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Abstracts
Oral Presentations

1

Twenty-four week safety, tolerability and efficacy of dolutegravir dispersible tablets in children 4 weeks to <6 years old with HIV: results from IMPAACT P1093

Ruel T[1], Farhad M[2], Alvero C[2], Acosta E[3], Singh R[4], George K[5], Montanez N[5], Popson S[6], Bartlett M[6], Dayton D[8], Anthony P[7], Buchanan A[9], Brothers C[9], Vavro C[9], Koech L[10], Vhembo T[11], Hazra R[12], Townley E[13], Wiznia A[14]

1UCSF Benioff Children's Hospital, San Francisco, San Francisco, United States, 2Harvard T.H. Chan School of Public Health, Boston, USA, 3School of Medicine, University of Alabama at Birmingham , Birmingham , USA, 4GlaxoSmithKline, Collegeville, USA, 5FHI 360, Durham, USA, 6Frontier Science Foundation, Boston, USA, 7University of Southern California, Los Angeles, USA, 8MacDonald Research Laboratories, Los Angeles, US, 9ViiV Healthcare , Research Triangle Park, USA, 10Kenya Medical Research Institute/ Walter Reed Project Clinical Research Centre, Kericho, Kenya, 11University of Zimbabwe College of Health Sciences Clinical Trials Research Centre, Harare, Zimbabwe , 12National Institute Child Health and Human Development, NIH, Bethesda, USA, 13National Institute of Allergy and Infectious Disease, NIH, Bethesda, USA, 14Albert Einstein College of Medicine, The Bronx, USA

Background: Dolutegravir (DTG) is recommended for first-line treatment of adults and children with HIV-1 due to its potency, high barrier to resistance, and tolerability. A 5mg dispersible tablet (DTG-DT) pediatric formulation is being evaluated in IMPAACT P1093, an ongoing phase I/II open-label dose-finding study. Here we present 24-week safety, tolerability and efficacy results among participants 4 weeks to <6 years old.

Methods: After initial 4-week dose evaluation with an intensive pharmacokinetic cohort, additional participants were enrolled to assess long term outcomes at proposed dosing. DTG-DT was dosed according to age and WHO weight-band (3 to <6 kg: 5 mg; 6 to <10kg: if <6 months 10mg, if ≥6 months 15mg; 10 to <14kg: 20mg, 14 to <20kg: 25mg), and given with a background antiretroviral (ARV) regimen including ≥ one active agent based on genotype. Clinical and laboratory assessments occurred between day 5 and 13, and at weeks 4, 8, 12, 16, 24, 32, 40 and 48 (+/- 3 days). Safety analysis included cumulative data to April 30, 2019.

Results: Among 51 children enrolled from 9 countries (55% female, 75% Black), baseline median (interquartile range) HIV RNA [log10(c/ml)] was 4.3 (3.3;5.8), CD4 count (cells/mm3) was 1866 (1189;2384) and CD4% was 24.2(20.0;31.0); 86% were ARV-experienced. Thirty-four (67%) had HIV RNA data at week 24. The proportion(95%CI) with HIV RNA <400c/ml at 24 weeks was 88% (64,99) for 4 wks to <6 mo (n=17), 89% (52,100) for 6 mo to <2 yrs (n= 9), and 75% (35,94) 2 yrs to <6 yrs (n=8). The proportion (95%CI) with HIV RNA <50c/ml at 24 weeks was 41%(18,67), 67%(30,93), and 63%(25,92) respectively. While 25 (49%) experienced an adverse event of Grade 3 or higher, none were assessed as related to DTG, and no events led to permanent discontinuation. One death was reported from gastroenteritis and not considered drug-related. DTG-DT palatability was rated average, good, or very good for 98% of respondents.

Conclusions: In P1093, once-daily weight-band dosing of DTG-DT was well-tolerated in children 4 weeks to <6 years old, with a robust antiviral effect and improvement in CD4 parameters.

2

Pediatric dolutegravir (DTG) dosing recommendations derived from combined P1093 and ODYSSEY Population Pharmacokinetic analysis

Singh R[1], *Baker M[2], Thapar M[3], Gibb D[4], Turkova A[4], Ford D[4], Ruel T[5], Wiznia A[6], Farhad M[7], Alvero C[7], Green J[8], Bollen P[9], Colbers A[9], Burger D[9], Acosta E[10]*

[1]GlaxoSmithKline, Collegeville, United States, [2]ViiV Healthcare, Nyon, Switzerland, [3]ICON plc, Marlow, United Kingdom, [4]MRC Clinical Trials Unit at University College London, London, United Kingdom, [5]University of California atSan Francisco, San Francisco, United States, [6]Jacobi Medical Center, Bronx, United States, [7]Harvard TH Chan School of Public Health, Boston, United States, [8]ViiV Healthcare, Brentford, United Kingdom, [9]Radboud University Medical Center, Nijmegen, Netherlands, [10]University of Alabama at Birmingham, Birmingham, United States

Background: HIV treatment options remain limited in children. The recent Tivicay (dolutegravir, DTG) pediatric regulatory submissions propose WHO weight-band based recommendations for once-daily dosing in children ≥4 weeks of age using combined datasets from two pediatric studies: IMPAACT P1093 and ODYSSEY (PENTA20). These doses were informed by the Population PK (PopPK) analysis described below.

Methods: P1093 is a Phase I/II, non-comparative pharmacokinetic (PK) and safety study in HIV-1 infected children (≥4 weeks to <18 years of age). ODYSSEY is a non-inferiority, phase II/III study comparing the efficacy and toxicity of DTG plus 2 NRTIs vs. standard of care in infants and children. Intensive and sparse PK samples following dosing with film coated tablets (FCT), granules and dispersible tablet (DT) formulations in the fasted state and without regard to food were collected in P1093; intensive PK samples using FCTs and DTs in fasted state were collected in ODYSSEY. A PopPK model was developed with data from P1093 (1711 concentrations from n=151 participants) and ODYSSEY (939 concentrations from n=88 participants) to characterize PK, covariates, and associated variability. The final PopPK model simulated exposures across weight bands, doses, and formulations which were compared with established adult reference data.

Results: Of N=239 participants included, baseline age ranged from 0.17-17.5 years and weight from 3.9-91 kg, 50% were male and 80% were black. The model described study data and associated variability well with estimated mean (interindividual variability) CL/F=1.03L/h (29%) and V/F=13.6 L (107%). Based on observed and simulated data, dose stratification by age (<6 months and ≥6 months) in the 6 to <10 kg weight band (10 and 15 mg DTG DT, respectively) was proposed to account for metabolic enzyme maturation. The proposed doses are 5mg DT in 3 to <6kg; 10 mg DT in 6 to<10kg and <6 months, 15mg DT in 6 to <10kg and ≥6months, 20mg DT in 10 to <14kg, 25mg DT in 14 to <20kg and 30mg DT or 50 mg FCT in >20kg. At these doses, the simulated 24- hour concentration (C24h) was consistent across weight bands, similar to observed data, and met the minimum target concentrations of 0.697µg/mL. Similarly, simulated 24-hour area-under-the-curve (AUC24h) met the minimum target (46 h*µg/mL) across weight bands. Simulated maximum concentration (Cmax) results were 0.96 to 1.79-fold those observed historically in adults at the approved dose of DTG 50 mg BID (4.15 µg/mL). The safety exposure-response analysis demonstrated no relationships between PK parameters and adverse events.

Conclusions: Using FCT and DT formulations, DTG dosing in children ≥4 weeks of age on an age/weight-band basis provides comparable exposures to those historically observed in adults. Observed PK variability was higher in this pediatric population and no additional safety concerns were observed.

3

Safety, pharmacokinetics, and efficacy of low-dose E/C/F/TAF in virologically suppressed children ≥2 years old living with HIV

***Natukunda E*[1]**, *Liberty A*[2], *Strehlau R*[3], *Hellstrom E*[4], *Hakim J*[5], *Kaur H*[6], *Maxwell H*[6], *German P*[6], *Shao Y*[6], *Brainard D*[6], *Pikora C*[6]

[1]Joint Clinical Research Centre, Kampala, Uganda, [2]Chris Hani Baragwanath Academic Hospital, Soweto, South Africa, [3]Empilweni Services and Research Unit, Rahima Moosa Mother and Child Hospital, Department of Paediatrics and Child Health, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa, [4]Be Part Yoluntu Centre, Western Cape, South Africa, [5]University of Zimbabwe, Avondale, Zimbabwe, [6]Gilead Sciences Inc., Foster City, United States

Background: Elvitegravir (EVG)/cobicistat/emtricitabine/tenofovir alafenamide(TAF) (E/C/F/TAF) is a single-tablet regimen (STR) approved for HIV treatment in children ≥6y and ≥25 kg. Previous data reported no bone or renal toxicity of E/C/F/TAF in 50 children 6-<12y. We report safety, pharmacokinetics (PK), and efficacy from interim analyses of the first clinical trial of low-dose E/C/F/TAF tablet in young children with HIV.

Methods: Virologically suppressed children (≥2y), 14-<25 kg, HIV-1 RNA <50 c/mL for ≥6 months, CD4 ≥200 cells/µL received low-dose E/C/F/TAF (90/90/120/6mg) once daily in a, single-arm, open-label trial. Adverse events (AE), laboratory data, and proportion of participants with virologic suppression were assessed through W24. Steady-state PK of E/C/F/TAF was evaluated; EVG AUCtau and TAF AUCtau in children were compared to those in E/C/F/TAF-treated adults (150/150/200/10 mg).

Results: 27 children were enrolled; median age 6y (range 3-9y), median weight 19 kg (15-24 kg), 63% female, 89% Black, median CD4 count 1061 cells/µL (383-2401 cells/µL). Most common AEs were upper respiratory tract infection (6 participants [22%]), cough (5 [19%), decreased appetite (4 [15%]). All AEs were grade 1 or 2; no child discontinued STR for AE. 27 participants (100%) maintained HIV-1 RNA <50 c/mL by M=E at W16, with 10/11 (91%) at W24 (one participant had HIV-1 RNA between 200 to <400c/mL). Mean change (% change) in CD4 count from baseline was -95 cells/µL (-0.3%) at W24. EVG and TAF geometric mean AUCtau estimates were modestly (<2-fold) higher in children vs adults. Exposures of all analytes remained within range of historical data. Most children found swallowability, acceptability, and palatability favorable at all timepoints assessed.

Conclusion: E/C/F/TAF low-dose STR was acceptable with high virologic suppression. E/C/F/TAF exposures in young children were within range of adult historical data. Safety and efficacy of low-dose STR in young children are consistent with full-strength STR efficacy in older populations.

4

SAFETY, PHARMACOKINETICS AND ACCEPTABILITY OF THE ABC/3TC/LPV/r GRANULES (4-in-1) IN CHILDREN LIVING WITH HIV (3-20KG) IN UGANDA: LOLIPOP STUDY

*Andrieux-Meyer I[5], **Mwanga-Amumpaire J[1]**, Kekitiinwa A[2], Musiime V[3], Najjingo E[1], Kisitu G[2], Nazzinda R[3], Muthoni Ouattara G[4], Kyomuhendo F[4], Diallo M[5], Cressey T[6], Salvadori N[6]*

[1]Epicentre, Mbarara, Uganda, [2]Baylor College of Medicine Children's Foundation, Kampala, Uganda, [3]Joint Clinical Research Centre, Kampala, Uganda, [4]Drugs for Neglected Diseases initiative, Nairobi, Kenya, [5]Drugs for Neglected Diseases initiative, Geneva, Switzerland, [6]Program for HIV Prevention and Treatment, Chiang Mai, Thailand

Background: Lopinavir/ritonavir (LPV/r) in combination with Abacavir (ABC) and Lamivudine (3TC) is the primary 1st line treatment option for children living with HIV (CLHIV) under 3 years in many countries. To date, this triple combination has not been available for young children in a fixed dose combination (FDC). In partnership with DNDi, Cipla Ltd has developed a strawberry-flavoured ABC/3TC/LPV/r (30/15/40/10 mg) "4-in-1" granule FDC formulation for children. The aim of the LOLIPOP study is to assess the safety, pharmacokinetics (PK) and acceptability of the 4-in-1 FDC for the first time in children.

Methods: This is an ongoing phase I/II, open label, partially randomized, crossover trial of the 4-in-1 (test formulation [T]) versus ABC/3TC 60/30 mg in dispersible tablets plus LPV/r 40/10 mg pellets (reference formulation [R]) in 50 CLHIV in Uganda (NCT03836833). Study drugs are dosed by WHO weight bands (WB): 3-5.9 kg (WB1), 6-9.9 kg (WB2), 10-13.9 kg (WB3) or 14-19.9 kg (WB4). Children in WB2-4 were randomly assigned (1:1) by WB to R followed by T for 21 days each ("RT") or to T followed by R for 21 days each ("TR"). Children in WB1 only received the 4-in-1 for 21 days. Intensive PK sampling were performed after 21 days of treatment with each formulation. Safety was assessed during the whole study period, efficacy at the end of the study and an acceptability questionnaire collected after 21 days on the 4-in-1.

Results: As of February 2020, 33 children had been enrolled: 29 in WB2, 3 and 4 (14 assigned to RT and 15 to TR); 4 children in WB1, 9 in WB2, 9 in WB3 and 11 in WB4. At baseline, mean age was 2.7 (±1.5) years, weight 11.3 (±3.8) kg and CD4 percentage 34% (±8.5). All children completed the study except two (one lost to follow-up and one withdrew consent). With the 4-in-1, the geometric mean (GM) AUC0-12 for ABC, 3TC and LPV were 5,479, 6,059 and 88,398 ng.h/mL, respectively, and GM for Cmax were 1,754, 1,125 and 10,103 ng/mL, respectively; two children in WB1 (with severe wasting secondary to failure to thrive) had LPV C12 <1,000 ng/mL however one remained virologically suppressed and one became virologically suppressed. At the end of the study, 30/31 (97%) children had VL<400 cp/mL (versus 29/33 (87%) at baseline), including 20/31 (65%) with VL<50 cp/mL (versus 16/33 (48%) at baseline). Of 101 Treatment-Emergent AEs reported, 96 were mild, 4 moderate and 1 severe; none led to treatment discontinuation; one was serious (pneumonia) and started while on the reference formulation. Of the 31 caregivers, 30 (97%) reported administering the 4-in-1 as "very easy" or "easy", and 22 (71%) reported that the child had no difficulty in swallowing it.

Conclusion: In the first 31 CLHIV who completed the study, the 4-in-1 was safe, well-accepted and effective in achieving or maintaining viral suppression. The 4-in-1 provided adequate drug exposures of each component in WB2, 3 and 4, but a larger sample size in WB1 is needed to fully evaluate drug exposures in this WB.

5

The “DTGs” of DTG for children and adolescents living with HIV (CALHIV): Descriptions, Trends, and Gaps of rolling out dolutegravir in CALHIV in Mbeya, Tanzania.

***Bacha J*[1,2,3]**, *Mayalla B*[1], *Jiwa N*[1], *Mwita L*[1], *Campbell L*[1,2,3]

[1]*Baylor College Of Medicine Children's Foundation - Tanzania, Mbeya, Tanzania, United Republic of,* [2]*Baylor International Pediatric AIDS Initiative (BIPAI) at Texas Children’s Hospital, Baylor College of Medicine, Houston, United States,* [3]*Baylor College of Medicine, Houston, United States*

Background: In 2019, Tanzania procured dolutegravir (DTG) and began a country-wide rollout of DTG including new antiretroviral therapy (ART) initiations, as well as shifting existing patients to DTG regimens. We describe characteristics and outcomes of this DTG rollout for children and adolescents living with HIV (CALHIV) in Mbeya, Tanzania.

Materials and Methods: Retrospective chart review was conducted to describe characteristics and outcomes of CALHIV who received DTG as part of their ART at the Baylor College of Medicine Children’s Foundation – Tanzania Centre of Excellence (COE) in Mbeya, Tanzania between 1 March 2019 (when DTG became available) and 31 December 2019. HIV viral load(VL) suppression was defined as VL<1000 copies/mL.

Results: In 2019, 681 CALHIV received DTG, representing 46.0% (681/1497) of all CALHIV on ART and 59.6% (681/1142) of CALHIV eligible for DTG by weight (>20kg) at the COE. TLD was used in 66.0% (449/681), followed by 23.9% (163/681) on ABC-3TC-DTG and 10.1% (69/681) on AZT-3TC-DTG.

Among the cohort, 50.0% (341/681) were female, average age was 13.9 years (range 5.0-19.9 years), average time on ART prior to DTG was 5.4 years (range 0-14.4 years). Initial WHO stages: 40.4% (275/681) WHO 4, 26.7% (182/681) WHO 3, 16.3% (111/681) WHO 2, and 16.6% (113/681) WHO 1; of those with WHO treatment stages (n=638), 97.8% (624/638) were T-stage 1. Nutrition status by BMI revealed 22.9% (156/681) with severe malnutrition, 37.9% (258/681) with moderate malnutrition, and 39.1% (266/681) with normal nutrition. In our DTG cohort, 12.6% (86/681) were new ART initiations, 62.4% (425/681) were shifted from a NNRTI regimen, and 25.0% (170/681) were shifted from a PI regimen.

Outcomes revealed no severe drug toxicity and no discontinuations of DTG, with 94.9% (646/681) remaining active in COE care and 5.1% (35/681) transferred out. Multi-month prescriptions were used in 77.2% (526/681) of DTG patients. At the end of the study period, 84.1% (499/593) of patients on DTG with documented VL were suppressed, compared to 76.1% (448/589) of VLs prior to DTG. Among those with pre- and post-DTG VLs (n=117), 63.6% (42/66) of unsuppressed became virally suppressed, and 94.1% (48/51) of suppressed remained suppressed. Two adolescents became pregnant while on a DTG regimen, with both delivery healthy full term infants with no signs of birth defects and with initial DBS tests negative.

Conclusion: DTG was well tolerated and effective in our clinically diverse cohort of CALHIV, and it use resulted viral suppression for many previously unsuppressed CALHIV. These results encourage continued use and scale up of DTG among eligible CALHIV.

6

Acceptability of a new 4-in-1 Abacavir/Lamivudine/Lopinavir/Ritonavir paediatric fixed-dose combination: the caregiver-child dyads' perspective

Rotsaert A[1], Nöstlinger C[1], Collin O[2], Lee J[3], Andrieux-Meyer I[3], Diallo M[3], Waweru M[4], Kyomuhendo F[4], Were L[4], Ouattara G[4], Nkeramahame J[5], Kekitiinwa A[6], Musiime V[7]

[1]Department of Public health, Institute of Tropical Medicine, Antwerp, Belgium, [2]Makerere University, Kampala, Uganda, [3]Drugs for Neglected Diseases initiative (DNDi), Geneva, Switzerland, [4]Drugs for Neglected Diseases initiative (DNDi), Nairobi, Kenya, [5]Epicentre, Mbarara, Uganda, [6]Baylor College of Medicine Children's Clinical Centre of Excellence, Kampala, Uganda, [7]Joint Clinical Research Centre, Kampala, Uganda

Background: Worldwide 1.8 million children below 15 years were living with HIV in 2018 and only half of these have access to anti-retroviral (ARV) medication. Main obstacles to access remain availability of age-appropriate ARV formulations that are easy to swallow and have an acceptable taste. Cipla Ltd. and Drugs for Neglected Diseases initiative (DNDi) have developed a strawberry-flavoured Abacavir/Lamivudine/Lopinavir/Ritonavir (30/15/40/10mg) fixed-dose combination of granules in a capsule (4-in-1) for HIV-infected children weighing 3-25kg. This study assessed caregivers' perceived acceptability and related factors compared to Lopinavir/Ritonavir (40/10mg) pellets plus dual Abacavir/Lamivudine (60/30mg) dispersible tablets.

Materials and methods: A phase I/II, open label, randomized cross-over pharmacokinetic, safety and acceptability study (LOLIPOP) with an embedded qualitative component was carried out in three sites in Uganda (two in Kampala, one in rural Mbarara). Thirty-three children weighing between 3 and 19.9 kg were recruited. To assess acceptability, 18 semi-structured, qualitative interviews (of the overall 20 planned interviews) were conducted with purposively sampled caregiver-child dyads. Data were transcribed and analysed inductively using Nvivo12 and a thematic analysis approach. In addition, data on caregivers' and children's acceptability and adherence to treatment were collected through structured questionnaires. Questionnaires were analysed descriptively to assess concordance between the two data sources.

Results: All caregivers, irrespective of their children's weight, found the 4-in-1 formulation highly acceptable. Factors contributing to high acceptability were the appealing flavour, ease of administration (using mainly local cow milk, porridge or water as available, even when breastfeeding), easy storage and the child's acceptance. Overall, caregivers found the 4-in-1 easier to use than the pellets/tablets combination. Self-reported high short-term adherence was achieved due to effective support received from health providers and visible improvements in children's health. Administration instructions enabled caregivers to find most effective and individually tailored ways to administer the 4-in-1 and to overcome struggles such as initial vomiting. Questionnaire data and interviews were concordant confirming high acceptability.

Conclusions: In this sample, the 4-in-1 granule formulation was highly accepted among all weight-bands compared to the pellets/tablets combination due to treatment-related factors. In addition, health providers' comprehensive support to caregivers allowed individual tailoring of administering the treatment to the children, which increased short-term adherence.

7

A validated outpatient department HIV screening tool for children 18 months to 14 years as efficient as index testing in Uganda

*Katureebe C[1], **Ashburn K[2]**, Machekano R[2], Gill M[2], Adler M[3], Itoh M[4], Nazziwa E[3], Kazooba P[5], Kiyonga A[5], Rivandeneiro E[6], Gross J[6], Kekitiinwa A[7], Magongo E[1], Taasi G[1], Matovu J[1], Bitarakwate E[5]*

[1]Uganda Ministry of Health, Kampala, Uganda, Kampala, Uganda, [2]Elizabeth Glaser Pediatric AIDS Foundation, Washington, DC, United States, [3]Division of Global HIV and TB, Centers for Disease Control and Prevention, Kampala, Uganda, [4]Division of Global HIV and TB, Centers for Disease Control and Prevention, Lusaka, Zambia, [5]Elizabeth Glaser Pediatric AIDS Foundation, Kampala, Uganda, [6]Division of Global HIV and TB, Centers for Disease Control and Prevention, Atlanta, United States, [7]Baylor College of Medicine Children's Foundation, Kampala, Uganda

Background: While progress has been made in HIV case identification and linkage to care and treatment for adults, children and adolescents continue to lag behind. The lower HIV prevalence among children exacerbates challenges in case identification, requiring testing of large numbers of children to identify those living with HIV. In 2019, the number needed to test (NNT) to identify one new HIV-positive child was 64 in outpatient departments (OPD) and 31 through index testing in Uganda. We aimed to develop and validate an HIV screening tool for children and adolescents to optimize testing resources and provide targeted testing for those most likely to be HIV positive.

Materials and methods: In 2018, we developed a simple HIV screening tool based on a mother's HIV positive status or having any 2 of 5 symptoms (sickly in last 3 months, recurring skin problems, weight loss, not growing well, or history of TB) for children and adolescents (18 months - 14 years) in OPDs in Uganda. The proposed screening tool had a sensitivity of 83.6% (95% CI: 68.1 – 92.4) and specificity of 62.5% (95% CI: 55.0 – 69.4). Between September and December 2019, the screening tool was validated among children and adolescents in 15 different health facility OPDs and community-based settings across four regions, and analyzed for sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and NNT, accounting for inter-cluster correlations. All children and adolescents were tested for HIV according to national guidelines.

Results: 11,342 children and adolescents were enrolled in the validation sample; median age six years (IQR: 1.5 – 14), 47% males and HIV positivity was 1%. The tool had a sensitivity of 87.8% (95% CI: 80.9 – 92.5), specificity of 62.6% (95% CI: 54.8 – 69.7), PPV of 2.4% (95% CI: 1.9 – 2.8), NPV of 99.8% (95% CI: 99.7 – 99.9), and NNT of 43 (95% CI: 36 - 53). In OPD only, the tool had a sensitivity of 88.1% (95% CI: 80.8 – 92.8), specificity of 69.0% (95% CI: 61.9 – 75.3), PPV of 3.7% (95% CI:2.7 – 5.0), NPV of 99.8% (95% CI: 99.6% – 99.9%), and NNT of 28 (95% CI: 20 - 38). Of the 115 children who tested HIV positive, 46 (40%) had mothers with unknown or "reported" HIV negative status.

Conclusions: This screening tool, validated in OPD and community settings, had high sensitivity and reasonable specificity. It focuses testing resources on children and adolescents more likely to be living with HIV, and significantly reduces the NNT from 64 under current testing algorithms to 43 across both settings and 28 in OPDs, making targeted OPD testing as efficient as pediatric index testing in Uganda. This tool can supplement existing testing guidelines for providing an HIV test to all children with HIV positive mothers by including additional symptom related indicators for children with mothers who have an unknown or negative HIV status, avoiding 68% of unnecessary HIV tests. Use of such a screening tool should balance the potential to expedite the rate of case identification with the possibility of missing the diagnosis of a child or adolescent living with HIV.

8

Point of Care SAMBA-II vs Centralized Laboratory Viral Load Assays among HIV-1 Infected Children, Adolescents and Young Adults in Rural Zimbabwe: A Randomized Controlled Trial

Kouamou V[1], *Mapangisana T[2], Machekano R[2], Manasa J[1,3], Maposhere C[3], Mutetwa R[3], Mutsvangwa J[3], Shamu T[4,5], Bogoshi M[6], Israelski D[6], McCarty K[7], Katzenstein D[3,8]*

[1]University of Zimbabwe, Harare, Zimbabwe, [2]University of Stellenbosch, Cape Town, South Africa, [3]Biomedical Research and Training Institute, Harare, Zimbabwe, [4]Newlands Clinic, Harare, Zimbabwe, [5]University of Bern, , Bern, Switzerland, [6]Gilead Sciences Inc, Foster City, United States of America, [7]Chidamoyo Missionary Hospital, Hurungwe, Zimbabwe, [8]Stanford University School of Medicine, Stanford, United States of America

Background: To achieve the third 95-95-95 global target by 2030, access to viral load (VL) monitoring and more effective VL suppression (VLS) are needed. The Simplified Amplification-Based Assay (SAMBA II), near point of care (POC) semi-quantitative HIV VL test was introduced at selected rural hospitals in February 2018.

Methods: We randomized children, adolescents and young adults (CAY) on ART for >1 year at Chidamoyo Hospital Clinic (CHC) and 8 rural ART outreach sites (ROS) to VL monitoring by one of two methods. VL was assayed by either Roche Ampliprep®/COBAS® Taqman48® HIV-1 v2.0 at the provincial referral laboratory (PRL) or by POC SAMBA II, Diagnostics for the Real World at CHC at 0, 6 and 12 months. To switch drugs, 2 sequential VL>1000 copies/ml were required. The turn around time (TAT) from a blood sample to CHC charting and drug switching were compared. VL outcomes at 12 months were assessed by study arm (POC vs PRL), age, gender, care site (ROS vs CHC) and treatment regimen (non-nucleotide reverse transcriptase inhibitor, NNRTI vs boosted protease inhibitor, PI).

Results: Of 390 CAY enrolled, half were from ROS, 347 (89%) completed 12 months follow-up and 43 (11%) did not; 5 died, 14 transferred care and 24 were lost to follow up. 78 (20%) had a baseline VL>1,000 copies/ml (virological failure). The median age (IRQ) and ART duration were 15 (5-25) and 6 (3-9) years, respectively. Over half (59%) of the participants were female and 39% were on a boosted PI. A higher rate of VLS was seen at baseline among those enrolled at ROS vs CHC (85% vs 76%, respectively, p= 0.022). The confirmatory testing remained slightly higher in the POC vs PRL arms; 82% vs 63%, respectively at 6 months (p=0.07) and 89% vs 78%, respectively at 12 months (p=0.325). The TAT for confirmatory results from the POC laboratory were significantly shorter at 6 and 12 months. The median months (IQR) to confirmatory result for POC vs PRL was 2.7 (1.4-2.9) vs 3.5 (2.5-5.8) at 6 months (p=0.004) and 4.0 (2.1-4.4) vs 4.5 (3.5-6.3) (p=0.027) at 12 months, respectively. However, the mean time (□STD) to switch regimens from the first VL>1,000 copies/ml by PRL vs POC was not significantly different (8.2+5.6 vs. 7.3+5.5 months respectively, p=0.493). At 12 months, VLS was 80% and 81% by POC vs PRL monitoring, respectively. VLS on NNRTI was higher (85%) than on PI regimens (74%) (p=0.01). Persistent VLS defined as VL <1000 at 0, 6 and 12 months was 68% in ROS and 57% in CHC care (p <0.032). At 12 months, 36/347 (10%) had >1,000 copies/ml on PI regimens after a median (IRQ) of 7.3 years (5.2-8.3) of ART.

Conclusions: POC VL provided earlier and efficient confirmation of VLS, but with similar results for drug switching. Persistent VLS was significantly greater over 12 months in participants in care at ROS and was less likely among PI recipients regardless of ROS or CHC care. Because of PI failure, access to Integrase strand transfer inhibitor-based third line regimens are needed to achieve 95% VLS among CAY in rural Zimbabwe.

9

"Right under our nose": A simple screening tool to identify HIV-positive children outside of the PMTCT program at outpatient departments in Malawi

Tallmadge A[1], Stillson C[1], Nyirenda G[1], Nyambi N[1], Banda C[1], Gunda A[1], Muyaso M[2], Namachapa K[2], Eliya M[2]

[1]Clinton Health Access Initiative, Lilongwe, Malawi, [2]Ministry of Health, Department of HIV/AIDS, Lilongwe, Malawi

Background: In Malawi, only 67% of children living with HIV are on life-saving treatment. Linkage to treatment for known infected children is high, but identifying undiagnosed children who have dropped out of the PMTCT cascade or were infected postnatally is a persistent challenge. These children likely account for most of the remaining gap in pediatric treatment coverage. It is costly and impractical to test all children for HIV, every time they visit a health facility. However, the lack of specific screening guidance for children has led to ineffective and inconsistent testing in high-volume entry points like outpatient departments (OPDs). Therefore, despite having frequent contact with the health facilities, these children are often left undiagnosed until they present with advanced disease. Through systematic screening, there is a unique opportunity to identify these "missed" children earlier and link them to life-saving care.

Materials and Methods: Through a national taskforce, a screening tool was developed for use in facility OPDs. The tool was formatted as a simple checklist and screened children 2-12 years old, focusing on their mother's testing history instead of clinical or behavioral risk factors. Mothers without a documented HIV negative result after the end of breastfeeding were referred for HIV testing and, if positive, their children were also referred. If the mother was not available and the child had no record of a negative HIV test result after the end of breastfeeding, the child was referred for testing. The tool was piloted at 32 public health facilities in Malawi from July-September 2019. Baseline testing practices were evaluated from April-June 2019, through review of facility registers at each pilot facility. Following the completion of the pilot, focus group discussions (FGDs) were conducted at each pilot facility. Discussions were captured on contact summary forms for analysis. The forms were abstracted into Microsoft Excel and coded thematically with themes tabulated for frequency.

Results: 8811 screening slips were collected during the pilot period. The median age of children screened was 5.3 years (IQR: 3—7). 22.0% of available mothers were referred for testing based on screening (1827/8288). Of those tested, 1.9% tested newly positive (28/1474). Overall, 8.3% of children were screened in for testing (658/7897). Of those tested, 3.9% tested newly positive (17/437). Baseline analysis showed that in the pre-intervention period 11.4% of children presenting to OPDs at the pilot facilities were being tested (2750/24221) and 1.1% were testing positive (29/2750). Introduction of the screening tool thereby reduced testing volumes by 27% while increasing yields 270% from baseline. 640 screening personnel participated in FGDs. Discussions revealed high acceptance of the screening tools, high willingness to use the tools if nationally adopted, and high usability of the tools by non-clinical lay cadres.

Conclusions: Systematic screening of mothers and children for HIV testing is feasible and can reduce testing volumes, while increasing the number of HIV-positive children identified, leading to more efficient testing within resource constraints and earlier identification and linkage of HIV infected children. These results will inform revisions to the screening tool in anticipation for national adoption.

10

Finding the remaining unidentified children living with HIV: Opportunities through index testing

***Amzel A*[1]**, *Srivastava M*[1], ***Gleason M*[1]**, *Lee L*[1]

[1]*USAID, Washington, United States*

Background: Index testing serves as an effective and efficient case-finding strategy for children living with HIV (CLHIV) <15 years of age who were missed through early infant diagnosis (EID) and routine testing; however, this case-finding modality has been slow to scale. PEPFAR's Country Operational Plan 2020 Guidance (COP20) recommends 100% of biological children of women living with HIV (WLHIV) be tested to improve case identification. In this descriptive analysis, we examined PEPFAR program data and total fertility rate (TFR) by country to estimate the number of biological children <15 years of age that could be tested and the subsequent number of children living with HIV (CLHIV) identified, if all WLHIV 15-49 years old on ART not previously evaluated for index testing were assessed.

Methods: The authors analyzed PEPFAR data from 23 countries and the TFR obtained from the respective country's most recent Demographic and Health Surveys (DHS) to approximate the numbers of: 1) WLHIV 15-49 years old on ART who have not been reported as an index client; 2) total number of biological children that could be elicited from index WLHIV; and 3) CLHIV that could be identified if all WLHIV on ART who have not been reported as an index client were assessed. PEPFAR indicators reviewed include: TX_CURR (current on treatment) and HTS_INDEX (index testing) for women between 15-49 years of age, and the average testing yield by country for children found through index testing from July 1, 2018 to December 31, 2019 (FY18Q4 to FY20Q1).

Results: In the 23 PEPFAR countries included in this analysis, 7,509,333 WLHIV aged 15-49 were documented on ART as of December 31, 2019 (FY20Q1). Only 2,430,721 WLHIV (32%) were reported as having been offered index testing cumulatively from July 1, 2018 to December 31, 2019 (FY18Q4 to FY20Q1). We estimate a remaining gap of 5,081,238 WLHIV (68%) on ART who could be assessed for index testing. Using the respective TFR for each country [2.3-6.6 children per woman], a crude estimate of 21,518,082 biological children could be elicited from these WLHIV through index testing. Using the respective pediatric index testing yields by country, testing all of the estimated biological children of WLHIV on ART could identify as many as 869,140 CLHIV.

Conclusions: There is an urgency to identify CLHIV of all ages and initiate them on lifesaving treatment. Maximizing coverage of index testing for WLHIV of childbearing age (15-49 years) currently on ART has the potential to make a powerful contribution to close the first 95 gap for children.

11

Factors associated with late presentation of HIV-infected infants for Early Infant HIV Diagnosis (EID) services in Kenya

Langat A[1,2], *Yonga I[5], Boniface O[1], Callahan T[4], Onyango B[5], Waruru A[1], Singa B[7], Githuka G[3], Tylleskar T[2], Omoto L[1], Oyule S[6], Muli J[6], Barmasai K[3], Simiyu T[5], Ng'anga L[1], Katana A[1], Modi S[4]*

[1]Centers For Disease Control And Prevention, Kenya, Nairobi, Kenya, [2]Centre for International Health, University of Bergen, Bergen, Norway, [3]National AIDS and STI Control Program (NASCOP), Ministry of Health, Nairobi, Kenya, [4]Division of Global HIV & TB, U.S Centers for Disease Control and Prevention, Atlanta, USA, [5]Health Population and Nutrition Office, USAID Kenya , , Kenya, [6]The U.S. Military HIV Research Program (MHRP), Nairobi, Kenya, [7]Kenya Medical Research Institute (KEMRI), Nairobi, Kenya

Background: Every HIV-infected infant indicates a missed opportunity in Prevention of Mother to Child Transmission (PMTCT) programs. In Kenya efforts to scale-up early infant HI-diagnosis (EID), have led to significant gains, but slightly over half of the HIV exposed infants receive HIV testing within the first 8 weeks of life. We assessed factors associated with late enrolment into HIV-exposed infants (HEI) services (which included EID), for HIV-positive infants in sites supported by the US President's Emergency Plan for AIDS Relief (PEPFAR) Kenya.

Methods: We abstracted routine clinical data on all infants with a HIV-positive PCR result from 1347 PEPFAR-supported health facilities (October 2016–September 2018). We aggregated the data from all sites in STATA and used univariate and multivariate logistic regression to examine the association of baseline characteristics to timing of HEI enrollment. Late HEI enrolment was defined as >8 weeks from the time of birth and used maternal time of anti-retroviral therapy (ART) initiation as a proxy for maternal HIV diagnosis since actual date of HIV diagnosis was not available.

Results: Of 4091 HIV-positive infants, only 4011 who had date of birth recorded were included in the analysis The median infant age at HIV diagnosis was 13 weeks (interquartile range [IQR], 4–64 weeks), and most (2669 [66.4%]) were enrolled late for HEI services. The mothers of the HIV positive infants who enrolled late, slightly more than half were aged 24–34 years (1,291 [51%] of the 2505 who had maternal age recorded), did not attend antenatal clinics (ANC) (46.7% [1247/2669]), were newly diagnosed as HIV positive at presentation to MCH (64.5% [1722/2669]), and initiated ART in the postnatal period (60.5% [1615/2669]).

Factors that were independently associated with late HEI enrollment were lack of maternal ANC attendance (adjusted odds ratio [aOR], 1.54 [95% confidence interval (CI): 1.27–1.85]), new maternal HIV diagnosis (aOR, 1.38 [95% CI: 1.17–1.63]), lack of maternal prophylaxis (aOR, 1.96 [95% CI: 1.64–2.35]), HEI identification in outpatient (aOR, 14.2 [95% CI: 7.35–27.6]) or inpatient settings (aOR, 8.92 [95% CI: 4.16–19.1]), and late infant immunization (aOR, 1.63 [95% CI: 1.31–2.03]).

Conclusions: Ensuring that mothers attend ANC early to receive HIV testing and are prepared to access EID services for their infants could help improve outcomes for infants. Finally, routine HIV screening in outpatient and in-patient settings may identify HIV-positive infants who were missed in the maternal child health clinics.

Abstract 12 is withdrawn

13

Development and Validation of the HIV Adolescent Readiness for Transition Scale (HARTS)

***Zanoni B*[1]**, *Archary M*[2], *Sibaya T*[2], *Musinguzi N*[3], *Haberer J*[4]

[1]Emory Universoty School Of Medicine, Atlanta, United States, [2]University of KwaZulu-Natal, Durban, South Africa, [3]Mbarara University of Science and Technology, Mbarara, Uganda, [4]Massachusetts General Hospital, Boston, United States of America

Background: Adolescents living with perinatally acquired HIV have low rates of retention in care and viral suppression after transition to adult care. In many settings, timing of transition to adult care is arbitrarily assigned and often occurs with little or no preparation. We designed and validated the HIV Adolescent Readiness to Transition Scale (HARTS) to determine when an adolescent is ready to transition to adult care and to identify at-risk adolescents who may need further interventions prior to transition.

Materials and Methods: We iteratively adapted existing transition readiness scales that were created for children with chronic illnesses in North America for use with HIV transition in South Africa by conducting focus groups with healthcare providers (n=11), and adolescents (n=20 in 2 groups) before transition to adult care. We then administered the HARTS questionnaire to 131 adolescents to determine the psychometric properties of the questionnaire. We assessed test-retest variability with 13 (10%) adolescents who took the questionnaire before and after their clinic visits. Based on item response theory, we used generalized linear equation models with the overall score and with the individual domains. In addition, we correlated the responses to self-described transition readiness and age using liner regression. We then validated the scale by prospectively administering it to 199 new adolescents in a different South African setting prior to their transition and measured their viral suppression (viral load <200 copies/ml) one year after transitioning to adult clinic. Transition outcomes were evaluated using multivariable logistic regression based on the continuous HARTS value and covariates with a p value of less than 0.2 on bivariate analysis.

Results: We identified 4 domains that were important to HIV transition readiness: disclosure, health navigation, self-advocacy, and health literacy. The initial questionnaire contained 16 individual questions. Factor loading for each question ranged from 0.21 – 0.76. One question had a factor load <0.1 and was eliminated from the final questionnaire, leaving 15 questions for the final HARTS. For the test-retest variability, the mean score on test 1 was 36.3 and 36.9 on test 2 with no statistical difference in means (p=0.69). Positive correlations with self-described transition readiness were significant with the overall HARTS score (p<0.0004) and domains of health navigation (p=0.028), self-advocacy (p=0.0014), and health literacy (p=0.0023). Overall scores and each domain increased with age but not significantly. In the prospective analysis, overall HARTS scores ranged from 2 to 56. For participants receiving first-line antiretroviral therapy, each 10-point increase in HARTS score was associated with 0.53 odds of viral failure (p=0.001; 95% CI 0.36 – 0.77) in our multivariable model adjusting for age at antiretroviral therapy initiation, sex, disclosure status, drug and alcohol use, peer support, and self-esteem. Age alone at time of transition was not significantly associated with viral suppression 12 months after transition to adult care.

Conclusion: The HARTS questionnaire is a validated scale that can be used to determine which adolescents may require additional interventions prior to transitioning to adult care to improve retention in care and viral suppression.

14

Point-of-Care Viral Load Testing Among Adolescents and Young Adults Living with HIV in Haiti: A Randomized Control Trial

***Reif L*[1,5]**, *Belizaire M*[2], *Seo G*[1], *Rouzier V*[1,2], *Joseph B*[2], *Apollon S*[2], *Abrams E*[3,5,6], *Arpadi S*[3,4,6], *Elul B*[5], *Pape J*[1,2], *McNairy M*[1,7], *Fitzgerald D*[1], *Kuhn L*[4,5]

[1]Weill Cornell Medicine, New York, United States, [2]GHESKIO Center, Port-au-Prince, Haiti, [3]ICAP at Columbia University, Mailman School of Public Health, Columbia Irving Medical Center,, New York, United States, [4]Gertrude H. Sergiesvsky Center, Vagelos College of Physicians and Surgeons, Columbia University Irving Medical Center, New York, United States, [5]Department of Epidemiology, Mailman School of Public Health, Columbia University Irving Medical Center, New York, United States, [6]Department of Pediatrics, Vagelos College of Physicians and Surgeons, Columbia University Irving Medical Center, New York, United States, [7]Division of General Internal Medicine, Department of Medicine, Weill Cornell Medicine, New York, United States

Background: Adolescents living with HIV have poor antiretroviral therapy (ART) adherence and viral suppression outcomes. HIV viral load (VL) monitoring is an opportunity to reinforce antiretroviral therapy (ART) adherence. Standard VL testing requires high laboratory capacity and coordinated transfer of samples and results between clinic and laboratory which can result in delayed or mis-placed results. Point-of-care (POC) VL testing is an alternative that may return results faster, strengthen adherence counseling, and lead to improved outcomes.

Methods: We conducted an unblinded randomized trial comparing POC VL testing to standard VL testing among 150 adolescents and young adults, ages 10-24 years, living with HIV in Haiti. Participants were randomized 1:1 to the POC arm for a POC VL test with same-day result and adherence counseling or standard care (SOC) arm for a laboratory-based VL test with result and ART adherence counseling given 1 month later. VL testing was repeated 6 months later for both arms. The primary objective was to compare the efficiency of VL testing between the arms; secondary objectives included effects on ART adherence and viral suppression at 6 months.

Results: Participants were between the ages of 12-24 years and 70% acquired HIV perinatally. Participants had been on ART for an average of 6 years, and 57% had a VL <1,000 copies/ml at enrollment. Participants in the POC arm were more likely to receive their VL test result with adherence counseling within 6 weeks of blood collection than participants in the SOC arm (94.7% vs. 80.1%; p<0.01). Associations between VL >1000 copies/ml and low self-reported ART adherence were stronger in the POC arm (OR: 6.57; 95%CI: 2.12-25.21) than in the SOC arm (OR: 2.62; 95%CI: 0.97-7.44) suggesting more accurate self-reporting of ART adherence in the POC arm. The proportion of participants with a VL <1,000 copies/ml at month 6 did not differ by arm (POC: 58.7% vs. SOC: 57.3%; p=0.87).

Conclusions: POC VL testing was efficiently implemented in this low-resource setting and among an adolescent and young adult population. POC VL testing provided faster time to VL test results and adherence counseling and was also associated with greater accuracy in ART adherence reporting. This may enable clinicians to more accurately identify poor ART adherence and high VL in this high-risk population and provide counseling or regimen changes sooner, preventing or mitigating HIV disease progression or the development of ART drug resistance. POC VL testing is a pragmatic intervention that can reduce inefficiencies in the VL testing process, and enable clinicians to make faster decisions to benefit adolescents and young adults living with HIV.

15

Antiretroviral Drug Transition and Adverse Event Monitoring among Adolescents 15 to 19 years of age in Kenya

Syowai M[1], Vakil S[1], Odhiambo S[1], Atandi D[1], Moraa G[1], Gikura M[3], Odhiambo J[3], Oramisi V[4], Imbuki E[4], Ngugi C[4], Fayorsey R[2]

[1]RISE and ICAP at Columbia University, Nairobi, Kenya, [2]RISE and ICAP at Columbia University, New York, United States of America, [3]The Palladium Group, Nairobi, Kenya, [4]Ministry of Health, NASCOP, Nairobi, Kenya

Introduction: Antiretroviral treatment (ART) optimization is critical to ensure viral suppression (VS) amongst children and adolescents. ART optimization in Kenya began in 2017 with the introduction of dolutegravir (DTG)-based first-line regimen for adolescents and adults living with HIV. We describe the ART transition, retention, VS, and adverse events (AE) among adolescents living with HIV (ALHIV) in Kenya.

Method: A retrospective observational study using de-identified patient-level data from the Kenya National Data Warehouse, 1 July 2019 to 30 June 2020, from 918 facilities. Descriptive statistics were used to summarize patient demographics, regimen distribution, retention, VS, and AE among ALHIV (15 – 19 years) and chi-square tests were calculated to determine level of significance of VS between DTG and efavirenz (EFV) -based regimen.

Results: 22,237 ALHIV, 54.2% females, mean age 17 years (IQR: 16-18), 80.3% (17,865) were on first-line ART, 19.4% (4,325) on second-line and 0.03% (7) on third-line ART. Of 17,865 ALHIV on first-line regimen, 47% (8,376) were on DTG-based ART, 40% (7,189) on EFV-based ART and 13% (2,300) on other regimen. Of 17,659 (79%) with viral load (VL) results, 14,853 (84%) were VS (< 1000copies/ml): 90% VS (5,962/6,619) for DTG-based ART and 83% VS (4,502/5,404) for EFV-based ART, p < .0001.

AE were reported for 10% (2,152) ALHIV, but only 6% (119) were graded. The top five Aes were anemia 25.5% (549), headache 14.1% (303), abdominal discomfort/pain 10% (215), hyperlipidemia 9.2% (199) and suicide ideation 6.4% (138). Top five ungraded AE were anemia 27% (549%), headache 14.3% (291), hyperlipidemia 9.8% (199), abdominal discomfort/pain 9.4% (191), and suicide ideation 6.8% (138) whereas the top five graded Aes were gynecomastia 27.7% (33), abdominal discomfort/pain 20.2% (24), nausea 19.3% (23), skin rash/hypersensitivity reaction 11.8% (14), and headache 10.1% (12).

Forty-eight Aes had DTG or EFV listed as a causative agent (DTG – 25% (12) and EFV 75% (36). Headache was the only listed DTG-associated AE, while EFV associated Aes were gynecomastia 91.7% (33), central nervous system 5.5% (2) and dizziness/spinning sensation/vertigo 2.8% (1). There were no severe Aes (SAE) associated with DTG whereas there were 13 SAEs due EFV, all of which were gynecomastia.

Six-month retention for 1,154 ALHIV with Aes and at least six months of follow-up time revealed 93% (1,074) retention in care. VS for adolescents with AE and VL in past 12 months was 81% (1,638). Ninety-nine percent (106/107) of ALHIV with ART related AE had a recent VL result and 98% (104) were VS. VL results were available for all (12/12) DTG-associated AE and 89% (32/36) EFV-associated AE. VS was 100 % (44/44) for those with VL result.

Conclusion: One in ten ALHIV 15-19 years on ART in Kenya had a reported AE. ALHIV on DTG-based regimen had higher rates of viral suppression and no SAEs reported compared to EFV-based regimen. Retention and VS remained good amongst ALHIV with documented AE. However, there is a need to improve the capacity of health care providers to grade and report on severity of AEs.

16

Bringing HIV and SRH services closer to Adolescents Girls and Young Women in Eswatini through a comprehensive mobile HIV and SRH package

***Wusumani S*[1]**, *Khumalo P[1], Siwela M[1], Maziya N[1], Dlamini F[1], Makwindi C[1], Miller N[2]*

[1]Elizabeth Glaser Pediatric Aids Foundation, Mbabane, Swaziland, [2]Pact, Mbabane, Swaziland

Issue: Adolescent girls and young women (AGYW) lag on every aspect of the 90-90-90 UNAIDS targets and are the hardest hit by the HIV epidemic. Vulnerability among AGYW is exacerbated by gender-based violence, lack of access to health services and education and policies that do not translate into action. In April 2018 Pact working with Elizabeth Glaser Pediatric AIDS Foundation (EGPAF) and Johns Hopkins Center for Communication Programs (CCP) started a project called Insika or Triple R (Ready, Resourceful and Risk Aware). The project aims to prevent new HIV infections and reduce vulnerability in AGYW in 24 rural and urban communities in Eswatini.

Description: The Insika project has five mobile clinical outreach vehicles to reach AGYW within their communities mainly at community centres, local shops, churches, and near schools. Before a mobile outreach visit is conducted, outreach home visitors and life mentors go through the community informing and inviting AGYW and other community members to attend the event. Each outreach unit has a team comprising of a nurse, HTS counsellor, expert client, and driver. The outreach services include: HIV testing and counselling, family planning services, screening and treatment for sexually transmitted infections, pregnancy testing and condoms, including education sessions on these topics, and antiretroviral treatment (ART). The mobile unit visits the same area at least once a month.

Lessons learned: From October 2018-March 2020, EGPAF carried out 1,191 mobile outreach events in 24 communities spread across all 4 regions of Eswatini. During outreaches 19,643 AGYW aged 10-24 years were reached of which 10,048 (51.2%) screened eligible for HIV testing. Of those eligible 19,936 (98.9%) were tested for HIV and 147 (1.5%) tested HIV positive. Eighty (54.4%) of the AYGW identified positive were initiated on ART. Of all AYGW reached 18,801 (95.7%) were screened for STIs; 59 (0.3%) screened positive for STIs and were referred for treatment. Family planning counselling and services were provided to 14,317 AYGW: 329 (2.3%) received implant; 850 (5.9%) injectables; and 814 (5.7%) oral contraceptives and 9,417 (68.0%) received condoms. Fifty-four of 275 AYGW receiving a pregnancy test had a positive pregnancy test.

Next steps: Bringing integrated, friendly and comprehensive services to AGYW outside the health facility during convenient hours is feasible and can increase demand and uptake of services. The Insika project should continue and additional services such as Pre-exposure Prophylaxis (PrEP) can be provided to ensure that AGYW can conveniently access essential HIV prevention and sexual reproductive services.

17

Archived HIV-1 Drug-Resistance Variants in Cellular Reservoirs and its Determinants among Vertically-Infected Adolescents failing Antiretroviral Therapy

***Fokam J*[1,2,6], *Mpouel Bala M*[1,2], *Santoro M*[3], *Takou D*[1,3], *Colizzi V*[1,4], *Perno C*[1,5], *Ndjolo A*[1,2]

[1]*CIRCB: Chantal Biya International Reference Centre for research on HIV/AIDS prevention And management, Yaounde, Cameroon,* [2]*Faculty of Medicine and Biomedical Sciences, University of Yaoundé I, Yaounde, Cameroon,* [3]*Faculty of Medicine and Surgery, University of Rome Tor Vergata, Rome, Italy ,* [4]*Evangelic University of Cameroon , Bandjoun, Cameroon,* [5]*Chair of Microbiology, University of Milan, Milan, Italy,* [6]*Faculty of Health Sciences , Buea, Cameroon*

Introduction: Adolescents with vertical HIV infection (AVHI) have the highest risk of mortality due to failure to antiretroviral treatment (ART), likely favoured by accumulation of drug resistance mutations (DRMs) in cellular reservoirs as children grow-up. Our study objectives were to evaluate HIV-1 genotypic profile between circulating-RNA compared to proviral-DNA of APHI failing ART, and determine factors associated with archived of DRMs in cellular reservoirs.

Methods: Within the scope of the EDCTP READY-Study, we conducted a study amongst AVHI (10-19 years) receiving ART in health facilities of Centre-Cameroon in 2019. WHO-clinical staging, CD4-count and plasma viral load (PVL) were performed. For those experiencing virological failure (VF), defined as PVL≥1000 copies/mL, HIV-1 polymerase gene was sequenced from both plasma (circulating-RNA) and buffy-coat (proviral-DNA) using a validated in-house genotyping assay at the Chantal BIYA International Reference Centre (CIRCB) in Yaoundé, Cameroon. Patterns of HIV-1 DRMs and molecular phylogeny were compared between circulating-RNA and proviral-DNA using Stanford HIVdb and MEGAv.10 respectively; with p-value<0.05 was considered significant.

Results: Out the 296 eligible AVHI enrolled, 30% (89) experienced VF, from whom 81 pairs of sequences were successfully generated from both circulating-RNA and proviral-DNA samples of each participant. HIV-1 subtyping concordance was 100% between circulating-RNA and proviral-DNA, CRF02_AG was the predominant viral clade (65%) and 2 potential novel viral recombinants were identified (F2/A1 and F1/G clades). DRMs were significantly detected in circulating-RNA compared to cellular proviral-DNA (93% vs. 85%, p=0.001); and only 34.2% (27/79) concordant DRMs profile was found between circulating-RNA and proviral-DNA. Importantly, 27.0% (21/79) had archived DRMs that were identified solely in proviral-DNA. Factors associated with archived DRMs in cellular reservoirs were the WHO clinical-stage 3/4 (OR: 7.1; p<0.001) and lower/moderate concentrations of PVL, between 3-5 log copies/mL, (OR: 4.9; p=0.01).

Conclusion: ART failure is concerning amongst AVHI (i.e. about one-third) in Cameroon, thus confirming their vulnerability. Events of VF are consistent with circulating DRMs (plasma). Though plasma sample remains the standard biomarker for detecting DRMs in clinical settings, approximately one quarter of those AVHI failing ART have resistant mutations archived in cellular reservoirs. Predictors of archived DRMs in reservoirs are poor clinical status and moderate PVL.

18

Deficits noted at 11 years in children with HIV starting early antiretroviral therapy in fine motor dexterity and auditory working memory

***Laughton B*[1]**, *Barnabas S[1], Kidd M[2], Zuidewind P[1], Naidoo S[3], Janse van Rensburg A[1], Glashoff R[3,4], Van Zyl G[4,5], Otwombe K[6], Violari A[6], Boivin M[7,8], Cotton M[1]*

[1]Family Centre for Research with Ubuntu, Stellenbosch University , Cape Town, South Africa, [2]Centre for Statistical Consultation, Stellenbosh University, Cape Town, South Africa, [3]Department of Pathology, Stellenbosch University, Cape Town, South Africa, [4]National Health Laboratory Services, Cape Town, South Africa, [5]Division of Virology, Stellenbosch University, Cape Town, South Africa, [6]Perinatal HIV Research Unit, University of the Witwatersrand, Johannesburg, South Africa, [7]Department of Neurology and Ophthalmology, Michigan State University, East Lansing, USA, [8]Department of Psychiatry, Michigan State University, East Lansing, USA

Background: A longitudinal neurodevelopmental substudy of participants at the Cape Town site of the Children with HIV Early AntiRetroviral Therapy (CHER) trial showed benefits of early antiretroviral therapy (ART). Post-trial, this cohort of children with perinatally acquired HIV (CPHIV) continued follow-up and neuropsychological assessments were conducted along with children who were perinatally HIV-exposed and uninfected (CHEU) and children who are HIV-unexposed (CHU).

Materials and methods: A cross-sectional descriptive study of the longitudinal cohort. CHER children had clinical visits since enrolment from a median of 7 weeks of age. After the CHER trial ended in 2011, viral loads and CD4 counts were done yearly. CHEU and CHU children from similar neighbourhoods were enrolled concurrently and had annual clinical visits, however due to attrition, additional children were recruited between 5-9 years of age. Below, we present outcomes of a comprehensive neuropsychological battery at 11 years conducted in participants' preferred language. CHER treatment arms were combined into one CPHIV group and ANOVAs were used to compare outcomes of the 3 groups (CPHIV, CHEU, CHU).

Results: Of 164 enrolled, 161 (84 CPHIV, 41 CHEU, 36 CHU), were assessed at median [Q1;Q3] of 11.1 [11;11.3] years (two CPHIV participants had relocated and one CHU was lost to follow-up). CPHIV children commenced ART at a median age[IQRQ1;Q3] of 9.1[7.4;12] weeks. Forty-five (53%) undergoing planned ART interruption at median [Q1;Q3] start age 51[48;103] weeks and duration 35[25;56] weeks. At 11 years 65 (77%) were still on their first ART regimen: AZT/3TC/LPV-r, 11% had AZT substituted with Abacavir and the rest on various regiments. Median [Q1;Q3] CD4% was 38[34;43] and CD4 absolute count was 915[709;1169]. HIV viral load was detectable in 18 (21%), with median copies/ml 156(range 22 – 1841). Seventeen had previous diagnosis of HIV encephalopathy of which 14 resolved. On neuropsychological battery there was no difference between groups on visual motor integration tests (Beery-VMI and Rey Complex Figure test) or verbal fluency (animal naming). There were significant differences for fine motor dexterity (Purdue pegboard: preferred hand CPHIV worse than CHU p =0.01, both hands CPHIV and CHEU scores worse than CHU p <0.01). The Kaufman Assessment Battery for children 2nd edition (KABC-II), found for Sequential Processing (working memory), CPHIV scored lower than CHEU and CHU (mean standard scores 79, 84, 84 respectively p= 0.02), also influencing the global Mental Processing Index with CPHIV scoring lower than CHU (p= 0.05). No difference were seen between groups on the KABC-II global nonverbal index (p = 0.73) nor other subtests.

Conclusion: Despite early ART and careful clinical management, persistent mild deficits were noted at 11 years for fine motor dexterity tests and auditory working memory (also noted at 7 and 9 years – see accompanying abstract), In contrast to global deficits described in other studies in CPHIV. These findings suggest that rehabilitation should be planned and implemented early. Further exploration is required to determine effects of other risk factors e.g. attention problems, previous HIV encephalopathy, HIV reservoir, immune markers and early brain development measured by neuroimaging.

19

A multi-country analysis of the impact of COVID-19 on HIV services for children and adolescents living with HIV

*Gleason M[1], Fernando N[1], Srivastava M[1], **Traub A[1]**, Vrazo A[1], **Amzel A[1]***

[1]USAID, Washington, United States

Background: The impact of the COVID-19 pandemic on HIV service delivery is not yet well understood. Our analysis reviews USAID PEPFAR program data to assess the impact of the COVID-19 pandemic on services for children living with HIV (CLHIV).

Materials & Methods: We analyzed pediatric HIV program data trends from 13 countries for children 0-14 years of age from FY20 Q1 (October 1, 2019 to December 31, 2019), FY20Q2 (January 1 to March 31, 2020), and FY20Q3 (April 1, 2020 to June 30, 2020), and described the relative change in testing volume and positivity, CLHIV new and currently on antiretroviral therapy (ART), and viral load coverage (VLC) and suppression (VS).

Results: The number of children HIV tested remained steady from Q1 to Q2 (309,053 vs. 297,667), and then dropped in Q3 (173,696), a 41.6% decrease (123,971). Q3 was when host-government restrictions were enacted to mitigate COVID-19.

During Q1 and Q2, similar numbers of CLHIV were newly identified (7,169 vs. 7,216) while Q3 (5,517) showed a 23.5% drop (1,699). Despite the decrease in numbers of CLHIV identified, testing positivity increased from Q1/Q2 to Q3 (2.3% /2.4% vs. 3.2%).

There was an increase in CLHIV newly initiated on ART from Q1 to Q2 (6,742 vs. 7,580) with a subsequent 24.8% decrease from Q2 to Q3 (5,700). Despite the decrease in newly initiated CLHIV on ART from Q2 to Q3, linkage rates remained high across the three quarters (94% vs. 105% vs. 103%).

The number of CLHIV on treatment increased across all three quarters from 179,327 (Q1) to 183,873 (Q2), to 186,132 (Q3), with less growth from Q2 to Q3 than from Q1 to Q2 (2,259 vs. 4,546). When including the number of newly initiated CLHIV on ART in the growth calculation--where the proportion of quarterly loss is defined as treatment growth minus new on treatment divided by current on treatment x 100-- there are similar but minimal losses of CLHIV noted in Q2 at -1.65% (Q2 loss = [4,545 - 7,580]/183,873 x 100) and Q3 at -1.85% (Q3 loss = [2,259-5,700]/186,132 x 100).

VLC dropped from Q1 to Q2 to Q3 (80.9% to 76.3% to 74.4%) while VS rates rose slightly across the three quarters (70.6% to 73.4% to 74.3%).

Conclusions: In 13 PEPFAR-supported countries, rates of HIV testing, treatment initiation, and viral load testing in CLHIV decreased during the COVID-19-pandemic; while HIV testing positivity increased, linkage and retention have been maintained and VS rates improved slightly. The reduction in testing with a concomitant increased positivity yield in Q3 may reflect reduced number of facility-based visits and admissions with more targeted HIV testing through indexing, however, additional data analyses are recommended to better understand these results. The decreasing trends across the pediatric clinical cascade should continue to be closely monitored during the COVID-19 pandemic and program adaptations to increase access to essential services for CLHIV should be rapidly implemented. Now more than ever, sustaining life-saving HIV services for children during COVID-19 must be a priority.

20

Challenges of remdesivir pediatric development for SARS-CoV-2 infection in a pandemic

***Pikora C*[1]**, *Bamford A[2], Luzuriaga K[3], Wiznia A[4], Rojo Conejo P[5], Giaquinto C[6], Muller B[7], Burchett S[8], Mackey J[1], Vu A[1], Timbs L[1], Kido A[1], Maxwell H[1], Brainard D[1], Osinusi A[1]*

[1]Gilead Sciences Inc., Foster City, United States, [2]Great Ormond Street Hospital for Children, London, United Kingdom, [3]University of Massachusetts Medical School, Worcester, United States, [4]Jacobi Medical Center and Lewis M. Fraad Department of Pediatrics, Bronx, United States, [5]Hospital Universitario 12 de Octubre, Spain, Madrid, Spain, [6]Pediatric Infections Diseases Unit at the Department of Woman's and Child's Health of the University of Padova, Padova, Italy, [7]Northwestern University Feinberg School of Medicine, Chicago, United States, [8]Boston's Children's Hospital, Boston, United States

Background: Surveillance data from the US, Europe, and China showed that, relative to adults, a small proportion of children have been diagnosed with COVID-19 and even fewer developed severe disease with fatal outcomes. However, understanding of the clinical course of SARS-CoV-2 infection in the pediatric population is evolving, and identification and study of effective antivirals against this disease are ongoing. Remdesivir (RDV) has demonstrated in vitro and in vivo activity against SARS-CoV-2 and favorable clinical efficacy and tolerability in patients with moderate or severe COVID-19 infection.

Materials & Methods: We assessed the challenges of designing a pediatric study of RDV for COVID-19 infection during the pandemic compared to pediatric development of treatments for other infectious disease indications.

Results: The pediatric development of drugs for many other infectious diseases relies upon adult experience with the drug in addition to well-characterized disease in the target population. The pediatric development of RDV for COVID-19 was a novel experience in that knowledge of the clinical presentations in children, including multisystem inflammatory syndrome in children (MIS-C), was evolving. Furthermore, adult safety and efficacy data were still pending at the time that a study and overall pediatric strategy were needed. The choice of doses to treat COVID-19 in children was based on prior physiologic pharmacokinetic (PK) modeling for treatment of Ebola virus, and the dosing duration was aligned with the adult dosing strategy. PK bridging of efficacy from adults to children needed to rely on obtaining useful PK data in children; however, intensive PK sampling in children with COVID-19 would not be practical, and a modified sparse sampling approach was instead considered. The formulation route and physicochemical characteristics would also need to be safe and practical for children in whom limited data exist on solubilizers such as cyclodextrin. Identification of the proper age range to study RDV needed to consider current pediatric disease epidemiology and likelihood of severe disease over the age spectrum. Limited experience with RDV in the pediatric population also necessitated frequent safety laboratory tests and virologic sampling. PK sampling, in addition to safety labs, would be challenging in regard to maximum blood volume limits, especially in very small children. Virologic sample collection methods also needed to be assessed based on the availability of validated assays at the time of study design. Lastly, pediatric development would need a single regulatory plan across the US and EU to be implemented at a very fast pace.

Conclusions: Despite these challenges, we were able to develop clinical, PK, operational, and regulatory strategies that has led to an FDA and EU-approved pediatric development plan for RDV. Ongoing accumulation of pediatric clinical data from published observations, key stakeholder input, data from adult studies, and input from regulators provided a basis for the ongoing CARAVAN study: Clinical Administration of RDV After Covid-19 Diagnosis in Children.

21

A multi-country analysis of the impact of COVID-19 on uptake of multi-month dispensing for children living with HIV on antiretroviral therapy

Fernando N[1], *Gleason M[1], Amzel A[1], Traub A[1], Vrazo A[1], Srivastava M[1]*

[1]US Agency For International Development , Washington, USA

Background: Key priorities during the COVID-19 pandemic include sustaining high quality HIV clinical care services, continuity of antiretroviral therapy (ART) for clients, and decongestion of health facilities to minimize transmission of COVID-19. Stable children living with HIV (CLHIV) on ART are eligible for multi-month dispensing (MMD), however, policy uptake is variable in terms of age ranges and eligibility criteria determining 'stable' clients. With the COVID-19 pandemic, a number of countries rapidly advanced policies to allow CLHIV to receive MMD.

Materials & Methods: USAID PEPFAR program data was reviewed to assess the uptake and proportion of CLHIV receiving MMD of ART during the COVID-19 pandemic. Quarterly trends of MMD data for CLHIV 0-14 years of age were analyzed from fiscal year (FY) 20 during Q1 (October 1, 2019 to December 31, 2019), Q2 (January 1, 2020 to March 31, 2020) and Q3 (April 1, 2020 to June 30, 2020) across 12 USAID PEPFAR-supported countries. MMD was defined categorically as dispensing ART at intervals of <3 months, 3-5 months, or >6 months. Relative changes in MMD coverage across the three dispensing timeframes, in relation to the change in treatment volume, across the three quarters are described.

Results: From Q1 to Q3, the average percentage of CLHIV receiving greater than a 3 month supply of ART nearly doubled, from 34.8% [range 10% to 77%] in Q1 to 41.4% [range 15% to 90%] in Q2, to 60.9% in Q3 [range 30% to 95%]. Rates of dispensing <3 months of ART across countries showed a concomitant fall from 65.2% in Q1 [range: 23% to 90%], to 58.6% in Q2 [range: 10% to 85%], to 39.3% in Q3 [range: 5% to 70%]. The percentage of CLHIV on ART receiving >6 months MMD also increased from Q1 to Q3, with 3% receiving >6 months MMD in Q1 compared to 3.5% in Q2 and 6.7% in Q3.

Conclusions: While inclusion of stable CLHIV on ART in MMD policies was previously not rapidly adopted, the proportion of CLHIV now accessing MMD, especially during Q3 when COVID-19 pandemic restrictions were in effect, is encouraging. Continuing efforts to ensure all stable CLHIV on ART are allowed access to at least 3 months MMD should remain a priority, especially as countries begin to lessen COVID-19-restrictions. MMD should be the standard of care for stable CLHIV which allows families to synchronize visits, decongests health facilities, and focuses resources on newly diagnosed and virally unsuppressed clients.

22

A multi-country analysis of the impact of COVID-19 on HIV services for pregnant and breastfeeding women and their infants

*Traub A[1], Srivastava M[1], Amzel A[1], Gleason M[1], Fernando N[1], **Vrazo A[1]***

[1]USAID, Washington, United States

Background: With the COVID-19 pandemic straining health care systems, ensuring pregnant and breastfeeding women and their infants have access to essential services has become a critical global priority. This analysis reviews USAID PEPFAR program data from Fiscal Year 2020 (FY20) to determine the impact of COVID-19 on HIV testing and treatment for pregnant women (PW) and their HIV-exposed infants (HEI).

Materials & Methods: We analyzed USAID PEPFAR data from 11 countries, comparing the relative changes from the FY20Q2 (January 1, 2020 to March 31, 2020) to FY20Q3 (April 1, 2020 to June 30, 2020) reporting periods. Variables reviewed include the number of PW tested for HIV (including testing coverage), identified as HIV-positive and new and current on antiretroviral therapy (ART), as well as the number of HEI tested by 12 months. In addition, we compared FY19Q2 and FY19Q3 (January 1, 2019 to June 30, 2019) to the same FY20 quarters' trends to better understand the impact of COVID-19 on HIV services.

Results: 754,847 PW were tested in FY20Q2, and 691,902 in FY20Q3 (8.3% reduction). A reduction in testing also occurred between FY19Q2 and FY19Q3, but to a lesser extent (846,110 vs 821,574; 2.9% reduction). Antenatal care testing coverage for PW remained similar in all quarters of FY19 and FY20, between 96.2% to 97.6%. Decreases in the number of PW testing from FY19Q2 and FY19Q3 (1,667,884) to FY20Q2 and FY20Q3 (1,446,749) reflect a reduction in the number of sites being supported by USAID implementing partners in FY20.

In FY20Q2, 39,560 HIV-positive PW were seen at their first prenatal appointment (ANC1), compared to 36,382 PW seen in FY20Q3 (3,178; 8.0% reduction). FY19Q2 and FY19Q3 (46,587 vs 43,780) showed a similar but lesser reduction of 6.0% (2,807). Positivity yields remained constant from FY19 to FY20, with all quarters between 5.2% to 5.5%.

Total PW on ART in FY20Q2 and Q3 was 39,390 and 36,273 (7.9% reduction) respectively. While FY19Q2 and FY19Q3 was a similar but lesser reduction of 6.7% (45,907 vs 42,851) ART coverage for PW was similar in FY19 and FY20 with all quarters between 97.9% and 99% in all countries except in Nigeria, where ART coverage substantially decreased from 99% to 72% from FY20Q2 to FY20Q3.

In FY19Q2 and FY19Q3, 40,320 and 42,637 HEI were tested by 12 months of age respectively (5.7% increase). In FY20Q2 and FY20Q3, 38,626 and 36,027 HEI were tested respectively (6.7% decrease).

Conclusions: In 11 PEPFAR-supported countries, there was a slightly larger percent reduction between Q2 and Q3 in FY20 when compared to the same quarters in FY19 in PW tested at ANC1, and confirmed as HIV-positive and on ART, with no significant change in ANC testing and ART coverage. A similar finding is noted in HEI tested by 12 months of age. Despite modest reductions across the PMTCT cascade, these results demonstrate that women have continued to seek these essential services during the COVID-19 pandemic. The trends in service uptake should continue to be closely monitored.

23

Use of a Walk-In HIV and STI Testing Model for At Risk Youth Ages 13 to 24 - Assessment of the Impact of the COVID-19 Pandemic on Testing Services

Sanders L[1], Lopez I[2], Tetlow A[1], McKinney M[1], Emmanuel P[1]

[1]University Of South Florida Department Of Pediatrics, Tampa, United States, [2]University Of South Florida Morsani College of Medicine, Tampa, United States

Background: The University of South Florida Department of Pediatrics' Ybor Youth Clinic (YYC) serves youth from the ages of 13 to 24. The clinic location was chosen to serve the large number of disenfranchised youth who frequent the neighborhoods surrounding it, and it was built to serve their needs. Services include HIV and STI testing and treatment, prevention services and counseling, sexual and reproductive health care, referrals to specialized care for physical and emotional trauma, and linkage to other youth programs in the community.

Crucial to the clinic's success is its youth-friendly atmosphere and the ability to offer free walk-in testing. Evidence supports the concept of providing healthcare for youth in an environment tailored to them, while the walk-in testing provides flexibility and convenience. This year's COVID-19 pandemic resulted in a switch from walk-in to appointment-based testing in March 2020 and provided a unique opportunity to compare both approaches to testing in our youth population.

Methods: The YYC maintains a database to track patient demographics, services provided, and other information. We analyzed data extracted from January 1, 2017 to July 31, 2020 to assess testing services provided, the rates of infections identified, and the effect of COVID-19 on these measures.

Results: From 2017 through 2018, youth testing increased 11% and an additional 28% from 2018 to 2019 likely due to increased awareness of YYC services and an expansion of walk-in testing hours to accommodate increased demand. In 2019, YYC case finding rates were 23% for bacterial STIs and 2.9% for syphilis. We identified 9/52 (17%) of new HIV infections in Hillsborough County youth aged 13-24 through our walk-in testing.

At the end of March and in April 2020, we modified services in response to COVID-19. Walk-in testing was discontinued and other services cut back. We instituted screening measures for patients coming to clinic, followed university recommendations for cleaning and PPE, minimized patient time in clinic, and switched appointments to telehealth when possible. By mid-April modifications were in place that allowed the accommodation of all youth calling to schedule testing. Overall, average monthly clinic visits declined by 42% (215 to 125) from May to July compared to the first 2 months of 2020. The average number of youth getting gonorrhea and chlamydia testing monthly declined by 35% (151/month vs 98). Absolute numbers of HIV testing declined by only 3% (96/month vs 93). Syphilis testing via RPR increased by 29% (50/month vs 66) attributable to the ease of performing the test when blood was also being drawn for HIV testing. Case finding rates for all infections were similar to 2019 levels.

Conclusions: The free walk-in testing model used at the YYC is a very effective way to engage youth who might otherwise avoid the healthcare system and results in high rates of detection of both STIs and HIV. The COVID-19 pandemic has had a significant impact on clinic testing for bacterial STIs, but HIV and syphilis testing were not impacted, likely due to higher consent rates for these tests during appointments. The contribution of social distancing and decreased perceived risk to these changes is not clear. Monitoring utilization of services and measuring behavior change during this pandemic will help providers adapt to the changing needs of youth and further progress towards EHE.

24

Extent of in utero transfer of tenofovir from mother to fetus: a paired analysis of hair specimens collected at birth from a cohort in the United States

Pintye J[1], *Huo Y*[2], *Kacanek D*[2], *Zhang K*[3], *Kuncze K*[3], *Okochi H*[3], *Gandhi M*[3]

[1]*University of Washington, Seattle, United States,* [2]*Harvard TH Chan School of Public Health, Boston, United States,* [3]*University of California San Francisco, San Francisco, United States*

Background: As efforts intensify to eliminate vertical HIV transmission, and pre-exposure prophylaxis use burgeons among women of reproductive age, the likelihood of women receiving tenofovir (TFV)-based regimens during pregnancy increases. Understanding pharmacokinetics of in-utero TFV transfer is critical for interpreting safety. To evaluate in-utero TFV transfer, we measured TFV hair levels at delivery among women living with HIV (WLHIV) receiving tenofovir-disoproxil-fumarate (TDF)-based antiretroviral therapy (ART) and their infants in the United States.

Methods: Hair samples were collected at or shortly after childbirth from WLHIV and infants enrolled in the Surveillance Monitoring for ART Toxicities Study of PHACS between 06/2014-07/2016. TFV hair levels from mother-infant pairs were analyzed using validated liquid chromatography/tandem mass spectrometry methods. The lower limit of quantification (LLQ) was 0.00200 ng/mg and the upper limit of quantification (ULQ) was 0.400 ng TFV/mg. Weight-normalized TFV hair concentrations were log-transformed. We calculated individual ratios of infant-to-maternal hair TFV concentrations to determine degree of transfer and Spearman correlation coefficients. To explore covariates associated with transfer, we used univariable linear regression to estimate the percent change in unadjusted mean log10-transformed ratios associated with having the characteristic versus not.

Results: We measured TFV hair levels among 116 mother-infant pairs with TDF-based ART exposure during pregnancy; within this group, 103 (89%) mothers had TFV levels >LLQ and were included in the analysis with their infants. Median maternal age was 32 years (IQR 26-36); 70% self-identified as non-Hispanic Black, and median gestational age at birth was 38 weeks (IQR 38-39). Median time from birth to hair collection was 3 days (IQR 1-14). Eighty-two (80%) infants had TFV hair levels >ULQ; only 1 maternal hair level was >ULQ. Median concentration of TFV was 0.02 ng/mg (IQR 0.01-0.04) in maternal hair and 0.40 ng/mg (IQR 0.40-0.40) in infant hair. The mean log10 ratio of infant-to-maternal TFV levels was 1.08 (95% CI 0.97-1.20) and the correlation coefficient between maternal and infant TFV levels was 0.221 (p=0.02). TFV transfer was 60% lower from mothers who had preterm deliveries compared to term (mean log10 ratio 0.72 vs. 1.12, p=0.04) and 42% lower from mothers who had C-section deliveries compared to vaginal (mean log10 ratio 0.98 vs. 1.21, p=0.04). TFV transfer was also lower from mothers who used TFV during the 1st trimester when compared to TDF use in other trimesters (mean log10 ratio -0.28 vs. 1.11, p<0.001). There was a trend towards 36% lower TFV transfer among mother receiving integrase strand transfer inhibitors (INSTIs) compared to those who did not (mean log10 ratio 0.96 vs. 1.15, p=0.10); we did not observe associations (p<0.10) between TFV transfer and other characteristics in this limited sample.

Conclusions: To our knowledge, this is the first evaluation of mother-to-infant tenofovir transfer using hair concentrations. Prior studies assessed in-utero TFV exposure via short-term metrics and similarly found high rates of TFV transfer, with our study confirming that such transfer is cumulative. In exploratory models, transfer was lower among mothers who had preterm delivery, those with only 1st trimester TDF use, and those with C-section deliveries. Our data contribute to ongoing discussions regarding which ART regimens can minimize infant toxicities while maximizing protection.

25

Children who are HIV-Exposed and Uninfected Exhibit Immune Suppressive Plasma Biomarker Profiles

***Khaitan A*[1]**, *Li W*[1], *Roose A*[1], *Oyungu E*[2], *Jang J*[1], *McHenry M*[1], *Yu Q*[1]

[1]*Indiana University School Of Medicine, Indianapolis, United States,* [2]*Moi University School of Medicine, Eldoret, Kenya*

Background: Children born to mothers with HIV have worse health and survival outcomes compared to HIV-unexposed (HU) children, but the biological mechanisms that might be contributing to these deficits have been grossly unexplored. In children with perinatal HIV, chronic immune activation lies at the heart of HIV-associated comorbidities, including delayed growth and neurocognitive development and early onset cardiovascular and metabolic disease. Despite a negative HIV status, there are reports that children who are HIV-exposed, uninfected (HEU) also exhibit greater immune activation than their HU counterparts in early infancy, but whether this persists beyond infancy is unknown. Here we examined pro- and anti-inflammatory plasma biomarkers and soluble immune checkpoints (ICP) in children who are HEU and HU between ages 18-36 months.

Materials and Methods: We performed a comprehensive analysis of 81 plasma biomarkers in a cohort of Kenyan children, comprised of 44 who are HEU and 38 who are HU between ages 18-36 months old. Plasma levels of biomarkers including 65 pro- and anti-inflammatory cytokines/chemokines/growth factors and 16 soluble inhibitory and co-stimulatory ICPs were determined using the 65-Plex Human ProcartaPlex kit (EPX650-10065-901, Invitrogen) and the Human Immuno-Oncology Checkpoint Protein Panel (MilliporeSigma), respectively. Biomarker levels from children who are HEU and HU were compared using the Mann-Whitney U test. We used Bayesian model averaging (BMA) to jointly consider multiple plasma biomarkers in a logistic regression model and identify a parsimonious subset of those most useful for predicting HEU vs. HU status in children, with a posterior effect probability (PEP) ≥0.5 considered to be evidence of a significant association.

Results: Of the 16 ICPs, HEU had significantly higher plasma levels of soluble T-cell immunoglobulin and mucin-domain containing-3 (TIM-3; p=0.002) and CD40 (p=0.02) compared to HU. In the 65-plex panel, we identified a subset of proinflammatory cytokines/chemokines/growth factors that were lower in HEU compared to HU: IL-12 (p=<0.001), leukemia inhibitory factor (LIF; p=0.01), macrophage migration inhibitory factor (MIF; p=0.01), TNF-related weak inducer of apoptosis (TWEAK; p=0.004) and A proliferation inducing ligand (APRIL; p=0.03); granulocyte colony-stimulating factor (G-CSF; p=0.01), fibroblast growth factor-2 (FGF-2; p=0.02), CXCL13 (p=0.03), CCL24 (p=0.02), CXCL11 (p=0.04), CXCL9 (p=0.04), and CCL20 (p=0.03). Based on BMA, IL-12 (PEP=0.968), CD40 (PEP=0.746), and IL-13 (PEP=0.619) were the most robust predictors of HEU vs. HU status in children.

Conclusions: Children who are HEU do not exhibit more immune activation by plasma biomarkers than their HU peers between 18-36 months. Interestingly children who are HEU had higher levels of soluble TIM-3, a key inhibitory ICP that has been associated with HIV disease progression in persons living with HIV. Similarly, soluble CD40 that exerts immunosuppressive effects by negatively regulating CD40-CD40L interactions was elevated in children with HEU. Contrary to our expectation, children who are HEU also had lower levels of some proinflammatory cytokines, chemokines and growth factors. Thus, our comprehensive plasma biomarker panels revealed an immune suppressive rather than inflammatory profile in children who are HEU. Further investigation is needed to understand whether these perturbations result in weakened functional immune responses to vaccines or infections in children who are HEU.

26

Time to first positive HIV-1 DNA PCR in infants infected with subtype B HIV-1 is delayed in the presence of maternal antiretroviral use

Balasubramanian R[1], *Zhao Y[1], Dominguez K[2], Nesheim S[2], Fowler M[3], Shapiro D[4]*

[1]University Of Massachusetts Amherst, Amherst, United States, [2]Centers for Disease Control and Prevention, National Center for HIV, Viral Hepatitis, STD, and TB Prevention, Atlanta, USA, [3] Department of Pathology, Johns Hopkins University School of Medicine, Baltimore, USA, [4]Center of Biostatistics in AIDS Research, Harvard T. H. Chan School of Public Health, Boston, USA

Background: Early diagnosis of HIV infection in infants is associated with reduced morbidity and mortality. However, accurate diagnosis of HIV infection in infants is challenging as serological tests are only reliable when given after 15-18 months of age. HIV-1 DNA or RNA amplification assays are recommended in infants under 15 months of age. Knowledge of the performance of these assays is essential to inform HIV diagnosis guidelines. To this aim, we evaluated the association of maternal/infant antiretroviral use with time to first positive HIV-1 DNA polymerase chain reaction (PCR) test, in non-breastfed infants infected with HIV-1 subtype B virus.

Materials and Methods: We combined data on non-breastfed HIV-infected infants born to HIV-positive mothers from two prospective U.S. cohorts: the Women and Infants Transmission Study (WITS) (n=129) and the Perinatal AIDS Collaborative Transmission Study (PACTS) (n=299). HIV-positive infants with non-missing information on maternal/infant prophylaxis and at-least one HIV-1 DNA PCR test were included. Time to first positive DNA PCR was estimated by infant or maternal prophylactic regimen from Weibull proportional hazards models for interval censored outcomes, with adjustment for covariates including maternal CD4+ cell count and viral load closest to the time of delivery, mode of delivery, gestational age, and infant birth weight. Due to the high concordance between maternal and infant ARV regimen, the effect of each exposure was estimated in separate models.

Results: Maternal antiretroviral (ARV) regimens during the trimester delivery and labor occurred included: no ARV (n=198), single nucleoside analog reverse transcriptase inhibitor (NRTI) (n=89), single-dose nevirapine (sdNVP) with zidovudine (ZDV) (n=10), sdNVP only (n=6), 2-3 NRTIs without sdNVP (n=11), 2-3 NRTIs with sdNVP (n=8), combination ARV therapy with Non-Nucleoside Reverse Transcriptase Inhibitors and/or Protease Inhibitors (cART) (n=106). Infant prophylactic ARV regimens included: no ARV (n=355), ZDV (n=70), other (n=3).

Time to first positive DNA PCR was significantly associated with maternal ARV regimen ($p < 0.001$), with a delayed time to test positivity in the cART group relative to the Single NRTI group (hazard ratio = 0.16, 95% CI: 0.08-0.34); this association remained after adjustment for potential confounders ($p<0.001$, hazard ratio=0.22, 95% CI: 0.07-0.47). At 30 days after birth, the probability of a positive HIV-1 DNA PCR test remained significantly lower in the cART group (0.14, 95% CI: 0.08-0.23) relative to the Single NRTI group (0.60, 95% CI: 0.46-0.76). Infant ARV regimen was not significantly associated with time to first positive DNA PCR ($p=0.99$) in a univariate Weibull model.

Conclusions: Time to first positive HIV-1 DNA-PCR in infants infected with HIV-1 subtype B differs according to maternal/infant antiretroviral regimen and is longer with exposure to maternal cART, which may have implications for scheduling infant HIV PCR diagnostic testing and confirming final infant HIV status.

27

Higher hospitalization rates in children born HIV-exposed uninfected in British Columbia, Canada, between 1990 and 2012

Li S[1], Albert A[2], Piske M[3,4], Janssen P[5], Alimenti A[2,6], Jesson J[2], Côté H[2,3], Sauvé L[2,6]

[1]University Of British Columbia, Vancouver, Canada, [2]Women's Health Research Institute, BC Women's Hospital and Health Centre, Vancouver, Canada, [3]Department of Pathology and Laboratory Medicine, University of British Columbia, Vancouver, Canada, [4]BC Centre for Excellence in HIV/AIDS, Vancouver, Canada, [5]School of Population and Public Health, University of British Columbia, Vancouver, Canada, [6]Department of Pediatrics, University of British Columbia, Vancouver, Canada

Background: Globally, approximately 1.5 million children are born to women living with HIV each year and are predominantly HIV-exposed but uninfected (CHEU). Compared to children who are HIV-unexposed uninfected (CHUU), CHEU face higher risk of clinical complications, including infections, but it remains unclear whether this is attributable to in-utero HIV exposure, maternal antiretroviral therapy (ART), or other factors. This study investigated hospitalizations among CHEU by antenatal ART exposure timing.

Methods: This retrospective controlled cohort study used data from health administrative databases. Maternal and child data were collected on CHEU and CHUU born in the province of British Columbia, Canada, between 1990-2012. CHEU and CHUU were matched 1:3 for age, sex, and maternal forward sortation area (first three digits of postal code). We determined the adjusted odds ratios (aOR) between in-utero HIV exposure, antenatal ART exposure, and child hospitalization outcomes via conditional logistic regression, adjusting for preterm birth and maternal risk factors.

Results: From 1990-2012, a total of 446 CHEU and 1333 CHUU were included. Compared to CHUU, a higher proportion of CHEU were born preterm (19.1% versus 7.1%). CHEU also showed a greater prevalence of any hospitalization (47.3% versus 29.8%), hospitalization within the first month of life (42.9% versus 29.0%), within the first year of life (40.8% versus 28.1%), and intensive care unit (ICU) admission ever (28.5% versus 9.2%). After adjusting for preterm birth, CHEU experienced higher odds of hospitalizations (aOR 2.30, 95% CI 1.81-2.91), hospitalizations within the first year of life (aOR 2.05, 95% CI 1.62-2.60), and ICU admissions (aOR 3.38, 95% CI 2.38-4.79), compared to CHUU. The most prevalent diagnosis of ICU admissions among CHEU was neonatal withdrawal symptoms from maternal use of drugs of addiction, while that among CHUU was dental caries followed by asthma. While CHEU whose mothers had initiated ART pre-conception tended towards higher odds of any hospitalization (aOR 1.66, 95% CI 0.98-2.81) compared to CHEU born to mothers who initiated ART during pregnancy, pre-conception ART tended towards a protective effect for ICU admissions (aOR 0.51, 95% CI 0.25-1.08). Differences in the proportion of infection-related hospitalizations (9.0% versus 7.5%) was not significant. Infection-related hospitalizations were primarily respiratory tract infections among both CHEU and CHUU. Within a subset of children born between 2000 and 2012, for whom detailed maternal substance use data were available, these findings remained. Maternal smoking and substance use identified as a risk in pregnancy were also associated with increased odds of hospitalization among CHEU.

Conclusion: In British Columbia, CHEU experienced increased odds of hospitalization relative to control CHUU. A substantial number of them occurred within the first month of life among CHEU and were ICU admissions, particularly neonatal abstinence syndrome. Antenatal exposure to ART for the entire gestational period tended towards lower severity of hospitalizations, requiring fewer ICU admissions, compared to antenatal exposure to ART initiated during pregnancy. Infection-related hospitalizations were infrequent and not significantly different between CHEU and CHUU. These findings may inform care of mothers of CHEU and strategies to reduce hospitalizations among CHEU.

28

Longitudinal evolution of maternal viral loads during pregnancy and postpartum among women living with HIV in South Africa.

Moyo F[1,2,3], Haeri Mazanderani A[1], Kufa T[1,2], Sherman G[1]

[1]Centre for HIV & STIs. National Institute for Communicable Diseases, Sandringham, Johannesburg, South Africa, [2]School of Public Health. University of the Witwatersrand, Parktown, Johannesburg, South Africa, [3]Paediatric HIV Diagnostics Division, Wits Health Consortium, Parktown, Johannesburg, South Africa

Background: Maternal viraemia is associated with HIV transmission to infants. Using a national laboratory dataset, we describe maternal viral load (HIV VL) evolution during pregnancy, around delivery and up to 15-months postpartum among women living with HIV (WLHIV) within the public health sector in South Africa.

Methods: HIV VLs and pregnancy-related tests performed January 2016-December 2017 from the National Health Laboratory Service's Corporate Data Warehouse were used to create a synthetic cohort of pregnant WLHIV aged 15-49 years. Syphilis screening was assumed to occur at first antenatal care visit (fANC). A syphilis-screening test without prior or concurrent HIV VL test identified newly diagnosed, pregnant WLHIV initiating antiretroviral therapy (ART). Cohort entry was at fANC and follow-up was until 15-months from estimated date of delivery. HIV VL changes during follow-up were described using fractional polynomial models. Proportions of viraemic women at different time-points were calculated. Piecewise linear regression models determined factors associated with HIV VL decline during follow-up.

Results: Amongst 178 319 pregnant WLHIV in the cohort, median age was 29.2 years, interquartile range (IQR) (24.8-33.9) and median baseline CD4 count was 407 (258-579) cells/mm3. At fANC, 85 545 (48.0%) conceived on-ART, 88 877 (49.8%) were newly diagnosed with HIV and ART status was unknown for 3 897 (2.2%). The cohort contributed 345 174 HIV VL measurements: median=2 (IQR 2-3) HIV VLs per woman during follow-up. Overall, baseline pregnancy HIV VLs were a median log10 VL 1.9 copies/mL (IQR) (0-3.5), 1.3 (0-2.2) around delivery and < undetectable (0-2.0) postpartum. Mean predicted HIV VLs started at 2.0 log10 VL copies/mL at baseline decreasing to 1.4 and 1.3 at delivery and postpartum respectively. At delivery, 36.9% and 14.3% of pregnant WLHIV were viraemic at VL ≥50 and ≥1000 copies/mL respectively for the entire cohort. Median log10 VLs were 1.3 (0.0-2.7) among 40 660 (47.5%) women who conceived on-ART with a baseline HIV VL vs. 2.8 (0.0-4.2) among 32 325 (36.4%) women newly diagnosed with HIV during pregnancy with an HIV VL after three months of ART. Proportions of viraemia (VL ≥50) were 39.3% vs. 34.9% at delivery and 37.0% vs. 33.2% postpartum for women newly diagnosed with HIV during pregnancy and women conceiving on ART respectively. Among 38 659 (25.1%) women with a baseline pregnancy VL ≥1 000 copies/mL, 13 592 (35.2%) had a VL ≥1 000 and 12 703 (32.9%) had a VL <1 000 copies/mL after median time of 3.7 (2.6-6.0) months. Being older (≥25 years), having CD4 ≥200 and VL <50 copies/mL at baseline was associated with sustained HIV VL decline.

Conclusion: Despite decline in maternal HIV VLs during pregnancy, only 63% reached VL <50 copies/mL by the time of delivery. Women with VL ≥50 copies/mL in pregnancy and postpartum periods require prioritization for interventions to ensure VL suppression.

29

Maternal PrEP use in HIV-uninfected pregnant women in South Africa: Role of Stigma in PrEP initiation and persistence

***Moran A*[1]**, *Myer L*[2], *Coates T*[3], *Mashele N*[2], *Gorbach P*[1], *Bekker L*[4], *Joseph Davey D*[1,2]

[1]*Department of Epidemiology, Fielding School of Public Health, University Of California, Los Angeles, Los Angeles, United States,* [2]*Division of Biostatistics and Epidemiology, School of Public Health and Family Medicine, University of Cape Town, Cape Town, South Africa,* [3]*David Geffen School of Medicine, University of California, Los Angeles, Los Angeles, United States,* [4]*The Desmond Tutu HIV Centre, University of Cape Town, Cape Town, South Africa*

Pre-exposure prophylaxis (PrEP) is an important HIV prevention method for people at high risk for HIV transmission. PrEP can be an important HIV prevention tool for pregnant and postpartum women because it is user-controlled chemoprophylaxis which is safe to take during pregnancy and breastfeeding. There is limited research on maternal PrEP use in South Africa. We assessed PrEP initiation and persistence in pregnant and postpartum women in Cape Town, South Africa.

The PrEP in pregnancy and postpartum study (PrEP-PP) is an observational cohort study which enrolls pregnant women at their first antenatal care (ANC) visit and follows participants through 12-months post-partum in a community clinic in a high HIV prevalence community (20% HIV prevalence in pregnancy). Aside from standard ANC visits, trained study staff ask about socio-demographics, sexual behaviors, PrEP and HIV stigma (previously validated) and are screened for HIV, sexually transmitted infections (STIs) and intimate partner violence. Participants are offered PrEP at baseline following HIV risk reduction counseling. We measured PrEP initiation at baseline, retention at 3-month follow up and persistence at 3-month follow up (having taken 25+ of last 30 PrEP doses in past month, verified by pill count) using multivariable logistic regression controlling for gestational age, gravidity, education level and partner HIV testing. PrEP-related stigma is measured through two scales of three questions each: internalized (α=0.852) and anticipated (α=0.784) PrEP-related stigma (e.g. negative internal feelings or anticipated judgement for taking PrEP).

We enrolled 425 HIV-uninfected pregnant women at their first antenatal visit, median age was 25 years (IQR 22-30) and gestational age at baseline was 20 weeks (IQR: 13-29). Overall, 92% of women (n=390) initiated PrEP at baseline, 8% (n=36) of participants reported high internalized PrEP stigma and 25% (n=107) reported high anticipated PrEP stigma at baseline. Compared to participants with low internalized PrEP stigma, participants with high internalized stigma had higher odds of not accepting PrEP at baseline (aOR=21.1, 95%CI: 9.3 – 49.7). Compared to participants with low anticipated PrEP stigma, participants with high anticipated stigma were at higher odds of not initiating PrEP at baseline (aOR=2.4, 95%CI: 1.1 – 4.8). Among participants who initiated PrEP at baseline, those with high anticipated stigma had lower odds of retention compared to those with low anticipated stigma (aOR= 0.47, 95%CI: 0.3 – 0.8) and participants whose partners had not been tested for HIV or whose testing status was unknown had higher odds of retention compared to those whose partners had been tested (aOR=1.85, 95%CI:1.1-3.1). Participants with high internalized stigma had lower odds of retention compared to those with low internalized stigma (aOR= 0.38, 95%CI: 0.1 – 1.1). Adherence did not differ by PrEP-related stigma at baseline.

PrEP-related stigma is an important barrier for both PrEP uptake and PrEP retention among pregnant and postpartum women at risk of HIV acquisition. Efforts to distribute PrEP among pregnant women must consider anticipated PrEP stigma as a barrier to optimal maternal PrEP use. Interventions which focus on normalizing PrEP use in pregnancy are urgently needed for HIV prevention scale up and impact.

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30

Trends in pediatric antiretroviral treatment in U.S. President's Emergency Plan for AIDS Relief-supported countries in sub-Saharan Africa —2016–2019

***Rabold E*[1]**, *Bain R*[1], *Bhatkoti R*[1], *Carpenter D*[1], *Modi S*[1], *Rivadeneira E*[1], *Battey K*[1], *Patel M*[1]

[1]*CDC, Atlanta, United States*

Background: The United Nations Programme on HIV/AIDS (UNAIDS) reports only 54% of children living with HIV (CLHIV) are on antiretroviral treatment (ART) compared with 62% of adults with HIV, despite global initiatives focused on closing this gap. Robust modeling approaches can improve assessment of temporal trends in CLHIV on ART relative to adults.

Methods: We used quarterly data from the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) from October 1, 2016 to September 31, 2019 to fit three generalized linear models (GLMs) for time series data for each of 17 countries in Africa receiving PEPFAR support. We assumed the counts data was Poisson distributed and used a log-link, fitting the three models to the pediatric (<15 years) and adult (≥15 years) populations of each country. We included all countries where PEPFAR supports direct HIV service delivery with >95% data disaggregated by age. Model 1 estimated the annual percent change in number of facilities providing ART. Model 2 estimated the annual percent change in CLHIV and adults with HIV on ART, with the 3rd model adjusting for the number of facilities. Statistically significant differences between a country's pediatric and adult populations were conservatively determined by non-overlapping 95% confidence intervals. R version 3.6.1 and the tscount package version 1.4.1 were used in this analysis.

Results: All results reflect annual percent changes. All countries increased the number of facilities providing services to children (range 1.0-21.2%, median 8.6%), with the annual growth in number of facilities outpacing that of adults in three countries (Zambia: 17% vs. 12%; Cameroon: 12% vs. -1%; Namibia: 21% vs. 18%) and the increase comparable to the respective adult increase in all other countries. Adjusting for number of facilities resulted in different estimates of annual percent change of CLHIV on treatment for countries across Model 2 and Model 3. After adjustment, nine (DRC, Eswatini, Mozambique, Nigeria, South Sudan, Tanzania, Uganda, Zambia, and Zimbabwe) of 17 countries demonstrated positive annual growth in the number of CLHIV on treatment, with four (DRC: 48.5%; Mozambique: 21.2%; South Sudan: 20.2%; Zambia: 40.5%) exceeding 10% annual growth. In contrast, all counties increased the number of adults living with HIV on ART, with 11 exceeding 10% annual growth. Of the eight countries with no annual percent increase in CLHIV on treatment, four (Cōte d'Ivoire: -1.2%; Cameroon: -5%; Namibia: -3%; South Africa: -9%) increased facilities by more than 10% per year. DRC, Mozambique, and Zimbabwe demonstrated annual growth in children on treatment that exceeded that for adults (49% vs. 36%; 21% vs. 15%; and 4% and 0%, respectively). Except for Zambia and South Sudan, where annual growth was similar with overlapping confidence intervals, annual growth in adults on ART outpaced annual growth in CLHIV for the remaining 12 countries.

Conclusions: Despite all countries increasing the number of facilities providing treatment for CLHIV, only half increased the number of CLHIV on treatment. Decentralization of pediatric treatment services may be insufficient to capture children not yet on treatment, with factors other than proximity of facilities impacting treatment initiation and retention. Our results emphasize the need for more focused, data-driven efforts to expand HIV treatment for CLHIV.

31

Model Informed Prediction of Dolutegravir Pharmacokinetics in the Neonates

***Chandasana H*[1]**, *Goyal N*[1], *Baker M*[2], *Singh R*[1]

[1]*Glaxosmithkline, , United States,* [2]*ViiV Healthcare, , United States*

Background: Antiretrovirals are essential in neonates for both prevention of HIV infection in infants born to HIV infected mothers and for the treatment of those neonates who become infected with HIV. Dolutegravir is an integrase inhibitor approved for the use in HIV-infected adult and children ≥4 weeks and ≥3 kg in US and it has potential for the treatment of HIV infection and prophylaxis in the neonates. Safety, tolerability and pharmacokinetics (PK) have been studied in pediatric subjects (IMPAACT P1093 (NCT01302847) and PENTA ODYSSEY (NCT02259127)). Selection of optimal dose(s) and prediction of PK in neonates in clinical trials is very challenging. The objective of this work was to characterize PK and select starting doses in the neonates using modeling and simulation.

Methods: Population PK model developed using available exposure data from pediatric subjects >4 weeks of age was used to predict PK in neonates. Allometric scaling along with enzyme maturation characteristics (UGT1A1 and CYP3A4) were included in the model to predict dolutegravir clearance in this population. The absorption from the marketed dispersible tablet and from newly developed liquid formulation was assumed to be similar. Clinical trial simulations were performed using NONMEM® version 7.3 (ICON, Ellicott City, MD).to evaluate PK with different dosing scenarios. Virtual neonates with age between 0 and 30 days with weight range 2-4 kg simulated based on World Health Organization and Centers for Disease Control and Prevention infant weight for age information.

Results: A combination of different dolutegravir single and multiple dose strategies including daily vs every other day dosing were simulated in the neonates with the aim to achieve Ctrough population exposure (GM) > 697 ng/mL for the first month of life. Exposure metrics (AUC, Ctrough and Cmax) were calculated for each potential regimen and corresponding weight. In addition to this, adequate sensitivity analysis was performed to assess impact of model assumptions dose regimen recommendations in neonates.

Conclusions: Conducting clinical trials in the neonatal population during drug development remains a major challenge. Accurate prediction of drug disposition in neonates and young infants is an extremely difficult task due rapidly changing enzyme ontogeny. This model-based simulation can be effectively employed to guide selection of starting doses for the neonate clinical trials to expedite the dose optimization process.

32

Absence of selection for integrase inhibitor resistance via the Q148H pathway in HIV-1 subtype F integrases: Evaluation of treatment outcomes, replicative capacity, and drug resistance

Rozenszajn, M.[1], *zoha Momin, Z.*[3], *Sanchez, D.*[1], *Arazi Caillaud, S.*[2], *Bologna, R.*[2], *Mangano, A.*[1], *Kimata, J. T.*[3], *Aulicino, P.C.*[1]

[1] *Laboratorio de Biología Celular y Retrovirus-UVEM. Hospital de Pediatría "J.P. Garrahan"- CONICET;* [2] *Servicio de Epidemiología e Infectología, Hospital de Pediatría "J.P. Garrahan";* [3] *Department of Molecular Virology and Microbiology, Baylor College of Medicine, Houston, Texas, USA- * Authors equally contributed to the work*

Background: Raltegravir (RAL) is currently the preferred first-line regimen for HIV-1-infected neonates, and an alternative first-line regimen for children for whom approved dolutegravir dosing is not yet available (under 6 y.o). In previous studies, we found that HIV-1 drug resistance (HIVDR) to RAL through the pan-resistance Q148H pathway is impeded in individuals from Argentina carrying BF recombinants with subtype F IN genomes. Our aim was to evaluate the impact of IN subtype on treatment outcomes to a RAL-based ART in a clinical setting from Argentina, and to investigate the mechanisms associated with HIVDR to Integrase Inhibitors (INIs).

Materials and Methods: Treatment outcomes and IN subtype were retrospectively evaluated in 41 HIV-1 infected children and adolescents receiving a RAL-based ART rescue regimen at Garrahan Hospital. A 900bp HIV-1 IN fragment was sequenced from PBMC or plasma samples. Subtype was assigned by phylogeny using MEGA5.1. HIVDR was investigated in cases with virologic failure (VF), defined as ≥2 detectable VL measurements after achieving virologic suppression (VS). Kaplan-Meier curves were used to evaluate the probability of VS and VF during follow-up. Formal comparisons between groups were made using chi-square, log rank test, or Mann Whitney U tests. In vitro phenotypic characterization of resistant viruses was performed by introducing N155H and Q148H INI-DRMs into NL4-3 infectious molecular clones with subtype B or F integrase: NL4-3 (B), ARMA159 (CRF12_BF) and URTR23 (BF recombinant with 163K polymorphism). Infectious virus stocks were generated by transfection of 293T cells and evaluating replication in CEMx174 cells. IC_{50} to RAL or Dolutegravir (DTG) of each IMC was determined by TZM-bl assay.

Results: Patients were grouped according to HIV-1 subtype in IN: 24/41 (58.5%) subtype F, 17/41 (41.5%) subtype B. Median age at initiation of the RAL-based ART was 13,2 years, median number of previous ART regimens 2; and median VL at RAL initiation 4,26 log_{10} copies/mL. Baseline characteristics did not differ significantly between the groups. 75% of patients achieved VS, at a mean time of 120 days (B) vs 152,5 days (F), (p=0,9980). VF occurred in 52% of B and 58% of F, at a mean time of 254 days (B) vs 466 days (F), (p=0,2023). Upon VF, e*mergence of INI-DRMs was associated to Q148H+G140S or N155H pathways in subtype B and to N155H or T97A pathways in subtype F.* Introduction of N155H increased the IC_{50} of NL4.3 and URTR23 to RAL (19-fold) but had no effect on susceptibility to DTG. However, introduction of Q148H (+/-G140S) reduced susceptibility to RAL and DTG in NL4.3 while abolishing URTR23's and ARMA159's ability to replicate. This effect of H148 was also observed in context of the ARMA159 integrase.

Conclusions: Resistance to RAL in subtype F IN genes through the Q148H pathway is impeded both *in vivo* and *in vitro* due to a severe loss of IN function. This may limit cross-resistance to dolutegravir and bictegravir in most individuals infected with BF recombinants from Argentina. Whether differences in the mutational rates of INI-DRMs are responsible for the slower rate of VF in subtype F merits further study.

33

Expanded index testing and community-based testing modalities in Nigeria are effective in identifying children living with HIV

Traub A[1], *Firth J[1], Obanubi C[1], Fayorsey R[2], Adetosoye Moses A[3], Fadare O[2], Grabbe K[3]*

[1]United States Agency for International Development (USAID), Washington, United States, [2]International Center on AIDS Care and Treatment (ICAP), New York City, United States, [3]Jhpiego, Baltimore, United States

Background: With one of the highest rates of new HIV infections, and an estimated 220,000 children living with HIV (CLHIV), Nigeria represents a critical country for improved pediatric case finding. Starting in FY19 Q3 (April 2019), targeted community testing and improved index testing started being scaled up in four states in Nigeria including Adamawa, Akwa Ibom, Cross River, and Niger states in line with national drive for HIV epidemic control. Index testing, the testing of at-risk contacts of HIV-positive persons (including their biological children), has been shown to yield high positivity rates and be essential in identifying asymptomatic CLHIV. This study assessed the change in pediatric case identification from FY19 Q1 (October 1, 2018) to FY20 Q2 (March 31, 2020) when community-based testing and index testing modalities were scaled up.

Materials and Methods: We analyzed quarterly trends of HIV testing program data for children 0-14 years of age from October 1, 2018 (FY19 Q1) to March 31, 2020 (FY20 Q2) in Adamawa, Akwa Ibom, Cross River, and Niger states. The pediatric population was defined as 0 to 14 years of age. Facility index testing referred to testing biological children of HIV positive parents at the facility, while community index testing occurs at the household or other community location. Mobile testing referred to all other community level testing. This analysis describes the positivity and volume by type of testing modality.

Results: The testing positivity across all modalities increased from 10.1% (FY19 Q1) to 17.9% (FY20 Q2) with 203 HIV- positive children newly diagnosed in FY19 Q1 and 451 HIV-positive children in FY20 Q2. Community testing began in FY19 Q3 with 1 positive child (0.3% of all positives) identified through community index testing, and increased to 199 positive children (44.1% of all positives) identified through a combination of community index (84, 18.6% of all positives) and mobile testing in FY20 Q2. Mobile testing began in FY20 Q1 with 109 positive children (23.2% of all positives), and increased to 115 positive children (25.5% of all positives) in FY20 Q2. The proportion of all tests that were index testing increased from 9.2% (FY19 Q1) to 27.1% (FY20 Q2) ($p<0.001$) and the proportion of HIV-positive children identified through index testing increased from 23.2% (FY19 Q1) to 43.7% (FY20 Q2) ($p<0.001$). Volume of positives from facility index testing increased from 47 positive children (23.2% of all positives) in FY19 Q1 to 113 positive children (25.1% of all positives) in FY20 Q2. The overall proportion of facility-based tests, when index testing is excluded, decreased (29.9% decrease, $p<0.001$) from FY19 Q1 to FY20 Q2, however the volume of children identified through non-index facility-based testing dropped less, from 156 to 139 (11% drop).

Conclusion: The increase in volume of HIV-positive children diagnosed, as well as increased overall positivity when community and index testing are scaled up, reflects the efficiency and impact of community and index testing for pediatric case identification.

34

Evaluating the performance of the GeneXpert HIV-1 Qualitative assay as a consecutive test for a new early infant diagnosis algorithm

***Mukendi A*[1,2,3]**, *Kufa T*[1,4], *Murray T*[1,3], *Burke M*[5], *Strehlau R*[5], *Technau K*[5], *Tiemessen C*[1,2], *Sherman G*[1,2,3], *Mazanderani A*[1]

[1]*Centre for HIV and STIs, National Institute for Communicable Diseases, Johannesburg, South Africa,* [2]*School of Pathology, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa,* [3]*Paediatric HIV Diagnostics, Wits Health Consortium, Johannesburg, South Africa,* [4]*School of Public Health, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa,* [5]*Empilweni Services and Research Unit, Rahima Moosa Mother and Child Hospital, Department of Paediatrics and Child Health, School of Clinical Medicine, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa*

Background: Due to comprehensive prevention of mother-to-child transmission (PMTCT) programmes, the proportion of HIV-exposed infants and young children infected with HIV has markedly declined over the past decade. This in turn has reduced the positive predictive value (PPV) of diagnostic assays, resulting in an increase in the proportion of false-positive results and necessitating review of early infant diagnosis (EID) algorithms to ensure acceptable accuracy. The WHO recommends the use of an indeterminate range whereby potentially false-positive results can be differentiated from clearly positive cases based on the cycle threshold (Ct) of HIV-detected PCR results. This practice has been used within South Africa's National Health Laboratory Service since 2013, but has been associated with a high indeterminate rate of approximately 17% of all HIV-detected PCR results. As an alternative to this approach, the performance of the GeneXpert HIV-1 Qualitative (Xpert EID) assay was evaluated as a consecutive test for infants with an HIV-detected PCR screening test on the Cobas® AmpliPrep/Cobas® TaqMan HIV-1 Qualitative Test v2.0 (CAP/CTM v2.0).

Materials and Methods: Retrospective analysis of a longitudinal cohort of HIV-exposed infants for whom concurrent Xpert EID and CAP/ CTM v2.0 birth testing was performed at four tertiary sites in Gauteng, South Africa between June 2014 and December 2019. All infants with a CAP/CTM v2.0 HIV-detected screening test, concurrent Xpert EID test and subsequent confirmatory CAP/CTM v2.0 test on a separate specimen were included. Performance of the Xpert EID in predicting final HIV status was determined as proportions with 95% confidence intervals. A comparison of indeterminate CAP/CTM v2.0 results as per verification practices in South Africa (Ct >33 and/or relative fluorescence intensity <5), with discordant CAP/CTM v2.0/ Xpert EID results was performed.

Results: A total of 150 infants met the inclusion criteria of which 6 (3.9%) had an Xpert result discordant with final HIV status: 5 (3.3%) false-negatives and one (0.7%) false-positive. As a consecutive assay, the Xpert EID yielded a sensitivity of 96.5% (95% CI: 92.0% - 98.9%), specificity of 85.7% (95% CI: 42.1% - 99.6%), PPV of 99.3% (95% CI: 95.7% - 99.9%), negative predictive value of 54.5% (95% CI: 32.5% - 74.9%), and overall accuracy of 96.1% (95% CI: 91.5% - 98.5%). If discordant CAP/CTM v2.0/ Xpert EID results were used as criteria to verify indeterminate results instead of current practice, the number of indeterminate screening results would be reduced from 18 (12.6%) to 11 (7.2%) - 42.1%, without increasing the false-positive rate.

Conclusion: The addition of the Xpert EID as a consecutive test for specimens with an HIV-detected PCR screening result has the potential to improve the PPV and reduce the indeterminate rate, thereby reducing diagnostic challenges and time to final diagnosis.
Keywords: Early Infant diagnosis, indeterminate, paediatric HIV, Birth HIV PCR, Prevention of mother-to-child transmission

35

Change in sexual behavior and partner communication following oral HIV self-testing among adolescents and young adults in Kenya

***Driver M*[1]**, *Katz D*[2], *Manyeki V*[3], *Mungala C*[3], *Otiso L*[4], *Mugo C*[2], *McClelland S*[1,2,5], *Kohler P*[2,6], *Simoni J*[7], *Inwani I*[3], ***Wilson K*[2]**

[1]University Of Washington Department of Epidemiology, Seattle, United States, [2]University Of Washington Department of Global Health, Seattle, United States, [3]University of Nairobi/Kenyatta National Hospital, Nairobi, Kenya, [4]Liverpool VCT, Nairobi, Kenya, [5]University of Washington Department of Medicine, Seattle, United States, [6]University of Washington Department of Child, Family, and Population Health Nursing, Seattle, United States, [7]University of Washington Department of Psychology, Seattle, United States

Background: HIV testing is a key step to linkage to care and prevention services. Adolescents and young adults (AYA) have lower rates of HIV testing compared to adults in sub-Saharan Africa. HIV self-testing (HIVST) is a promising strategy to improve testing uptake among AYA because it is more convenient and private than provider-assisted testing. While HIV testing is an important part of prevention services, it is unclear whether completing HIVST influences sexual behavior among AYA. We evaluated whether HIVST was associated with changes in sexual behaviors and HIV risk perception among AYA who completed oral HIVST in Kenya.

Materials and Methods: This analysis used data from participants enrolled in a community-based oral HIVST study in an urban settlement in Kenya. Eligible AYA were between ages 15-24 with negative or unknown HIV status. Participants were recruited and enrolled from one of three channels: home-based testing, pharmacies, and 'hotspots' (bars, nightclubs). Surveys at enrollment and at 4-months post-HIVST assessed any condomless sex in the last 30 days (any reported vaginal or anal sex act without a condom); consistent condom use with casual and main partners (every single time vs. sometimes/almost never/never); talking to sexual partners about HIV testing (yes vs. no); and HIV risk perception (moderate/large/very large chance of getting HIV in the next year vs. small/almost none/none). Multivariate negative binomial regression was used to evaluate change in behaviors and risk perception between baseline and 4-month follow-up overall and by gender and channel.

Results: Of 244 eligible participants, most (85.2%) were ages 18-24, and 63.8% were female. Approximately one third (32.6%) were recruited from home-based testing, 19.2% from pharmacies, and 48.2% from hotspots. At enrollment, 87.9% reported sexual activity with a main partner (90.0% among males and 87.4% among females) and 69.6% reported sexual activity with a casual partner (81.3% among males and 63.6% among females). Overall, participants reported greater prevalence of talking to partners about HIV testing at follow-up compared to baseline (87.1% vs. 66.0%, adjusted PR [aPR]=1.30; 95%CI=1.15-1.48). In contrast, fewer participants reported consistent condom use with casual partners at follow-up compared to baseline (29.1% vs. 43.6%, aPR=0.67; 95%CI=0.49-0.91). This decline was only observed in females (23.0% vs. 44.0%, aPR=0.52; 95%CI=0.32-0.83) and not males (37.5% vs. 43.1%; aPR=0.96; 95%CI=0.62-1.48). No differences were observed between baseline and follow-up in condomless sex acts (48.9% vs. 50.9%, aPR=1.08; 95%CI=0.91-1.28), consistent condom use with main partners (29.3% vs. 31.0%, aPR=0.88; 95%CI=0.65-1.20), or HIV risk perception (40.9% vs. 39.7% moderate-to-very large, aPR=1.00; 95%CI=0.83-1.20).

Conclusion: AYA reported greater likelihood of discussing HIV testing with their sexual partners following HIVST. A decline in reported condom use with casual partners, though not main partners, was observed among females. This suggests that receiving a negative HIVST result may help initiate conversations about testing with sexual partners but may reduce the individual's or partner's motivation to use condoms in casual partnerships. HIVST programs should consider integrating client-centered counseling to support preventive behaviors following receipt of HIVST while recognizing the unique perspectives and challenges experienced by this population.

36

High Rates of Primary and Secondary Syphilis Infections in HIV-Positive Adolescent and Young Adult Men Who Have Sex With Men in Atlanta, GA

Loerinc L[1], *Scheel A[1], Jordan-Thompson S[2], Gillespie S[3], Camacho-Gonzalez A[2]*

[1]Emory University School of Medicine, Atlanta, United States, [2]Department of Pediatrics, Division of Pediatric Infectious Diseases, Emory University School of Medicine, Atlanta, United States, [3]Department of Pediatrics, Emory University School of Medicine, Atlanta, United States

Background: The rates of primary and secondary syphilis infections have continued to increase in the United States since 2001. Men who have sex with men (MSM) consistently represent the majority of these cases, and nearly half of infections in MSM occur in HIV-positive individuals. HIV and syphilis co-infection has been associated with lower CD4 T-cell counts, higher HIV viral loads, and increased HIV transmission. The purpose of our study was to determine incidence rates of primary and secondary syphilis infections in HIV-positive adolescent and young adult MSM in Atlanta, GA and compare them to nationally reported data. We also aimed to determine reinfection and treatment rates for individual patients in this group.

Materials and Methods: Retrospective chart review was conducted for all patients aged 13-24 at Grady Ponce and Family Youth Clinic (GPFYC) in Atlanta, GA from 2009-2018. Data were collected on demographics, syphilis infection and resolution, clinical symptoms, reported sexual history, and treatment received. Syphilis infection was determined by positive screening with RPR and a positive Treponemal confirmatory test. Resolution of infection was determined by a 4-fold drop in RPR titer. Reinfection was determined by a 4-fold increase in RPR titer or a 2-fold increase in RPR titer with high clinical suspicion and treatment by a provider. Number of syphilis infections and corresponding treatments were calculated using frequencies and percentages. Overall incidence and incidence of reinfections were calculated by dividing new syphilis cases by corresponding person follow-up time. Incidence is presented as new cases per 10 person-years with associated 95% confidence intervals (CI).

Results: 375 sexually active HIV-positive MSM were included. Mean age at the onset of the follow-up period was 19.4 (+/- 2.1) years. 348 patients (92.8%) were African American, 11 patients (2.9%) were Hispanic, 9 patients (2.4%) were white, and 7 patients (1.9%) identified as other. 203 patients (54.1%) had at least one primary or secondary syphilis infection over the study period. 115 patients (30.7%) had one infection, 52 patients (13.9%) had two infections, 26 patients (6.9%) had three infections, and 10 patients (2.7%) had more than three infections. The 10-year syphilis incidence rate (95% CI) was 2.44 (2.20-2.71). For re-infected patients, the 10-year syphilis incidence rate (95% CI) was 8.10 (7.10-9.20). 316 patients (91.3%) had documented treatment, 9 patients (2.6%) had no documented treatment, and 21 patients (6.1%) had unknown treatment status.

Conclusion: Our study demonstrates disproportionately high numbers of syphilis infection and reinfection in HIV-positive MSM, even when compared to high rates in this population nationally. If left untreated, syphilis may lead to serious long term health complications and increased HIV transmission. It is well documented that screening for co-sexually transmitted infections, including syphilis, remains suboptimal in HIV-positive MSM despite national recommendations. Our data support the urgent need for HIV-care clinics to increase adherence to routine screening protocols.

37

Overlapping Significant Life Events are associated with HIV Viral Non-Suppression among Youth in Clinics in Rural East Africa

***Mwangwa F*[1]**, *Charlebois E[2], Ayieko J[3], Olilo W[3], Black D[2], Peng J[2], Kwarisiima D[1], Kabami J[1], Blazer L[4], Petersen M[5], Kapogiannis B[6], Kamya M[1,7], Havlir D[2], Ruel T[2]*

[1]Infectious Diseases Research Collaboration, Kampala, Uganda, [2]University of California, San Francisco , San Francisco, United States, [3]Kenya Medical Research Institute(KEMRI), Nairobi,, Kenya, [4]University of Massachusetts Amherst, , Amherst, United States, [5]University of California, Berkeley, Berkeley, United States, [6]Eunice Kennedy Shriver National Institute of Child Health and Human Development National Institutes of Health, Bethseda, United States , [7]Makerere University College of Health Sciences, Kampala, Uganda

Background: The HIV-care continuum among Youth Living with HIV (YLWH) is thought to be influenced by life events that may be part of normal psycho-social development but affect engagement with treatment. However, data on the prevalence of disruptive life events among YLWH in rural sub-Saharan Africa and their association with viral suppression are limited.

Methods: SEARCH Youth (NCT0384872) is a cluster-randomized trial testing a package of youth-focused interventions in 28 HIV clinics in rural Uganda and Kenya. In the intervention arm, a tablet-based care-planning tool is used to assess potential barriers to treatment including age, alcohol use, HIV disclosure status, and major recent life-events such as start/stop school or employment, change in residence, divorce/separation or relationship strife, new sexual partner, family death, sickness, incarceration, family strife, and pregnancy or birth. We used multivariable logistic regression adjusted for clinic clustering to evaluate the association of potential barriers with viral suppression (<400 copies/mL, any ART status) at the time of enrollment.

Results: Among 900 participants (83% female), 885 (98%) completed HIV viral load testing. The age distribution (years) of subjects was 15-17 (19%),18-20 (32), 21-22 (29%), and 23-24 (20%). ART had been started at enrollment (12%), ≤ 6 months prior (21%), or >6 months prior and they remain in care (62%) or have since disengaged from care (4%). The prevalence of alcohol use was (17%), disclosure of HIV status to family (81%) and disclosure to a partner (54%).
The most common life events were pregnancy (16%), moving (16%), sickness (9%), start/stop job or school (9%), family death (8%), relationship strife or divorce/separation (8%), and a new sexual partner (8%) with 17% reporting overlapping (≥2) life-events.
Overlapping life events (aOR 0.52, 95% CI 0.35-0.77; p=0.001) and alcohol (aOR 0.56, 95% CI 0.38-0.84; p=0.004) were associated with viral non-suppression. While increasing age (aOR 1.08, 95% CI 1.02-1.15; p=0.011) and disclosure to family (aOR 2.00, 95% CI 1.4-2.8; p=0.001) or partner (aOR 1.71, 95% CI 1.2-2.4; p=0.001) were associated with viral suppression.

Conclusions: In this contemporary cohort of youth living with HIV in rural Africa, overlapping major life-events, alcohol use, and lack of disclosure were associated with viral non-suppression while disclosure to a partner or family was associated with suppression. Systematic and routine assessment of life events could allow providers and patients to identify and address barriers to treatment, potentially improving clinical outcomes in this vulnerable population.

38

Qualitative Analysis of a mobile WhatsApp group messaging intervention for adolescents living with HIV in Kenya

Chory A[1], Martin R[1], Aluoch J[2], Njoroge T[2], Ashimosi C[2], Scanlon M[1], Apondi E[2,3,4], Nyandiko W[2,3,4], Vreeman R[1,2]

[1]Arnhold Institute for Global Health, Icahn School of Medicine at Mount Sinai, New York, United States, [2]Academic Model Providing Access to Healthcare (AMPATH), Eldoret, Kenya, [3]Moi Teaching and Referral Hospital, Eldoret, Kenya, [4]Department of Child Health and Paediatrics, School of Medicine, College of Health Sciences, Moi University, Eldoret, Kenya

Introduction: Mobile platforms are novel and scalable technologies for intervention delivery. There are few studies using these platforms to target adolescents living with HIV (ALWH) in low- and middle-income countries. We conducted an observational pilot study to assess engagement and value of a WhatsApp group messaging intervention to deliver peer support and mental health counseling to ALWH in western Kenya.

Methods: Participants (N=29) were ALWH aged 10-19 years, HIV-disclosed and engaged in care at a comprehensive HIV clinic in Kenya. Participants were enrolled for six months and provided with a SIM card and smartphone with WhatsApp chat application installed. We used a multimedia curriculum that was informed by formative qualitative work with an ALWH cohort, and included group discussion modules on stress management, drug and alcohol abuse prevention, intimate relationships, and issues related to HIV adherence, disclosure, and stigma. A trained pediatric HIV adherence and disclosure counselor facilitated the group chats to encourage positive support between participants, to introduce weekly group discussion topics, and to answer questions. Participants were given a pseudonym to maintain confidentiality in the chats. All WhatsApp chats from the six month intervention were downloaded and translated into English for analysis. Inductive thematic analysis of the transcripts was led by two researchers (AC and RM) who identified preliminary codes and subsequent themes using Dedoose software (Sociocultural Research Consultants, LLC). Preliminary codes were further refined, reviewed and analyzed by an additional researcher (JA). Participants aged 18 years or older provided informed consent; participants younger than 18 years of age provided assent and consent from the minors' caregivers.

Results: Participants demonstrated particular interest in conversations around HIV literacy, navigating relationships, and experiences with stigma. Adolescents discussed side effects of ARVs, provided support and suggestions to ALWH experiencing challenges around adherence, and HIV transmission methods. Participants shared the value of trustworthy relationships and the importance of intentional disclosure to friends and romantic partners. They identified the emotional impact of non-disclosure in their relationships and the steps they take to maintain secrecy, including hiding medication bottles and sneaking away from a group to keep time. Adolescents described challenges in the school setting, including maintaining adherence without accidental disclosure and navigating HIV-related stigma by teachers and classmates. Participants described similar stigma and disclosure related experiences in the home, and offered tactics and solutions to these challenges. Religion played a significant role, providing a sense of hope and protection for the ALWH. Evening prayer was considered a priority and routinely led by participants. Notable barriers to participation in the group included scheduling conflicts with school related responsibilities, parents limiting cell phone use, and prolonged community loss of electricity which prevented charging of cell phones.

Conclusion: The content discussed suggests that this could be a valuable platform for ALWH, as it provides an opportunity to share experiences, fears, questions and advice related to HIV that would otherwise remain secret. Future studies should further investigate ALWH engagement in WhatsApp delivered interventions for peer support, including assessing its effectiveness in improving HIV adherence and clinical outcomes.

39

High Prevalence of Asymptomatic Sexually Transmitted Infections at Baseline Clinic Visit Following HIV Diagnosis in Atlanta Youth

Scheel A[1], *Loerinc L[1], Jordan-Thompson S[2], Gillespie S[3], Camacho-Gonzalez A[2]*

[1]Emory University School Of Medicine, Atlanta, United States, [2]Department of Pediatrics, Division of Pediatric Infectious Diseases, Emory University School of Medicine, Atlanta, USA, [3]Department of Pediatrics, Emory University School of Medicine, Atlanta, USA

Background: The IDSA Primary Care Guidelines recommend routine screening for co-sexually transmitted infections (STIs) for all HIV-positive men who have sex with men (MSM) and transgender women (TW) who present for initial enrollment in HIV care. The Centers for Disease Control and Prevention further recommends routine screening for co-STIs in this group at all anatomic sites (urogenital, pharyngeal, and rectal), especially since many of these infections are asymptomatic. Despite these guidelines, screening for co-STIs in this population remains suboptimal. The need to intensify screening is critical as STIs are known to enhance transmission of HIV, as well as play a role in recruiting immune cells to the site of infection providing increased substrate for HIV replication. The purpose of our study is to determine the number of HIV-positive adolescent and young adult (AYA) MSM and TW who presented with co-STIs at any anatomic site during their initial enrollment visit in a HIV primary care clinic in Atlanta, GA.

Methods: Retrospective chart review was conducted for all patients aged 13-24 at Grady Ponce and Family Youth Clinic (GPFYC) in Atlanta, GA from 2009-2018. Data were collected on all co-STIs diagnosed during enrollment in HIV care, including diagnosis and resolution dates, site of infection, clinical symptoms, reported sexual practices, and treatment received. Co-STIs included chlamydia (CT), gonorrhea (GC), syphilis, herpes simplex virus (HSV), human papilloma virus (HPV), and lymphogranuloma venereum (LGV). Statistical analysis was performed to determine the number, type and site(s) of sexually transmitted infections. Infections are reported as whole number counts and percentages.

Results: 237 HIV-positive MSM and TW who presented for enrollment in HIV care within 3-months of HIV diagnosis were included. 95% identified as male, while 11 participants (4.6%) identified as TW. 217 (91.6%) identified as African American. Mean age at HIV diagnosis was 20.3 (+/- 2) years. There were 149 STIs identified in 101(42.6%) participants; 63 (26.5%) participants presented with one infection, 30 (12.7%) with two, and 8 (3.4%) with three or more infections. HPV was the most common STI with 45 (30.2%) infections, followed by 37 (24.8%) syphilis infections, 31 (20.8%) GC infections, 30 (20.1%) CT infections, 4 (2.7%) LGV and 2(1.3%) HSV. The rectum was the most common anatomical site for CT representing 16 (53.3%) infections, followed by 10 (33.3%) urogenital and 4 (13.3%) oropharyngeal infections. Similarly, the rectum was the most common anatomical site for GC with 12 infections (38.7%), followed by 11 (35.5%) oropharyngeal and 8 (25.8%) urogenital. Asymptomatic infections in this population were common with 26 (70.3%) syphilis, 18 (60.0%) CT, and 16 (51.6%) GC infections displaying no subjective or objective physical signs of infection.

Conclusions: The high prevalence of co-STI's in this population highlights the importance of baseline screening and further supports the current guidelines. Our findings suggest that the majority of co-STIs at baseline are asymptomatic, emphasizing the need for 3-site anatomical testing,. Enrollment visits highlight a unique opportunity for intervention. Further work is needed to increase routine co-STI testing for HIV-positive AYA MSM and TW at enrollment in HIV care.

40

Cascades of care for preventing vertical HIV transmission in Canada

Li S[1], Boucoiran I[2], Tan B[3], Singer J[4], Kakkar F[2], Lee T[4], Brophy J[5], Money D[6], Alimenti A[6], Vaudry W[7], Comeau J[8], Bitnun A[9], Wong A[10], Sauvé L[6]

[1]University Of British Columbia, Vancouver, Canada, [2]CHU Ste-Justine, Université de Montréal, Montréal, Canada, [3]University of Saskatchewan, Saskatoon, Canada, [4]CIHR Canadian HIV Clinical Trials Network, Vancouver, Canada, [5]Children's Hospital of Eastern Ontario, University of Ottawa, Ottawa, Canada, [6]Women's Hospital and Health Centre of British Columbia, University of British Columbia, Vancouver, Canada, [7]Stollery Children's Hospital, University of Alberta, Edmonton, Canada, [8]IWK Health Centre, Dalhousie University, Halifax, Canada, [9]Hospital for Sick Children, University of Toronto, Toronto, Canada, [10]University of Regina, Regina, Canada

Background: In the era of combined antiretroviral therapy (cART), vertical HIV transmission (VT) has declined dramatically. However, missed opportunities for VT prevention among pregnant women and their infants remain a concern. The cascade of care is a tool that estimates engagement in care and encompasses a continuum of services from diagnosis to virologic suppression. This study investigated cascade of care indicators for mother-infant pairs in the Canadian Perinatal HIV Surveillance Program (CPHSP).

Materials and methods: The CPHSP is an active surveillance system that collects data on VT across all 13 provinces and territories in Canada. Data are collected at the 23 participating sites via annual retrospective chart reviews of mother-infant pairs. The current analysis was restricted to live infants born to women living with HIV (WLWH) in Canada from 2008-2018. Measures of success included maternal diagnosis prior to the second trimester (<13 weeks of gestation), initiation of antenatal antiretroviral therapy (ART) before the third trimester (<28 weeks of gestation), undetectable maternal viral load (VL) near delivery (<50 copies/ml), infant prophylaxis (four or more weeks of ART), finalizing of infant HIV status (two or more HIV tests at two weeks of age or later), and linkage to care within one year if infected. Linkage to care was defined as having a recorded immunological or clinical status, as evidence of clinical appointment. Proportions were presented for each step in the cascade of care and further stratified by infant year of birth, mother exposure risk category, and infant province of birth.

Results: 2651 mother-infant pairs were included. Of all women, 2107 (79.5%) were diagnosed prior to the second trimester, 2067 (78.0%) started ART before the third trimester, and 2115 (79.8%) achieved an undetectable VL near delivery. Among all infants, 2420 (91.3%) received appropriate prophylaxis and 2242 (84.6%) had sufficient testing to finalize their HIV status. Among infected infants (n=37), 34 (91.9%) were linked to care. Analysis by infant year of birth showed an increase in the proportion of women achieving an undetectable VL near delivery, from 159 (67.1%) in 2008 to 228 (88.0%) in 2018. When stratified by exposure risk category, women who reported injection drug use had the lowest engagement in care, with 336 (65.4%) diagnosed before second trimester, 141 (63.5%) initiating ART before third trimester, and 326 (63.4%) achieving an undetectable VL near delivery. When stratified by infant province of birth, Alberta, Saskatchewan, and Manitoba experienced the lowest rates for maternal engagement in care indicators.

Conclusions: This population-level analysis demonstrated promising trends of maternal and infant engagement in HIV care in a Canadian setting. However, gaps in care remain a significant concern for certain populations of pregnant WLWH and their infants. As Canada strives to improve the continuum of HIV care, exploring the factors associated with lower engagement in care is needed on order to enhance targeted health strategies to reduce VT.

41

Opportunity Analysis for HIV Risk and Acquisition Among Pregnant Adolescent Girls and Young Women in Antenatal Care Services in Ten African Countries

***Lenz C*[1]**, *Ahimbisibwe A[2], Akuno J[4], Ashburn K[1], Corneliess C[1], Lailari A[1], Makwindi C[3], Namubiru M[5], Jelagat Odionyi J[4], Ombija M[1], Sunguti J[2], Van de Ven R[6]*

[1]EGPAF, Washington D.C., United States, [2]EGPAF Malawi, , , [3]EGPAF Eswatini, , , [4]EGPAF Kenya, , , [5]EGPAF Uganda, , , [6]EGPAF Tanzania , ,

Background: HIV transmission risks remain high among adolescent girls and young women (AGYW) in sub-Saharan Africa. Approximately 270,000 new HIV infections among AGYW (15-24) occurred in 2018. AGYW also have high rates of unplanned pregnancies, and pregnancy and the early postpartum periods are a time when there is an increased risk of HIV acquisition per unprotected sex act. The Elizabeth Glaser Pediatric AIDS Foundation (EGPAF) analyzed program data to understand HIV trends and potential prevention opportunities among pregnant AGYW and antenatal care (ANC) clients in our programs.

Methods: Cross-sectional analyses of routinely reported program data and service packages were conducted for EGPAF supported regions in ten countries (Cameroon, Cote d'Ivoire [CDI], Democratic Republic of Congo [DRC], Eswatini, Kenya, Lesotho, Malawi, Mozambique, Tanzania, and Uganda). We identified the number/proportion of HIV-positive pregnant women in ANC and women attending prevention of mother-to-child transmission (PMTCT) services. The indicators were analyzed from October 2018 to December 2019 and disaggregated by country and age (15-19, 20-24, 25+ years).

Results: Proportionally, 46% of new ANC clients were age 15-24-years (n=453,961); 16.6% (n=161,729) were 15-19 years and 29.5% (n=292,232) were 20-24 years. Comparing the 10 countries, Lesotho had the highest proportion of AGYW in ANC with 54.5% (n= 21,666), followed by Mozambique (53.1%; n= 98,496) and Uganda (48.6%; n= 91,066). Overall, 98.8% of new ANC clients (15-24) had a known HIV status at first ANC visit. Of those entering ANC with known HIV status, HIV-positivity was associated with age, with 2.6% of those age 15-29 years HIV-positive; 5.3% of those 20-24 years; and 9.4% of those 25+ years. At 16.9%, Eswatini had the highest rate of HIV-positive new ANC clients age 15-24 years, followed by Lesotho (11.8%) and Kenya (8.2%). The countries with the lowest proportion of HIV-positivity among AGYW age 15-24 years were DRC (0.67%) and CDI (1.2%). Of those with confirmed HIV-positive status, 95% of pregnant girls (15-19 years) and 97% of pregnant young women (20-24 years) were receiving ART. Of the ten countries analyzed, five offer PrEP to HIV-uninfected individuals, (Kenya, Lesotho, DRC, Eswatini, Uganda), most of which are starting PrEP programs for this population. 7,388 youth 15-24 years received PrEP in Uganda, Eswatini, Kenya, and Lesotho January-September 2019.

Conclusions: In all countries, a high proportion of new ANC clients were AGYW. ANC offers an important opportunity to reach AGYW and their partners, especially those in discordant/unknown-status relationships, with HIV prevention, care and treatment in addition to other SRH services, including FP. While the rate of HIV-positivity increased with age, being highest among those 25+ years, a significant proportion of AGYW were HIV-positive, ranging from a low of 0.7% in low HIV prevalence countries like DRC to 17% in high prevalence countries like Eswatini. The vast majority of HIV-positive pregnant AGYW were receiving ART. Services such as PrEP for prevention of HIV acquisition for AGYW, who form nearly half of ANC/PMTCT clientele and the majority of whom will be HIV-uninfected, were relatively limited, and need to be scaled up, particularly in high prevalence settings.

42

Continuous quality improvement improves retention of clients in prevention of mother-to-child transmission of HIV program (Wakiso District, Uganda)

Naikazi G[1], *Namaganda S[1], Babirye B[1], Ngobi D[1], Amuge M[1], Tumukugize V[1], Nakubulwa S[1], Busingye P[1], Mugabe P[1], Baluku J[1], Agolor C[1], Businge J[1], Nakaweesi J[1], Namukwaya Z[2], Namukanja P[3]*

[1]Mildmay Uganda, Entebbe Road,Naziba Hill Lweza,, Uganda, [2]Infectious Diseases Institute, Makerere College of Health Sciences, Makerere University,, Uganda, [3]Division of Global HIV & TB, US Centers for Disease Control and Prevention, Kampala, Uganda

Background: Mother-to-child transmission of HIV (MTCT) accounts for 90% of new HIV infections in children globally. Low retention in care of pregnant and breastfeeding mothers living with HIV continues to hinder prevention of MTCT (PMTCT) efforts. In December 2017, Wakiso District reported a 61% maternal retention rate versus the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) 95% target. This shortfall was mainly due to shortage of midwives and documentation gaps. A continuous quality improvement (CQI) project was undertaken to address the existing retention gap. We evaluated the effect of CQI interventions on retention rates.

Materials and Methods: We retrospectively assessed 12-months retention among pregnant and breastfeeding women living with HIV (December 2017–December 2019) at 51 PEPFAR-supported health facilities in Wakiso District. CQI interventions included reviewing patient chart, updating antiretroviral therapy (ART) registers, following up mothers who were lost to care through line-listing and follow up by peer mothers via phone calls and home visits, and initiating pre-visit reminder calls. We tried all the other interventions first with slow retention progress. In July 2018, we complemented an intervention to recruit 15 midwife volunteers to support PMTCT clinics and retention audits that is when the rates changed. In January 2020, 12-months maternal retention cohort data were extracted from the Ministry of Health database (DHIS2) with month zero being the ART start date, and retention rates were calculated by the proportion of active PMTCT mothers receiving ART in the 12-month cohort out of the net current cohort (original cohort plus transfers-in minus transfers-out). We conducted a trend analysis for nine quarters from December 2017 to December 2019 and used the Mann-Kendall test to determine monotonic trend from beginning to the end of the study period. P-values <0.05 were considered statistically significant.

Results: Retention rates from 51 health facilities by quarter were 61%(October-December,2017),63% (January–March, 2018), 69% (April–June, 2018), 70% (July–September, 2018), 79% (October–December, 2018), 80% (January–March, 2019), 83% (April–June, 2019), 88% (July–September, 2019), and 93% (October–December, 2019). We found positive trends over time for 12-month maternal retention (p=0.008).

Conclusion: Maternal retention at 12 months improved 32% over the study period We found CQI initiatives such as using data teams, including midwives and peer mothers in retention audits updating registers in a timely manner, deploying additional human resources in PMTCT clinics is key for better outcomes, and conducting pre-visit reminder calls and home visits can significantly improve maternal PMTCT retention. These interventions can be scaled up to other districts nationally with minimal resources because they are cost effective.

43

Higher prevalence of stunting and lower length, weight, and head circumference among HIV-exposed uninfected infants

***Neary J*[1]**, *Langat A[2], Singa B[3], Kinuthia J[4], Itindi J[3], Nyaboe E[3], Ng'anga' L[2], Katana A[2], John-Stewart G[1], McGrath C[1]*

[1]University of Washington, Seattle, United States, [2]Division of Global HIV & TB, Division of Global HIV & TB (DGHT), US Centers for Disease Control and Prevention Kenya, Nairobi, Kenya, [3]Kenya Medical Research Institute, Nairobi, Kenya, [4]Departments of Obstetrics & Gynaecology, Research & Programs, Kenyatta National Hospital, Nairobi, Kenya

Background: HIV-exposed uninfected (HEU) children have increased risk of morbidity and poor growth compared to HIV-unexposed uninfected (HUU) children. With the growing population of HEU globally, there is need and opportunity to leverage programmatic data to monitor growth outcomes among HEU children.

Methods: We analyzed growth data from a prevention of mother-to-child transmission (PMTCT) survey enrolling mother-infant pairs attending week 6 and month 9 immunizations at 140 clinics in Kenya between July-December 2013. HIV-infected women were oversampled in 30 clinics in western Kenya, an area of high HIV prevalence. Primary outcomes, including weight-for-age (WAZ), length-for-age (LAZ), head circumference-for-age (HCAZ) z-scores and underweight (WAZ<-2), stunting (LAZ<-2), and microcephaly (HCAZ<-2), were compared between HEU and HUU infants at week 6 and month 9. Generalized Poisson and linear regression models accounting for clinic-level clustering were used to determine prevalence ratios (PR) to examine correlates of primary outcomes. Covariates associated with outcomes at p<0.05 in univariate analysis were included in multivariable analysis.

Results: Among 2,457 mother-infant pairs surveyed, 456 (19%) infants were HEU (16% at 6 weeks; 22% at 9 months) and 2,001 (81%) were HUU (84% at 6 weeks; 79% at 9 months). Sixty-five percent of HIV-infected mothers were on antiretroviral therapy and 19% were on monotherapy (AZT) during pregnancy. All HEU infants received nevirapine for PMTCT and, at the 9-month visit, 97% of HEU were on cotrimoxazole. At week 6 immunizations, HEU infants had lower birth weight (3.11 vs. 3.23 kg, p=0.009) and fewer were currently breastfeeding (96% vs 99%, p<0.001) than HUU infants. At month 9, fewer HEU than HUU infants were currently breastfeeding (72% vs 98%, p<0.001). At 6 weeks, HEU infants had lower mean WAZ (-0.41 vs. -0.09; p=0.0009) and LAZ (-0.99 vs. -0.31; p=0.001) than HUU. At 9 months, HEU had lower mean LAZ (-0.60 vs. -0.07; p=0.005) and HCAZ (-0.10 vs. 0.41; p=0.02) than HUU infants. Stunting prevalence was higher among HEU than HUU infants at both 6 weeks (34% vs 18%, p<0.001) and 9 months (20% vs 10%, p<0.001). In adjusted analyses, HEU had lower mean LAZ at week 6 (-0.77, 95%CI: -1.33, -0.26; p=0.008) and month 9 (-0.67, 95%CI: -1.11, -0.23; p=0.003) and were nearly twice as likely to be stunted than HUU (week-6 adjusted PR [aPR]: 1.92, 95%CI: 1.32, 2.79, p=0.001; month-9 aPR: 1.89, 95%CI: 1.23, 2.88, p=0.004). Additionally, in adjusted analyses, HEU infants had lower mean WAZ than HUU at week 6 (-0.27, 95%CI: -0.48, -0.07; p=0.008), but not at month 9. Microcephaly was twice as prevalent among HEU than HUU (14% vs 7%, p=0.03) at month 9. Compared to HUU infants, HEU had lower head circumference at month 9 (-0.59, 95%CI: -1.11, -0.23; p=0.008), but this was attenuated after adjustment (p=0.080).

Conclusion: HEU children had an increased risk of stunting and poor length, weight, and head growth compared to HUU children. Mechanisms to leverage routinely collected data to monitor growth and nutrition strategies to improve length growth in this vulnerable population are needed.
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44

Adoption of WHO's HIV retesting policy for HIV-negative women during the breastfeeding period in 10 high HIV-burden African Countries

***Burmen B*[1]**, *Omollo M*[1], *Obunga J*[1], *Muttai K*[1,2], *Oketch D*[1]

[1]*Kenya Medical Research Institute, Nairobi, Kenya,* [2]*National AIDS Control Council, Nairobi, Kenya*

Background: We evaluated how the 2016 WHO recommendation for HIV retesting for HIV-negative breastfeeding women and their HIV-negative sexual partners in the postpartum period to reduce the risk of mother to mother-to-child transmission of HIV, was adopted in 10 high HIV-burdened African countries.

Methods: An online search was used to retrieve 10 country-specific HIV treatment guidelines dated 2015 to 2019 from Kenya, Zambia, Tanzania, Uganda, Zimbabwe, Malawi, Lesotho, Botswana, Namibia, and Rwanda. Each guideline had to specify that the WHO 2016 guidelines (launched in 2015) were used to guide its' development. Frequency summaries were used to document how different countries adapted WHO guidelines into their country-specific guidelines.

Results: All (100%) countries had adopted the WHO HIV-resting policy for breastfeeding women in their HIV treatment guidelines with variations in: timing for initial testing in the postnatal period (50% at the 6th-week postpartum immunization visit, 40% at 6 months' postpartum and 10% with test-timing unspecified); frequency of repeat testing (60% recommended retesting 3-monthy, 20% 6-monthly, 10 % as per the general population, and 10% with schedule of repeat testing unspecified); and in timing of the last HIV test during the postpartum period (30% recommended the last test be at the end of breastfeeding, 30% three months after cessation of breastfeeding, 10% yearly and 10% had the timing of last HIV test unspecified).
Only 40% of the guidelines had recommendations for repeat HIV-testing for the mother's sexual partner, at a schedule akin to that that recommended for the breastfeeding mother (25%), recommended only offering HIV testing for the male partner (50%) and encouraged male partner involvement (25%).

Conclusions: Despite the time lapse between reviewed guidelines and updated clinical guidelines, and the absence of detailed information on rationale for country-specific recommendations and actual clinical practices, HIV retesting schedules for HIV-negative breastfeeding mothers in high-HIV burden settings during the postpartum period are suboptimal for timely identification of new infection. This is further worsened by limited guidance on HIV retesting for their sexual partners. We recommend the routine policy and practice assessments to align HIV health policies to country-specific HIV statistics.

45

The changing face of paediatric HIV: A review of the evolving clinical characteristics of a paediatric and adolescent patients at a clinic in Johannesburg, South Africa.

***Keal J*[1]**, *van Dongen N[1], Sorour G[1], Levin L[2], Dunlop J[3,4], Technau K[1]*

[1]Empilweni Services and Research Unit, Rahima Moosa Mother and Child Hospital, Department of Paediatrics and Child Health, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa, Johannesburg, South Africa, [2]Right to Care, Johannesburg, South Africa, [3]Anova Health Institute, , Johannesburg, South Africa, [4]Division of Community Paediatrics, Department of Paediatrics and Child Health, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, , Johannesburg, South Africa

Background: HIV-infected adolescents, aged between 10 and 19 years, represent a vulnerable and growing population. With a decline in perinatal HIV transmission, a shift in paediatric HIV services towards caring for adolescents has been observed. There is growing concern about the incidence of non-communicable diseases, and the effects of long-term ART exposure on this sub-population. This review was conducted to understand the relationship between age, duration of ART exposure and adolescent patient clinical characteristics over the past 15 years.

Materials and Methods: Prospective longitudinal data were analysed from the clinical visit database of a Hospital-based paediatric and adolescent HIV clinic in Johannesburg. We assessed the cohort by taking cross-sectional samples from four different years (2005, 2010, 2015 and 2020). For each year, the age, nadir CD4 count, duration on ART, and BMI were compared.

Results: In 2005, adolescents made up 12% of the cohort (N=96) compared with 71% in 2020 (N=799; P<0.0001). The nadir CD4 count improved, with 35% having a CD4<200 cells/uL in 2005 compared with 25% in 2020 (p<0.0001). In 2005 62% of patients had been on treatment for a duration of 1 year or less (N=308) compared with 2020 where 50% of the cohort had been on treatment for >10 years (N=754) (p<0.0001). In 2005, less than 1% (N=1) of the sample population had a BMI >25 which increased to 4% (N=56) in 2020 (p<0.0001) with 1% (N=19) recording a BMI >30.

Conclusions: These data demonstrate the aging of the paediatric HIV programme, to care for increasing numbers of HIV-infected adolescents. With improved access to ART, a more immune-competent cohort at ART initiation is seen. In line with global trends, the number of adolescents who classify as overweight is rising. The prevention and treatment of non-communicable diseases in adolescents on ART long-term is an important focus area.

46

Cognitive outcomes at 7 and 9 years after the Children with HIV Early Antiretroviral (CHER) trial

van Wyhe K[1,2], *Laughton B[2], Cotton M[2], Boivin M[3,4], Kidd M[7], Meintjes E[5], van der Kouwe A[6], Thomas K[1]*

[1]ACSENT Laboratory, Department of Psychology, University of Cape Town, Cape Town, South Africa, [2]Family Centre for Research with Ubuntu, Department of Paediatrics and Child Health,Stellenbosch University, Cape Town, South Africa, [3]Department of Psychiatry and Neurology and Ophthalmology, Michigan State University, East Lansing, United States of America, [4]Department of Psychiatry, University of Michigan, Ann Arbor, United States of America, [5]Biomedical Engineering Research Centre, Division of Biomedical Engineering, Department of Human Biology, University of Cape Town, Cape Town, South Africa, [6]Athinoula A. Martinos Center, Massachusetts General Hospital, Charlestown, United States, [7]Centre for Statistical Consultation, University of Stellenbosch , Cape Town, South Africa

Introduction: Many children living with HIV (CHIV+) display impaired cognition. Although early combination antiretroviral therapy (ART) produces the best cognitive outcomes, more long-term outcome data are needed, especially in high-burden settings such as sub-Saharan Africa.

Materials and Methods: This longitudinal study investigated cognitive performance, at 7 and 9 years of age, of participants randomised to three intervention strategies within the Children with HIV Early antiRetroviral (CHER) trial (Cape Town site): deferred ART (ART-Def; n=22); immediate time-limited ART for 40 weeks (ART-40W; n=30); and immediate time-limited ART for 96 weeks (ART-96W; n=18). We also recruited control children who were HIV-exposed but uninfected (CHEU; n=28) and HIV-unexposed (CHU; n=35). Participants completed a battery of standardized tests assessing fine motor dexterity, visual-motor integration, auditory working memory (WM), receptive language, visual-spatial processing and problem-solving, and executive functioning (EF). Mixed-model repeated-measures ANOVAs assessed differences over time between (a) CHIV+ (ART-Def + ART-40W + ART-96W) and CHIV- (CHEU + CHU) groups, (b) ART-Early (ART-40W + ART-96W), ART-Def, CHEU, and CHU groups, and (c) ART-Def, ART-40W, ART-96W, CHEU, and CHU groups.

Results: Analyses comparing CHIV+ to CHIV- detected significant Time x Group interaction effects. For fine motor dexterity, CHIV+ performed worse than CHIV- at 7 years ($p<.01$) but improved to equivalence at 9 years. For WM and EF, CHIV+ performed similarly to CHIV- at 7 years but worse at 9 years ($p<.06$ and $<.04$). For visual-spatial processing and problem-solving, CHIV+ ($p<.04$) but not CHIV- showed significant performance improvement over time. Analyses comparing ART-Early to ART-Def and controls detected one significant Group effect (WM: CHU performed significantly better than ART-Early and CHEU [$p<0.01$ and $<.04$], and also better than ART-Def [$p=.05$]) and one significant Time x Group interaction (fine motor dexterity: ART-Def performed significantly worse than ART-Early, CHEU, and CHU at 7 years [$p=.02$, $<.001$, and $<.001$, respectively] but improved to equivalence by 9 years [ps >.17]). Finally, analyses comparing the three CHER treatment arms and two control groups detected significant effects of Time for most outcome variables (scores were better at 9 than at 7 years; ps <.001). There were no significant Group effects and one significant Time x Group interaction: For fine motor dexterity, ART-Def performed worse than ART-96W, CHEU, and CHU at 7 years ($p<.04$, $<.001$, and $<.001$) but improved to equivalence by 9 years (ps >.20).

Conclusions: All ART-treated CHIV+, regardless of their treatment arm, remain at risk for cognitive deficits over early school ages, but the nature of these deficits may change over time as neuropsychological development proceeds (e.g., deficits in fine motor dexterity at 7 years, deficits in auditory working memory and executive functioning at 9 years). Of interest, however, is that the neurocognitive developmental trajectories for treatment groups and controls were similar for most domains (i.e., there were performance improvements from 7 to 9 years in all groups). The identified deficits may have negative consequences for these children's future learning, reasoning, and adaptive functioning; hence, future investigations must examine possible persistence into and beyond adolescence, and should address remediation goals.

Abstract 47 is withdrawn

48

Low access to viral load monitoring and poor virological outcomes in children and adolescents living with HIV in West Africa

***Dahourou D*[1]**, *Malateste K[2], Desmonde S[3], Eboua T[4], Takassi E[5], Renner L[6], d'Almeida M[7], Amorissani-Folquet M[8], Sylla M[9], Leroy V[3]*

[1]Institut de Recherche en Sciences de la Santé, Ouagadougou , Burkina Faso, [2]Inserm U1219, Université de Bordeaux, Institut de Santé Publique, d'Epidémiologie et de Développement, Bordeaux, France, [3]Inserm, U1027, Université Paul Sabatier Toulouse 3, Toulouse, France, [4]CHU de Yopougon, Abidjan, Côte d'Ivoire, [5]CHU Sylvanus Olympio, Lomé, Togo, [6]Korlebu Hospital, Accra , Ghana, [7]CNHU de Cotonou, Cotonou, Bénin, [8]CHU de Cocody, Abidjan, Côte d'Ivoire, [9]CHU Gabriel Touré, Bamako, Mali

Background: Reaching 90% of all people receiving antiretroviral therapy (ART) to be virally suppressed implies access to viral load measurement (VL) for all patients receiving treatment. We assessed the progress to the third 90-90-90 UNAIDS target and factors associated with viral suppression in the International epidemiological Databases on AIDS (IeDEA) paediatric West African Cohorts (pWADA).

Methods: The pWADA database involves nine paediatric clinics in five countries (Benin, Côte d'Ivoire, Ghana, Mali, Togo). All children and adolescents living with HIV (CALHIV) aged 0-19 years, ART-naïve at enrolment except for prevention of mother-to-child transmission, and diagnosed between 2004 and 2018 were included. We described the cumulative incidence of CALHIV accessing to VL monitoring ≥6 months after ART initiation and associated factors in a Fine & Gray model, where death/ lost-to-follow-up (LTFU, last clinical visit >12 months) are competing risks. Among those accessing VL ≥6 months post ART, we described factors associated with Viral Success (VL <500cp/mL) in a logistic regression model.

Results: Overall, 7570 CALHIV were enrolled of whom 72% (5475/7570) initiated ART at a median age of 5 years (Interquartile range [IQR]: 2-9 years); 80% were treated with a non-nucleoside reverse transcriptase inhibitors regimen. Children were on ART for a median time of 3 years (IQR: 1-7 years) and 55.2% (3020/5475) had at least one VL measurement ≥6 months after ART initiation; 14% died (7.8% within 6 months) and 22% were LTFU (7.6% within 6 months). The 12-month cumulative incidence of VL access was 28.8% (95% Confidence Interval [95%CI]: 27.5-30.2). This was 46.0%, 54.6% and 59.9% at 24, 36 and 48 months post-ART, respectively. Adjusted for center, gender, clinical stage, CD4 count and weight-for-age z-score at ART initiation, children aged <2 years (Ajusted Hazard ratio [aHR]: 0.62; 95%CI: 0.53-0.73), aged 2-4 years (aHR: 0.80; 95%CI: 0.68-0.93) and aged 5-9 years (aHR: 0.80; 95%CI: 0.68-0.93) were significantly less likely to access VL compared to those aged 10-15 years. This was also true for CALHIV who initiated ART before 2013, compared to those initiating treatment more recently (≥2013). We also note disparities across centers, where access to VL was less likely in centers that had to send samples to a central laboratory. Among CALHIV with a VL measurement, 53% (1611/3020) were virologically suppressed (VS). Adjusted for center, age, clinical stage, CD4 count and weight-for-age z-score at ART initiation, VS was less likely among those who initiated ART <2013 compared to ≥2013. Finally, among the 2808 CALHIV in active follow-up (patients seen at least once in the past 12 months prior to database closeout), 84% had a VL measurement, among whom 56% were suppressed.

Conclusions: In West Africa, between 2004-2018, overall access to VL in CALHIV remains low. Despite a significant increase in VL monitoring in recent years, we found that only 53% were VS (56% among those in active follow-up), far from reaching the third 90-90-90 target. Additional support is needed for CALHIV on ART, including improving access to VL testing, more potent drug regimens and the strengthening of treatment adherence interventions.

49

Time to repeat viral load testing following an unsuppressed viral load among adolescents and young adults in Kenya

Mugo C[1,3], *Wilson K[2], Onyango A[1], Njuguna I[3], Mburu C[1], Richardson B[2], Oyiengo L[4], Inwani I[3], John-Stewart G[2], Wamalwa D[1], Kohler P[2]*

[1]University of Nairobi, Nairobi, Kenya, [2]University of Washington, Seattle, United States of America, [3]Kenyatta National Hospital, Nairobi, Kenya, [4]Ministry of Health, Nairobi, Kenya

Introduction: Viral load (VL) information is key in determining success and changes required in HIV care for adolescents and young adults (AYA). Following an unsuppressed VL, Kenya's HIV treatment guidelines require a repeat VL test is performed to rule out treatment failure, 3 months after establishing that the patient has good compliance to the treatment. We assessed VL data to determine its utilization in the care of AYA on ART in Kenya.

Methods: VL data for AYA ages 10-24 years in the period April 2017 to May 2019 in 117 sites in 28 counties were abstracted from the Kenya national HIV program database. Eligible records included being on ART for at least 6 months with at least 6 months of follow-up time following the first monitoring VL in the dataset. We summarized demographics, treatment after first VL, and repeat testing following unsuppressed VL (≥1000 copies/ml). Among records with unsuppressed VL, we calculated the proportion with any repeat VL, a repeat VL within 6 months, and median (interquartile range [IQR]) number of months between first unsuppressed VL and the repeat VL.

Results: We abstracted 40,928 VL records for 23,969 AYA, of whom 16,722 (70%) were eligible for this analysis. Of those, 11,845 (71%) were female, median age 19 (IQR: 13-23), with 6105 (37%) from counties with a HIV prevalence ≥10%. Median ART duration was 39 months (IQR: 18-77), while 13,830 (83%) were on a nevirapine/efavirenz based regimen and 2,539 (15%) on a protease inhibitor.

Among 16,722 eligible AYA, 3,928 (23%) had an unsuppressed VL at first measurement. Only 2,268/3928 (58%) had any repeat VL in the dataset, and 1,153 (29%) had a repeat VL within 6 months after the unsuppressed VL. Among the 2,268 with a repeat VL, the median time between unsuppressed VL and the repeat VL was 6 months (IQR: 4-8). Among 1,303 AYA with 2 consecutive unsuppressed VL, 715 (55%) had information on ART regimen after their second VL, with 483 (68%) indicating no change of regimen.

Conclusion: A substantial proportion of AYA on ART had unsuppressed VL, with less than a third receiving a repeat VL assessment within 6 months, and less than half of those with persistent VL failure having a change of regimen. Strategies to improve VL testing practices among health care workers are needed to improve outcomes of AYA on ART.

50

Clinical outcomes of infants identified HIV-positive at birth through routine point-of-care early infant HIV diagnosis; a pilot program in Eswatini

Khumalo P[1], *Chouraya C[1], Masuku T[1], Mchunu S[1], Mpango L[1], Nhlabatsi B[2], Mthethwa N[2], Cohn J[3]*

[1]Elizabeth Glaser Pediatric Aids Foundation, Mbabane, Swaziland, [2]Ministry of Health, Mbabane, Swaziland, [3]Elizabeth Glaser Pediatric AIDS Foundation, Geneva, Switzerland

Background: It is important to understand the long-term impact of early infant HIV diagnosis (EID) at birth before countries incorporate birth testing into EID programs. Our study aimed to measure clinical outcomes of infants identified HIV-positive at birth, at 12 months after initiation in antiretroviral therapy.

Methods: This was a retrospective cohort study conducted in three maternities in Eswatini, piloting routine POC EID at birth. We abstracted data for all infants identified HIV-positive at birth from 1 August 2017 through 30 June 2019 from electronic databases and health facility-based registers. Data collected included demographic characteristics, ART initiation, retention in HIV care, and viral load testing. Data was summarized through frequencies and proportions using SPSS version 21.

Results: Thirty-one infants identified HIV-positive at birth were included in the study, of which, 61.0% (n=19) were females and 39.0% (n=12) were males. At study follow-up, the median age was 18 months (IQR 16-27). Of these 31 infants, 96.8% (n=30) were initiated on ART and 3.2% (n=1) died before ART initiation. The median age at ART initiation was 21 days (IQR 15-47). The median time from result reception by caregivers to ART initiation was 20.5 days (IQR 14–45). At 12 months ART follow-up, 76.6% (n=23) of infants were active on treatment; 16.7% (n=5) had died and 6.7% (n=2) were lost to follow-up. At 12 months, 73.9% (n=17) infants retained in HIV care had viral load information, of which, 29.4% (n=5) had viral load less than 20 copies/mL, 41.2% (n=7) had viral load of 20 -1,000 copies/mL and 29.4% (n=5) had viral load above 1,000 copies/mL.

Conclusion: Retention and viral load suppression (viral load <1,000 copies/mL) rates for children identified HIV-positive at birth was lower compared to the retention (87.6%) and viral load suppression (93.7%) for children less than 2 years old in Eswatini. Additionally, mortality of infants tested at birth is higher than for overall children less than 2 years living with HIV in Eswatini which was 3.5% in 2018. However, children infected at birth have a higher mortality if they get identified later at 6-8 weeks, thus birth testing might be helping in addressing that gap. As Eswatini scales up EID at birth, there is a need to improve time to ART initiation and to ensure the quality of care for HIV-positive infants tested at birth is sustained.

51

Fidelity to a lay cadre-administered HIV risk screening tool used among orphans and vulnerable children in community settings in Tanzania

Gill M[1], Antelman G[2], Jahanpour O[2], Urasa P[3], Barankana A[4], Koler A[4], Massenge T[2], Komba T[2], Luhanga I[5], van de Ven R[2]

[1]Elizabeth Glaser Pediatric AIDS Foundation, Washington, United States, [2]Elizabeth Glaser Pediatric AIDS Foundation, Dar es Salaam, Tanzania, [3]Ministry of Health, Community Development, Gender, Elderly and Children , Dodoma, Tanzania, [4]Pact Tanzania, Dar es Salaam, Tanzania, [5]CSK Research Solutions, Dar es Salaam, Tanzania

Background: HIV risk screening tool validation studies have not typically included process evaluations to understand tool implementation. We assessed fidelity to administration of a 12- item tool used by community case workers (CCW) as part of a community program for orphans and vulnerable children (OVC) aged 2-19 years.

Materials and Methods: This cross-sectional study took place March-April 2019 in Dar es Salaam and Tabora Regions in Tanzania. CCW responsible for HIV risk screening participated in focus group discussions (FGD) and were observed conducting the screening in households with OVC and caregivers. Research staff accompanied CCW on household visits. Staff observed HIV risk screenings by CCW using structured checklists to capture if questions were asked or reworded. Quantitative data were summarized and qualitative data from FGD were thematically analyzed to address screening tool perceptions and experiences.

Results: CCW (n=32) were observed 1-14 times each for 166 observations total. Four FGD were conducted each with 8-9 participants (n=34). Mean FGD participant age was 39 years (SD 10); 47% were female. Among 10 items directed to all beneficiaries, none were asked consistently. Questions were skipped; most frequently malnutrition in 34% of observed screenings and poor health in last three months in 19% of screenings. Questions regarding pregnancy/having a child of one's own and sexual activity, directed to adolescents only (≥ 10 years, n=85), were skipped in 45% and 20% of observations respectively. CCW answered some questions themselves based on presumed knowledge of household members (pregnancy), by visual assessment only (malnourishment) or because the question was asked during another child's screening in same household (any member of household prescribed TB treatment). Overall, CCW reported ease with asking questions, though they reworded questions viewed as containing harsh language, characterizing those as socially inappropriate to ask.

Conclusions: We found sub-optimal fidelity to the CCW-administered risk screening tool delivered in homes to OVC and their caregivers. Screening tool administration could be improved with ongoing mentorship of CCW. Community input could inform phrasing and translation of screening items to standardize language in a culturally appropriate way.

52

Reaching the 1st 95: Maximizing index testing coverage in children of women living with HIV

Srivastava M[1], *Lee L[1], Gleason M[1], Amzel A[1]*

[1]US Agency For International Development, Washington, United States

Introduction: Of the 1.7 million children living with HIV (CLHIV) <15 years of age at the end of 2018, only 55% were receiving antiretroviral therapy (ART). A major gap in the pediatric clinical cascade is identification of CLHIV who were missed through early infant diagnosis and routine testing services. Index testing is an important strategy to identify these "missed" CLHIV. Across PEPFAR programs, testing the biological children of women living with HIV (WLHIV) has shown high testing yield. The PEPFAR Country Operational Plan 2020 guidance recommends that 100% of biological children of WLHIV should have a documented HIV test result. In this descriptive analysis, total fertility rate (TFR) is compared to the numbers of index contact children to characterize the potential pediatric index testing gap in PEPFAR-supported countries.

Methodology: PEPFAR index testing data from 23 countries and the TFR obtained from each country's most recent Demographic and Health Surveys were analyzed. The average number of children elicited from WLHIV from October 1, 2018 to December 31, 2019 was compared to the country TFR. The index testing cascade for the 23 countries during the same time period was also analyzed by number of WLHIV assessed for index testing, number of biological children elicited, number of biological children tested and those with a positive test result.

Results: PEPFAR program data from October 1, 2018 to December 31, 2019 showed that 1,453,001 biological children were elicited from 1,898,817 WLHIV resulting in a child:WLHIV ratio of 0.77 (range 0.08 - 2.11). Of 1,453,001 children elicited, 1,165,089 were tested (80%), and of those tested, 41,813 CLHIV were identified (yield 3.6%).

For each of the 23 countries, the ratio of elicited children to WLHIV in PEPFAR programs was less than the TFR (range 2.3 - 6.6 children per woman). South Sudan had the highest number of elicited children from WLHIV at 2.1 (TFR 6.2 children per woman) with Dominican Republic being the lowest at 0.08 (TFR 4.0 children per woman).

Conclusion: When compared to the country TFR, the substantially lower number of biological children elicited from each WLHIV undergoing index testing suggests a large gap of potentially unidentified CLHIV. In addition, sub-optimal testing coverage of those children who are elicited reflects challenges to testing children even when elicited. In order to reach 95-95-95 for CLHIV, it is critical that programs understand the reasons for these gaps and prioritize interventions to increase the number of biological children elicited from all WLHIV, and that all of those children elicited have their HIV status confirmed - and, if HIV-infected, are rapidly initiated on lifesaving treatment.

53

Expand HIV Testing in Youth at an Urban Children's Hospital – Sustainable or Not?

Courville T[1], *Petru A*[1]

[1]*UCSF Benioff Children's Hospital Oakland, Oakland, United States*

Background: Despite advances in prevention and treatment, 30% of all new HIV infections globally and 21% in the United States (US) are estimated to occur among youth; however, in the US only 22% of sexually active youth report having ever been tested. Early testing, linkage to care and initiating treatment is crucial to achieve the goal of zero new transmissions. UCSF Benioff Children's Hospital Oakland (UBCHO) was one of only two pediatric sites funded by Gilead's HIV FOCUS project between 2014-2016 to develop infrastructure and create a sustainable program for routine, opt-out HIV testing in youth and increase the opportunity to decrease HIV transmission through early diagnosis and treatment initiation.

Materials and Methods: UBCHO is an urban teaching hospital in Alameda County, CA, one of the 48 highest burden US counties identified in "Ending the HIV Epidemic" campaign. Approximately 15,000 youth are seen annually at 7 sites where teens receive care: Teen Clinic, 2 school-based clinics, Primary Care clinic, Emergency Department, the Juvenile Justice Center and inpatient. Prior to 2014, testing was "opt-in" based on risk. Since 2014, opt-out testing was implemented utilizing progressively more sensitive Abbott® 3rd, 4th (2014) and 5th generation (2017) tests. A Program Coordinator (2014-2016) funded by FOCUS provided oversight, analyzed data and developed various modalities to encourage offering/testing, including: a Best Practice Advisory in the EHR, posters, newsletters, provider "report cards", incentives, and inservices. Sustainability of HIV offering and testing was analyzed over three time periods: Pre-FOCUS (2011-2013), FOCUS (2014-16) and the Sustainability Phase (2017-2019).

Results: Testing increased from an average of 17.3% Pre-Focus to 23% during the Focus years, but dropped to 13.6% in the Sustainability Phase (SP) despite average offer rates of 52% (FOCUS) and 58.6% (SP). There were 18 new infections identified in total (gender: 12 male/6 female; race/ethnicity: 17 Black/1 Latino; sexual identity 11 MSM/7 Heterosexual, ages 16-22 years of age) with more new positives identified in the Pre-FOCUS years than during FOCUS or SP (9, 7 and 2, respectively). Acute HIV infection was identified more frequently during FOCUS than in Pre-FOCUS or SP (5, 1 and 0 AHI, respectively).

Conclusions: HIV offering and testing at Children's Hospitals present unique challenges. While there were more new HIV infections identified during early study phases, maintaining a sustainable program with a dedicated coordinator is key to identification of new positives in this vulnerable age group and in the prevention of new cases through the offering of PrEP to those acknowledging risk but testing negative and providing early treatment to positives. Ongoing funding is essential to identify obstacles to testing in all clinical settings, to improve the offering and testing rates for HIV infection.

54

PK and safety of F/TAF with boosted 3rd agents in children with HIV

Castaño E[1], Deville J[2], Zuidewind P[3], Vedder J[4], German P[4], Mathias A[4], Wang H[4], Maxwell H[4], Brainard D[4], Pikora C[4]

[1]Hospital del Nino, Panama City, Panama, [2]David Geffen School of Medicine, University of California, Los Angeles, Los Angeles, United States, [3]Tygerberg Hospital, Cape Town, South Africa, [4]Gilead Sciences Inc., Foster City, United States

Background: Coformulated emtricitabine/tenofovir alafenamide (F/TAF) 200/25 mg is a preferred NRTI backbone in children ≥25 kg in the US when used with unboosted third agents. To simplify dosing for children, a single F/TAF dose is proposed for use in either boosted or unboosted antiretroviral (ARV) regimens. This applies to the adult strength tablet (200/25 mg) for ≥25 kg and the low-dose tablet (LDT) (120/15 mg) for 14-<25 kg. A previously reported PK-PD analysis in children provided support for a positive risk-benefit outcome in using a single dose with any third agent. We now report pharmacokinetics (PK), safety and efficacy of F/TAF in a limited number of children ≥6y using F/TAF with ritonavir (r) boosted atazanavir (ATV), darunavir (DRV) or lopinavir (LPV).

Methods: This study is a prospective, single-arm, open-label, 2-part, 48-week clinical trial to evaluate switching to the adult or LDT formulations of F/TAF (200/25 mg or 120/15 mg) administered once-daily in virologically suppressed children (6 to <12y) weighing ≥25 kg or 14-<25 kg, respectively. Adverse events (AEs) and laboratory tests were assessed. Bone mineral density (BMD) was measured by dual-energy X-ray absorptiometry.

Results: We enrolled 12 children; median age 10y (range 6-11y), median weight 32 kg (17.7-45.5 kg), 58% female, 50% Black, median CD4 count 1033 cells/µL. In the nine children weighing ≥25 kg (Group 1), six received LPV/r and three received DRV/r. For the three children weighing 14-<25 kg (Group 2), two received LPV/r and one ATV/r. The median (Q1, Q3) duration of exposure was 69.4 weeks (24.0, 81.0) and 47.4 weeks (9.0, 53.3) for Groups 1 and 2, respectively. No participant had a serious AE or AE leading to study drug discontinuation. At week 24, the median (Q1, Q3) change in eGFR (Schwartz formula) from baseline was -3.6 mL/min/1.73cm2 (-15.7, 19.2). The median change in spine height-age (HA)-adjusted BMD Z-score at weeks 24 and 48 was -0.03 (-0.12, 0.08) and -0.06 (-0.22, 0.04), respectively. The median change in total body less head HA-adjusted BMD Z-score at weeks 24 and 48 was -0.13 (-0.41, 0.12) and 0.07 (0.11, 0.16), respectively. Mean TAF and TFV exposures in group 1 (n=6 on LPV/r and n=1 on DRV/r) were higher than adult mean exposures but TFV exposures were 34% (Cmax) to 54% (AUCtau) lower than those in TDF-treated children 6-<12y of age from a previous study.

Conclusion: Children living with HIV receiving the weight appropriate F/TAF at both adult or LDT strengths with various boosted third agents demonstrated persistent favorable renal and bone safety profiled out to Week 48. These findings support the safety of F/TAF given at a dose predicted to be effective and safe in both boosted and unboosted ARV regimens and the continued investigation of F/TAF with boosted third agents in additional children.

55

Plasma Exposure-Viral Load Response Analysis for Dolutegravir in Children with HIV-1: Results from IMPAACT P1093

***Singh R*[2], *Acosta E*[3], *Buchanan A*[4], *Green J*[4], *Brothers C*[4], *Wiznia A*[5], *Alvero C*[6], *Farhad M*[5], *Bartlett M*[7], *Popson S*[7], *Townley E*[9], *Hazra R*[8], *George K, Ruel T*[1], *Vavro C*[4], *Baker M*[4]

[1]*UCSF Benioff Children's Hospital, San Francisco, San Francisco, USA,* [2]*GlaxoSmithKline, Collegeville , USA,* [3]*University of Alabama at Birmingham, Birmingham, USA,* [4]*ViiV Healthcare, Research Triangle Park, US,* [5] *Albert Einstein College of Medicine, The Bronx, USA,* [6]*Harvard T.H. Chan School of Public Health, Boston, USA,* [7]*Frontier Science Foundation, Boston, USA,* [8]*National Institute Child Health and Human Development, NIH, Bethesda, USA,* [9]*National Institute of Allergy andInfectious Disease, NIH, Bethesda, USA,* [10]*FHI 360, Durham, USA*

Background: The approval of antiretroviral dosing in children is generally based on matching adult pharmacokinetic exposure parameters. However, higher variability in pediatric exposures suggests that efficacy may not be presumed to be identical to that in adults. Therefore, we evaluated the relationship between dolutegravir (DTG) exposure and virologic response in children.

Methods: P1093 is a Phase I/II, open-label PK and safety study. The probability of virologic response (VR, HIV-1 RNA <50 or <400 copies/mL at Weeks 4, 24 and 48) was modelled as a function of DTG exposure (C24, Cavg or AUC0-24) based on sampling between days 5-10, weeks 4, 12 and 24; covariates included baseline viral load (VL), CD4+ count, CDC HIV infection stage and baseline VL ≥100,000 copies/mL. Logistic regression analyses were performed using NONMEM (version 7.4.3).

Results: A total of 143, 135 and 112 VL observations were available at Weeks 4, 24 and 48, respectively. DTG exposure parameters (C24, AUC0-24 and Cavg) were not predictive of VR within the dose ranges tested, suggesting that exposures were at the maximum of the exposure-response curve. This may also be attributed to small sample size per dose and higher PK variability. Graphic display of exposure-response relationships for short and long-term versus C24 demonstrate lack of correlation. Baseline VL ≥100,000 copies/mL was a significant predictor of response and associated with a lower probability of achieving a VR of HIV-1 RNA <50 copies/mL ($p<0.001$).

Conclusions: In IMPAACT P1093, a wide range of exposures (C24, AUC0-24 and Cavg) were observed at tested doses. DTG exposure metrics did not predict VL response, suggesting that the doses tested maintained exposures near maximum drug effect, while baseline VL remained a significant predictor of response. These results suggest that matching pediatric PK exposure parameters to those in adults is a reasonable approach for dose determination of DTG-containing formulations.

56

Weight trajectory in children and adolescents who switched to TAF-based regimens

***Rakhmanina N*[1], *Cunningham C*[2], *Cotton M*[3], *Natukunda E*[4], *Rodriguez C*[5], *Gaur A*[6], *Kosalaraksa P*[7], *Liberty A*[8], *Xiang S*[9], *Liu Y*[9], *Zhong L*[9], *Brainard D*[9], *Martin H*[9], *Pikora C*[9]

[1]*The George Washington University and Children's National Health System, Washington D.C., United States,* [2]*Duke University School of Medicine, Durham, United States,* [3]*Stellenbosch University, Tygerberg Academic Hospital, Cape Town, South Africa,* [4]*Joint Clinical Research Centre, Kampala, Uganda,* [5]*University of South Florida, Morsani College of Medicine, Tampa, United States,* [6]*St. Jude Children's Research Hospital, Memphis, United States,* [7]*Khon Kaen University , Khon Kaen, Thailand,* [8]*Chris Hani Baragwanath Academic Hospital, Soweto, South Africa,* [9]*Gilead Sciences Inc., Foster City, United States*

Background: The 2016 WHO estimates a ~24% prevalence of overweight and obesity among children and youth aged 5-19 years and have found increasing obesity in children globally. Weight gain with the use of antiretroviral (ARV) medications has become a focus of concern for adults living with HIV. Integrase strand transfer inhibitor (INSTI)-based regimens may also result in weight gain; however single-tablet regimens frequently include both INSTI and tenofovir alafenamide (TAF) in their co-formulation. Children, with fewer co-morbidities compared to adults, are likely to provide for a less confounded analysis when evaluating weight changes as height and weight related to growth track along standardized growth curves, potentially facilitating the understanding of the impact of individual ARV agents. We report the first evaluation of weight changes at Week (W) 48 in virologically suppressed children and adolescents switching from various ARV regimens to a TAF-based regimen.

Methods and materials: We conducted four prospective, single-arm, open-label, 48-week clinical studies (GS-US-380-1474, GS-US-311-1269, GS-US-292-0106 and GS-US-292-1515) to evaluate the safety and efficacy of switching from a suppressive multidrug regimen to either elvitegravir/cobicistat/emtricitabine/TAF (E/C/F/TAF) or bictegravir/F/TAF (B/F/TAF) or F/TAF plus a third ARV agent in children 6 to <18y weighing ≥25 kg. Weight and height were obtained at baseline and at each visit to W48. The variables of interest included demographics, Tanner stage, weight, and body mass index (BMI).

Results: We evaluated 223 participants through W48 after switching to a TAF-based regimen across the four trials. Of these participants, 43% were male, 21% were from the USA and 12% were at Tanner Stage 5. The majority (88%) switched to either B/F/TAF or E/C/F/TAF from a suppressive INSTI, non-nucleoside reverse transcriptase inhibitor (NNRTI)- or protease inhibitor (PI)-based ARV regimen. Univariate analysis showed that younger age, lower BMI percentile at baseline, female sex, and an earlier Tanner stage were all associated with an increased BMI percentile at W48. Multivariate linear regression showed that younger age, lower baseline BMI percentage, and female sex were associated with an increased BMI percentile at W48. The proportion of pediatric participants who were overweight and obese at baseline was 7% and 6%, respectively, and increased at W48 to 13% and 10%, respectively. Approximately 10% (19/193) of underweight/normal weight participants at baseline shifted to overweight at W48 and 2% (3/193) shifted to obese at W48. In a multivariate logistic regression analysis consisting of all demographic and ARV-related variables, only baseline BMI percentile was predictive of increased risk of shifting to an overweight or obese category (odds ratio 1.11, 95% CI 1.06, 1.17, p<0.001).

Conclusions: Weight gain over 48 weeks observed in these children and adolescents living with HIV who switched to TAF-based regimens were most closely associated with baseline BMI. Weight gain in this population is consistent with the 2016 WHO findings in this age group.

57

Acceptability & palatability of low dose B/F/TAF & E/C/F/TAF in children (≥2y) with HIV

Liberty A[1], *Strehlau R*[2], *Rakhmanina N*[3], *Chokephaibulkit K*[4], *Koziara J*[5], *Kaur H*[5], *Shao Y*[5], *Maxwell H*[5], *Brainard D*[5], *Pikora C*[5]

[1]*Chris Hani Baragwanath Academic Hospital, Soweto, Zimbabwe,* [2]*Empilweni Services and Research Unit, Rahima Moosa Mother and Child Hospital, Department of Paediatrics and Child Health, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa,* [3]*The George Washington University and Children's National Health System, Washington D.C., United States,* [4]*Siriraj Hospital, Mahidol University, Bangkok, Thailand,* [5]*Gilead Sciences Inc., Foster City, United States*

Background: Single-tablet regimens (STRs) offer ease of administration that optimizes adherence in adults. Previous reports of high levels of acceptability and adherence to full-strength STRs of bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) and elvitegravir/cobicistat/F/TAF (E/C/F/TAF) in children ≥6y are aligned with findings in adults. Younger children (<6y) take antiretroviral regimens consisting of multiple tablets and/or liquid medication that require meticulous dosing. Little information is available regarding adherence, acceptability, and palatability of STRs in this young pediatric population. B/F/TAF and E/C/F/TAF have been now been formulated into low-dose tablets (LDTs). We report data on acceptability, palatability, adherence, and efficacy of B/F/TAF and E/C/F/TAF LDTs in pediatric clinical trials participants ≥2y.

Methods & Materials: We conducted two prospective, single-arm, open-label, 2-part, 48-week (W) clinical studies to evaluate safety and efficacy of switching from a suppressive multidrug regimen to the LDT formulation of either B/F/TAF (30/120/15 mg, ~14x6.5 mm) or E/C/F/TAF (90/90/120/6 mg, ~16x7 mm) STR in children (≥2y) weighing 14 to <25 kg. LDTs could be split for ease of swallowability. Palatability and acceptability were assessed by investigator survey of participants and/or caregivers on product taste, size, and swallowability. Assessments were conducted at baseline, W4, W24, and W48. Efficacy (HIV-RNA analysis; Missing=Excluded) and adherence (pill counts) were assessed at each visit.

Results: Twelve children switched to B/F/TAF in Study 1; median age 6y (range 3-9y), median weight 20.1 kg, 58% female, 58% Black, all vertically infected. Twenty-seven children switched to E/C/F/TAF in Study 2; median age 6y (range 3-9y), median weight 19.3 kg, 61% female, 89% Black, 93% vertically infected.

At baseline, two and four children required split B/F/TAF and E/C/F/TAF LDTs, respectively, which declined to one child at W24 for each treatment. When taken whole, 73-86% rated tablet size "okay" from baseline to W24 for B/F/TAF and 73-86% for E/C/F/TAF. Ease of swallowing was rated "easy" to "super easy" for 64%-88% from baseline to W24 for B/F/TAF and 91-96% for E/C/F/TAF. Whether taken whole or split, 83-92% rated the taste of B/F/TAF or E/C/F/TAF "neutral/good/super good" from baseline to W24.

At W24, 12/12 participants given B/F/TAF and 16/17 given E/C/F/TAF maintained HIV-1 RNA <50 c/mL. Median (Q1, Q3) duration of exposure was 42.3 (40.1, 49.3) weeks and 24.1 (24.1, 32.1) for B/F/TAF and E/C/F/TAF, respectively. Mean (SD) study drug adherence was 97% (6%) and 97% (6%) for B/F/TAF and E/C/F/TAF, respectively. Most participants given either B/F/TAF or E/C/F/TAF had a median of ≥90% adherence. Adherence of ≥95% was observed in 10 (85%) and 23 (83%) on B/F/TAF and E/C/F/TAF, respectively.

No participant discontinued study drug due to an AE (related to palatability/acceptability or otherwise).

Conclusions: A high percentage of children ≥2y with HIV, switching from a multidrug regimen, found either B/F/TAF or E/C/F/TAF LDT acceptable and palatable. Likewise, the majority were able to maintain high rates of adherence and virologic suppression, with no LDT-related issues leading to study drug discontinuation. These findings support the patient/caregiver perceived advantages of using STRs in young children with HIV and the need for continued evaluation of novel antiretroviral drugs formulations.

58

HIV-infected treatment-experienced children and adolescents from Sub-Saharan Africa: clinical outcomes on third-line antiretroviral treatment in the New Horizons drug donation program

Tiam A[1], *Machecano R[1], Walner K[1], Namusoke-Magongo E[3], Chirwa L[4], Masaba R[5], Khumalo P[6], Lwaka C[5], Tumwebaze R[7], Mulenga L[4], Mofenson L[1], Rakhmanina N[1], Study team N[9]*

[1]Elizabeth Glaser Pediatric Aids Foundation, Washington, United States, [2]University of Bergen, Bbergen, Norway, [3]Ministry of Health, Kampala, Uganda, [4]University Teaching Hospital, Lusaka, Zambia, [5]Elizabeth Glaser Pediatric AIDS Foundation, Nairobi, Kenya, [6]Elizabeth Glaser Pediatric AIDS Foundation, Mbabane, Eswatini, [7]Elizabeth Glaser Pediatric AIDS Foundation, Kampala, Uganda, [8]Children's Hospital, Washington, USA, [9]New Horizons , Multiple cities, Multiple

Background: Viral load (VL) scale-up has highlighted significant rates of treatment failure among HIV-infected children and adolescents on ART in sub-Saharan Africa. The aim of this study was to describe virologic and immunologic characteristics of children and adolescents with treatment failure on second-line antiretroviral treatment (ART) and to describe their clinical outcomes on third-line ART.

Methods: This is an observational cohort study collecting prospective data from patients aged 0-24 years on third-line ART in Eswatini, Kenya, Uganda, and Zambia. We collected data from clinical record of patients initiated on darunavir (DRV) and/or etravirine (ETR) as part of third-line ART through the New Horizons drug donation program sponsored by Johnson & Johnson. Baseline demographic, clinical and laboratory data (CD4 cell count, HIV RNA VL, genotypic resistance) were collected at the starting point of initiating third-line ART and summarized using descriptive statistics and median (IQR).

Results: From December 2018 to November 2019, 152 participants were enrolled; 57.2% (87/152) were male; median (min-max) age at initiation of third line was 12.8 (1.3 – 21.8) years. Prior second-line ART was PI-based, including lopinavir/ritonavir in 67.1% (n=102) and atazanavir/ritonavir in 17.8% (n=27). The NRTI backbone included lamivudine plus zidovudine in 20.4%, abacavir in 53.3%, or TDF in 23.0%. Most participants with available VL assessment (85.5%; n=130/152) had elevated VL within six months prior to switching: median (min-max) VL was 4.8 log (1.3 – 6.5). Of the 123 patients with baseline resistance results, 89 (68.5%) had thymidine analog mutations (TAMs), 62.9% (n=56/89) TAM1 and 73.0% (n=65/89) TAM2 pathways. PI resistance mutations were observed in 71 (79.8%), with 70.4% (n=50/71) having accumulated >3 PI mutations. At six months on DRV/ETR based third-line ART, of the 58 participants with VL results, 72.4% (n=42/58) had viral suppression. At twelve months on third-line ART, of 36 participants with VL results, 80.6% (n=29/36) had viral suppression.

Conclusion: Treatment-experienced pediatric and adolescent patients failing a second-line PI-based ART had high level HIV viremia and high levels of NRTI thymidine analog and PI mutations. Among those patients with VL results available at 6 and 12 months on third-line ART containing DRV and/or ETR, the majority achieved virologic suppression.

59

Optimized ART regimen transition: Experiences at ICAP supported facilities in Manzini, Eswatini.

Mutiti A[1], *Nxumalo H[1], Magagula B[1], Mudekereza R[1], Kamiru H[1], Kidane A[1], Mthethwa N[2], Bongomin P[1], Tsiouris F[1]*

[1]ICAP at Columbia University, Mailman School of Public Health, New York, USA, [2]Ministry of Health Eswatini, Mbabane, Swaziland

Background: Optimal and sustained viral suppression (VS) is crucial to ensure long term HIV control among adolescents living with HIV (ALHIV). Among ALHIV attending HIV care at ICAP-supported health facilities in the Manzini region of Eswatini and receiving suboptimal non-nucleoside reverse transcriptase (NNRTI)-based ART regimens, low rates of VS have been observed. From October 2018 ICAP supported the introduction of dolutegravir (DTG) to optimize ART regimens. We describe some of the processes and potential barriers encountered during the introduction DTG-based regimens among a cohort of ALHIV.

Methods: Between October and December 2018 , we trained health care workers (HCW) at ICAP supported sites in Manzini to intiate the transition of males (including ALHIV) weighing ≥40kg and women >50 years to DTG-based regimens as per 2018 Eswatini HIV guidelines. A 2nd training on updated guidelines was held in June 2019 and included guidance for optimization of ART regimens in all populations including children and adolescent females. It also included client-centered approaches, counselling guidance on the benefits and risks of DTG and recommendations for contraception use in female ALHIV. In addition, we provided support on quantification, consumption monitoring and uptake of DTG among ALHIV. During the period October 2018 to May 2020, we reviewed the implementation of the transition guidance, related barriers and DTG uptake, using routine program data.

Results: Transition to DTG-based regimens started early in October 2018 for male ALHIV, as the initial national transition guidance had recommended transition to only males weighing ≥40kg and women >50 years if viral load (VL) >1000 copies/ml. Access to DTG among female ALHIV only started from June 2019, following an update of the 2018 Eswaini ART guidelines. During this phase, children weighing ≥20kg and those switching to second-line were put on DTG-based regimen. In addition ALHIV were transitioned to DTG -based regimens regardless of VL if on NVP-based regimen, while for those on EFV, a VL ≥200 copies/ml was the threshold for switch to DTG. ALHIV on either NVP or EFV with VL ≥ above 200 copies/ml who met the criteria for treatment failure were switched to DTG-based second-line regimen. Though access to DTG increased over time particularly from June 2019 , it was much slower among females due to health provider hesitance in prescribing DTG due to persistent concerns on DTG and neural tube defects (NTD). At the beginning of Phase I transition among a cohort of 908 ALHIV on ART, 410 (45.2%) were on EFV-based regimens, 475 (53.2%) on NVP-based and none on DTG-based regimens while 20 months into transition , 605 (66.7%) ALHIV were on DTG-based, 141 (15.5%) on EFV-based,none on NVP-based regimens and those on LPV/r and ATV/r being 83 (9.1%) and 79 (8.7%), respectively. The majority, 76.6% (108), of those remaining on NNRTI were female.

Conclusion: Our findings highlight a lengthy process in the adaptation and implementation of recommendations for DTG use among ALHIV. Continuous changing guidance, complex criteria for transitioning and incomplete information regarding NTD risk related to DTG were potential barriers to accessing optimal regimens for female ALHIV on ART.

60

Antiretroviral Drug Optimization and Viral Suppression Amongst Children and Adolescents Living with HIV in four States in Nigeria

*Oliveras E[1], Strachan M[1], **Ijaiya M[2]**, Dare B[2], Emerenini F[4], Fadare O[4], Yakubu T[4], Immanuel C[4], Anyanwu P[4], Makadi S[4], Olowu A[4], Ogundare Y[2], Atuma E[2], Obanubi C[5], Curran K[1], Fayorsey R[3]*

[1]Jhpiego, Washington, United States, [2]Jhpiego, Abuja, Nigeria, [3]ICAP at Columbia University, New York, US, [4]ICAP at Columbia University, Abuja, Nigeria, [5]United States Agency for International Development, Abuja, Nigeria

Background: Globally rates of viral suppression (VS) amongst children and adolescents living with HIV (CALHIV) lag behind adults. To improve VS, WHO recommends transition to optimal antiretroviral treatment (ART) drug regimens for children and adolescents with either a dolutegravir-based regimen (DTG) or a lopinavir/ritonavir-based regimen (LPV/r) based on weight. To rapidly scale-up the transition, the PEPFAR/USAID-funded RISE project trained and mentored prescribers, educated and sensitized clients and caregivers, and improved stock management through inter-state and intra-state re-distribution, weekly review meetings to harmonize clinic appointments with available stock, and regular clinic and supply chain interaction. This study assessed changes in VS (< 1000 copies/ml) among CALHIV in four states in Nigeria: Adamawa, Akwa Ibom, Cross River, and Niger.

Materials and Methods: We analyzed de-identified, individual patient level data from the electronic medical records of CALHIV <19 years who were active on ART between October 2019 and June 2020. We report on changes in ART regimens and VS amongst CALHIV at 90 health facilities supported by RISE in Nigeria.

Results: The number of CALHIV on ART increased from 2767 at the end of October 2019 to 3544 by June 2020. The proportion of CALHIV on optimal regimens (DTG or LPV/r-based) increased from 53% (1,591/2,766) in October 2019 to 90% (2,954/3,290) in March 2020, and 99% (3,514/3,544) in June 2020. The number of CALHIV on abacavir/ lamivudine/lopinavir/ritonavir increased from 79 to 1448, and the number on abacavir/lamivudine/dolutegravir increased from 38 to 383, while the number on tenofovir/lamivudine/dolutegravir increased from 1474 in October 2019 to 1683 in June 2020. By June, 92% (561/607) of children 0-4 years were on a LPV/r-based regimen, 64% (599/937) and 35% (326/937) of 5-9 years were on a LPV/r or DTG-based regimen, 33% (287/874) and 67% (582/874) of 10-14 years were on or LPV/r or DTG -based regimen and 98% (1,115/1,126) of 15-19 years were on a DTG-based regimen.

Viral load (VL) coverage among eligible CALHIV increased from 69% (1,402/2,030) in October 2019 to 77% (2,177/2,834) in June 2020. Among those who received a VL result, the percentage with VS increased from 57% (866/1,521) in October to 66% (1,490/2,253) in June ($p<0.001$). Rate of VS increased steadily among CALHIV on DTG-based regimens, rising from 66% (556/844) in October 2019 to 78% (824/1,057) in June 2020. VS was higher amongst older children 5-19 years at all time points and increased over time among all age groups except those under 5 years of age, where it remained at 50% (141/279) in June .VS was higher among CALHIV who newly initiated under RISE than among those who were continuing on ART (76% vs 65%, $p<0.001$) in June 2020.

Conclusion: The transition of CALHIV to optimal ART regimens has been paralleled by an increase in VL coverage and VS, except for children <5 years. As CALHIV remain on these regimens, we anticipate that suppression will continue to increase. However, there is a need to provide adherence support to

61

Optimisation of First-Line Antiretroviral Therapy (ART) for Children Living with HIV in Uganda: Translation from policy to action

***Namusoke Magongo E*[1]**, *Nabitaka V[2], Kirungi G[1], Katureebe C[1], Adler M[3], Nazziwa E[3], Nawaggi P[2], Nyamugisa Ochora E[4], Tibenderana H[5], Kasuule K[6], Lubega S[7], Musinguzi J[1]*

[1]Ministry of Health, AIDS Control Program, Kampala, Uganda, [2]Clinton Health Access Initiative, Kampala, Uganda, [3]Centers for Disease Control and Prevention, Division of Global HIV and Tuberculosis, Kampala, Uganda, [4]United Nations International Children's Emergency Fund, Kampala, Uganda, [5]United State Agency for International Development , Kampala, Uganda, [6]USAID Strategic Information Technical Support project, Kampala, Uganda, [7]Medical Access Uganda Limited, Kampala, Uganda

Background: Uganda has been optimising ART for children: in 2014 the Nucleoside Reverse Transcriptase Inhibitor (NRTI) backbone changed from Zidovudine/Lamivudine (AZT/3TC) to Abacavir/Lamivudine (ABC/3TC); introduction of Lopinavir/ritonavir pellets (LPV/r) in 2016 and Dolutegravir in 2018 for children ≥20kg. Despite these efforts, 52.2% of children aged 3-10 years were still receiving AZT/3TC/NVP(Nevirapine) as first-line ART by June 2018. The aim of the current optimisation strategy (July 2018 to date) is to transition children with viral load
< 1000 copies/ml from AZT/3TC to ABC/3TC, and Nevirapine or Efavirenz (high burden of pretreatment drug resistance) to LPV/r pellets/tablets or Dolutegravir-containing first-line ART. Children with viral load > 1000 copies/ml on Nevirapine or Efavirenz are immediately switched to second line ART without waiting for a repeat viral load result. We describe below, lessons learned during implementation of the ongoing strategy.

Description: Between June-2018 to September-2019; an optimisation checklist, line-listing tool, standard operating procedures and job aides were developed. The check-list was used to identify eligible children for optimisation at the health facilities. These were transferred to the line listing tool for tracking. Using data from the national reporting system (DHIS-2) and web-based ART ordering system (WAOS), supply chain planning was done. Weekly national planning meetings, cascaded trainings and post-training mentorships were conducted. ART optimisation indicators were incorporated into the weekly PEPFAR surge dashboard to monitor implementation.

Lessons Learned: 71% (6,085/8486) children 3months to <3 years were initiated on LPV/r pellets. Due to global shortage, 1.14% (250/21,898) children 3-<10 years were transitioned to LPV/r tablets from June 2018 to September 2019. 64.7% (6,381/9854) children < 15 years weighing ≥20 Kgs were initiated on Dolutegravir in the same period. Proportions of children on AZT/3TC backbone reduced from 76.8% to 48% by June 2019. At patient level, changing regimens comes with additional challenges such as effectively communicating changes in dosing schedules or administration procedures. A real-time reporting platform has been instrumental in monitoring the process.

Conclusions: The key barrier to ART optimisation for children was inadequate stock of antiretroviral drugs. Dispensing messages for health care workers and a caregiver literacy manual are being developed to address the communication challenges. Continuous mentorship is needed to operationalise changes in guidelines at facility level.

62

Associations of Nevirapine-based ART regimens with neuropsychological outcomes in HIV-positive children

Fairlie L*[1]**, *Chernoff M[2], Cotton M[3], Bwakura-Dangarembizi M[4], Violari A[5], Familiar-Lopez I[6], Barlow-Mosha L[7], Kamthunzi P[8], McCarthy K[9], Jean-Philippe P[10], Laughton B[3], Palumbo P[11], Boivin M[6,12,13]

[1]Wits Reproductive Health & HIV Institute, University of the Witwatersrand, School of Clinical Medicine , Johannesburg, South Africa, [2]Center for Biostatistics in AIDS Research, Harvard T.H. Chan School of Public Health. , Boston, USA , [3]Family Centre for Research with Ubuntu, Department of Paediatrics and Child Health, Tygerberg Hospital, Stellenbosch University, Tygerberg, South Africa, [4]Harare Family Care CRS, University of Zimbabwe, College of Health Sciences Clinical Trials Unit, Harare, Zimbabwe, [5]University of Witwatersrand, Chris Hani Perinatal HIV Research Unit, Soweto, Republic of South Africa, [6]Department of Psychiatry, Michigan State University, East Lansing, USA , [7]Makerere University-Johns Hopkins University Research Collaboration (MU-JHU CARE LTD) CRS , Kampala,, Uganda, [8]University of North Carolina Project–Lilongwe, Malawi CRS , Lilongwe , Malawi , [9]FHI 360 , Durham, USA , [10]National Institute of Allergy and Infectious Diseases, National Institute of Health , Rockville, USA , [11]Geisel School of Medicine at Dartmouth , Lebanon, USA, [12]Department of Neurology & Ophthalmology, Michigan State University , East Lansing, USA, [13]Department of Psychiatry, the University of Michigan , Ann Arbor, USA

Background: IMPAACT P1104s compared neuropsychological outcomes over 96 weeks in HIV-positive (HIV+) children with matched HIV unexposed (HU) and HIV-exposed uninfected (HEU) children, aged 5 to 11 years at 6 sites in Sub-Saharan Africa. Here, we explore HIV-illness related associations with neuropsychological outcomes in the HIV+ cohort.

Methods: HIV+ children had participated in IMPAACT P1060, which compared efficacy of nevirapine (NVP) versus lopinavir/ritonavir (LPV/r). 96% of eligible P1060 participants enrolled in P1104S. For P1104S, neuropsychological evaluations of KABC cognitive ability, TOVA attention-impulsivity and BOT-2 motor domains were assessed at 0, 48 and 96 weeks. In HIV+ children, clinical, antiretroviral and laboratory (immunological and virological) data from P1060 were combined with clinical and neuropsychological and caregiver data from P1104S to explore associations with neuropsychological outcomes using linear mixed-effects multivariable regression analysis, controlling for personal and caregiver characteristics. Adjusted means with 95% confidence intervals were presented.

Results: The 246 HIV+ children (45% male, mean age at P1104s entry 7.1 yrs (SD 1.2)) had median ART initiation at 15 months (IQR 8.2, 25.2), nadir CD4 count of 632 cells/mm3 (IQR 427, 874); 233 (95%) had a peak viral load >100,000 copies/ml. 164 (67%), 7 (3%) and 71 (29%) were receiving LPV/r, efavirenz (EFV)- and NVP-based ART respectively; 61% had ≥ stage 3 WHO clinical stage.

Use of NVP or EFV at P1104s study start or during follow-up were associated with lower neuropsychological scores compared to LPV/r, which persisted when controlling for nadir CD4 percent and time-varying HIV viral load. Other predictors of poorer scores in KABC domains included low birth weight, WHO stage 4 disease and serious illness history but not elevated VL on P1060 or P1104.

Conclusions: Children receiving nevirapine or efavirenz while on P1104s had poorer neuropsychological scores as assessed by the KABC, BOT-2 and TOVA than those on lopinavir/ritonavir.

63

Retention and viral suppression among child -caregiver pairs enrolled in family centered differentiated model of care in Kenya, 2019

***Mutisya I*[1]**, *Katana A[1], Omoto L[1], Masamaro K[1], Ngugi E[1], Ng'ang'a L[1]*

[1]CDC, Nairobi, Kenya

Background: The majority of HIV infected children < 15 years enrolled in care also have caregivers also living with HIV. Most clinics in Kenya give monthly clinic appointments for children for frequent follow up due to the low viral suppression in this age group. A family centered differentiated model of care with three monthly appointments for child-caregiver pairs who were virally suppressed was started in 2018. Our study evaluated the 12 month retention and viral suppression rates among child-caregiver pairs enrolled on 3 monthly clinic appointments in 6 counties in Kenya .

Methods and materials: The family centered care is a differentiated model of care for children and care givers living with HIV enrolled in care. Children who have care givers enrolled in the facility are referred to as 'paired' while those who do not have are classified as 'unpaired'. Using the national guidelines, the paired and unpaired categories are further classified as 'stable' or 'unstable'. Stable group has among other parameters are virologically suppressed at entry and do not have active comorbidities. Stable child-caregiver pairs received aligned clinic appointments, multi-month dispensing, caregiver training on support for children living with HIV (CLHIV) and family centered psychosocial support. We reviewed data for stable children0-15 years and caregivers enrolled in family centred differentiated care in 5 counties. Data were collected for the period January 1, 2019– December 31, 2019. We evaluated aggregate program data for the following; number of child-caregiver pairs with documented viral load uptake, viral suppression and 12 months retention months.

Results: The total number of children< 15 years was 2,453 and 2,258 caregivers. Viral load uptake was 97% for children and 99% for caregivers while viral suppression was 98% for both children and caregivers. Overall 12 month retention for children was 99.8% and caregivers was 99.9%. Four children and 2 caregivers were lost to follow up while 39 and 29 children and caregivers were transferred out respectively. The median frequency of clinic appointments was 3-4 in 12 months.

Conclusions: Universal retention and viral suppression is achievable for children and caregivers enrolled in family centered model of care. Pediatric HIV treatment programs should consider implementation of family- centered HIV care which substantially reduces clinic visits and has good treatment outcomes.

64

Virological failure is consistent with acquired HIV drug resistance among vertically-infected adolescents: evidence from the EDCTP-READY study.

Njume D[1,4], *Fokam J[1,2,3], Pabo W[1,5], Takou D[1], Mbuagbaw L[4], Santoro M[6], Mpouel Bala M[1,2], Tala V[1,2], Chenwi C[1,2], Beloumou G[1], Djupsa S[1], Semengue Ngoufack E[1,6,7], Nka Durand A[1,6,7], Teto G[1], Dambaya B[1], Ateba F[8], Tetang Ndiang S[9], Koki Ndombo P[2,8], Njom-Nlend A[9], Colizzi V[1,6,7], Perno C[1,6,10], Ndjolo A[1,2]*

[1]'Chantal Biya' International Reference Centre For Research On Prevention And Management Of HIV/AIDS(CIRCB), Yaoundé, Cameroon, [2]Faculty of Medicine and Biomedical Sciences, University of Yaoundé 1, Yaoundé, Cameroon, [3]National HIV Drug Resistance Group, Ministry of Public Health , Yaoundé, Cameroon, [4]Faculty of Health Sciences,University of Buea , Buea, Cameroon, [5]Faculty of Science, University of Buea, Buea, Cameroon, [6]University of Rome Tor Vergata, Rome, Italy, [7]Evangelic University of Cameroon, Bandjoun, Cameroon, [8]Mother and Child Centre of the 'Chantal BIYA' Foundation, Yaoundé, Cameroon, [9]National Social Welfare Hospital, Essos, Yaoundé, Cameroon, [10]University of Milan, Milan, Italy

Background: With recent increase uptake of antiretroviral therapy(ART) and subsequent global decrease in HIV-associated mortality, adolescents living with perinatal HIV infection (ALPHI) continue to experience persistently high mortality rates.This burden is borne more by those in Sub-Saharan Africa (SSA), particularly in the Cameroonian context. Hence, we aimed to assess response to ART, acquired HIV Drug resistance (HIVDR) and its underpinning factors among ALPHI.

Materials and methods: A cross-sectional and analytical study was conducted amongst consenting ALHIV in two reference urban paediatric centres and at the 'Chantal Biya' International Reference Centre for research on HIV prevention and management (CIRCB), Yaoundé, Cameroon. WHO clinical staging, self-reported adherence, immunological status (CD4 count) and plasma viral load (PVL) were assessed. Cases of virological failure (VF:PVL>1000copies/ml) had genotypic resistance testing performed and drug resistance mutations interpreted with Standford HIVdbv8.8. Seven early warning indicators (EWIs) for HIVDR were evaluated. Data were analysed with EpiInfo v7.2.2.6, using Chi-square or Fisher exact test (where applicable) for categorical data and Student t test for quantitative data; with a $p<0.05$ considered statistically significant.

Results: Out of 196 ALPHI, 56.1%(110) were female, median age was 16[IQR: 14-18] years, 61.7%(121) were on non-nucleoside reverse transcriptase inhibitors (NNRTI)-based regimens and 30.1%(59) were poorly adherent. Clinical failure rate (WHO-stage III/IV) was 9.2%. Median CD4 was 541[330.5-772] cells/mm3, immunological failure rate (CD4<250cells/mm3) was 15.8% and associated with late adolescence (OR=1.24 [1.03-1.50], p=0.02), female gender (p=0.04) and poor adherence (p=0.04). VF rate was 34.2% (67/196), associated with poor adherence (p=0.02) and being on NNRTI-based ART (p=0.02). HIVDR rate was 92.2%, higher with first-line ART (95.9% /OR=5.66[0.58-74.82]. By drug-class, 89.1% had NNRTI-DRMs, 78.1% NRTI-DRMs and 4.7% PI/r-DRMs; with 81.3% dual-class resistance. Using 70% acceptable efficacy threshold, the most potent drugs were tenofovir (72.0%) for NRTI and all PI/r. 12 viral strains were found (76.5% recombinants versus 23.5% pure subtypes). Following EWI, driving factors of HIVDR were delayed drug pick-up (81.7%), drug stock outs (75%) and sub-optimal viral suppression (71.1%).

Conclusion: Among Cameroonian ALPHI on ART, immunological failure is consistent with poor adherence, late age and female adolescents. However, VF is high because of a very high HIVDR rate, driven by poor adherence and being on low genetic barrier first-line ART. TDF and PI/r appear highly active for managing ART failure. Thus, a successful transition of ALPHI to adult care requires: improving drug supply, enhancing adherence to ART, use of newer innovative drugs and early detection of therapeutic failure, targeting mainly female and late age adolescents receiving first-line ART.

65

Significant life events and viral suppression outcomes in children starting antiretroviral therapy in South Africa

*Paris-Davila T[2], **Cambeiro J[3]**, Mutiti A[4], Arpadi S[4], Magashoa M[5], Rivadenieira E[6], Abrams E[4], Teasdale C[1]*

[1]CUNY Graduate School of Public Health & Health Policy, New York, United States, [2]University of North Carolina at Chapel Hill, Chapel Hill, United States, [3]Macauley Honors College of Hunter College, CUNY, New York, United States, [4]ICAP-Columbia University, New York, United States, [5]US Centers for Disease Control and Prevention (CDC), Pretoria, South Africa, [6]CDC, Atlanta, United States

Background: Viral suppression (VS) is critical for treatment success in children living with HIV (CLHIV) on antiretroviral therapy (ART). Little is known about the effect of significant life events on adherence to ART and VS outcomes in children. We examined whether specific life events, as reported by caregivers of children initiating ART in South Africa, were associated with VS outcomes in the first 12 months on treatment.

Methods: The pediatric enhanced surveillance study (PESS) enrolled CLHIV 0-12 years of age at the time they were identified as ART-eligible at five PEPFAR-supported health facilities in Eastern Cape Province, South Africa between 2012 and 2015. Children received routine HIV care per national guidelines, including viral load (VL) monitoring. Clinical and laboratory data were abstracted from medical charts. At quarterly study visits, caregivers answered questions about the occurrence over the previous three months of 10 significant life events including moving homes, new caregivers, new partners of caregivers, caregiver job loss, new siblings, and family deaths. Children who started ART and had at least one VL measure between 6 and 18 months after ART initiation were included in this analysis (VL measure closest to 12 months after ART initiation was used). Life events were analyzed individually according to whether a caregiver ever reported each event at any visit between ART initiation and the 12-month VL. We examined the relationship between ever reporting individual life events and lack of VS >50copies/mL (lower limit of detection) at 12 months on ART using univariable relative risk regression models fitted with the Poisson link function. Estimates were calculated for two age groups corresponding to first-line ART regimens, children <3 years, who were on abacavir (ABC)+lamivudine (3TC)+ lopinavir/ritonavir (LPV/r), and children ≥3 years, who were on ABC+3TC+efavirenz (EFV).

Results: Of the 397 children enrolled, 308 (77.6%) were included in the analysis; 166 (53.9%) <3 years old and 142 (46.1%) were ≥3 years old. Median age of HIV diagnosis for all children was 29.6 months (interquartile range [IQR]: 7.7-93.4) and median log VL at enrollment was 5.6 (IQR 4.9-6.3). Overall, 167 (54.2%) children achieved VS <50 copies/mL by 12 months; 65 (39.2%) children <3 years old and 102 (71.8%) children ≥3 years. The most commonly reported life events were moving into a new home (17.5% ever reported), new partner for caregiver (14.3%), caregiver lost job (13.0%), and a family death (13.0%). For children <3 years, a caregiver job loss and a caregiver having a new partner were associated with significantly greater risk of not achieving VS (Relative risk (RR): 1.46, 95% CI: 1.15-1.85; RR 1.36, 95% CI: 1.02-1.81, respectively). For children ≥3 old, a caregiver having a new partner was also associated with significantly greater risk of not achieving VS (RR 2.1, 95% CI:1.27-3.48).

Conclusions: Our data demonstrate that for CLHIV on ART, a caregiver losing a job or having a partner may be important markers of risk for not achieving viral suppression. These findings are novel and underscore the complex array of social and psychological factors influencing treatment outcomes.

66

Children newly diagnosed with HIV in the UK and Ireland between 2000 and 2018: a population- level overview

***Peters H*[1]**, Francis K[1], Crichton S[2], Judd A[2], Thorne C[1], Collins I[2]

[1]*Integrated Screening Outcomes Surveillance Service, UCL Great Ormond Street Institute of Child Health, London, United Kingdom,* [2]*MRC Clinical Trials Unit at UCL, Institute of Clinical Trials & Methodology, University College London, London, United Kingdom*

Background: In recent years, the UK/Ireland vertical HIV transmission rate has declined to <0.3% among pregnant women diagnosed with HIV. Very few transmissions to diagnosed women still occur in the UK/Ireland, with the majority of children seen for HIV care now being born to undiagnosed women or born abroad. We explore the changing characteristics of children diagnosed with HIV and seen for care in the UK/Ireland in 2000-2018 using two observational population-level surveillance datasets.

Methods: All children aged <16 years at HIV diagnosis are reported to the Integrated Screening Outcomes Surveillance Service (part of Public Health England's Infectious Diseases in Pregnancy Screening Programme) and followed up longitudinally in the Collaborative HIV Paediatric Study throughout their paediatric HIV care. Descriptive statistics summarise characteristics of 1606 children diagnosed with HIV between 2000-18 at first diagnosis in the UK and Ireland by place of birth (domestic versus abroad) and calendar year of diagnosis.

Results: Paediatric HIV diagnoses peaked at 150 in 2003-04, declining to 20-50 in 2012-18 ($p<0.001$). The proportion of children born abroad increased from 63% in 2000-04 to 73% in 2012-18 ($p<0.01$), with the majority from sub-Saharan Africa. Ninety-seven percent (1452/1497) of all children acquired HIV vertically. Median [IQR] age at HIV diagnosis declined from 2.4 years [0.3,4.9] among domestic-born children born before 2005 to 0.3 years [0.1,1.6] since 2010, versus 9.2 years [5.9, 12.3] and 3 years [2.3, 4.5] in children born abroad, respectively. The proportion of children with AIDS at diagnosis declined from 32% in 2000-04 to 12% from 2015-18 among domestic-born children, and 20% to 15% among children born abroad, respectively. Of all the children diagnosed in the whole study period (2000-2018), two-fifths were identified as having HIV following symptomatic presentation. Domestic-born children were more likely to be diagnosed following their mother's diagnosis (37% vs 12% of those born abroad, $p<0.001$); 85% of these maternal diagnoses were the result of antenatal screening (either during the pregnancy resulting in the transmission or in a subsequent pregnancy) in the UK/Ireland. Nearly half of children born abroad and a third of domestic-born children were diagnosed following HIV diagnosis of another family member in the UK/Ireland. An increasing proportion of children born abroad had already been diagnosed abroad before arrival in the UK, increasing from 9% in 2000-04 to 62% since 2015 ($p<0.001$), and 60% of those diagnosed abroad received antiretroviral therapy prior to arrival in the UK/Ireland.

Conclusions: Declines in new paediatric HIV diagnoses reflect the success of prevention of vertical transmission domestically and globally. In the UK specifically there is an uptake of over 99% of the HIV screening test in pregnancy, supported by the work of the Infectious Diseases in Pregnancy Screening Programme. An increasing proportion of children born abroad are now arriving in the UK already diagnosed and on treatment. In later calendar years, children were diagnosed at younger ages with less advanced disease stage, irrespective of place of birth. Paediatric HIV surveillance remains vital in ensuring this vulnerable population receives high quality specialist care and optimal health outcomes.

67

Trends in the prevalence of overweight and obesity among children and adolescents living with perinatally-acquired HIV in the UK and Ireland.

Byrne T[1], Collins I[2], Judd A[2], Foster C[3], Riordan A[4], Thorne C[1], Bamford A[1,2,5], Klein N[1], Turkova A[2,5], Crichton S[2], on behalf of the Collaborative HIV Paediatric Study (CHIPS) Steering Committee

[1]UCL Great Ormond Street Institute of Child Health, University College London, London, UK, [2]MRC Clinical Trials Unit, Institute of Clinical Trials & Methodology, University College London, London, UK, [3]Imperial College Healthcare NHS Trust, London, UK, [4]Alder Hey Children's NHS Foundation Trust, Liverpool, UK, [5]Great Ormond Street Hospital for Children, NHS Foundation Trust, London, UK

Introduction: Prevalence of overweight and obesity is rising in children and adolescents in the UK, increasing the risk of end organ disease. Additionally, weight gain has been associated with use of certain antiretroviral drugs/classes, although with limited paediatric data. We assessed prevalence of overweight and obesity, and associated risk factors among children and adolescents living with perinatally-acquired HIV (CLWHIV), in the UK/Irish Collaborative HIV Paediatric Study (CHIPS).

Methods: Body mass index-for-age z-scores (zBMI) were calculated for CLWHIV in follow-up to October 2019 and categorised using WHO reference data (overweight:>+1SD to ≤+2SD, obese:>+2SD). Prevalence of the combined outcome of overweight/obesity at ages 5, 10 and 15-years were estimated by sex and calendar year of measurement (<2005, 2005-2009, 2010-2014, ≥2015). These were compared to population-level prevalence at age 5 and 10-years from the National Child Measurement Programme (from 2006) and at age 15-years from the Health Survey for England (from 2015).
Multivariable logistic regression models explored risk factors for overweight/obesity at age 15, separately for males and females. These include: viral load, CD4 count, CDC disease stage, duration on ART, duration on protease inhibitors and integrase inhibitors at age 15 years, zBMI at age 10-years and a priori ethnicity, country of birth and calendar year of zBMI measurement.

Results: Of 2,171 participants ever followed in CHIPS, 1,922(88.5%) with perinatally-acquired HIV had at least 1 height/weight measurement with a total of 53,614 measurements reported during follow-up. 902(46.9%) were male and 1,509(79.1%) black-African ethnicity, median duration of follow-up was 10.5 years [IQR, 7.4-13.1]. In male CLWHIV, prevalence (95% CI) of overweight/obesity was stable across calendar years and decreased with increasing age: 34.6%(30.1-39.2%) at 5-years, 28.4%(24.9-32.1%) 10-years, 21.1%(18.5-25.0%) 15-years. In contrast, prevalence among males in the general population increased with age over the calendar period [22.9-24.0% at 5, 34.4-36.4% at 10 and 36% at 15-years].
Among female CLWHIV, prevalence of overweight/obesity at age 5 was stable over calendar years at 30.3%(26.2-34.7%), comparable to population estimates [21.3-31.1%]. The prevalence among female CLWHIV increased with age and over calendar years: at 10-years rising from 31.3%(25.2-38.0%) in 2005-2009 to 39.5%(29.2-50.7%) ≥2015); at 15-years rising from 33.9%(26.9-41.5%) 2005-2009 to 46.3%(38.8-54.0%) ≥2015. This compares to population estimates of 30.8-32.2% at 10 and 44% at 15-years.
At age 15-years, in multivariable models for males, only higher zBMI at age 10-years (aOR 8.0 (95% CI 5.3-12.1)) and later calendar year of zBMI measurement (1.1 (1.0-1.1)) were associated with overweight/obesity, and for females, only higher zBMI score at age 10-years (6.16 (4.43-8.56)).

Conclusion: Prevalence of overweight/obesity in CHIPS was highest among females at age 15 years and increased over calendar years but was comparable to the general population. The analysis was limited by the lack of reference population data matched by ethnicity. There was no evidence of association of overweight/obesity at age 15-years with HIV-related clinical status or ART drug class, although there were insufficient numbers to explore the effect of new drugs e.g. tenofovir alafenamide, and the impact of these parameters should be further explored as CLWHIV become adults.

68

Cascade of care in children and adolescents with HIV in Russian Federation

Turkova A[1], *Voronin E[3], Plotnikova Y[2], Samarina A[4], Milanzi E[1], Rozenberg V[3], Okhonskaya L[3], Latysheva I[3], Plynsky A[2], Fertikh E[4], Crichton S[1], Jackson C[1], Judd A[1], Collins I[1]*

[1]MRC Clinical Trials Unit at University College London (UCL), London, United Kingdom, [2]Irkutsk AIDS centre, Irkutsk Regional Center for the Prevention and Control of AIDS and Infectious Diseases (IOC AIDS), , Russian Federation, [3]Republican Clinical Infectious Diseases Hospital, , Russian Federation, [4]The City HIV centre, St. Petersburg City AIDS Center, , Russian Federation

Background: There are limited published data on the paediatric HIV care continuum in Russia. We explored characteristics of children and adolescents living with HIV attending paediatric HIV clinics in Russia. We adapted the UNAIDS 90-90-90 cascade of care to assess uptake of antiretroviral therapy (ART) among children/adolescents diagnosed with HIV, virological suppression and immune recovery after ART start by key age groups and calendar year of ART initiation.

Methods: Patients aged <18 years at HIV diagnosis from three Russian clinics participating in the European Pregnancy and Paediatric Infections Cohort Collaboration (EPPICC) were included. Patients were followed from first presentation to HIV care until death, loss to follow-up, transfer to adult care or last visit (data cut-off 1/10/2016). We categorised patients into two groups, those diagnosed with HIV during "childhood" (age<10), and those diagnosed during "adolescence" (age≥10). As our study denominator was patients already diagnosed, we did not measure the first "90" of the UNAIDS cascade. Instead, among those who initiated ART and were subsequently followed for ≥12 months, we summarised proportions with virological suppression (<1000 copies/mL) and good immune status (WHO none/mild immunosuppression-for-age) at 12(±3) months after ART start, by age group and calendar year of ART initiation. In addition, among patients in care in 2015/2016 with ≥12 months follow-up, we summarised proportions of patients who: (i) initiated ART, (ii) were virologically suppressed and (iii) had good immune status at time of their last visit.

Results: Of 922 patients included, 793(86%) were diagnosed in childhood, of whom 92% had perinatally acquired HIV, and 129(14%) were diagnosed in adolescence, of whom 12% had perinatally acquired HIV, 24% heterosexually-acquired, and 52% unknown mode of acquisition. 423(54%) of those diagnosed in childhood and 100(77%) diagnosed in adolescence were female, median[IQR] age at diagnosis was 1.5[0.6-2.6] and 16.7[15.8–17.3] years, respectively. Median CD4 count at diagnosis was 643[369 -1007] and 508[274-695] cells/mm3, 165/762(21%) and 23/113(20%) were late presenters (defined as WHO severe immunosuppression-for-age or AIDS at diagnosis), respectively. Median duration of follow-up from diagnosis was 6.4[3.5-9.5] and 2.4[0.8-4.3] years respectively. Overall, 36(3.9%) died (35 diagnosed in childhood, 1 in adolescence) and 16(1.7%) (all diagnosed in childhood) were lost to follow-up. 5(<1%) and 93(72%) transferred to adult care respectively. By last paediatric visit, 734(92%) and 70(54%) had initiated ART at a median age of 2.2[0.9–4.8] and 16.6[15.1–17.3] years, respectively.
In patients diagnosed in childhood who initiated ART before 2008, 33/63(52%) were virologically suppressed at 12-months, rising to 146/195(75%) among those initiating ART ≥2012 (p<0.001); 65/74(88%) and 173/192(90%) had good immune status at 12-months of ART, respectively. Most adolescents initiated ART from 2012 onwards, with no clear trends by calendar time; 13/21(62%) were virologically suppressed and 13/21(62%) had good immune status 12 months later. Among patients in care in 2015/16, 619/656(94%) diagnosed in childhood and 39/48(81%) in adolescence had initiated ART, of whom 508/619(82%) and 20/39(51%) were virologically suppressed and 568/607(94%) and 30/38(79%) had good immune status at last visit, respectively.

Conclusions: The proportion of children diagnosed aged <10 years and on ART who achieved virological suppression improved over calendar year of ART start, and the HIV care continuum shows good progress towards 90% ART initiation and virological suppression UNAIDS targets. A lower proportion of those diagnosed in adolescence initiated ART and were virologically suppressed, emphasising need for targeted support towards ART initiation to achieve the targets.

Abstract 69 is withdrawn

70

"HIV is the easy part": A qualitative study on perceived biopsychosocial needs among U.S. parents who have internationally adopted children living with HIV

Fair C[1], Olivero R[2], Crowell C[3], Bryant Y[4], Piper M[5], Alger S[6], Bingaman A[7]

[1]Elon University, Elon, United States, [2]Helen DeVos Children's Hospital of Spectrum Health, Grand Rapids, United States, [3]Seattle Children's Hospital, Seatlle, United States, [4]Children's National Health Center, Washington, United States, [5]Brown School, Washington St. Louis University, St. Louis, United States, [6]George Washington University, Washington, United States, [7]Research Triangle Institute, Cary, United States

Background: An increasing number of U.S. families seek to adopt children born with HIV outside the country. This study explored parental views of adoptees' biological, psychological, and social factors that influence their child's well-being, commonly known as biopsychosocial needs.

Methods: We conducted 60-minute, semi-structured, audio-recorded interviews with a purposive snowball sample of 44 parents (43 mothers) of 51 internationally adopted children with living HIV (IACH) recruited from three U.S. pediatric infectious diseases clinics, as well as several closed FaceBook groups for adoptive parents. Interview questions explored adoption-related experiences and their child's biopsychosocial needs. Transcripts were coded for emergent themes.

Results: All parents identified as white (mean age 37.3 years, from 12 states) and 38 (86%) as Christian. Few were familiar with HIV prior to adoption. Mean age of adoptees at enrollment was 8.1 years (range 3-19); 33 (65%) were females, 33 (65%) were from African countries. Few serious medical concerns were noted; the most common included hearing issues, vitamin D deficiency, and short stature. Many participants indicated, "HIV is no big deal" and few struggled with ART adherence. All children were on ART and 49 (96%) were virally suppressed. Adoption-related issues related to perceived inadequate pre-adoption care, trauma, and language barriers took precedence over HIV-related medical issues. Associated psychosocial problems included attention deficit disorder, learning disability, and reactive attachment disorder. One parent stated, "I would say that she brought home more orphanage or institutional behaviors that we needed to address than HIV. I just told someone the other day her HIV diagnosis was one of the easiest parts of adopting her." Participants described the initial challenges that IACH experienced due to cultural differences between their country of origin and their new home. Concerns around disclosing HIV status to the child and others were common. Parents sought to protect their child from HIV-related stigma by carefully limiting disclosure to those within immediate family. They also worked to build their child's self-confidence and offered ways to manage questions that might come up related to their diagnosis. Several parents described role playing with their child to practice answering questions about their medication or illness. To avoid accidental disclosure several had medications mailed to the home rather than filled at their local pharmacy. The majority of participants received emotional and/or financial support from family, and reported that they were well-connected to medical care. Most participants reported anticipating challenges during adolescence related to sexuality and disclosure.

Conclusions: Serious medical issues relating to HIV were not common. However, adjustment and attachment issues emerged as pressing concerns, highlighting the importance of behavioral health treatment for IACH. Parents of IACH could benefit from collaborating with medical and mental health providers around issues of disclosure.

71

Measuring Symptoms of Depression, Anxiety, and PTSD among Children and Adolescents Living with and Affected by HIV in Sub-Saharan Africa: A Systematic Review

McCoy B[1,2], McAteer C[2,3], Sang F[2,4], Nyandiko W[2,4], Vreeman R[1,2,4]

[1]The Arnhold Institute for Global Health, Icahn School of Medicine at Mount Sinai, New York, United States, [2]Academic Model Providing Access to Healthcare (AMPATH), Eldoret, Kenya, [3]Department of Pediatrics, Indiana University School of Medicine, Indianapolis, United States, [4]Department of Child Health and Paediatrics, College of Health Sciences, Moi University School of Medicine, Eldoret, Kenya

Background: Children and adolescents living with and affected by HIV face unique mental health and psychosocial challenges. This systematic review sought to identify which tools measuring symptoms of depression, anxiety, and PTSD have been used in studies of children and adolescents living with and affected by HIV in sub-Saharan Africa and to evaluate tool quality in terms of cultural adaptation and validation within these populations. We hypothesized that few of the identified tools would be adapted for and validated in the populations they were being used.

Materials and Methods: Online bibliographic databases, including MEDLINE, EMBASE, and PsycINFO, were searched on July 31, 2019 using the following search strategy: ("HIV" or "HIV infections") and [("depression," "depressive disorder," "mood disorder," "anxiety," "anxiety disorders," "stress disorders, post-traumatic," or "quality of life"), "psychometrics," or [("depression," "depressive disorders," "mood disorders," "anxiety," "anxiety disorders," "stress disorders, post-traumatic," or "quality of life") and ("mass screening" or "surveys and questionnaires")]] and "Africa". The bibliographies of identified articles and reviews were also examined. Two reviewers selected articles validating or using quantitative tools measuring symptoms of depression, anxiety, or PTSD among children and adolescents (ages 0-19 years) living with and affected by HIV in sub-Saharan Africa. Articles on the same study sample using the same quantitative measures were counted only once within our results. Data were extracted from the selected articles regarding the sample characteristics, study setting, measurement strategy, and cultural adaptation. In addition, we evaluated the quality of the measures identified using the Terwee quality criteria tool.

Results: Searches returned 1971 unique articles, of which 27 met inclusion criteria. Eight sub-Saharan African countries were represented among the included articles with South Africa being the most common study site. Study samples ranged in age from 2 to 19 years. Twenty-five of the included studies used a measure of depression with the Children's Depression Inventory being the most frequently used tool. Of the seven identified articles describing use of a measure of anxiety and seven describing use of a measure of PTSD, the most frequently employed measures were the Children's Manifest Anxiety Scale-Revised and the Child PTSD Checklist, respectively. Two studies sought to validate measures of depression – the Beck Depression Inventory-II and versions of the Children's Depression Inventory. We did not identify any article describing the validation of a measure of anxiety or PTSD symptoms which met inclusion criteria. Few of the included studies culturally adapted their measure(s) beyond translation prior to use. Even fewer met criteria for a positive rating on any domain of the Terwee quality criteria tool.

Conclusions: Despite the burden of HIV and comorbid mental health problems among children and adolescents in sub-Saharan Africa, few standardized, adapted measures of common mental health conditions have been developed and used. Further work to adapt and validate measures of mental health conditions in these populations is desperately needed to better characterize the mental health challenges faced by youth and inform the development of mental health interventions for these populations.

72

Disclosure to South African children about their own HIV status over time

***Wu M*[1]**, Shiau S[2], Strehlau R[3], Liberty A[4], Patel F[3], Burke M[3], Murnane P[5], Violari A[4], Kuhn L[1,6], Arpadi S[1,6,7]

[1]Department of Epidemiology, Mailman School of Public Health, Columbia University, New York, United States, [2]Department of Biostatistics and Epidemiology, Rutgers School of Public Health, Piscataway, United States, [3]Empilweni Services and Research Unit, Rahima Moosa Mother and Child Hospital, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa, [4]Perinatal HIV Research Unit, Chris Hani Baragwanath Hospital, University of the Witwatersrand, Johannesburg, South Africa, [5]Department of Epidemiology & Biostatistics, University of California, San Francisco, San Francisco, United States, [6]Gertrude H. Sergievsky Center, College of Physicians and Surgeons, Columbia University, New York, United States, [7]Department of Pediatrics, College of Physicians and Surgeons, Columbia University, New York, United States

Background: Disclosure of HIV infection to children about their own status is essential for HIV treatment adherence and prevention of transmission. In a prior cross-sectional study, we reported that only 9% of children ages 4–9 years living with perinatally-acquired HIV (CHIV) in Johannesburg, South Africa had been told their diagnosis. This study aims to assess the extent of pediatric disclosure over time.

Materials and Methods: From February 2013 through April 2018, 548 CHIV ages 4–9 years were followed in a longitudinal cohort study at two sites in Johannesburg, South Africa: Rahima Moosa Mother and Child Hospital's Empilweni Services and Research Unit and Chris Hani Baragwanath Hospital's Perinatal HIV Research Unit. At each visit, caregivers were asked whether the child had been told their HIV positive status (i.e., full disclosure). Cumulative incidence of disclosure among the entire study sample and by baseline child and caregiver characteristics were calculated with Kaplan-Meier analysis. Clinically important or statistically significant characteristics ($p<0.05$) were included in a multivariable Cox regression model to evaluate predictors of pediatric disclosure among children undisclosed to at baseline (n=498).

Results: By the end of follow-up, 303 of 548 caregivers had reported their child receiving full disclosure. Mean length of follow-up was 2.9 years (standard deviation 1.4). Overall cumulative incidence of first-time disclosure was 70.3% (95% confidence interval [CI]: 60.0, 79.9). Disclosure incidence was 13.5% (95% CI: 10.9, 16.7), 21.2% (95% CI: 18.0, 24.9), 37.9% (95% CI: 33.9, 42.2), and 55.0% (95% CI: 50.6, 59.5) at 1, 2, 3, and 4 years post-enrollment, respectively. The log-rank test was statistically significant for child age at enrollment ($p<0.0001$), child sex ($p=0.0157$), study site ($p<0.0001$), and whether the child's mother was alive at enrollment ($p=0.0425$). In addition to these variables, disclosure to someone at the child's school or crèche was added to the Cox regression model. Predictors of disclosure included child age ($p<0.0001$), child sex ($p=0.0351$), and someone at school or crèche knowing the child's HIV status ($p=0.0102$). Girls had 1.4 times the adjusted hazard of receiving disclosure versus boys. Compared with children ages 4–5, children age 6 had 3.0 times, children age 7 had 6.7 times, and children ages 8–9 had 7.8 times the adjusted hazard of receiving disclosure. Finally, children for whom their HIV status was reportedly known at school or crèche had 1.4 times the adjusted hazard of receiving disclosure versus children for whom their HIV status was reportedly unknown.

Conclusions: In a longitudinal cohort of CHIV in South Africa, cumulative incidence of pediatric disclosure per the Kaplan-Meier method was approximately 70% by the end of follow-up. Girls, older children, and children whose HIV status had been disclosed to someone at school or crèche experienced higher hazard of pediatric disclosure. It is important that healthcare professionals encourage age-appropriate disclosure as early as possible, support families during the disclosure process, and provide psychological and emotional support for CHIV who learn of their HIV diagnosis.

73

Trends in clinical and socio-demographic characteristics of HIV-positive children up to 10 years of age at enrollment in CA-IeDEA sites

*Kim H[4], Zivich P[2,3], **Twizere C[1]**, Shi Q[4], Brazier E[5,6], Hoover D[7], Adedimeji A[8], Bukuru H[9], Niyongabo T[1,9], Lelo P[11], Nsonde D[12], Nash D[5,6], Anastos K[8,13], Yotebieng M[13]*

[1]Centre National de Réference en matière de VIH/SIDA Burundi, Bujumbura, Burundi, [2]Department of Epidemiology, Gillings School of Public Health, University of North Carolina at Chapel Hill, Chapel Hill, USA, [3]Carolina Population Center, University of North Carolina at Chapel Hill, Chapel Hill, USA, [4]Department of Public Health, School of Health Sciences and Practice, New York Medical College,, Valhalla, USA, [5]City University of New York, Institute for Implementation Science in Population Health (ISPH)New York, New York, USA, [6]City University of New York, Graduate School of Public Health and Healthy Policy, New York, USA, [7]Department of Statistics and Institute for Health Care Policy and Aging Research, Rutgers The State University of New Jersey, Rutgers, USA, [8]Department of Epidemiology and Population Health, Albert Einstein College of Medicine/Montefiore Medical Center, Bronx, USA, [9]CHUK/Burundi National Univers, Bujumbura , Burundi, [10]Division of Clinical Education, Rwanda Military Hospital,, Kanombe, Kigali, Rwanda, [11]Pediatric Hospital Kalembe Lembe,, Lingwala, Kinshasa, Democratic Republic of Congo, [12]CTA Brazzaville, Brazzaville, Republic of Congo , [13]Department of Medicine,Albert Einstein College of Medicine, Bronx,, USA

Background: For over a decade, the World Health Organization (WHO) has recommended that all infants born to women living with HIV be tested for HIV ideally between the ages of 4-6 weeks, and those found to be HIV infected initiate ART immediately. To assess progress in the timely diagnosis and enrollment in care of children living with HIV (CLHIV), we examined the trends in clinical and socio-demographic characteristics at time of enrollment into the HIV care at the clinics that participate in Central Africa International epidemiology Database to Evaluate AIDS (CA-IeDEA).

Methods: Children ≤ 10 years old enrolled at time of enrollment into HIV care in four of the five CA-IeDEA participating countries were eligible for inclusion. The primary outcome variables of interest include: age, weight-for-age (WAZ), height/length-for-age Z score (HAZ), and WHO-defined immunological suppression at enrollment into care at the IeDEA site.

Results: Between 2007-2018, 4,446 children ≤10 years old were enrolled at CA-IeDEA participating sites. Of those, 3,078 children were included in this analysis (36.7% from DRC, 36.6% from Rwanda ,13.5% from Burundi and 13.1% from ROC). The mean age (SD) decreased from 57.3(months in 2007 to 28.0 (months in 2018 with huge variation among countries: a decrease from 62.3(and 63.0 (months in 2007 to 11.2 (and 30.4 (months in 2018, respectively, in Rwanda and ROC; an initial monotonic decrease from 51.9 (months to 18.2 (months in 2015 before increasing back to 50.6 (months in 2018 in DRC and monotonous increase in Burundi from 32.9 (in 2008 to 64.3 (months in 2018. Similar but less pronounced trends were observed for WAZ, HAZ, and WHO immunological suppression.

Conclusions: Despite the WHO recommendations on early infant diagnosis of HIV-exposed infants, the mean age at enrollment in care for HIV-infected children in 2018 was more than 30 months in all countries other than Rwanda. These results indicate a need for further efforts to optimize the Early Infant Diagnosis services across the region.

74

Mental health management integration into adolescent HIV treatment services in Bangkok, Thailand

Songtaweesin W[1], Thisayakorn P[2], Saisaengjan C[1], Pholphet K[1], Nadsasarn R[1], Lonhin S[1], Deeklum P[1], Kawichai S[1], Puthanakit T[1,3]

[1]Center of Excellence for Pediatric Infectious Diseases and Vaccines, Chulalongkorn University, Bangkok, Thailand, [2]Department of Psychiatry, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand, [3]Department of Pediatrics, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand

Background: In response to recent calls by the World Health Organization to integrate mental health care to routine health services, we conducted a study on the feasibility of this in our adolescent HIV services. This study aimed to describe the occurrence of mental health disorders (MHDs), focusing on depression and suicidal attempts among Thai adolescents living with HIV (ALHIV).

Materials and Methods: A study was conducted among a cohort of adolescents living with HIV (ALHIV) aged between 15-26 years attending adolescent HIV services at King Chulalongkorn Memorial Hospital. Integrated mental health services were provided in the form of general assessment by pediatricians and psychologists. If an MHD was clinically suspected, referral to a psychiatrist was made for diagnosis and management, which included emergency management for suicidal attempts. MHDs were diagnosed by a psychiatrist using DSM-IV criteria. A cross-sectional data analysis was conducted.

Results: From July 2017 to June 2020, 346 ALHIV were followed-up in adolescent services with a median age of 18.7 (IQR 17.1-21.3) years, 278 (80%) had perinatally-acquired HIV (PHIV) and 68 (20%) horizontally-acquired HIV (HHIV). Thirty-four ALHIV (21 PHIV and 13 HHIV) had psychiatrist-confirmed MHDs, including major depressive disorder (n=27), post-traumatic stress disorder(n=3), bipolar disorder (n=2), and anxiety disorders(n=2). Median (IQR) age at diagnosis of MHDs was 21.5 (19.1-23.4) years. There were 11 men who have sex with men (MSM), 3 transgender women (TGW), 13 cisgender females and 7 cisgender males. MHDs were seen in 21 (7.6%, 95% CI 4.4-10.7) of those with PHIV and 13 (19.1%, 95%CI 9.8-28.5) of those with HHIV (p=0.004). Compared to cisgender males, after adjustment for HIV acquisition route, there was a trend of cisgender females being at higher risk of MHDs (aOR 2.23 (95%CI 0.9-5.8). MSM and TGW were 4.4 (95%CI 1.1-17.2) and 9.3 (95%CI 1.8-48.4) times more likely to have MHDs respectively. Among the 34 adolescents with MHDs, 3 had suicidal ideation with no attempts made and 10 actually attempted suicide (4 drug overdoses, 4 wrist cuttings, 1 hanging, 1 jumping off a building). Suicidal attempts were more common among HHIV 62% (8/13) compared to PHIV 9.5% (2/21) (p=0.001). The median follow-up time for those with MHDs linked to psychiatric care was 15.2 (IQR 3.9-28.1) months. Three quarters 25/34 (73.5%) had improvement or resolution in their MHDs after treatment.

Conclusions: Approximately 12% of ALHIV had psychiatrist-confirmed MHDs, which was was 4-9 times more likely in MSM and TGW compared to cisgender patients, possibly due to the double-stigma they experience of both HIV and gender stigma. Those with HHIV are more at risk of committing suicide compared to PHIV. Mental health emergency service plans are essential, particularly for suicide management which should incorporated into staff training for adolescent HIV services.

75

The Outcomes of Transition from Pediatrics to Adult Care among Adolescents and Young Adults with HIV at a Tertiary Care Center in Bangkok

***Rungmaitree S*[1]**, *Thamniamdee N*[1], *Phongsamart W*[1], *Lapphra K*[1], *Wittawatmongkol O*[1], *Maleesatharn A*[1], *Chokephaibulkit K*[1,2]

[1]*Department of Pediatrics, Siriraj Hospital Mahidol University, Bangkok, Thailand,* [2]*Siriraj Institute of Clinical Research, Bangkok, Thailand*

Background: Adolescents and young adults with HIV (AYHIV) are at relatively higher risk of loss to follow up and treatment failure. Transitioning grown-up perinatally HIV-infected individuals from pediatric to adult care is challenging.

Materials and Methods: We reviewed the medical records of AYHIV who were transferred from pediatric to adult HIV clinic for at least 1 year between December 1, 2011- November 30, 2017. Demographic and clinical data including CD4 cell count, viral load, antiretroviral (ARV) regimen and viral resistance at the most recent pediatric clinic visit before and at 1, and 2 years following transition were collected. The outcomes evaluated were rate of retention in care and viral suppression (< 40 copies/mL). Multivariate analysis was used to evaluate factors associated with viral suppression.

Results: Of 101 AYHIV who were transferred, 97% were perinatal infection, 54% were female, median age at transition was 20 (range 15-24) years old, 50% were transferred to adult clinic in the study center. Before transition, 69% had viral suppression and 51% were receiving protease inhibitor (PI) based ARV regimen. At 1 year of transition, 92.1% retained in care and 71.1% had viral suppression. The respective rates at 2 years following transition, 88.0% and 76.7% were retained in care and had viral suppression, respectively. Factors associated with viral suppression are transition age 20 years or older (odd ratio [OR] 4.38, 95% confidential interval [CI] 1.41-13.65; p=0.011) and receiving non-nucleoside reverse transcriptase inhibitor (NNRTI) based regimens (OR 6.05, 95% CI 1.55 - 23.58; p=0.010) which was the first-line treatment regimens in these AYHIV.

Conclusion: Transition from pediatric to adult clinic was found more successful when occurring after 20 years old of age. The AYHIV who never had treatment failure before transition were more likely to achieve viral suppression after transition underscores the importance of adherence supports in the pediatric clinic.

76

Peer-supported community-based HIV self-testing is highly acceptable to Adolescents and Young Adults in Nairobi, Kenya.

Lapsley R[1], *Beima-Sofie K[1], Moraa H[2], Manyeki V[2], Inwani I[2], Mungwala C[2], Kohler P[1,3], Simoni J[1,4], McClelland R[1,5,6], Farquhar C[1], Wilson K[1]*

[1]Department of Global Health, University of Washington, Seattle, United States, [2]University of Nairobi/Kenyatta National Hospital, Nairobi, Kenya, [3]Department of Child, Family, and Population Health, Nursing, University of Washington, Seattle, United States, [4]Department of Psychology, University of Washington , Seattle, United States, [5]Department of Epidemiology, University of Washington, Seattle, United States, [6]Department of Medicine, University of Washington, Seattle, United States

Background: Adolescents and young adults (AYA) have lower rates of HIV testing compared to adults in sub-Saharan Africa. Traditional facility-based HIV testing services (HTS) have not fully engaged AYA, nor been designed to meet their needs. Community-based delivery of oral HIV self-testing (HIVST) has been shown in limited settings to be a promising approach that may increase testing uptake for AYA. Understanding experiences of AYA who have used HIVST in a real world setting is important to tailor and optimize this alternative approach in resource-limited settings and improve overall AYA testing and treatment goals. This qualitative study explored experiences and recommendations for future HIVST services among AYA in Kenya.

Methods: This qualitative study was nested in a prospective cohort study evaluating uptake and completion of oral HIVST in Nairobi, Kenya. Eligible AYA were 15-24 and recruited through three community-based distribution channels: homes, pharmacies, and 'hotspots' (bars/nightclubs), by teams of local peer educators and HIV Testing Services (HTS) counselors. We conducted nine focus group discussions (FGDs) stratified by channel (three groups per channel), and age (15-17, 18-24). FGD participants were recruited from the parent cohort after completing HIVST (all confirmed HIV negative) and a 4 month follow-up survey. All FGDs were mixed gender, audio recorded, transcribed, and translated into English when necessary. Thematic content analysis by two independent coders was used to identify HIVST experiences, influences on behavior, and future testing preferences.

Results: Of 61 AYA participants, 66% were female and 72% were 18-24 years old; 31% had "steady" partners, 25% had "casual" partners, and 42% were "single". Participants valued HIVST because it promoted AYA autonomy, was more convenient than clinic based (HTS), and avoided possible perceived judgement from health care workers during standard HTS. AYA appreciated that they could self-test when, where, and with whomever they wanted. In addition, several AYA reported that self-testing experience gave them confidence to test again, and promoted positive behavior change including greater use of condoms during sex to remain HIV-negative. Negative tests were also powerful motivators for AYA engaged in transactional sex to negotiate condom use with clients. When asked about future HIVST preferences, AYA wanted access to individualized, ongoing professional support during and after testing, including post-test counseling and linkage to care. Specifically, AYA wanted to have multiple options to obtain this support, including in-person and via social media. They also requested multiple venues to access HIVST, including bars, pharmacies, and youth centers. Participants wanted trained peers to be involved in all aspects of HIVST. AYA felt that peers could relate to them and were uniquely qualified to encourage and distribute HIVST to AYA, as well as assist in linking to care or prevention services.

Conclusions: Peer-supported, community-based delivery of HIVST is highly acceptable to AYA because it provides convenient and autonomous testing experiences with the potential to reinforce HIV prevention behaviors. Future community-based HIVST programs should include multiple distribution points and trained peer educators in all steps of distribution, testing, and follow-up to optimize this testing strategy.

77

The Provision of School-based Support for Adolescents and Youth Living with HIV in Boarding Schools in Homa Bay and Turkana, Kenya: The Red Carpet Program

Akuno J[1], Simiyu R[1], Akello Okoth E[1], Kose J[2], Lenz C[3], Rakhmanina N[3]

[1]Elizabeth Glaser Pediatric AIDS Foundation, , Kenya, [2]EGPAF Global , , Kenya, [3]EGPAF Global, Washington D.C., United States

Introduction: Adolescents and youth spend a significant amount of time at school, especially boarding schools, where they reside away from their families and communities for 9 months of the year. In schools, adolescents and youth living with HIV (AYLHIV) encounter factors that can enhance or hinder their treatment success. The Elizabeth Glaser Pediatric AIDS Foundation (EGPAF), funded by the ViiV Positive Action Fund, implemented a comprehensive tailored intervention in Kenya, the Red Carpet Program (RCP). The broader package focused on improving linkage to HIV treatment, adherence, and retention in care, with the school-based activities concentrated primarily on the provision of adherence and retention support.

Methods: EGPAF implemented this boarding school-based RCP initiative in coordination with the Ministry of Education and the Ministry of Health, targeting learners who are AYLHIV in 87 schools in Homa Bay and Turkana Counties from March 2016 to September 2019. Elements of RCP support in schools included the provision of psychosocial support; the establishment of bi-directional linkages with healthcare facilities; capacity building and sensitization sessions for school staff, parents, and adolescent advocates on HIV support; HIV/SRH education; and stigma reduction. The strengthening and integration of MOE structures, including the multi-disciplinary school health committee and facility/sub-county adolescent youth peer advisory groups supported the design and implementation of the school-based activities with RCP focal persons. Trained and sensitized school staff supported AYLHIV to receive treatment literacy education and counseling as well as disclosure and adherence support, such as private storage space, monitored refills, and support focused on positive living and avoiding treatment disruptions.

Results: By the end of project year three, all 87 schools had established a bi-directional linkage with 66 health facilities to support AYLHIV. A total of 561 school managers were sensitized, 476 adolescent advocates received capacity building training. Sensitized managers committed to the development of creating HIV responsive environments in line with the RCP response school criteria. At the end of PY3, 63 schools had implemented school health committees, adherence counselling, confidential storage, and access to HIV medication for AYLHIV. At the end of PY2, over 33,000 learners – both HIV positive and negative, had been reached with HIV education, including information on PrEP and SHR, and anti-stigma interventions at participating schools. 546 AYLHIV disclosed their status to a sensitized school representative and subsequently received treatment and adherence support. By September 2019, the overall suppression rate among AYLHIV in RCP facilities was 87% for younger adolescents (10-14 years), 90% for older adolescents (15-19 years).

Conclusion: RCP school-based interventions highlight the effectiveness and feasibility of providing boarding school-based support for AYLHIV and integrating adherence support at boarding schools. Increases in disclosure and use of adherence and PSS initiatives by AYLHIV underlines the acceptability and need for this type of support. Approaches to tackle stigma in schools and provide holistic support remain priority areas and gaps for all AYLHIV.

78

Perceived Social Support among Adolescents and Young Adults Living with HIV

***Neary J*[1]**, *Beima-Sofie K[1], Dyer J[1], Agot K[2], Wilson K[1], Bosire R[2], Badia J[2], Kibugi J[2], Shah S[3], Inwani I[2], Kohler P[1], John-Stewart G[1]*

[1]University of Washington, Seattle, United States, [2]Impact Research and Development Organization, Kisumu, Kenya, [3]Northwestern University Medical School/Bioethics Program at Lurie Children's Hospital, Chicago, United States

Background: Adolescents and young adults living with HIV (ALHIV) have poorer retention in care and medication adherence than adults. Social support among ALHIV is not well characterized and may influence medication adherence, engagement in care, and clinical outcomes.

Methods: The Data-informed Stepped Care to Improve Adolescent Outcomes (DiSC) cohort includes ALHIV 10-24 years receiving HIV care at nine health facilities in Western Kenya. The 12-item Multidimensional Scale of Perceived Social Support (MSPSS) was used to assess perceived social support from family, friends, and significant others (4 items each). Response options for each item were on a 5-point Likert-type scale. Means and t-tests were used to compare older (15-24 years) and younger (10-14 years) ALHIV.

Results: Among 1,144 ALHIV, median age was 17 years (interquartile range: 14-20); 26% were younger (10-14 years) and 74% were older (15-24 years). Thirty-four percent were male and 70% were enrolled in school. The overall mean MSPSS score was 3.46 (range: 1-5; standard deviation [SD]=0.61); 3.86 (SD=0.79) for family, 3.34 (SD=0.94) for friends, 3.24 (SD=1.13) for significant other subscales.
Mean MSPSS scores did not differ between males and females. Compared to younger ALHIV (mean overall MSPSS: 3.28), older ALHIV had higher mean overall MSPSS scores (3.53; $p<0.001$). Compared to older ALHIV, younger ALHIV reported higher perceived family support (3.96 vs. 3.82; $p=0.010$) but lower friend (3.23 vs. 3.37; $p=0.019$) and significant other support (2.59 vs. 3.47; $p<0.001$).
School enrollment was associated with higher mean MSPSS scores among ALHIV 20-24 years (3.79 vs 3.55; $p=0.004$), driven by more support from friends and family. Secondary and college education was associated with higher MSPSS scores among ALHIV 15-24 years compared to primary education (3.64 and 3.83 vs. 3.37, respectively; $p<0.001$ for both).
MSPSS scores were associated with resilience scores in ALHIV (β: 0.083; $p<0.001$ after adjusting for age), and were not associated with depression.

Conclusions: Older, educated, and more resilient ALHIV have higher perceived social support. While family support is higher in younger than older ALHIV; as ALHIV age, friends play a critical role in providing support. Leveraging social support or addressing under-supported ALHIV could improve ALHIV health outcomes.

79

Improving pediatric and adolescent HIV services through integrated peer support: A case of the Young People and Adolescent Peer Support (YAPS) Model in Uganda

Chimulwa T[1], Kabanda J[2], Nazziwa E[2], Lukabwe I[1], Magongo E[1], Nawaggi P[3], Ricotta A[4], Willis N[4], Musinguzi J[1], Katureebe C[1], Nasaba R[5]

[1]Ministry of Health, Kampala, Uganda, [2]Centers for Disease Control and Prevention, Uganda, Entebbe, Uganda, [3]Clinton Health Access Initiative, Kampala, Uganda, [4]AFRICAID-Zvandiri, Harare, Zimbabwe, [5]Catholic Relief Services Uganda, , Uganda

Background: Outcomes of viral load suppression and retention among Adolescents and Young people (AYP) living with HIV continue to lag behind worldwide. In December 2017, the performance against targets for Uganda's clinical care cascade for adolescents and young people (AYP) was poor where 74.3% of the identified AYP positives were linked to treatment, 53.5% retained in care and only 73% virally suppressed. To address these gaps, in 2018, Uganda with her partners conducted a bench marking visit to Zimbabwe to learn of Zvandiri CATS model and eventually designed the young people and adolescent peer support (YAPS) model. We share the adaptation processes and preliminary results from the pilot.

Description: With technical assistance from Africaid, Uganda developed necessary tools and materials including: implementation strategy; training manuals; standard operating procedures for the YAPS, a robust monitoring and evaluation plan; and reporting systems. In July 2019, the model was piloted in selected 48 PEPFAR supported health facilities (HFs) located in 9 districts. In this model, the districts identify and train selected YAPS aged 18-24 years to provide care and support services to their peers across the 95-95-95 cascade at both facility and communities. The YAPS are supervised and mentored by the HF staff

Lessons learned: Between July 2019 and March 2020, a total of 83,200 and 43,056 AYP had received health education and pre-test counseling respectively. Up to 69.8% tested for HIV with a positive yield of 3.6%. Out of the positives, 96.1% were linked to care and started ART. The YAPS brought back 72.2% of all AYPs that had disengaged from Care and made 113,378 referrals to other services. When AYP are well selected, trained, supervised and mentored, they are capable of making significant contributions to the 95-95-95 cascade for their peers. Key success factors included having full government leadership and meaningful involvement of young people throughout the adaptation and implementation stages of the program.

Conclusion: Preliminary results demonstrate the importance of institutionalized peer support in improving HIV care services and outcomes for AYP living with HIV. The lessons learned will be vital in informing the national scale up of the model.

80

Improving Identification of Sexually Transmitted Infections (STIs) among Youth Living with HIV

Koay W[1,2], *Richards K[1], Griffith C[1], Fortuna G[1], Ferrer K[1,2], Meyers J[1], Williams T[1], Rakhmanina N[1,2,3]*

[1]Children's National Hospital, Washington, United States, [2]George Washington University, Washington, United States, [3]Elizabeth Glaser Pediatric AIDS Foundation, Washington, United States

Background: Sexually transmitted infections (STIs) are a major public health problem in the United States, with a high burden among youth living in Washington, DC, one of the national "hotspots" of the HIV epidemic. Genital testing (i.e.: urine) is recommended for routine STI screening in the US, and extragenital STI testing (i.e.: pharyngeal and rectal) is recommended by the Centers for Disease Control and Prevention only for men who have sex with men (MSM). To improve diagnostics for STIs in youth living with HIV (YLHIV), we implemented extragenital screening, in addition to genital STI screening among all YLHIV in care who reported a history of oral and/or anal sex.

Methods: We collected data on enhanced STI screening for gonorrhea (GC) and chlamydia (CT) with urine plus pharyngeal and/or rectal specimens among YLHIV (≥13 years) who self-reported oral and/or anal sex, independent of gender and sexual orientation. When desired, patients were offered to self-collect oral and rectal swabs for testing. We collected demographic and viral suppression data, acceptance of extragenital STI testing and self-collection of swabs, and positive rates of GC/CT. Descriptive statistics were used for analysis.

Results: From March 2019 through February 2020, 108 YLHIV (46.3% male; 53.7% female; median age 18.7 years; 94.4% black) received genital and extragenital GC/CT screening at 227 encounters. Twenty eight YLHIV (53.6% female; 46.4% male; 92.3% of males self-identified as MSM) had extragenital testing with pharyngeal and/or rectal tests at 39 encounters. The majority of STI tests were with urine only (n=187); 16 tests included both urine and pharyngeal tests; 2 tests included both urine and rectal tests; 3 tests included both pharyngeal and rectal tests; 18 tests in 13 YLHIV included all 3 sites for GC/CT. Among all GC/CT tests, 9/223 (4.0%) urine, 5/37 (13.5%) pharyngeal and 4/23 (17.4%) rectal tests were positive. For all the positive urine tests, none received rectal STI screening, and only 1/8 (12.5%) received pharyngeal STI screening, which was positive for pharyngeal GC. At the time of the positive GC/CT test, two YLHIV had suppressed HIV viral load <20 copies/mL, and the majority (73.3%) had HIV RNA <200 copies/mL. Acceptance of pharyngeal testing was high; however, the majority of female YLHIV refused rectal testing. Of the 15 females who agreed to pharyngeal testing, only 3/15 (20.0%) received rectal testing. The majority of MSM self-collected rectal swabs for STI testing, but preferred the healthcare provider to perform the pharyngeal swabs. Most female participants who agreed to extragenital testing preferred to have the healthcare provider perform both pharyngeal and rectal swabs.

Conclusion: Extragenital STI screening with pharyngeal and rectal tests identified higher rates of STIs in males and females compared to standard of care urine testing in our cohort of YLHIV. Most pharyngeal and rectal GC and CT infections would have been missed if urine-only STI screening was performed. Routine extragenital STI screening should be considered in all sexually active youth in areas of high HIV and STI epidemic to decrease the incidence of HIV and STIs within these communities.

81

Adolescents disengaged from HIV care in Kenya: qualitative insights

***Enane L*[1,2]**, *Apondi E[2,3], Omollo M[2], Toromo J[1], Bakari S[2], Okoyo J[2], Morris C[4], Brown S[5], Fortenberry J[6], Nyandiko W[2,7], Wools-Kaloustian K[2,8], Elul B[9], Vreeman R[2,7,10,11]*

[1]The Ryan White Center for Pediatric Infectious Disease and Global Health, Department of Pediatrics, Indiana University School Of Medicine, Indianapolis, United States, [2]Academic Model Providing Access to Healthcare (AMPATH), Eldoret, Kenya, [3]Moi Teaching and Referral Hospital, Eldoret, Kenya, [4]Indiana University-Purdue University of Indianapolis, Indianapolis, United States, [5]Department of Biostatistics, Indiana University School of Medicine, Indianapolis, United States, [6]Section of Adolescent Medicine, Department of Pediatrics, Indiana University School of Medicine, Indianapolis, United States, [7]Moi University, College of Health Sciences, School of Medicine, Department of Child Health and Pediatrics, Eldoret, Kenya, [8]Division of Infectious Diseases, Department of Medicine, Indiana University School of Medicine, Indianapolis, United States, [9]Department of Epidemiology, Mailman School of Public Health, Columbia University, New York, United States, [10]Icahn School of Medicine at Mount Sinai, Department of Health System Design and Global Health, New York, United States, [11]Arnhold Institute for Global Health, New York, United States

Background: Adolescents living with HIV (ALHIV, ages 10-19) experience poor retention in care. Limited detailed qualitative data exist on factors underlying disengagement. We examined reasons for disengagement among ALHIV that were lost to program (LTP).

Methods: This qualitative study included ALHIV from two large HIV clinics in the AMPATH program in western Kenya who had attended ≥1 visit in the 18 months prior to data collection, but who had not attended clinic ≥60 days past their last scheduled visit. ALHIV and their caregivers were traced in the community and invited to complete semi-structured interviews informed by a socioecological framework.

Results: Interviews were conducted with 32 LTP ALHIV and 25 caregivers. Adolescents averaged age 17.2. Most were female (69%), orphaned (mother/father deceased, 63%), and cared for by someone that was not a biological parent (53%). Twelve (38%) were food-insecure. Reasons for disengagement varied, but centered on family-level factors, particularly when adolescents were orphaned and/or newly living with caregivers who lacked the knowledge or resources to support them in care. Stigma within families resulted in failure to disclose to family members and dropping out of care to avoid disclosure. ("I couldn't come because I never wanted them to know.") Enacted stigma also resulted in situations of neglect of the adolescent's care. ("The family abandoned her.") Transportation time and costs were a frequent challenge, one made more difficult when new caregivers were responsible for orphaned adolescents. Adolescents also anticipated stigma and feared disclosure of their status at clinic or school. ("The school refused me permission to come [to clinic] and I always fear disclosing my status to them.") Mental health issues also led to disengagement. ("I just gave up with life.") Poor experiences with clinic staff deterred some from returning to care. ("I feared coming back because I will be quarreled with by the nurses.")

Conclusions: Reasons for LTP centered on family-level factors, stigma, and financial challenges. Adolescents who were orphaned or experience other family-level challenges or financial hardships may require targeted interventions to remain engaged in care. Stigma presents a central barrier to retention.

82

Baseline factors associated with time to lost to follow up of adolescent girls and young women enrolled in DREAMS program for HIV prevention in Kenya

***Njenga J*[1]**, *Obwiri W[1], Talam N[2], Mbaire C[3], Ojiambo V[4], Gathogo J[5], Gitonga J[6], Barker J[1]*

[1]DGHT, Center for Disease Control and Prevention, CDC, Nairobi, Kenya, [2]US Department of Defense, DOD, Nairobi, Kenya, [3]PEPFAR Coordination Office, Nairobi, Kenya, [4]USAID Kenya and East Africa, Nairobi, Kenya, [5]Hope World Wide Kenya, Nairobi, Kenya, [6]National Aids Control Council, MoH, Nairobi, Kenya

Introduction: The determined, resilient, empowered, AIDS-free, motivated and safe (DREAMS) initiative targets adolescent girls and young women (AGYW) aged between 9 and 24 years with interventions to address factors that make AGYW particularly vulnerable to HIV. The principal tenet of the program is provision of multiple evidence-based services; AGYW retention in DREAMS is essential to ensure beneficiaries receive full package of interventions for maximum HIV prevention effect. However, few studies and reports have described AGYW retention in DREAMS and associated factors.

Methods: We used routine DREAMS program data to retrospectively follow AGYW for 24 months from enrolment into the program. Only AGYW enrolled between October 2015 and October 2017 were included. Stratified Cox regression analysis was used to assess factors associated with time to lost to follow up (LTFU) with county of residence as the stratification factor. Beneficiaries were censored at 24 months if they were still active or their reason for exit was not LTFU.

Results: Of 202,454 AGYW included, 13,934 (6.7%) were LTFU. Compared to AGYW aged 15-19, those aged 9-14 had 1.35 times hazard of exiting the program by 24 months ($z=12.73$, $p<0.0001$) while those aged 20-24 had 1.22 times hazard of exiting ($z=8.66$, $p<0.0001$). The number of AGYW reporting gender-based violence (GBV) 12 months prior to enrolment was 123,229 (61%) but there was no association between GBV and survival time, ($z=3.35$, $p=0.0645$). AGYW in school had 0.55 times hazard of being LTFU by 24 months compared to AGYW not in school ($z=-25.6$, $p<0.0001$). AGYW enrolled in October-December 2017 quarter had 28.71 times hazard of being LTFU compared to those enrolled in Oct-Dec 2015 quarter ($z=3.35$, $p=0.0008$).

Conclusion: We found that an AGYW's age at enrollment or her being in school are significant correlates of her retention time in DREAMS. Experiencing GBV prior to enrolment was surprisingly not significantly associated with survival time, although the number of AGYW reporting experiencing GBV was high. There was higher risk of LTFU among the youngest and oldest age groups and may therefore need different efforts to retain them in the program. Efforts should be made to ensure AGYW remain in school. Implementers should explore individual, contextual and program factors as to why more recent enrollees have a shorter time retention compared to initial cohorts.

83

Predictors of engagement in HIV care for young people with perinatal HIV in England

Le Prevost M[1], Ford D[1], Crichton S[1], Foster C[2], Bamford A[1,3], Judd A[1]

[1]MRC Clinical Trials Unit at UCL, London, United Kingdom, [2]Imperial College Healthcare NHS Trust, London, United Kingdom, [3]Great Ormond Street Hospital for Children NHS Foundation Trust, London, United Kingdom

Background: Most studies of engagement in care (EIC) in people living with HIV use a simplistic definition of EIC based on the number of clinic visits per year, and examine limited predictors of EIC. We adapted an existing EIC algorithm for adults living with HIV in England, for use in young people (YP). We then applied it to YP with perinatal HIV (PHIV) in the Adolescent and Adults Living with Perinatal HIV (AALPHI) cohort in 2013-2015. A wide range of potential predictors of EIC from the AALPHI dataset were explored.

Methods: The algorithm predicts when the next clinic visit will be scheduled within 1-6 months following the current visit, based on routinely collected clinical data including antiretroviral therapy (ART) management, CD4 count and HIV viral load (VL). Time since AALPHI interview date (baseline) was split into 1 month periods across 12 months of follow-up. Each person-month was classified as engaged in care (patient had a clinic visit or not yet due for clinic visit) or not engaged in care (patient overdue a clinic visit). Logistic regression models (allowing for clustered data) explored multivariable predictors ($p<0.05$) of being engaged in care, adjusting for a priori variables (time from interview date, sex, age, ethnicity, country of birth). Potential baseline predictors across the following 7 domains were considered: sociodemographic; risk behaviour; mental health; cognition; clinic factors; ART adherence/ disclosure and HIV; and HIV markers (CD4 count and VL, CD4 nadir, previous CDC event, on efavirenz, ART interruption in year prior to baseline).

Results: Of 306 young people, 179 (59%) were female, 262 (86%) black ethnicity and 180 (59%) born abroad. At baseline, median [IQR] age was 17 [15-18] years, and 202 (69%) had viral load ≤50c/ml. 87% of 3,585 person-months were classified as engaged in care. Multivariable predictors associated with poorer odds of being engaged in care were: baseline VL>50c/mL vs. VL≤50c/mL (ref) (OR 0.47, 95% CI 0.30, 0.75, p=0.002); Asian/mixed ethnicity, vs. black ethnicity (ref) (OR 0.44, 95% CI 0.25, 0.78, p=0.02); ever self-harmed vs. not (ref) (OR 0.55, 95% CI 0.32, 0.95, p=0.03); self-assessed adherence as bad/not so good vs. good/excellent (ref) (OR 0.46, 95% CI 0.25, 0.84, p=0.004) and not on ART vs. on ART (ref) (OR 0.64, 95% CI 0.64, 1.21,) p=0.04).

Conclusions: Identifying which YP are less likely to engage in care may allow targeted interventions to support YP to attend clinic, which is crucial to improve their health outcomes. VL and ethnicity, which are easily available in clinic, are strongly associated with EIC. In addition, assessment of self-harm and self-rated adherence may help clinics identify young people at risk of lower EIC, while at the same time facilitate multidisciplinary clinic support to address YP's mental health needs.

84

Healthcare worker perspectives on adolescent disengagement from HIV care in western Kenya: a qualitative study

***Enane L*[1,2]**, Apondi E[2,3], Toromo J[1], Omollo M[2], Bakari S[2], Morris C[4], Brown S[5], Fortenberry J[6], Nyandiko W[2,7], Wools-Kaloustian K[2,8], Vreeman R[2,7,9,10]

[1]The Ryan White Center for Pediatric Infectious Disease and Global Health, Department of Pediatrics, Indiana University School of Medicine, Indianapolis, United States, [2]Academic Model Providing Access to Healthcare (AMPATH), Eldoret, Kenya, [3]Moi Teaching and Referral Hospital, Eldoret, Kenya, [4]Indiana University-Purdue University of Indianapolis, Indianapolis, United States, [5]Department of Biostatistics, Indiana University School of Medicine, Indianapolis, United States, [6]Section of Adolescent Medicine, Department of Pediatrics, Indiana University School of Medicine, Indianapolis, United States, [7]Moi University, College of Health Sciences, School of Medicine, Department of Child Health and Pediatrics, Eldoret, Kenya, [8]Division of Infectious Diseases, Department of Medicine, Indiana University School of Medicine, Indianapolis, United States, [9]Icahn School of Medicine at Mount Sinai, Department of Health System Design and Global Health, New York, United States, [10]Arnhold Institute for Global Health, New York, United States

Background: Healthcare workers (HCW) managing adolescents living with HIV (ALHIV, ages 10-19) play a critical role in the retention of this key population in HIV care. We sought to understand ALHIV barriers and facilitators to care, and potential interventions, from the perspectives of HCW in western Kenya.

Methods: This qualitative study included HCW managing ALHIV at clinical sites within the USAID-PEPFAR-funded Academic Model Providing Access to Healthcare (AMPATH) HIV treatment program in Kenya, which serves over 160,000 people living with HIV. Semi-structured interviews based on a socio-ecological framework, conducted by a trained facilitator, queried HCW experiences of adolescent disengagement, perceived barriers and facilitators to retention, and proposed interventions.

Results: Twenty-eight HCW at 10 clinics participated, including 11 clinical officers, 8 outreach workers, 5 nurses, 3 social workers, and one psychologist. HCW were predominantly female (64%), averaged age 37 years (range 23-60), and had a median of 10 years of experience in HIV care. HCW identified multiple factors influencing ALHIV retention at the levels of the adolescent, family, clinic, school, and community; with family-level factors being the most prominent. They emphasized timely, supportive disclosure to adolescents to facilitate HIV education and avoid problematic reactions if disclosure was late and/or inadvertent. Family-level barriers included orphanhood; living with extended family or on the street; stigma within families; failure to disclose the adolescent's status to relatives or school administrators who could otherwise help support engagement; gaps in caregiver education about HIV and caregivers' own disengagement from treatment. Attending boarding school interfered with clinic attendance, with some ALHIV disengaging to avoid disclosure of their status. This was overcome when support systems were in place at school. Adolescent relationships to HCW were important, and HCW sought further training to provide adolescent-friendly care. HCW favored increasing the availability of adolescent-friendly services, improving counseling, providing disclosure support, peer support, and stigma-reduction interventions.

Conclusions: ALHIV experience multilevel barriers to retention in care. Retention is facilitated by several factors that create an enabling environment for ALHIV to engage in care. HCW recognize a need for interventions to establish supportive networks to improve ALHIV engagement in care and clinical outcomes.

85

A Qualitative Examination of Perceived Stigma and Its Impact on Health Status and Care Preferences Among Kenyan Adolescents Living with HIV

Callen G[1], Sang F[2], Munyoro D[2], Chory A[3,4], Aluoch J[2], Scanlon M[3,4], McHenry M[1,2], Apondi E[2,5], Enane L[1,2], Nyandiko W[2,5], Wools-Kaloustian K[1,2], Vreeman R[2,3,4]

[1]Indiana University School Of Medicine, Indianapolis, United States, [2]Academic Model Providing Access to Healthcare (AMPATH), Eldoret, Kenya, [3]Arnhold Institute for Global Health, New York, USA, [4]Icahn School of Medicine at Mount Sinai, New York, USA, [5]Moi University, Eldoret, Kenya

Background: Adolescents living with HIV (ALWH) face unique challenges to achieving long-term antiretroviral therapy (ART) adherence and virologic suppression. ALWH in sub-Saharan Africa frequently identify perceived stigma as one such challenge. This study investigated ALWH experiences with perceived stigma to understand the sources, its relationship to mental health and treatment adherence, and its effects on individual preferences for peer support and mental health care delivery.

Methods: ALWH aged 14-19 years, aware of their HIV status, on ART, and enrolled at either one urban or periurban HIV clinic in Western Kenya were included in this study. Semi-structured interviews were conducted to address key domains of mental health, stigma, adherence, peer support, and care preferences. Interviews were conducted in Kiswahili, English, or both and then audio-recorded, translated, and transcribed. Thematic analysis was led by two investigators (GC and FS) to identify and extract themes related to these key domains. We used a software program (Dedoose, SocioCultural Research Consultants, LLC) to conduct qualitative analyses.

Results: Nearly all participants reported experiencing perceived stigma, relating the source of this fear to previous experiences of enacted stigma or stories recounted to them by caregivers, schoolmates, and community-based peers. ALWH were most concerned about stigma from friends and peers who were not living with HIV in the form of vengeful disclosure, gossip, and social isolation. In order to protect themselves from stigma, participants stressed the importance of secrecy in terms of purposefully avoiding disclosing their status. Secrecy was directly related to the key domains of mental health, adherence, and peer support. Several participants identified feelings of isolation, estrangement, and fear as a result of secrecy. Coupled with purposeful non-disclosure, this secrecy led to non-adherence. Nearly every participant reported purposeful non-adherence when in the presence of friends, extended family, and visitors. When asked how their medication-taking behaviors would be different if their peers were also living with HIV, nearly every participant reported that it would be easier to maintain adherence. Despite identifying the impact of open status and having an HIV-positive community on treatment adherence, most participants reported not knowing other ALWH. Several adolescents identified secrecy as a barrier to developing a network of ALWH. One method for providing ALWH with a peer network is the development of clinic-based peer support groups. Participants with experience in these programs described them as beneficial to adherence by creating a community of ALWH who encourage one another and provide adherence reminders. Despite participant familiarity with these groups, many described barriers to accessing them, citing concerns of accidental disclosure. Notably, participants at the periurban facility reported their clinic did not provide peer support programming for ALWH. In order to expand access and preserve secrecy, participants suggested developing peer support groups that met both in-clinic and via mobile platforms. They similarly endorsed these multi-method strategies for delivery of mental health services. Several participants identified their preferred provision of these services to be through peer-to-peer counseling and recommended the utility of peer support groups for discussing mental health challenges.

Conclusions: ALWH describe multiple consequences of perceived stigma, including a perceived need for secrecy, hindering treatment adherence, increasing emotional burdens, and preventing ALWH from forming peer networks. Interventions that encourage peer support networks across various platforms, while respecting ALWH needs for secrecy, are imperative to improve long-term health outcomes, including mental health and ART adherence.

86

Factors associated with virologic failure and loss to follow up for adolescents living with perinatally-acquired HIV during transition to adult care: A prospective analysis

***Zanoni B*[1]**, *Archary M*[2], *Sibaya T*[2], *Musinguzi N*[3], *Haberer J*[4]

[1]*Emory Universoty School Of Medicine, Atlanta, United States,* [2]*University of KwaZulu-Natal, Durban, South Africa,* [3]*Mbarara University of Science and Technology, Mbarara, Uganda,* [4]*Massachusetts General Hospital, Boston, United States of America*

Background: Adolescents living with perinatally-acquired HIV have poor viral suppression and retention in care rates during and after transition from pediatric to adult based care. Timing of transition is often based on age but varies widely in different settings. Optimal timing, readiness, and preparation measures for adolescents living with HIV before transition to adult care are not currently known. We prospectively evaluated risk factors for loss to follow up and virologic failure among adolescents living with perinatally-acquired HIV during transition from pediatric care to adult based care.

Materials and Methods: We prospectively enrolled 199 adolescents living with perinatally-acquired HIV prior to transition from pediatric care to adult care in South Africa. At enrollment, adolescents completed a questionnaire asking demographic data and about alcohol/substance use, depression, stigma, self-esteem, social support, and transition readiness. Additional clinical data including age at antiretroviral therapy (ART) initiation, baseline CD4, baseline viral load, and disclosure status were extracted from medical records. Adolescents were followed for 12 months after transition to adult care to determine viral suppression (viral load <200 copies/ml) and retention in care (consistent pharmacy refills and appointments without a 3-month gap). We used bivariable and multivariable logistic regression to determine factors associated with virologic failure and loss to follow up after transition to adult care. Covariates with p values of less than 0.2 on bivariate analysis were included in our final multivariate models.

Results: Of the 199 adolescents who transitioned to adult care, 84 (43%) had virologic failure one year after transition and 21 (11%) were not retained in care. Older age at ART initiation (OR 1.19, p=0.008; 95% CI 1.05 – 1.35), female sex (OR 2.0, p=0.045; 95% CI 1.02 – 3.97), and alcohol consumption (OR 3.41, p=0.003; 95% CI 1.53 – 7.56) were associated with increased odds of virologic failure one year after transition to adult care. Disclosure of HIV status prior to transition (OR 0.48, p=0.035; 95% CI 0.24 – 0.95), receiving first line ART (OR 0.47, p=0.30; 95% CI 0.23 – 0.93), and higher transition readiness score (OR 0.97, p=0.03; 95% CI 0.94 – 0.99) were associated with lower odds of virologic failure one year after transitioning to adult care. Older age at ART initiation (OR 1.21, p=0.01; 95% CI 1.04 – 1.41) and abuse of inhalants (OR 5.19, p=0.04; 95% CI 1.10 – 24.45) were associated with being lost to follow up within one year of transition. Age at time of transition was not associated with viral suppression or retention in care one year after transition to adult care.

Conclusion: Despite age being the most common factor that determines timing of transition to adult care, age at transition was not associated with retention in care or viral suppression one year after transitioning from pediatric to adult care. However, modifiable factors such as disclosure, and drug or alcohol consumption did predict one-year outcomes. In addition, females, adolescents receiving second line ART, adolescents who initiated ART at an older age, and adolescents with lower transition readiness scores may benefit from additional interventions to improve their transition outcomes.

87

The last mile of PMTCT: A simple screening tool for targeted re-testing of postnatal mothers at outpatient departments in Malawi

Tallmadge A[1], *Stillson C[1], Nyirenda G[1], Nyambi N[1], Banda C[1], Gunda A[1], Muyaso M[2], Namachapa K[2], Eliya M[2]*

[1]Clinton Health Access Initiative, Lilongwe, Malawi, [2]Ministry of Health, Department of HIV/AIDS, Lilongwe, Malawi

Background: Mother to child transmission (MTCT) of HIV is the primary means of infection among infants in Malawi. Currently, the national strategy focuses on identifying HIV-positive women during ANC and enrolling them and their exposed infants into follow-up through the end of breastfeeding. However, there is no systematic guidance for identifying mothers who are infected between delivery and the end of breastfeeding or mothers who drop out of the PMTCT program. As such, postnatal infection is the primary driver of MTCT, accounting for over 70% of new childhood infections in Malawi. In lieu of costly universal postnatal maternal retesting, systematic screening could more efficiently identify mothers for targeted retesting.

Materials and Methods: Through a national taskforce, a tool was developed to screen breastfeeding mothers at outpatient departments in public health facilities. The tool was formatted as a simple checklist. All mothers who had not been tested for HIV at delivery, had not been tested within the last 6 months, or had defaulted from the PMTCT program were referred for HIV testing. Infants of known HIV-positive mothers were also screened for completion of EID testing milestones. The tool was piloted at 32 health facilities in Malawi from July-September 2019. Baseline testing practices were evaluated from April-June 2019, through review of facility registers at each pilot facility. Following the completion of the pilot, focus group discussions (FGDs) were conducted at each pilot facility. Discussions were captured on contact summary forms for analysis. The forms were abstracted into Microsoft Excel and coded thematically with themes tabulated for frequency.

Results: Of the 10515 mothers screened using the tool, 44% (4584/10515) were referred for testing, 81% tested (3720/4584) and 0.7% tested newly positive (26/3720). Overall, 1.4% of infants were screened in for testing (142/9854). Of the infants tested, 25% (24/95) were newly identified as exposed, 47% (45/95) were previously known as exposed but had missed a testing milestone and 27% (26/95) had unknown exposure but were screened in because the mother was deceased or had an inconclusive HIV result. 11.8% (2/17) of the tested infants were confirmed infected via nucleic acid testing. Baseline analysis showed that in the pre-intervention period, 7.6% of infants presenting to OPDs at the pilot facilities were being tested (1513/19784) and 2.3% were testing positive (35/1513). Introduction of the screening tool thereby reduced infant testing volumes by 82% while increasing yields 409% from baseline. 640 screening personnel participated in FGDs. Discussions revealed high acceptance of the screening tools, high willingness to use the tools if nationally adopted, and high usability of the tools by non-clinical lay cadres.

Conclusions: Using a screening tool effectively identified mothers who had defaulted from the PMTCT program, missed a testing milestone or seroconverted during breastfeeding, and linked them and their exposed infants into care. While a 44% referral rate may seem high, use of a screening tool was still significantly more efficient than universal retesting and holds potential to be more effective at bringing defaulters back into care. Additionally, if delivery ward testing was saturated, the referral rate would be reduced by nearly half. These results will inform revisions to the screening tool in anticipation for national adoption.

88

Effects of the Pratt pouch on completion of the six week infant nevirapine prophylaxis regimen in Uganda

Kazooba P[1], *Ashburn K[2], Khamasi R[1], Hererra N[2], Kisaakye L[3], Malkin R[4], Bitarakwate E[1]*

[1]Elizabeth Glaser Pediatric Aids Foundation, Kampala, Uganda, [2]Elizabeth Glaser Pediatric AIDS Foundation, Washington DC, United States, [3]Uganda Ministry of Health, Kampala, Uganda, [4]Biomedical Engineering, Duke University, Durham, United States

Background: The pre-filled, single-dose Pratt pouch could optimize dispensing infant nevirapine (NVP) prophylaxis to HIV-exposed infants to increase completion of the full six weeks infant NVP regimen. We compared infant initiation and completion of NVP prophylaxis, facility delivery and two-week postpartum visit attendance in HIV-infected pregnant women receiving infant NVP prophylaxis using the pouch compared to standard of care.

Materials and Methods: Nineteen health facilities with highest HIV positivity among pregnant women across nine districts in southwest and central Uganda were assigned to control and intervention groups. HIV-positive pregnant women enrolled at the intervention facilities received NVP pouches. Pouches were filled with premeasured doses of liquid NVP, according to Uganda national guidelines for infant NVP dosing. The pouches were integrated into the existing drug distribution system. During ANC, women received 14 pouches to cover the time until returning for the six day postpartum follow-up visit, with an additional eight pouches as a buffer in case women were delayed in returning to the health facility. HIV-positive women enrolled at the control facility received standard NVP syrup provided following delivery for postnatal prophylaxis administration to the infant. In a select number of intervention facilities, women received all 42 pouches needed to complete the six week regimen during ANC to compare any differences in key outcomes in dispensing 42 versus 14 pouches at ANC. Abstraction of medical record data in a cross-section of HIV-positive women attending ANC services and interviews with HIV-positive women during postnatal care visits were conducted at study sites. Unadjusted and adjusted logistic regression models were used to identify factors associated with facility delivery, postnatal care follow up visit, and completion of the full six week infant NVP prophylaxis regimen.

Results: Significantly more women in the intervention (n=292/316) versus control (n=169/340) group had facility deliveries, 92.4% versus 49.7%, p<.0001, postnatal visits within two weeks postpartum, 99.3% versus 36.1%, p<0.001, and reported infants completing the full six week infant NVP prophylaxis regimen, 95.5% versus 86.8%, p=.0002. Dispensing 42 pouches versus 14 pouches during ANC did not have a negative effect on these key outcomes. Significantly more infants received NVP within 72 hours of birth in the intervention group (97.4% versus 93.1%, p=0.006); and 17 of the 23 infants who received infant NVP more than 72 hours after birth were in the control group. For infants born outside of a facility with data on facility delivery and NVP at birth, 60/77 (77.9%) infants in the control group received NVP within 72 hours of birth compared to 23/24 (95.8%) infants in the intervention group. In multivariate models, intervention group was the only significant factor associated with facility delivery or completion of the full six week infant NVP prophylaxis regimen.

Conclusions: The Pratt pouch is an improved delivery method for dispensing pre-measured, single dose infant NVP prophylaxis; use of the pouch resulted in an overall increase in HIV-exposed infants receiving NVP within 72 hours of birth and in infants completing the full six-week NVP prophylaxis regimen and had other associated benefits including an increase in facility delivery and in women's adherence to postnatal maternal and child care services. Dispensing NVP at ANC versus the postnatal care visit helps ensure infants will receive NVP prophylaxis within 72 of birth, regardless of facility or out-of-facility delivery.

89

Uptake of 6-8 weeks HIV testing after implementation of HIV birth testing in Manzini, Eswatini.

MEDEKEREZA R[1], *NXUMALO H[1], MUTITI A[1], TSIOURIS F[1], MKHATSHWA S[1], DLAMINI P[1], KAMIRU H[1], KIDANE A[1], BONGOMIN P[1], NKAMBULE D[2], NHLABATSI B[2]*

[1]ICAP, Mbabane, Swaziland, [2]Ministry of Health , Mbabane, Eswatini

Background: Timing of HIV testing in HIV exposed infants (HEI) is critical to identify those with HIV infection for immediate ART initiation. ICAP, in partnership with the Ministry of Health of Eswatini, piloted HIV birth testing in the Manzini region from October 2017 to December 2019. Uptake of birth testing was 93% with an HIV positivity rate of 0.6%. Eswatini has now adopted birth testing as a standard of care and early infant diagnosis (EID) guidelines recommend testing at birth, 6-8 weeks, 9 months and 12 months. Eswatini uses a one-stop model of care to support integration of immunizations and HEI follow-up during the recommended testing points as a way to promote HIV testing uptake. We describe trends in HEI testing at 6-8 weeks of age two years before and after implementation of birth testing.

Methodology: We examined routinely collected cross-sectional data on 6-8 week testing coverage for the period of October 2015 to September 2017 (pre-birth testing implementation) and October 2017 to September 2019 (post birth testing implementation). In the cross-sectional analyses comparing 2 years before and 2 years after implementation, the expected number of HEI was determined using the number of HIV+ women having attended maternal, neonatal and child health (MNCH) services during the same periods as a proxy. Data reported from these periods were compared and tested for significance through ANOVA.

Results: Overall, a total of 11,272 HIV+ pregnant women were identified in the ICAP supported facilities from October 2015 to September 2019. During the same period, a total of 10,720 HEI received HIV testing at 6-8 weeks corresponding to 95% EID testing coverage. When looking at the pre-birth testing period (Oct 2015-Sept 2017), the average 6-8 week EID testing uptake was 98% (5,059 HEI /5,237 HIV + pregnant women). Following birth testing implementation, from October 2017 to September 2019, EID testing coverage at 6-8 weeks was 94% (5,661/6,035). Overall there was no difference or change in EID testing uptake at 6-8 weeks after implementation of birth testing (98% vs 94%; p=0.5).

Conclusion: While other countries where birth testing has been implemented have shown decreases in 6-8week testing uptake with the addition of birth testing, our data suggest no differences in testing uptake at 6-8weeks when comparing pre and post implementation data. This may be a result of integration of routine testing into infant follow-up/vaccination programs where uptake of vaccine is known to be quite high at 96%. While there are limitations in our interpretations of the findings given use of cross-sectional data, further analysis using cohort data should be conducted to understand full impact of birth testing on uptake on other testing points.

90

Depression and internalized stigma in pregnant and recently postpartum women in Lesotho

Greenberg L[1], *Hoffman H[2], Tukei V[4], Mokone M[4], Tiam A[1,3], Mofenson L[1], Freeman J[2], Masitha M[4], Nchepe M[5], Thabelo R[5], Guay L[1,3]*

[1]Elizabeth Glaser Pediatric AIDS Foundation, Washington, United States, [2]George Washington University Milken Institute School of Public Health, Washington, United States, [3]University of Bergen, Bergen, Norway, [4]Elizabeth Glaser Pediatric AIDS Foundation, Maseru, Lesotho, [5]Lesotho Ministry of Health, Maseru, Lesotho

Background: Prevalence estimates for prenatal or postpartum depression in sub-Saharan Africa vary widely. For HIV-positive women, internalized HIV-related stigma can create barriers to accessing healthcare services and cause depression. We evaluated the effect of the IMPROVE intervention (multidisciplinary teams, patient centered skills building with facility- and community-based health care workers, and early home visits) on maternal depression and internalized stigma.

Methods: Twelve health facilities were randomized to the IMPROVE intervention or routine service delivery. From July 2016 and November 2017 we enrolled 614 HIV-positive and 390 HIV-negative pregnant women and followed them for 12-24 months postpartum. We administered the 9-item Patient Health Questionnaire (PHQ-9) and 9-item internalized stigma scale (9-ISS) during pregnancy and every 6 months postpartum. PHQ-9 responses were categorized as no/mild depression (cumulative score <10) or moderate/severe depression (≥10). Questions from the 9-ISS were reviewed individually. We compared responses by HIV status and intervention arm stratified by HIV infection status. Bivariate tests of association were performed with the Fisher's exact test.

Results: Moderate/severe depression in PHQ-9 was relatively uncommon during pregnancy. Significantly more HIV-negative than HIV-positive women reported moderate/severe depression (13.5% vs 8.6%, respectively, p=0.046), with no differences by study arm or whether the participant was newly HIV diagnosed. Among HIV-positive women, antenatal depression was associated with fears of being denied care by family if sick, being rejected by family, being treated badly at work/school, being physically abused by partner, experiencing a relationship break-up, and becoming a social outcast if others discovered their HIV status. Postpartum, <10% reported moderate/severe depression, with no differences by arm or HIV status. For internalized stigma (9-ISS), significantly more HIV-positive women in the control arm reported fearing that they would be treated badly at work/school, experience relationship break-up, become a social outcast, or lose friends through 18 months postpartum but not at 24 months postpartum. Significantly more HIV-negative women in the control compared to intervention arm reported fearing that they would experience outcomes such as loss of job/livelihood, poor treatment at work/school, or becoming a social outcast if they were to test HIV-positive and others found out through 6 months postpartum, but not at 12 months.

Conclusion: The IMPROVE intervention, designed to improve quality and coordination of MCH/PMTCT services, was associated with lower internalized stigma in both HIV-positive and -negative women throughout much of the study period. The proportion of women reporting moderate/severe depression was low, but higher in HIV-negative than -positive women during pregnancy.

91

Assessment of Population level Impact of Prevention of Mother to Child transmission Program in Manhica district, Mozambique

Urso M[1], Guambe H[3], Tibana K[3], Bernardo E[3], Jadczak S[2], Gaffga N[2], Baughman D[2], Jessica G[1], Cox A[1], Juga A[1], Fuente-Soro L[5], Naniche D[5], Nhamposse T[4], Bhairavabhotla R[2], Ngeno B[2]

[1]Centers for Disease Control and Prevention, Maputo, Mozambique, [2]Centers for Disease Control and Prevention, Atlanta, United States of America, [3]Mozambique Ministry of Health, Maputo, Mozambique, [4]Manhica Health Research Center (CISM), Manhica, Mozambique, [5]ISG Global, University of Barcelona, Barcelona, Spain

Background: There are limited data on population level PMTCT program coverage and outcomes in Mozambique including the mother-to-child HIV transmission (MTCT) prevalence at the end of breastfeeding

Methods: We conducted a cross-sectional survey (October 2017−June 2018) that randomly selected children born alive in the last 48 months in Manhiça district; only the first selected child in each household was included. Mother's HIV-positive status was verified using her clinical records or by testing if unknown, and all children of HIV-positive mothers were tested. Structured interview data were merged with available clinical records for analysis. We estimated ART uptake, viral suppression, breastfeeding, and maternal and infant HIV positivity and mortality. We also estimated the HIV-free survival rate in children using the Kaplan-Meier estimator.

Results: Of 4826 households with a live childbirth, 3486 caregivers (72.2%) were interviewed. HIV prevalence in mothers was 30.8% (967/3136; 95% confidence interval: 29.2%−32.5%). Median age of the HIV-positive mothers at time of delivery was 28.7 (IQR, 23.4–33.4) years. Antiretroviral therapy (ART) data were available for 72.3% (699/967) mothers: 92.7% were receiving TDF+3TC+EFV, 5.9% were on AZT+3TC+NVP, and 1.4% were on second-line or other regimens. Only 47.1% (329/699) of HIV-positive mothers on ART had received a viral load test: 86.0% (283/329) had viral suppression. Mean duration of breastfeeding was 12.7 months for HIV-exposed children compared to 17.9 months for non-exposed children ($p < 0.01$). Overall, 31 maternal deaths occurred among 4826 survey participants, 11 among HIV infected mothers. Of 967 HIV-exposed children, 49 (5.1%, 95% CI: 3.8%−6.6%) were HIV-positive, and 33 had died (HIV-related, 6; non-HIV related, 22; unknown cause, 5). The HIV-free survival rate in HIV-exposed children at 48 months was 92.3% (95% CI: 88.2%−95.0%).

Conclusions: There is a high HIV prevalence among women of reproductive age in Manhiça with a high coverage of ART but a low coverage of viral load testing. National infant feeding policy was well implemented. MTCT prevalence is still high (5.1%) with high rates of child and maternal death. The PMTCT program could consider strategies to prevent new infections, increase viral load testing coverage, and decrease maternal and child mortality rates.

92

Improving retention and viral suppression among HIV positive pregnant women in Nampula Mozambique: results from a quality improvement collaborative.

Tsiouris F[1], *Rondinelli I[1], Boccanera R[4], Bonou M[2], Caliche H[1], Dougherty G[1], Francisco S[1], Pimentel de Gusmao E[1], Macul H[2], Manjate C[1], Matavel L[1], Mungambe O[2], Pereira I[3], Simbine E[1], Sutton R[1], Ussene E[2], Urso M[3], Vitale M[1], Walker L[1], Rabkin M[1]*

[1]ICAP at Columbia University, New York, United States, [2]Ministry of Health, Mozambique, Maputo, Mozambique , [3]US Centers for Disease Control (CDC), Atlanta, USA, [4]US Health Resources and Human Services Administration (HRSA), Washington, USA

Background: Although Mozambique has reduced mother-to-child transmission (MTCT) of HIV by achieving high testing and antiretroviral therapy (ART) coverage among pregnant and breastfeeding women (PBF), its MTCT rate remains amongst the world's highest. Approximately 15% of infants born to HIV-positive mothers acquire HIV by the end of breastfeeding largely due to suboptimal retention in care and failure to achieve viral load suppression (VLS) <1,000 copies/mL. We describe results of a quality improvement collaborative (QIC) as an approach designed to improve retention and VLS in this population.

Description: In collaboration with Mozambique's Ministry of Health, the U.S. Centers for Disease Control & Prevention, and the Health Resources & Services Administration, ICAP at Columbia University designed and implemented a QIC at 30 health facilities (HF) in Nampula Province. Over a 10-month period (October 2018-July 2019), participating HF aimed to improve 3-month retention and VLS from baseline to 90% among PBF enrolled in antenatal care (ANC). Teams at each HF used the same targets and indicators, conducted root cause analyses, designed and prioritized change ideas, used QI methods and tools to conduct rapid, iterative tests of change, received monthly supportive supervision (SS) visits, and convened quarterly to share results and best practices.

Lessons Learned: QI teams at the 30 HF tested 44 change ideas and received 327 SS visits. Three-month retention rates among all PBF improved from 55% to 74% and VLS improved from 55% to 70%. Among PBF newly diagnosed with HIV, 3-month retention rates improved from 51% to 72% and VLS rose from 55% to 68%. Among the PBF on ART at ANC enrollment, 3-month retention improved from 61% to 76% and VLS improved from 55% to 72%. Five HF (17%) achieved both aims. Successful interventions included linking PBF with nearby mentor mothers, modification of VL results management systems, and in-service training on adherence counseling skills.

Conclusions: The QIC led to robust improvement in 3-month retention and VLS amongst PBF, although only five HF achieved the aims of 90% retention and VLS. Focused support, empowerment of teams to develop and test local solutions and use of QIC methodology to accelerate the diffusion of innovations were critical to success.

93

Results of a cluster randomized study to evaluate the effect of a comprehensive service delivery intervention on HIV and maternal child health outcomes in HIV-positive and HIV-negative women

Tiam A[1], Tukei V[3], Greenberg L[1], Hoffman H[4], Viana S[1], Mofenson L[1], Ramatlapeng T[5], Mots'oane T[5], Nchephe M[5], Guay L[1]

[1]Elizabeth Glaser Pediatric Aids Foundation, Washington, United States, [2]University of Bergen, Bergen, Norway, [3]Elizabeth Glaser Pediatric AIDS Foundation, Maseru, Lesotho, [4]George Washington University, Washington, USA, [5]Ministry of Health, Maseru, Lesotho

Background: Progress has been made in reducing mother-to-child transmission, yet service delivery barriers that compromise health outcomes remain. We evaluated the effect of the IMPROVE intervention (multidisciplinary teams, patient centered skills building with health care workers [HCW] and facility and community lay workers, and early home visits) on maternal child health (MCH) and HIV outcomes in Lesotho.

Methods: Twelve health facilities were randomized to IMPROVE intervention or routine service delivery. A prospective cohort of HIV-positive and negative pregnant women were enrolled and followed for 12-24 months post-delivery. In-depth interviews (IDI) with women and focus group discussions (FGD) with providers explored service delivery experiences and HCW/lay supporter attitudes on feasibility of IMPROVE package integration in routine services. Descriptive statistics and bivariate tests of association were performed with Chi-square (or Fisher's exact) testing for categorical and t-tests (or nonparametric Wilcoxon test) for continuous indicators. IDI and FGD were audio taped and translated/transcribed with thematic analysis completed with RQDA.

Results: From July 2016 to November 2017, 614 HIV-positive and 390 HIV-negative pregnant women were enrolled. More HIV-positive women in the intervention arm delivered in a facility than control arm women (92.5% vs. 85.1%, p= 0.009). HIV-positive women in the intervention arm were more likely to maintain > 95% ART adherence than women in the control arm (76.6% vs. 65.5%, p= 0.005). Overall >90% of women achieved viral suppression (<1,000 copies/ml) with no difference between arms. Women in the intervention arm were more likely to have undetectable viral load 12 months after delivery than control arm women (82.9% vs. 72.2%, p=0.02). More HIV-positive women (41.3% vs. 29.6%, p=0.05) and HIV-negative women (47% vs. 33.5%, p=0.003) in the intervention vs control arm used contraception consistently. HIV-negative women in the intervention arm were more likely to have a repeat HIV test prior delivery than women in the control arm (77.4% vs. 63.6%, p=0.007). HCWs in the intervention arms felt they provided better care after implementing IMPROVE interventions and intervention arm women reported well-coordinated services with few delays.

Conclusion: Introducing multi-disciplinary teams using a patient-focused approach to MCH/PMTCT service delivery led to improved services and provider-patient relationships and improved health outcomes.

94

Lessons for retention in postpartum care in the South African prevention of mother-to-child transmission of HIV program

Sawry S[1], *N'Geno B[2], Mbatha P[1], Pals S[2], Modi S[2], Sherman G[3], Leigh B[4], Diallo K[4], Mogashoa M[4], Fairlie L[1]*

[1]Wits Reproductive Health and HIV Institute, University of the Witwatersrand, Faculty of Health Sciences, Johannesburg, South Africa, [2]Centers for Disease Control and Prevention (CDC), Atlanta, United States of America, [3]Department of Paediatrics and Child Health, University of the Witwatersrand and Centre for HIV and STIs, National Institute for Communicable Diseases, a division of the National Health Laboratory Services, Johannesburg, South Africa, [4]Centers for Disease Control and Prevention (CDC), Pretoria, South Africa

Background: Although prevention of mother-to-child transmission of HIV (PMTCT) interventions have been remarkably successful in reducing the number of children infected with HIV and improving maternal health, some gaps remain. To address some of these gaps, the OPPTIM (Optimised Postpartum PMTCT Testing for Infants and their Mothers) clinical trial in Johannesburg, South Africa, was designed to evaluate approaches to maternal viral load (VL) monitoring and infant HIV testing strategies to improve postnatal PMTCT outcomes. This interim operational analysis was aimed at determining factors that affect retention in care to prevent further attrition from the study and understand which women are at highest risk of attrition.

Methods: OPPTIM is an ongoing non-blinded operational research study that enrolled HIV-positive postpartum women and their HIV-negative infants presenting for immunization visits at 6-14 weeks (between July 2018 and April 2019), from two primary health care facilities in inner city Johannesburg. Women were randomised equally, in blocks of 20, to either Arm 1 (standard of care laboratory-based VL monitoring at enrolment, 6, 12 and 18 months), or Arm 2 (enhanced VL monitoring with increased frequency of VL testing using a GeneXpert point-of-care instrument at enrolment, and 6, 9, 12, 15 and 18 months). In this interim analysis, we included all enrolled women who had infants aged at least 12 months by February 2020 and should therefore have had at least 2 follow-up visits at infant ages of 6 and 12 months. Retention was assessed by the number of mother-infant pairs who: (1) attended at least one follow-up visit; or (2) attended all follow-up visits. We investigated potential risk factors for poor retention during the early follow-up period (from enrolment to 12 months) using descriptive statistical methods and univariate logistic regression.

Results: At enrolment, the median age of the 398 mothers was 30 years (Interquartile range (IQR): 26-35), 54% were not from South Africa, 53% started ART during their pregnancy and 9% had elevated viral loads (>1000 copies/ml). Overall, 17% of women never attended any follow-up study visits while 40% of women missed at least 1 follow-up visit. Of the 398 women, 31% and 28% did not attend their 6- and 12-month visits, respectively. Women with an elevated VL at study entry were significantly more likely to have never attended at least one follow-up visit (odds ratio (OR): 3.85; 95% confidence interval (CI): 1.84-8.04). Women younger than 25 years (OR: 2.07; 95% CI: 1.20-3.53), born in South Africa (OR: 1.56; 95% CI: 1.04-2.33) and with elevated VL at study entry (OR: 5.67; 95% CI: 2.50-12.83) were significantly more likely to have ever missed a follow-up visit. There were no significant differences in retention by study site, study arm, or starting ART before vs during pregnancy.

Conclusions: Overall retention in the OPPTIM study was moderate, with a substantial proportion of missed visits. Even with POC testing strategies, PMTCT programs that provide enhanced support for younger women, those with high viral loads early in the post-partum period, and women of South African origin may help to improve retention.

95

A comparison of the outcomes of women retained versus lost during the prevention of mother to child HIV transmission (PMTCT) cascade: the IeDEA-Kenya PMTCT cohort

Humphrey J[1], *Musick B[1], Griffith B[1], Kipchumba B[2], Alera M[3], Songok J[4], Mwangi W[2], Kosgei W[2], Yiannoutsos C[1], Wools-Kaloustian K[1]*

[1]Indiana University, Indianapolis, United States, [2]Moi Teaching and Referral Hospital, Eldoret, Kenya, [3]Academic Model Providing Access to Healthcare, Eldoret, Kenya, [4]Moi University College of Health Sciences, Eldoret, Kenya

Background: Retention in care and viral suppression are major challenges for pregnant and postpartum women living with HIV (WLHIV) in resource-limited settings. However, few studies have characterized the clinical and virologic outcomes, including mother-to-child transmission (MTCT) of HIV, for women and infants after they are lost to follow-up (LTFU) from integrated HIV and maternal and child health (MCH) services. We examined these outcomes in the International Epidemiology Databases to Evaluate AIDS Consortium in East Africa within an enhanced sub-cohort in Kenya.

Methods: We implemented enhanced data collection in a prospective cohort of pregnant and postpartum WLHIV and their infants at five MCH (i.e., antenatal and postnatal) clinics affiliated with the Academic Model Providing Access to Healthcare (AMPATH) in western Kenya. Retained women ≥ 18 years of age were enrolled at the antenatal clinic during the third trimester and re-encountered, along with their infants, at 2 months post delivery. For women who became LTFU (last visit > 90 days) after enrolling in the antenatal clinic and who were ≤ 6 months postpartum at the time of study enrollment, community tracing was conducted to ascertain their outcomes. The primary outcomes were viral suppression (VS < 1,000 copies/mL) and MTCT (positive infant HIV DNA PCR). Descriptive analyses were used to compare groups.

Results: A total of 338 women were enrolled from 3/2018 to 1/2019: 239 (71%) were retained and 99 (29%) were LTFU. A total of 77 additional LTFU women were not enrolled due to inability to trace secondary to poor locator information (n=61), moving > 3-hour drive away (n=12), or refusal to be encountered (n=4). Among retained women, 65% (n=155) were on antiretroviral treatment (ART) prior to pregnancy, and of these women, VS during the third trimester was 96%. Overall, 95% (n=228) of pregnant women retained in care at enrollment in the study remained retained at 2 months postpartum, and of these women, postpartum VS was 93%. For LTFU women, 18 became LTFU during pregnancy and 81 during the postpartum period (median 11 [IQR 5-18] weeks postpartum); 25% reported a silent transfer (ST) to another facility, and 55% were virally suppressed (68% ST vs. 51% disengaged from care; p<0.001 compared to VS among retained women at study enrollment). MTCT among infants of retained versus LTFU women was 0.9% and 5.6%, respectively (p=0.016).

Conclusion: Viral non-suppression and MTCT were higher among LTFU women and infants compared to retained women and infants. These findings highlight the utility of tracing to improve outcomes ascertainment in the PMTCT population and the urgent need for interventions to improve retention in care for this vulnerable population.

96

Effective Community Engagement and Participation, key to Nigeria achieving the elimination of Mother to Child Transmission (eMTCT) by 2021

Okorie G[1], *Oladele T*[1]

[1]*National Agency for the Control of AIDS, Abuja, Nigeria*

Background: Nigeria contributes 30% world burden of Mother to Child Transmission of HIV (MTCT). 2017 Nigeria eMTCT programme data showed that, of the estimated nine million yearly pregnancies, only 60% accessed HTS at health facility; 165,474 (2% of pregnant women) estimated mothers needing PMTCT, only 64.811 (39.2%) have been identified and of those identified, only 24,026 (47.2%) delivered at facility offering PMTCT; Nigerian body of Obstetrics and Gynecology are opposed to any interface with community providers of ANC services e.g. Traditional Birth Attendants (TBA). This intervention was aimed at finding sustainable solution to challenges of pregnant women not accessing HIV services at health facility and to cub the attritions along the eMTCT cascade.

Method: A draft framework to strengthen interface between the community actors and health service providers for PMTCT was designed by National stakeholders coordinated by National Agency for the control of AIDS and FMoH. 21 districts with high burden of HIV were selected for test run. A high level advocacy to state, and community stakeholders and technical sessions ensured understanding of staff of SMoH of the need to interface with TBAs on the provision of PMTCT services. TBAs were identified, trained on HIV basics and referrals; their facilities mapped and linked to formal health facilities for referrals. Baseline PMTCT data were collected from 42 PHC that received referrals from the TBAs. Testing was provided at the mapped TBA shops by health facility personal for 9 months. Identified positives were referred to health facilities for HIV care. Members of HIV networks ensured follow up and enrollment of any identified positive. Data set have been validated by National M&E system.

Result: A total of 104,576 pregnant women were reached within 9 months across the 42 PHCs of which 789 were HIV positive (0.75 positivity). This represents 40% increase of access to HTS by pregnant women across the districts; 95% facility delivery by identified positives was also recorded. The number of infants who accessed HIV prophylaxes also increased by 5% indicating community deliveries that were referred by TBAs. The TBAs engaged in this exercise now have sustainable interface with personnel from facilities. This also popularized the existence of network groups with resultant reduction in stigmatization and discrimination and improved uptake of PMTCT services.

Conclusions: This intervention demonstrated clearly that pregnant women patronize TBAs. It also shows clearly that strengthening the interface between community and health service providers improved uptake of PMTCT services. The next step is the adoption and dissemination of the framework as policy in Nigeria.

97

Early life developmental trajectories of HIV exposed uninfected children – Results from a longitudinal study in Limpopo, South Africa.

Evans D[1], *Coetzee L[1], Robertson-Sutton A[2], Hamer D[3,4], Fink G[5], Yousafzai A[6], Tarullo A[7], Leppänen J[8], Rockers P[3]*

[1]Health Economics and Epidemiology Research Office, Department of Internal Medicine, School of Clinical Medicine, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa, [2]Limpopo Department of Health, Limpopo Province, Limpopo, South Africa, [3]Department of Global Health, Boston University School of Public Health, Boston, Massachusetts, USA, [4]Section of Infectious Diseases, Department of Medicine, Boston University School of Medicine, Boston, Massachusetts, USA, [5]Swiss Tropical and Public Health Institute, , Switzerland, [6]Department of Population and Global Health, Harvard T.H. Chan School of Public Health, , USA, [7]Department of Psychological and Brain Sciences, Boston University, , USA, [8]Faculty of Medicine and Health Technology, Tampere University, , Finland

Background: HIV-exposed uninfected (HEU) children have substantially increased morbidity and mortality, predominantly from infectious causes, compared with children born to uninfected mothers (HIV-unexposed uninfected, HUU). As the number of HEU children continues to increase worldwide, it is important to understand the consequences of exposure to HIV and antiretroviral therapy (ART) in utero or during infancy on child development outcomes.

Setting: Data were collected from 317 caregiver-child dyads at three waves—just after birth, at 7 months, and at 17 months of age— as part of an ongoing cluster-randomized trial in rural Limpopo, South Africa that aims to evaluate the impact of home visits by community health workers.

Methods: HIV exposure was based on the mother self-report of status. A household asset index was used to divide the sample into wealth tertiles. The WHO self-reporting questionnaire (SRQ-20) was used to assess maternal depressive symptoms. We used WHO standards to calculate length-for-age z-scores (LAZ) and weight-for-age z-scores (WAZ) and the Caregiver Reported Early Development Instruments (CREDI) as a measure of overall child development. We estimated mean differences between HEU and HUU children in these outcomes at 7 and 17 months of age.

Results: 306 children were included in the analysis (50.3% female; median birth weight 3.1kg, IQR 2.9-3.4; median birth length 50cm, IQR 49-51; 29.9% had no siblings). In total, 71 (23.2%) were HEU, and 235 (76.8%) were HUU children.

Mothers who were HIV positive (n=71; 95.6% on ART) were slightly older than uninfected mothers (median 33 years, IQR 28-38 vs. 29, IQR 24-35). At the first wave, HIV infected and uninfected mothers were similar in terms of being employed (10.0% vs. 12.5%), being single, divorced, separated or widowed (63.2% vs. 55.7%) or reportedly receiving a government grant in the past month (26.8% vs. 33.8%). Compared to uninfected mothers, mothers who were HIV positive were less likely to have completed a Grade 12 education (22.5% vs. 45.0%; RR0.50, 95% CI 0.31-0.79) and more likely to be from the lowest wealth tertile (42.3% vs 30.3%; RR1.39, 95% CI 0.99-1.95). Both groups had similar mean SRQ-20 symptom scores at the first wave (1.59 SD2.95 vs. 2.03 SD2.91), and both groups reported higher symptom scores at wave 2 (3.66 SD4.25 vs. 3.36 SD4.03) and wave 3 (3.45 SD4.82 vs. 3.92 SD4.95), respectively.

At 7 months, HEU children (n=67) had a lower mean LAZ (-0.52 SD1.12 vs. -0.00 SD1.25; $p<0.05$) and WAZ (0.10 SD 1.13 vs. 0.47 SD1.19; $p<0.02$). No differences in mean LAZ or WAZ were observed at 17 months, but the rate of underweight (WAZ <-2SD) was higher in HEU children (4.9% vs. 0.5%; $p=0.01$). HEU children performed as well as HUU children on the motor, cognitive, language domains of the CREDI at 7 and 17 months. At 17 months, HEU children had higher socioemotional developmental scores than HUU children (mean 0.05 SD0.89 vs. -0.26 SD0.91; $p=0.016$).

Conclusion: HIV affects those of lower socioeconomic status at a disproportionately high rate. We found increased linear growth faltering among HEU children at 7 months of age but not at 17 months of age. We also found evidence that HEU was associated with lower weight. We found no relationship between HEU and overall child development, possibly due to the high coverage of ART among HIV positive mothers.

98

Metabolic syndrome and neurocognitive functioning in youth with perinatally-acquired HIV and youth who are HIV-exposed uninfected

Shiau S[1], Yu W[2], Jacobson D[2], Nichols S[3], Geffner M[4], Chen J[5], Dirajlal-Fargo S[6], McFarland E[7], Surowiec K[8], Jao J[9]

[1]Department of Biostatistics and Epidemiology, Rutgers School of Public Health, Piscataway, USA, [2]Center for Biostatistics in AIDS Research, Harvard T.H. Chan School of Public Health, Boston, USA, [3]Department of Neurosciences, University of California, San Diego, La Jolla, USA, [4]The Saban Research Institute, Children's Hospital Los Angeles, Los Angeles, USA, [5]Department of Pediatrics, Drexel University College of Medicine, Philadelphia, USA, [6]University Hospitals Cleveland Medical Center and Rainbow Babies and Children's Hospital, Case Western Reserve University, Cleveland, USA, [7]Department of Pediatrics, University of Colorado School of Medicine, Aurora, USA, [8]Department of Pediatrics, New Jersey Medical School, Newark, NJ, , Newark, USA, [9]Department of Pediatrics, Northwestern University Feinberg School of Medicine, Chicago, USA

Background: Studies in the general population and adults with HIV have linked metabolic syndrome (MetS) and its components [abdominal obesity, elevated triglycerides, low HDL cholesterol, high blood pressure (BP), and impaired fasting glycemia] to neurocognitive impairment. We investigated whether these associations extend to youth living with perinatally-acquired HIV (YPHIV) or who are HIV-exposed uninfected (YPHEU).

Methods: Participants were selected from the Adolescent Master Protocol (AMP) of the Pediatric HIV/AIDS Cohort Study (PHACS) network (451 YPHIV, 227 YPHEU), enrolled from 2007-2009 in the USA including Puerto Rico. The analysis included youth with a neurocognitive function exam at ≥10 years (baseline) and all five MetS components (based on International Diabetes Federation criteria) measured between 1 year before and 3 months after that exam. Neurocognitive index scores included Wechsler Intelligence Scale for Children (WISC-IV; 10-16 years) or Wechsler Adult Intelligence Scale (WAIS-IV; ≥16 years) full-scale IQ, and verbal comprehension, perceptual reasoning, working memory, and processing speed domains. A sub-group of YPHIV completed a second neurocognitive exam 3 years later and were included in a longitudinal analysis. Within YPHIV and YPHEU separately, we assessed the association between each binary MetS component and each neurocognitive index (baseline) or change in neurocognitive index (longitudinal) by fitting linear regression models using generalized estimating equations with robust variance, unadjusted and adjusted for potential confounders including age, sex, race/ethnicity, primary language, income, Tanner stage, and, for YPHIV only, age at antiretroviral therapy (ART) initiation, nadir CD4, peak viral load (VL), and ART regimen type.

Results: A total of 418 (350 YPHIV and 68 YPHEU) participants were included in baseline analyses. Median age was 12.8 years (range 10-19) for YPHIV (54% female; 64% non-Hispanic Black) and 11.6 years (range 10-16) for YPHEU (53% female; 51% non-Hispanic Black). At baseline, 89% YPHIV had a CD4 count >350 cells/µL, 69% had VL ≤400 copies/mL, and 46% were on PI-based ART. Median age at ART initiation was 2.96 years. At baseline, 15% and 3% of YPHIV and 18% and 7% of YPHEU met criteria for ≥2 and ≥3 MetS components, respectively. At baseline, among YPHIV, no associations between MetS components and neurocognitive indices were observed. Among YPHEU, however, those with elevated triglycerides had lower mean scores in verbal comprehension (-10.0; 95% CI: -17.7, -2.2), perceptual reasoning (-7.9; 95% CI: -13.2, -2.5), and full-scale IQ (-7.5; 95%CI: -14.6, -0.5) and those with impaired fasting glycemia had a lower mean verbal comprehension (-12.7; 95% CI: -24.7, -0.7) score in adjusted models. In adjusted analyses among 183 YPHIV, raised BP was associated with lower mean perceptual reasoning scores over time (-4.3; 95% CI: -8.8, 0.2). In addition, meeting ≥2 MetS components was associated with lower mean processing speed scores over time (-5.3; 95% CI: -9.6, -1.1).

Conclusions: Some components of MetS in YPHIV (raised BP) and YPHEU (elevated triglycerides, impaired fasting glycemia) are associated with lower neurocognitive performance in childhood and adolescence. Early elucidation of modifiable metabolic risk factors associated with neurocognitive outcomes could improve short- and long-term outcomes as these individuals age into adulthood.

99

RESPONSE TO HEPATITIS B VACCINATION AMONG HIV-EXPOSED UNINFECTED CHILDREN IN CANADA

Dorval S[1], *Boucoiran I[2], Valois S[3], Taillefer S[3], Lamarre V[1], Soudeyns H[3], Ovetchkine P[1], Kakkar F[1]*

[1]Department of Pediatrics, Division of Infectious Diseases, Université de Montreal, CHU Sainte-Justine, Montréal, Canada, [2]Department of Obstetrics and Gynecology, Université de Montreal , Montreal, Canada, [3]Centre Maternel et Infantile sur le SIDA, CHU Sainte-Justine, Montreal, Canada

Background: Ensuring an appropriate response to vaccination among children who were HIV exposed and uninfected (cHEU) is essential to reducing their morbidity and mortality from infectious diseases. The objective of this study was to assess immunological response to Hepatitis B vaccine (HBV) among cHEU according to two different vaccination schedules.

Methods: Retrospective study of mother infant pairs enrolled in the Centre Maternel et Infantil sur le SIDA (CMIS) cohort (Montreal, Canada). Anti-HBs IgG titers (CMIA architect assay, Abbott) was routinely assessed for all women at the first antenatal visit. For infants, HBV was given according to the provincial guidelines at the time (three doses, at 0, 1, 6 months 1998-2012, or 2, 4, and 18 months 2012-2016). Children who had anti-HBs IgG titers (CMIA architect assay, Abbott) after 3 doses of HBV were included. A titer of >10mUI/ml was considered as protective.

Results: 91 mother-infant pairs were included. All mothers were prescribed antiretroviral therapy; median maternal CD4 T-lymphocyte count at time of delivery was 549 cells/mm3; 22% were immunosuppressed with CD4 <350 cells/mm3, and 21,6% had a detectable HIV viral load (VL). Overall, 50% of mothers (41/82) were not immune to hepatitis B in the first trimester of pregnancy – including 9,5% (8/84) with evidence of Hepatitis B infection. Of those not immune, 16,5% (14/85) were vaccinated during pregnancy. 56 children (61,5%) received their 3 doses according to the 0, 1, 6 months (early) schedule and 35 (38,5%) according to the 2,4, 18 months (delayed) schedule. Median time of serological testing after the third dose was 2 years (IQR 1-5) in the early group, and 3 years (IQR 1-4 years) in the delayed group. Overall, 25.3% of the children were not immune to HBV after vaccination. There was a significant difference in proportion of non-responders according to vaccine schedule, with 33.9% non-response in the early group, and 11.4% in the delayed group (p=0.016). There was no difference proportion of children sero-protected among those born to mother with detectable vs. undetectable VL (12.5% vs. 20.7%, p=0.46) or those born to mothers with vs without immunosuppression at time of delivery (30 vs 24%, p=0.58). There was no association between maternal anti-HbSAg titer in first trimester and child's anti-HbSAg titer following vaccination (coef= -0.04, p=0.51). In a multivariate logistic regression model including maternal delivery CD4 count, first trimester anti-HBV titer, and timing of vaccination, only timing remained a significant predictor of subsequent sero-protection (delayed vs. early, OR 3.95, p=0.05).

Conclusion: In this resource-rich setting with low HIV and HBV seroprevalence, a high proportion of women with HIV were not immune to hepatitis B in early pregnancy, and a significant proposition of cHEU were not immune following vaccination. Timing of vaccination (early vs late) had an effect on sero-protection among children. Given the risks of infectious diseases related morbidity and mortality among cHEU globally, further work needs to be done to ensure appropriate response to vaccination in this population.

100

Characteristics and outcomes of coinfection-exposed infants born to women living with HIV in the UK

***Peters H*[1]**, *Francis K*[1], *Webb S*[2], *Smeaton L*[2], *Thorne C*[1]

[1]*Integrated Screening Outcomes Surveillance Service, UCL Great Ormond Street Institute of Child Health, London, United Kingdom,* [2]*Infectious Diseases in Pregnancy Screening Programme, Public Health England , London, United Kingdom*

Background: Sexually-acquired and blood-borne coinfections are frequent among people living with HIV. Infants born to women living with HIV who also have coinfection(s) during pregnancy may be at increased risk for adverse outcomes, including vertical or congenital infection requiring increased management and monitoring. We describe the current picture of infants born to women living with HIV and coinfection in pregnancy using observational population-level surveillance data.

Methods: The Integrated Screening Outcomes Surveillance Service (ISOSS) is part of Public Health England's Infectious Diseases in Pregnancy Screening Programme, and conducts active surveillance of all pregnancies in women living with HIV and their children in the UK. ISOSS is currently expanding to cover pregnancies to all women who screen positive for the other two screened for infections in pregnancy in the UK: syphilis and hepatitis B (HBV). Data on screened for co-infections as well as Hepatitis C (HCV) among pregnancy women living with HIV have been collected since 2008, alongside details on infant exposure to and/or any confirmed congenital infections. Descriptive statistics summarise characteristics and outcomes of coinfection-exposed (syphilis, HBV and HCV) infants born to women living with HIV in the UK 2009-18 reported to ISOSS by December 2019.

Results: Among 10675 infants born to women living with HIV in 2009-2018, 83% (8832) had information on maternal coinfection. Overall 7.2% (636/8832) of infants were coinfection-exposed: 4.7% (413/8832), 1.4% (126) and 1.4% (120) to HBV, HCV and syphilis respectively. Twenty infants were exposed to more than one coinfection: 4 HBV/HCV, 10 HBV/syphilis, 5 HCV/syphilis, 1 to all.
Among coinfection-exposed infants: 19% were born to mothers diagnosed with HIV during pregnancy (versus 16% born to non-coinfection exposed, p=0.107), and median maternal age was 33 years (IQR: 29, 37). Most infants with coinfection exposure were born to mothers born abroad (92% v 84% in non-exposed, p<0.001); 15% of exposed infants were born <37 weeks gestation (vs 12% non-exposed, p=0.048). Injecting drug use was more common as the likely mode of maternal HIV acquisition among infants born to coinfected women (8.5% v 0.5% in non-exposed, p<0.001);among infants born to women with HCV coinfection this reached 37%. Congenital infection was reported in 0.8% (5/636) of coinfection-exposed infants: syphilis (3), HBV (1), HCV (1) and 0.3% (2/621) infants were diagnosed with HIV, consistent with the overall HIV transmission rate.

Conclusions: One in 14 infants born to women living with HIV in the UK are exposed to coinfections, underscoring the importance of monitoring sexual health in pregnancy. Detection allows for appropriate management of mother and infant to prevent congenital infection and/or other adverse pregnancy outcomes, and an ongoing awareness of the possibility of acquiring a new infection throughout pregnancy offers opportunities to retest if this is considered necessary. ISOSS is uniquely placed to monitor the management and outcomes of all the screened for infections in pregnancy in the UK, and as the expansion gets underway valuable insights will be gained in order to inform national guidelines and policy. Looking to the future, ISOSS will also be able to track other coinfections in pregnancy (including HCV) that may arise as the landscape continues to change.

101

High HIV infection rates among children under five years of age identified as TB presumptive in sub-Saharan Africa

Denoeud-ndam L[1], *Masaba R[2], Tchounga B[3], Siamba S[2], Zemsi A[3], Ouma M[2], Youm E[3], Zoung-Kanyi Bissek A[4], Okomo G[5], Casenghi M[1], Cohn J[1], Tiam A[6,7]*

[1]EGPAF, Geneva, Switzerland, [2]EGPAF, Nairobi, Kenya, [3]EGPAF, Yaounde, Cameroon, [4]Ministry of Health, Yaounde, Cameroon, [5]Ministry of Health, Nairobi, Kenya, [6]EGPAF, Washington, United States, [7]University of Bergen, Bergen, Norway

Background: Children <5 years of age are at high risk of developing and dying of active TB disease. In addition, HIV infection increases the severity of TB infection in this vulnerable population. We assessed the rate of HIV infection and its association with active TB disease and outcomes among children under age 5 with presumptive TB in 12 district hospitals of Kenya and Cameroon.

Materials and Methods: We conducted a stepped-wedge randomized control trial, where children aged less than five years of age who had presumptive diagnosis of TB based on symptom-screening were enrolled into the study. They were followed through TB diagnosis and treatment. We interviewed caregivers and abstracted clinical information including HIV status at baseline and during follow up visits. Data were entered into an electronic case report form and analyzed to compare children's characteristics and outcomes in HIV infected versus uninfected or with status unknown, using Fisher exact test. The protocol was approved by institutional review boards and we obtained written informed consent from caregivers for the children to participate.

Results: Between May 2019 and March 2020, 275 TB presumptive children were enrolled. Mean age was 1.9 years (± 1.3), 151 (55%) were male. At enrolment, 149 (54%) knew their HIV status (12 (4%) HIV exposed but negative, 27(10%) HIV positive, 110 (40%) HIV unexposed). 126 children (46%) were of unknown HIV status. 20 of the 27 (74%) HIV-infected children were already on ART; 12/27 (44%) had been screened with presumptive TB at the HIV clinic whereas 15/27 (56%) had been screened for TB in other pediatric entry points.
Active TB diagnosis was clinically or bacteriologically confirmed in 54% (13/24) of HIV-infected versus 41% (81/199) of HIV-negative or unknown (P=0.27). Of the 94 children with active TB, 14% (13/94) were HIV-infected and 7% (7/94) remained of unknown HIV status on TB treatment initiation.
TB-HIV co-infected children presented more frequently with cough (100% versus 67%), loss of appetite or failure to thrive (62% versus 28%) abnormal pulmonary auscultation (54% versus 16%), dehydration (15% versus 2%), moderate or severe acute malnutrition (69% versus 32%), compared to children without HIV or with unknown HIV status (P<0.05).
Overall TB case fatality rate was 8% (7/94) with a rate of 6% (5/81) among HIV-negative or unknown and 15% (2/13) among HIV-infected children, P=0.25.

Conclusions: We observed high rates of HIV infection among children with presumptive diagnosis of TB. Children with TB/HIV co-infection had a poorer clinical condition and the case fatality rate among them was almost twice as high as the overall mortality in the cohort. A number of children did not know their HIV status calling for strengthening of early infant diagnosis and integration with TB screening programs.

102

High Prevalence of Hepatic Steatosis in Children with Perinatally Acquired HIV Starting Antiretroviral Therapy Beyond Infancy

***Rose P*[1]**, *Nel E*[1], *Innes S*[1]

[1]*Stellenbosch University, Cape Town, South Africa*

Background: Despite the high prevalence of non-alcoholic fatty liver disease (NAFLD) in adults with HIV, little is known about this problem in children. Our aim was to evaluate the prevalence of hepatic steatosis and fibrosis in South African children with perinatally acquired HIV (PHIV) and HIV-uninfected (HU) children, evaluating both traditional and HIV-specific risk factors.

Methods: This cross-sectional study, conducted from April to December 2019, enrolled well school-aged children participating in an ongoing cohort study. Both PHIV and HU were included. Demographic and clinical data were collected. All children had transient elastography (TE) and controlled attenuation parameter (CAP) performed using the Fibroscan Mini 430 (Echosens, Paris, France) after an overnight fast. Hepatic steatosis was defined as CAP ≥238dB/m and hepatic fibrosis as a liver stiffness ≥7.1kPa.

Comparisons of categorical variables used the Chi-square or Fisher's exact test. For parametric and non-parametric continuous variables, the t-test and Wilcoxon test were used as appropriate. Multivariate logistic regression analyses identified predictors for hepatic steatosis in PHIV and HU separately. All analyses were two-tailed and $p<0.05$ was considered statistically significant.

Results: 138 children were evaluated. The median age was 12.5 years [IQR 11.2-13.5 years], 73 (53%) were female, 43 (31%) were PHIV and 95 (69%) were HU. All PHIV were on antiretroviral therapy (ART) since early life. A total of 18/138 (13%) children had evidence of hepatic steatosis: 1/2 (50%) obese, 4/14 (29%) overweight and 13/122 (11%) lean children. There were 3/95 (3%) HU children and 1/43 (2%) PHIV with evidence of hepatic fibrosis.

Eight (19%) PHIV children [5/10 (50%) who initiated ART beyond infancy and 3/33 (9%) who started ART during infancy] and 10/95 (11%) HU children had hepatic steatosis (p=0.02). There was no significant difference in HIV stage, ART regimen, CD4 count (absolute or %), viral load or nadir CD4 count (absolute or %) between PHIV children with and without hepatic steatosis. There was no significant difference in duration of ART, duration of suppression of HIV viraemia, nadir CD4 count or whether the ART regimen contained a protease inhibitor or non-nucleoside reverse transcriptase inhibitor between PHIV children initiating ART after infancy and those initiating ART during infancy. In multivariable logistic regression analysis, the only significant risk factor for hepatic steatosis was obesity or overweight in HU children (OR 9.6; 95% CI 2.0-45.8) and starting ART beyond infancy in PHIV children (OR 9.9; 95% CI 1.4-68.4).

Conclusions: PHIV children starting ART beyond infancy had a higher prevalence of hepatic steatosis compared to PHIV children starting ART during infancy. Early ART may protect PHIV children from developing NAFLD. Further longitudinal studies are needed to monitor for the development and progression of hepatic steatosis, NASH and hepatic fibrosis in PHIV children and to elucidate the possible mechanisms though which early ART may protect PHIV from developing hepatic steatosis.

Author	Paper Title	Abst#	Page #
Amzel, A.	Finding the remaining unidentified children living with HIV: Opportunities through index testing	10	11
Amzel, A.	A multi-country analysis of the impact of COVID-19 on HIV services for children and adolescents living with HIV	19	19
Amzel, A.	A multi-country analysis of the impact of COVID-19 on HIV services for pregnant and breastfeeding women and their infants	22	22
Ashburn, K.	A validated outpatient department HIV screening tool for children 18 months to 14 years as efficient as index testing in Uganda	7	8
Ashburn, K.	Effects of the Pratt pouch on completion of the six week infant nevirapine prophylaxis regimen in Uganda	88	87
Bacha, J.	The "DTGs" of DTG for children and adolescents living with HIV (CALHIV): Descriptions, Trends, and Gaps of rolling out dolutegravir in CALHIV in Mbeya, Tanzania.	5	6
Balasubramanian, R.	Time to first positive HIV-1 DNA PCR in infants infected with subtype B HIV-1 is delayed in the presence of maternal antiretroviral use	26	26
Brothers, C.	Pediatric dolutegravir (DTG) dosing recommendations derived from combined P1093 and ODYSSEY Population Pharmacokinetic analysis	2	3
Burmen, B.	Adoption of WHO's HIV retesting policy for HIV-negative women during the breastfeeding period in 10 high HIV-burden African Countries	44	44
Byrne, T.	Trends in the prevalence of overweight and obesity among children and adolescents living with perinatally-acquired HIV in the UK and Ireland.	67	66
Callen, G.	A Qualitative Examination of Perceived Stigma and Its Impact on Health Status and Care Preferences Among Kenyan Adolescents Living with HIV	85	84
Chandasana, H.	Model Informed Prediction of Dolutegravir Pharmacokinetics in the Neonates	31	32
Chimulwa, T.	Improving pediatric and adolescent HIV services through integrated peer support: A case of the Young People and Adolescent Peer Support (YAPS) Model in Uganda	79	78
Chory, A.	Qualitative Analysis of a mobile WhatsApp group messaging intervention for adolescents living with HIV in Kenya	38	38
Courville, T.	Expand HIV Testing in Youth at an Urban Children's Hospital – Sustainable or Not?	53	52
Dahourou, D.	Low access to viral load monitoring and poor virological outcomes in children and adolescents living with HIV in West Africa	48	47
Denoeud-ndam, L.	High HIV infection rates among children under five years of age identified as TB presumptive in sub-Saharan Africa	101	101
Diallo, M.	SAFETY, PHARMACOKINETICS AND ACCEPTABILITY OF THE ABC/3TC/LPV/r GRANULES (4-in-1) IN CHILDREN LIVING WITH HIV (3-20KG) IN UGANDA: LOLIPOP STUDY	4	5
Dorval, S.	RESPONSE TO HEPATITIS B VACCINATION AMONG HIV-EXPOSED UNINFECTED CHILDREN IN CANADA	99	99
Driver, M.	Change in sexual behavior and partner communication following oral HIV self-testing among adolescents and young adults in Kenya	35	35
Enane, L.	Adolescents disengaged from HIV care in Kenya: qualitative insights	81	80
Enane, L.	Healthcare worker perspectives on adolescent disengagement from HIV care in western Kenya: a qualitative study	84	83
Evans, D.	Early life developmental trajectories of HIV exposed uninfected children – Results from a longitudinal study in Limpopo, South Africa.	97	96
Fair, C.	"HIV is the easy part": A qualitative study on perceived biopsychosocial needs among U.S. parents who have internationally adopted children living with HIV	70	69
Fairlie, L.	Associations of Nevirapine-based ART regimens with neuropsychological outcomes in HIV-positive children	62	61
Fokam, J.	Archived HIV-1 Drug-Resistance Variants in Cellular Reservoirs and its Determinants among Vertically-Infected Adolescents failing Antiretroviral Therapy	17	17
Gill, M.	Fidelity to a lay cadre-administered HIV risk screening tool used among orphans and vulnerable children in community settings in Tanzania	51	50
Greenberg, L.	Depression and internalized stigma in pregnant and recently postpartum women in Lesotho	90	89
Humphrey, J.	A comparison of the outcomes of women retained versus lost during the prevention of mother to child HIV transmission (PMTCT) cascade: the IeDEA-Kenya PMTCT cohort	95	94
Keal, J.	The changing face of paediatric HIV: A review of the evolving clinical characteristics of a paediatric and adolescent patients at a clinic in Johannesburg, South Africa.	45	45
Khaitan, A.	Children who are HIV-Exposed and Uninfected Exhibit Immune Suppressive Plasma Biomarker Profiles	25	25
Khumalo, P.	Bringing HIV and SRH services closer to Adolescents Girls and Young Women in Eswatini through a comprehensive mobile HIV and SRH package	16	16
Khumalo, P.	Clinical outcomes of infants identified HIV-positive at birth through routine point-of-care early infant HIV diagnosis; a pilot program in Eswatini	50	49
Kido, A.	Safety, pharmacokinetics, and efficacy of low-dose E/C/F/TAF in virologically suppressed children ≥2 years old living with HIV	3	4
Kido, A.	Challenges of remdesivir pediatric development for SARS-CoV-2 infection in a pandemic	20	20
Kido, A.	PK and safety of F/TAF with boosted 3rd agents in children with HIV	54	53
Kido, A.	Weight trajectory in children and adolescents who switched to TAF-based regimens	56	55
Kido, A.	Acceptability & palatability of low dose B/F/TAF & E/C/F/TAF in children (≥2y) with HIV	57	56
Koay, W.	Improving Identification of Sexually Transmitted Infections (STIs) among Youth Living with HIV	80	79

Kouamou, V.	Point of Care SAMBA-II vs Centralized Laboratory Viral Load Assays among HIV-1 Infected Children, Adolescents and Young Adults in Rural Zimbabwe: A Randomized Controlled Trial	8	9
Langat, A.	Factors associated with late presentation of HIV-infected infants for Early Infant HIV Diagnosis (EID) services in Kenya	11	12
Lapsley, R.	Peer-supported community-based HIV self-testing is highly acceptable to Adolescents and Young Adults in Nairobi, Kenya.	76	75
Laughton, B.	Deficits noted at 11 years in children with HIV starting early antiretroviral therapy in fine motor dexterity and auditory working memory	18	18
Le Prevost, M.	Predictors of engagement in HIV care for young people with perinatal HIV in England	83	82
Lenz, C.	Opportunity Analysis for HIV Risk and Acquisition Among Pregnant Adolescent Girls and Young Women in Antenatal Care Services in Ten African Countries	41	41
Lenz, C.	The Provision of School-based Support for Adolescents and Youth Living with HIV in Boarding Schools in Homa Bay and Turkana, Kenya: The Red Carpet Program	77	76
Li, S.	Higher hospitalization rates in children born HIV-exposed uninfected in British Columbia, Canada, between 1990 and 2012	27	27
Li, S.	Cascades of care for preventing vertical HIV transmission in Canada	40	40
Loerinc, L.	High Rates of Primary and Secondary Syphilis Infections in HIV-Positive Adolescent and Young Adult Men Who Have Sex With Men in Atlanta, GA	36	36
Mccoy, B.	Measuring Symptoms of Depression, Anxiety, and PTSD among Children and Adolescents Living with and Affected by HIV in Sub-Saharan Africa: A Systematic Review	71	70
Moran, A.	Maternal PrEP use in HIV-uninfected pregnant women in South Africa: Role of Stigma in PrEP initiation and persistence	29	29
Moyo, F.	Longitudinal evolution of maternal viral loads during pregnancy and postpartum among women living with HIV in South Africa.	28	28
Mudekereza, R.	Uptake of 6-8 weeks HIV testing after implementation of HIV birth testing in Manzini, Eswatini.	89	88
Mugo, C.	Time to repeat viral load testing following an unsuppressed viral load among adolescents and young adults in Kenya	49	48
Mukendi, A.	Evaluating the performance of the GeneXpert HIV-1 Qualitative assay as a consecutive test for a new early infant diagnosis algorithm	34	34
Mutisya, I.	Retention and viral suppression among child -caregiver pairs enrolled in family centered differentiated model of care in Kenya, 2019	63	62
Mutiti, A.	Optimized ART regimen transition: Experiences at ICAP supported facilities in Manzini, Eswatini.	59	58
Mwangwa, F.	Overlapping Significant Life Events are associated with HIV Viral Non-Suppression among Youth in Clinics in Rural East Africa	37	37
Naikazi, G.	Continuous quality improvement improves retention of clients in prevention of mother-to-child transmission of HIV program (Wakiso District, Uganda)	42	42
Namusoke-Magongo, E.	Optimisation of First-Line Antiretroviral Therapy (ART) for Children Living with HIV in Uganda: Translation from policy to action	61	60
Neary, J.	Higher prevalence of stunting and lower length, weight, and head circumference among HIV-exposed uninfected infants	43	43
Neary, J.	Perceived Social Support among Adolescents and Young Adults Living with HIV	78	77
Njenga, J.	Baseline factors associated with time to lost to follow up of adolescent girls and young women enrolled in DREAMS program for HIV prevention in Kenya	82	81
Njume, D.	Virological failure is consistent with acquired HIV drug resistance among vertically-infected adolescents: evidence from the EDCTP-READY study.	64	63
Okorie, G.	Effective Community Engagement and Participation, key to Nigeria achieving the elimination of Mother to Child Transmission (eMTCT) by 2021	96	95
Peters, H.	Children newly diagnosed with HIV in the UK and Ireland between 2000 and 2018: a population- level overview	66	65
Peters, H.	Characteristics and outcomes of coinfection-exposed infants born to women living with HIV in the UK	100	100
Pintye, J.	Extent of in utero transfer of tenofovir from mother to fetus: a paired analysis of hair specimens collected at birth from a cohort in the United States	24	24
Rabold, E.	Trends in pediatric antiretroviral treatment in U.S. President's Emergency Plan for AIDS Relief-supported countries in sub-Saharan Africa —2016–2019	30	31
Reif, L.	Point-of-Care Viral Load Testing Among Adolescents and Young Adults Living with HIV in Haiti: A Randomized Control Trial	14	14
Rose, P.	High Prevalence of Hepatic Steatosis in Children with Perinatally Acquired HIV Starting Antiretroviral Therapy Beyond Infancy	102	102
Rotsaert, A.	Acceptability of a new 4-in-1 Abacavir/Lamivudine/Lopinavir/Ritonavir paediatric fixed-dose combination: the caregiver-child dyads' perspective	6	7
Rozenszajn, M.	Absence of selection for integrase inhibitor resistance via the Q148H pathway in HIV-1 subtype F integrases: Evaluation of treatment outcomes, replicative capacity, and drug resistance	32	33
Ruel, T.	Twenty-four week safety, tolerability and efficacy of dolutegravir dispersible tablets in children 4 weeks to <6 years old with HIV: results from IMPAACT P1093	1	2
Ruel, T.	Plasma Exposure-Viral Load Response Analysis for Dolutegravir in Children with HIV-1: Results from IMPAACT P1093	55	54
Rungmaitree, S.	The Outcomes of Transition from Pediatrics to Adult Care among Adolescents and Young Adults with HIV at a Tertiary Care Center in Bangkok	75	74

Sanders, L.	Use of a Walk-In HIV and STI Testing Model for At Risk Youth Ages 13 to 24 - Assessment of the Impact of the COVID-19 Pandemic on Testing Services	23	23
Sawry, S.	Lessons for retention in postpartum care in the South African prevention of mother-to-child transmission of HIV program	94	93
Scheel, A.	High Prevalence of Asymptomatic Sexually Transmitted Infections at Baseline Clinic Visit Following HIV Diagnosis in Atlanta Youth	39	39
Shiau, S.	Metabolic syndrome and neurocognitive functioning in youth with perinatally-acquired HIV and youth who are HIV-exposed uninfected	98	98
Songtaweesin, W.	Mental health management integration into adolescent HIV treatment services in Bangkok, Thailand	74	73
Srivastava, M.	A multi-country analysis of the impact of COVID-19 on uptake of multi-month dispensing for children living with HIV on antiretroviral therapy	21	21
Srivastava, M.	Reaching the 1st 95: Maximizing index testing coverage in children of women living with HIV	52	51
Strachan, M.	Antiretroviral Drug Optimization and Viral Suppression Amongst Children and Adolescents Living with HIV in four States in Nigeria	60	59
Syowai, M.	Antiretroviral Drug Transition and Adverse Event Monitoring among Adolescents 15 to 19 years of age in Kenya	15	15
Tallmadge, A.	“Right under our nose”: A simple screening tool to identify HIV-positive children outside of the PMTCT program at outpatient departments in Malawi	9	10
Tallmadge, A.	The last mile of PMTCT: A simple screening tool for targeted re-testing of postnatal mothers at outpatient departments in Malawi	87	86
Teasdale, C.	Significant life events and viral suppression outcomes in children starting antiretroviral therapy in South Africa	65	64
Tiam, A.	HIV-infected treatment-experienced children and adolescents from Sub-Saharan Africa: clinical outcomes on third-line antiretroviral treatment in the New Horizons drug donation program	58	57
Tiam, A.	Results of a cluster randomized study to evaluate the effect of a comprehensive service delivery intervention on HIV and maternal child health outcomes in HIV-positive and HIV-negative women	93	92
Traub, A.	Expanded index testing and community-based testing modalities in Nigeria are effective in identifying children living with HIV	33	33
Tsiouris, F.	Improving retention and viral suppression among HIV positive pregnant women in Nampula Mozambique: results from a quality improvement collaborative.	92	91
Turkova, A.	Cascade of care in children and adolescents with HIV in Russian Federation	68	67
Twizere, C.	Trends in clinical and socio-demographic characteristics of HIV-positive children up to 10 years of age at enrollment in CA-IeDEA sites	73	72
Urso, M.	Assessment of Population level Impact of Prevention of Mother to Child transmission Program in Manhica district, Mozambique	91	90
van Wyhe, K.	Cognitive outcomes at 7 and 9 years after the Children with HIV Early Antiretroviral (CHER) trial	46	46
Wu, M.	Disclosure to South African children about their own HIV status over time	72	71
Zanoni, B.	Development and Validation of the HIV Adolescent Readiness for Transition Scale (HARTS)	13	13
Zanoni, B.	Factors associated with virologic failure and loss to follow up for adolescents living with perinatally-acquired HIV during transition to adult care: A prospective analysis	86	85