T7, Coffité P8, Leroy V7

1Inserm U1027, Université Paul Sabatier Toulouse 3, 
2CNHU Hubert K. Maga, 3CHU Cocody, Service Pédiatrie, 
4Hôpital des Enfants Albert Royer, 5Inserm U1219, Bordeaux Population Health, Univ. of Bordeaux, ISPED, , 
6Hôpital pédiatrique, CHU Charles de Gaulle, 7CePreF-enfant, 8CHU Tokoin, 9Hôpital Gabriel Toure , 9CIRBA, 
10Korle Bu Hospital, 11CHU Yopougon, Service Pédiatrie, 12Regional IeDEA coordination, Pacci

Background: Estimates of malnutrition among HIV-infected adolescents in sub-Saharan Africa are lacking, and growth evolution on antiretroviral therapy (ART) has been little investigated among children after 10 years of age. How growth does evolve during adolescence among perinatally HIV-infected children? Could anthropometric data be used as predictive markers of HIV evolution? We assessed growth evolution and its associated factors among adolescents in the paediatric IeDEA West African cohort (pWADA), and explore the association between growth evolution and death or loss to follow-up (LTFU) using a joint modelling approach.

Methods: All HIV-infected adolescents aged between 10 and 15 years old in the pWADA cohort, with at least one available measure of weight and height during this period and before 10 years were included. Growth was described using Body-Mass-Index (BMI)-for-age Z-score (BAZ), according to the WHO Child Growth Standards. Correlates of growth evolution were studied using a linear mixed model (1). In parallel, a survival model (2) was run to describe time to death or LTFU (no contact since 6 months) since age 10 years (baseline time). Then, a joint model combining models 1 and 2 was conducted to assess the effect of BAZ value and slope over time on the risk of death or LTFU (no combined criteria). Adjustment variables were gender, country, age and CD4 at ART initiation, CD4 cell count and stunting (Height-for-Age Z-score < -2 SD) at baseline.

Results: Since 2005, 1860 children were included in this analyses (55% of the cohort). Median age at last visit was 12.3 years (InterQuartile Range [IQR] = 10.9-14.3). At baseline, 54% were boys, 18% were wasted (BAZ< -2 SD), 26% stunted, and 16% had severe immunodeficiency (CD4 cell count<350 cells/mL). ART was initiated before 2 years of age for 9% of them, between 2 and 5 years for 30% and between 5 and 10 years for 62%; 35% were severely immunodeficient at ART.

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initiation. Between 10 and 15 years, 4% died (median age 11.5y, IQR: 10.6-13.2) and 11% were LTFU (median age 12.3y, IQR: 11.0-13.7). BAZ decreased significantly, of -0.06 SD by month, with a more important decrease for males, immunodeficient and stunted children at baseline (model 1). Probability to death was higher for severely immunodeficient and malnourished children at baseline (model 2). In the joint model, probability of death was two-time higher when BAZ value was decreased by one unit (associated Hazard Ratio [aHR] = 2.2, Confidence Interval [CI] 95% = 1.6-3.3). BAZ slope over time was not associated significantly with a higher risk of death (p=0.201). Probability of LTFU was not associated with growth evolution.

Conclusions: Malnutrition is a great concern among HIV-infected adolescents even on ART, and growth need to be monitored routinely. Decreasing BAZ between two visits was associated with a higher risk of death during follow-up, independently of the advancement of HIV infection. The joint modelling approach could help to investigate growth over time as a marker for other types of adverse events (CD4 drop or viral rebound), to improve pediatric HIV care follow-up in resource-limited settings.

Abstract 101
Hospitalization and Death Among HIV-positive Asian Adolescents

Singtorei T1, Kerr S5, Chokephaibulkit K1, Phanuphak N4, Gatechompol S5, Hansudewechakul R2, Hanh D6, Tran D6, Homkham N6, Sohn A1

1Treat Asia/amfar – The Foundation For Aids Research, 2HIV-NAT, The Thai Red Cross AIDS Research Centre, 3Faculty of Medicine Siriraj Hospital, Mahidol University, 4Thai Red Cross AIDS Research Centre, 5Chiangrai Prachanukroh Hospital, 6Hung Vuong Hospital, 7Children’s Hospital 1

Background: As perinatally HIV-infected (PHIV) adolescents age into adults, they are at risk for long-term clinical complications and death associated with poorer adherence to antiretroviral therapy (ART) and retention.

Methods: PHIV and HIV-uninfected (HU) adolescents were enrolled in a prospective study to monitor human papillomavirus (HPV) infections in sexually active youth in Thailand and Vietnam from 2013-2016. HU controls were matched by sex, age, and lifetime number of sexual partners. Patients were tested for HPV and other sexually transmitted infections (STIs; C. trachomatis, N. gonorrhoeae, T. pallidum, herpes simplex virus 2). The cumulative incidence of hospitalization and/or death were calculated for the number of events by the total person-years of follow-up (PYFU). Covariates with p <0.1 in univariate analyses were included in a multivariate model. Median values are provided with interquartile ranges.

Results: A total of 284 adolescents were followed for a median of 142 (135-145) weeks: PHIV (N=140):HU (N=144), 67% female, 95% Thai. At enrollment, the median age was 19 (18-20) years, and median lifetime partners were 2 (1-5) persons; of the PHIV, 94% were taking ART, median log HIV-RNA was 1.6 (1.3-2.8) with 31% <40 copies/mL, and median CD4 was 581 (404-808) cells/mm3. There were 40 hospitalizations (5.24 per 100 PYFU overall; 7.71 per 100 PYFU for PHIV, 2.67 per 100 PYFU for HU) and 3 deaths (0.39 per 100 PYFU) among 28 adolescents. The most common causes of hospitalization included: PHIV (N=30) – pneumonia (n=10; Nocardia [n=2], tuberculosis [n=1], Pneumocystis [n=1], penicilliosis [n=1], other [n=5]), trauma (n=6), cerebral infection (n=6; toxoplasmosis [n=2], other fungal [n=1], tuberculosis [n=1], other [n=2]), sepsis (n=4; Salmonella [n=2], penicilliosis [n=2]), and other infections (n=4); HU (N=10) – trauma (n=3), pregnancy complications (n=3), appendicitis and other infections (each n=2). All deaths were among PHIV adolescents and were due to pneumonia (n=2) and sepsis (n=1). The combined events were higher among PHIV than HU adolescents (unadjusted incidence rate ratio [IRR] 3.15, 95%CI 1.49-6.67; p=0.003). In a multivariate model, after adjusting for alcohol use and any STI, two factors were independently associated with an increased risk of hospitalization and/or death: HIV infection (IRR 2.36, 95%CI 1.08-5.15, p=0.03) and low (<18.5kg/m2) body mass index (IRR 2.01, 95%CI 1.05-3.84, p=0.04).

Conclusions: PHIV adolescents were more likely to be hospitalized, which was frequently due to opportunistic infections, despite having
access to ART, monitoring, and other clinical services. That all deaths were among those with HIV and due to infectious causes raises serious concerns about how clinics and PHIV youth are managing challenges with lifelong adherence, despite the clinical resources frequently available at these referral centers. The results also emphasize the need for sexual and reproductive health services for youth, and support for PHIV adolescents as they transition to adult life.

Abstract 102

Monitoring the 3rd 90: are we on track with the youth?

Ngugi E¹, Natukunda A², Chen T¹, Nganga L¹, Mwangi J¹, Mustisya I¹, Masamaro K¹, Katana A¹, Young P¹

¹Division of Global HIV & TB (DGHT), US Centers for Disease Control and Prevention (CDC), ²University of California (UCSF) Global programs for Research & Training

Background: Kenya has implemented the UNAIDS 90-90-90 strategy; the “3rd 90” target has implications for patient outcomes and secondary HIV prevention. As of September 2016, approximately 970,000 persons living with HIV were on antiretroviral therapy (ART) in Kenya and a total of 1,646,632 viral load (VL) tests had been done cumulatively by September 2016.

Methods: In a nationally-representative cross-sectional survey conducted during October 2015-September 2016, dried blood spot (DBS) samples were collected from 2561 persons aged ≥ 15 years on ART >= 12 months from 50 health care facilities in Kenya. Students were defined as those in school during the study period. HIV-1 RNA quantification was performed on 2522 of the collected DBS samples. Dried blood spot strips were prepared whole blood on Whatman 903 DBS filter in the HIV-Lab for analysis using Abbott m200rt system. We assessed VL suppression (VL<1000 copies/ml) rates and factors associated with non-suppression using logistic regression.

Results: Of the 2522 patients with samples analyzed for VL, 759 (30.1%) were men. Median age was 41 years (inter-quartile range [IQR] 35-49) and 100 (4.2%) were youth aged 15-24 years; all youth were students. Median time on ART was 4.8 (IQR 2.5–7.2) years; 2489 (99%) were on NNRTI-based regimens at ART initiation. Overall viral suppression (VL<1000 copies/mL) was shown in 2109 (84.2%) (95% confidence interval CI 82.7-85.6) and was similar among females and males (p=0.527). Suppression was lower, 54.2% (95% CI 40.1–68.3%), among adolescents aged 15-19 years and highest among persons aged 55-59 years (90.3%, 95% CI 85.6–94.9%); Students had lower suppression rates, 55.3% (95% CI 39.4–71.1%), compared to employed persons at 87.7% (95% CI 82.5–90.0%). In multivariable linear regression, being a student was independently associated with non-suppression, adjusted odds ratio (AOR) 6.74(95% CI 1.13-40.28, p<0.0001), however, there was no difference in viral suppression by sex, age,CD4 at ART initiation, WHO stage, disclosure and initial regimen.

Conclusions: Viral suppression among ART patients in Kenya is approaching 90%, but adolescents,youth and students show substantially lower rates of suppression. Identifying and implementing effective service delivery models and interventions to help youth in schools to achieve VLS should be prioritized.

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Insulin resistance in South African perinatally HIV-infected adolescents on antiretroviral therapy: a cross-sectional study

Frigati L¹², Jao J³, Mahtab S², Asafu Agyei N³, Myer L², Zar H²

¹Stellenbosch University, ²University of Cape Town, ³Icahn School of Medicine Mount Sinai

Background: Access to antiretroviral therapy (ART) has reduced morbidity and mortality in perinatally HIV-infected (PHIV) children, but metabolic complications of ART including
insulin resistance (IR) in adolescents are poorly understood.

Methods: We evaluated IR in a cross-sectional analysis of PHIV and HIV-uninfected adolescents enrolled in the Cape Town Adolescent Antiretroviral cohort (CTAAC). Adolescents 9-14 years old and on ART for >6 months were eligible. The Homeostatic Model Assessment (HOMA) was used to assess IR calculated from fasting insulin and glucose measurements at enrollment. IR was defined as HOMA >2.5 for pre-pubertal and >4.0 for pubertal adolescents. Multiple linear regression was used to examine adjusted associations between HOMA and both HIV-related and traditional cardiovascular risk factors.

Results: Of 403 adolescents, 356 were PHIV. Median age was 12.1 (IQR:10.7-13.3) years for PHIV and 11.5 (IQR:9.9-13.1) for uninfected adolescents. 49% of PHIV and 60% of uninfected adolescents were female. Median duration on ART was 7.5 (IQR:4.7-9.2) years with 123 (35%) of PHIV adolescents starting ART between 0-2 years of age, 97 (27.6%) between 3-5 years and 131 (37.3%) between 6-14 years of age. The most common regimens included Abacavir (72%) and Lopinavir/ritonavir (59%). Median triglycerides were 79.7 mg/dL (IQR:62.0-106.3) in PHIV and 62.0 mg/dL (IQR:44.3-70.9) in uninfected controls (p<0.0001). Median waist circumferences were 61cm (IQR:58-66) and 62.5cm (IQR:57-70) for PHIV and uninfected adolescents. Overall, 20.1% had IR, but rates of IR did not differ between groups or by duration of ART exposure. Among PHIV adolescents, waist circumference (β=0.007, p=0.035), hypertriglyceridaemia (β=0.074, p=0.013), and ever use of Abacavir (β=0.071, p=0.022), were associated with increased HOMA, while viral load >1000 copies/mL (β= -0.062, p=0.013) was associated with decreased HOMA after adjusting for age, gender, body mass index and Tanner stage.

Conclusions: In a South African cohort of PHIV adolescents, IR did not appear significantly different from uninfected adolescents. In addition to traditional risk factors such as waist circumference and hypertriglyceridaemia, Abacavir exposure may be associated with increased HOMA, and this finding needs further exploration.

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Psychological Adjustment of Perinatally HIV-Infected Youth in Cape Town, South Africa

Perez A†, Brittain K‡, Stein D*, Zar H‡, Myer L†, Hoare J‡

†Division of Epidemiology and Biostatistics & Centre for Infectious Disease Epidemiology and Research, University Of Cape Town, ‡Department of Psychiatry and Mental Health, University of Cape Town, *Department of Pediatrics and Child Health, University of Cape Town, †Medical Research Council Unit on Child & Adolescent Health

Background: Mental health is a documented risk factor for increased morbidity and mortality, especially in vulnerable groups like the growing number of perinatally HIV-infected (PHIV+) youth across Africa. The extent to which mental health and psychological adjustment is affected by chronic HIV infection in PHIV+ is largely unknown, with very few studies including appropriate comparator groups of HIV-uninfected (HIV-) youth. We examined psychological adjustment in PHIV+ and HIV- youth participating in the Cape Town Adolescent Antiretroviral Cohort (CTAAC).

Methods: This cross-sectional analysis from CTAAC included 466 PHIV+ youth (eligibility 9-14 years, on ART >6 months, disclosed about their HIV status and recruited from services across the city) and 97 HIV- controls drawn from comparable communities; data from the 18-month follow-up visit was used. Participants and their care-givers completed the Strengths and Difficulties Questionnaire (SDQ) which consists of 5 subscales measuring emotional, conduct, peer-relation, and hyper-activity difficulties as well as prosocial strengths in youth; the four difficulty scores are then summed into a total difficulties score. Raw scores were standardized using age-and-sex adjusted normative data. Linear regression was used to compare self-reported total difficulty scores between PHIV+ and HIV- youth and to investigate variables associated with poorer scores on each of the subscales for both self-reported and care-giver reported scores.
Results: The mean age was 13.5 years in PHIV+ youth and 13.3 years in HIV- controls, with 51% and 44% of participant’s male, respectively. The median age at ART initiation was 4.2 years [IQR 2.7-5.5]. The reliability of the SDQ was reasonable across subscales for self-reported (Cronbach’s Alpha, 0.36 – 0.65) and caregiver reported (Cronbach’s Alpha, 0.26-0.64) scores. PHIV+ youth reported fewer total difficulties, on average, compared to HIV-youth on self-reported measures (mean: 5.8 vs. 9.2;p<0.001). After adjusting for age, gender, socio-economic status, primary caregiver, and having repeated a grade, PHIV+ youth reported fewer difficulties, on average, on self-reported subscales for emotional (β: -0.97; 95%CI: -1.43,-0.51), conduct (β: -0.43; 95%CI: -0.77,-0.1), hyperactivity (β: -0.95; 95%CI: -1.34,-0.57), peer relation (β: -0.84; 95%CI: -1.21,-0.47) and total difficulties (β: -3.2; 95%CI: -4.37;-2.03), with better prosocial adjustment on the prosocial subscale (β: 0.49; 95%CI: 0.16;0.83), compared to HIV- controls. When stratified by age and gender, associations between HIV status and self-reported total difficulties persisted. Having repeated a grade did not have a statistically significant impact on adjusted models for self-reported and caregiver reported total difficulties. Older age and higher socio-economic status were predictive of better scores on the hyperactivity subscale in adjusted models for caregiver and self-reported scores in PHIV+ youth.

Conclusions: PHIV+ youth in this setting seemed to perform significantly better than their HIV- counterparts on self-reported and caregiver reported measures of psychological adjustment. It is possible that more frequent contact with health services by PHIV+ compared to HIV- youth may explain the observed associations. However, contradictions with studies measuring neuro-cognitive functioning in PHIV+ youth may indicate poor psychometric capacity of SDQ for identifying difficulties in youth of this context, suggesting a need for more culturally appropriate measures of psychopathology and functioning. The implications and consistency of these findings within Africa require ongoing attention.

Abstract 105
Substance use and sexual behaviour among perinatally-infected adolescents and same-age, HIV-uninfected peers in South Africa

Britain K,1,2, Hoare J, Phillips N, Zar H,3, Stein D,4, Myer L1,2
1Division of Epidemiology & Biostatistics, School of Public Health & Family Medicine, University of Cape Town,
2Centre for Infectious Disease Epidemiology & Research, School of Public Health & Family Medicine, University of Cape Town, 3Department of Psychiatry & Mental Health, University of Cape Town, 4Department of Paediatrics & Child Health, University of Cape Town, 5Medical Research Council Unit on Child & Adolescent Health

Background: A growing population of perinatally-infected children is aging into early and later adolescence, but there are few data on how they transition through this critical developmental stage in sub-Saharan Africa, where the burden of HIV is highest. Sexual and behavioural experimentation are common during adolescence, but are complicated in perinatally-infected adolescents by their health status, as well as the need to adhere to antiretroviral therapy (ART) and reduce the risk of onward transmission of HIV to sexual partners. A better understanding of the emergence and drivers of substance use and sexual behaviours is needed in this context, including comparisons to same-age, HIV-uninfected peers.

Materials & Methods: Using enrolment data from the Cape Town Adolescent Antiretroviral Cohort, we explored report of substance use and sexual behaviour among perinatally-infected adolescents ages 9-14 years and using ART >6 months and an HIV-uninfected comparator group. Behaviours were assessed by trained fieldworkers using an interviewer-supported, self-administered tool (“Teen Talk”) that was formatted to be adolescent-friendly. Interviews were conducted in participants’ home language and separate from caregivers, at a study visit conducted separately from routine medical care; and a urine toxicology screen tested for common illicit substances. We compared substance use and reported behaviours between HIV-infected and –
uninfected adolescents and examined the effect of risky behaviours on self-reported adherence (≥1 missed ART dose during the preceding 30 days) and elevated HIV viral load (VL >50 and >1000 copies/mL, respectively) in logistic regression models.

**Results:** Between July 2013 and March 2015, 508 perinatally-infected and 110 HIV-uninfected adolescents (median age: 11.9 years; 50% female) were enrolled and included in analysis. Report of ever smoking tobacco or marijuana or ever sniffing substances was uncommon in both groups (overall: 2%, 1% and 0.3%, respectively); 2% of participants in both groups tested positive for marijuana and/or Mandrax (Methaqualone). Ever use of alcohol was more frequently reported, and was slightly more common among HIV-uninfected participants (12% vs 8% in HIV-infected; p=0.180). 3 HIV-uninfected and 1 HIV-infected participant reported a history of sexual intercourse. Among HIV-infected participants, report of any risky behaviour was strongly associated with older age [adjusted odds ratio (aOR): 1.43; 95% CI: 1.16-1.75] and male gender (aOR: 2.19; 95% CI: 1.13-4.25). After adjustment for age and gender, report of any risky behaviour was associated with report of ≥1 missed ART dose during the preceding 30 days (aOR: 2.01; 95% CI: 1.06-3.80), but not with elevated VL >50 or >1000 copies/mL.

**Conclusions:** Among this cohort of perinatally-infected children entering early adolescence, the prevalence of reported substance use and sexual behaviour was low and comparable to that of same-age, HIV-uninfected peers. Longitudinal data are needed to explore the emergence of these behaviours as this population ages into later adolescence, and to further explore the potential association between risky behaviours and non-adherence to ART.

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**Abstract 106**

**Prevalence, barriers and facilitators of age appropriate transition from pediatric to adult care among HIV infected adolescents at Kenyatta National Hospital**

Grewal G1, Obimbo E1, Wamalwa D1, Inwani I2

1University Of Nairobi, 2Kenyatta National Hospital

**PREVALENCE, BARRIERS AND FACILITATORS OF AGE APPROPRIATE TRANSITION FROM PEDIATRIC TO ADULT CARE AMONG HIV INFECTED ADOLESCENTS AT KENYATTA NATIONAL HOSPITAL**

Grewal G.K, Obimbo E.M, Wamalwa D, Inwani I

University of Nairobi, Kenyatta National Hospital, Nairobi

**Background:** Rates of HIV infection among adolescents in Kenya continues to rise and due to wide access to life saving anti-retroviral, there has been an improvement in survival rates, resulting in more individuals who must eventually transition from pediatric to adult care. HIV-infected youth must learn to navigate a complex health regime and the social stigma and discrimination that are associated with HIV. The study determined the proportion and described barriers and facilitators to age appropriate transition of HIV infected adolescents from pediatric to adult HIV services presenting between the age of 15 to 24 years at the Comprehensive HIV care services at Kenyatta National Hospital.

**Methods:** This was a mixed method cross-sectional study. 96 HIV infected adolescents between the ages of 15-24 years were recruited using consecutive sampling over a period of four months. A standard questionnaire and clinical data abstraction form were used and different variables were analyzed using a statistical package for social services version 23 and associations were presented using odd’s ratio with 95% CI using Chi-square test. A p-value of < 0.05 was considered significant. In depth interviews were also conducted with a total of 38 HIV infected adolescents and 11 key informants using purposive sampling approach. All interviews were transcribed verbatim and analyzed which were then reported in form of themes and quotes.

**Results:** Our study determined a prevalence of 67.1% of HIV infected adolescents who had transitioned by the age of 19 yrs. Most participants described feeling unprepared for transition and described anxiety and specific worries during the transition process. Participants indicated that the change was overwhelming, and used phrases like: “being scared,” “a shock,” and “don’t know what to expect” to describe first hearing about transition. All key informants agreed that transition to adult care was an important issue that was increasing in urgency as
Abstract

Early clinical and social outcomes at and after transfer from pediatric to adult HIV care in Asia

Sohn A1, Chokephaibulkit K2, Lumbiganon P3, Hansudewechakul R4, Gani Y5, Nguyen L6, Mohamed T7, Sethaputra C1, Singtoroj T1, Kerr S8

1TREAT Asia/amtAR - The Foundation for AIDS Research, 2Department of Pediatrics, Faculty of Medicine Siriraj Hospital, Mahidol University, 3Division of Infectious Diseases, Department of Pediatrics, Faculty of Medicine, Khon Kaen University, 4Chiangrai Prachanukroh Hospital, 5Hospital Sungai Buloh, 6National Hospital of Pediatrics, 7Pediatric Institute, Hospital Kuala Lumpur, 8HIV-NAT, The Thai Red Cross AIDS Research Centre

Background: The Study of Transitioning Asian Youth (STAY) is a pilot prospective cohort study in Southeast Asia enrolling adolescents and young adults (AYA) at and after transition from pediatric to adult HIV care.

Methods: Patients between 16-24 years who were transferred to adult care within 12 months, knew about their HIV status, and without severe neurocognitive impairment were recruited from clinics in Thailand (N=3), Malaysia (N=1) and Vietnam (N=1). Study procedures took place at their “sending” pediatric clinic (Thailand and Vietnam) or their “receiving” adult clinic (Malaysia). Data at study enrollment are presented. Median values are provided with interquartile ranges.

Results: Between March-December 2016, 83 AYA were enrolled; median age 20 (19-21) years, median 7.5 (6.3-9.4) years after disclosure. For those whose transition date was the first adult clinic visit (n=65), the median post-transition time to enrollment was 4.7 (0.9-8.6) months; for those whose transition date was the last pediatric clinic visit (n=18), the median post-transition time was 7.4 (2.8-8.9) months. Almost all (93%) were perinatally infected, 63% were female, 88% were Thai; 92% were in WHO stage 1, with a highest ever stage of 3 or 4 in 57%; 77% self-reported no significant medical events in the past 12 months. Median lab values included creatinine 0.70 (0.60-0.86) mg/dL, total fasting cholesterol 170 (153-196) mg/dL and triglycerides 100 (77-135) mg/dL, CD4 611 (483-834) cells/mm3; 85% had HIV-RNA <40 copies/mL. All were on antiretroviral therapy (ART; median 13.2 [10.0-15.7] years); 35% had prior mono/dual antiretroviral use. Current regimens included efavirenz (20%), nevirapine (21%), tenofovir (63%), protease inhibitors (39%).

Median 30-day self-reported adherence by visual analogue scale was 95 (90-100)% The most common housing was in a house (73%), with 13% in orphanages, care homes, or shelters; 32% lived with biological parents, and 32% with relatives or adoptive parents. Forty-five percent were employed (47% full-time), and 65% were currently in school or a training program. Of those not in school, 40% had attended university or vocational school. Forty-nine percent were single, 36% had ≥1 partner but were not married, 7% were married; 42% had ever had sex, 6% had ever been pregnant. Almost half (46%) reported being very prepared to make their transfer, and were very (42%) or somewhat (49%) comfortable receiving care at their adult clinics. In the past 3 months, 29% had used alcohol, 9% had used tobacco.

Conclusion: Two thirds of adolescents had transitioned to adult care however significant barriers remain including stigma. The major facilitator for successful transitioning was adolescents who were exceptionally mature for their age and took ownership over their care. However, identification of best practices to support successful transition to adult-oriented health care is in its early stages, and more research is needed to identify universal components of effective transition programs.
Many felt that they needed to keep their HIV status secret (55%), were unequal in their relationships because of their HIV infection (44%), and that they sometimes, rarely, or never had someone they could trust to talk with about their feelings (64%) or who understood their problems (62%).

**Conclusions:** Our cohort of predominantly perinatally HIV-infected AYA had high rates of viral suppression, immunologic recovery, and advanced educational attainment at transition out of pediatric HIV care. However, the majority were concerned about the negative impact of having HIV, and felt they lacked adequate social support and people in their lives they could trust with their personal problems.
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Malnutrition, growth response and metabolic disorders within the first 24 months of ART initiation in HIV-infected children treated before the age of two years in West Africa


1Inserm U1027, Université Paul Sabatier Toulouse 3, 2Inserm U1219, University of Bordeaux, ISPED, 3MONOD Project, ANRS 12206, Centre de Recherche Internationale pour la Santé, 4Centre Muraz, 5Paediatric Department, Centre Hospitalier Universitaire de Cocody, 6PACCI Programme, Site ANRS, Projet Monod, 7Paediatric Department, Centre Hospitalier Universitaire Yaïdago Ouédraogo, 8Paediatric Department, Centre Hospitalier Universitaire Charles de Gaulle, 9Centre de Prise en charge de Recherche et de Formation (CePReF-enfants), 10EA 8, Université-Paris Descartes ; Immunology, Hematology, rhumatologie Unit, Hopital Necker Enfants Malades-Assistance Publique Hopitaux de Paris., 11Paediatric Department, Centre Hospitalier Universitaire de Yopougon

Background: Healthcare of HIV-infected children in resource-limited settings faces several challenges, which one of them is malnutrition. We described baseline malnutrition, growth evolution and metabolic disorders within the first 24 months of antiretroviral therapy among children initiated on ART <2 years in West Africa.

Methods: all HIV-1-infected children, <2 years were initiated on an initial LPV/r based-ART cohort for 12 months before being enrolled at 13-month for those in virological success in a randomized simplification trial, assessing LPV/r vs EFV-based ART, in Ouagadougou, Burkina Faso, and Abidjan, Côte d’Ivoire. Weight-for-age, Height-for-age and Weight-for-height Z-scores (WAZ, HAZ, WHZ) defined malnutrition (Z-score <−2 Standard Deviations [SD]), using WHO growth references. Malnutrition at baseline was studied using a multivariate logistic regression and growth evolution within the first 24 months of ART using linear mixed models, with random intercept, slope for time and unstructured variance-covariance matrix.

For WAZ and WHZ evolution, a spline term was added at six months to take into account the change of slope at this period. All analyses were adjusted by age, sex, country, immunodeficiency by age and viral load at ART initiation. Metabolic parameters were measured each six month and compared to the baseline value.

Results: Between 2011 and 2013, 161 children were enrolled: 64% were from Abidjan, 54% were females. At baseline, median age was 13.6 months [IQR 7.7; 18.4], 53% were underweight (WAZ), 51% stunted (HAZ), and 36% wasted (WHZ). During the 24 months of follow-up, 14 infants died (9%), 2 were lost-to-follow-up (1%), 3 withdrew their consent (2%). Overall, malnutrition at baseline was more likely for children living in BF vs CI, those never breastfed, the oldest (12-24 months), and with a low birth weight. Sex and immunodeficiency for age were not associated to any type of baseline malnutrition. Growth improvement occurred mainly within the first 6 months on ART (Monthly estimated mean increase: WAZ and WHZ: +0.12 SD/+0.02 SD for 0-6 and 6-24 months respectively; HAZ: +0.03 SD for the 0-24 months period). It was greater for the most severely malnourished children at baseline, but a substantial part remained malnourished after 24 months (20% for underweight, 32% for stunting and 8% for wasting). There were no differences in any growth parameters evolution per arm. ART initiation was associated with an increase of hypercholesterolemia (38% at 24 months vs 8% at baseline, p<0.001) and a decrease of anemia (21% at 24 months vs 74% at baseline, p<0.001) and hypoalbuminemia (0% at 24 months vs 50% at baseline), with no difference according to the initial nutritional status.

Conclusions: Prevalence of malnutrition was high at ART initiation. Growth on ART improved regardless of the HIV disease status, but a part of children remained malnourished after 2 years on ART. Management of malnutrition could be optimized with a regular assessment of anthropometric indicators, in order to offer an adapted nutritional support. Lipid disorders were observed, which is concerning and need to be monitored carefully to reduce the long-term cardiovascular risk, especially among children in a lifelong therapy process.
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Antiretroviral resistance among early treated HIV-infected children after five years follow-up in the ANRS-Pediacam cohort in Cameroon

Kenne Malaha A1, Tjiokem M1, Tetang Ndiang S1, Tagnouokam Ngoupo P2, Ateba Ndongo F4, Penda F1, Kfutwah A5, Yuya Septoh F1, Tchatchueng J6, Warszawski J6,7,8, Faye A8,9,10,11, ANRS - PEDIACAM Study Group

1Centre Pasteur of Cameroon, Epidemiology and Public Health Unit, 2Centre Pasteur of Cameroon, Virology Unit, 3Centre Mère et Enfant de la Fondation Chantal Biya, 4Hôpital Laquintinie, Hôpital du jour, 5Equipe 4 (VIH et IST) - INSERM U1018 (CESP), 6Assistance Publique des Hôpitaux de Paris, Service Epidémiologie et Santé Publique, Hôpital de Bicêtre, 7Université Paris Sud, 8Université de Paris 7 Diderot, Sorbonne Paris Cité, 9Assistance Publique des Hôpitaux de Paris, Pédriatrie Générale, Hôpital Robert Debre, 10INSER UMR 1123 (ECEVE)

Background: Early initiation of combined antiretroviral therapy (cART) in children has been shown to be very life saving, helping improvement of immune reconstitution and decreasing HIV-related morbidity and mortality. However, administration of cART at this age is challenging because of some drugs formulation not suitable for children and could lead to virological failures (VF). We estimated the frequency of VF and described mutations associated to resistance in early treated HIV-infected children followed in the ANRS-Pediacam cohort.

Materials and methods: Pediacam is a prospective cohort launched in Cameroon in 2007 and constituted of HIV-infected children (HIC) and HIV-uninfected children born to HIV-infected or uninfected mothers. HIC were included during the first week of life or at diagnosis before 7 months of age. They were followed every 3 months from inclusion to 24 months, then every 6 months till 5 years, with viral loads measurements at each visit. Virological failure (VF) was defined for children on cART for at least 6 months as plasma viral loads >1000 copies/ml on two consecutive measurements. ARV resistance was assessed using ANRS procedures if the second viral load was still >1000 copies/ml after therapeutic education. We used Medians (interquartile range) for descriptive analysis of quantitative variables, Frequencies and Percentages for categorical variables; while t tests and χ2 were performed to compare characteristics of the individuals.

Results: Of 210 HIV-positive children enrolled, 14 died before treatment, 9 lost to follow up, 1 confirmed as HIV-negative and 30 received cART <6 months. A total of 156 children were therefore considered for analyses. Among them, 54.5% (85/156) were female, 65.1% received PMTCT prophylaxis at birth. The median age at cART initiation was 4.4 months (IQR 3.9-5.9). The median durations between cART initiation and respectively first viral load >1000 copies/ml and genotyping were 10.6 months (IQR 7.6-21.2) and 30.5 months (IQR 16.6-45.0) to genotyping. No significant difference was found between children with and without VF or a genotyping test. Overall, 40.4% (63/156) experienced VF and ARV resistance was assessed for 33 children. No resistance was found in 27.3% (9/33) of them. Resistance to 3TC (77.4%), NVP (50.0%), EFV (46.4%), AZT (16.1%) and D4T (16.1%) was found for reverse transcriptase inhibitors (RTI), and IDV (9.4%) and LPV/r (9.4%) for protease inhibitors (PI). No resistance to ABC, TDF, DDI, NFV, and ATV/r was found. Respectively 42.4% and 30.4% were resistant to one and two/all drugs of current ART regimen. The most frequent mutations observed were H69K/Q (87.9%); L89I/M (87.9%); and M36I/L (81.8%) for PI; and; M184I/V (60.6%); K103N (21.2%); and Y181C (18.2%) for RTI.

Conclusions: High-level virological failure was observed in children in routine clinical care. This could lead to management difficulties especially with 3TC, a central drug present in almost all cART regimens in Cameroon. There is a need to improve ART adherence in the paediatric population and to reinforce better use of genotyping test.
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Aging-out of HIV infected children <15 years old into adulthood in a Kenyan cohort, 2009-2015

Mutisya I, Waruru A1, Mureithi C2, Achwoka D1, Motoku J1, Njoroge A2, Ngugi E1, Katana A1, Ng’ang’a L1

1 CDC, Division of Global HIV/TB, 2 Eastern Deanary AIDS relief Program

Background: In 2016, pediatric HIV estimates have dropped globally; in Kenya, the estimated children living with HIV (CLHIV) dropped by 40% to from 159,000 to 98,000. Success in pediatric HIV treatment has led to increased survival of HIV infected children into adolescence and adulthood. During the 2 years of implementing acceleration of Children’s Treatment (ACT) initiative 2015/2016, the net growth of the Kenya pediatric ART cohort was 9,000, despite initiating ART to 27,000 CLHIV in the same period. While attrition through mortality and loss to follow up are known contributors to net growth of ART cohorts; we do not know what proportion of children age out of the pediatric ART cohort by virtue of turning 15 years. Our study sought to determine the proportion and factors associated with CLHIV aging out of the pediatric ART cohort into the adult ART cohort.

Methods: We used HIV program data from electronic medical records (EMR) of 14 sites serving urban slums in Nairobi for the period January 1st 2009 through December 31st 2015. Children were defined as age 0-14 and aging-out as attaining ≥ 15 years during follow-up. We used extended Cochran-Mantel-Haenszel stratified test of association to test for differences in proportions of socio-demographic and treatment characteristics across year of enrollment; χ2 test to compare proportions and non-parametric equality of medians test to compare differences in medians. We calculated aging out rates per 1000 child-years and fitted Cox proportional hazards models to test for associations of aging out with selected characteristics.

Results: We analyzed 2,156 records of children age <15 years old at the time of entry into HIV care. Median age at enrollment was 56.5 months, interquartile range (IQR) 21.7-102.1 months. Median age at enrollment increased from 58.3 months [IQR 11.9, 107] in 2009 to 65.8 months [IQR 28.3,108.7] in 2015, p=0.004. Aging out rate was 7.1% corresponding to 153/2156 children and a rate of 8.2 [95% CI 7.0-9.6] per 1000 child-years. ART uptake was 81.5% and increased from 68.8% in 2009 to 86.1% in 2015, p<0.001. Factors associated with aging-out were: being on ART [adjusted hazard ratio (aHR) 5.294 (95% CI 2.43-11.5)]; ever changing ART [aHR 4.2 (95% CI 3.0-5.9)]; and ever received IPT [aHR 4.3 (95% CI 2.8-6.6)].

Conclusions: A significant proportion of children are aging out of pediatric into the adult ART cohort ; the rate of aging out is higher among children on ART and those who ever received IPT. Aging out should be considered when determining the net growth of pediatric ART cohorts.

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HIV drug resistance among children in Malawi: Multi-year surveillance results and clinical outcomes

Wadonda-Kabondo N1, Buck W6, Sexton J2, Chang J3, Luhanga M1, DeVos J4, Moyo K5, Ng’ambi W5, Phin S6, Yang C5, Weigel R8

1 U.S. Centers For Disease Control And Prevention - Malawi, 2 ASPH/CDC Allan Rosenfield Global Epidemiology Fellowship, 3 Baylor College of Medicine Children’s Foundation Malawi, 4 University of California - Los Angeles, 5 U.S. Centers for Disease Control and Prevention, 6 National HIV Reference Laboratory - Ministry of Health, 7 Lighthouse Trust, 8 Liverpool School of Tropical Medicine

Background: The evolution of HIV drug resistance (HIVDR) among children on antiretroviral therapy (ART) has a limited evidence base, with no published studies specific to Malawi. We adapted the WHO adult strategy for surveillance to determine prevalence of baseline and acquired HIVDR and describe HIV drug resistant mutations
(DRM) in a cohort of HIV-1 infected children on ART over time.

**Materials and Methods:** ART-naïve HIV-1 infected children (<15 years) starting on a standard ART regimen of stavudine/lamivudine/nevirapine (d4T/3TC/NVP) between 2008-2010 were recruited at three sentinel sites in Lilongwe. Samples were collected to assess virologic failure (VF) (viral load >1000 copies/mL) and HIVDR at baseline, 12, 24, and 36 months. Demographics, clinical information, and prevention of mother to child transmission of HIV (PMTCT) history were recorded at each visit. Stanford HIVDR Database intermediate-to-high DRMs were reported and include nucleoside reverse transcriptase inhibitor (NRTI), non-nucleoside transcriptase inhibitor (NNRTI), and protease inhibitor (PI) mutations.

**Results:** In this cohort (n=378), the mean age was 2.5 years and 111(29%) had PMTCT exposure to single-dose nevirapine. A total of 255(68%), 184(49%), and 136(36%) samples were provided at 12, 24, and 36 month study points, respectively. Samples (n=953) were analyzed over a 36-month treatment period where NRTI (n=132), NNRTI (n=137), and PI (n=7) DRMs were captured among 80(21%) children. For NRTIs and NNRTIs, the proportion of mutations observed was lowest at baseline (6% and 8%) and highest at 12 months (22% for both). Few children (n=2) demonstrated PI DRMs for an overall study prevalence of 1%. Between the 12 and 36 month study points, VF decreased from 22% to 15%. Resistance to current first-line antiretroviral drugs (ARVs) used in Malawi included lamivudine/3TC (18%), zidovudine/AZT (8%), nevirapine/NVP (25%), efavirenz/EFV (25%), and tenofovir/TDF (6%).

**Conclusions:** This study offers insight into evolution of DR in real life conditions. HIVDR to current first-line ARVs was high (21%) compared to what is typically observed in adult populations in Malawi. The proportion of DRMs was highest among NNRTIs and NRTIs for NVP, 3TC, and EFV. The study experienced high attrition, and it is possible that many of the patients who died, were lost to follow-up, or did not have a sample collected also had VF and HIVDR that was not captured. However, children who remained in care and on treatment demonstrated encouraging viral suppression trends.

**Abstract 112**

**Retention in care of children living with HIV in resource constraint setting: the case of Nepal**

**Deuba K**

1 Save the Children International stationed at National Centre For AIDS and STD Control, Ministry Of Health

**Background:** The need for efficient retention in HIV care is more evident than ever because of the expansion of earlier ART initiation and the shift towards 'Test and Treat'. This study assesses different steps of HIV care cascade (from diagnosis to viral load suppression) among children living with HIV (CLHIV) in Nepal. We also examined retention in care, mortality and Loss To Follow-Up (LTFU) over time by age (0-4 and 5-14 years) and gender.

**Methods:** We calculated the number of CLHIV using UNAIDS developed Spectrum and Epidemic Projection Package using census, surveillance data and national programme data. We reviewed the program data of all HIV-infected children (1363) registered till the end of 2015 in 65 ART centres in 59 districts of Nepal. The retention in care was defined as the percentage of children alive and on ART at 12, 24, 36 and 48 months. LTFU was defined as having not visited ART centre for 90 days.

**Results:** Of 1589 estimated CLHIV, 815 (51.3%) were male, and 774 (48.7%) were female. 1363 (86%) of the total estimated children were diagnosed with HIV by the end of 2015. Of the total estimated CLHIV, 76% linked to HIV care. Only half of the CLHIV have access to ART, and one-third (35%) had tested for viral load. Only one-quarter of CLHIV remained virologically suppressed (<1000 copies/mL) at their most recent tests. The retention rate was 94%, 94%, 89% and 84% at 12 months, 24 months, 36 months and 48 months respectively. No substantial difference in the retention in care was observed by gender, but the difference was observed by age group. LTFU was increased from 3% in 2012 to 6% in 2016, and the substantial difference was observed by age group (54 years old vs. 5-14 years old: 11% vs. 2% at 12 months). Similarly, we found a significant
difference in mortality rate over time by age group (≤4 years old vs. 5-14 years old: 14% vs. 6% at 36 months).

Conclusions: Young children (≤4 years old) are experiencing higher LTFU and mortality than children 5-14 years old. Future efforts should improve access to and retention in care of young CLHIV in Nepal.

Abstract 113
Assessment of Pediatric HIV Testing and Linkage to HIV Care and Treatment in Lesotho, 2014

Harris T1, Schaaf A1, Hartsough K1, Tau P1, Gadisa T1

1ICAP at Columbia University's Mailman School of Public Health

Background: In 2015, 13,000 children were living with HIV in Lesotho, which has the second highest global HIV prevalence. Lesotho's HIV program has made substantial progress; however, challenges to achieve universal treatment access persist. As such, challenges across the HIV care continuum – pediatric testing uptake, timely linkage to care, and immediate ART initiation--need to be identified and addressed.

Methods: A Presidents Emergency Funding for AIDS Relief (PEPFAR)-funded evaluation was conducted from May-June 2016. Routine data was abstracted from HIV testing and counseling (HTC), pre-ART, and ART registers and HIV care cards for children age 0-14 years receiving services in 2014 in 62 facilities in five high HIV burden districts prioritized for the Lesotho Accelerating Children on Treatment (ACT) initiative. Data was limited to services provided within the testing facility, as no system for tracking inter-facility transfers exists. Descriptive and univariate analyses were conducted to identify factors associated with testing and testing positive. Statistical analyses accounted for clustering by health facility, using generalized linear mixed models.

Results: HTC registers recorded 24,443 children tested in 2014-3% positive, 97% negative, and <1% indeterminate. Most tested were aged 10-14 years (37%). More boys were tested than girls (56% vs. 44%) and among those tested, females were more likely to test HIV-positive (2.9% vs. 2.4%, p=0.028). Positivity differed by age - <1 year: 2.8%, 1-4 years: 2.9%, 5-9 years: 3.1%, 10-14 years: 2.1% (p=0.047). Including non-HTC register data, 674 children tested positive and 436 (65%) were enrolled in care at the same facility. Of the 436 in care, 333 (76%) initiated ART; 53% (167/317) initiated within one month. Children initiated on ART were more likely to be active in care than those not initiated (68% vs. 11%, p<0.0001).

Conclusions: Poor retention observed among children not started on ART suggests that successful implementation of immediate ART initiation should be prioritized to increase retention. More boys were tested likely due to the voluntary medical male circumcision program that includes boys aged 10-14 years. Opportunities for testing more females aged 10-14 should be identified to support HIV prevention among adolescent girls and young women by providing a forum for prevention messaging/counseling.

Abstract 114
Substitution of stavudine in children and adolescents on combination ART: describing the impact on virological outcomes

Fick C1,2, Sawry S1,2, Kachingwe E1, Maribe A1, Fairlie L1,2

1Wits Reproductive Health and HIV Institute, 2University of the Witwatersrand

Introduction: Stavudine-containing regimens were the mainstay of ART in many low- and middle income countries, until concerns about long-term side effects necessitated that it be replaced by newer agents. This prompted a change in WHO guidelines for ART in children in 2010. In South Africa, guidance since April 2010 recommends that children and adolescents on ART be switched, once virally suppressed, from stavudine onto a newer NRTI (Abacavir or Tenofovir). The implications...
of broadly implemented ART backbone switches on the durability of viral suppression in HIV-infected children and adolescents has not been adequately explored in routine clinical settings. This study investigated the effect of switching from stavudine to another NRTI on viral suppression.

Methods: We conducted a retrospective review of clinical records from a large paediatric ART clinic in Johannesburg, South Africa. Children (0-19 years) in care in April 2010, on a stavudine-containing ART regimen for at least 12 months, who had never experienced a drug or regimen switch and who had 2 consecutive suppressed viral loads in the previous 12 months, were included in the study. Incidence of viral rebound (viral load >400 copies/ml) between 2010 and 2015, was calculated using survival analysis. Person-time at risk started at time of drug substitution or at the first visit after 1st April 2010 for those who never switched from d4t to another NRTI (T0) and ended 12 months later or censored at the first event of viral rebound, death, transfer out or loss to follow-up. Multivariate Cox proportional hazard models were used to estimate the association between viral rebound and potential risk factors.

Results: In total, 727 children were included in the analysis: at T0, all were virally suppressed, median age was 9.5 years (IQR:6.4-12.4) and median duration on ART was 37.8 months (IQR:26.7-49.8). Among these, 568 (78%) had undergone an NRTI switch and 159 (22%) had not, with no statistically significant differences in degree of immune suppression, weight-for-age, height-for-age or BMI-for-age Z-scores between the two groups at T0. More children in the switch group were initiated on EFV-containing regimens compared to the non-switch (76% vs 62%; p<0.05). At 6 months, 265 person-years (pys) were observed; the overall incidence of viral load rebound was 9.4/100pys (95%CI:6.4-13.9) among 576 children. The incidence in children who switched was 7.4/100pys (95%CI:4.5-12.4), compared to 15.4/100pys (95%CI:8.3-28.7) in non-switches. At 6 months those who switched were significantly less likely to experience rebound (HR:0.4, 95%CI:0.2-0.9). No other risk factors (prior elevated viral load, age, sex, time on ART) were significantly associated with rebound in univariate analyses. At 12 months, switching was not associated with rebound.

Conclusion: In routine clinical care, the implementation of a single NRTI switch in children and adolescents with prior viral suppression resulted in a reduced risk of viral rebound within 6 months after the switch. At 12 months there was no difference in rebound between the groups. This provides some reassurance that single drug substitutions to newer NRTIs is unlikely to have adverse effects on the durability of viral suppression.

Abstract 115

Antiretroviral therapy (ART) for children 18 months to 5 years in Rwanda: Faster ART initiation and better growth

Arpadi S1, Lamb M1, Nzeyimana I1, Vandebriel G1, Anyalechi E2, Wong M1, Smith R1, Rivadeneira E2, Kayirangwa E3, Malamba S3, Musoni C3, Koumans E1, Nsanzimana S4

1ICAP Columbia University, 2US Centers for Disease Control and Prevention, 3US Centers for Disease Control and Prevention, 4Rwanda Biomedical Center

Background: Although it is well established that early ART initiation reduces morbidity and mortality for HIV-infected children less than one year of age, there is less evidence of benefit for older children. In 2012, the Rwandan national guidelines recommended ART for all HIV-infected children 5 and under regardless of CD4 or clinical status. Implementation of this policy change provided an opportunity to compare outcomes for HIV-infected children aged 18 months to 5 years.

Methods: We conducted a retrospective study to compare HIV-infected children ages 18-60 months enrolled into care before (standard cohort) and after 2012 guidelines implementation (treat all cohort). Proportionality proportional to size sampling selected 100 sites from among 421 providing services to HIV-infected children as of August 2013. At these sites, medical records were abstracted from all children 18-60 months enrolled between June 2009-July 2011 (standard) and July 2012-April 2015 (treat all), with follow-up information abstracted up to 14 months after
enrollment. ART eligibility was based on national guidelines applicable at the time. First date of ART pharmacy pickup was used as ART initiation date. Repeated measures analyses were used to estimate and compare average change in WHO weight-for-age z-score (WAZ) since enrollment, and for children initiated on ART, average change in WAZ since ART initiation.

**Results:** Medical records were abstracted for 392 children: 241 and 151 in the standard and treat all cohorts respectively. At enrollment the mean age (standard deviation) was 3.1 years (1.0) for the standard and 3.0 years (1.1) for the treat all cohort, p = 0.16. In the standard cohort, 59% initiated ART within one year versus 89% in the treat all cohort; the median (Interquartile range [IQR]) time to ART initiation was 68 days (IQR 14-494) among the standard cohort and 9 days (IQR 0-28) in the treat all cohort (p<0.0001). Of those initiating ART in the treat all cohort, 49% would not have been eligible for ART initiation under national 2009 guidelines. Three hundred twenty nine (84%) were included in WAZ change assessment. At 12 months post enrollment, the mean WAZ among the treat all cohort was WAZ 0.28 units higher than in the standard cohort (p = 0.09). In repeated measures analyses, the treat all cohort experienced an average 0.30 unit greater increase in WAZ over enrollment baseline compared to the standard cohort (95% CI: 0.07 to 0.53; p=0.01). Among those initiating ART, the mean WAZ at ART initiation among the treat all cohort was 0.22 units higher than the standard cohort (p = 0.21). Following ART initiation the change in WAZ was similar in both cohorts (beta = 0.12, 95% CI: -0.11 to 0.35, p= 0.31).

**Conclusions:** In Rwanda the 2012 guidelines resulted in nearly 90% of children starting on ART within one year of enrollment; nearly half would have been ineligible according to previous guidelines. As change in WAZ from enrollment was higher in children in the treat all cohort, a more favorable growth pattern was observed among HIV-positive children following implementation of the 2012 guidelines.

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**Abstract 116**

**Factors associated with Seronegativation in early treated children with vertically transmitted HIV infection in Cameroon**


1Service d'Epidémiologie et de Santé Publique, Centre Pasteur Du Cameroun, 2Centre Hospitalier d'Essos, 3Centre Mère et Enfant, Fondation Chantal Biya, 4Hôpital Laquintinie, 5Faculté de Médecine et de Sciences Pharmaceutiques, Université de Douala, 6Service de Virologie, Centre Pasteur du Cameroun, 7Assistance Publique des Hôpitaux de Paris, Hôpital de Bicêtre , 8INSERM U1018, CESP - Équipe VIH et IST, 9Université de Paris Sud , 10Assistance Publique des Hôpitaux de Paris, Hôpital Robert Debré, 11Université Paris Diderot, 12INSERM UMR 1123, ECEVE

**Background:** Negative serological test in early treated HIV-infected children is not a rare phenomenon now. But, the mechanism explaining the absence of HIV-antibodies is not completely described. Here, we explored characteristics associated with the absence of HIV-antibodies in early treated children followed during five years in the ANRS-Pediacam cohort.

**Methods:** From November 2007 to December 2010, HIV-infected children followed from first week of life or at diagnosis before 7 months of age, and HIV-uninfected children followed from first week of life born to HIV-infected or -uninfected mothers were included after parental consent in the ANRS-PEDIACAM cohort in Cameroon. HIV-infected children were offered free combined antiretroviral therapy (cART) according to national guidelines. Children follow-up was planned from inclusion to five years of age. During follow-up, HIV serology was carried out in HIV-infected children using a fourth-generation ELISA from fifteen months of age. Retrospectively, we defined and compared two groups of children using serological test and viral load accordingly: seronegative group (children with at least one negative serological test during follow-up) and control group (children with positive serological test who
maintained HIV viral load under 1000 copies/ml during follow-up).

Results: In total, 210 HIV-infected infants (55.7% female) were included with 106 (50.5%) at the Mother and Child Center of the Chantal Biya Foundation, 61 (29.0%) in Essos Hospital Center in Yaounde and 43 (20.5%) in Laquintinie Hospital in Douala. Of the 210 HIV-infected infants enrolled, 13 (6.2%) died untreated. Of the remaining 197 infants, 5 (2.5%) refused cART and to continue follow-up, and 192 (97.5%) started cART at a median age of 4.1 months [Interquartile range (IQR): 3.2 – 5.6]. The median duration of cART from initiation to this evaluation was 4.7 years [IQR: 4.5 – 4.8]. HIV serology was performed at least one in 144 HIV-infected children considered in this analysis. The median age at first HIV serology was 20.3 months [IQR: 18.3 – 22.8]. Of the 144 children tested, 28 (19%) children were seronegative and 26 (18 %) fulfilled the control group criteria. Age at cART initiation less than 3 months (39% vs 12%, p=0.04), short delay from cART initiation to first viral load suppression [(3.31 months, IQR: 2.97-6.46) vs (5.27, IQR: 3.17-6.06), p<0.001], and pre-term birth or gestational age less than 38 weeks (39% vs 15%, p=0.04) were significantly associated with absence of HIV-antibodies. No difference was observed between the two groups concerning gender, PMTCT prophylaxis, mode of delivery, cART regimen at initiation, and other social and economic characteristics of mother.

Conclusion: These results reinforce the interest of early cART and underline the fact that lack of children maturation could influence the production of HIV-antibodies. There is a need to continue this exploration in order to facilitate the discussion of physicians with families in order to save adherence.

Abstract 117

Gaps in management of children and adolescents on ART with virologic failure: lessons learnt from a viral load service quality assessment in Kenya

Mutisya I1, Wangari E1, Muthusi J1, Boylan A2, Chun H2, Broyles L2, Katana A1

1CDC, 2CDC

Background: According to 2016 national ART data, there are 115,000 children and adolescents on ART in Kenya. Viral load testing has been scaled up in the past 2 years with approximately 73% uptake in this population (2016 ). Appropriate management of virologic failure (VF) is essential in improving outcomes and preserving future ART treatment options for children and adolescents. Our study evaluated viral suppression rates and management of VF among adolescents and children.

Methodology: A viral load (VL) service quality assessment (SQA) was conducted in March 2016 in select high burden counties in Kenya that account for 75% of people living with HIV (PLHIV) . Health facilities were eligible for inclusion if they had >500 patients on ART and offered both maternal, child and adolescent services: 25 ART sites were purposively selected and evaluated. Children (0-9 yrs) and adolescents (10-19 yrs) who initiated ART between 1/1/2014 and 8/31/2015, with at least one documented VL at the date of abstraction were included. Key variables abstracted were demographics, HIV treatment and viral load levels. Data were analyzed using SAS and Epi info.

Results: Medical records were reviewed for 540 children and adolescents; 280 children and 260 adolescents. Median age was 7.8 years and inter quartile range [IQR] (4.0 - 12.8years). Males were 48.5%. ART regimens were 87.4% non -nucleoside reverse transcriptase (NNRTI) and 12.6% protease inhibitor (PI) based. PI based regimen was more likely in children compared to adolescents, 18.6% vs 1.3 %, p-value=<.001.
Of the 540 VL tests ordered: 459 (85%) were routine and 10 (2%) were targeted (suspected treatment failure) and 71 (13%) were for “other” reasons. Viral suppression defined as VL < 1000 copies/mL was 79.5%; 77% in children and 83% in adolescents. There was no significant difference in viral suppression for clients on PI regimen compared to Nevirapine, OR 0.7(0.12-4.06) p-value=0.69. Documented poor adherence was associated with VF, OR 12.22(3.35-44.65), p=<.001. Of the 189 with VF, only 36% received 1st enhanced adherence counselling (EACC), 16% received 2nd EACC and 10% 3rd EACC. Among patients with documented virlogic failure, only 26% had a repeat VL; of those, 90% had VF on repeat viral load. Only 13% of those with VF on a repeat VL were switched to second line antiretroviral therapy.

Conclusion: Results of SQA revealed gaps in management of children and adolescents failing on ART: lack of timely repeat viral load test, suboptimal adherence sessions and sustained VF even on the follow up viral load. Urgency is required to implement systematic management of VF, provision of enhanced age appropriate adherence support and timely regimen switch for those eligible.

Abstract 118

Prevalence of minority HIV-1 drug resistant quasi-species in children patients at virologic failure in a rural KwaZulu-Natal cohort.

Mthiyane H1, Danaviah S2

1Wits, 2AHRI

Background: Missed minority drug resistance mutations (DRMs) may pave a way to therapy failure in a short period of time. Therefore, the use of sensitive assays to monitor the presence of minority DRMs in HIV-1 infected individuals especially children is important and urgently needed for better patient management. Assays have been developed including next generation sequencing (NGS) that are able to identify a larger proportion of quasi-species including those bearing minority DRMs within a patient's viral population. This intervention is crucial particularly among children who would require antiretroviral therapy (ART) for their lifetime. Therefore, the aims of this study was to (1) describe the prevalence of minority HIV quasi-species harbouring DRMs in paediatric patients at virologic failure in a rural KwaZulu-Natal (KZN) paediatric cohort using NGS technology and (2) to compare the genotypes generated using Sanger sequencing with NGS.

Study design: This retrospective study was conducted on archived samples (n= 34) collected from August 2011 to June 2014 from infants and children ≤15 years of age on first-line ART (13 on PI-based regimen and 21 on an NNRTI-based regimen) and experiencing virologic failure (defined as two successive viral load results >1000 copies/ml) from a rural KwaZulu-Natal cohort.

Methods: Thirty four patients were genotyped using both Sanger sequencing and NGS. A 1.3kb region of the Pol gene was genotyped using Sanger sequencing, while the whole 9.7kb HIV genome was sequenced using NGS. All electropherograms were analysed using the Geneious V8.0.5 software system for the presence of drug resistance mutations including minority drug resistance mutations. Sequences were assembled against an HIV-1 subtype C reference sequence from South Africa. For NGS a reference sequence was annotated with known HIV resistance mutations within the protease and RT genes. Drug resistance mutations were identified using the RegaDB which references the Stanford, Rega and ANRS resistance algorithms and analysed in correlation with selected clinical and demographic data in STATA v11.

Results: NGS was able to detect minority DRMs in eleven (32.3%) samples which were missed by Sanger sequencing. NGS also detected an additional three (8.8%) specimens that harboured DRMs but were found to be susceptible by Sanger sequencing. Patients on PI-based regimen had a lower prevalence of mutations compared to those on an NNRTI-based regimen.

Conclusion: The presence of minority DRMs among paediatric patients is likely to obstruct the use of ART and consequently predispose patients to therapy failure. This emphasises the critical importance of using specific and
sensitive assays for the detection of minority DRM early in treatment particularly among children. We noted that children on PI-based regimen, while at a lower prevalence still harboured DRMs that remained undetected by conventional Sanger sequencing. Finally, this study emphasised the need to apply more sensitive assays to accurately distinguish patients failing due to the emergence of minority DRMs from those that are non-adherent in order to maximize the efficacy of the limited range of anti-retroviral drugs currently in use in South Africa.

Abstract 119

HIV-infected adolescents on anti-retroviral therapy: a retrospective descriptive cohort study of breast abnormalities documented during routine care

Dunlop J1,2, Firnhaber C1,2, Schnippel K1,2, Makura C1, Levin L1, Vujovic M1, Rayne S1,2, Stemming W2

1Right To Care, 2University of Witwatersrand, 3Helen Joseph Hospital

Background: HIV antiretrovirals (ART) cause breast abnormalities in adults, especially efavirenz (EFV). Little is known about the prevalence of these adverse effects in adolescents receiving ART. This study describes clinical and demographic characteristics of adolescents with breast conditions.

Methods: A retrospective file review looking for clinical notes describing abnormal breast conditions in adolescents receiving ART at three facilities in South Africa. Patients aged 10-19 presented at the clinics from 1 January to 31 December 2014. Descriptive statistics will be reported and an analysis conducted to determine whether there is a significant increase in breast conditions on with EFV.

Results: 631 patient records were reviewed, 37 patients (5.9%) had an abnormal breast event documented of which 24/37 (64.9%) were male. 41 abnormal breast events were observed in 37 patients. Breast conditions developed at 1.5 years older than normal breasts (p<0.0005). 48.8% of breast events were described as gynaecomastia or lipomastia (n=20) with 7.3% being severe (n=3). 43.6% suffered from comorbid lipodystrophy (n=19) with 84.2% having received stavudine (D4T) (n=16/19). At abnormal breast event, 71% of patients had CD4 counts >500 cells/µl and were virologically suppressed (n=29). Adherence to ART was good (>90% of doses taken) in 63.4% with abnormal breast conditions (n=26). Significantly more cases of breast abnormalities were noted in patients receiving EFV compared to other NNRTI and PI regimens (p<0.0005). All patients with breast abnormalities had been exposed to EFV, for a median duration of duration of 5.5 years (IQR:3.8-8.5). D4T was also related to the development of abnormal breast conditions (p=0.28) possibly through the lipodystrophy pathway with 59.5% having been exposed to D4T for a median duration of 4.9yrs (IQR:1.8-7.2). 16 events resulted in substitution of EFV (39.0%), five led to a change from D4T and three resolved once substituted from EFV to nevirapine.

Conclusion: 5.9% of patients had an abnormal breast condition. EFV and D4T use, male gender and increased age were associated with breast conditions (p<0.05). EFV substitution was the most common intervention (n=16/41). Further study is needed to better understand this phenomenon.

Abstract 120

Impact of therapeutic food supplementation on lipid profiles of malnourished HIV infected children in Uganda

Tatwangire Orikiliza J1,2, Kikaire B1, Nakawesi J1, Kambugu A1, Lamorde M3, Turtwetenka D1, Mugasha C1, Mubiru F2, Normark J1, Achan J1, Musiime V6, Ndezi G6, Mbona Tumwesigye N1, G. Doherty D1, Lithander F8, Spiers P9, Mullen A10, Hennessey M9

1Infectious Diseases Institute, College of health Sciences, Makerere University, 2Department of Immunology, School of Medicine, Trinity College Dublin, 3Pediatrics Department, Mildmay-Uganda, 4Division of Infectious Diseases, Department of Clinical Microbiology, Umeå
Introduction: Malnutrition with HIV infection precipitates profound metabolic derangements. The objective of this study was to compare serum lipid profiles of HIV-infected malnourished and well-nourished-children (WNC) and to determine the impact of ready to use therapeutic food (RUTF) on lipid profile after 12 weeks of supplementation. Malnutrition was defined as weight-for-height-z-score < -2SD expected for age or mid upper arm circumference < 12.5 cm with no oedema.

Study design: This was a prospective cohort study of HIV-infected children aged 6 months to 12 years, on antiretroviral treatment (ART) or ART-naïve. A blood sample was taken after an overnight fast and processed immediately, hemolysed samples were excluded. Ethical approvals were received at all levels.

Results: At baseline 156 patients (76 male) were recruited, of whom 85 (54.5%) were malnourished; the median (IQR) age was 5.2 (2.8-8.8) years. Only 92/156 completed the 12 week visit. Of the ART-naïve and ART-experienced children 62.1% and 49.4% were malnourished respectively. Immunosuppression (<30% CD4+ T cell) among ART-naïve patients was 80% (53/66) compared to 46% (39/85) of the ART-experienced. Majority of ART-experienced children 59/81 (72.8%) had detectable viral loads ≥20cps/ml. The median viral load among the ART-naïve was 240,753cps/ml (IQR: 2SD expected for age or mid upper arm circumference <12.5 cm with no oedema).

After RUTF supplementation the mean total cholesterol among the ART-naïve was similar to the WNC; increase in HDL was statistically significant (0.8±0.5 to 1.1±0.5; p<0.004). Baseline lipids in ART-experienced compared with ART-naïve children demonstrated higher levels of total cholesterol (4.1±1.1 vs 3.1±1.0 mM; p≤0.001), HDL (1.1±0.5 vs 0.5±0.3 mM; p≤0.0001) and LDL (2.2±0.8 vs 1.6±1.0 mM; p≤0.001) respectively.

Conclusion: HIV-infected-children who are malnourished compared to the WNC have lower HDL cholesterol which is normalized by RUTF supplementation for 12-weeks. ART-experienced children have significantly raised serum lipids compared to ART-naïve children indicating that ART can profoundly affect lipid metabolism.

Prevalence of renal abnormalities in HIV-infected children and adolescents – a multicentric study

Oliveira F1, Fraga A1,2, Tavares M4, Virtuoso M4, Campos T6, Mouzinho A5, Stone R6, Marques J6

1Unidade de Infeccologia Pediátrica, Departamento de Pediatria, Hospital Universitário de Santa Maria, Centro Académico de Lisboa, 2Serviço de Pediatria, Hospital De São Bernardo, Centro Hospitalar de Setúbal, EPE, 3Serviço de Pediatria, Hospital do Divino Espirito Santo de Ponta Delgada, EPE, 4Serviço de Pediatria, Centro Hospitalar de São João, EPE, 5Serviço de Pediatria, Centro Hospitalar do Algarve, EPE, 6Serviço de Pediatria, Hospital Prof. Doutor Fernando da Fonseca, EPE, 7Unidade de Nefrologia Pediátrica, Departamento de Pediatria, Hospital Universitário de Santa Maria, Centro Académico de Lisboa

Background: The increasing survival of patients with human immunodeficiency virus (HIV) infection, under effective antiretroviral therapy (ART) may lead to an increasing prevalence of some comorbidities due to HIV infection and/or ART, such as kidney disease. This study aimed to identify the prevalence of renal abnormalities (RA) among HIV-infected children and adolescents followed up in Portuguese hospitals and to identify risk factors for RA in our cohort.

Materials & Methods: Retrospective, multicentric, cross-sectional cohort study. The RA group included patients with at least one criteria: proteinuria/hematuria in two subsequent samples; renal ultrasound or
biopsy abnormalities; systemic hypertension; estimated glomerular-filtration-rate (eGFR) less than 90 ml/min/1.73m² (less than 60ml/min/1.73m² defined as chronic kidney disease-CKD), using the Schwartz formula. Statistical analysis was performed with SPSS statistics, using t-student test for continuous variables and chi-square or fisher test for categorical variables. A multivariable logistic regression was performed to identify factors independently associated with RA.

Results: We included 145 children and adolescents followed in four hospitals: 61% females; median age 10.6 (IQR 4.4-15.6) years; 53% from Portugal and 42% with African parents; 94% infected by mother-to-child transmission; 98% HIV-1; 24% subtype G; 86.9% on ART with a median duration of 2.3 (IQR 0.6-5.5) years. Actual viral load was undetectable in 67.7%. Distribution by CDC immunological staging: stage-1 76%; stage-2 19.3%; stage-3 4.1%. HIV non-related and HIV-related non-renal comorbidities were present in 14% (n=20) and 40% (n=58) respectively. RA were found in 24% (n=35); proteinuria 11%, hematuria 7.6%, eGFR <90ml/min/1.73m² 9% (CKD 2%), altered renal ultrasound 2.8%, altered renal biopsy 0.7% and hypertension 2.1%.

In a multivariate analysis including age, gender, HIV type and HIV non-related comorbidities as covariates, non-vertical transmission (OR 6.5, CI 95% 1.2-39.5, p=0.031) and actual treatment with emtricitabine/tenofovir (FTC/TDF) (OR 5.4, CI 95% 1.0-28.5, p=0.045) and abacavir-based schemes (OR 6.4, CI 1.4-29.8, p=0.018) were associated with RA. TDF without FTC was being taken by 7 patients without RA and none of the RA group.

No significant difference was found between groups regarding viral load and CD4-staging at the start of actual ART, CD4 nadir, actual viral load and non-renal HIV-related comorbidities. There was a non-significant trend in the RA group for a higher prevalence of HIV non-related comorbidities (28.6% vs. 15.5%, p=0.132) and for an older age at the beginning of ART (5.06.2 vs. 3.34.2, p=0.164).

Conclusions: In our cohort we found no significant correlation between RA and clinical/immunological severity, which may be due to the low number of severely immunosuppressed patients. TDF was related to RA only when associated to FTC, and deserve further investigation. The prevalence of CKD (2%) was lower than the reported in HIV-infected children in North America (4.7%) and Europe (9.7%) and that may be the trend in the years to come. The prevalence of subclinical RA in HIV-infected children is unclear. In our cohort, 24% of the children had some type of RA, which emphasizes the importance of kidney complications screening.

Abstract 122

Effectiveness of outpatient nutritional rehabilitation based on ready-to-use food in Senegalese children and adolescents infected with HIV: The multicenter SNAC’s Study

Ndiaye S1, Varloteaux M2, Diop K1,2, Coulibaly M2, Masson D2, Niasse F3, Cames C2

1 Centre regional de Recherche et de Formation à la prise en charge Clinique, CHU de Fann, 2 Institut de Recherche pour le Developpement, UMI233/U1175/Universite de Montpellier, 3 Division de Lutte contre le Sida et les IST, Ministere de la Sante et l’Action Sociale, 4 Sidaction, 5 Conseil National de Lutte contre le Sida

Background: Severe acute (SAM) and moderate acute (MAM) malnutrition are common and associated with mortality in HIV-infected children and adolescents, even when on antiretroviral treatment (ART). Ready-to-use food (RUF) is effective and widely used in outpatient nutritional rehabilitation of children <5 years with SAM. However, the effectiveness of such nutritional rehabilitation in older children and adolescents is unknown. The SNAC’s Study aims to assess effectiveness of RUF protocols in 12 HIV clinics in Senegal.

Methods: SAM and MAM were defined as body mass index z-score (BMI-z) < -3 and ≥ -3 to < -2 , respectively. RUF, namely Plumpy Nut™ and Plumpy Sup™, were provided every 2 weeks and prescribed by weight to SAM and MAM children, respectively, aged 6 months to 19 years. Successful nutritional rehabilitation (SNR) was defined as reaching a z-score for BMI-z > -1.5. Laboratory monitoring was performed at enrollment and at last visit.
Multiple logistic regression was used to assess factors associated to SNR.

Results: Overall, 185 children were enrolled, 79 SAM and 106 MAM, 39% were girls, median age was 11.7 years (IQR: 8.1–14.3), 56% were followed-up in decentralized study sites, 87% were on ART of whom 47% presented with a viral load < 300 copies/ml at enrolment. Most patients, 72%, experienced SNR, 18% failed to gain weight and/or to consume RUF and were discontinued, 8% defaulted and 2% died. MAM children were more likely to achieve SNR than MAS children (84% vs 57%, P=0.001). Median time to achieve SNR was 98 days (IQR: 59–182) in MAM and 154 days (96–266) in SAM children (P=0.003). Independent risk factors for SNR were presenting with MAM rather than SAM (adjusted odds ratio = 3.5, 95% CI: 1.6–7.5), to be younger (6 mo–10 years versus 10-19 years of age: 2.8, 1.1–7.0), to be enrolled in a regional clinic (2.3, 1.0–5.0) and presenting with a better immunologic status (CD4 count ≥ 350 cells/ml vs. < 350).

Conclusion: RUF therapies are feasible and effective in undernourished HIV-infected children and adolescents, including in a decentralized setting. The results suggest that rehabilitation is shorter and more effective when initiated at an early stage of malnutrition and advocate for the integration of RUF therapies in the global HIV care of children.

Abstract 123
Low immunization coverage of the Expanded Immunization Program in HIV-infected children initiated on ART before the age of two and its determinants in Abidjan and Ouagadougou, Project MONOD ANRS 12206

DAHOAROU D,1,2, Asité-N’Guessan S,4, Mea V,5, Diméglio C,1, Amorissani-Folquet M,1, Yonaba C,4, Malateste K,1, Yé D,1, Timité-Konan M,9, Desmonde S,4, Ahoba I,9, Leroy V,

1Centre Muraz, 2MONOD Project, ANRS 12206, Centre de Recherche Internationale pour la Santé, 3Inserm, Unité U1219, Université Bordeaux, 4Inserm, Unité U1027,

Objective: Thank to the access to antiretroviral treatment (ART), HIV-infected children survive, but their vulnerability to residual infectious diseases remains, justifying the National Expanded Program on Immunization (EPI) recommendations in this population, especially in low-income countries where the infectious disease spectrum is important. We assessed the vaccine coverage and its associated factors in HIV-infected children at their time of inclusion before the age of two in a research project in Abidjan, Côte d’Ivoire and Ouagadougou, Burkina Faso.

Methods: All confirmed HIV-infected children, less than two years of age, and whose parents have given their written consent were included from 2011 to 2013 in the ANRS 12206 MONOD therapeutic cohort to receive a lopinavir-based ART for 12 months. At inclusion, all EPI immunizations planned at birth for BCG, at 6, 10, and 14 weeks for diphtheria–tetanus–pertussis polio tetravalent, Hib and HBV monovalent, and at 9 months for yellow fever and measles monovalent, and their related dates were recorded. Those with incomplete vaccine program had catching-up doses. At baseline, the EPI immunization coverage was measured, and its socio-demographic associated factors studied using a logistic regression.

Results: Between 05/2011 and 01/2013, 161 children were initiated on ART at median age of 13.7 months. At inclusion, vaccination coverages were: BCG: 85% (95% Confidence Interval [CI]: 78% - 90%); Oral polio vaccine coverage was 52% (CI: 41% - 61%) in Abidjan and 81% (CI: 69% - 90%) in Ouagadougou; 3-dose diphtheria–tetanus–pertussis-polio: 70% (95%CI: 63% - 77%), 3-dose Hepatitis B: 58% (95%CI: 50% - 66%); 3-dose Haemophilus influenzae b: 56% (95CI: 48% - 64%). In univariate analysis, there were several trends in associated non-immunization factors: mother alone in charge of the child, living in Abidjan rather than Ouagadougou, child being ever breastfed, and not having hospitalised
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Improving the transition to adult HIV care for perinatally HIV-infected adolescents, Thailand

Sricharoenchai S1, Lolekha P2, Na Nakorn Y3, Boonyyasidhi V1, Manaboriboon B1, Leowsrisook P4, Punpanich Vandepitte W2, Martin M2, Nuchanard W2, Dunier Y2, Kanakool S1, Yuvaseeve C1, Sontaratjwong P1, Jongchotchatchawal N2, Chokaphaibulkit K1

1Department of Pediatrics, Siriraj Hospital, Mahidol University, 2Division of Global HIV/AIDS and Tuberculosis Thailand/Asia Regional Office, Thailand Ministry of Public Health (MOPH) – US Centers for Disease Control and Prevention (CDC) Collaboration, 3Queen Sirikit National Institute of Child Health, Thailand MOPH

Background: HIV-infected adolescents are living longer and transitioning to adult HIV care. We implemented an 18-month clinic-based intervention, The Happy Teen Program, at two hospitals in Bangkok, to prepare HIV-infected adolescents for the transition to adult HIV care services. We evaluated adolescent’s satisfaction with and barriers to transition.

Materials and Methods: The Happy Teen Program consisted of a one-day group workshop, 2 half-day group sessions, and 3 individual sessions centered on 4 strategies: health knowledge, coping skills, sexual risk, and life goals. The group sessions focused on increasing youth’s knowledge about self-care, antiretroviral drug management, transitioning to adult care, health insurance, communication skills, self-esteem, family planning, sexual risk reduction, education, and career planning. Individual sessions focused on preparing for the transition. Counselors used a standardized questionnaire to collect information from participants in a face-to-face or telephone interview at 12 months after completing the program.

Results: Between March 2014 to July 2016, 192 participants joined the program. Of these, 158 (82.3%) participants returned for follow-up at 12 months. Among the 158 participants, 154 (97.5%) were perinatally acquired HIV infection, 86 (54.4%) were male, the median age was 17 (range: 14-21) years, 133 (84.2%) were students, 14 (8.9%) were employed, 151 (95.6%) resided with caretakers or relatives, and 157 (99.4%) were receiving ART (median duration 13 years).

Twelve months after completing the program, 36 (22.8%) participants had transitioned to adult HIV care services; 12 (33.3%) at the same hospital and 24 (66.7%) transferred to another hospital. The reasons for not transition among 122 (77.2%) participants included transition process was underway (73, 59.8%), age <18 years (41, 33.6%), participating in clinical studies (6, 5%), refusal for transition (2, 1.6%).

Among 36 transitioned participants, median age at transition was 20 (range: 16-23) years. The reasons for transition included a change in health insurance scheme (19, 52.8%), age ≥18 years (14, 38.9%), convenience (2, 5.6%), and the need for special service at an adult clinic (1, 2.8%). Most participants completed all appointments at adult clinics (34, 94.4%), and were satisfied with adult HIV care (34, 94.4%). Transitioned participants reported some difficulties in the transition including the perception that adult providers were unfriendly (4, 11.1%), did not provide good medical care (2, 5.6%), difficult to understand (1, 2.8%), did not maintain confidentiality (1, 2.8%), the care was disorganized (6, 16.7%), long wait time (4, 11.1%), and long distance to the clinic (3, 8.3%). Participants reported that The Happy Teen Program was helpful for the transition (35, 97.2%), provided good guidance for care...
in adult clinics (33, 91.7%), and promoted confidence in the transition (36, 100%). At 6.6 months into the transition, 28 (77.8%) participants were virologically suppressed (<40 copies/mL) and the median CD4 count was 520 (range: 24-1,357) cells/mm³.

Conclusions: The Happy Teen Program helped HIV-infected adolescents transition to adult care. Transition preparation should begin in the pediatric clinic with the collaboration of adult providers to anticipate and resolve barriers. The long term impact of the transition program on behavioral and biologic outcomes requires ongoing follow-up.

Abstract 125

Maximizing targeted testing to improve HIV yield among children and adolescents in Rwenzori region, Uganda

Bitimwine H1, Musiime F1, Ajuna P1, Tumbu P1, Kekitiinwa A1

1Baylor College of Medicine Children’s Foundation-Uganda

Background: The Anti-retroviral therapy (ART) coverage for Uganda among children (<15 years) was 32%, compared to 52% for HIV positive adults by June 2015. This was closely linked to the low identification of HIV infected children and adolescents through existing HIV Testing Service (HTS) models. In Rwenzori region, HIV testing yield was low for children (0.7%) and adolescents (1%). Baylor-Uganda implemented targeted HTS models to improve HIV yield among children and adolescents and thus close the ART gap in the Rwenzori region. We determined the HIV yield from these models.

Methods: In the period March-June 2016, we provided HTS to children and adolescents 18months-19 years using the following models: HTS outreaches to dwelling homes of orphans and vulnerable children (OVC); Know your child Status Campaigns (KYCS); HTS outreaches to children of female sex workers (FSWs), fisher folks (FFs) and tea plantation workers; and evening HTS points targeting adolescents after work/school hours. We summarized the HIV yield for the different models in proportions and frequencies.

Results: Of the 4,091 children and adolescents tested, 2,135 (52%) were females and 2,030 (50%) adolescents (10-19 years). The overall HIV yield from all models was 53/4,091 (1.3%). The HIV yield among adolescents (10-19 years), children (5-9 years) and those under 5 years was 30/2,030 (1.5%), 20/1,234 (1.6%) and 3/824 (0.4%) respectively. The HIV yield was highest through HTS outreaches at OVC dwelling homes 7/271 (2.6%) and lowest through outreaches to children of tea plantation workers 0/214 (0%). The HIV yield through HTS outreaches to children of FSWs, children of FFs, KYCS campaigns and evening HTS points was 10/610 (1.6%); 3/283 (1.1%); 16/836 (0.9%) and 14/815 (1.7%) respectively.

Conclusion: A relatively high HIV yield was achieved through HTS outreaches at OVC dwelling homes; for children of FSWs, FFs and through Evening HTS; A low yield through outreaches to children of tea plantation workers and KYCS campaign. Therefore, deliberate efforts should be made to scale up HTS to OVC dwelling homes, children of FSWs and fisher folks, and evening HTS for adolescents; and consider to discontinue HTS outreaches to children of tea plantation workers and scale down or modify KYCS campaigns.

Abstract 126

Toward the first 90: Identifying and testing younger populations for HIV at community outreach events in Kenya

Okoko N1, Guze M2, Ndolo S1, Nyanaro G1, Bukusi E1, Cohen C2, Penner J1, Kulzer J3

1Kenya Medical Research Institute (KEMRI); Family AIDS Care and Education Services (FACES), 2Department of Obstetrics, Gynaecology and Reproductive Sciences, University of California San Francisco, San Francisco, CA, USA, 3University of British Columbia, Vancouver, British Columbia, Canada
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Background: Low HIV status awareness among children and adolescents, 12,940 new HIV infections among children and rising adolescent AIDS-related deaths in Kenya is a cause for concern given the association of delayed HIV identification with poor health outcomes. This study examined HIV testing outcomes and characteristics of younger (age <19) populations attending targeted community outreach events (TCOEs).

Methods: In Homa Bay, Migori, and Kisumu counties in Kenya 492 TCOEs with HIV testing and identification were conducted in 148 health facility catchment areas supported by the HIV program Family AIDS Care & Education Services (FACES) over five months from July – December 2015. Aggregated HIV testing (mean number tested), yield (mean number identified HIV positive), and gender among eligible children (age <15) and adolescents (age 15-19) at TCOEs were captured in a REDCap database. Negative binomial models were used to assess age and gender differences in HIV testing and yield.

Results: Among 14,603 individuals tested at TCOEs, 67% (N=9788) were children (age <15) and 33% (N=4815) were adolescents (age 15-19). Among children, 54% (N=5291) were female with 0.2% (N=10) HIV positive; 46% (N=4497) were males including 0.2% (N=8) HIV positive. Among adolescents, 51% (N=2457) were female with 0.5% (N=13) HIV positive; 49% (N=2358) were male including 0.2% (N=4) HIV positive. Adolescents were less likely to be tested at TCOEs compared to children (IRR: 0.46; 95% CI: 0.34, 0.62; p<0.01). Although fewer males than females tested overall (IRR: 0.85; 95% CI: 0.78, 0.93; p<0.01), the decrease in males testing from the children age group to the adolescent age group was smaller than in females (IRR: 1.13, 95% CI: 1.02, 1.25, p=0.02). There was no significant difference in age and gender among those testing positive.

Conclusions: Targeted community outreach events reached twice as many children as adolescents for HIV testing and identification and female HIV testing declined in adolescence. The TCOE approach appears useful in reaching children, however a better understanding of what type of community approaches would draw adolescents, particularly females, is needed.

Abstract 127

Piloting very early infant diagnosis of HIV in Lesotho: acceptability and feasibility among mothers, health workers and laboratory personnel

Gill M1,2, Mokone M3, Tukei V3, Ncheph M2,4, Phalatse M2,4, Guay L1,2,5, Tiam A1,2, Mofenson L1,2

1The Elizabeth Glaser Pediatric AIDS Foundation, 2Project SOAR (Supporting Operational AIDS Research), 3The Elizabeth Glaser Pediatric AIDS Foundation, 4Lesotho Ministry of Health, 5The George Washington University, Department of Epidemiology and Biostatistics, Milken Institute School of Public Health

Background: Mortality associated with intra-uterine HIV infection rises rapidly within weeks after birth. Current guidelines recommend infant HIV testing at age six weeks, but very early infant diagnosis (VEID) – testing at birth–two weeks – followed by immediate initiation of antiretroviral therapy (ART) has potential to avert mortality associated with intra-uterine transmission. However, our understanding of acceptability and feasibility of VEID among mothers, health workers (HW) and laboratory staff is limited.

Materials & Methods: VEID was piloted in an observational prospective cohort of HIV-positive pregnant women and their infants in 13 Lesotho health facilities from July 2014 to October 2016. Semi-structured interviews were conducted March-July 2016 with 20 HIV-positive women attending 6-week or 14-week postnatal visits in eight study facilities in three districts. Counselors/study nurses (n=18) and district/central laboratory staff (n=9) involved in VEID were also interviewed. Interview themes included acceptability of birth, subsequent HIV testing and early treatment, perceived VEID challenges and HIV birth testing procedures and how well they were performed. Thematic analysis was conducted using MAXqda (V10).

Results: Nearly all mothers interviewed were happy to know their child’s HIV status at birth and respondents were supportive of national implementation of birth testing. Mothers and HW did not indicate that birth testing affected subsequent acceptance of infant HIV testing or
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Clinic attendance. No respondents expressed a challenge with early ART initiation (though only the perspective of HW was captured, as all mothers interviewed had HIV-negative children). Some women expressed concern about obtaining blood from newborns and stated they received limited counseling about infant HIV testing in general. HW and laboratory staff reported challenges with follow-up systems for mothers delivering at home, and expressed concern regarding the limited number of diagnostic machines, reagent stock-outs and increased workload that would accompany additional testing requirements. DNA-PCR testing was conducted at one central laboratory and communication among clinic and laboratory staff around specimen and results transfer was limited. All groups reported turnaround time delays for all EID, and that sometimes results were never received. Laboratory staff felt delays would be exacerbated by adding a test to the algorithm.

Conclusions: While respondents found VEID acceptable, the study raised questions about its feasibility. Strategies to address the challenges within the existing EID system can include strengthening counseling on infant HIV testing, improving the processes for specimen transfer and communication of results, and improving client tracing procedures for women who deliver at home. In order to start HIV-positive infants on the lifesaving treatment as early as possible, policymakers will need to consider the most appropriate course of action, such as implementing birth testing or strengthening the current clinic and laboratory system without an additional test.

Abstract 128

Characterization of patterns of retention of mothers and their children in an HIV/ART clinic in Southern Mozambique

Nhampossa T1, Fernandez S2,3, Maculuve S1, Augusto O1, Ruperez M1,2,3, González R1,2,3, Fuente-Soro L1,2,3, Bernardo E1,4, Macete E1, Menendez C1,2,3, Naniche D1,2,3, Lopez-varela E1,2,3

1Centro de Investigação em Saúde de Manhiça (CISM), 2ISGlobal, Barcelona Ctr. Int. Health Res. (CRESIB), 3Hospital Clinic- Universitat de Barcelona, 4Manhiça District Health Services

Objective: It is often assumed that children and their caregivers either stay in care together or abandon together, but few studies have actually evaluated this. We sought to describe the pattern of care among a cohort of HIV infected children and mothers enrolled in care at the Manhiça District Hospital (MDH).

Methods: This was a retrospective review of routine HIV clinical data collected under in a larger prospective HIV cohort study at the Manhiça District Hospital. Children initiating HIV care at the MDH from February 2013 to November 2015 who had been on ART for at least 12 months at the time of the study were selected and matched to their mother’s clinical data. Vital status was ascertained through the health and demographic surveillance system in place at the Manhiça District. Retention in care was estimated 12 months after first consultation for mothers and children. We used Kaplan–Meier estimates and competing risks (death or transfer) to estimate the effect of mother’s pattern of care in their child’s retention.

Results: A total of 395 children initiated HIV care during the study period and 237(60%) were matched to their mother’s clinical data. Finally, 203 children on ART for over 12 months were included in the analysis. At the time of the child’s first consultation, their median age was 2.3 years (IQR:1.0-6.3) and 54% were female. A total of 30% of the mothers had not initiated care, and 9% initiated the same day. Of those already in care, 47.6% were on ART. One year after ART initiation, 15.8% of children were LTFU and 9.9% had died or been transferred out. A total of 23.7% of children had a mother who was LTFU during their first 12 months of treatment. This group was in turn three times as likely to be LTFU (sHR 3, 95%CI 1.4-6.3, p=0.01).

Conclusion: A family-centered care approach to care is required to facilitate retention and improve health outcomes among mothers and their children.
Abstract 129

Epidemiology and Early Childhood Outcomes of HIV-Infected Children in Zimbabwe: A Secondary Data Set Analysis, 2015

Nyamundaya T, Mutede B, Mahomva A, Gombe N

1Elizabeth Glaser Pediatric AIDS Foundation (EGPAF), 2Zimbabwe Field Epidemiology Training Program

Background: Delays in pediatric HIV diagnosis are associated with high morbidity and mortality. Highly centralized testing leading to long turnaround time (TAT) of results contributes to delays in HIV early infant diagnosis (EID). EGPAF hosts an EID electronic database (EDB) utilized by 1223 sites in Zimbabwe. The EDB tracks EID results and facilitates prompt issuing of positive results and fast tracked commencement on ART. Analysis of this national dataset has potential to provide insight into the national and local-level EID steps, which may inform critical interventions to enable ending pediatric AIDS in Zimbabwe.

Methods: In 2016, a retrospective secondary data set analysis was conducted by EGPAF. Excel was utilized to generate frequencies, medians, interquartile ranges and graphs. The dataset had a total of 2740 EID entries with unique identifiers. Records with critical information missing were not considered in the dataset analysis. Confidentiality was assured and maintained through coding of data to exclude personal variables, password protection and no patient identification information was analysed.

Results: The median age at dried blood spot (DBS) specimen collection was 14 weeks (Q1=7; Q3=43). Out of 63 districts, three major cities and one peri-urban district contributed 20% yield of DNA PCR positive results. Overall median TAT was 35 days (Q1=21; Q3=62), with the laboratory incurring the largest length of time in the TAT process, at 15 days (Q1=10; Q3=21). The median time from sample collection to ART initiation was 8.8 weeks (Q1=5.1; Q3=10.7). By August 2015, 50% were on ART, 4% lost to follow, 2% transferred out, 6% died whilst 38% of the entries had a pending outcome.

Conclusion: High median age at testing, long TAT and late ART initiation has potential to contribute to high early morbidity and mortality. As program implementers in Zimbabwe focused on the care and treatment of HIV-positive children, we need to further decentralize EID services and introduce point-of-care diagnostics to reduce TAT to better meet the needs of children infected with HIV. MOHCC should consider targeting high yield geographic areas such as major cities with pediatric HIV prevention services to avert new infections.

Abstract 130

Retention and viral suppression of newly diagnosed and known HIV positive pregnant women on Option B+ in Kenya

Abuogi L, Akama E, Nimz A, Blat C, Maloba M, Cohen C, Oyaro P

1University Of Colorado, Department of Pediatrics, 2Family AIDS Care and Education Services, 3University of Colorado, School of Medicine, 4University of California San Francisco

Background: Kenya introduced continuous antiretroviral treatment (ART) for all pregnant women living with HIV (Option B+) in 2014. We describe the uptake of viral load (VL) testing and outcomes, comparing newly diagnosed HIV positive (NP) and Known Positive (KP) pregnant women in western Kenya.

Methods: A retrospective cohort study of 164 HIV-positive pregnant women presenting for antenatal care (ANC) at five clinics September to November 2014 and followed through February 2016 was conducted. Virologic testing was conducted per Kenyan National Guidelines for pregnant women six months after (ART) initiation or six months from last VL, if already on ART. KP (defined as women with HIV diagnosis prior to current pregnancy) were compared to NP regarding virologic
suppression and retention in care. Categorical variables were analyzed by χ2 or Fisher’s exact tests. Discrete interval variables were analyzed by Wilcoxon rank-sum.

Results: At first ANC visit, NP were younger (24.2 years (SD 4.6) vs 28.2 years (SD 5.6), p<0.001) compared to KP. The majority of NP (96%) were initiated on Option B+ while over half of KP (58%) started ART for clinical/immunological criteria (p<0.0001). KPs were more likely than NPs to have a VL performed following guidelines (64% vs 33%; p<0.001). Among those tested, virologic suppression was high in both groups (92% KP vs. 100% NP; p=0.31). More KPs (83%) vs. NPs (66%) remained active in care at end of the follow up (p=0.02). Uptake of infant testing was higher among KP (87%) vs. NP (69%) (p<0.01). Two (2%) infants were HIV infected at six weeks, both from newly diagnosed mothers (p=0.15).

Conclusion: Women newly diagnosed with HIV during pregnancy show poorer uptake of VL and worse retention in care than those diagnosed prior to pregnancy. Elimination of mother-to-child transmission targets will require a greater focus on newly diagnosed mothers.

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Increasing early case identification for children through implementation of routine HIV screening for women at 6 week postnatal visit in Kenya, 2016

Kegolī S1, Motoku J1, Muriithi C1, Njoroge A1, Waithera I1

1Eastern Deanery AIDS Relief Program

Background: During the 2 years of the Accelerating Children’s HIV/AIDS Treatment initiative, Kenya intensified pediatric case finding by rolling out routine HIV screening among women who bring in infants for the 6 week immunization. This was to leverage on the high uptake of immunization services across the country which averages >90% for the 6 week pentavalent 1 immunization. Our study sought to evaluate proportion of HIV exposed and infected infants identified through this initiative in a program setting.

Method: A retrospective analysis was carried out by reviewing clinical data for mother’s infants’ pairs attending in 14 Maternal and Child Health clinics supported by Eastern Deanery Aids Relief Program (EDARP), Nairobi between 1st January 2016 to 31st December 2016. Documentation of HIV exposure status was assessed for all infants attending 6 week immunization clinic in the study period. HIV exposed infants (HEI) were defined as follows, 1) New HEI: infants of HIV infected women identified at the 6 week visit; and, 2) Known HEI infants of HIV infected women whose HIV status is known prior to the 6 week immunizations visit. Age at enrollment, timing of maternal HAART and infant prophylaxis were obtained using descriptive statistics. Data were analyzed using STATA version 12.1 software package.

Results: A total of 3,215 infants received 6 week pentavalent 1 immunization. Median age was 6.4 weeks (range 6.1 to 6.7). Of these, 1,414 (44%) had a documented HIV exposure status. And 532 were HEI, translating to 38% HIV exposure status at 6 weeks immunization. Of the 532 HEI, 96% (513) were known HEI and 4% (19) were new HEI p value 0.000. Uptake of maternal HAART during pregnancy was at 510 (99.4%) for known HEI and 6 (31.6%) for New HEI, P value 0.000. Uptake of infant Nevirapine at 6 weeks was 99.8% (512) for known HEI and 0 for new HEI, P value 0.000. Of the 19 new HEI at 6 weeks, 1 (5.3%) was confirmed to be HIV infected by PCR compared to 8 (1.6%) of the 513 known HEI, P value 0.229.

Conclusion: Routine screening for HIV exposure status for women at 6 weeks postnatal visit results to early identification of infants at risk of HIV infection and those already infected. Newly identified HEI are more likely to be HIV infected compared to previously known HEI. Therefore, efforts should made to strengthen and expand routine HIV screening for women at the 6 week postnatal visit in order to provide interventions for infants at risk of HIV infection and early infant diagnosis and treatment for those who are already HIV infected.
Abstract 132

Keep our future generation alive: Reinforce routine HIV testing for children

Savory T1, waMwanza M2, Lumpa M3, Chitala M3, Washington M2, Chilengi R1, Sikazwe I1

1Centre for Infectious Disease Research Zambia CidrZ, 2Centers for Disease Control and Prevention

Background: Zambia has made great strides in tackling the HIV/AIDS epidemic. By the end of 2015, over 58% of HIV infected people were on treatment; anti-retroviral treatment (ART) services are decentralized; prevention-of-mother-to-child-transmission (PMTCT) treatment of HIV has changed from single dose to full ART, resulting in reduced HIV infected children being born of HIV+mothers from 7% to 2%. Despite these achievements, UNAIDS Spectrum model estimates 36,000 HIV+ children are not identified through HIV testing annually due to various factors including poor provider initiated testing and counseling (PITC), which averaged 3% in 2015. Unfortunately, their model does not identify these children by age, which makes it difficult to evaluate policy options. We set out to estimate the number of unidentified HIV+ children by age born between 2006-2015 in the 338 CIDRZ-supported facilities in the Lusaka, Western, and Eastern Provinces of the Zambia to devise policies to address the gap in identifying HIV infected children.

Materials & Methods: Some of the input data included perinatal transmission rates from African literature for mothers not on ART, with single, double dose or full ART, and seroconversion rate during breastfeeding from untreated mothers. Also from literature, we used the child mortality rates for HIV+ and HIV- children due to HIV and non-HIV related causes. We incorporated Zambia data that shows 98% of the mothers breastfeed their children up to 24 months, and from CIDRZ databases showing the number of pregnant mothers on different treatment options and the number of children initiated on treatment for each of the 10 years. We evaluated the impact to two policy options within the year 2015.

1. Enforced routine pediatric testing. We assumed 80% of the under 2 year olds and 50% of the 3-5 year olds visit the clinic annually, and we increased the PITC rate to 90%.
2. School screening drives. In addition to other health care activities, HIV testing would be provided during drives. We assumed 80% of the children attend pre or primary school and would be reached through drives, and a pediatric treatment acceptance rate of 70%.

Results: Between 2006 and 2015, an estimated 30,203 HIV+ children died from HIV-related conditions. By the beginning of 2015, 14,348 HIV-infected children remained untested, unidentified, and therefore untreated. Our model estimated that in 2015, an additional 39% untested HIV+ children could have been identified with reinforced PITC, and that would have prevented 52% of HIV related child deaths. Conducting school screening drives in 2015 would have identified 50% of untested HIV+ children (5-10-year-old), who if identified and treated could have reduced HIV related child deaths by 54%.

Conclusions: Our model demonstrates that improved HIV testing at health facilities augmented by school screening could identify in one year up to 7,937 (58%) additional HIV+ children in need of treatment. Besides the potential reduction in morbidity and mortality, a policy change in this direction could also result in early detection and treatment of other childhood diseases and reduction in school absenteeism and overall improved school performance.

Abstract 133

Repeat HIV testing during pregnancy in Kenya: an economic evaluation

Rogers A1, Turan J1, Helova A1, Eaton E1, Mennemeyer S1

1University Of Alabama At Birmingham

Background: Repeat HIV testing during late pregnancy may identify women who seroconvert after an initial negative HIV test early in pregnancy, allowing these women to adopt lifelong antiretroviral therapy (ART) for
the sake of their own health as well as to prevent mother-to-child transmission of HIV. We evaluated the cost-effectiveness of repeat HIV testing during late pregnancy in Kenya, compared to a single antenatal test in early pregnancy alone.

Methods: We used TreeAge software to model a decision tree with the initial decision node comparing the alternative HIV testing strategies and the successive branches representing subsequent prepartum decisions. At delivery of the infant, each branch culminated in a state-transition model following the mother-infant pair in one-month cycles for a ten-year horizon. All inputs were drawn from the literature and were varied across their range or distribution in univariate and probabilistic sensitivity analyses.

Results: In the base case, the retesting strategy was very cost-effective for the Kenyan setting at $1,098 per quality-adjusted life year (QALY) saved, yielding fewer infant HIV infections (757), infant deaths (30), and maternal deaths (178) per 100,000 women. Results were sensitive to low cumulative incidence of HIV during pregnancy and monthly cost of maternal ART (thresholds of 1% and $45, respectively). Probabilistic sensitivity analyses confirmed the base-case analysis.

Conclusions: This modeling study indicates that repeat HIV testing is likely to be cost-effective and result in fewer infant HIV infections. In an era of immediate initiation on lifelong ART for mothers identified as being HIV-positive during pregnancy, retesting for HIV not only improves maternal health outcomes but may also contribute to the elimination of perinatal HIV transmission in Kenya.

Abstract 134

Factors associated with HIV-exposed infants’ non-attendance at scheduled visits during a nationally representative observational cohort study, South Africa 2012-2014

Ngandu N1, Jackson D2, Lombard C4, Nsibande D3, Magasana V1, Goga A1

1South African Medical Research Council, 2UNICEF, 3University of the Western Cape, 4University of Cape Town, 5University of Pretoria

Background: Regular postnatal follow-up of the increasing population of HIV exposed uninfected infants (HEU) is the weakest link in current programmes to prevent mother-to-child HIV transmission (PMTCT). We sought to identify factors associated with non-attendance at scheduled follow-up study visits, including an 18-month visit for infant HIV testing, amongst a nationally representative sample of HEU in South Africa (SA), a high HIV prevalence setting. Child Health and PMTCT SA guidelines recommend monthly HEU follow-up in the first year of life and three-monthly thereafter, until five years. Additionally, HEU should be tested for HIV at 18 months to determine final PMTCT outcome.

Materials & Methods: Secondary analysis of data was conducted, from a nationally representative observational cohort study of HEU and their primary caregivers, recruited in public health facilities (October 2012 and September 2014). During this time PMTCT policy transitioned from antiretroviral treatment (ART) guided by criteria (PMTCT Option A, October 2012-March 2013) to ART for all HIV positive pregnant and lactating women (PMTCT Option B, April 2013-September 2014). Participants were eligible for enrolment (N=2650) if they were 4-8 weeks old, receiving their six-week immunisation and HIV antibody positive, but not PCR positive. All enrolled infants were scheduled for follow-up 3-monthly from 3 till 18 months or till PCR positive or death (n=6 expected follow-up visits). Each visit was scheduled to coincide with the child’s recommended routine health visit, where possible. We assessed fifteen baseline (at 4-8 weeks post-delivery) maternal and early HIV care characteristics associated with the frequency of ‘Missed visit’ (MV) between 3 and 18 months, ‘MV-frequency’, using a negative binomial regression model adjusted for total number of expected visits. A logistic regression model was used to identify characteristics associated with MV at 18-months, ‘18-month MV’.

Results: MV were lowest at 3 (32.7%) and 18 months (31.0%) and highest at 12 months
HEU born to mothers not on ART by 6-week postpartum had a significantly increased incidence rate of ‘MV-frequency’ (adjusted incidence rate ratio (aIRR) 1.2(95% confidence interval (CI) 1.1-1.4), p<0.0001), and odds of ‘18-month-MV’ (adjusted odds ratio (aOR) 1.3(CI 1.1-1.6), p=0.006). In addition, ‘MV-frequency’ was higher amongst HEU with unknown nevirapine intake (aIRR 1.4(CI, 1.1-1.8), p=0.020), compared with nevirapine users. HEU born to mothers older than 24 years, had a significantly reduced incidence rate of ‘MV-frequency’ (25-34 years aIRR 0.9(CI, 0.8-1.0), p=0.010 and 35-50 years aIRR 0.8 (CI, 0.7-1.0), p<0.012) and significantly reduced odds of ‘18-month-MV’ (25-34 years aOR 0.7(CI 0.5-0.9), p=0.001 and 35-50 years aOR 0.7(CI, 0.5-0.9), p<0.011). Shorter clinic travel time (<30 minutes) lowered ‘MV-frequency’ (aIRR 0.7(CI 0.6-0.9), p ≤0.004).

Conclusions: To reduce postnatal MV amongst HEU, concerted efforts are needed to initiate maternal ART before six weeks postpartum, improve uptake of infant nevirapine prophylaxis, reduce travel time to clinics and provide support for young women. These findings largely relate to an Option A regimen at baseline; additional research is needed to evaluate infant missed visits under PMTCT Option B+ policy, where infants mainly receive six weeks of nevirapine, and mothers receive lifelong ART.

Abstract 135

Seroprevalence of trans-placentally acquired anti-measles antibodies in HIV exposed vs HIV unexposed infants at 6 months of age

Jain S1, Seth A1, Khare S2, Chandra J1

1Lady Hardinge Medical College, 2National Centre For Disease control

Background: Measles is one of the vaccine preventable diseases in the world accounting for a large proportion of childhood morbidity and mortality. HIV exposed infants are more vulnerable to acquire measles infection and also at a younger age as compared to HIV unexposed infants. World Health Organisation recommends measles vaccination starting at 6 months of age in HIV exposed infants. However in India, these infants are given measles vaccination at 9 months of age, like all other healthy infants.

Objective: To compare sero-prevalence of trans-placentally acquired anti-measles antibodies in HIV exposed and HIV unexposed infants at 6 months of age and assess the proportion of HIV exposed infants undergoing sero-conversion after immunization with measles vaccine.

Methods: In this prospective longitudinal study carried out in Kalawati saran children hospital in Northern India, we estimated measles IgG antibodies in serum of 49 HIV exposed and 50 HIV unexposed infants aged 6-7 months. Measles vaccine was then administered to HIV exposed infants. Assessment for measles IgG antibodies was repeated 8-12 weeks post immunization.

Results: Measles IgG antibodies were detected in 2/49 (4.1%) HIV exposed and 16/50(32%) HIV unexposed infants (p< 0.001). Post vaccination, sero-prevalence of measles antibodies increased to 38.5% (p< 0.001) in the exposed infants.

Interpretation: HIV exposed infants have less proportion of measles antibodies at 6 months age and are therefore more vulnerable to measles than HIV unexposed infants. Sero-conversion in response to a single dose of measles vaccine administered at 6 months age is low in these infants, signifying the need of additional dose(s) of measles/measles containing vaccine.

Conclusion: Larger proportion of HIV exposed infants lacked protective levels of anti-measles antibodies at 6 months of age in comparison to HIV unexposed infants. HIV exposed infants showed a statistically significant seroconversion following measles vaccination at 6 months of age. However, seroconversion rate is low, signifying the need of additional dose(s) of measles/measles containing vaccine.
Abstract 136

Factors associated with non-return for infants’ HIV test results in Uganda

Elyanu P1, Atuyambe L2, Nakanjako D3, Musoke P3, Kekitiinwa A4, Sewankambo N3

1University Of Texas School Of Public Health, 2Makerere University School of Public Health, 3Makerere University College of Health Sciences, 4Baylor College of Medicine

Background: In 2014, 20% of HIV-infected infants in Uganda did not initiate ART because caregivers did not return for their infants’ HIV test results. Limited knowledge exists regarding reasons for non-return. We determined factors associated with failure to return for HIV-exposed infants’ HIV test results, and identified facilitators and barriers to returning.

Methods: We prospectively followed a cohort of 425 HIV-exposed infants first HIV tested between August 2015 and January 2016 in three health facilities in Uganda for 90 days post-test date. Caregivers who had not returned for results within 90 days were classified as “not-returned”. Predictors of non-return were determined using multivariable logistic regression. We conducted 49 in-depth interviews with caretakers who returned (n=29) and did not return (n=20). Key informant interviews were conducted with 36 health workers/community personnel. Interviews were transcribed, translated, and coded; thematic content analysis was performed.

Results: Of 425 infants (median age 6.9 weeks, IQR 6.3-8.9), 54.6% were boys; 4.2% tested HIV positive. Most (99%) caregivers were infants’ biological mothers, mean age 27 (SD 6) years; 98% of mothers received triple antiretroviral therapy for PMTCT. Twelve percent (52/425) did not return for the infants’ test result. Health facility type (health center vs. hospital: OR =3.4 (95%CI: 1.4, 6.0; p=0.005) and distance lived from the health facility [<5km vs. 5-10km: OR: 3.4 (95% CI: 1.1, 10; p=0.03), and >10km vs. 5-10km: OR: 6.1 (95%CI: 1.8, 20; p=0.004)] were associated with non-return.

Reasons for non-return were non-disclosure of HIV status, lack of money for transportation, stigma, negative experiences with healthcare workers, and fear of facing the infant’s test results. Reasons for return included needing to know the infants’ HIV status and receive appropriate care, disclosure of HIV status, positive healthcare worker-client interaction, and medicine availability. Caretakers suggested the following solutions to non-return: 1) provide same day test results and effective counseling; 2) provide client-friendly services; 3) follow-up with those who do not return; 4) Provide incentives (food/transportation); and 5) empower women financially with funds for small businesses.

Conclusion: Non-disclosure, stigma, lack of transportation and fear of facing results were reasons for non-return for infants’ HIV test results. Disclosure support, same day test results, client-friendly healthcare services including quality counselling and provider-patient relations could improve return rates.

Abstract 137

PMTCT and clinical profile of hospitalized HIV-infected children in an era of high pMTCT uptake and efficacy.

Du Plooy E1, Frigati L1, Cotton M2, Rabie H1,2

1Department of Paediatrics and Child Health, Tygerberg Children’s Hospital and Stellenbosch University, 2Children’s Infectious Diseases Research Unit Tygerberg Hospital and Stellenbosch University

Background: Combination antiretroviral therapy (cART) for all HIV-infected pregnant and lactating women with post-exposure prophylaxis for HIV-exposed infants prevents mother-to-child transmission of HIV. This has been the standard of care in Cape Town, South Africa since May 2013. Despite high uptake and coverage, transmission still occurs. Through describing the profile of young infected children, we aimed to broaden our understanding of the current risk factors for transmission, identify failures in the diagnostic and care pathways and describe the associated morbidity and mortality.
Materials & Methods: Between February 2015 and January 2016, we prospectively documented the hospitalization of children 18 months and younger with newly diagnosed or previously confirmed HIV. Data on maternal HIV and pregnancy history, as well as child HIV-history and clinical status were documented and descriptive analysis performed.

Results: Sixty-three children were screened and 55 enrolled (6 declined; 2 unavailable for consent). The median age was 5.7 (IQR 3 - 12.5) months; 33 (60%) were male. Forty-six children (83%) were identified as HIV-exposed at birth. The majority, 31 (67%), of their mothers were aware of their HIV diagnosis prior to pregnancy. However, only 20 (65%) attended antenatal care, with 7 (23%) interrupting cART initiated prior to pregnancy. Twenty-three women (50%) began cART during pregnancy: 11/31 (35%) known to be HIV-infected prior to pregnancy and 12/15 (80%) diagnosed during pregnancy (p=0.4). Of these 23 women, 6/11 (55%) of previously known and 4/12 (33%) diagnosed during pregnancy were not retained in care (p=0.4). Children with unknown HIV-exposure risk were older: 9.3 (IQR 5.9 – 12.8) vs 4.5 (IQR 2.2 – 12.6) months (p=0.195). The median duration from HIV diagnosis to cART initiation was 8 (IQR 5 – 30) days in known-risk children; 15/46 (27%) successfully initiated cART prior to admission and remained in care. At time of hospitalization 5 children (9%) had discontinued previously initiated cART.

Seven children (13%) died in hospital, with 14/55 (25%) (13 with known risk) requiring intensive care admission. The median hospitalization duration was 17 days, similar in those with known (23 [IQR 12 – 30.5] days) vs unknown risk (15.5 [IQR 10 – 32.3] days) (p=0.67).

Conclusion: We identified poor antenatal clinic attendance and cART-treatment interruption in women aware of their status prior to pregnancy as the driver of newly infected infants. Despite HIV being diagnosed relatively early, mortality and morbidity were high. Identifying these women and supporting them before, during and after pregnancy is the challenge. Enhanced infant post-exposure treatment guidelines must be considered in these children.

Abstract 138

Experiences and perceptions of community-based mentor mothers (cMM) supporting HIV-positive pregnant/postpartum women on lifelong antiretroviral therapy in Southwestern Kenya

Helova A1, Abuogi I1, Onono M1, Bukusi E2, Wangaa P1, Odhiambo G3, Akama E3, Nalwa W4, Odeny T5, Musoke P1, Turan J6

1Department of Health Care Policy and Organization, School of Public Health, University of Alabama at Birmingham; 2Department of Pediatrics, University of Colorado Denver; 3Kenya Medical Research Institute, The Research Care and Training Program, Center for Microbiology Research; 4Centre for Global Health Research, Kenya Medical Research Institute; 5Migori County Referral Hospital, Kenya Ministry of Health; 6Department of Epidemiology, University of Washington

Background: Community-based mentor mothers (cMM) are HIV-positive mothers providing peer support to HIV-positive pregnant/postpartum women in the community with the aim to enhance lifelong antiretroviral therapy (ART) adherence and retention in care.

Methods: To explore the perceptions of cMMs on their role in supporting HIV-positive pregnant/postpartum women, we completed 24 in-depth interviews with cMMs from ten communities in Kenya between April-May 2016. Transcripts were coded with Dedoose software using a coding framework based on

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the literature, interview guides, and emerging themes from transcripts, and fine-coded using an inductive approach. Main themes were explored in longitudinal questionnaire data collected by cMMs during their home visits for 159 women and their infants at 6-weeks postpartum.

**Results:** cMMs expressed high acceptability of their work in the community and health facilities, and emphasized their positive impact on HIV-positive women and their infants. They described provision of health education; making linkages to HIV care, prevention of mother-to-child transmission (PMTCT) and maternal and child health (MCH) services. The cMMs reported serving as role models and confidantes, supporting acceptance of HIV status, providing encouragement about the potential of having an HIV-negative child; assisting with partner disclosure/communication, and providing tangible support (development of birth plans, picking up medications). Additionally, cMMs described personal benefit through self-empowerment and increased income. Reported challenges included possible inadvertent disclosure of clients’ HIV status, transportation, and cultural barriers/myths. Positive impact of home visits described by cMMs was reflected in questionnaire data. At 6-weeks postpartum, 96% of women visited at home self-reported 100% adherence to ART as well as increase in disclosure to male partner to 96% from 84%; all infants were on preventive HIV regimen and 99% were properly adhering, 94% of infants had been tested for HIV, 89% were delivered at the hospital, and 99% were exclusively breastfed and immunized.

**Conclusions:** Kenya, similar to other countries, is in a need of innovative approaches to overcome challenges associated with the scale-up of lifelong ART services. This study suggests that a cMM strategy may play an important role in enhancing PMTCT as well as MCH in Kenya and may have positive effects on the cMMs themselves.

**Abstract 139**

**Tying the loose ends-Missed opportunities for EMTCT among HIV Positive women in Kenya**

**Ngugi E,1 Mutisya I,1 Muthusi J,1 Chen T,1 Waruru A,1 Ngeno B,2 Geller A,2 Katana A,1 Chun H,2 Broyles L2**

1Division of Global HIV & TB (DGHT), US Centers for Disease Control and Prevention (CDC), 2Division of Global HIV & TB (DGHT), US Centers for Disease Control and Prevention (CDC),

**Background:** In 2014 Kenya implemented routine viral load (VL) testing and Option B+ to eliminate mother-to-child HIV transmission (MTCT). We assessed VL implementation and site level interventions among pregnant and breastfeeding women who were known HIV-positive and previously enrolled in care (KP), or newly diagnosed new positive (NP).

**Methods:** The VL Service Quality Assessment surveyed 25 ART and PMTCT sites in Kenya, including all pregnant and breastfeeding women seen during Jan 2014–Aug 2015 at these sites with routine or targeted VL testing; 656 charts were reviewed. We used Chi-squared and Fisher's exact tests for differences in proportions, the Kruskal-Wallis test for differences in medians, and logistic regression for associations between predictor variables and viral suppression (VS).

**Results:** Of 514 women with available data, there were 339 (66.0%) KP and 175 (34.0%) NP; median age was 29.6 years (interquartile range [IQR] 26.0–33.6). Median gestational age at enrolment was 19.0 weeks (IQR 11.8-25.3) and 20.5 (IQR 15.1-27.1) for KP and NP, respectively. Median time to 1st VL test from ANC enrolment was 5.0 months (IQR 1.7-8.4) for KP and 6.3 months (IQR 4.0-8.7) for NP. Overall VS (VL<1000 copies/ml) percent was 77.2% (95% CI 72.2 - 82.2); 76.3% and 78.9% for KP and NP, respectively. Women aged <25 years were more likely than older women to have virologic failure (VF, VL≥ 1000 copies/ml), AOR=3.5 (95%CI, 1.58–7.74). Median time to first enhanced adherence counselling (EAC) was 3.5 (1.0 - 8.0) months and 53%, 32% and 26% had 1st, 2nd and 3rd EAC documented, respectively. Median time to...
repeat VL was 2.5 (0.5–6.8) months: 16 (26%) still had VL≥1000 after repeat VL, and 9 (56%) changed regimens. Women on non-nucleoside reverse transcriptase inhibitor (NNRTI) regimens as first line therapy were more likely to have VF than those on first line protease inhibitor-based treatment, AOR=22.2 (95% CI, 4.1-120.9).

Conclusions: Missed opportunities exist in timely VL testing, adherence counselling, and regimen changes in PMTCT programs. There is an urgent need to implement service delivery models that focus on young women and enhance early attendance to ANC and comprehensive services in order to achieve eMTCT.

Abstract 140

Maternal Humoral Immune Correlates of Mother to Child Transmission of HIV-1 in the Setting of Peripartum Antiretrovirals

Mutucumarana C1,2,3, Eudailey J1, Mcguire E1, Vandergrift N1, Tegha G4, Chasela C5, Ellington S6, van der Horst C7, Kourtis A6, Permar S1, Fouda G1

1Duke Human Vaccine Institute, 2Duke University School of Medicine, 3Doris Duke Charitable Foundation, 4University of North Carolina, UNC Project, 5University of Witwatersrand, Division of Epidemiology and Biostatistics, 6Centers for Disease Control and Prevention, Division of Reproductive Health, 7University of North Carolina School of Medicine, Division of Infectious Diseases

Background: More than 150,000 annual pediatric HIV-1 infections occur due to mother to child transmission (MTCT) despite the availability of antiretrovirals (ARVs). In the pre-ARV era U.S. Women and Infants Transmission study (WITS), we previously reported that maternal HIV envelope-specific anti-V3 IgG, CD4 binding site antibodies, and tier 1 virus neutralization predicted reduced HIV-1 MTCT. As the majority of pediatric HIV infections occur in clade C HIV-infected populations with increased access to ARVs, we studied a Malawian HIV-infected pregnant women cohort from the Breastfeeding, Antiretrovirals, and Nutrition (BAN) study. We sought to determine if immune factors in the setting of ARVs predict reduced MTCT and help eliminate pediatric HIV-1.

Methods: Plasma from a subset of BAN clade C HIV-infected Malawian mothers (n=88, 45 transmitting and 43 non-transmitting) and their infants were studied. Women and infants received ARVs at delivery, and the majority of peripartum MTCT was during pregnancy (91%). Binding antibody multiplex assays, HIV-1 neutralization assays, and soluble CD4 blocking ELISAs measured plasma IgG against multiclade HIV Env antigens, neutralizing capacity, and CD4 binding site antibodies, respectively. A multivariable logistic regression model analyzed the association of maternal and infant immune responses with peripartum MTCT risk.

Results: No significant association was detected between maternal anti-clade C V3 IgG (OR 0.57, p=0.42) or tier 1 neutralization (OR 1.37, p=0.70) and MTCT. Surprisingly, plasma blocking of the CD4 binding site (OR 1.06, p=0.03) and maternal anti-clade C V1V2 IgG (OR 1.62, p=0.04) were associated with increased MTCT independent of maternal viral load. Maternal anti-V1V2 IgG transfer efficiency to infants was not associated with transmission (OR 1.00, p=0.67).

Conclusions: This study revealed an association between high maternal CD4 binding site antibodies and anti-V1V2 IgG and transmission. Distinct humoral immune correlates of MTCT in the BAN and previous studies could be due to differences between transmission mode, virus clade, or maternal antiretroviral use. The association between specific maternal antibody responses and in utero transmission, distinct from potentially protective maternal IgG in the WITS cohort, underlines the importance of investigating additional cohorts with well-defined transmission modes to understand the role of maternal antibodies during HIV-1 MTCT.
Abstract 141

Adolescent Human Immunodeficiency Virus Disclosure: Characteristics of Patients and Parents, and Association with the Timing and Methods of HIV Disclosure

Olivero R1

1Helen DeVos Children’s Hospital of Spectrum Health

Background: Children perinatally-infected with HIV have a chronic condition requiring lifelong engagement in medical care. During adolescence, medical providers and parents consider disclosing the HIV-positive status to the adolescent. HIV disclosure can be stressful for parents, with common themes of concern surrounding privacy, confidentiality, the ability of the adolescent to understand necessary health concepts, and causing or worsening behavioral issues. There are gaps in the medical literature related to HIV disclosure in adopted children and in children less than 12 years, and how various demographic and neuropsychiatric factors influence parental preferences regarding the timing and techniques of HIV disclosure. The objective of this study is to describe details of adolescent HIV disclosure, and to determine whether patient demographics or neuropsychiatric issues influence parental comfort with disclosure.

Materials and Methods: The study was conducted in the Pediatric Infectious Diseases clinic at Helen DeVos Children’s Hospital as a voluntary cross-sectional survey of parents of perinatally HIV-infected children aged 6-16 years. Demographic information, details of the adoption (if applicable), country of origin, presence of or concern for neuropsychiatric issues, and opinions regarding disclosure were collected. A univariate analysis was used to compare data between the disclosed and non-disclosed groups.

Results: 41 sets of parents of patients participated; 5 additional sets of parents were eligible but did not have a routine appointment during the study period. Patient demographics included: 56% female, mean age 10.4 years, 88% adopted, 76% African in origin with 49% born in Ethiopia. Less than 10% of patients had neuropsychiatric diagnoses but 20% of parents had concerns for neuropsychiatric issues. 66% of patients were in the disclosed group; 89% of parents thought disclosure was done at appropriate age, 85% reported that disclosure was a positive or neutral experience, and 85% reported that disclosure helped the adolescent adhere to their medication regimen. Patients in the non-disclosed group were significantly younger than the disclosed group (7.6±1.6 vs 11.9±2.6, p<0.001) and parents in the disclosed group thought that a younger age was appropriate for disclosure (7.5±2.5 vs 10.4±1.3, p<0.001). Demographic features and adoption status were not associated with either group, though adoption from Ethiopia was more common in the disclosed group (59% vs 29%, p=0.062). In the disclosed group, a parent most commonly disclosed to the adolescent, followed by orphanage staff; 59% of parents reported that at least one tool was used (most commonly a pediatric HIV disclosure book), and 67% reported no issues with disclosure. In the non-disclosed group, 100% of parents thought that a parent should disclose to the adolescent, and 92% felt a book would be helpful. The prevailing concerns in the non-disclosed group included confidentiality and privacy.

Conclusions: In our predominantly adopted, perinatally-infected pediatric cohort, HIV disclosure most often takes place by 8 years. Parents of the non-disclosed group reported that an older age (9-10) is appropriate for disclosure, citing concerns for confidentiality and privacy. Disclosure was reported as a positive experience with appropriate timing by most parents, and the preferred tool for disclosure was a book.

Abstract 142

Long-term outcomes of perinatally HIV-infected adolescents accessing care in a tertiary state hospital in Cape Town, South Africa

Van Heerden L1,2, Cotton M1,2,3, Frigati L1,2

1Stellenbosch University, 2Tygerberg Hospital, 3FAMCRU
Background: Approximately 2 million adolescents were living globally with HIV in 2014. HIV is the leading cause of death in adolescents in Africa and the second leading cause of death for adolescents worldwide. Perinatally HIV-infected adolescents (PHIV) often have chronic complications due to late access to ART and ART side effects. There is relatively little information on their psychosocial outcomes although adolescence may be a risk factor for not taking ART. The aim of this study was to describe a cohort of PHIV adolescents attending Tygerberg Hospital, a tertiary hospital in the Western Cape.

Material and Methods: A retrospective descriptive study (folder review) describing all HIV-infected adolescents between the ages of 10 to 19 years attending the Infectious Diseases Clinic at Tygerberg Hospital during a 12 month period in 2015 was performed.

Results: Ninety-eight (25%) of approximately 400 patients attending the Tygerberg Paediatric Infectious Diseases clinic were adolescents. Of these 55 (56%) were female. Median age at first clinic visit was 4.9 years (IQR 1.5-9.4). Median age at most recent clinic visit was 14 years (IQR 10-19). The majority were WHO stage 3 and 4 at diagnosis (74%).

Twenty-eight (28%) were on their original ART regimen with no switch of drug for side effects, failure or intolerance. Seventy-six (77%) remained on their first regimen with a single drug switch due to side effects. Fifty of sixty-one (82%) starting on Efavirenz remained on it. Of 94 with a viral load available at last clinic visit, 71 (81%) were virologically suppressed.

The following chronic medical complications were documented: 23 (23%) with chronic lung disease with 58 (59%) having had previous Pulmonary Tuberculosis (PTB), 2 (2%) having had multidrug-resistant Tuberculosis and 1 (1%) having had Extremely Drug Resistant Tuberculosis. Four (4%) were documented to have cardiac disease, 1 (1%) had HIV nephropathy, 80 (80%) had dermatological complications and 41 (42%) had central nervous system complications disease such as seizures and neurodevelopmental delay. The median number of hospitalizations since diagnosis was 3 (1-4) and no adolescent died in 2015.

Regarding disclosure, 67 (68%) were fully disclosed to, 20% had no documentation and 11 (14%) not disclosed to. Seven of eleven not disclosed to had severe neurological disease. Forty-five (55%) attended mainstream school and 34 (34%) a special school/care centre. Forty-six (47%) had failed a grade and 33 (33%) failed more than one grade. Five (5%) were known to be on antidepressants. Fifty-six (57%) had been referred to a social worker for psychosocial issues. Contraception was only documented in 5 (5%) with 2 (2%) pregnant.

Conclusions: Despite late access to ART and minimal additional resources, the adolescents had reasonably good outcomes. There are fewer chronic medical complications than noted in other African cohorts. However, there are significant psychosocial and educational issues and more focused interventions are needed to address these.

Abstract 143
Systemic biomarkers of inflammation and immune activation are associated with radiographic findings of chronic lung disease among HIV+ adolescents in Nairobi, Kenya

Attia E1, West T 1-2-3, Maleche Obimbo E4, Zhong D5, McGrath C3, Kiplinnes C6, Cagle A2, Sakr S6, Njuru C6, Chung M3, Kicska G5, Crothers K1

1Division of Pulmonary and Critical Care Medicine, University Of Washington, 2International Respiratory and Severe Illness Center, University of Washington, 3Department of Global Health, University of Washington, 4Department of Paediatric and Child Health, University of Nairobi, 5University of Washington, 6Coptic Hope Center for Infectious Diseases, Coptic Hospital

Background: Chronic lung disease (CLD) is an important complication of HIV among adolescents in Africa. Radiographic manifestations of CLD are common in this population and reflect a spectrum of pathophysiologic processes. We hypothesized that biomarkers of inflammation (IL-6) and immune/monocyte activation (sCD14, sCD163) are associated with radiographic CLD patterns.
Materials & Methods: We performed a cross-sectional study of 50 clinically stable, perinatally-infected HIV+ adolescents enrolled in the Coptic Hope Center for Infectious Diseases in Nairobi. Subjects underwent high-resolution chest CT and phlebotomy for serum biomarkers. We also collected demographic, anthropometric, CD4, antiretroviral therapy (ART), and exposure data. A radiologist blinded to clinical data interpreted the CT scans, and CT findings were categorized by patterns of abnormality: fibrotic (fibrosis, linear scars, traction bronchiectasis, honeycombing); interstitial (reticular abnormalities, cysts, micronodules); airway/obstructive (bronchial wall thickening, bronchiectasis, emphysema); infectious (consolidation, tree-in-bud opacities, lymphadenopathy). We compared biomarkers by CT patterns, using Wilcoxon rank-sum tests.

Results: Mean age was 13 (SD 3) years, 56% were male, 22% were malnourished, and 34% had secondhand smoke and 84% indoor biofuel exposure. Over 1/3 had prior pulmonary infections. Most (94%) were on ART; median CD4 was 672 cells/µL [IQR 406-870]. Median IL-6 was 0.34 pg/mL [IQR 0.19-0.68]; sCD14: 2227 ng/mL [1852-2811]; sCD163: 306 [226-482]. IL-6 and sCD163 were moderately correlated (r=0.3, p=0.02). Biomarkers did not vary significantly by clinical characteristics, including age, sex, CD4, ART, and malnutrition. Thirty-nine (78%) adolescents had CT abnormalities. Adolescents with the fibrotic pattern (n=9) had higher median sCD14 (2825 [2576-3357] vs 2121 [1839-2470], p=0.02) than those without the fibrotic pattern. Those with the interstitial pattern (n=13) had higher sCD163 (502 [242-626] vs 292 [222-422], p=0.08). Adolescents with the infectious pattern (n=9) had higher IL-6 (0.74 [0.68-1.78] vs 0.29 [0.17-0.44], p=0.004) and sCD163 (509 [302-626] vs 292 [221-454], p=0.02). We detected no associations between the airway/obstructive pattern (n=17) and biomarker concentrations.

Conclusions: Circulating biomarkers of inflammation and immune/monocyte activation are associated with specific radiographic patterns of CLD among HIV+ adolescents with immune reconstitution and preservation. This suggests that circulating biomarkers of inflammation and immune activation may reflect particular patterns of pulmonary injury.
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children with young adolescents, older adolescents and young adults with children.

Conclusion: Change between age groups should be considered when conducting cohort analyses in children and adolescents with chronic disease. There is significantly increased risk of LTFU in adolescents, particularly in older adolescents. The high proportion of girls amongst 15-19 year olds and low proportion of advanced disease suggest that this group is predominantly likely to have acquired HIV sexually. The potential difference of risk of LTFU of adolescents with sexually acquired HIV compared with horizontally infected adolescents warrants further investigation.

Abstract 145

Cumulative Viremia, Treatment History, and Immune Status in Youths with Perinatal HIV Infection - The ANRS EP38 IMMIP Study

Avettand-Fenoel V1,2, Scott-Alagara D1, Montange T1, Le Chenadec J1, Viard J3, Dollfus C1, Warszawski J1, Rouzioux C1,2, Blanche S3, Buseyne F1

1Institut Pasteur, 2Université Paris-Descartes, 3AP-HP, 4INSERM

Background: Cumulative exposure to viral replication has been consistently associated with morbidity and mortality in HIV-infected patients under successful combined antiretroviral treatment (cART) over several years. Long-term maintenance of adherence and viral control can be challenging, particularly in children and adolescents. We previously described associations between cumulative viremia, cell-associated HIV-DNA, and naïve CD4 T-cell levels in perinatally infected youths over the age of 15 years. Here, we assessed whether cumulative viremia was associated with treatment history and biomarkers of inflammation and T-cell function.

Methods: The ANRS-EP38-IMMIP study included youths who acquired HIV during the perinatal period. Cumulative viremia was defined as the area under the curve of HIV RNA load over the last 10 years before the study. Plasma inflammatory markers were quantified using ELISA or Luminex technology. SEB-specific cytokine production by CD4 T cells was assessed by flow cytometry. Linear regression was used for univariate and multivariate analysis of cumulative viremia.

Results: The present analysis focused on the 57 patients with undetectable plasma HIV RNA at the time of the study. Their median (interquartile range) age was 18 (16-19) years and their CD4 T-cell count was 642 (522-949) cells/µl. Cumulative viremia was negatively associated with the duration of the last period of uninterrupted cART (estimate [95% confidence interval]: -315.6 [-569.1;-62.1], P = 0.01) and positively with the number of cART interruptions (708.26 [34.2;1382.3], P = 0.04), but not total duration of cART (-327.0 [-728.3;74.3], P = 0.11). It was positively associated with current CD8 T-cell count (2.5 [0.1;4.9], P = 0.04), neopterin (511.7 [70.6; 952.8], P = 0.02), and soluble tumor necrosis receptor 2 (3424.9 [741.5;6108.3], P = 0.01) levels. It was negatively associated with the percentage of polyfunctional CD4 T cells (-3281.3 [-4820.5;-1742.1], P < 0.0001). These associations were significant in multivariate analysis including age, sex, and CD4 T-cell count.

Conclusions: Lower cumulative viremia was associated with reduced immune activation and improved T-cell function in youths with long-term HIV infection and suppressed viral replication. However, cART interruptions were associated with higher cumulative viremia. Our data support the importance of adherence to treatment in HIV-infected youths.

Abstract 146

 Desire to prove fertility and contraceptive misconceptions delay family planning and condom use until after pregnancy among Kenyan adolescents

Crouthamel B1, Velonjara J1, O'Malley G1, Wiggins M1, Matemo D2, John-Stewart G1, Unger J1, Drake A1

1University of Washington, 2Kenyatta National Hospital

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Background: Adolescent girls have a high risk of unintended pregnancy and HIV acquisition in Kenya. We conducted a mixed methods study to characterize contraceptive knowledge and determinants of use among postpartum adolescents.

Methods: We recruited postpartum HIV-uninfected adolescents from 2 maternal-child health clinics in Western Kenya to participate in a survey and focus group discussion (FGD); 4 FGDs were conducted, stratified by site and age (14-18, 19-21). We also recruited health care providers offering family planning (FP) services to participate in a survey and 2 FGDs (1/site).

Results: Overall, 32 adolescents and 28 providers participated. Median provider age was 36 (interquartile range [IQR]: 31-47), and median number of years providing FP was 5 (IQR: 3-10). Misconceptions about FP and HIV risk were common among both providers and adolescents. Nearly half (40%) of providers believed intrauterine devices (IUDs) increased risk of HIV acquisition, and 63% believed they were unsafe to use among HIV-infected women. Adolescents were familiar with condoms for HIV and pregnancy prevention, but believed condoms were only appropriate when a partner was known to be HIV-infected, rather than when partners HIV status was unknown or concordant negative. Providers identified lack of training, experience, and counseling time as barriers to offering the full range of FP methods; they limited counseling to short-term methods when there were long queues or if they lacked knowledge or experience with other methods. Limited counseling options coupled with lack of training and experience with implants and IUDs contributed to lower use of these methods among young women at risk for HIV. Prior to marriage and/or childbearing adolescents lacked family and community support for FP, but adolescents also said they did not use FP because they felt it was important to prove their fertility prior to childbearing. However, after they became mothers adolescents received encouragement and familial/community support to use FP and had increased awareness of FP benefits.

Conclusions: Adolescents would benefit from novel strategies to receive better contraceptive support and education prior to childbearing (including dual method use with condoms) and improved provider training to prevent unintended pregnancies and HIV transmission.

Abstract 147

Psychiatric disorders among HIV infected Adolescents in Montreal

Kakkar F1, Valois S2, Lamarre V1,2, Renaud C1,2, Soudeyns H1,2, Lapointe N1,2

1University Of Montreal, Sainte-Justine Hospital Center, 2Centre Maternel et Infantile sur le SIDA

Background: The incidence of psychiatric disorders among perinatally HIV infected children who are on effective antiretroviral therapy (ART) is not well known, despite the neurotropic effects of the virus, and concerns about the potential ART associated neurotoxicity. The objective of this study was to document the incidence of psychiatric disorders among perinatally HIV infected children in Montreal.

Methods: Clinical records and the database of the Centre Maternel et Infantile sur le SIDA (CMIS) (Montreal) cohort (1988-2015) were reviewed to identify all children who were diagnosed with a psychiatric disorder according to DSM IV criteria. Patients were excluded if they were followed at CMIS less than 5 years, were non-perinatally infected, were less than 13 years of age, or died before the age of 18.

Results: Out of a total of 184 HIV infected children followed at CMIS, 93 met the inclusion criteria. Of these, 8.6% were diagnosed with a psychiatric disorder (psychoses with hallucinations=2, psychosis without hallucinations=1, major depression with suicide attempt=2, major depression without suicide attempt, n=3). Mean age at psychiatric diagnosis was 14 (range 10-17 years). The majority (62.5%) were on effective ART at the time of their diagnosis, with sustained viral suppression. There was a higher proportion of psychiatric diagnosis among children born during the era of cART availability (2000-2014), vs. those for whom only sequential ART was available (1980-2000) (14% vs. 8.2%), though not statistically significant. The overall
incidence of psychosis (4.3%) and suicide (2.1%) was higher that reported in the general Canadian population of adolescents (0.5% and 0.001% respectively).

Conclusions: In this cohort of perinatally infected children, the incidence of psychiatric disorders was 8.6% in adolescence, and appears significantly higher than among the general population of Canadian adolescents. These findings and specific causative factors need to be confirmed in larger studies.

Abstract 148

A study of non-disclosure and associated factors among perinatal HIV-infected children and adolescents in Bangkok, Thailand

Kingkaew W1, Anugulruengkitt S2,3, Jantarabenjakul W6,7, Phophonphitak S1, Kasipong N1, Bureechai S1, Thamsala S1, Sophonphan J1, Bunupuradah T1, Puthanakit T1,2,3

1HIV-NAT, The Thai Red Cross AIDS Research Centre, 2Department of Pediatrics, Faculty of Medicine, Chulalongkorn University, 3Research Unit in Pediatric Infectious Diseases and Vaccines, Faculty of Medicine, Chulalongkorn University

Introduction: Disclosure of HIV status to children is essential for disease management but is not well characterized in resource-limited setting. This study aimed to describe the prevalence of disclosure/non-disclosure and associated factors of non-disclosure in a cohort of perinatal HIV-infected children and adolescents.

Methods: We conducted a cross-sectional study of HIV disclosure status in all perinatal HIV-infected children age > 6 years at HIV-NAT, the Thai Red Cross AIDS Research Centre, Bangkok, Thailand. HIV disclosure status of each child and caregiver were collected by pediatricians by interview children and their caregivers in each scheduled clinic visits during January-December 2016. Descriptive statistics and disclosure prevalence were calculated. Univariate analysis and multivariate logistic regression were performed to assess the association of non-disclosure.

Results: Two hundred thirty six children were enrolled, current median (IQR) age was 18.5 (15.8-20.6) years, 51.6% were female, median CD4 was 663 (491-917) cells/mm3. Two hundred thirty four (99%) children were using antiretroviral therapy and 78% had plasma HIV RNA <50 copies/ml. One hundred fifty four (65%) children had at least 1 of parents alive and 33 (14%) live in orphanage house.

Prevalence of HIV disclosure was 91% (214/236). Median age at disclosure was 12.1 (10.7-13.7) years. Twenty two (9%) children were HIV non-disclosure. The reasons of non-disclosure were caregiver felt that the child is too young 10 (45%), child had delayed cognitive development (i.e. from HIV encephalopathy) 9 (41%), caregiver is not ready to disclose i.e. not know how to do 2 (9%), and caregiver fear of HIV stigma 1 (5%). In multivariate regression, factors associated with non-disclosure were age ≤15 years (aOR 22, 95%CI 6.8-70.9, p<0.001), and living in orphanage vs. community (aOR 6.5, 95%CI 1.6-25.7, p=0.01). Other variables such as parent alive and current CD4 were not significantly associated with non-disclosure.

Conclusion: One-tenth of perinatal HIV-infected children and adolescents were non-disclosure in our pediatric cohort. Younger age and living in orphanage were significantly associated with non-disclosure. Health care provider should give more psychosocial support to these children and caregiver in disclosing process.

Abstract 149

Screening for HIV-associated cognitive disorders in perinatally infected adolescents: validation of the IHDS.

Phillips N1, Thomas K1, Stein D1,2, Myer L1, Sacktor N6, Zar H1, Hoare J1

1University Of Cape Town, 2South African Medical Research Council, 3Johns Hopkins University
**Background:** Perinatally acquired HIV-infection has adverse neurocognitive consequences for children living with the virus. To date, there are no screening tools to determine the risk of HIV-associated cognitive disorders in this vulnerable cohort.

**Materials and Methods:** We sought to test and validate the use of the International HIV Dementia Scale (IHDS) as a screening tool for risk of HIV-associated cognitive disorders in a sample of perinatally HIV-infected adolescents drawn from the Cape Town Adolescent Antiretroviral Cohort (CTAAC). Each participant completed a comprehensive neuropsychological test battery and the IHDS. The neuropsychological test battery assessed neurocognitive functioning in the following cognitive domains: general intellectual functioning, attention, motor coordination, language, working memory, verbal memory, visual memory, visual spatial ability, processing speed and executive function. We statistically developed composite cognitive domain scores for each of the listed domains comprised of different combinations of the various neuropsychological tests making up the battery. Using those composite cognitive domains scores we then classified each participant according to the youth HAND criteria established by Hoare et.al. in 2016.

**Results:** Cross tabulation sensitivity analysis testing various cut off scores on the IHDS revealed that the IHDS yields more true positives than false positives with a sensitivity of 85.22% when using a cut-off score of 10.5 (i.e. >10.5 = no risk, <=10.5 = moderate - high risk). Furthermore we found that: 1) there are significant differences in cognitive ability between HIV-infected children and controls scoring above 10.5 on the IHDS and those scoring less, the same was true for the HIV-infected group alone, 2) a strong positive correlation between the IHDS and cognitive ability which demonstrates that as cognition improves so do scores on the IHDS (i.e. better cognitive ability is associated with higher scores on the IHDS), 3) ROC analysis produced an area under the curve of >.5 indicating that the IHDS performs better than chance detection of neurocognitive impairment.

**Conclusions:** Statistical analysis of the usability of the IHDS revealed that this tool could be useful as a screen for neurocognitive impairment in perinatally HIV-infected adolescents. A validated quick screening tool for use in this vulnerable population will be valuable in low resources settings, like South Africa.

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**Abstract 150**

**Experience and impact of HIV naming (disclosure) in adolescents with perinatal HIV in England**

**Judd A**, **Rowson K**, **Evangeli M**, **Thompson L**, **Le Prevost M**, **Sturgeon K**, **Brice S**, **Foster C**, **Gibb D**, on behalf of the Adolescents and Adults Living with Perinatal HIV (AALPHI) Steering Committee

**Background:** Informing children about their HIV status (HIV naming) is a critical aspect of disease management, and WHO guidelines now recommend naming in primary school years. Delayed HIV naming may affect mental and physical health, but there is little evidence. We describe circumstances around and predictors of age at HIV naming, and impact of age at naming on self-reported antiretroviral adherence and wellbeing outcomes, in the AALPHI cohort.

**Methods:** 296 PHIV aged 13-21yrs recruited in England from 2013-15, and all aware of their HIV status, underwent computer-assisted interviewing. Predictors of older age at naming, including sex, born in UK/Eire v elsewhere (both a priori), age at ART start, ever diagnosed with encephalopathy, cognitive function (NPZ-6), CDC diseases stage (N/A/B v C), death of parents, fostered/adopted, and language spoken at home, were explored using linear regression. The effect of age at naming on various outcomes was explored using logistic (for ever drugs, alcohol, smoking; missed ART in last 3 days), ordered logistic (no. people told about HIV, no. people able to talk about HIV), and linear (Hospital Anxiety & Depression Scale, quality of life (PedsQL), self-perception about HIV) regression models.

**Results:** Of 295/296 PHIV with naming data, 118(40%) were male, median age 17 years [IQR 15,18] (range 12,22), 252(85%) black
African, 171(58%) born outside the UK, 99(36%) one/both parents had died. 219 recalled age at HIV naming: median 12 years [11,13] (range 3,17). 98(34%) were told at home, 161(55%) at hospital, 17(6%) did not remember, 19 other. 121(41%) were told by a doctor, 55(19%) a nurse, 93(32%) parent/carer, 26 other. 35(12%) already knew by looking up medicines (2), overhearing conversations (10), other (13). After adjustment for a priori factors (both p>0.2), the only predictor of older age at naming was cognitive function (0.73 years older (95%CI 0.1-1.4) for every 1 point worse, p=0.025). Age at naming did not predict any outcomes either before or after adjustment (all p>0.08).

Conclusions: Median age at HIV naming was 12 years, conforming to previous UK guidelines, although 25% were ≥13 yrs. Older age at naming among those with poorer cognition might be expected as cognition levels may relate to the ability of a young person to understand their diagnosis, potentially impacting on when caregivers think a child is ready to know their diagnosis. We saw no effect of older age at naming among those with worse CDC disease stage. Age at naming did not predict study outcomes 5 years later, although other factors at the time of naming or afterwards may be more important, for example, how HIV is named, how this impacts on onward disclosure, and ongoing communication about HIV within the family.

Abstract 151

Late initiation of ART results in poor longitudinal treatment outcomes in perinatally HIV-infected adolescents in South Africa

Chandiwana N1, Fairlie L1, Sawry S1, Chasela C2, Musenge E2, Kachingwe E1

1Wits Reproductive Health And HIV Institute, 2Wits School of Public Health

Background: Scale-up of prevention of mother-to-child transmission (PMTCT) of HIV, coupled with increased access to antiretroviral therapy ART has resulted in many children surviving into adolescence and young adulthood. HIV-infected adolescents on ART are at high risk of poor treatment outcomes yet few studies describe longitudinal outcomes and compare treatment outcomes among adolescents in high HIV burden resource limited settings.

Methods: We analysed routinely collected patient-level data from patients aged 10-19 years enrolled in care from January 2004 to December 2016 at a large paediatric ART clinic in South Africa. Kaplan Meier estimates were calculated for mortality, loss to follow up, LT FU, transfer out and virological suppression. Crude and adjusted hazard ratios (HR) of the ART outcomes were calculated using Cox proportional hazard models.

Results: Of 1963 adolescents included in the analysis, half (52%, 1020) initiated ART in preadolescence (age<10 years), compared to in adolescence (≥10-19 years) (48%, 943). At ART initiation, the median absolute CD4 was 217 (interquartile range, IQR 69-413), 590 (43%) children had viral loads above 100000 copies/ml, 71% of children had advanced disease (WHO stage 3 and 4) and majority of patients initiated on an efavirenz-based regimen (95%). Children who initiated ART in adolescence had more markers of advanced clinical disease at the start of treatment as reflected by lower CD4 counts (p<0.000), WHO stage 3 or 4 (p=0.002), severe anaemia (p<0.000), lower weight-for-age (p<0.000), and higher levels of stunting (p<0.000) at ART initiation. At last follow up visit, 460 (24.4%) adolescents were still alive and in care, 285 (14.5%) were LTFU, 1156 (59%) transferred to another facility, and a further 62 (3.2%) had died. ART initiation in adolescence [adjusted hazard ratio (aHR), 5.58; 95% CI: 2.33 to 13.36, severe anaemia at ART start (aHR, 5.55; 95% CI 1.71 to 18.04) and WAZ ≤ -3 at ART start (aHR, 5.42; 95% CI 2.21 to 3.31) were found to be independently associated with mortality at last visit. Adolescents who were not retained in care were more likely to be LTFU if they started ART in adolescence (aHR, 2.31; 95% CI: 1.56 to 3.41).

Conclusions: Delayed ART initiation results in poorer long term treatment outcomes in HIV-infected adolescents, especially for those that have markers of severe disease at the start of ART. With high HIV- related mortality among HIV infected adolescents starting ART late, more efforts should be made to find and start children and adolescents on treatment early.

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Abstract 152

Retention in ART care amongst Adolescents attending an urban clinic in Durban, South Africa

Kindra C1,2, Kindra G2, Archary M1,2, Bobat R1,2

1King Edward VIII Hospital, Department of Paediatrics, 2Department of Paediatrics and Child Health, Nelson Mandela School of Medicine, University of KwaZulu-Natal

Background: Adherence and retention in care are critical in attaining the UNAIDS 90-90-90 goals. Adolescents are particularly challenging and a recent systematic review reported a retention rate of 83% (95%CI 68%-93%) amongst adolescents on ART. It is imperative to identify good practices which aid retention in care in an African context.

The adolescent clinic at King Edward VIII Hospital functions within a combined Paediatric and Adult HIV clinic, with dedicated adolescent-friendly days. Each adolescent is managed by a multidisciplinary team, including a doctor, lay counsellor, social worker and nurses and is seen by the same staff at each visit to allow continuation of care and bonding. Facilitated group counselling is also provided.

Methods: A retrospective chart review of all adolescents (10 years-19 years) attending the clinic between January 1996 – December 2015 was conducted. Analysis was conducted using STATA12.O; Mantel-Haenszel estimates were calculated and multivariate logistic regressions performed.

Results: Amongst the 357 eligible patients were identified, 343 files were available for analysis and the remaining 14 files were incomplete. All patients were black African of Zulu ethnicity and 43.7% are female. Most were WHO stage 3 at ART initiation (67.4%). Median age at diagnosis and ART initiation were 97 months and 102.4 months respectively. Most adolescents (62.6%) had lost one or both parents. Almost 87% of the adolescents were still being actively followed-up at the time of this analysis; with 28 (8.2%) being transferred; 16 (4.7%) lost to follow-up and 1 (0.3%) death. Predominantly, 256 (74.6%) were still on their 1st line ART regimens (EFV based ART); 86 (25.1%) on 2nd line (Protease-inhibitor based ART); and 1 (0.3%) on 3rd line. Current or past history of TB was present in 228 (66.5%) of the adolescents. On multivariate analysis, controlling for current age, being on a once daily combination pill was almost 80 times protective for retention in care (OR 0.05; 95%CI 0.01-0.39; P=0.004).

Conclusions: Provision of adolescent-friendly days with dedicated staff results in a 90% retention in-care of adolescents, even in a busy urban clinic in South Africa. Once daily fixed dose preparations can further improve retention in adolescents.
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