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Once-Daily Integrase Inhibitor (Insti) With Boosted Darunavir is Non-Inferior to Standard of Care in Virogically Suppressed Children, Week 48 Results of the Smile PENTA-17 Trial

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Background: INSTI+Darunavir/r, a regimen with a high-resistance barrier, avoiding NRTI toxicities, might be a switching option in children LWHIV.

Methods: SMILE is a randomised non-inferiority trial evaluating safety and antiviral effect of once-daily INSTI +Darunavir/r versus standard-of-care (SOC) in HIV-1 infected, virologically-suppressed children 6-<18 years. The primary outcome is the proportion with confirmed HIV-RNA≥50c/mL up to week 48. Analyses were intention-to-treat, using Kaplan-Meier method (10% non-inferiority margin).

Results: 318 participants were randomised (Africa 53%, Europe 24%, Thailand 15%, Latin America 8%), INSTI+DRV/r:158(DTG: 153, EVG: 5); SOC:160. Median (range) age was 14.7years (7.6-18.0); weight 47.8kg (22.1-96.3); CD4 count 782cells/mm3 (227-1647); 61% female; 59% NNRTI; 41% PI.Median follow-up was 64.3 weeks with no loss to follow-up. By 48 weeks, 8 INSTI+DRV/r vs 12 SOC had confirmed HIV-RNA≥50c/mL; difference (INSTI+DRV/r-SOC) -2.5% (95% CI: -7.7, 2.6), showing non-inferiority. No major PI (0/11) or INSTI (0/6) resistance mutations were observed. There was 1 new severe CDC stage B event in INSTI+DRV/r and none in SOC. There were 4 SAEs (4 participants) in INSTI+DRV/r vs 5(4) in SOC (p=0.986); 13 grade 3/4 AEs (13 participants) in INSTI+DRV/r vs 25(19) in SOC (p=0.280). Self-reported mood/sleep disorders were infrequent and similar between arms. By week 48, difference between arms (INSTI+DRV/r-SOC) in mean CD4 count change from baseline was -48.3cells/mm3 (95% CI: -93.4,-3.2; p=0.036); numbers with CD4 count ≤500cells/mm3 were low and similar between arms [21(14%) INSTI+DRV/r vs 15(10%) SOC; p=0.234]; no significant differences were observed for CD8%, CD8 count and CD4%/CD8% ratio. Difference between arms (INSTI+DRV/r-SOC) in mean LDL and HDL change from baseline was +4.7mg/dL (95% CI: -0.7, 10; p=0.088) and -4.1mg/dL (95% CI: -6.7,-1.4; p=0.003), respectively. Weight and BMI increased more in INSTI+DRV/r than SOC [difference: 1.97kg (95% CI: 1.1, 2.9; p<0.001), 0.66kg/m2 (95% CI: 0.3, 1.0; p<0.001)].

Conclusions: In virologically-suppressed children, switching to INSTI+DRV/r was non-inferior virologically, with similar safety profile, to continuing SOC. Changes in CD4%, CD4 count, HDL-cholesterol, weight and BMI were slightly different in INSTI+DRV/r vs SOC although clinical relevance needs further investigation. SMILE data corroborate adult findings and provide evidence for an alternative NRTI-sparing regimen for children and adolescents.

2

B/F/Taf in Virologically Suppressed Adolescents and Children: Two-Year Outcomes in 6 to <18 Year Olds And Six-Month Outcomes in Toddlers

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Background: Bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) 50/200/25 mg is a single-tablet regimen recommended for adults and children weighing ≥25 kg living with HIV-1 due to its high barrier to resistance, low drug-drug interaction potential, and no food restrictions. Despite recent innovations, the limited availability of once-daily, palatable single-tablet-regimen formulations for infants and young children remains problematic. We present long term safety, efficacy, and tolerability outcomes in virologically suppressed 6 to <18-year-olds (>25 kg) who received B/F/TAF through 96 weeks (W), and results in younger children aged ≥2 yrs (14 to <25 kg) who received a new formulation, B/F/TAF low-dose tablet (LDT, 30/120/15 mg) through 24W.

Methods: Pediatric patients with HIV-1 RNA <50 c/mL ≥6 months and CD4 ≥200 cells/µL at screening were enrolled in an open-label trial (NCT02881320) to receive B/F/TAF 50/200/25 mg (Cohort 1: 12 to <18 yrs, ≥35 kg; n=50) (Cohort 2: 6 to <12 yrs, ≥25 kg; n=50) or B/F/TAF LDT (Cohort 3: >2 yrs, 14 to <25 kg; n=22) for 48 weeks followed by an extension phase. Adverse events (AE), laboratory tests, HIV-1 RNA, and acceptability/palatability of the adult and low dose tablets were assessed.

Results: Overall enrollment by country was: South Africa 42%, US 23%, Thailand 22% and Uganda 13%. Baseline characteristics (median, range) were: for Cohorts 1/2, age 12 (6-17) yrs, weight 39 (25-123) kg, CD4 count 810 (337-1991) cells/µL, 59% female, 69% Black, 93% vertically infected; for Cohort 3, age 6 (3-9) yrs, weight 19 (14-24) kg, CD4 count 962 (365-1986) cells/µL, CD4% 32 (24, 46); 50% were female, 73% Black, 100% vertically infected. For Cohorts 1/2, the median (range) duration of exposure to B/F/TAF was 151 (20-179) weeks. All participants from Cohorts 1/2 (n=100/100) had HIV-1 RNA <50 c/mL at W24 and 98% (98/100) at W48 by US FDA Snapshot Algorithm, while proportion suppressed at W96 was 99% (95/96) (missing=excluded). For Cohort 3, the median (range) duration of B/F/TAF exposure was 55 (24-84) weeks, and 91% (n=20/22) had HIV-1 RNA <50 c/mL at W24 (FDA Snapshot).

No participant developed treatment-emergent resistance. Study drug-related AEs reported in > 1 participant included abdominal discomfort (n=3) and transient neutropenia (n=2). One participant discontinued around W20 due to an AE (grade 2 insomnia and anxiety, Cohort 2). All participants from Cohorts 1/2 reported B/F/TAF size/shape acceptable and taste as palatable; in Cohort 3, ≥84% participants (or caregivers) reported acceptability and ≥91% reported favorable palatability for the LDT through 24W.

Conclusion: This week 96 (B/F/TAF 50/200/25 mg) and week 24 (B/F/TAF LDT 30/120/15 mg) efficacy, safety, acceptability and palatability data combined with the previously reported PK data continue to support the use of the first, unboosted, INSTI-based STR of B/F/TAF for the treatment of HIV 1 infection in adolescents and children 6 to <18 years of age weighing ≥ 25 kg and provides similar support for the use of B/F/TAF LDT for children aged >2 yrs weighing 14 to <25 kg. Evaluation of an age-appropriate B/F/TAF formulation in infants and children < 2 yrs is planned.

3

Pharmacokinetics and Safety of Dispersible- and Immediate-Release FDC Dolutegravir/Abacavir/Lamivudine in Children with HIV Weighing ≥14 kg: Preliminary Results from IMPAACT 2019

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Background: Children with HIV have limited pediatric-friendly fixed dose combination (FDC) formulations. IMPAACT 2019 is a Phase I/II, multi-site, open-label dose confirmation study examining the pharmacokinetics (PK), safety, and tolerability of immediate-release (IR) and a novel dispersible tablet (DT) formulation of abacavir (ABC)/dolutegravir (DTG)/lamivudine (3TC). Here we report preliminary PK and Week 4 safety results for IR and DT ABC/DTG/3TC FDC once-daily in children weighing ≥14 kg.

Methods: Children <12 years of age were enrolled across five weight bands (WB) in Botswana, South Africa, Thailand, and the United States. Data presented include: WB3 14-<20 kg (ABC 300 mg/DTG 25 mg/3TC 150 mg DT); WB4 20-<25 kg (ABC 360 mg/DTG 30 mg/3TC 180 mg DT); and WB5 ≥25 kg (ABC 600 mg/DTG 50 mg/3TC 300 mg IR). At entry, children were either treatment-naïve or treatment-experienced with HIV VL <200 copies/mL on a stable non-NNRTI-containing ARV regimen for ≥6 months. Treatment-experienced children switched to ABC/DTG/3TC at entry. Intensive PK assessments were performed 5-10 days after entry, with samples collected at time 0 (pre-dose), 1, 2, 3, 4, 6, 8, and 24 hours post-dose following an overnight fast (low-fat light snack permitted ≥2 hours prior to observed dose). IR tablets were swallowed whole. DT were dispersed in 20mL water. WB targets were geometric mean (GM) point estimates within the following ranges: DTG AUC0-24h of 35.1-134 µg·h/mL and C24h of 0.67-2.97 µg/mL, ABC AUC0-24h of 6.3-50.4 µg·h/mL, and 3TC AUC0-24h of 6.3-26.5 µg·h/mL. PK parameters were calculated using noncompartmental methods (Phoenix WinNonlin®). For each WB, acceptable safety criteria included: no deaths/life-threatening adverse events (AEs) related to study drug, or Grade 3+ AEs or permanent discontinuation related to study drug in ≥2 participants.

Results: Twenty-one children (10 female) underwent intensive PK assessments (7 per WB). Children were a median (range) 8.2 (5.8-11.3) years of age, 21.6 (16.5-37.1) kg, and all were treatment-experienced. For WB3, WB4, and WB5, the GM (CV%) DTG AUC0-24h was 71.5 (23.5%), 84.5 (26.3%), and 71.8 (13.9%) µg·h/mL, respectively, and C24h was 0.79 (44.2%), 1.35 (95.6%), and 0.98 (27.9%) µg/mL, respectively. GM (CV%) ABC AUC0-24h was 15.1 (40.3%), 17.3 (19.2%), and 25.7 (14.6%) µg·h/mL, in WB3, WB4, and WB5, respectively. GM (CV%) 3TC AUC0-24h was 13.0 (15.6%), 14.5 (16.5%), and 21.7 (26.2%) µg·h/mL, in WB3, WB4, and WB5, respectively. Two grade 2 events in one child in WB4 and one grade 1 event in WB5 were related to DTG. One child in WB3 experienced a grade 3 eGFR decrease and serum creatinine increase (with values in normal range) unrelated to study drug. All AEs resolved without intervention and no children discontinued study treatment due to AEs.

Conclusion: PK targets were met for IR and DT ABC/DTG/3TC in children ≥14kg and these formulations were well-tolerated. Additional data in children <14 kg and long-term safety/tolerability data are forthcoming. These findings provide reassurance for the dosing of these FDC formulations in children ≥14 kg and are expected to support global efforts to expand the availability of pediatric-friendly DTG-containing FDCs in alignment with WHO WB dosing.

4

Long-term Safety & Efficacy of Elvitegravir/Cobicistat/Emtricitabine/Tenofovir Alafenamide Fumarate (E/C/F/TAF) Single-Tablet Regimen in in Children and Adolescents Living with HIV

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Background: Elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide fumarate (E/C/F/TAF) is a once-daily, integrase strand transfer inhibitor (INSTI)-based single-tablet regimen (STR) for the treatment of HIV-1 infection. The current study is evaluating E/C/F/TAF in children and adolescents living with HIV. This analysis presents long term safety and efficacy data in study participants ≥2 years weighing ≥14kg.

Methods & Materials: Pediatric participants on a stable anti-retroviral regimen with HIV-1 RNA <50 copies/mL for ≥6 months prior to baseline and treatment-naïve adolescents were enrolled in this open-label study (NCT 01854775) and switched to E/C/F/TAF. Cohort (C) 1 (12 to <18 years; ≥35 kg, treatment-naive) and C2 (6 to <12 years; ≥25 kg) received E/C/F/TAF 150/150/200/10 mg for ≥96 weeks and C3 (≥ 2 years; 14 to < 25 kg) received E/C/F/TAF 90/90/120/6 mg low dose tablet (LDT) for ≥48 weeks at this analysis. Adverse events (AEs) and laboratory tests, including bone and renal biomarkers, were assessed. Bone mineral density (BMD) is measured by dual-energy X-ray absorptiometry every 48 weeks and z-scores and height-adjusted z-scores are determined. We report data through W96 for C1 and C2 and through W48 for C3.

Results: In C1, C2 and C3, 50, 52 and 27 participants were enrolled, respectively, with median age of 15, 10, and 6 years; overall, 58% of participants were female, 81% Black, and 85% vertically infected. RNA < 50 copies/mL was 97.8% (C1) and 100% (C2) at Week 96, and 96.3 (C3) at Wk 48. Median CD4 count change from baseline was 240 (C1) and -45 (C2) cells/µL at Week 96, and -187 cells/µL (C3) at Wk 48. Most AEs were mild or moderate in severity and no AE led to study drug discontinuation. One participant in C1 had a serious AEs considered study drug related by the investigator (grade 2 autoimmune uveitis, grade 2 visual impairment [n=1]). Median change from baseline in estimated GFR (Schwartz formula, mL/min/1.73m^2) C1 and 2 at Wk 96 was -19.5, -2.2 and C3 at Wk 48 was 9.6. Median % change in BMD for C1 and 2 at Week 96 was +9%, +9.1% and for C3 at Wk 48 +4.6% for spine and +2.7%, +7.2% and +6.5% for total body less head.

Conclusions: In pediatric participants living with HIV who initiated ART or were virologically suppressed on ART, switching to E/C/F/TAF maintained high rates of virologic suppression through 48 or 96 weeks of treatment in children 2y and older weighing 14 to <25kg and in children 6 to <18y weighing ≥25 kg. E/C/F/TAF was well tolerated through 48 and 96 weeks, respectively, with an acceptable bone safety profile. Decreases in eGFR seen in children 6 to <18y weighing ≥25 kg up remained stable through Week 96 and are consistent with inhibition of renal tubular creatinine (Cr) secretion by cobicistat and age-related physiological changes. These safety and efficacy findings support the use of E/C/F/TAF for treatment-experienced, virologically suppressed children and treatment naïve-adolescents living with HIV.

5

Pharmacokinetics, Safety and Acceptability of a Single Dose of Abacavir/Lamivudine/Lopinavir /Ritonavir (4-In-1) Fixed-Dose Granule Formulation In Neonates: PETITE Study

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Background: Early infant HIV diagnosis enables the rapid initiation of antiretroviral therapy (ART) from birth. ART is also increasingly used as 'presumptive' treatment for neonates at high-risk of HIV acquisition. However, initiating ART in neonates is challenging due to lack of dosing information and appropriate formulations. A paediatric fixed-dose granule formulation containing 30mg abacavir (ABC), 15mg lamivudine (3TC) and 40/10mg lopinavir/ritonavir (LPV/r), referred to as the '4-in-1', was developed to treat infants and young children with HIV. Whether this fixed dose combination (FDC) could be used for neonates is unknown. We evaluated the pharmacokinetics (PK), safety and acceptability of the 4-in-1 in neonates and report the results following the first planned interim analysis.

Material and Methods: The PETITE study is an ongoing Phase I/II, open-label, single arm, single centre, two-stage clinical trial conducted in South Africa. In Stage 1, neonates exposed to HIV (gestational age ≥38 weeks and birth weight of ≥2000 - 4000 g) received single dose(s) of the 4-in-1. The first 8 neonates received one single dose (1 capsule with milk) in the 2nd week of life, followed by intensive PK sampling. After establishing no safety concerns, a second group of 8 neonates received a single dose of the 4-in-1 on two separate occasions, the first dose within 3-14 days of life and the second 10-14 days later, with intensive PK sampling after each dose. Safety visits were performed 1 week after each PK visit and included clinical/laboratory evaluations and electrocardiograms. An interim analysis was planned to review pre-defined safety and PK criteria after completion of Stage 1 and before moving to a multi-dose strategy. LPV geometric mean exposure (AUC0-12) was required to fall between 20 and 100 µg.hr/mL.

Results: Eighteen neonates (72% female) were enrolled, 2 discontinued prior to receiving the 4-in-1. Sixteen neonates with a median (range) birth weight of 3,130 (2,790 - 3,590) g completed the study. All 24 intensive PK sampling visits were performed between day 7 and 22 of life. ABC, 3TC and LPV mg/kg doses were 8.6 (6.6-11.4), 4.3 (3.3-5.7) and 11.5 (8.8-15.2). As expected, the geometric mean (90% CI) AUC0-12 of ABC and 3TC were high: 29.87 (26.3-33.93) µg.h/mL and 12.61 (10.72-14.83) µg.h/mL, respectively. LPV exposures were below the predefined target, geometric mean AUC0-12 was 3.49 (2.13-5.72) µg.h/mL. RTV concentrations were detectable in only 4/120 (3%) of samples. There were no adverse events related to study drug. One serious adverse event occurred (viral pneumonia requiring short-term hospitalisation). All QTcF calculations were within normal limits. None of the neonates experienced difficulty in swallowing the 4-in-1 and none refused the medication.

Conclusions: The high mg/kg ABC and 3TC doses imposed by the 4-in-1 FDC in neonates were safe following a single dose, but LPV/r exposures were extremely low. Significant LPV/r dose increases would be required to achieve therapeutic LPV exposures, unduly increasing ABC/3TC exposures, and thereby preventing use of the 4-in-1 in neonates. Other pediatric solid formulations of LPV/r and ABC/3TC that allow different drug ratios should be studied in neonates.

6

Clinical Impact and Cost-Effectiveness of Viral Load Testing (VLT) to Inform the Transition to Pediatric Dolutegravir (DTG) in Antiretroviral Therapy (ART)-Experienced Children With HIV in South Africa

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Background: The WHO promotes transition to dolutegravir (DTG)-based ART for all children with HIV (CWH) established on ART. Viral load testing (VLT) may improve outcomes by identifying children with virologic failure (VF) who need a full 2nd line regimen containing DTG instead of a single drug substitution. We projected the clinical impact and cost-effectiveness of using VLT to inform transition to DTG for CWH in South Africa.

Methods: We modeled a cohort of 8-year-old CWH in South Africa on ABC/3TC/EFV as 1st-line ART in the CEPAC-Pediatric model, simulating 3 strategies: 1) remain on ABC/3TC/EFV (No DTG, as a comparator); 2) transition to ABC/3TC/DTG (DTG); and 3) VLT-based switch to DTG (DTG+VLT: ABC/3TC/DTG with virologic suppression [VS, VLT shows RNA<1,000c/ml]; ZDV/3TC/DTG with VF, RNA>1,000c/ml). DTG+VLT includes a 3-month delay between VLT and result receipt, followed by regimen switch. The following assumptions were made in the base-case: at simulation start, 70% of the cohort had VS, 15% had VF with NRTI-resistance, and 15% had VF without resistance. The probability of 24-week VS post-switch was greatest for children with baseline VS [96%], compared to children with VF and NRTI resistance [90% on ZDV; 80% on ABC] or VF without resistance [50%]. Risk of VF after 24-week VS was greater for children switched to ZDV/3TC/DTG (0.4%/month, assumed due to twice-daily dosing) than for children maintained on ABC/3TC/DTG (0.2%/month). One-time VLT cost was $25; monthly ART costs were $14 (ABC/3TC/DTG) and $10 (ZDV/3TC/DTG). Other input parameters were identical between strategies. Model outcomes included life expectancy (LE), per-person costs, and incremental cost-effectiveness ratios (ICERs, $/life-year-saved [$/LYS]), calculated from discounted (3%/year) LYs and costs. We considered ICERs <$3,000/LYS to be cost-effective (~0.5x South Africa's per-capita GDP).

Results: No DTG led to a projected undiscounted (discounted) LE of 33.10 (19.29) years and lifetime per-person costs of $21,680 ($12,000). Both DTG strategies increased LE and decreased costs, compared to No DTG: 39.43 (21.16) years and $21,710 ($11,340) for DTG, and 38.95 (21.06) years and $21,580 ($11,260) for DTG+VLT. DTG+VLT had lower life expectancy than DTG largely due to the higher VF risk associated with twice-daily ZDV/3TC/DTG. The ICER of DTG compared to DTG+VLT was $850/LYS.

In univariate sensitivity analyses, doubling ABC/3TC/DTG costs or using a point-of-care VLT made DTG+VLT cost-effective compared to DTG. Plausible variations in VS proportion at model start (30-100%) and VLT costs (0.5x-2x) did not change the finding that DTG was cost-effective. In multivariate sensitivity analyses, DTG+VLT became cost-saving when ZDV/3TC/DTG led to better long-term suppression for all children (post-suppression VF risk: 0.3%/month) and ABC/3TC/DTG simultaneously led to worse short-term VS for children failing with resistance (24-week VS: 70%).

Conclusions: The clinical and economic value of using VLT to guide DTG rollout depends substantially on the effectiveness and cost of ZDV compared to ABC after switch, as well as the time required to receive and act on VLT results. As children switch to DTG, long-term data about these key outcomes should be prioritized; using our current assumptions, VLT to inform switch to DTG provides little value.

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Weight Gain in Children and Adolescents on Dolutegravir vs Standard-of-Care in the ODYSSEY Trial

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Background: Dolutegravir is associated with excessive weight gain in adults. We present the first randomised data in children and adolescents.

Methods: ODYSSEY is a randomised multi-country trial evaluating dolutegravir (DTG) + 2NRTIs versus standard-of-care (SOC) in children starting first or second-line ART. We compared weight, height and BMI-for-age Z-scores (BAZ) between treatment arms using normal regression models adjusting for first-/second-line, randomisation stratification factors and baseline measurements. Proportions becoming newly overweight (BAZ>1-≤2) or newly obese (BAZ>2) are described.

Results: 707 children were randomised (sub-Saharan Africa 88%, Thailand 9%, Europe 4%); 311 started first-line (80% ABC/3TC, 19% TDF/3TC(FTC); 92% efavirenz-based in SOC); 396 second-line (54% ABC/3TC, 26% TDF/3TC(FTC); 72% lopinavir/ritonavir in SOC); 49% were female. At baseline, median age (IQR; range) was 12.2 (9.1, 14.9; 2.9-18.0) years; weight (IQR) 31(23, 43)kg, height 138(125, 153)cm, BMI 16.3(14.9, 18.5)kg/m2, BAZ -0.6(-1.4, 0.1); 11% had WHO-defined severe thinness/thinness, 5% were overweight, 1% obese; 50% were pubertal/postpubertal. Median follow-up was 142(124, 159) weeks.

Weight, height and BAZ increased more in DTG than SOC with adjusted difference in means (DTG-SOC) at 96 weeks of 1kg (95%CI 0.3, 1.7; p=0.004), 0.8cm (95%CI 0.2, 1.4; p=0.007) and 0.14 Z-score (95%CI 0.02, 0.26; p=0.018) respectively. Early differences between groups stabilised. Treatment differences at 96 weeks in BAZ were similar in males and females (heterogeneity p=0.42), children aged <12 and ≥12 years (p=0.95), prepubertal and pubertal/postpubertal participants (p=0.54), participants starting first- and second-line ART (p=0.746), and those starting TDF vs other (p=0.61). Findings were similar for weight and height.

Overall, 14(4%) children/adolescents in DTG and 9(3%) in SOC were newly overweight or obese at 96 weeks (p=0.29).

Conclusions: Children grew better after starting DTG. Small differences between arms in weight, height and BMI stabilized before 2 years, with few becoming newly overweight/ obese in either arm. DTG-based ART was not associated with excessive weight gain in children and adolescents.

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Dolutegravir and Weight Gain to Adolescents Living with HIV at Baylor Mwanza-Tanzania

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Introduction: Dolutegravir (DTG) has been approved for the use in adolescents with HIV. It's highly effective and well tolerated drug by adolescents and adults. DTG is an integrase strand inhibitor that has been associated with weight gain in adults, however this relationship has not been well described in adolescents living in Tanzania, where stunting and malnutrition are problematic. The aim of this study was to assess the weight gain in adolescents using ART regimens that contain Dolutegravir.

Methodology: This was a retrospective study conducted at Baylor COE in Mwanza –Tanzania from January 2020 to December 2020. It involved all adolescents (10 – 19yrs) living with HIV on Dolutegravir based regime for more than six months both newly initiated on ART and those switched from other regimen. Clinical data such as sex, age, WHO stage, HVL, CD4, initial and final body weight, body mass index (BMI), and adherence were collected. HVL and CD4 count were taken before. Comparison of the weight before (the visit of DTG switch) and after (visit after six months of being on DTG). Overweight and obesity was defined by BMI per age. Data was obtained from the electronic medical record (EMR).

Results: A total number of 229 adolescents were enrolled in the study of which 99/229 (43.2%) were female, 21/229(9%) were newly enrolled and 208/229(91%) switched from other regimen. 70(30.5%) had WHO stage I and II and 159 (69. 4%) had stage III and IV. Majority were suppressed 220/229 (96.0%) with HVL of < 1000. 222/229 (96.9%) patients had CD4> 350celld /mm3 and 165 (72%) had good adherence as per pill count.

225/229 (98.3%) adolescents had normal BMI for age and 4/229 (1.7%) were overweight and none had severe or moderate malnutrition before DTG. After six months of being on DTG based regimen 206/229 (90%) of adolescents gained weight 23/229(10%) had no weight gain. Among those who gained weight 83/186 (44.6%) gained 0-2.5 kg, 78/186(41.9%) gained 2.6 - 5kg, 16 (8.7%) gained 5-10kg and 9/186 (4.8%) gained more than 10kg. Before switch to DTG 4/229(1.7%) adolescents were overweight compare to 20/229(8.7%) who were overweight (16) and obese (4) after being on DTG for 6 months.

Conclusion: There was five times increase of adolescents with obesity after being on DTG based regimen for six months. There is need to have a close monitoring of adolescent weight when on DTG .and need for more health education about effect of overweight and obesity.

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Longitudinal Study on Insulin Resistance and Metabolic Syndrome in Children with Perinatal HIV Infection and HIV Exposed Uninfected Children in South Africa

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Introduction: HIV is associated with insulin resistance and Metabolic Syndrome, driven by HIV-associated immune dysregulation and by antiretroviral therapy (ART). However, few longitudinal studies have been conducted in children living with perinatally-acquired HIV (CLpHIV). We evaluated the trajectory of insulin resistance and Metabolic Syndrome in CLpHIV compared to children who are HIV-unexposed and uninfected (CHUU), and children who are HIV-exposed and uninfected (CHEU).

Methods: The study included children previously part of the Children with HIV Early antiRetroviral (CHER) trial and P1060 trial followed at Tygerberg Children's Hospital in South Africa between 2014 and 2020, along with CHEU and CHUU from the same communities. The cohort comprised 485 children, with 141 CLpHIV, 169 CHEU and 175 CHUU, with a median age at baseline of 9 years. The main outcome was the Homeostatic Model Assessment of Insulin Resistance (HOMA-IR), and secondary outcomes included LDL cholesterol, triglyceride-to-HDL ratio, android fat mass and systolic blood pressure. We used a mixed effects model to model the progression of metabolic indicators over time in each HIV group, with age as a categorical variable to account for the expected decline in HOMA-IR towards the end of puberty. Directed Acyclic Graph analysis was used to identify covariates, whereafter the following were considered as confounders: gender, height, age group, Tanner puberty stage and ethnicity.

Results: Adjusted mean HOMA-IR was 15% (95%CI: 2%–29%) greater in CLpHIV than CHUU. Adjusted mean triglyceride-to-HDL ratio was 48% (95%CI: 35%–62%) greater in CLpHIV than CHUU, and the adjusted mean LDL was 0.25 mmol/L greater in CLpHIV than CHUU (95%CI: 0.11–0.40). In all analyses, no significant difference was found between CHEU and CHUU.

Conclusions: CLpHIV have persistently elevated insulin resistance, triglyceride-to-HDL ratio and LDL cholesterol into puberty, and therefore should be monitored carefully for subclinical cardiovascular disease and receive appropriate preventative interventions, as CLpHIV will have a lifelong exposure to HIV-associated immune dysregulation and ART.

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Virological Failures and Genotypic Resistance in Children and Adolescents Randomised to Dolutegravir-Based ART vs. Standard-of-Care in the ODYSSEY Trial

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Background: ODYSSEY, a multi-country randomised trial, demonstrated superior treatment efficacy for dolutegravir (DTG) plus two NRTIs versus standard-of-care (SOC) in children ≥14kg (median age 12 years [range:3-18]) starting first- and second-line ART. We describe virological and drug resistance outcomes by 96 weeks.

Methods: Virological failure (VF) was defined as confirmed viral load (VL)≥400c/mL after week 36 or lack of virological response by week 24 with ART switch. Participants with VF were retrospectively tested for post-failure resistance up to week 96, using the latest sample with VL≥1000c/mL after failure and prior to treatment change; the corresponding baseline sample was sequenced if ≥1 major IAS mutation was identified.

Results: 311 children started first-line ART (154 DTG, 157 SOC [92% efavirenz]) and 396 started second-line (196 DTG, 200 SOC [72% lopinavir/r, 25% atazanavir/r]). NRTI backbones were ABC/3TC (80% first-line, 54% second-line), TDF/XTC (19%, 26%), ZDV/3TC (1%, 19%), and ABC/TDF (0%, 0.8%). On first-line, 11(7%) DTG vs. 30(19%) SOC experienced VF by 96 weeks, and on second-line, 31(16%) DTG vs. 40(20%) SOC. Samples were tested for all 112 failures: median time from VF to resistance test was 24[IQR:12-47] weeks. 47(42%) had post-failure resistance test at week 96, 60(54%) were tested earlier (16 due to treatment change, 44 no later sample available with VL≥1000c/mL or later sample failed to amplify); the remaining 5(4%) failed to amplify on all samples. On first-line, post-failure resistance tests were available as follows: reverse transcriptase (RT)/protease (PR) (11 DTG, 29 SOC), integrase (IN) (10 DTG); on second-line: RT/PR (28 DTG, 39 SOC), IN (22 DTG).

First line ART: No participants on first-line DTG had a major IAS drug resistance mutation post-failure (0/11 NRTI/NNRTI/PI; 0/10 INSTI). On SOC, 18/29(62%) participants had NRTI resistance post-failure (DTG vs. SOC p<0.001), 27/29(93%) NNRTI resistance (p<0.001) and 0/29 PI resistance. Of 13 with NRTI resistance post-failure and a baseline resistance test, all developed at least one new NRTI mutation; 18/19(95%) developed new NNRTI resistance.
Second line ART: 20/28(71%) DTG vs. 28/39(72%) SOC had at least one NRTI mutation post-failure; 21/28(75%) vs. 35/39(90%) had NNRTI resistance; and 2/28(7%) vs. 2/39(5%) had PI resistance. Among DTG vs. SOC participants with a major resistance mutation post-failure and baseline result, 0/16 DTG vs. 3/23 SOC (p=0.26) developed new NRTI resistance, 0/18 vs. 3/26 (p=0.26) new NNRTI resistance and 1/2 vs. 1/1 new PI resistance.

On DTG, 4/22(18%) on second-line developed INSTI resistance (2 Q148R/K, 1 G118R, 1 G118R+R263K); 3/4 were on ZDV/3TC.

Conclusion: ODYSSEY demonstrated that DTG has a high genetic resistance barrier in children, preventing emergent resistance to NRTIs. We identified no post-failure resistance to any drug class amongst children initiating first-line DTG, significantly less than first-line SOC. Among those on second-line DTG, there was no new NRTI resistance, however 4 children developed new INSTI resistance. These results support using DTG-containing regimens for children starting first-line or second-line ART, but ongoing adherence support is required for children on second-line.

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Hypertensive Disorders in Pregnancy and HIV: A Province-Wide Cohort Analysis During 2018 and 2019 in the Western Cape, South Africa

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Background: Antiretroviral therapy (ART) in pregnant women with HIV (PWH) may be associated with hypertensive disorders of pregnancy (HDP) including gestational hypertension, pre-eclampsia, eclampsia and HELLP syndrome. Studies suggesting an association between HDP and ART were conducted when ART was initiated for advanced HIV disease only. In the population of pregnant women during 2018 and 2019, before dolutegravir roll-out, we evaluated whether the prevalence of HDP differed between PWH not receiving ART (ART-none), PWH initiating ART during pregnancy (ART-pregnancy), PWH initiating ART preconception (ART-preconception) and pregnant women without HIV. Secondarily, PWH with ART-preconception were compared by calendar period of ART initiation to evaluate if initiation under earlier (pre-2013; 2013-2015) compared to universal ART guidelines (2016-2019) was associated with HDP.

Methods: All women with a pregnancy outcome from 01 January 2018 to 31 December 2019 in the Western Cape Provincial Health Data Centre (PHDC) were included. The PHDC integrates data from multiple electronic platforms according to individual unique identifiers issued to all those accessing provincial health services. Basic information is routinely electronically collected on all deliveries in the province. Individual women were linked to the electronic HIV register to identify PWH and ART history, to a facility administration database for HDP ICD10 codes, antihypertensive drug dispensing codes and the laboratory database for CD4 counts. Women were classified as having HDP based on ICD-10 code or first-time prescription of antihypertensive drugs <140 days before delivery. Women with chronic hypertension prior to pregnancy without superimposed pre-eclampsia, eclampsia or HELLP syndrome were not considered to have HDP. Unadjusted and adjusted prevalence ratios (PRs) for HDP were calculated using log-binomial regression.

Results: Among 180553 women with a pregnancy outcome, 33978 (18.8%) were PWH and 13677 (7.6%) had HDP. Among PWH, 3827 (11.3%) were classified as ART-none, 9868 (29.0%) ART-pregnancy and 20283 (59.7%) ART-preconception. ART-none had the highest HDP prevalence (9.8%) and ART-preconception the lowest (6.9%). Unadjusted PRs (95% confidence interval (CI)) for HDP in ART-none, ART-pregnancy and ART-preconception compared to women without HIV were 1.28 (1.16-1.41), 0.92 (0.85-0.99) and 0.90 (0.84-0.95) respectively. Adjusted for maternal age, multiparity and multifetal pregnancy PRs (95% CI) were 1.12 (1.02-1.24), 0.87 (0.81-0.93) and 0.74 (0.71-0.79) in ART-none, ART-pregnancy and ART-preconception respectively. ART duration and CD4 at delivery were not associated with HDP. Amongst PWH on ART-preconception, unadjusted PRs (95% CI) for HDP by ART initiation period were 0.75 (0.66-0.86; N=6668) and 0.80 (0.71-0.91; N=8323) for 2016-2019 and 2013-2015 respectively compared to pre-2013 (N=5292). Adjusted for maternal age, multiparity and multifetal pregnancy, PRs (95% CI) were attenuated to 0.95 (0.82-1.08) and 0.92 (0.82-1.04) for 2016-2019 and 2013-2015 respectively compared to pre-2013.

Conclusion: In this large province-wide analysis, compared to women without HIV, for PWH no ART was associated with a higher prevalence of HDP and ART started prior to or during pregnancy was associated with a lower prevalence of HDP. These are reassuring findings observing no excess risk of HDP in PWH receiving ART during 2018 and 2019. Future analyses will examine associations of HDP with ART regimens.

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Bone Mineral Density/Content of Postpartum Mothers Taking Treatment Including DTG Vs EFV, TDF Vs TAF in Pregnancy and Their Infants: Randomized IMPAACT 2010 Trial

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Background: Dolutegravir (DTG), efavirenz (EFV), tenofovir disoproxil fumarate (TDF) and, in future, possibly tenofovir alafenamide fumarate (TAF) are important drugs for pregnant women with HIV, but little is known about the impact of their use in pregnancy and postpartum on maternal and infant bone.

Material and Methods: Pregnant women with HIV-1 in 9 countries were randomized 1:1:1 to start open-label DTG+FTC/TAF, DTG+FTC/TDF, or EFV/FTC/TDF at 14-28 weeks gestational age (GA). The planned enrolment was 213 mother-infant pairs (71 per arm). DXA scans were performed at 7 sites in sub-Saharan Africa using Hologic systems in a subset of mothers at week ~50 postpartum (hip and lumbar spine) and infants at age ~26 weeks (whole body and lumbar spine). Central DXA analysis was performed by a trained technologist. Pairwise comparisons of maternal bone mineral density (BMD) Z-scores and infant bone mineral content (BMC) were performed using two-sample t-tests.

Results: One hundred and fifty-four maternal DXAs were available from week 50 postpartum. Baseline characteristics were similar between treatment arms. By week 50 postpartum, mean (SD) study treatment duration was 66.0 (8.5) weeks, 139 (90%) had breastfed (mean (SD) duration of 43.9 (15.0) weeks) and 95 (62%) mothers had received medroxyprogesterone acetate. Mean (SD) maternal hip BMD Z-scores were -0.45 (0.71) in the DTG+FTC/TAF arm, -0.50 (0.73) in the DTG+FTC/TDF arm, and -0.57 (0.73) in the EFV/FTC/TDF arm. Mean (SD) spine BMD Z-scores were -1.40 (1.08) in the DTG+FTC/TAF arm, -1.57 (1.07) in the DTG+FTC/TDF arm, and -1.64 (1.05) in the EFV/FTC/TDF arm. There were no apparent differences in maternal hip or spine BMD Z-scores between treatment groups (p-values ≥0.26).

Of the infant week 26 DXAs done, 104 (54%) whole body and 157 (83%) spine scans were available for analysis. Birth characteristics were similar across arms. At time of DXA, infants were a mean (SD) age of 5.8 (0.6) months, 134/165 (81%) were still breastfeeding, and 153 (93%) had received co-trimoxazole. Mean (SD) whole body BMC was 143.4 (31.0) grams in the DTG+FTC/TAF arm, 137.4 (31.1) grams in the DTG+FTC/TDF arm, and 133.5 (29.0) grams in the EFV/FTC/TDF arm. Excluding head measurements, mean (SD) BMC was 73.3 (18.4) grams in the DTG+FTC/TAF arm, 70.5 (18.7) grams in the DTG+FTC/TDF arm, and 69.0 (16.0) grams in the EFV/FTC/TDF arm. Mean (SD) spine BMC was 2.9 (0.5) grams in the DTG+FTC/TAF arm, 2.8 (0.5) grams in the DTG+FTC/TDF arm, and 2.6 (0.5) grams in the EFV/FTC/TDF arm. Mean spine BMC was close to ½ SD (25g) and significantly lower in the EFV/FTC/TDF arm compared to the DTG+FTC/TAF and DTG+FTC/TDF arms (respective difference (95% CI) of 0.22 (0.02, 0.42) grams (p-value=0.028) and 0.20 (0.01, 0.40) grams (p-value=0.042)). There were no apparent differences between treatment groups for whole body BMC or whole body without the head BMC measurement.

Conclusions: At week 50 postpartum, maternal BMD was similar across study arms. Further analysis is underway of the clinically meaningful ½ SD difference in lumbar spine BMC observed at week 26 in infants exposed to maternal EFV vs DTG.

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Impact of the COVID-19 pandemic on perinatal HIV prevention In Canada: Canadian Perinatal HIV Surveillance Program

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Background: With Canada currently in its third wave of the COVID-19 pandemic, significant public health resources continue to be diverted to pandemic control, with concerns that many non-COVID medical conditions, including the prevention and treatment of HIV, may have been adversely affected. Annual HIV vertical transmission rates in Canada were <2% prior to the COVID-19 pandemic. There are concerns that regional and national lockdowns and lack of available public health resources for HIV control may have compromised the care available to pregnant women living with HIV (PWLWH). The objectives of this study were to determine the impact of COVID-19 on access to optimal therapy among PWLWH, and the impact of vertical transmission in Canada.

Material and Methods: Using data from the Canadian Perinatal HIV Surveillance Program, access to optimal care during pregnancy, and vertical transmission rates were compared in the pre-COVID-19 period (2015-2019) to the COVID-19 period (May-Dec 2020). 23 Canadian pediatric HIV centres report data yearly on all mother-infants pairs, including detailed maternal characteristics, pregnancy combination antiretroviral treatment (cART) and infant outcomes. Sub-optimal treatment was defined as one of "no treatment" or "ART" (< 3 antiretroviral drugs) or <4 weeks of consecutive combined antiretroviral therapy (cART) immediately prior to birth. The analysis was restricted to infants born in Canada to mothers with documented HIV infection who were referred to one of the participating sites within three months of their birth. Positive infants were identified as having HIV on the basis of detection of HIV by virologic assay on 2 separate occasions beyond 4 weeks of life.

Results: The number of HIV exposed infants per year has increased over time, with 250 infants born in 2020. In 2020, 32% came from the province of Ontario, 17% from Alberta, 24% from Quebec, 14% from Saskatchewan, 7% from British Columbia and 4% from Manitoba; 60% were Black, 21% were Indigenous, and 13% were white. Overall, 63% of women acquired HIV heterosexually, 13% through injection drug use (IDU) and 4.4% perinatally. The proportion and number of pregnant women sub-optimally treated in May-December 2020 versus 2015-2019 were 7.7% (12/155), as compared to 6.6% (86/1297) respectively. The corresponding transmission rates were 3.2% (5/155) versus 1.3% (17/1297), respectively. Among those who had acquired HIV through IDU, the sub-optimal treatment rate was 26.1% during COVID-19, versus 13.6% in the pre-COVID-19 period.

Conclusions: The perinatal transmission rate increased in Canada from 1.3% (2015-2019) to 3.2% during the pandemic, a clinically important increase in a country with low HIV vertical transmission rates, and it is the highest reported rate in over 5 years. Notably, the sub-optimal treatment rate among women acquiring HIV through IDU increased from 13.6% to 26.1%, suggesting this group may have been at highest risk. These data serve as an alarming signal that there may have been problems in accessing care for addictions, prenatal care and HIV specific care in the first waves of the pandemic. Additional attention to at-risk populations is needed as the pandemic continues to affect Canada.

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A Comparative Multi-Country Analysis of the Impact of COVID-19 on HIV Services for Pregnant and Breastfeeding Women and Their Infants

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Background: HIV service delivery adaptations during the COVID-19 pandemic ensure timely prevention of mother-to-child HIV transmission (PMTCT) services. This analysis updates a 2020 International Pediatrics Workshop oral presentation and compares USAID PEPFAR PMTCT program data from 12 countries before and during COVID-19.

Methods: Quarterly (Q) PMTCT program data was collected (October 1, 2019 and September 30, 2020). Chi-squared tests and percent change compared results on HIV testing and treatment before (average of Q1 and Q2 data [Q1/2]) and during COVID-19 (Q3 and Q4).

Results: Women attending and tested at ANC1 decreased from Q1/2 to Q3 by 3.4% and 3.8%, respectively. From Q3 to Q4, attendance and testing increased by 5.5% and 4.4%, respectively. Testing coverage was similar in Q3 as Q1/2, but decreased by 1% in Q4 ($p<0.001$). PWLHIV identified and on ART decreased from Q1/2 to Q3 by 4.5% and 4.9%, then increased from Q3 to Q4 by 6.7% and 7.4%, respectively. Positivity decreased from 8.0% in Q1/2 to 7.9% in Q3, then increased to 8.1% in Q4 (Q3 vs. Q4 $p<0.001$). ART coverage for PWLHIV was stable during FY20.

HEI tested ≤2 months and testing coverage was similar in Q3 vs Q1/2, then decreased by 4.7% and 10.6% in Q4 (Q3 vs. Q4, $p<0.001$) respectively. HEI tested at 2-12 months decreased by 5% between Q1/2 and Q3 while testing coverage was stable; both increased in Q4 by 9% and 2.2% (Q3 vs. Q4, 2.2%, $p<0.001$), respectively.

Conclusions: During COVID-19, there were decreases in ANC1 testing coverage, HEI tested ≤2 months, and testing coverage. As COVID-19 restrictions lessened in Q4, ANC1 positivity, ART coverage and HEI 2-12 month testing coverage increased. PMTCT services should continue to be adapted to serve mothers and infants during the COVID-19 pandemic to ensure continuity of treatment.

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Early Infant Diagnosis of HIV and Linkage to Antiretroviral Therapy in the Context of COVID-19 in Fifteen Sub-Saharan African Countries

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Background: Among the 1.3 million pregnant women living with HIV in 2019, only 60% of their infants received early infant diagnosis (EID) testing by two months of age. We describe changes in EID testing, diagnosis, and linkage to antiretroviral treatment (ART) for infants with HIV in the context of the global COVID-19 pandemic.

Methods: We analyzed U. S. President's Emergency Plan for AIDS Relief (PEPFAR) Monitoring, Evaluation and Reporting data from 15 countries in sub-Saharan Africa (Cameroon, Côte d'Ivoire, Democratic Republic of the Congo, Eswatini, Kenya, Lesotho, Malawi, Mozambique, Nigeria, South Africa, South Sudan, Tanzania, Uganda, Zambia, and Zimbabwe) with complete data for the following indicators: number of infants with a first EID test by two months of age, proxy two-month EID coverage (number of infants with an EID test / reported number of pregnant women living with HIV receiving antenatal care), number of infants with HIV diagnosed by 12 months of age initiated on ART, and 12-month proxy ART linkage (number of infants with HIV initiated on ART / number of infants with HIV). We calculated the percent change for each indicator, by country and overall, across two time periods, representing the six months both before and during the early phase of the COVID-19 pandemic (Period A: October 2019-March 2020 and Period B: April-September 2020). To understand seasonal variation, we calculated the percent change over the same six-month periods in the prior year (Period C: October 2018-March 2019 and Period D: April-September 2019). We classified percent change within +/-3.0% as minimal change.

Results: During April-September 2020 (Period B), 273,163 infants received EID testing by two months of age at PEPFAR-supported sites in 15 countries, with minimal change compared to October 2019-March 2020 (Period A, +0.6%). Overall, EID coverage increased from 76.8% to 80.1% from Period A to Period B (+4.3%). During the same time periods the prior year (Period C to D), EID coverage increased by 14.7%. Eight countries reported increased EID coverage during Period B, and two countries reported decreased EID coverage. During Period B, 5,554 infants were diagnosed with HIV by 12 months of age, which represented a 9.8% decrease compared to Period A. ART linkage decreased from 90.8% to 87.8% from Period A to Period B (-3.4%). During the same time periods the prior year (Period C to D), minimal change was observed in ART linkage (+0.4%). Six countries reported increased ART linkage during Period B, and four countries reported decreased ART linkage.

Conclusion: During the COVID-19 pandemic, EID coverage increased, though gains seen were less than in the prior year; ART linkage declined during the

pandemic. Sharing best practices from countries that saw gains may support improvements in comprehensive care for HIV-exposed infants during the ongoing pandemic. Additional analyses are necessary to understand how country-specific characteristics, including timing and implementation of mitigation strategies, affected EID coverage and linkage to ART.

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The Impact of COVID-19 on HIV Services for Children Living with HIV Across 14 Countries

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Background: Healthcare delivery has been affected by the COVID-19 pandemic, particularly for children living with HIV (CLHIV). This analysis compares USAID PEPFAR HIV services for CLHIV (<15 y/o) before and during COVID-19.

Materials & Methods: We analyzed 14 countries' quarterly (Q) CLHIV program data from October 1, 2019 to September 30, 2020. Chi-square tests and percent change compared pre-COVID-19 results from September 2019 to March 2020 (average of Q1 and Q2 data [Q1/2]) to results during COVID-19 from April to September 2020 (Q3 and Q4) for testing volume, CLHIV identified, positivity, new antiretroviral therapy (ART) initiations, number of CLHIV currently on ART, continuity of treatment (COT), viral load coverage (VLC) and viral suppression (VS).

Results: The total number of tests conducted and the number of CLHIV who were newly identified decreased from Q1/2 (Q1/2 tests: 461,726; CLHIV: 9,305) to Q3 (Q3 tests: 263,628; CLHIV: 6,551) by 42.9% and 29.6%, respectively. From Q3 to Q4 (Q4 tests: 332,129, CLHIV: 6,425) testing increased by 26.0%, but Q4 remained below the Q1/2 levels by 28.1%, while CLHIV identified had no significant difference. Positivity increased from 2.0% in Q1/2 to 2.5% in Q3 ($p<0.001$), but then decreased to 1.9% in Q4 (Q3 vs. Q4 $p<0.001$).

CLHIV newly initiated on ART decreased from Q1/2 to Q3 by 24.5% and increased from Q3 to Q4 by 5.1% (9,219; 6,956, and 7,314 for Q1/2, Q3, and Q4 respectively). COT decreased by 3.0% ($p<0.001$) from Q1/2 to Q3, but then increased by 3.6% ($p<0.001$) from Q3 to Q4. VLC decreased from Q1/2 to Q3 and Q3 to Q4 by 5.8% ($p<0.001$) and 1.2% ($p<0.001$) respectively. VS increased from Q1/2 to Q3 and Q3 to Q4 by 1.8% ($p<0.001$), and 2.0% ($p<0.001$) respectively.

Conclusions: Across the 14 countries, the total number of HIV tests conducted for <15 y/o, CLHIV identified, CLHIV initiated on ART, COT, and VLC declined significantly; while VS increased significantly during COVID-19. As COVID-19 restrictions eased in Q4, the total number of tests conducted, CLHIV initiated on ART, COT, and VS significantly improved, while positivity decreased. HIV programs must continue to adapt to ensure essential services for CLHIV are provided as the COVID-19 pandemic continues.

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Pediatric and Adolescent HIV Viral Load Coverage and Suppression Rates in the Context of the COVID-19 Pandemic in 14 Sub-Saharan African PEPFAR Countries in 2019 and 2020

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Background: The COVID-19 global pandemic has limited access to HIV services and antiretroviral therapy (ART) adherence for children and adolescents living with HIV. We describe viral load coverage (VLC) and VL suppression (VLS) rates in children and adolescents during the COVID-19 pandemic in 14 countries supported by the U.S. President's Emergency Plan for AIDS Relief (PEPFAR).

Methods: We analyzed PEPFAR monitoring, evaluation, and reporting data for children (0–9 years) and adolescents (10–19 years) living with HIV from facilities in Cameroon, Côte d'Ivoire, Democratic Republic of the Congo, Ethiopia, Lesotho, Kenya, Malawi, Mozambique, Nigeria, South Africa, Tanzania, Uganda, Zambia, and Zimbabwe. To describe the potential effect of COVID-19, we compared data from January to December 2019 (pre-COVID) and January to December 2020 (during COVID) for the following indicators: number of patients with a VL result in the medical or laboratory record, number of patients with suppressed VL under 1000 copies/mL, VLC (patients with a VL result/total eligible for a test on ART), and VLS (number of patients suppressed/number of patients with a VL result). We report percentage change for VL tests and differences in percentage points for VLC and VLS. Results were disaggregated by sex for VLC and VLS.

Results: A total of 234,373 children had a documented VL during the pre-COVID period, with VLC rate of 75.2%. across all countries. During COVID, there was a 4.4% reduction in number of children with a documented VL (n=224,066) and the overall VLC rate decreased to 72.8%. In 10 countries, the VLC rate increased during COVID (range, 0.7%–19.8%); however, four countries experienced steeper declines (range, 2.8%–59.8%). For adolescents, the number with a documented VL increased by 4.8% from 465,438 to 487,609 between pre-COVID and during COVID. However, VLC rates among all countries combined, decreased from 81.8% to 80.9%. The VLC rate increased during COVID in nine countries (range, 0.6%–16.9%) but decreased in five countries (range, 2.6%–49.0%). There was a decrease in VLC among female and male children (3.0% and 1.8% respectively) and a decrease among female and male adolescents (1.1% and 0.8% respectively).

Overall, VLS rates among children increased from 69.9% (n=163,886) pre-COVID to 77.1% (n=172,713) during COVID. Similarly, VLS rates among adolescents increased from 76.4% pre-COVID (n=355,375) to 83.4% during (n=406,495). VLS rates increased in all

countries during COVID, ranging between 0.2– 15.4% and 0.6–16.2 % for children and adolescents. Male children and adolescents had a larger increase in VLS compared to females (7.7% vs 6.7% and 8.1% vs 6.2% respectively).

Conclusions: Viral load testing and coverage was affected in varying degrees across all countries for children and adolescents. Countries that increased VLC rates during the pandemic could offer strategies to maintain patient access to VL testing and to overcome common barriers to VLC during COVID. Although VLC rates decreased in some countries, pediatric and adolescent VLS rates increased during the pandemic, which shows the feasibility of implementing and scaling strategies to improve outcomes for children and adolescents living with HIV.

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Knowledge and Perceptions of Covid-19 Among Young People Living With HIV in Malawi and the Impact of the Pandemic on Their Health and Wellbeing

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Background: Inadequate COVID-19 literacy is associated with poor adherence to preventative behaviours. Recent data suggest poor COVID-19 knowledge among adults in Malawi.

Young people living with HIV (YPLHIV) face psychosocial challenges related to their chronic disease. Data regarding their knowledge of COVID-19 and the impact of the pandemic on their lives are lacking. This study aims to address this knowledge gap among YPLHIV attending Baylor Children's Foundation Malawi (BCFM), the largest paediatric and adolescent HIV service in Malawi.

Methods: A cross-sectional prospective study was conducted whereby YPLHIV aged ≥14 years attending two BCFM Teen Clubs in November/December 2020 were recruited. Informed consent/assent were obtained from the guardian/YPLHIV. Data relating to COVID-19 knowledge and perceptions and the impact of the pandemic on their health and wellbeing were collected using a self-complete questionnaire (English/Chichewa). Descriptive statistics were used for data analysis (SPSS v24).

Research Ethics approval was granted by the Malawi College of Medicine Research Ethics Committee (#P.09/20/3141).

Results: A total of 164 YPLHIV with a median (IQR) age of 16(15-18) years (46% female) participated. Radio/TV was the primary source of COVID-19 information (92%). Over a quarter (28%) reported COVID-19 as a "Western made virus to depopulate Africans" although 83% were aware it was first identified in China and has spread globally. Fever (86%) and cough (82%) were commonly recognised symptoms, although only 52% reported runny nose/nasal congestion as presenting symptoms. Awareness of asymptomatic infection was low (10%). Knowledge of droplet transmission of COVID-19 was high (92%), although 31% reported animal transmission as common. The majority agreed with social distancing (76%) and wearing masks (90%) as preventative measures. However, 29% reported eating ginger/okra as protective and 40% believed the warm/humid weather in Malawi reduces transmissibility. Three quarters (76%) recognised COVID-19 as primarily a self-limiting illness in healthy people, although 27% reported herbal medications as treatment options.

A third (31%) of YPLHIV reported worsening HIV treatment adherence during the pandemic and 43% were unable to obtain medication before they ran out despite the clinic remaining open. Financial constraints (73%), transport difficulties (57%) and reduced group psychosocial support through Teen Clubs (50%) were identified barriers. Social vulnerabilities included interrupted education (56%), family conflict (23%), social isolation (60%) and parental unemployment (59%) with 37% reporting seeking casual employment to help support their families. A quarter (74%) feared contracting COVID-19 and 62% reported feelings of sadness.

Conclusion: This is the first study reporting knowledge gaps and misconceptions about COVID-19 among YPLHIV in Malawi. The data further highlight healthcare barriers and the psychosocial impact of the pandemic on this marginalised population. Exclusion of younger adolescents was a limitation, as the questionnaire was not developmentally-appropriate for this age-group.

The findings of this study have prompted strengthening of COVID-19 health education and the search for innovative measures (e.g., digital psychosocial support) to optimise service delivery at BCFM and can guide interventions in other HIV healthcare settings nationally. It is criticial that policymakers and governments ensure access to healthcare services for chronic diseases is maintained during the COVID-19 pandemic.

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More Frequent Viral Load Testing, With Point-Of-Care Tests Has No Impact on Viral Suppression in Postpartum HIV-Positive Women in a Randomized Controlled Trial in 2 Clinics in Johannesburg, South Africa

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Background: Elevated maternal viral load (VL) increases HIV transmission risk for breastfeeding infants. We describe results from a non-blinded randomised controlled trial in Johannesburg comparing 3-monthly point-of-care (POC) VL testing (arm 2), to 6-monthly standard-of-care (SOC) laboratory-based VL testing (arm 1) in HIV-positive post-partum women on first-line antiretroviral treatment. We evaluated differences in VL suppression rates per arm at 6, 12, and 18 months.

Methods: Mother-child dyads were enrolled at the child's 6/10/14-week clinic visit. Women were randomized 1:1 to arm 1 or 2. For arm 2, trained nurse clinicians and field workers used Cepheid GeneXpert IV for POC VL testing.
We fit a generalized linear mixed model with VL suppression at enrolment, 6, 12, and 18 months as the outcome, indicator variables for time, study site, study arm, and interaction variables(time x site, time x arm, site x arm, time x site x arm). The model included a random effect for study ID to account for correlation among multiple VL from the same woman over time. All interaction terms were nonsignificant and were removed from the model. The final model tested for a difference by study arm, pooling across timepoints.
Results: At baseline, women in arms 1 and 2 were well-balanced for socio-economic status and there was no difference between arms. Mean age in years 30.3 (5.35 standard deviation); the majority of participants, 217 (53.5) were not born in South Africa; with 188 (46.5) born in South Africa. Further, 225 (55.8) women were married/cohabiting; 396 (98.3) had a secondary or higher education; 221(54.8) women were unemployed; 352 (87.3) received some form of financial support:303 (75.2) received financial support from the child's father and 67(16.6) received a social grant. VL suppression rates were high throughout the study, with no difference at each time point between arms (p-value 0.8937) after adjusting for baseline VL suppression; in arm 1 and 2 respectively, 94.0% and 88.6% at baseline, 96.2% and 91.2% at 6 months, 94.1% and 91.6% at 12 months and 94.1% and 94.3 % at 18 months.

Conclusion: In our study, there was no significant difference in VL suppression rates between 6-monthly SOC and 3-monthly POC VL testing in HIV-positive postpartum women. VL suppression rates were high overall, indicating PMTCT programme success.

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Usability and Feasibility of an HIV POC Viral Load to Identify Infants at High Risk of MTCT at Birth in Primary Healthcare Clinics in Mozambique

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Background: Most resource-limited countries face challenges in implementing viral load testing within their public health programs due to limited laboratory infrastructure, capacity, and skill.Point-of-care Viral Load (POC VL) testing in pregnant and breast-feeding women could provide an opportunity for faster identification and management of virologic failure that may contribute to preventing mother-to-child transmission. This analysis aims to describe the usability and feasibility of mPima viral load at maternity wards in Mozambique's primary healthcare facilities.

Materials and Methods: Mother/child pairs were recruited at Maternity wards at 14 primary health facilities (clusters) in Mozambique. Seven of the health facilities (Intervention Arm) tested the mothers with POC VL at birth. The other 7 (Control Arm) sent mothers sample to the central laboratory for viral load testing. Nurses from maternity wards were trained to process POC VL on mPima (Abbott) device. A microcentrifuge was provided for plasma separation. Mothers with viral load above 1000cp/mL in Arm A at birth were referred for adherence counseling according to national guidelines. All HIV negative babies at birth received enhanced prophylaxis according to the national guidelines. At visit 3 (3 months after) all mothers had a viral load performed (laboratory based or POC). Data was collected using data collection forms (DCFs). Generalized estimating equations with an exchangeable working correlation was used for statistical analysis to account for clustered data. Only pairs that had both visit 1 and 3 viral loads were included in the analysis.

Results: For this analysis, 845(54,7%) Arm A and 700 (45,3%) Arm B mother-child pairs were included. In Arm A, 747 (88,4%) of patients had a viral load processed with POC with fresh samples. In total. in arm A 87,8 % of results of viral load processed were communicated to the mothers within 24 hours. In arm A 24,2% of mothers had viral load above 1000 cp/mL at birth compared to 35,7 % in Arm B (p=0,0001). The main risk factors associated with unsuppressed viral load at birth were: time since HIV diagnosis, mother's age, number of ANC visits attended and whether HIV status was disclosed. In both arms, there was a reduction of the percentage of unsuppressed viral load from visit 1 to visit 3 but in arm B this was more significant (35,7% vs 26,4% p=0,0002). In Arm A from those mothers who had a viral load above 1000 copies/mL at birth and received counseling, only 14.7% manage to suppress (<1000 copies/mL) at month 3. The error rate for POC VL was 6.1% but due to extra plasma availability, the majority were repeated using the same sample.

Conclusions: Use of POCVL testing is feasible in maternity wards of primary healthcare settings in Mozambique. Centrifugation was simplified with microcentrifuges and possible in maternity wards. The availability of the viral load result before discharging the mother, gave opportunity to counsel the mother for better adherence. Nevertheless, having the result available might not be the only factor contributing for viral load suppression. Quality of counseling and social factors should be also considered.

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Key Clinical and Programmatic Outcomes of HIV-Exposed Infants in the International Epidemiology Databases to Evaluate AIDS Consortium

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Background: Clinical outcomes and uptake of key health services among HIV-exposed infants are incompletely understood, despite a steady number born worldwide each year. Receipt of antiretrovirals by infants and their mothers, early infant diagnosis and definitive diagnostic testing, anthropometric and developmental measurements, and susceptibilities to mortality and loss to follow-up (LTFU) are largely known based on single-program or country reports. To complement existing data, we analyzed these indicators in a unique global dataset of linked mother-infant records from the International epidemiology Databases to Evaluate AIDS (IeDEA) consortium.

Material and Methods: Infants documented as having a mother with HIV were eligible if enrolled in care at <18 months at clinics providing routine HIV services in five IeDEA regions: East Africa (EA; 52 Kenya sites; born 2001-2018), Central Africa (CA; 113 sites in Republic of Congo, Democratic Republic of Congo, Burundi; 2001-2020), West Africa (WA; 8 sites in Côte d'Ivoire, Ghana, Togo, Benin; 2002-2018), Southern Africa (SA; 21 Umoyo+ sites in Malawi; 2010-2015), and CCASAnet (1 Brazil site; 1997-2017). We estimated cumulative incidence functions of DNA PCR testing, HIV diagnosis (positive RNA, DNA PCR, or >18-month serology), LTFU (>6 months since visit), and death through 24 months of age using proportional subdistribution hazards models accounting for relevant competing risks (e.g., death for LTFU, LTFU for death), with risk periods starting at enrollment. DNA PCR data were unavailable in CCASAnet, and maternal data were unavailable in WA.

Results: Overall, 74,103 infants (39,336 EA, 10,699 CA, 6,503 WA, 15,770 SA, 1,795 CCASAnet) were included, enrolled at median age <2 months in all regions. Receipt of maternal triple-therapy ranged from 87% in EA to 66% in CCASAnet, with between 17% (WA) and 92% (CCASAnet) of infants receiving antiretroviral prophylaxis. Preterm birth (<37 weeks' gestation) was more common in CA (19%) and CCASAnet (18%) than in EA (5%), as was small-for-gestational-age (30%, vs. 20% in EA and 26% in CCASAnet). Between 10% (EA) and 21% (CCASAnet) were low birth weight (<2,500 grams), with between 2% (SA) and 22% (WA) underweight-for-age at 6 weeks. Almost all EA and CA infants ever breastfed, compared with 4% in CCASAnet. Cumulative incidences at 24 months ranged from 12% (WA) to 94% (EA) for DNA PCR testing, 2% (WA) to 11% (EA) for HIV diagnosis, 56% (EA) to 99% (WA) for LTFU, and 1% (WA) to 5% (EA) for death. The median age of HIV diagnosis was between 3 (CCASAnet) and 8 (EA) months. Among those DNA PCR tested, median age at first DNA PCR was <2 months in all regions; the cumulative incidence of DNA PCR testing at 2 months was 8% in WA, 42% in CA, 71% in EA, and 81% in SA.

Conclusions: While maternal triple-therapy uptake was high, there was marked regional and temporal heterogeneity in key clinical and programmatic outcomes, with especially high percentages of infants LTFU in the first two years of life. Continued efforts are needed to keep infants in care for appropriate HIV prevention and diagnosis services and to reduce infection and mortality.

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Determinants of HIV-Free Survival in the Era of Lifelong Universal Antiretroviral Therapy (ART): Pooled Analysis of PEAWIL and IMPROVE Studies, Lesotho

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Background: We assessed factors associated with HIV-free survival (HFS) among HIV-exposed infants, pooling data from two Lesotho cohorts in the universal ART era.

Methods: PEA-WIL, an observational study (6/2014-9/2018), and IMPROVE, a randomized trial (7/2016-7/2019), enrolled HIV-positive pregnant women attending antenatal care (ANC) in Lesotho under universal ART guidelines, with mother-baby follow-up through 12-24 months postpartum, to evaluate a facility-based intervention package to improve patient care. There was no significant difference in HFS between arms, so arms were combined. Kaplan Meier analysis was used to estimate mortality and HFS rates, censoring for loss to follow-up or withdrawal; multivariate logistic regression was used to identify factors independently associated with HFS.

Results: A total of 1,205 HIV-positive women were enrolled in combined cohorts; median maternal age was 28 (IQR:24–32) years and 80.1% were married/living with a partner. At delivery, 99.3% of women were receiving ART. Of 1,178 (96.4%) live births, 8.4% were preterm, 97/1,103 (17.9%) had a birth weight <2500 g, and 91.4% were breastfed at birth with 35.9% breastfed for >6 months. Estimated 2-year HFS was 93.4% (95%CI 92–95%)—most rapid decline from birth-6 months, plateauing at age 1 year. In adjusted analyses, HFS was significantly associated with maternal age (≥25 vs. <25 years) (aOR 2.4, 95% CI 1.4–4.3), HIV disclosure to partner (aOR=2.0, 95% CI 1.04-3.8), gestational age at birth (>37vs≤ 37-weeks) (aOR=3.7, 95%CI 1.6–8.4), and breastfeeding for >6 months (aOR=2.4, 95%CI 1.2-5.0). In a multivariate model with birth weight instead of gestational age, birth weight <2,500 g was associated with lower HFS (aOR=0.4, 95%CI 0.2–0.8).

Conclusions: In an era of universal ART in pregnant women, higher HFS was associated with older maternal age, partner disclosure, and breastfeeding for at least six months; while lower in infants born preterm or low birth weight.

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Increased Infectious-Cause Hospitalization Among Infants Who Are HIV-Exposed Uninfected Compared to HIV-Unexposed

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Background: Increased risk of morbidity and hospitalization has been observed in children who are HIV-exposed but uninfected (HEU) compared to HIV-unexposed and uninfected (HUU), although studies in the era of universal maternal antiretroviral treatment (ART) are limited.

Methods: We investigated hospitalization between 29 days and 12 months of life in a prospective South African cohort of infants who were born between February 2017 and January 2019 (HEU=455; HUU=458) to mothers with similar socio-economic circumstances. All mothers known with HIV during pregnancy received ART (53% of whom were on ART at conception). We reviewed infant hospital records and classified and graded infectious diagnoses using a standardized tool. We examined factors associated with infectious-cause hospitalization using mixed-effects Poisson regression.

Results: Infants HEU vs. HUU had higher all-cause and infectious-cause hospitalization (58/455; 13% vs. 32/458; 7%; p=0.004 and 47/455; 10% vs. 27/458; 6%, p=0.014 respectively). In infants HUU, the number of hospitalizations per month peaked at 4-6 months, whereas in infants HEU, monthly hospitalizations reached twice the number and peaked at 8 months. Infectious causes accounted for most hospitalizations (97/126; 77%). More infants HEU than HUU were hospitalized with severe or very severe infections (4% vs. 3% severe; 6% vs. 3% very severe; p=0.041). Mortality (<1%) did not differ between groups. More infants HEU than HUU were born preterm (14% vs. 10%; p=0.048) and infants HEU were breastfed for shorter duration (median duration 3 (IQR 1-6) vs 6 (IQR 2-12) months, p<0.001; 44% vs. 68% breastfed for ≥3 months, p<0.001). Mothers with HIV reported stopping breastfeeding before 3 months due to concerns about HIV transmission in 22% of cases. Infants HEU vs. HUU had higher rates of infectious-cause hospitalization (aIRR=2.8; 95% CI 1.5-5.4) after adjusting for sex, vaccination status, maternal age and education, and type of housing. Up-to-date vaccination status was associated with decreased rates of hospitalization (aIRR=0.52; 95% CI 0.29-0.95). The association of HIV exposure with infectious-cause hospitalization remained significant (aIRR=2.0; 95% CI 1.0-3.8) when breastfeeding duration and preterm birth were incorporated in a separate model. Both were significant mediators of infectious-cause hospitalization: infant hospitalization rates were 10% lower for each additional month of breastfeeding and twice as high if infants were preterm. Although increased incidence of preterm birth and shorter duration of breastfeeding among infants HEU vs. HUU contributed to increased hospitalization, they did not account for all the increased risk. Among infants HEU, neither timing of maternal ART initiation nor maternal HIV disease indicators near delivery (CD4 count and viral load) were significantly associated with infant infectious-cause hospitalization.

Conclusion: Infectious-cause hospitalization rates were higher among infants HEU vs. HUU, likely partly due to higher incidence of prematurity and lower breastfeeding rates among infants HEU. Interventions to support breastfeeding could partially mitigate this risk. Considering the substantial size of the infant HEU population, the increased infectious disease burden in these infants will place increased strain on pediatric health services in sub-Saharan Africa.

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Growth of Children HIV-Exposed and Uninfected in The Context of Lifelong Maternal Antiretroviral Therapy in Malawi

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Background: In 2019, there were 570,000 children HIV-exposed and uninfected (CHEU) in Malawi. Current evidence on CHEU growth is limited, although early studies demonstrated CHEU have impaired growth compared to children HIV-unexposed. We retrospectively analyzed child anthropometrics and identified protective and risk factors against underweight and stunted growth among CHEU at 2 years of age in Malawi.

Materials and methods: Infants HIV-exposed and mothers enrolled in a prospective cohort within a national evaluation of Malawi's prevention of mother-to-child HIV transmission programme (2014-2018). For 1,228 mother-infant pairs followed for 24 months, anthropometry was measured at baseline (age 1–6 months), visit 1 (9–22 months), and visit 2 (18–33 months). Weight-for-age (WAZ) and length-for-age (LAZ) z-scores were calculated using World Health Organization Growth Standards. Logistic regression models restricted to children aged 24 months (± 3 months) at visit 2 were used to identify factors associated with stunted (LAZ<-2) or underweight (WAZ<-2) growth, corrected for intra-site correlation. Covariates were selected a priori based on literature; variables with p<0.300 in bivariate analysis were included and backward elimination was used to select the final explanatory variables with p<0.100.

Results: Among 1,228 CHEU, WAZ and/or LAZ was available for 98.2% (1206/1228) at baseline, 97.7% (738/755) at visit 1, and 97.0% (558/575) at visit 2. At baseline (N=1,228), 49.7% of infants were female, median age was 2 months (IQR: 2,4), 97.6% were breastfed, and 51.1% were enrolled in CHEU follow-up care. Baseline median maternal age was 29 years (24,33); 46.9% of mothers were receiving antiretroviral therapy (ART) before pregnancy, 46.3% started antenatally, and 6.4% started postpartum. At baseline, visit 1, and visit 2, median WAZ was -0.67 (IQR: -1.53,0.12), -0.42 (-1.13,0.33), and -0.81 (-1.43,-0.11), and median LAZ was -2.15 (-3.37,-1.02), -1.23 (-2.04,-0.38), and -1.74 (-2.66,-0.98), respectively.

Among CHEU with visit 2 anthropometry, 41.8% were stunted, and 9.5% were underweight. Adjusting for sex, child age, and maternal employment, protective factors against stunting were milk (11% breastmilk; 89% non-breastmilk) consumption in the past 7 days (adjusted odds ratio [aOR],0.63 [95% CI: 0.40–0.99]) and co-trimoxazole prophylaxis (aOR,0.51 [0.34–0.77]). Risk factors for stunting were low birthweight (defined as <2500 grams; aOR,1.72 [1.26–2.36]), child infectious disease diagnosis (i.e., pneumonia, meningitis, diarrhoea, or malaria) in the past year (aOR,1.45 [1.09–1.94]), and child ever admitted to hospital once (aOR,1.50 [1.03–2.20]). Adjusting for sex and child age, protective factors against being underweight included child's health reported as "well" (aOR,0.16 [0.04–0.70]), child in CHEU care (aOR,0.04 [0.00–0.78]), and co-trimoxazole prophylaxis (aOR,0.51 [0.28–0.92]). Risk factors for being underweight included low birthweight (aOR,4.39 [1.94–9.94]), child infectious disease diagnosis in the past year (aOR,2.37 [1.19–4.71]), mother being underweight (defined as mid-upper arm circumference <24cm; aOR,2.14 [0.88–5.20]), child ever admitted to hospital more than once (aOR,13.47 [3.06–59.31]), and living >1 hour away from the clinic (aOR,2.18 [1.02–4.65]).

Conclusion: Over a third of CHEU presented with impaired growth outcomes. Enrolment in CHEU follow-up care and/or co-trimoxazole prophylaxis reduced probability of underweight and stunted growth, supporting current guidelines for CHEU monitoring and care in Malawi.

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There is No Substitute for Hard Work(Ing Dolutegravir): Outcomes of Single Drug Substitutions Among CALHIV Shifted to a Dolutegravir Antiretroviral Regimen in Mbeya and Mwanza, Tanzania

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Background: As dolutegravir (DTG) is being rolled out globally for CALHIV, many questions remain on the effectiveness of a single ARV drug substitution when shifting patients to DTG-containing regimen, especially in countries where the NRTI backbone ARV options are limited. We report the virologic suppression rates of CALHIV shifted to DTG regimens using only a single drug substitution (SDS) from the Baylor Tanzania HIV clinics in Mbeya and Mwanza, Tanzania.

Materials and Methods: Retrospective chart review was conducted to assess the clinical characteristics of CALHIV who received DTG as part of their ART at the Baylor College of Medicine Children's Foundation – Tanzania Centres of Excellence (COEs) in Mbeya and Mwanza, Tanzania between 1 March 2019 (when DTG became available) and 30 November 2020. HIV viral load(VL) suppression was defined as VL<1000 copies/mL. The SDS cohort was defined those CALHIV who kept the same two NRTIs backbone (i.e. ABC or AZT or TDF + 3TC) when shifting to a DTG regimen (e.g. TLE toTLD).

Results: Of the 1703 total CALHIV received DTG, there were 634 (37.2%) involved SDS changes. Among the SDS cohort with pre- and post-DTG viral loads, viral suppression rates improved from 86.8% (547/630) pre-DTG to 92.9% (409/440) post-DTG overall. Of the SDS patients were previously unsuppressed (n=75), 84.0% (63/75) were able to become virally suppressed on a DTG regimen.

When analyzing the TLE to TLD cohort alone, 91.7% (11/12) of previously unsuppressed CALHIV became suppressed with the SDS of DTG via TLD, and 92.7% (76/82) of those previously suppressed (or unknown VL) remained suppressed on TLD.

The cohort also included 48 patients on TDF-3TC-Protease Inhibitor (PI) regimens, of which only 54.2% (26/48) were suppressed on a PI regimen. After a SDS to TLD, 92.3% (41/45) successfully became suppressed, including 90.9% (20/22) of those previously unsuppressed.

Conclusion: Single drug substitutions with DTG alone was highly effective in virally suppressing our cohort of CALHIV in Tanzania. A large majority of CALHIV previously non-suppressed while on NNRTI or PI-based regimens subsequently became suppressed with SDS of DTG. These results are especially encouraging in settings where NRTI backbone ARV options and/or HIV resistance testing is limited.

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Pediatric ARV optimization in a real-world setting: Dolutegravir transition in Mozambique

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Background: Dolutegravir (DTG) is recommended for first and second line antiretroviral therapy for children and adolescents living with HIV and is being scaled up globally to optimize treatment. However, barriers to adoption and supply distribution can hinder sustainable uptake. We describe rollout of DTG 50mg tablets for children weighing ≥20kg in Gaza and Inhambane provinces, Mozambique following national guideline updates in September 2019.

Methods: Clinic records from children 0-14 years with an HIV clinic visit between September 2019 and February 2020 were extracted from clinical databases in 16 health facilities. Among children aged ≥5 years (proxy for weight ≥20kg), we described treatment switches, defined as change in anchor drug for any reason, ignoring changes only to NRTI backbones. Among those on DTG-based regimens during the 6-month study period, we described treatment changes and available viral load (VL) outcomes.

Results: Of 3,107 children aged ≥5 years, 2,488 (80%) switched ART regimens during this period; 950 (38%) children switched ≥ 2 times; 11 changed 5-6 times. Of those who switched, 2,009 (81%) switched to DTG-based ART per national guidelines: 336 (17%) switched from PI-based, 1,616 (80%) from NNRTI-based ART, 36 (2%) had both PI and NNRTI switches, and 21 (1%) switched from other regimens. However, 711/2488 (29%) on DTG switched to other regimens within 6 months: 317 to PI, 387 to NNRTI and 7 to both drug classes. At last visit, 75% (2,311/3,092) of children were on DTG, excluding 15 without any documented regimen during follow-up. Among children ever on DTG, 1,607/2,596 (62%) were on continuous DTG for ≥2 months (median [IQR] 4.2 [3.1-5.0] months). Of these, 85 children had VL results available at median 2.9 [1.1-4.7] months after DTG start; 68 (80%) had undetectable VL <50 copies/mL.

Conclusions: This study highlights progress towards DTG transition for eligible children. However, rollout should be accompanied by ongoing training and forecasting support to minimize stock-outs and avoid non-clinically justified switches that may contribute to multiple changes. More consistent VL testing is also needed to monitor effectiveness. Addressing these issues, particularly as introduction of additional pediatric formulations are imminent, will help ensure timely uptake and continuous treatment for children.

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Co-trimoxazole prophylaxis for children born to mothers with HIV: predicted impact of different strategies on mortality up to the age of two years

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Background: WHO guidelines recommend co-trimoxazole prophylaxis for all children born to mothers with HIV from 6 weeks until the end of breastfeeding or 18 months, whichever is later. Although co-trimoxazole reduces mortality for infants living with HIV, recent evidence suggest lack of benefit for children HIV-exposed but uninfected (CHEU). Regardless, offering co-trimoxazole to all HIV-exposed infants may be beneficial for HIV-positive infants who miss early infant diagnosis (EID). Modelling could help quantify the predicted impact of alternative co-trimoxazole strategies on death.

Materials and methods: We used a decision-tree model for HIV-exposed children from 6 weeks to 2 years, assuming 100% breastfeeding for 18 months. The model incorporated: perinatal/postnatal HIV-transmission; HIV testing at 6 weeks, 9 months and end of breastfeeding; and antiretroviral therapy uptake.
Four country scenarios were considered: Zimbabwe, Cote d'Ivoire, Mozambique, Uganda. UNAIDS 2019 country-specific estimates and country-supplied information were used for: perinatal/postnatal HIV transmission; EID coverage; population size. The following were estimated using published literature: death rates (modelled in 3-month periods) for CHEU (cumulative 3.7% between 6wks-2yrs), HIV-positive children on ART (6.5%), HIV-positive children not on ART (53.6%); ART uptake in a child known to be HIV-positive (80%); relative risk for death (co-trimoxazole vs no co-trimoxazole) in HIV-positive children (0.57) and CHEU (1.00). Probabilities of having 9-month and end-of-breastfeeding HIV testing used expert opinion (50% if previously tested; 30% if not). Initial models considered 100% co-trimoxazole uptake to provide best-case scenarios.
Six strategies were considered:
(1) Co-trimoxazole until end-of-breastfeeding and final confirmation of negative HIV status at 18 months or after cessation of breastfeeding if >18 months (current strategy)
(2) Co-trimoxazole for 3 months (continue/restart with positive test result)
(3) Co-trimoxazole for 6 months
(4) Co-trimoxazole for 9 months
(5) Co-trimoxazole for 12 months
(6) Only start on positive test result
In scenarios 2-5 co-trimoxazole was continued or restarted with a positive age appropriate HIV testing. The predicted number of deaths between 6weeks-2 years was modelled. Results are presented as absolute risk differences compared to a "base-case" of no co-trimoxazole use.

Results: In the absence of any co-trimoxazole use ("base-case"), predicted mortality varied from 5.70% in Zimbabwe to 7.08% in Cote d'Ivoire. The smallest benefits of co-trimoxazole were in Zimbabwe, which had lowest vertical transmission and highest EID: risk differences for strategies 1-6 were 0.85% (a reduction from 5.70% in "base-case" to 4.85% in "treat all")/0.25%/0.32%/0.43%/0.48%/0.23%, respectively. The largest benefits were in Cote d'Ivoire which had the highest vertical transmission and lowest EID; risk differences were 1.42%/0.51%/0.67%/0.85%/0.93%/0.40%. In Zimbabwe, this translates into 544/160/205/275/307/147 deaths saved per year for strategies 1-6, respectively, compared to a baseline of 3648 deaths. Equivalent numbers for Cote d'Ivoire are 270/97/127/162/177/76, compared to 1345 deaths.

Conclusions: Changing current guidelines is predicted to increase mortality in all settings, assuming complete co-trimoxazole uptake. The benefits of the current policy are greatest where vertical transmission is highest and EID coverage is lowest. Alternative strategies that reduce co-trimoxazole duration may be a reasonable alternative in countries with low vertical transmission and high EID coverage.

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Risk factors for post-discharge mortality following hospitalization for severe acute malnutrition in Zimbabwe and Zambia

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Background: HIV-positive children discharged from hospital following management of complicated severe acute malnutrition (SAM) have a high risk of mortality. Few studies have examined mortality in the antiretroviral therapy (ART) era.

Objective: To ascertain 52-week mortality among children discharged from hospital following management of complicated SAM and to identify independent predictors of mortality.

Methods: A prospective cohort study was conducted among children aged 0-59 months, hospitalized for complicated SAM between July 2016 and March 2018 at three tertiary hospitals in Zambia and Zimbabwe. SAM was defined as weight-for-height Z score (WHZ) <-3 or mid-upper-arm circumference (MUAC) <115mm or nutritional edema. Baseline clinical, demographic, household and caregiver data were collected. Inpatient management of SAM and HIV followed WHO-adapted country guidelines, with follow-up visits conducted by the study team at 2, 4, 12, 24 and 48 weeks post-discharge. Illnesses identified during follow-up were managed by study physicians with referral for readmission when indicated. Children not receiving ART were referred to the hospital HIV/ART clinics. Vital status was ascertained by phone calls for those who defaulted follow-up. Mortality analysis was conducted through 52 weeks post-discharge, using univariable and multivariable Cox regression models to identify independent risk factors for death, and to investigate whether HIV modifies these associations.

Results: Among 745 children, median age 17.4 months (interquartile range (IQR) 12.8, 22.1), 21.7% were HIV-positive, 16.6% were HIV-exposed but uninfected and 64.4% had edema. HIV-positive compared to HIV-negative children were significantly older, more wasted, underweight, stunted, and less likely to have edema. Seventy [9.4% (95% confidence interval 7.4, 11.7)] children died and 26 exited during hospitalization; 649 were followed post-discharge. At discharge, 43.9% had ongoing SAM and only 50.7% of HIV-positive children were on ART. The median (IQR) follow-up time was 48.4 (39.9, 50.9) weeks. Vital status was ascertained for 604 (93.1%), of whom 55 [9.1% (95%CI 6.9, 11.7)] died at median 16.6 weeks (IQR 9.4, 21.9) with evidence of high ongoing mortality risk throughout follow-up.

Children who died were more wasted (mean WHZ -3.4 versus -2.1, P<0.001; mean MUAC 110mm vs. 124mm, P<0.001), underweight (mean WAZ -4.7 vs. -3.2, P<0.001) and stunted (mean HAZ -3.7 vs. -3.0, P=0.002), and had been hospitalized longer than those who survived (median 16 (IQR 8, 21) vs. 12 (7, 14) days, P=0.002). Overall, 20.0% (95%CI 13.5, 27.9) and 5.6% (3.8, 7.9) of HIV-positive and HIV-negative children, respectively, died (adjusted hazard ratio (aHR) 3.83, 95%CI 2.15, 6.82). Mortality among the HIV-positive children was similar according to discharge ART status (HR 1.09, 95%CI 0.49, 2.45). Additional independent risk factors for mortality were ongoing SAM (aHR 2.28, 95%CI 1.22, 4.25), cerebral palsy (aHR 5.60, 95%CI 2.72, 11.50) and non-edematous SAM (aHR 2.23, 95%CI 1.24, 4.01), with no evidence of interaction with HIV status.

Conclusion: HIV-positive children have almost four-fold higher mortality than HIV-negative children in the year following hospitalization for SAM, regardless of ART status. A better understanding of causes of death, an improved continuum of care for HIV and SAM, as well as targeted interventions to improve convalescence are needed.

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Estimated prevalence of prior HIV diagnosis among children living with HIV in Eswatini, Lesotho, Malawi, Tanzania, Zambia and Zimbabwe in the Population HIV Incidence Assessments (PHIA)

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Background: While there are an estimated 1.8 million children living with HIV (CLHIV), there are few data on the proportion of CLHIV who are undiagnosed. Data from the Population HIV Incidence Assessments (PHIA) in Eswatini (2016-17), Lesotho (2016-17), Malawi (2015-16), Tanzania (2016-17), Zambia (2016) and Zimbabwe (2015-16) were used to estimate the number and proportion of CLHIV 1-14 years with and without known HIV diagnosis.

Methods: PHIAs are nationally representative surveys measuring HIV outcomes. HIV rapid test data (PCR confirmatory testing for children <18 months) were used to calculate the number of CLHIV 1-14 years in each country and to estimate the proportion not previously known to have HIV. Mothers or guardians reported previous HIV testing of children and results. Detection of ARVs was conducted using dried blood spots (DBS). Children with prior negative or unknown HIV test results and without detectable ARVs were considered previously undiagnosed, all other children were considered to have known diagnosis. Survey weights with jackknife variance were used to generate national estimates of diagnosed CLHIV (population estimates derived from national statistical projections).

Results: 521 CLHIV were included in the study across the six countries; based on the survey prevalence estimates, there were 416,000 (95% probability bounds (PB) 356,00-476,000) CLHIV 1-14 years. Survey estimates of CLHIV by country were: Eswatini: 10,000 (95%PB 8,000-13,000); Lesotho: 13,000 (95%PB 9,500-16,000); Malawi: 119,000 (95%PB 90,000-148,000); Tanzania: 101,000 (95%PB 61,000-141,000); Zambia: 80,000 (95%PB 62,000-98,000); Zimbabwe: 93,000 (95%PB 70,000-116,000). In total, we estimate that 164,000 (95%PB 126,000-203,000) (39.5%) of all CLHIV 1-14 years had not been diagnosed. Estimates of undiagnosed CLHIV by country were: Eswatini: 2,000 (16.6%); Lesotho: 3,000 (23.7%); Malawi: 38,000 (32.2%): Tanzania: 50,000 (50.0%); Zambia: 41,000 (51.5%); Zimbabwe: 30,000 (31.8%). Missed diagnosis varied by age group in five countries. In Lesotho, Tanzania and Zimbabwe, CLHIV 1-4 years were the age group with the highest proportion who were undiagnosed; in Lesotho 53.3% of CLHIV 1-4 were undiagnosed compared to 11.8% of 5-9 year olds and 23.4% of 10-14 year olds; in Tanzania 70.1% of CLHIV 1-4 were undiagnosed compared to 41.1% of 5-9 year olds and 35.1% of 10-14 year olds and Zimbabwe 45.4% of CLHIV 1-4 were undiagnosed compared to 35.7% of 5-9 year olds and 22.9% of 10-14 year olds. In Malawi and Zambia, 10-14 year olds were the age group with the highest proportion of undiagnosed CLHIV; in Malawi 37.8% of CLHIV 10-14 were undiagnosed compared to 30.1% of 1-4 year olds and 27.8% of 5-9 year olds and in Zambia, 68.0% of CLHIV 10-14 were undiagnosed compared to 57.9% of 1-4 year olds and 42.0 % of 5-9 year olds. Proportions of undiagnosed CLHIV were similar across age groups in Eswatini (1-4 years: 16.8%, 5-9 years: 15.5%, 10-14 years: 17.5%).

Conclusion: Across six countries, we estimated that in 2015-2017 almost 40% of CLIHIV had not been diagnosed and were not on treatment. These findings show the uneven coverage of pediatric HIV testing and underscore the urgent need to address gaps in diagnosis and treatment for all CLHIV.

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A Costing Analysis of Index-Linked HIV Testing for Children and Adolescents in Zimbabwe

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Background: Index-linked testing refers to screening family, household or other contacts of a case for a disease. By testing children and adolescents in the household of an of HIV positive index, index-linked HIV testing (ILHIVT) could identify high risk children and adolescents earlier and more efficiently, compared to current strategies. We evaluated the incremental cost of integrating ILHIVT via three modalities into HIV services in Zimbabwe.

Methods: We estimated the provider cost of facility level HIV testing and the provision of index-linked testing for 2-18 year olds, using a mixed bottom-up and top-down approach at 2 urban facilities in Bulawayo, and 1 rural facility in Mangwe; these facilities do not routinely employ ILHIVT. The full cost of standard of care facility testing and diagnosis of children and adolescents was estimated over a 4-month period (May– August 2018). We measured the incremental cost of ILHIVT and diagnosis of children and adolescents (September– December 2018), provided by three modalities: clinic based; health-care worker testing in the household; and caregiver-testing in the household using oral mucosal transudate (OMT) tests. Costs estimated included personnel, consumables, overheads, building, equipment, training, start-up and transaction costs. Outcome and resource use data were collected through a combination of interviews, direct observation and review of study process data and facility registries. Costs were converted to 2019 constant US$.

Results: From May 2018 to August 2018, 2317 clinic-based standard of care HIV tests were administered. The 3 clinics screened 2087 index-cases, identified 1708 eligible children and adolescents of unknown HIV status, and of those, tested 1263 (74%): 41% in clinic; 48% via home-based testing; and 10% through assisted testing. ILHIVT yield was 0.6%, (i.e. 7 positive diagnoses). The cost per standard of care test was US$5.91 (average) in urban facilities and US$7.15 at the rural facility, while the cost per standard of care HIV diagnosis amongst 2-18 year olds ranged from US$ 139.76 to US$197.80. The average incremental cost of an index-linked HIV test was driven by the number of participants tested and uptake per modality. The lowest cost approach was home-based testing in the urban setting (US$6.69) and facility-based testing at the rural clinic (US$5.36). Testing by caregivers was the most expensive option: urban US$17.49; rural US$62.49.

Conclusions: To our knowledge, this study is the first to estimate the cost of ILHIVT in any setting. HIV case finding will become more costly as knowledge of HIV status and treatment coverage increase. Alternatives such as community-based HIV testing will be necessary in order to expand HIV testing and counselling services. While ILHIVT allows for greater access to children and adolescents – a particularly difficult to reach population – compared to current standard of care; uptake is a key driver of the cost per test administered. To ensure efficiency when scaling up ILHIVT, the acceptability of testing modality needs to be considered and alternatives that could increase yield such as ILHIVT of the entire household, as opposed to solely targeting children/adolescents, need to be explored.

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Rapid antiretroviral NNRTI-based initiation among youth living with HIV outcomes in the National AIDS program in Thailand

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Background: The Thai National AIDS program (NAP) recommended rapid ART initiation regardless of CD4 levels since 2014. We assessed treatment outcomes among youth living with HIV (YLHIV) aged 15-24 years, initiating Non-nucleoside reverse transcriptase inhibitor (NNRTI)-based antiretroviral therapy (ART) in the NAP, and determined factors associated with virological failure (VF).

Methods: Data of YLHIV initiating NNRTI based ART from 2014-2019 from the NAP database was extracted; follow-up data were available until May 2020. We classified YLHIV into 3 groups based on duration from registration (HIV positive test) to ART initiation: 1) <1 month (Rapid ART), 2) 1-3 months (Intermediate ART), and 3) >3 months (Delayed ART). VF was defined as VL ≥ 1000 copies/mL after at least 6 months of first-line ART. Mortality, loss to follow-up (LTFU) and VF rates were calculated per 100 person-years of follow-up (PY). Factors at ART initiation (baseline) associated with VF were analysed using generalized estimating equations with a Poisson link. Factors included age, gender, HIV stage, CD4 cell count, first ART regimen and calendar year.

Results: Of 19,824 YLHIV who started ART, 78% were male. Median (interquartile range, IQR) age was 21 (20-23) years and CD4 count was 338 (187-498) cells/mm3. After registration, 12,216 (62%) started ART within one month, 4,272 (22%) started from 1-3 months and 3,337 (17%) started >3 months. Proportion with rapid ART steadily increased from 60% in 2014 to 67% in 2019 (p for trend<0.001); overall median CD4 of those starting Rapid ART was (345, IQR (208-501) cells/mm3). Most YLHIV started with EFV- based regimens (89%), followed by NVP-(10%) and RPV-based ART (1%). The overall median duration of first-line therapy was 2 (IQR1-3) years. The attrition outcomes showed 1,762 (9%) YLHIV were LTFU (3.96 (95%CI 3.78-4.15)/100 PY), and 325 (2%) YLHIV died (0.73 (95%CI 0.65-0.81)/100 PY). Only 17,512 YLHV (88%) had plasma HIV measured 6-12 months after starting treatment. 15,908 (91%) achieved viral suppression < 200 copies/mL. Overall, 2,512 experienced VF (5.87 (95%CI 5.65-6.11) per 100 PY), and 964 (38%) patients switched regimens (2.15 (95% CI 2.02-2.29) /100 PY). The highest VF rate was 6.76 (95%CI 6.19-7.39) /100 PY, in YLHIV initiating ART >3 months after registration. In the multivariate model, compared to the rapid ART group, the adjusted Incidence rate ratio (aIRR) for VF was 1.47 (95% CI 1.33-1.63) in the delayed ART group, and 1.14, 95%CI 1.03-1.25 in those starting ART 2-3 months after registration. Other factors associated with an increased rate of VF were female sex, age < 20 years, initiating with NVP and EFV based ART, pre-ART CD4 < 350 cells/mm3 or an unknown pre-ART CD4.

Conclusions: In the Thai NAP, the proportion of YLHIV starting ART <30 days after HIV diagnosis significantly increased from 2014 to 2019. These rapid ART initiators had a significantly lower risk of VF compared to those where initiation was delayed to 1-3, or >3 months. However despite increasing rapid ART rates with predominantly EFV-based regimens, VL suppression was below the 95% UNAIDS target. DTG-roll out should be expedited.

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Optimizing antiretroviral treatment and viral suppression for adolescents and young people living with HIV by implementing Operation Triple Zero (OTZ) in four states in Nigeria

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Background: In Nigeria, adolescents (10-19 years) account for about 23% of the total population, and 7% of people living with HIV (PLHIV); treatment outcomes for adolescents and youth living with HIV (AYPLHIV) are quite low. RISE-Nigeria commenced Operation Triple Zero (OTZ) in 33 facilities across four states in February 2020 to improve treatment outcomes. This analysis reviews the effect of OTZ on treatment outcomes among AYPLHIV six months after implementation.

Materials/Method: The OTZ model focuses on health system modifications, adolescent-centeredness and involvement in health, and education of caregivers and health workers. Case managers were identified and trained on non-judgmental approaches to counselling and optimal antiretroviral therapy (ART) for AYPLHIV; Clinic settings modified with adolescent-friendly themes; all services integrated and systems for peer-to-peer adherence support strengthened; Extended and weekend clinic hours established, with an appointment system for age bands 10–14, 15-19 and 20–24 years; Viremia clinics established for the virally-unsuppressed AYPLHIV; Case-based learning introduced for capacity building of health workers; Talent nurturing and skill development incorporated into AYPLHIV club meetings; and HIV status disclosure support offered to caregivers with opportunity for caregivers interaction during OTZ meetings facilitating peer-to-peer learning.

Results: After 6 months, AYPLHIV enrollment into OTZ increased from 615/3306 (18.6%) to 3595/4304 (83.5%); p-value <0.001. Optimal regimen utilization pre-intervention was 284/765 (37.1%%), 285/760 (37.5%), and 709/1526 (46.5%) preintervention, and increased to 807/819 (98.5%), 985/991 (99.4%), and 2478/2484 (99.8%); p-value <0.001 post intervention for age bands 10-14, 15-19, 20-24 years respectively. Viral load coverage (VLC) was 255/765(33.3%), 230/761(30.2%), 492/1772(27.7%) pre-intervention and increased to 740/819(90.1%), 806/991(81.3%) and1794/2484 (72.2%); p-value <0.001 in respective age bands post-intervention. Viral suppression (VS) rate increased from 390/586(66.6%), 286/552(51.8%) and 1155/1690(68.3%) pre-intervention to 611/749 (81.6%), 700/844(82.9%), and 2030/2384(85.2%); p-value<0.001 in respective age bands post-intervention. Overall VS was higher 2487/2935 (84.7%) among OTZ enrollees compared to non-enrollees 852/1040 (81.9%); p-value 0.03.

Conclusion: OTZ implementation improved the use of optimal ARV regimen, VLC, and VS among AYPLHIV. These results validate the use of integrated, asset-based strategies to improve HIV treatment outcomes among AYPLHIV.

Keywords: Operation triple zero (OTZ), HIV regimen optimization, adolescents, young persons living with HIV.

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Projecting life expectancy for youth with non-perinatally- and perinatally-acquired HIV in the United States

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Background: Youth with HIV (YHIV) are the least likely age group in the US to achieve virologic suppression. Estimating life expectancy (LE) is critical to understand how to support this population as it ages.

Methods: Using a microsimulation model, we projected LE for three race/ethnicity-matched US-based cohorts starting at age 18 with characteristics based on Adolescent Medicine Trials Network for HIV/AIDS Interventions, National Health and Nutrition Examination Survey (NHANES), and published data. Two cohorts were YHIV engaged in care and prescribed antiretroviral therapy: 1) non-perinatally-acquired (YNPHIV) and 2) perinatally-acquired (YPHIV); the third was a cohort of youth without HIV (YWOH). Race/ethnicity was: 61/24/15% Black/Hispanic/White. YNPHIV/YPHIV/YWOH were 85/47/50% male. For YNPHIV and YPHIV, inputs included starting CD4 (527 and 635 cells/μL), likelihood of virologic suppression (96 and 80%), mean adherence (for both YNPHIV and YPHIV: <25 years: 82%, ≥25 years: 91%). Among YNPHIV/YPHIV/YWOH, demographics included: 80/3/3% men who have sex with men (MSM), 14/12/12% heterosexual with low socioeconomic status (SES) (a proxy for high-risk heterosexual contact), 0/82/82% heterosexual with high SES, 6/2/2% people who inject drugs (PWID). We report life expectancy loss relative to the highest LE, by YNPHIV/YPHIV/YWOH demographics. We modeled an ideal YHIV scenario: starting CD4 750 cells/μL, 99% adherence to care.

Results: Among female YNPHIV/YPHIV vs. YWOH, LE loss was 12.0/ 3.9 years. Among male YNPHIV/YPHIV vs. YWOH, LE loss was 7.5/3.2 years. By race/ethnicity, Hispanic individuals had the highest LE. Among YNPHIV/YPHIV/YWOH, for female White vs. Hispanic individuals, LE loss was 12.2/3.6/4.3 years; for male White vs. Hispanic individuals LE loss was 9.3/3.3/3.8 years; for female Black vs. Hispanic individuals, LE loss was 4.9/5.1/5.9 years; for male Black vs. Hispanic individuals, LE loss was 15.7/7.7/8.8 years. Among YPHIV/YWOH, heterosexual with high SES had the highest LE. For female heterosexual with low vs. high SES, LE loss was 7.8/9.1 years; for male heterosexual with low vs. high SES, LE loss was 6.5/7.6 years; for female PWID vs. heterosexual with high SES, LE loss was 18.3/20.3 years; for male PWID vs. heterosexual with high SES, LE loss was 10.6/ 12.0 years; for MSM vs. heterosexual with high SES, LE loss was 5.5/ 6.3 years. Among female YNPHIV, female heterosexual with low SES had the highest LE. For female PWID vs. female heterosexual with low SES, LE loss was 10.5 years. Among male YNPHIV, male MSM had the highest LE. For male heterosexual with low SES vs. MSM, LE loss was 1.0 year; for male PWID vs. MSM, LE loss was 5.1 years. Among YNPHIV/YPHIV vs. YWOH, LE loss was 10.1/3.4 years; in the ideal scenario, LE loss was 7.7/0.5 years.

Conclusions: Model-projected LE for YHIV differed substantially compared to YWOH as well as between YNPHIV and YPHIV; this was determined more by differences in distributions of sex, race/ethnicity and HIV acquisition/SES than HIV-related mortality. With ideal HIV care, LE remained lower in YNPHIV, but similar for YPHIV compared to YWOH. Focused interventions are needed to reduce differences in mortality driven by social factors.

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Hospitalisation rates for youth living with perinatally acquired HIV transitioning to adult care

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Background: Antiretroviral therapy (ART) has dramatically improved survival and reduced hospitalisation for people living with HIV (LWHIV). UK adults and children LWHIV have published admission rates of 2.7 and 5 per 100 person years (100 PY) respectively. Complex challenges amongst ageing perinatally infected (PaHIV) cohorts may impact on hospitalisation. We explored hospitalisation rates for PaHIV adolescents (10-19 years) and young people (20-35 years) transitioning from paediatric to adult services.

Methods: Retrospective observational cohort study of PaHIV aged 10+ years attending a specialist centre between 1st September 2016-31st August 2019. Patients exited the study at the date the study ended/ transfer of care (TOC)/ loss to follow up (LTFU) or death. Primary outcome was overnight admission to hospital. Maternity and admission to other hospitals were excluded. Data collected at baseline and admission from electronic patient record included: cause, frequency/duration of hospitalisation, plasma HIV viral load (VL) and CD4 lymphocyte count. Rates of admission per 100 PY (95% CI) were calculated by age group (10-19, 20-35 years). Analysis was performed using negative binomial regression with generalised estimating equations. StataTM 16.1 was used for all analyses.

Results: Two hundred and fifty-five PaHIV contributed 689 person-years of follow up. One hundred and forty-three (56%) were female, 212 (83%) of a Black ethnicity group, median transition age 17.8 years (range 15.2-20.1). At study entry median age was 19 years (IQR 16-22), VL <200 copies/ml in 197/255 (77%) and 226 (89%) had CD4 counts >200 cells/µl.

Sixty-two admissions occurred amongst 36/255 (14%) individuals, resulting in 558 nights (median five nights, IQR 2-9, range 1-103). One person died (CNS lymphoma) with a further seven (2.7%) exiting before the study ended; six TOC and one LTFU. Overall incidence of admission was 8.9 per 100 PY (95% CI, 7.0- 11.5); 3.0 (95% CI 1.5-.6.0) per 100 PY aged 10-19 years and 13.3 (7.0-17.4) per 100 PY aged 20-35 years (adjusted incidence rate ratio 2.0 (95% CI 0.98-4.1). Factors significantly associated with admission in regression analysis: CD4 count <200 cells/ul, HIV VL >200copies/ml or a previous CDC C-diagnosis.

55/62 (89%) admissions were HIV related, 28/62 (45%) with new/current CDC C-diagnoses; seven with Mycobacteria (11%), four presumed/suspected Pneumocystis pneumonia (6%), five with HIV wasting (8%) and three lymphoma (5%).

47 of all admissions (76%) were due to infections; respiratory 23/62 (37%), gastrointestinal twelve (19%), dermatological four (6%), symptomatic HIV after stopping ART two (3%) and others included meningitis, sepsis and urinary tract infections. Non-infective causes included surgery three (5%), psychoses three (5%), asthma two (3%), non-cirrhotic portal hypertension two (3%) and ART drug reaction one (2%).

Conclusion: In this perinatal cohort, rates of admission were four-fold higher in young adults compared to adolescents and were higher than published rates in the UK for children or adults LWHIV. A previous CDC-C diagnosis, plasma viraemia and immunosuppression were associated with future hospitalisation. Most admissions were HIV-related with CDC C-diagnoses documented in half. These findings highlight the continuing adherence challenges for adults born with HIV and the need for enhanced multidisciplinary support post transition.

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Increasing Capacity to Detect Neurocognitive Impairment among Adolescents and Young Adults with Perinatally Acquired HIV in Thailand: Validity of the NeuorScreen tablet application.

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Background: Adolescents and young adults (AYA) with perinatally acquired HIV (PHIV) often present with neurocognitive impairment (NCI), which is associated with diminished academic performance, suboptimal medication adherence, poor mental health, poor decision-making, and greater HIV transmission risk behaviors (e.g., condomless sex). Assessing and detecting NCI, however, is not widely accessible in low- and middle-income countries (LMICs), such as Thailand, where the current study took place. Neurocognitive assessment for NCI typically requires significant time and professional expertise (e.g., psychologists/neuropsychologists) – resources unavailable in many LMICs. Furthermore, available tests in LMICs are often simple translations of tests from high-income countries without LMIC-specific norms. NeuroScreen is a brief, highly automated and easy-to-administer (by all levels of clinical staff) tablet application to assess neurocognition and detect NCI. It consists of 12 subtests assessing learning, memory, executive functions, processing speed, working memory, and motor speed. NeuroScreen was adapted for Thailand via language and content translation by Thai psychologists, review by AYA and clinical staff (who found the app acceptable, highly understandable, and easy-to-use), and generation of stratified, community regression-based Thai AYA norms (N = 200; 13–24 years). This study compared test performance between AYA with PHIV and demographically-similar HIV-negative AYA.

Methods: AYA (50 PHIV; 49 HIV-negative) recruited from Bangkok and Chiang Mai were administered the Thai-version NeuroScreen by nurses who received one half-day training in its use. Raw scores were converted to demographically-adjusted (age, sex, education) T-scores based on the Thai norms. Global deficit scores (GDS) were calculated for each participant where GDS of ≥0.5 indicated NCI. Mean GDS scores were compared between HIV groups via independent samples t-test; chi-square analysis compared proportions of participants between groups with: test scores >2 SD below the normative mean and GDS ≥0.5.

Results: Median age was 18 years (IQR 16,20), median education was 11 years (IQR 11,13), and 57% were female. Median NeuroScreen completion time was 25 minutes (IQR 24,26). HIV groups did not differ on age, sex or education. On three tests of processing speed and one test of complex working memory, a greater proportion of the participants with PHIV had scores >2 SDs below the normative means; no other such differences were found for the other eight tests. Participants with PHIV had significantly worse GDS scores (Mean = 0.74, SD = 0.72) than their HIV-negative counterparts (Mean = 0.41, SD = 0.47), $t = 2.73$, $p < 0.01$. Fifty-five percent of PHIV participants had GDS scores ≥0.5 compared to 27% of HIV-participants, $X2 (1, N = 96) = 8.24$, $p<0.01$.

Conclusion: NeuroScreen is a brief, easy-to-use tablet app requiring minimal training to administer that has been adapted for use in Thailand with local AYA norms. The app was able to detect neurocognitive deficits commonly observed among PHIV youth. These findings are consistent with previous research on NCI in PHIV AYA using multi-hour, expert-administered paper-and-pencil neurocognitive test batteries. NeuroScreen demonstrates great potential to increase capacity in Thailand to identify neurocognitive challenges among AYA with PHIV and other vulnerable populations, and guide prevention/intervention opportunities.

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Development of a transition readiness score for adolescents living with perinatally-acquired HIV and transitioning to adult care

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Background: Adolescents living with perinatally-acquired HIV (ALHIV) have poor viral suppression and retention in care after transition from pediatric to adult based care. Timing of transition is often based on age but varies widely in different settings. Optimal timing and readiness for transition to adult care are not currently known.

Methods: We prospectively enrolled 199 ALHIV prior to transition from pediatric to adult care in South Africa. At enrollment, adolescents completed a questionnaire asking about alcohol/substance use, depression, stigma, self-esteem (Rosenberg self-esteem scale), social support (Adolescent social support scale), and transition readiness (HIV Adolescent Readiness for Transition Scale (HARTS)). Additional demographic and clinical data 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). We used factors associated with viral suppression in the bivariable and multivariable logistic regression models among adolescents not using drugs to calculate a transition readiness score using a point scoring system based on the regression coefficients. We used the Homer-Lemeshow Goodness of fit test for calibration and calculated the Area Under the Curve to determine the model's discrimination.

Results: Of the 199 adolescents who transitioned to adult care, 84 (43%) had viral suppression one year after transition. On multivariable analysis, adolescents on first-line ART (AOR 13.92; 95%CI 4.18-46.40; p<0.001), with documented HIV disclosure (AOR 2.75; 95% CI 0.1.21-6.23; p=0.015), and higher HARTS score (AOR 1.60; 95%CI 1.17-2.21; p=0.004) were associated with higher odds of viral suppression one year after transition, while females (AOR 0.40; 95% CI 0.19-0.85; p=0.018), older age (years) at ART initiation (AOR 0.81; 95% CI 0.71-0.94; p=0.004), and ever using alcohol (AOR 0.29; 95% CI 0.13-0.68; p=0.004) were associated with lower odds of viral suppression one year after transition to adult care. Based on these findings transition readiness scores were calculated and divided into tertiles of low, intermediate, and high probability of viral suppression after transition. The discrimination performance was good with an area under the curve of 0.85 (95% CI 0.79-0.90). The overall sensitivity of the intermediate/high transition readiness category compared to low transition readiness category in determining viral suppression one year after transitioning to adult care was 96.4 (95% CI 89.9 – 99.3) with a sensitivity of 27.7 (95% CI 19.6 – 36.9) and positive predictive value of 50.0 (95%CI 42.1 – 57.9). For the high transition readiness category compared to intermediate/low transition readiness, the transition readiness score had a sensitivity of 56.0 (95% CI 44.7 – 66.8), specificity of 86.6 (95% CI 78.9 – 92.3), and positive predictive value of 75.8 (95% CI 63.3 – 85.8) for the prediction of viral suppression one year after transition to adult care.

Conclusion: This transition readiness score can be used to identify adolescents who are ready to transition to adult care. For adolescents with lower transition readiness scores, it may identify additional areas for intervention to prepare adolescents for transition to adult care.

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Strategies used in countries with successful mother-infant pair tracking

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Background: Globally, new infant HIV infections continue for several reasons, including undiagnosed maternal infections and interruptions in maternal treatment. This abstract examined programmatic data, identifying countries with high coverage rates of Early Infant Diagnosis (EID) and HIV-exposed infants (HEI) final outcome (FO) ascertainment, and highlights the programmatic strategies being implemented.

Methods: Routinely collected programmatic data from 14 U.S. Agency for International Development (USAID)-supported PEPFAR countries from October 2019 to September 2020 (fiscal year [FY] 20) were used to assess 2-month EID coverage and 18-month FO ascertainment. Top performers were identified as those countries having the highest recorded EID 2mo coverage and FO ascertainment.

Results: The average EID2mo and FO ascertainment for the 14 countries was 65.1% and 58.6% respectively. Eswatini, Lesotho, Nigeria and South Africa achieved the highest rates of EID2mo, ranging from 82.0% to 96.5%, and FO ascertainment, ranging from 70.3% to 86.5%. All four countries implement community and facility mentor mother programs and provide clients with mHealth services, appointment reminders, and joint mother-infant pair services. Three countries implement birth cohort monitoring registers. Only Lesotho and Eswatini use continuous quality improvement approaches (CQI). Finally, only Lesotho incorporates point-of-care (POC) EID and only South Africa includes birth testing.

Conclusions: Top performing countries implemented a combination of strategies to promote continuity of treatment for mother-infants pairs along the PMTCT cascade, including using mentor mother programs, establishing mother-infant pair clinics and utilizing mHealth. However, only Lesotho is using POC machines to ensure rapid turnaround times, which may be contributing to Lesotho's high performance in both EID 2mo and FO, and only South Africa is implementing routine testing at birth and 10 weeks, which may be contributing to South Africa having the highest EID2mo coverage. Further analyses are needed to understand to what degree these interventions contributed to the outcomes of the PMTCT programs in these countries, and if additional innovative strategies are needed.

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Participatory PMTCT: community engagement for co-created PMTCT programming in 2 districts of Zimbabwe

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Background: Zimbabwe has a mother-to-child transmission (MTCT) rate of 7.8%. Community engagement in intervention design is recommended to improve acceptability, feasibility and effectiveness of PMTCT programs. Our aim was to conduct participatory action research (PAR) workshops to identify contextual risk factors and co-create a MTCT risk screening tool and maternal motivation package.

Methods: From August-September 2020 we conducted 12 PAR workshops at 8 health facilities in Bulilima and Makoni Districts, Zimbabwe. PAR workshops engaged key stakeholder groups of ≤15 participants: male partners, village health workers, health care workers, pregnant and lactating women and adolescent girls and young women (AGYW). A semi-structured facilitation guide explored the knowledge, perceptions and practices that increase MTCT risk in project communities and identification of subpopulations at increased risk. Participatory activities including brain storming, listing and sorting, use of visual aids and storytelling were used to facilitate participant engagement. PAR activities were documented through written, oral and visual methods and qualitative data analyzed thematically, including within and between group comparisons.

Results: A total of 174 stakeholders participated in 12 PAR workshops. PAR workshops revealed key themes on community MTCT risk perception across 4 ecological domains for consideration in tool design and program strategy:

1) Community: cultural and religious 'hotspots' between and within communities create increased MTCT risks. Participants emphasized need to engage communities at all stages of program implementation, not just at sensitization and evaluation. Communities perceive most PMTCT programs as 'missing' the most vulnerable and at risk.

2) Institutional: Low male- and youth-friendliness of health facility environments were seen as a critical limiting factor of effective MTCT risk reduction. Communities desire 'differentiated PMTCT' – with a Ministry endorsed menu of strategies that can be tailored to community context (i.e., outreach in conservative Apostolic communities).

3) Interpersonal: an emphasis on couples communication (not just biomedical intervention) for disclosure, partner HIV testing, and approval to have HIV-exposed infants tested for HIV. Adolescents and Young Women who are pregnant are marginalised and shamed by communities and health facility staff, limiting PMTCT information provided to AGYW and opportunities to identify and mitigate individual-level risk factors.

4) Individual: Communities conceptualise MTCT risk as being exclusively for women with known HIV positive status, with limited knowledge about the PMTCT cascade for HIV negative women. Communities desire simplified information in local languages that assist with problem-solving, not just identifying MTCT risks.

Participatory methods were adapted to support active participation for stakeholder groups, for example, AGYW preferred storytelling as a means of expressing their knowledge by depersonalising. All groups expressed their desire for adaptable PMTCT programming tailored to the needs of multiple target groups within the same community (men, AGYW, religious groups).

Conclusions: PAR workshops meaningfully engaged community stakeholders in the co-design of a parental motivation package and job aid for community- and facility-based MTCT risk identification and action. Future research is required to measure the impact of engaging communities in participatory co-design on PMTCT program outcomes.

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Population-level risk factors for vertical transmission of HIV within the national prevention of mother-to-child transmission programme in South Africa: An ecological analysis

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Background: Although South Africa has an overall mother-to-child transmission (MTCT) of HIV rate <5%, case rates remain high. Identifying population-level predictors of MTCT additional to maternal viral load (VL) may inform targeted interventions to further reduce paediatric HIV incidence.

Methods: We conducted an ecological analysis of routine laboratory HIV-related test-data belonging to a synthetic cohort of women of reproductive age living with HIV (WRLHIV), identified from the National Health Laboratory Service's Corporate Data Warehouse (NHLS CDW) between 2016 and 2017. As routine laboratory data lacks a marker of pregnancy, criteria based on syphilis screening and timing of HIV-related tests were used to differentiate pregnant from non-pregnant WRLHIV. Pregnant WRLHIV were followed from cohort entry at the first antenatal care (fANC) visit (estimated by the syphilis test date), through delivery to 15 months post-delivery. Follow-up for non-pregnant WRLHIV started at cohort entry on 01 January 2016 to 31 December 2018. HIV VLs performed at cohort entry, delivery (for pregnant WRLHIV) and at cohort exit described maternal viraemia (VL ≥50 copies/mL) stratified by pregnancy status. Percentages, medians (IQR) described study data. A negative binomial regression model determined the association between MTCT cases (HIV PCR positive children <24 months between 2016 and 2018) and the number of viraemic WRLHIV at different time points, controlling for number of WRLHIV aged <25 years at cohort entry and other routine sub-district level variables (fANC booking <20 weeks gestation rate, antenatal client start on antiretroviral therapy (ART) rate and HIV prevalence rate among pregnant women).

Results: From 262 sub-districts, 3 386 507 WRLHIV were identified with 178 319 (5.3%) meeting criteria for pregnancy. Median age (years) at cohort entry was 29.4 (24.6-33.7) for pregnant WRLHIV and 34.0 (33.0-35.0) for non-pregnant WRLHIV (p <0.001). Median proportions of women with fANC booking <20 weeks gestation, maternal HIV seroprevalence during ANC and ART coverage during ANC were 68.2% (62.9%-72.8%), 31.5% (23.4%-35.7%) and 94.8% (89.7%-97.8%), respectively. Maternal viraemia was consistently higher in pregnant versus non-pregnant WRLHIV with median proportions across sub-districts at 42.9% (38.3%-59.3%) versus 35.0% (25.9%-49.0%) at cohort entry (p <0.001) and 36.3% (25.0%-48.4%) versus 29.6% (21.0%-42.6%) at cohort exit (p <0.001) respectively. At delivery, the median proportion of viraemic pregnant WRLHIV was 38.2% (27.3%-52.1%). In total, 4 535 children tested HIV PCR positive representing a median sub-district level case rate of 1 372 (914-2 077) per 100 000 live births. Maternal viraemia postpartum, maternal HIV seroprevalence and ART coverage during ANC positively correlated with cases of MTCT while higher proportions of women with fANC booking <20 weeks gestation associated with a decline in cases of MTCT.

Conclusion: Findings suggest that maternal viraemia postpartum, higher burden of maternal HIV, women initiating ART late in pregnancy and/or incident maternal HIV during pregnancy are significant population-level predictors of MTCT within the national PMTCT programme. Scale-up of HIV prevention services is required to lower maternal HIV prevalence while expanded access to HIV testing will fast-track ART initiation among WRLHIV. Increased VL monitoring is critical to improve VL suppression rates for elimination of MTCT.

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Risk factors for adverse pregnancy outcomes among pregnancy women living with HIV on ART

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Background: Women living with HIV (WLWH) had substantially worse pregnancy outcomes. Current WHO guidelines of prevention of mother-to-child transmission (PMTCT) recommend all pregnant WLWH initiate lifelong antiretroviral treatment (ART) in pregnancy regardless of viral counts or clinical stage of disease. However, there have been concerns that ART use may affect pregnancy outcomes in addition to vertical transmission. It is important to understand risks of adverse pregnancy outcomes among WLWH on ART to optimize PMTCT care.

Material and Methods: This nested cohort study evaluated adverse pregnancy outcomes including stillbirth (fetal death at ≥20 weeks' gestation), preterm birth (livebirth at ≤37 weeks' gestation; very preterm birth at ≤32 weeks' gestation) and neonatal death (infant death ≤28 days after birth), and explored potential risk factors including ART use, viral loads (VL) and sociodemographic. Data was obtained from a completed randomized clinical trial (NCT02400671) which assessed short messaging service to improve ART adherence and retention among pregnant WLWH throughout 2 years postpartum. Gestational age was determined by the ascertained last menstrual period date and documented delivery date. Women who had a miscarriage were excluded from analyses. Site-adjusted Cox proportional hazard regression and log-binomial regression with robust standard error were used to determine association.

Results: Among 774 pregnant women at enrollment, median age was 27 years (IQR 23-31), median gestational age was 24 weeks (IQR 18-30), and 226 (29.0%) were virally unsuppressed (VL ≥1,000 copies/mL). Half of women (55.1%) started ART before pregnancy. Most women (89.1%) received tenofovir (TDF)-based ART regimens with the remainder on zidovudine (ZDV)-based ART regimens. During 211.5 person-years of follow-up until delivery, 34 women had stillbirth (incidence rate 16.1 per 100 person-years). Stillbirth was associated with being in school at enrollment (site-adjusted hazard ratio [HR] 4.18, 95%CI 1-17.43; p=0.05) and living ≥1 hour from clinic (HR 2.54, 95%CI 1.03-6.26; p=0.04). Among 235 women enrolled at <20 weeks' gestation, those whose partner tested for HIV had lower risk of preterm birth (HR 0.36, 95%CI 0.13-1.01; p=0.05) and those with depression (PHQ9>5) had higher risk (HR 2.92, 95%CI 1.09-7.81; p=0.03).

Among 740 women with live births, 201 (27.2%) had preterm births (including 31 very preterm births) and 22 (3.0%) neonatal deaths occurred. Preterm birth was associated with unsuppressed VL in pregnancy (site-adjusted prevalence ratio [PR] 1.33, 95%CI 1.05-1.67; p=0.02) and non-completion of primary school (PR 1.30, 95%CI 1.00-1.67; p=0.05). Very preterm birth was more frequent with ZDV- than TDF-based ART (12.9% vs. 4.4%, p=0.005). Neonatal death was associated with preterm birth (PR 2.46, 95%CI 1.10-5.51; p=0.03). Duration on ART had no significant effect on stillbirth, preterm birth or neonatal death.

Conclusions: Risk of preterm birth was substantial and associated with viral non-suppression, ART regimen and neonatal death. Pre-pregnancy ART may decrease HIV transmission and preterm birth; underlying regimen-effects should be explored. Supporting education, depression counseling and partner involvement may help prevent adverse pregnancy outcomes.

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Barriers to Early Infant Diagnosis (EID) at different stages of infancy

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Background: Early infant diagnosis (EID) has proven to be an impactful intervention, but little investments have been made. The coverage in sub-Saharan Africa is still unacceptably low. To drive uptake while reducing the burden of multiple clinic visits, the WHO recommends testing of HIV-exposed infants to align with routine immunization and child development clinic visits. Facilitating access to timely and reliable diagnostics is critical in bridging the treatment coverage gap for children, particularly in low-resource settings.

Materials and Methods: In 2020, Paediatric Adolescent Treatment Africa (PATA) conducted open-ended, qualitative cross-sectional surveys with 95 health providers across 14 countries in sub-Saharan Africa. The survey questions aimed to assess the barriers health providers face when promoting the uptake of EID during the infant's first year of life. The data was organised and analysed thematically across three age categories of infancy.

Results: Survey results showered that the main barriers to performing EID at birth included shortage of skilled health providers to perform EID tests and caregivers' lack of information about EID, thus resulting in mothers' refusal for babies to be tested. Furthermore, some respondents highlighted that EID at birth was not a standard recommendation in their national guidelines. At two months, the two most cited barriers were mother-baby pairs being lost-to-follow-up (LTFU) and a shortage of testing equipment and consumables, including cartridges for point-of-care machines and dried blood spot (DBS) test kits. Reportedly, LTFU resulted due to a number of contributing factors, including fear of stigmatisation due to lack of private cubicles in facilities to do phlebotomy, high costs of transportation to distant health facilities. More than half of the providers also reported LTFU as the main barrier for EID at nine months. In this instance, LTFU was reported as a result of migration, change of caregivers, mothers leaving children at home when attending clinic visits, distance to the health facility, inaccurate contact details and/or no phones. EID at nine months was also negatively impacted by the exchange of inaccurate information between clients in the waiting area, resulting in mothers withholding consent for the child to be tested.

Conclusion: Although there were some common challenges across the stages of infancy, others were noted more prominently at one stage. Most of the current barriers to EID testing in infants are related to weaknesses in the health systems infrastructure and resources- particularly human resources, procurement of commodities, policy guidance. Equally important to highlight are the economic, social and behavioural status of the clients. Ending paediatric AIDS will require overcoming persistent barriers to EID testing. More investments need to be done in ensuring we keep mothers and their babies in care as a critical success factor for EID. To keep mothers and babies in care, we need to explain the importance of knowing the babies' HIV status and starting treatment as soon as possible. National guidelines and policies need to be revised to embrace testing at birth as a pillar of early infant diagnosis, while equally investing in capacitating human resources to match the demand.

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Pregnancy characteristics and outcomes among migrant women living with HIV recently arrived in the UK

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Background: Migration is an important aspect of the UK HIV epidemic. In 2015-18 over 80% of pregnancies to women living with HIV (WLWH) were to women born abroad, primarily from sub-Saharan Africa. Those arriving during or shortly before pregnancy may face a complex and intersectional set of challenges hindering achievement of optimal birth outcomes. Despite this, population level data has not yet been used to explore and describe this population and their pregnancy outcomes in the UK. Here we draw on such data from the long-running National Surveillance of HIV in Pregnancy and Childhood (NSHPC), in order to describe the demographics, HIV-related characteristics and birth outcomes of WLWH who recently arrived in the UK.

Methods: Data on WLWH arriving in the UK during pregnancy or the 12 months prior to conception ('recent migrants'), with an expected date of delivery 1/1/2009-31/12/2019 reported to the NSHPC by 19/6/2020 were analysed. The NSHPC collects data on all pregnancies in diagnosed WLWH in the UK, their infants and any children diagnosed with HIV. The population was stratified by time of arrival (pre-pregnancy or during pregnancy) to explore differences in maternal characteristics and birth outcomes between women arriving before versus during pregnancy.

Results: Between 2009 and 2019, the NSHPC recorded 635 'recent migrant' women. Most were of sub-Saharan African origin (n=497, 78.3%), and although 602 (95.0%) were on antiretroviral therapy (ART) at some point during pregnancy, only 199/583 (31.4%) were on treatment at conception. Of the 384/585 (65.9%) women starting ART in pregnancy where timing was known, 21 (5.4%), 264 (68.8%) and 99 (25.8%) started in the first, second and third trimester respectively. Overall, 164 women (27.7%) booked antenatal care at ≥24 completed gestational weeks. Of the 570 pregnancies resulting in a recorded live or still birth, 86 (15.1%) experienced an adverse birth outcome (8.9% preterm, 12.0% low birthweight, and 1.6% extended perinatal mortalities) with a greater burden of ≥1 adverse birth outcomes for pregnancies where the mother arrived in pregnancy (44/242, 18%) than in those arriving the year before (42/328, 12.8%). Overall, of the 412/570 mothers with known viral load at delivery, 82 (19.9%) delivered with a detectable viral load (15.0% in those arriving pre-pregnancy and 24.8% in those arriving during pregnancy). Of the 490/570 babies with known HIV status, six (1.2%) acquired HIV vertically (2.0% among those arriving whilst pregnant), compared to 0.3%-0.6% in the same period among all pregnancies in WLWH in the UK.

Conclusions: These findings bring new insights about the vulnerabilities that 'recent migrant' WLWH and their infants may experience. This research supports work already being carried out by PHE's Inequalities and Migrant Health strategies, as understanding the demographics and the burden of adverse outcomes lays the foundation for further monitoring. To ensure that they receive the best care possible in pregnancy and safely deliver healthy babies, structural and political barriers that recent migrants may experience should also be considered.

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Factors Associated with Recent HIV Infection Among Pregnant Women in Lilongwe, Malawi: A Case Control Study

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Background: Malawi, like many countries in sub-Saharan Africa, has reduced HIV maternal to child transmission (MTCT) by providing antiretroviral therapy to all HIV-infected pregnant women through its Option B+ program. As a result, a growing proportion of MTCT stems from women who seroconvert during pregnancy. Understanding which pregnant women are at highest risk of HIV acquisition can help focus scarce prevention resources to those at highest risk of seroconversion.

Methods: This is a case-control study conducted at Bwaila District Hospital in Lilongwe, Malawi from 2017-2019. Five-hundred HIV-infected pregnant women were enrolled in a behavioral intervention trial. At baseline, participants were screened for recent HIV infection with a validated testing algorithm consisting of Limiting Antigen Avidity Enzyme Immunoassay and quantitative viral load (VL) testing. Those with final normalized optical density 1.5 and VL 1000 copies/mL were classified as having recent HIV infection (cases). To identify factors associated with recent HIV infection, cases were compared to 350 HIV-uninfected pregnant women presenting to the same setting (controls). Bivariate associations were estimated using logistic regression. A multivariate model was developed using a backward elimination approach. Variables with a p-value <0.05 in bivariable analysis were included in an initial full model and variables were removed sequentially until all variables in the final model had a p-value <0.05.

Results: At enrollment, 416/500 HIV-infected pregnant women (83.2%) provided a blood sample; of these, 44 had recent HIV infection (10.6%) and were classified as cases. In the final multivariate model, the odds of recent HIV infection were higher among women with a syphilis rapid test (odds ratio (OR)=5.6, 95% confidence interval (CI)=1.4-21.8), a primary partner known to be HIV-infected (OR=7.8, 95% CI=2.1-28.9) or a primary partner of unknown HIV status (OR=4.5, 95% CI=2.2-9.2). Additionally, the odds of recent HIV infection were higher if the woman reported not being married to her primary partner (OR=4.0, 95% CI=1.2-13.1), or if either she or her partner had traveled overnight within the past six months (OR=3.1, 95% CI=1.4-6.7).

Conclusions: A set of biomedical and behavioral characteristics may put HIV-uninfected women at elevated risk of HIV acquisition with a need for combination HIV prevention approaches.

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Prevalence of depression among postpartum women on Isoniazid-Preventive Therapy and Efavirenz-based treatment for HIV—An exploratory objective of the IMPAACT P1078 randomized trial

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Background: We conducted an exploratory analysis to investigate possible neurocognitive toxicity in postpartum women on HIV treatment in response to a concern of an Isoniazid-Preventive Therapy (IPT)/efavirenz (EFV) interaction.

Material and Methods: Pregnant women on HIV treatment from 8 high-incidence tuberculosis countries were randomized in IMPAACT P1078 to 28 weeks of IPT started immediately (during pregnancy) or deferred to 12 weeks postpartum. Enrolled women were followed monthly until 48 weeks postpartum. Partway through study implementation, the Patient Health Questionnaire 9 (PHQ-9) was added to systematically evaluate depression symptoms at entry, quarterly antepartum, and postpartum weeks 4, 12, 24, 36, and 48. Given the delayed initiation, all women do not have evaluations at every time point. We summarized percentages of women with depression symptoms at postpartum visits and assessed the association of 11 baseline risk factors of probable depression (PHQ-9 ≥10) at 36 weeks postpartum using exact logistic regression, adjusted for gestational age stratum. Week 36 was selected post-hoc because it had a high prevalence of probable depression. Risk factors included study arm, EFV-regimen, Hepatitis B surface antigen status, Hepatitis C serology status, country, CD4 count, HIV viral load, age, Body Mass Index (BMI), Isoniazid and EFV acetylation status, and Cotrimoxazole use. Study arm effect modification by EFV use was also evaluated.

Results: Of 956 women enrolled, 749 (78%) had at least 1 PHQ-9 evaluation. At study entry, 691/749 (92%) women were Black African/Black of African origin, with median (Q1, Q3) age of 29 years (24, 33) and gestational age of 26 weeks (22, 30). Most women were WHO Clinical Stage I (88%), on an EFV-containing regimen (85%), and had undetectable HIV RNA levels (63%), with median CD4 count of 499 cells/mm3 (355, 689). Across postpartum visits, the percentage of women reporting at least mild depression symptoms (PHQ-9 ≥5) peaked at 12% (29/229) during Week 12, then decreased to less than 6% (30/689) at Week 48. Probable depression (PHQ-9 ≥10) was reported in 1.5%, 2.2%, 1.6%, 2.0%, and 0.7% of women at Weeks 4, 12, 24, 36, and 48, respectively. Cotrimoxazole use was associated with increased odds of probable depression at Week 36 [adjusted odds ratio (95% confidence interval): 3.1 (1.1, 20.3)]. There was no evidence of study arm differences in odds of probable depression, nor treatment effect modification by EFV use.

Conclusions: Timing of IPT initiation and EFV use were not associated with probable depression. Further study is advised to formally assess associations of risk factors with probable depression.

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Trends in characteristics and care of women diagnosed with HIV during pregnancy in the UK

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Background: Prompt HIV diagnosis and initiation of antiretroviral therapy (ART) in pregnancy are key strategies to prevent vertical HIV transmission and optimize health of HIV-positive mothers and their infants. We aimed to assess trends in characteristics, timing of diagnosis, and treatment of women diagnosed during pregnancy in the UK.

Material and methods: The Integrated Screening Outcomes Surveillance Service (ISOSS) conducts population-based surveillance of pregnancies in women living with HIV in the UK. Analyses were based on 11,140 pregnancies in 7922 women diagnosed before delivery with estimated date of delivery (EDD) in 2010-2019 (reported by December 2020). Trends were assessed using logistic regression and Cuzick's non-parametric test for trend.

Results: There were 1617 pregnancies with maternal HIV diagnosis established antenatally (14.5% of 11,140 total pregnancies), with a decline observed in the proportion with antenatal diagnosis from 21.7% (314/1446) in 2010 to 10.2% (83/817) in 2019 (p<0.001). Overall, 93.3% (1509/1617) of pregnancies with antenatal diagnosis were reported by hospitals in England, increasingly from those outside London (51.0% (160/314) in 2010, 62.6% (55/83) in 2019, p<0.001).

Among women with antenatal diagnosis, median maternal age at EDD was 31 years (interquartile range [IQR] 27-35) and remained stable over time (p=0.084). Women born in Sub-Saharan Africa accounted for a decreasing proportion of these pregnancies, declining from 74.7% (230/308) in 2010 to 48.1% (39/81) in 2019 (p<0.001). Correspondingly, women born in the British Isles and Europe accounted for an increasing proportion, rising from 12.0% (37/308) to 16% (13/81) (p=0.009) and 6.8% (21/308) to 25.9% (21/81) (p<0.001) between 2010 and 2019, respectively.

Median gestational age at diagnosis was 12 completed weeks (IQR 10-16) among 1592/1617 with data available, significantly declining from 13 weeks (IQR 10-17) in 2010 to 12 weeks (IQR 9-16) in 2019 (p=0.018). There was no change over time in the proportion with diagnosis in the third trimester (≥27 weeks) (p=0.830), which was 7.7% (122/1592) overall.

Among 1477 with data on first reported maternal CD4 count in pregnancy, the median was 354 cells/mm³ (IQR 227-513) and 19.4% (286/1477) had a count <200 cells/mm³, with no evidence of change observed over time in either figure (p=0.884 and p=0.483, respectively).

Among the 1544/1617 (95.5%) pregnancies with known outcomes, there were 1431 (92.7%) livebirths, 18 (1.2%) stillbirths, 66 (4.3%) spontaneous abortions, and 29 (1.9%) terminations. Of 1449 women with live- or stillbirths, 1431 had information on ART, of whom 1422 (99.4%) had some antenatal ART. Median gestational age at ART initiation was 20 weeks (IQR 16-24) (59 missing date), declining from 21 weeks in 2010 (IQR 19-25) to 16 weeks in 2019 (IQR 13-20) in 2019 (p<0.001). Despite this improvement, there was only weak evidence of a decline in the proportion starting ART in the third trimester over time (13.3% [181/1363] overall) (p=0.070).

Conclusions: Women diagnosed with HIV during pregnancy in the UK are diagnosed and initiated on ART earlier than in previous years. However, late identification persists and warrants further investigation, particularly given underlying shifts in demographic characteristics of this group.

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Feasibility and acceptability of administering the cross culturally adapted ACTG adherence questionnaire to Ugandan women living with HIV via Audio Computer Assisted Self Interview (ACASI) vs via Provider-Assisted Interview

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Background: Women living with HIV often face challenges in adherence to ART postpartum. In addition to routine annual viral load testing, effective methods are needed to monitor adherence. We sought to assess and compare the feasibility and acceptability of administering the adapted AIDS Clinical Trials Group (ACTG) adherence questionnaire via Audio Computer Assisted Self Interview (ACASI) vs via Provider-Assisted Interview (PAI).

Methods: The ACTG adherence questionnaire was administered in both English and Luganda as part of the cross cultural adaptation validation. Participants were randomly assigned the order in which they received each mode-language combination of administration: e.g., Day 1 AE (ACASI English), Day 2 – IL (Interviewer Luganda), Day 3 –AL (ACASI Luganda), Day 4 – IE (Interviewer English). The feasibility and acceptability questionnaire was administered on day 4 after the participant had experienced all four mode-language combinations. A McNemar test was used to determine whether participant perceptions differed regarding privacy, brevity, ease of use and truthfulness. Focus Group Discussions (FGDs) using semi-structured interview guides were conducted in the local language among 18 women.

Results: Of 33 women enrolled, 26 (79 %) completed all the four required visits. Although 25 (96%) of the women reported not owning a personal computer, 81% reported past computer use, 88% reported ACASI use was easy and 81% completed ACASI without any help. Most women (20, 77%) preferred ACTG administration via ACASI to PAI (p=0.0001). Notably, more women reported that they had privacy during ACASI compared to PAI (24, 92% vs.18, 69%, respectively p= 0.008). However, no differences were observed for ease of understanding (ACASI: 24, 92% vs PAI: 19, 73%, p=0.15), honesty of responses (ACASI: 25, 96% vs. PAI: 21, 81%, p=0.18) and brevity (ACASI: 15, 58% vs. PAI: 16, 61%, p=0.10) of ACTG administration. These results were consistent with the FGDs findings.

Conclusion: Both ACASI and PAIs were acceptable and feasible in this study. ACASI was the preferred mode of administration and was associated with providing better privacy compared to PAIs. ACASI-administered questionnaires could be used to improve the process of adherence assessment with higher perceptions of privacy by participants during routine ART clinic visits without increasing staff burden.

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Behavioural and Emotional Outcomes at 7 and 9 years in Children from the Children with HIV Early antiRetroviral (CHER) trial: A longitudinal investigation

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Introduction: Behavioural and emotional problems are well described in children living with HIV (CLWH). Although starting antiretroviral therapy (ART) early in life improves immunological and physical health outcomes in later childhood, few studies address the question of whether these behavioural and emotional problems are similarly attenuated.

Methods: This longitudinal-observational study investigated behavioural and emotional outcomes, at 7 and 9 years of age, of participants randomized to three intervention strategies within the 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 HIV-exposed uninfected (CHEU; n=28) and HIV-unexposed children (CHU; n=35). The children's caregivers were administered the Child Behavior Checklist (CBCL), the Behavior Rating Inventory of Executive Function (BRIEF), and a study-specific questionnaire gathering biographic, economic, social, and medical information. Data were collected between May 2012 and December 2017. Over the course of the study period, doctors from the research team saw CLWH every 3 months and controls every 6 months. For each BRIEF outcome, mixed-model repeated-measures ANOVAs assessed differences over time between CHIV+ (ART-40W, ART-96W, and ART-Def) and CHIV- (CHEU and CHU); ART-Early (ART-40W and ART-96W), ART-Def, CHEU, and CHU; and ART-40W, ART-96W, ART-Def, CHEU, and CHU. For CBCL Externalizing, Internalizing, and Total Problem outcomes, chi-squared tests assessed between-group differences in frequency of both borderline impairment (T=60–63) and clinically significant impairment (T ≥64).

Results: Most caregivers were the children's biological mothers (≥75% per group). Ninety percent of CLWH were virally suppressed, with CD4 percentages >35% at both 7 and 9 years. Seventy-six percent of children were in age-appropriate school grades. Among the measured sociodemographic variables, only home language was significantly different across the five groups. However, analyses suggested that variable had no significant effect on either BRIEF or CBCL outcomes. Regarding the BRIEF outcomes, all group average T-scores were <65 (scores above that cut-off indicate problems with emotional and behavioral aspects of the child's executive functioning) at both measurement points. Analyses detected no significant Time or Group main effects, and no significant Time x Group interaction effects (all ps >.17). Regarding the CBCL outcomes, analyses also detected no significant between-group differences (all ps >.08). At 9 years, 18% of CLWH presented with scores in the clinical range on Internalizing scale, while a further 17% presented with scores in the borderline range on that scale. The analogous numbers were 15% and 10% for each of the CBCL Externalizing scale and the CBCL Total problems scale.

Conclusions: These results suggest that, regardless of ART treatment strategy, children who start ART early and who thereafter have careful clinical monitoring and sustained viral suppression will have favourable (i.e., similar to healthy controls) emotional and behavioural outcomes at 7 and 9 years of age, and that their trajectory of emotional and behavioural development across that time period will also be similar to that of controls. Further investigation is warranted to understand the mechanisms of resilience in these children, particularly as they reach adolescence.

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An assessment of multi-month dispensing of antiretroviral therapy for children and adolescents across 10 African countries

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Background: Multi-month dispensation (MMD) allows people living with HIV (PLHIV), including children and adolescents <15years (CALHIV), to obtain treatment for longer periods, reducing frequency of facility visits and patient volume. Informed by national policies, the Elizabeth Glaser Pediatric AIDS Foundation (EGPAF) supports implementation of MMD for both CALHIV and PLHIV. In light of the COVID-19 pandemic and subsequent response, transitioning patients to MMD became an important strategy to ensure clients remain on ART.

Methods: We analyzed routinely reported PEPFAR-program data from October 2019-September 2020 from 10 countries in EGPAF-supported regions (Cameroon, Cote d'Ivoire, Democratic Republic of Congo, Eswatini, Kenya, Lesotho, Malawi, Mozambique, Tanzania, Uganda). MMD regimens were defined to include 3-5 months and >6 months dispensation. The proportion of PLHIV currently on treatment receiving MMD was calculated by taking the total reported number of PLHIV currently on treatment for each 3-month period and dividing by the number of PLHIV on an MMD regimen. Data was disaggregated by age (<15 and >15 years) and country.

Results: The proportion of clients on MMD increased across countries from October 2019 to September 2020 for both PLHIV and CALHIV populations. Malawi and Mozambique experienced the highest increase of CALHIV clients on MMD over the 12-months, with proportions increasing from 2% (n=232) to 91% (n=10,854) and 5% (n=734) to 53% (n=6,120) respectively. The proportion of CALHIV on >6 month MMD across countries increased from 10.6% to 14.6% by September 2020. This proportion for PLHIV (>15 years) increased more steeply from 10.2% to 28.7% over the same period.

Conclusion: The estimated proportion of CALHIV on MMD was lower compared to adults across countries. There was increased momentum of transitioning adults to MMD compared to CALHIV over time. There was an increasing trend of transitioning clients to >6 month MMD. The changing policy landscape could have contributed to this increase.

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A Systematic Review and Meta-Analysis of HIV Risk Screening Tools to Identify At-risk Children and Adolescents for HIV Testing

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Background: HIV risk screening tools can identify at-risk individuals in need of HIV testing, but the effectiveness of these tools for children/adolescents varies. We performed a systematic review and meta-analysis of studies that validated tools for <19 years old (y/o).

Methods: We searched 11 databases for publications between 2000-2020 and 23 abstract books from 2015-2020. Sources were included if they validated questionnaires to determine the need for HIV testing for <19y/o. We computed the tools' pooled sensitivity and specificity and the diagnostic odds ratio (DOR).

Results: After retrieving 7,318 sources and 5,025 abstracts, 61 full-text articles were reviewed. Of the 11 studies with 12 different tools, eight were conducted in outpatient settings, one in the community, one in an inpatient setting, and two in outpatient and inpatient settings. The studies were conducted across six countries: five high HIV prevalence and one low HIV prevalence country. Pooled sensitivity was 81% (70-88%) and pooled specificity was 71% (49-86%). The DOR was 10 (3-31).

Conclusions: The few studies that validate HIV risk screening tools for children/adolescents vary across countries and inpatient/outpatient settings. The validated tools in this review show a weak association between screening tool results and determining which at-risk children need an HIV test. Our pooled results show that 2/10 children and adolescents living with HIV (C/ALHIV) assessed with a risk screening tool may be screened out for testing. Further research is needed to validate context-specific HIV risk screening tools and explore alternative approaches to optimize the diagnosis of C/ALHIV.

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Abstract 50 was withdrawn

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Effect of HIV on the distribution of NK cell subsets and their phenotype in infants pre-ART initiation and at 10 months of age

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Background: NK cells play an important role in antiviral immune response. This study investigated the effect of HIV infection on the phenotype of NK cells in neonates prior to ART initiation and at 10 months of age.

Methods: 33 untreated HIV Infected (HEI) and 35 HIV Exposed Uninfected (HEU) infants were enrolled at 1-2 months of age from Maputo, Mozambique and were followed until 48 months of age. Flow cytometry was performed using 28 color panel on PBMC. NK cell subsets were defined based on CD56 and CD16 expression. Four subsets were identified: (1) CD56++CD16-, CyP, cytokine producers, (2) CD56+CD16+, CTX, cytotoxic, (3) CD56+CD16-, intermediate, and (4) CD56-CD16+ dysfunctional and were further analyzed for immune activation (IA), CD38 and CD2, immune regulation, NKG2A and TIGIT, and trafficking, CCR5, CX3CR1 and CCR2. Besides FlowJo, we performed an unbiased analysis using Artificial Intelligence (viSNE) and clustering (FlowSOM). Mann-Whitney T-test was performed to compare the frequency of subsets and metaclusters, and MFI of each marker within NK subsets and metaclusters between HEU and HEI infants and correlated with plasma virus load by Pearson correlation.

Results: At entry, in comparison to HEU, the HEI infants had a lower frequency of CyP NK ($p \leq 0.001$) and higher frequencies of CTX NK ($p \leq 0.05$) and dysfunctional NK ($p \leq 0.04$), with increased frequencies and MFI of the molecules CD38 ($p \leq 0.05$) and trafficking receptor CCR5 ($p \leq 0.05$) together with lower NKG2A in the 3 subsets ($p \leq 0.05$). Interestingly, frequency of the CD38+ CTX NK cells and MFI of CCR5 in Cyp NK cells showed a positive association with VL ($p=0.05$ $r=0.4$ and $p=0.004$ $r=0.6$, respectively) at entry. At 10 months of age, the frequency of dysfunctional NK cells remained high in viremic HEI infants ($p \leq 0.05$) compared to HEU with higher MFI of CD2 ($p \leq 0.01$), while NKG2A remained lower ($p \leq 0.05$). In addition, MFI of TIGIT, a checkpoint molecule was also in lower in CTX NK in viremic HEI ($p \leq 0.01$).

At entry, metacluster #10 in CTX NK cells with dim activation and inhibitory markers, was statistically significant in HEI compared to HEU. Compared to entry, at 10 mo. viremic HEI showed a decrease in meaclusters#20,23,28,29,35, and 36 which were identified as CTX NK cells with dim TIGIT expression. In contrast, in HEU there as an increase in dysfunctional NK, metaclusters #16 and 17, with dim TIGIT expression at 10 mo. compared to entry.

Conclusion: In conclusion, NK cells of viremic HEI infants at 1-2 mo. age are activated with increase in migration marker CCR5, reduction of the inhibitory receptor NKG2A, and high frequencies of dysfunctional NK cells compared to HEU. At 10 months, in viremic infants some of these markers persist with an increase in CTX NK cells expressing the inhibitory receptor TIGIT. These observations highlight the need to investigate the effect of HIV on the development and function of NK cells during early life and their role in HIV viral reservoir establishment.

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Impact of COVID-19 on Ugandan children with and without HIV

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Background: The spread of COVID-19 has impacted children's education, emotional wellbeing and physical activity worldwide. The present study aims to understand the mental, socioeconomic and physical activity impact of the pandemic on children living with HIV (HIV+) and without HIV (HIV-) in Kampala, Uganda.

Methods: We included children aged 10-18 years who filled out questionnaires at baseline (2017-2018, pre-pandemic) and 2 years later (March 2020-January 2021, pandemic) in an ongoing observational cohort study at Joint Clinical Research Centre, Kampala. We measured socio-economic variables and physical activity with a questionnaire that incorporated the WHO STEPS instrument and the Demographic and Health Surveys Wealth Index. Physical activity energy expenditure was calculated using compendium from the National Collaborative on Childhood Obesity Research. COVID questionnaires were adapted from the PhenX toolkits and the NIH Public Health Emergency and Disaster Research Response. Descriptive statistics and standard test statistics including Kruskal Wallis were used to compare pre-pandemic and pandemic variables.

Results: 198 children were included pre-pandemic (101 HIV+, 97 HIV-); 140 (71 HIV+, 60 HIV) had information collected during the pandemic. At baseline, median (Q1; Q3) age was 13 years (11; 15) and 52% were females. During the pandemic, overall, 91% of participants endorsed not experiencing any COVID-related symptoms, only one participant was tested and one was aware of a confirmed COVID-19 exposure. Overall, 43% claimed feeling worried in the past 2 weeks, specifically 45% of participants worried about being infected with COVID and 38% about missing school. 77% of participants stated their schools were closed and only 3% had access to a digital device at home. 70% of HIV+ stated that they could not physically come to the clinic, however 87% were still able to obtain their ART regularly. There was no change in poverty level: pre-pandemic, 40% of HIV+ children compared to 54% of HIV- negative lived in extreme poverty (living on ≤ $1.90 per day), and during the pandemic 44% vs 49% (p=0.90 comparing pre-pandemic vs pandemic for groups overall). During the pandemic, overall physical activity increased in both groups: weekly activity minutes increased with a median of 596 min/week (IQR:270-940) reported pre-pandemic and 1450 (IQR:1050-1890) during pandemic (p<0.001). Moreover, physical activity as measured by kcal/week also increased by 16% in both HIV+ and in HIV- (p<0.001 for groups overall pre-pandemic vs pandemic).

Conclusions: We found in this Ugandan cohort of adolescents, that despite little reported exposure or reported infection due to SARS-CoV2, there was a high level of anxiety about potential infection and missing school. There is an overall high level of economic insecurity that did not fluctuate during the pandemic. Despite difficulty accessing the clinic, due to closure and transportation, HIV+ were still able to obtain their ART. We hypothesize that due to the extensive closure of schools and the lack of digital devices in homes, children in an urban Ugandan setting had increased physical activity during the pandemic. Further research is warranted to address the new barriers to health care and education access to enhance children's wellbeing during the pandemic.

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IMARA SA: Piloting a family-based HIV/STI prevention package for South African adolescent girls and young women

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Background: Reducing HIV/STI risk among adolescent girls and young women (AGYW) in sub-Saharan Africa is a global priority. Although family-based interventions may improve sexual health outcomes among AGYW, few have been tested. Informed, Motivated, Aware, and Responsible Adolescents and Adults- South Africa (IMARA SA) is an evidence-based group HIV/STI risk reduction program, adapted for South African AGYW and their female caregivers (FC). Through separate and joint sessions for AGYW and their FC delivered over two days (~12 hours of content), the intervention addresses drivers of HIV and emphasizes strong AGYW-FC relationships and communication. We conducted a pilot study to assess the preliminary effectiveness, feasibility, and acceptability of IMARA SA among AGYW in the Western Cape, South Africa.

Material and Methods: AGYW-FC dyads were randomized to IMARA SA or a health promotion control arm and completed surveys at baseline and follow-up (6-10 months post). AGYW reported on their: 1) sexual risk behavior (i.e., condom use at last sex, consistency of condom use, substance use during sex, and number of sexual partners); and 2) PrEP adherence. We tested intervention effects on sexual risk behavior using Fisher's Exact tests (given sparse data) and PrEP adherence using multivariable regression. Feasibility was examined according to the number and percentage of AGYW who completed IMARA SA and acceptability was evaluated by AGYW responses to survey items and open-ended responses following the intervention.

Results: Sixty AGYW (mean age=17.1, range=15-19 years) were enrolled (30 per arm). At follow-up, three of four sexual behavior outcomes and the PrEP adherence outcome favored IMARA versus control participants but did not reach statistical significance. Feasibility and acceptability for IMARA SA were strong. Over 80% of AGYW randomized to IMARA completed the intervention, and 100% of AGYW were at least "satisfied" and 86% were "extremely satisfied" with the program. Open-ended surveys revealed very positive responses; one AGYW wrote: "I learned to value my body more and to show respect to all people around me. I learned how to communicate in a good way with my parents and how I should respond to them when they talk. I learned about sexuality and how risky sex without a condom is."

Conclusions: The IMARA SA intervention is a promising strategy to improve sexual health outcomes among South African AGYW. Recruiting, enrolling, and retaining AGYW in the 12-hour program was feasible, and the intervention was highly acceptable among AGYW. IMARA SA warrants further investigation in a fully-powered randomized controlled trial.

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Ritonavir concentrations in hair predict virological outcomes in HIV-infected adolescents with virological treatment failure to atazanavir/ritonavir-based second-line treatment

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Background: Sub-optimal adherence to antiretroviral therapy (ART) is responsible for most virological treatment failure in adolescent yet methods for objectively measuring adherence to ART are limited. Adolescent studies measuring antiretroviral levels in hair are scarce. In addition, ritonavir concentrations in hair are under-studied in both adolescents and adults, yet it is widely co-formulated with other protease inhibitors as a pharmacokinetic enhancer in second-line treatment in resource limited settings. This study assessed the relationship between ritonavir concentrations in hair and virological outcomes, self-reported adherence and modified directly administered antiretroviral therapy in HIV-infected adolescents who were virologically failing second-line ART in Harare, Zimbabwe.

Methods: HIV-infected adolescents on atazanavir/ritonavir-based second-line treatment for >6 months with viral load ≥1,000 copies/mL were randomized to either modified directly administered antiretroviral therapy (mDAART) plus standard of care (intervention) or standard of care alone (control). Questionnaires were administered; viral load and hair samples were collected at baseline and after 90 days. Treatment outcome was ritonavir concentrations in hair after follow-up. Virological suppression was defined as <1,000 copies/mL after follow-up.

Results: Fifty adolescents (13-19 years old) were enrolled, and 42 adolescents had ritonavir concentrations measured in hair at baseline and 90 days. Twenty-three (46%) were randomised to mDAART. Two female participants refused hair collection citing cosmetic disruption of their hairstyles and 6 participants were excluded from analysis because their hair had been shaved too short either at baseline or follow-up visits. Mean(SD); 95% CI ritonavir concentrations were 0.3(0.4); 0-0.9ng/mg hair and 0.6(0.4); 0–1.3ng/mg hair at baseline and follow-up respectively. After follow-up, suppressed (VL<1,000 copies/ml) participants, n(%) [18(43%)] had higher ritonavir concentrations [mean(SD); 95% CI] (0.7(0.4); 0.01-1.4ng/mg hair) compared to unsuppressed (VL ≥ 1,000 copies/ml) participants [24(57%)] (0.5(0.4); 0-1.1ng/mg hair)]. In bivariate regression analysis, ritonavir concentrations in hair were associated with decreased viral load from baseline to follow-up and virological suppression at follow-up [regression co-efficient(standard error); 95% confidence interval; p-value] [-0.1(0.04); -0.2- -0.01; 0.03] and [-0.3(0.1); -0.5-0.02; 0.04 respectively]. Ritonavir concentrations in hair were also associated with attending school consistently over the past 3 months [-0.3(0.2); -0.7- -0.0008; 0.05] and self-reported adherence by visual analogue scale at follow-up [0.01(0.005); -0.00005-0.02; 0.05]. Ritonavir concentrations were not associated with mDAART [-0.04(0.1); -0.3- 0.2; 0.7]. In multivariate logistic regression analysis, ritonavir concentrations in hair were associated with viral load suppression at follow-up [RC(SE); 95% CI; p-value] [-0.3(0.1); -0.5- -0.06; 0.01], self-reported adherence at follow-up [0.01(0.005); 0.004–0.02; 0.006] and being male [0.3(0.1); 0.08–0.5; 0.008]. Ritonavir concentrations were not associated with mDAART [0.2(0.1); -0.07–0.4; 0.2].

Conclusion: Ritonavir concentrations in hair predicted virological outcomes and were associated with self-reported adherence in HIV-infected adolescents with virological treatment failure to atazanavir/ritonavir-based second line ART. Ritonavir hair concentrations were, however, not associated with a home-based adherence intervention in this cohort of adolescents. Measuring ritonavir concentrations in hair in adolescents on protease inhibitor-based regimens could predict virological outcomes and assess adherence in this vulnerable group.

Key words: Adolescents, virological treatment failure, ritonavir hair concentrations, adherence.

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Using Narrative Films to Combat HIV-Related Stigma in Western Kenya: A Pilot Study of Adolescents Living with HIV and their Caregivers

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Introduction: HIV-related stigma negatively impacts the mental health and quality of life of adolescents living with HIV (ALHIV) and serves as a significant barrier to youths' adherence to antiretroviral medications. Interventions that effectively address stigma and misinformation about HIV infection are needed to improve outcomes for ALHIV. In this study, we piloted a series of four short, narrative films, the HIV Stigma Films, created collaboratively in Kenya and depicting Kenyan ALHIV's lived experiences of stigma and discrimination with Kenyan ALHIV and caregivers of ALHIV. We hypothesized that these films would decrease viewers' negative, stigmatizing attitudes and beliefs about HIV-infection.

Materials and Methods: Fifty-seven ALHIV (10 to 19 years) and 50 adult caregivers (≥ 18 years) of ALHIV were recruited from two AMPATH-affiliated pediatric clinics in Eldoret, Kenya. Participants viewed all four films and either completed pre- and post-viewing questionnaires, including an HIV/AIDS-related stigma and discrimination scale previously validated in East Africa, or participated in post-viewing focus groups. Follow-up visits were conducted after three months to assess for persistence in changes to viewers' attitudes and beliefs about HIV-infection. Quantitative data were analyzed using SPSS® with paired t-tests comparing pre- and post-viewing and pre-viewing and follow-up scores on the HIV/AIDS-related stigma and discrimination scale. Qualitative data were thematically coded and analyzed using Dedoose® software.

Results: Mean pre-viewing Shame (47.2 vs 43.9 out of 50; $p<0.05$) and Equity scores (19.8 vs 17.1 out of 20; $p<0.05$) on the HIV/AIDS-related stigma and discrimination scale were higher for adolescents than caregivers, suggesting lower baseline levels of stigmatizing attitudes and beliefs about HIV infection reported by adolescent participants. Immediately post-viewing, adolescents demonstrated significantly worse total scores (Mean Difference (MD) = -5.88; $p<0.05$) and scores on the Shame (MD = -1.35; $p<0.05$) and Discrimination (MD = -3.29; $p<0.05$) subscales. Caregivers' total and subscale scores were not significantly different immediately post-viewing but most trended towards improvement. At three-month follow-up, caregivers demonstrated significant improvement in total scores (MD = 11.83; $p<0.05$) and Discrimination (MD = 6.50; $p<0.05$) and Equity (MD = 2.92; $p<0.05$) subscale scores, whereas adolescents had no significant differences in scores from pre-viewing. Qualitative analysis of post-viewing focus groups for both groups revealed that participants believed the films 1) would have a positive impact on their communities and 2) on people living with HIV, 3) had changed their personal attitudes, beliefs, and/or knowledge about HIV infection, and 4) would be effective and appropriate for a wide variety of audiences in Kenya. Analysis of follow-up focus groups revealed these same themes. Several adolescents reported that the films led to positive changes in how their caregivers behave towards them.

Conclusions: The HIV Stigma Films show promise as an intervention to reduce stigmatizing attitudes and beliefs about HIV-infection, especially among caregivers of ALHIV. Findings from the adolescent group warrant additional exploration but may be at least partially explained by an increased awareness of HIV-related discrimination after viewing the films. Further work is needed to establish the HIV Stigma Films as an effective intervention to reduce HIV-related stigma and discrimination.

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Tenofovir, Lamivudine and Dolutegravir (TLD) among Rural Adolescents in Zimbabwe, a Cautionary Tale.

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Background: Tenofovir disoproxil fumarate (TDF), lamivudine (3TC) and dolutegravir (TLD) as a lower cost, safe and more effective single daily dose regimen is rolling out in Africa for people living with HIV. Although access to viral load (VL) testing is improving, drug switching to TLD may result, despite virologic failure (VF) and potential drug resistance. We followed children and adolescents enrolled in a community-based antiretroviral therapy (CBART) programme in rural Zimbabwe who were switched from specific ART regimens to TLD to determine the rate of virologic suppression on TLD.

Methods: We followed annual VL testing of 390 children and adolescents who enrolled in a CBART study in 2018-2019. Review of clinic records in July 2020 identified 184/390 who had switched to TLD in 2019-2020. VL testing was done by the near point of care Simplified Amplification-based Assays, the SAMBA II semi-Q (Diagnostics for the Real World, Sunnyvale California) at Chidamoyo Christian Hospital, rural Zimbabwe. Rate of virologic suppression on TLD (VL<1000 copies/ml) was determined and factors (gender, age, previous ART regimens) associated with VF on TLD were established using Fisher exact test. All statistical analysis was done on Stata 14.

Results: Overall, 184 children and adolescents on TLD were enrolled in this study. The median (IQR) age was 15 (11-19) years and above half of the participants were female (57%). Prior to switching to TLD, 63%(115/184) of the participants were receiving a WHO 1st line NNRTI, of which the majority 83%(96/115) were on TDF/3TC/EFV and 17% (19/115) on abacavir (ABC)/3TC + either EFV (18) or nevirapine (1). Thirty eight percent (69/184) were receiving a PI-containing regimen, of which the majority 81% (56/69) were on ATV/r/3TC + either ABC (53) or TDF (2) or zidovudine (1) and 17% (12/69) received LPV/r/3TC + either ABC (11) or TDF (1). One participant was on TDF/3TC/darunavir/dolutegravir. Prior to switching to TLD, 76% (139/184) were virologic suppressed (VL<1000 copies/ml). After a median (IQR) duration of 6.9 (5-9.1) months on TLD, virologic suppression was observed in 95% of the participants. Of the 10 participants with VL ≥1000 copies/ml, 90%(9/10) were failing on their previous regimens, suggesting a behavioural tendency. Participants with PI as prior ART regimens were more likely to fail on TLD compared to those with 1st line NNRTI (10.1% vs 2.6%, p=0.042). Although not statistically significant, older adolescents (>15 years old) were more likely to fail on TLD compared to younger ones. Gender was not associated with VF on TLD.

Conclusions: A high rate (95%) of virological suppression was observed among children and adolescents on TLD in rural Zimbabwe. However, VL monitoring and more effective adherence support need to be reinforced in this vulnerable population to maximize the efficacy of dolutegravir.

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Feasibility and Acceptability of a Peer Youth Led Curriculum to Improve HIV Knowledge in Northern Tanzania: Resilience and Intervention Experience from the Perspective of Peer Leaders

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Background: HIV peer youth led (PYL) interventions contribute to improved retention in care and psychosocial wellbeing. The study objective was to assess the feasibility and acceptability of a 12-month PYL HIV curriculum integrated into routine clinical care in Tanzania and evaluate change in participants' knowledge and impact of leadership on peer leaders' lives.

Material and Methods: The study took place from June 2018 to June 2019 in two clinical sites in Tanzania. Peer leaders previously participated in a mental health and life skills intervention called Sauti ya Vijana (The Voice of Youth; SYV) and were recommended for leadership by SYV facilitators and clinic staff. Peer leaders were trained and supervised weekly in curriculum delivery using a "train the trainer" model. Data were collected and analyzed using mixed methods. Fidelity checklists were used to measure adherence to the curriculum. Youth participants answered written pre- and post-knowledge questions and evaluated PYL teaching. Semi-structured interviews and the Connor Davidson Resilience scale were conducted with peer leaders before and after assuming the leadership role.

Results: Peer leaders (N=4 male; 3 female) demonstrated high fidelity (96%) to activities in each lesson and participant feedback was positive for curriculum delivery. Participants' knowledge improved in nine of ten sessions. All but one leader—who moved away before the study ended—demonstrated stable or improved resilience with a mean difference of 3.8 (SD=7.0). Qualitative thematic analysis of peer leader interviews revealed peer leaders' perception that the curriculum normalized the HIV experience; being a peer leader also improved leadership confidence. Nevertheless, anticipated stigma, difficulty disclosing HIV status, and varying PYL teaching ability remained barriers.

Conclusions: This study demonstrated that a PYL curriculum to improve HIV knowledge integrated into routine adolescent HIV clinic in Tanzania was feasible, acceptable, and improves knowledge while also benefiting peer leaders, supporting efforts to scale and sustain PYL interventions for YLWH.

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Trends in HIV self-testing among adolescent and youth populations across sub-Saharan Africa

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Background: HIV self-testing (HIVST) addresses barriers that impact HIV-testing uptake including fear, stigma/discrimination, waiting times, lack of confidentiality and difficulty reaching facilities. HIVST can also be a strategic approach to minimize client attendance at facilities to decongest and reduce risks concerning COVID-19. HIVST aims to increase HIV-testing for populations with low-uptake and high infection. The Elizabeth Glaser Pediatric AIDS Foundation (EGPAF) facilitates HIVST-kit provision through integration into active index, partner and recency testing; via provider-initiated testing & counselling; and following eligibility screening for HIV testing. Provider training and site-level mentorship on HIVST are ongoing in select EGPAF-supported countries to support implementation of the modality.

Methods: Routinely reported PEPFAR-program data from EGPAF-supported countries was analyzed to identify trends in HIVST uptake and distribution from October 2019 – January 2021. Data was disaggregated by age, sex, and distribution method – assisted or unassisted. Distribution methods include unassisted self-testing (limited or no instruction provided by a provider) and directly-assisted self-testing (provider demonstrates use). HIVST-kit distribution varies based on country policies i.e., by providers or outreach workers, over-the-counter, etc. Primary and secondary distribution of HIVST-kits may occur based on country policies (to sexual partners of HIV-positive ANC attendees, sexual partners/biological children of indexed clients above 12 years, siblings of CLHIV, FSWs clients).

Results: From October 2019–January 2021, 191,964 HIVST-kits were distributed across nine countries. Initially, in the first three months, five countries (CDI, DRC, Eswatini, Kenya, Uganda) reached 5,907 individuals with HIVST-kits, including 1,726 adolescents and youth (AY) 10-24 years. By 18 months, this increased to nine countries (adding Lesotho, Malawi, Tanzania, Cameroon) with 76,662 HIVST-kits reportedly distributed, including 29,085 to AY. Over the 18-month period, 68,911 HIVST-kits were distributed to AY, representing 36% of all HIVST-kits issued. The proportion of distributed-unassisted HIVST-kits was higher overall and among AY at 58% (n=110,843) and 58% (n=39,838) respectively. HIVST-kits were distributed to more females (64% of all dispensed tests to AY went to adolescent girls and young women (AGYW); while 21% (n= 14606) of all distributed tests went to young men (20-24) and 12% (n= 8281) to adolescent boys (15-19)). Proportionally, more adolescent boys and young men obtained unassisted HIVST-kits (66%) compared to AGYW (55%); this trend was seen across all age groups.

Conclusion: Over the 18-months, HIVST-kit distribution was scaled-up considerably across countries. The scale-up, particularly during the COVID-19 pandemic, speaks to the adaptability of the modality. Despite difficulty in drawing concrete conclusions from the data and limited follow-up around end-users and facility-linkages, the identified trends provide valuable insights. Unassisted HIVST distribution was more frequent, which could imply the favorability of obtaining and taking HIVST-kits privately, particularly among males. Distribution to AGYW (15-24) was higher compared to other AY groups, which may highlight their role as a gateway to linking partners or peers to testing and care services. Additional research is needed to understand distribution, use, and follow-up trends of HIVST to more adequately amend approaches to reach and engage hard to reach and vulnerable populations, including AY.

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Lopinavir Drug Exposures in African Children with HIV using Lopinavir/ritonavir Pellets Dosed per WHO Weight-Bands

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Background: Lopinavir/ritonavir (LPV/r) is widely used for the treatment of HIV in children younger than 3 years of age. Due to the poor palatability and cold storage requirement of the original liquid formulation of LPV/r novel solid formations of LPV/r have been sought. The first solid formulation for young children approved by the United States of America Food and Drug Administration were LPV/r oral pellets (or mini-'melt' tablets), stored in lopinavir/ritonavir (40/10mg) capsules, which allows the drug to be easily mixed with food (Cipla Ltd, India). The LIVING study assessed the effectiveness, safety, efficacy, acceptability and pharmacokinetics (PK) of the LPV/r pellets in routine treatment settings in Africa. Here, we report the PK of LPV in young African children administered the LPV/r pellets per World Health Organization (WHO) weight band dosing.

Method: Children enrolled in the LIVING study in Kenya and Uganda were included [ClinicalTrials.gov Identifier: NCT02346487]. LPV/r oral pellets were administered according to WHO weight bands: 2, 3, 4, 5, and 6 LPV/r capsules, twice daily, for children 3–5.9 kg, 6–9.9 kg, 10–13.9 kg, 14–19.9 kg, and 20–24.9 kg, respectively. During study follow-up, blood samples were collected for sparse PK evaluation at 1 month, and then every 6 months afterwards. A population PK model of LPV was developed using a nonlinear mixed-effects modeling approach (NONMEM®). Model evaluation was performed using Goodness-of-fit plots and visual predictive checks. For covariate analysis, children were classified with moderate underweight with a weight-for-age Z-score (WAZ) between -2 and -3 and with severe underweight if WAZ < -3. Individual LPV exposures, using area under the curve (AUC0-12), were predicated from the final model and compared with the expected range of 40–160 mg.h/mL reported in adults.

Results: A total of 2,998 LPV/r plasma concentrations were available from 514 children (52% female). Mean (SD) age was 3.28 ± 2.01 (range, 0.3-12.4) years, body weight was 12.56 ± 3.97 (4.6-25) kg and 17% and 9% of children were classified with moderate and severe underweight, respectively. LPV concentrations were best described by a one-compartment model with first order absorption (with lag) and elimination. Body weight influence LPV clearance (CL/F) and apparent volume of distribution (V/F), but the inclusion of possible maturational changes as a function of age or malnutrition status, did not improve the model. Population estimated CL/F, V/F, Ka and lag time of LPV were 1.56 L/h/13.6 kg, 24.10 L/13.6 kg, 0.46 h-1, 0.46 h, respectively. The predicted median LPV AUC0-12 (range) were 109 (96-126), 113 (98-133), 116 (102-133), 114 (101-131), 106 (96-118) mg.h/mL, for children 3–5.9 kg, 6–9.9 kg, 10–13.9 kg, 14–19.9 kg, and 20–24.9 kg, respectively.

Conclusion: LPV exposure in African children using the LPV/r pellets per WHO weight bands were within the reference range reported with liquid and tablet formulations.

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Exposure to two dolutegravir formulations in children in the ODYSSEY trial

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Background: Dolutegravir-based ART is the WHO preferred treatment for both adults and children living with HIV. Dolutegravir (DTG) formulations for children include film-coated tablets (FCTs) of different strengths and dispersible tablets (DTs). A bioequivalence study in healthy adults showed a 1.6-fold higher area under the curve (AUC) with DTs compared to FCTs. However, the relative bioavailability of different formulations in HIV-infected children may differ from healthy adults. This study aimed to assess bioavailability of DTs and FCTs in HIV-infected children in the ODYSSEY trial.

Methods: PK substudies were conducted within the ODYSSEY trial (NCT02259127) to evaluate PK of DTG in children on first-line and second-line antiretroviral therapy dosed using WHO weight-bands. We compared DTG pharmacokinetic (PK) parameters between DTs and FCTs in children weighing 14-<25kg. Non-compartmental PK analysis was performed to calculate PK parameters with Phoenix/WinNonlin64 software. For estimations of geometric mean ratios (GMR) and 90% confidence intervals (90%CI) a linear mixed-model was used.

Results: 64 PK curves were available: in 14-<20kg weight-band 19 children had 25mg FCT and 13 children 25mg DT; in 20-<25kg weight-band 14 children had 25mg FCT, 9 children 50mg FCT and 9 children 30mg DT. Paired data were available for 11 children. DTG C24h (concentration at 24h after observed DTG dose) was lower than adult C24h (0.83 mg/L) in children receiving 25mg FCT: geometric mean C24h (CV%) was 0.44 mg/L (50%) in weight-band 14-<20kg and 0.32 mg/L (94%) in weight-band 20-<25kg. DTG C24h was comparable to adults for 25mg DT in weight-band 14-<20kg and 50mg FCT and 30mg DT in weight-band 20-<25kg: 0.85 mg/L (67%), 0.75 mg/L (44%) and 0.76 (73%) respectively.
GMR (90%CI) for DTG AUC0-24 25mg DT versus 25 mg FCT was 1.76 (1.46-2.12) for children 14-<20kg. GMR (90%CI) for DTG AUC0-24 30mg DT versus 50 mg FCT was 1.12 (0.86-1.46) for children 20-<25kg.

Conclusion: DTG exposure in children receiving DTs was 1.76 times higher compared to FCTs of the same dose. 30mg DTs gave equivalent exposure to 50mg FCTs. These results are comparable with the bioequivalence data in healthy adults.

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Abacavir Weight-Band Dosing for Infants in the First 4 Weeks of Life

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Background: The World Health Organization (WHO) recommends abacavir (ABC) from 1 month of age in infants weighing ?3 kg. ABC liquid formulation (20 mg/mL) use from birth has been restricted due to limited ABC pharmacokinetic (PK) data in neonates. We recently developed a population PK model to inform dosing from birth using ABC PK data from neonates/infants. This model incorporates both body weight changes and metabolic enzyme maturation during early life. In order to achieve ABC plasma exposures within the range observed in older children, we proposed a 2 mg/kg twice daily dose for a 3.0 kg infant from birth to 4 weeks of age [Bekker et al CROI 2021]. While the WHO prefers weight-band dosing to mg/kg dosing for simplification, there are no ABC weight-band dosing recommendations for infants <4 weeks of life. Our objective was to determine the optimal weight-band doses for ABC liquid formulation in neonates with weights 2.0-5.0 kg.

Material and Methods: The ABC PK model was developed through pooling data from 3 studies administering ABC liquid formulation: (1) PACTG 321 (2) a Tygerberg cohort and (3) IMPAACT P1106. Studies 1 and 2 performed intensive PK sampling in term neonates exposed to HIV and on standard prophylaxis. Study 3 performed sparse PK sampling in term and low birth weight infants with HIV initiating ABC based ART after 1 month of life. ABC clearance (CL/F) was allometrically scaled according to infant body weight and post-natal age (PNA) described maturation in a non-linear manner. Using the final model, Monte Carlo simulations were run for neonates (birth weights: 2-4.5 kg) to identify the optimal ABC dosing strategy for three WHO weight-bands: 2.0-3.0 kg, 3.0-4.0 and 4.0-5.0 kg. The PK goal was to achieve ABC exposures (AUC0-12) in the range (3.2-25.2 mcg.hr/mL) reported in older children.

Results: Forty-five infants contributed 308 ABC concentrations; 21 neonates were <15 days of life. For studies 1, 2, and 3, the median (range) PNA was 1 (1-8) day, 9.5 (6-15) days, and 73 (41–190) days at first PK assessment; median (range) body weight of 3.1 (2.2-4.0) kg, 3.3 (2.9-4.4) kg and 3.8 (2.4-5.8) kg. Simulations predicted that the optimal ABC doses are 8 mg (0.4 mL), 10 mg (0.5 mL) and 12 mg (0.6 mL) twice daily in neonates with birth weights between 2-3 kg, 3-4 kg and 4-5 kg, respectively. ABC exposures were within the expected range except for a small proportion (<15%) of infants with higher exposures during the first week of life, however, no safety concerns were identified. ABC exposures decreased rapidly across all weight bands by approximately 25% at Week 2, and 55% at Week 4.

Conclusions: This ABC weight-band dosing strategy of 8 mg (2-3 kg), 10 mg (3-4 kg) and 12 mg (4-5 kg) twice daily in infants less than 4 weeks of age provides therapeutic exposures for both treatment/prophylaxis during this period of rapid maturation and growth. Using the same dose throughout the first 4 weeks of life will simplify implementation from a public health perspective.

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Assessing parental choice of Lopinavir/ritonavir granules intake to improve child adherence at Baylor-Mwanza, Tanzania.

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Introduction: Drugs formulations are one of the main obstacles to achieving viral suppression in children. A new policy introduced in 2020 by the Tanzania Ministry of Health included Lopinavir/ritonavir (LPV/r) in granules. This new formulation allows new and more attractive routes of administering medication to children older than three years. During counselling, different options were advised: to mix granules with soft food, to blend with liquids such as water or milk, or to pour directly into the child's tongue. This study's objective was to assess administration practices, challenges, and acceptability among caregivers whose children are on LPV/r granules.

Methods: The study was conducted at Baylor Clinic in Mwanza, Tanzania between September and October 2020. Caregivers whose children were on LPV/r granules for at least two weeks were sampled and interviewed. Data on administration practices, challenges encountered during administration and acceptability of LPV/r granules were collected.

Results: Out of the 72 caregivers interviewed, 52 (72%) and 44 (61%) were aware of the three options to administer the dose and found the process of mixing granules prior easier, respectively. Offering the granules with water was the preferable route for 52 caregivers (72%). Interestingly, 69% of caregivers who started by mixing granules with soft food had changed to water. At least three sachets per dose were prescribed for 94% of the children, and 72% (52) of the caregivers admitted administering it at once. Although 64% (46) have not claimed any problem while administering the granules, 25% (18) described vomiting and 11% (8) complained of the number of sachets per dose. More than half of the caregivers (57%) preferred to continue with LPV/r granules as it was easy to administer.

Conclusion: Although the suggested first option was mixing with food, the preferred option of administering LPV/r granules was with water. The majority of the caregivers well accepted the new administration route, being vomiting and dose size the biggest challenges observed.

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Caregivers perception on paedriatic Lopinavir/ritonavir formulations for HIV infected children at Baylor clinic, Mwanza-Tanzania.

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Background: Tanzania introduced and updated Lopinavir/ritonavir (LPV/r) based regimen as the first line regimen for children < 3 years in 2015 and < 15 years in 2017 respectively; tablet and solution were the only formulations available. LPV/r tablets were prescribed for children able to swallow tablets. However, most children were unable to swallow tablets were given solution and also led to introduction of LPV/r granules in 2019 which mask unpleasant taste of solution. Over a span of 5 years, there are children who have used different LPV/r formulations during the course of their treatment depending on age, weight, availability, ability to swallow tablets and caregivers' preferences. The objective of this study was to assess caregiver's perception regarding the different formulations administered.

Methods: This was a cross sectional study conducted at Baylor Clinic-Mwanza between September 21st and October 29th 2020. Participants were caregivers whose children were < 25 kg and on LPV/r pediatric regimen for ≥ 2 weeks. Structured questionnaire was administered to assess information on types of LPV/r formulations administered over the course of treatment between 2015 and 2020, reasons for change and caregiver preference on the LPV/r formulation administered.

Results: Of the 330 caregivers assessed, the majority 186(56%) were caregivers of children < 5 years old. Majority 172(52%) of caregivers had administered two,112(34%) administered one and 46(14%) administered all three of LPV/r formulations throughout their children therapy. Half 79(50%) of caregivers mentioned stock out as a reason that led to change of LPV/r formulation. Furthermore, 49(30%) and 36(20%) of caregivers cited weight gain and inability to swallow tablets as reason for change respectively. Of 46 caregivers who had used all three LPV/r formulations; 23(50%) preferred solution, 13(28%) tablets and 10(22%) granules. Those who had administered one formulation, 33(25%) administered LPV/r granules of which 23(50%) of them preferred to continue with the formulation.

Conclusion: LPV/r solution was most preferred formulation by majority of caregivers who has experience in administering all formulations and main reason for formulation change was stock out. Further studies with large sample size to assess perception and reasons for preference of LPV/r formulations.

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Effects of Long-term Treatment with Elvitegravir/Cobicistat/Emtricitabine/Tenofovir Alafenamide Fumarate (E/C/F/TAF) on Bone Safety Parameters in Children and Adolescents Living with HIV

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Background: Elvitegravir/cobicistat/emtricitabine/ tenofovir alafenamide fumarate (E/C/F/TAF) is a once-daily integrase inhibitor-based single-tablet regimen approved for use in pediatric participants ≥6 years old and weighing ≥25kg. We examined the effects of long-term treatment with E/C/F/TAF on bone safety parameters following 96 weeks of treatment in pediatric participants 6 years and older weighing at least 25kg and 48 weeks of treatment in children 2 years and older weighing 14 to <25kg.

Materials & Methods: Study participants were enrolled in an open-label study (ClinicalTrials.gov: NCT 01854775) to receive E/C/F/TAF 150/150/200/10 mg (Cohort [C] 1: 12 to <18 years, ≥35kg; C2: 6 to <12 years, ≥25kg) or 90/90/120/6 mg (C3: ≥2 years, 14 to <25kg) for 48 weeks, followed by an extension phase of an additional 48 weeks. C1 study participants were treatment naïve. C2 and C3 study participants on a stable ARV regimen (HIV-1 RNA <50 copies/mL for ≥ 6 months prior to baseline) switched to E/C/F/TAF. Bone safety was assessed through 48 (C3) to 96 (C1, C2) weeks of treatment based on bone mineral density (BMD) measured by dual-energy X-ray absorptiometry and biomarkers for bone formation and resorption. Z-scores and height-adjusted Z-scores for BMD and biomarkers were summarized.

Results: In C1, C2 and C3, 50, 52 and 27 participants were enrolled, respectively, with median age of 15, 10, and 6 years; overall, 58% of participants were female, 81% Black, and 85% vertically infected. Median % changes from baseline in spine and total body less head (TBLH) BMD (g/cm2) at Week 96 were +9% and +2.7% (C1), +9.1% and +7.2% (C2), and +4.6% and +6.5% (C3) at W48, respectively. Median change from baseline in spine BMD height-age (HA) Z-score was +0.14 (C1) and -0.2 (C2) at Week 96 and +0.14 (C3) at Week 48; median change from baseline in TBLH HA z-scores was -0.07, -0.32 and -0.06, respectively. Participants with a ≥4% decline from baseline in spine BMD at Week 96, C1 4.3%, C2 11.6% and at W48, C3 3.7%, whilst in TBLH were C1 0%, C2 4.4%, C3 0% respectively. Median change from baseline in serum PTH (pg/mL) at Week 96 was C1 +17.4, C2 +10.4 and at Week 48 C3 +5.1. Median change from baseline in serum bone specific alkaline phosphatase (ug/L) at Week 96 was C1 -4.65, C2 -16.67 and at Week 48 C3 +8.02. Median change from baseline in serum 25-hydroxyvitamin D (ng/mL) at Week 96 was C1 -0.8, C2 +1.2 and at Week 48 C3 -6.0.

Conclusion: The long-term BMD and bone biomarker data in children weighing ≥14 kg demonstrate no concern for bone safety associated with E/C/F/TAF in pediatric and adolescent participants and support its continued development in this population and extension for children <14 kg. Bone safety will continue to be monitored in the clinical study.

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Effect of dolutegravir on folate and vitamin B12 status among HIV-infected children and adolescents in the ODYSSEY trial

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Background: Neural tube defects (NTDs) are known to be associated with maternal folate and vitamin B12 deficiency, and initial surveillance studies suggested an increased risk of NTDs among infants conceived by women taking dolutegravir (DTG). We, therefore, compared folate and vitamin B12 levels among HIV-infected children aged 6-<18 years starting first- or second-line DTG-based antiretroviral treatment (ART) versus Standard of Care (SOC) at 3 Ugandan sites in the ODYSSEY trial.

Methods: Plasma folate was measured on stored samples at baseline and 4 weeks. Red blood cell (RBC) folate and vitamin B12 levels were measured using samples collected prospectively at ≥96 weeks. Samples were analysed in one laboratory using Elecys assays. Normal regression was used to compare change in plasma folate from baseline to 4 weeks (adjusted for baseline) and cross-sectional RBC folate and vitamin B12 between randomised arms, adjusting for site, sample date, first-/second-line ART and randomisation stratification factors.

Results: 229 children ≥6 years were randomised at participating sites; 51% female, at baseline, median (IQR) age was 12.3 years (9.0,14.7), CD4 was 501 cells/mm3 (228,795); 67% started second-line ART; 114 started DTG, 115 started SOC (40% lopinavir/ritonavir-, 37% efavarinez-, 23% atazanavir/ritonavir-based ART). The mean change in plasma folate from baseline (mean 6.1 ng/ml) to week 4 was 0.4 ng/ml (SE 0.3) in the DTG arm (n=110) vs. -1.1 ng/ml (SE 0.3) in the SOC arm (n=107) with a difference (DTG-SOC) of 1.6 ng/mL (95%CI 0.8, 2.3; p<0.01). At week ≥96, mean RBC folate was 888 pg/ml (SE 29) in the DTG-arm (n=109) vs. 855 pg/ml (SE 28) in the SOC-arm (n=105) with a difference of 73 ng/mL (95%CI 3, 143; p=0.04). Plasma and RBC folate levels varied by site, but there was no evidence for heterogeneity of treatment effects. At week ≥96, vitamin B12 levels were similar: 478 pg/ml (SE 21) in the DTG arm and 504 pg/ml (SE 26) in the SOC arm (p=0.42).

Conclusion: We found no evidence that DTG-based ART was associated with decreased levels of plasma folate or RBC folate; plasma folate levels at 4 weeks and RBC folate levels at week ≥96 were higher than on NNRTI-/PI-based ART though the mechanism is unclear. Vitamin B12 levels were similar in both arms. These results suggest any increased risk of NTDs in infants conceived on DTG is unlikely to be due to DTG causing decreased folate and vitamin B12 levels.

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Neuropsychiatric manifestations and sleep disturbances in children and adolescents randomised to dolutegravir-based ART vs standard-of-care in the ODYSSEY trial

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Background: Dolutegravir is associated with neuropsychiatric adverse events (NPAEs) in adults. We present first randomised data in children and adolescents.

Methods: ODYSSEY is an open-label, multi-centre, randomised trial, comparing efficacy and safety of dolutegravir-based ART (DTG) with standard of care (SOC) in children initiating first- or second-line therapy. We compared NPAEs, including serious adverse events (SAEs), grade ≥3 events, ART-modifying events and suicidality-related events, and patient/carer mood-and-sleep questionnaire responses in DTG versus SOC.

Results: 707 children ≥14kg were randomised (sub-Saharan Africa 88%, Thailand 9%, Europe 4%); 311 children started first-line (92% efavirenz-based in SOC); 396 second-line (98% PI-based). Median (IQR) age was 12.2 (9.1,14.9) years; 362 (51%) were male; median follow-up 142 (124,159) weeks.

There were 31 NPAEs (in 23 children): 18(15) in DTG vs 13(8) in SOC; hazard ratio for time to first NPAE (DTG vs SOC) was 1.87 (95%CI: 0.79, 4.41). 12 AEs were neurological: 6(6) in DTG vs 6(5) in SOC. 19 AEs were psychiatric: 12(10) in DTG vs 7(4) in SOC. Median(IQR) age and time from enrolment to first event were 15.9 (10.4,17.5) years and 72 (47,124) weeks respectively. Most NPAEs (23) were in children starting first-line; and most (22) occurred in males. Ten participants (5 DTG; 5 SOC) had 13 SAEs: 7 DTG (3 epilepsy/convulsions, 1 headache/hypertension, 1 depression, 1 parasuicide, 1 psychosis) vs 6 SOC (3 epilepsy/convulsions, 1 dizziness, 2 parasuicide). 12 children (8 DTG; 4 SOC) experienced 15 suicidality events: 10 suicidality ideation (6 DTG; 4 SOC) and 5 parasuicide (2 DTG; 3 SOC). ART-modifying NPAE(s) included 3 DTG (2 depression, 1 psychosis) and 2 SOC (1 parasuicide, 1 dizziness).

Small numbers of participants/carers reported symptoms of self-harm (8 DTG; 1 SOC,p=0.04), “life was not worth living”(17 DTG; 5 SOC,p=0.009) or suicidal thoughts(13 DTG; 0 SOC,p<0.001) in mood-and-sleep questionnaires; the reported symptoms were transient and did not lead to treatment change. There were no differences between treatment groups in low mood/feeling sad, problems concentrating, feeling worried or feeling angry/aggressive, time to fall asleep, nightmares/vivid dreams or sleep quality.

Conclusion: Numbers of NPAEs and reported neuropsychiatric symptoms were low. More participants reported neuropsychiatric symptoms in the DTG arm vs SOC, however, this difference should be interpreted with caution in an open-label trial.

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Mutations associated with ineffectiveness of HIV-1 protease inhibitors in children in Abidjan, Côte d'Ivoire

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Background: HIV protease inhibitors (PIs) select more mutations than any other class of antiretroviral drugs.The accumulation of these mutations induces PI resistance. In addition, the development of widespread cross-resistance in this class presents a real challenge in clinical practice, particularly in children, where there are difficulties related to the limited number of pediatric dosage forms, adherence, social environment, psychosocial factors and lack of biological monitoring. In Côte d'Ivoire, 2 PIs are available for triple therapy in children out of the 8 approved by the US Food and Drug Administration (US-FDA). But only one is frequently used as first-line treatment.The objective of our study is to identify minor and major mutations on the HIV-1 protease gene that may decrease protease inhibitor (PI) efficacy in children.

Material and methods: The determination of minor and major mutations in the HIV-1 protease gene and their interpretation were performed using ANRS techniques and algorithm (www.hivfrenchresistance.org). In order to specify the viral subtypes, the obtained consensus sequences were aligned with the reference sequences available in the GenBank (http://hiv-web.lanl.gov/). The sequences were aligned with the Clustal W software implemented in the BioEdit v7 program. Phylogenetic trees were made with Mega 7 software.

Results: From a cohort of 260 children, 61 were included in our study. The synthesis of the different phylogenetic analyses showed that CRF02_AG represented 85% of the viral subtypes isolated. Then the A subtypes, CRF06_cpx and CRF09_cpx represented 10%, 3% and 2% of the virus population, respectively. The frequency of PI resistance was 13%. Common minor mutations were M36I and K20I (100% respectively), H69K (88%), L89M and I54V (75% respectively) and G16E (50%).The major mutations were V82A (75%), M46I (63%), L90M (38%) and L76V (13%). We noted resistance to Indinavir (IDV) and Fosamprenavir/Ritonavir (FPV/r) (75% respectively), Nelfinavir (NFV) and Saquinavir/Ritonavir (SQV/r) (50% respectively), Atazanavir/Ritonavir (ATV/r) (38%) and Lopinavir/Ritonavir (LPV/r) (25%).

Conclusions: The study identified mutations in the HIV-1 protease gene associated with PI resistance in children and confirmed the predominance of CRF02_AG in Côte d'Ivoire. It identified mutations associated with ineffectiveness of HIV-1 protease inhibitors in children in Abidjan, Côte d'Ivoire.Lopinavir/Ritonavir (LPV/r) and Atazanavir/Ritonavir (ATV/r) are the 2 PIs used. The major mutation responsible for the resistance to LPV/r was L76V. The combination of mutations frequently associated with ineffectiveness of the 2 PIs was I54V-V82A-L90M-M46I for LPV/r and G16E-L90M-M46I for ATV/r. The study thus demonstrated the need for increased access to third-line options ideally guided by genotypic resistance testing. In anticipation, efforts should be made to reduce the price of ARVs and acquire other PIs such as TPV/r and DRV/r for children in Côte d'Ivoire.

Keywords: Resistance mutation, Child, HIV-1, Protease inhibitors, Côte d'Ivoire.

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Early Trends in HIV Drug Resistance Mutations Among Pediatric and Young Adult (0-24 years) Clients in Sub-Saharan Africa

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Background: Treatment-experienced patients are failing antiretroviral therapy (ART) throughout Sub-Saharan Africa. The resulting HIV Drug resistance mutations (DRMs) present an urgent need for genotyping in order to provide successful individualized treatment and help inform regional treatment optimization strategies. Rilpivirine (RPV)-containing injectable ART may be the future for many people living with HIV (PLWH), but are these treatments likely to succeed in regions where Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs) have been extensively used? Pediatric clients <20 kg will soon gain access to Dolutegravir (pDTG), but does optimization need to account for possible high levels of ABC resistance in the population to avoid functional monotherapy? This abstract looks at early resistance trends in treatment experienced pediatric and young adult clients in Eswatini.

Methods: This is a retrospective review of electronic medical records and genotype results from Baylor Clinic in Mbabane, Eswatini. All genotypes are from treatment-experienced clients, 0-24 years old, with at least two detectable viral loads on Protease Inhibitor (PI) -based ART. Dominant Nucleotide Reverse Transcriptase Inhibitor (NRTI) backbone was Abacavir (ABC)-based.

Results: 169 genotypes were performed between January 2014 and February 2021 (63% male, 37% female). 37 (22%) showed intermediate level or higher resistance to Lopinavir/ritonavir (LPV/r) needing a change of regimen; 16 of those also had low level or greater resistance to Darunavir (DRV), 15 of those with L76V mutations. Most common PI mutations were I54V (30/169; 18%), M46I (29/169; 17%) and V82A (29/169; 17%). Most common NNRTI mutations were K103N (36/169; 21%), Y181C (32/169; 19%) and E138A (24/169; 14%). 36% of genotypes (61/169) had intermediate level or higher resistance to Rilpivirine (RPV) by Stanford score: 23 with K101E/H/I/Q/P/RV/V. Most common NRTI mutations were M184V (85/169; 50%), M41L (25/169; 15%) and D67N (21/169; 12%). 44 genotypes were done on children ≤10 years old. Of those, 77% (34/44) had low level or greater resistance to ABC, mainly due to M184V, while 10 (23%) had intermediate or higher ABC resistance due to other, more clinically significant mutations.

Conclusions: Early trends in DRMs in Eswatini give insight into effective ART for our treatment-experienced clients. RPV is not available in Eswatini, however 36% of these treatment-experienced clients have high level RPV resistance. Patients in this analysis were not on an NNRTI regimen at the time of genotyping so additional NNRTI mutations will have been archived. For this reason, injectable RPV-containing regimens will be problematic in this treatment experienced population. For clients ≤10 years old, optimizing them to pDTG based regimens with ABC/3TC backbone may pose a risk of putting them on functional monotherapy. Pediatric surveillance resistance testing is needed in Eswatini and the region to inform national ART optimization guidelines.

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HIV Drug Resistance Patterns Among Highly Treatment-Experienced Children, Adolescents and Young Adults in Sub-Saharan Africa

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Background: There are limited studies of drug resistance among children, adolescents, and young adults failing antiretroviral treatment (ART) in sub-Saharan Africa (SSA). We evaluated baseline drug resistance patterns in children, adolescents, and young adults enrolled in the New Horizon's study, which provides darunavir (DRV) and/or etravirine (ETR) to children failing second-line ART.

Methods: From November 2018 to October 2020, we collected data from Eswatini, Kenya, Lesotho, Rwanda, Uganda, Zambia, and Zimbabwe among patients aged 0-24 years initiated on DRV and/or ETR. Data were abstracted from medical records at baseline and approximately every six months thereafter. Susceptibility to various drugs was determined using the genotypic susceptibility score (GSS) using the Stanford University HIV drug resistance database version 8.9.1 portal (hivdb.stanford.edu) and was classified as susceptible, intermediate-level, and high-level resistance.

Results: A total of 233 patients aged 0-24 years were enrolled and the median age at switch to DRV or ETR was 12.9 years. Immediately prior to DRV or ETR initiation, 80.1% had viral failure while receiving LPV/r plus dual NRTIs. Of those enrolled, 128 (55%) had documented baseline resistance results. Only 27% were susceptible to TDF or AZT and 82 (64.1%) were not susceptible to any NRTI. For NNRTIs, high-level resistance was found for NVP in 80%, EFV in 58%, while 45% remained susceptible to second-generation NNRTIs, doravirine (DOR) and ETR. Among PIs, high resistance was found for both LPV (58%) and ATV (50%), with 71% having cross-resistance, however, 62% remained susceptible to DRV with only 1% having high-level DRV resistance. Compared to adolescents and children under five years, PI resistance was higher in 5-9-year-olds (80.8% vs 60% vs 44.4%).

Conclusions: Highly treatment-experienced children/adolescents in SSA have accumulated high-level of resistance to NRTI, NNRTI, and commonly used PIs, but susceptibility to DRV and second generation NNRTI was retained in most.

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The road to success is paved with dolutegravir: Dolutegravir treatment success among in children and adolescents living with HIV (CALHIV) at the Baylor Tanzania Centres of Excellence.

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Background: Efficacy and safety data of novel antiretrovirals, such as dolutegravir (DTG), in children and adolescents often lags behind adult data, and can lead to hesitation and slow uptake by HIV clinicians. Beginning in 2019, the Baylor Tanzania program began an enthusiastic rollout of DTG among CALHIV. We describe outcomes and safety data of this DTG rollout among CALHIV enrolled at the Baylor Tanzania clinics in Mbeya and Mwanza, Tanzania.

Materials and Methods: Retrospective chart review was conducted to describe outcomes and safety data of CALHIV who received DTG as part of their ART at the Baylor College of Medicine Children's Foundation – Tanzania Centres of Excellence (COEs) in Mbeya and Mwanza, Tanzania between 1 March 2019 (when DTG became available) and 30 November 2020. HIV viral load(VL) suppression was defined as VL<1000 copies/mL.

Results: A total of 1703 CALHIV received DTG, representing 62.4% (1703/2727) of all CALHIV on ART and 78.1% (1703/2180) of CALHIV eligible for DTG by weight (>20kg) at the COE. TLD was used in 57.0% (970/1703), followed by 39.2% (667/1703) on ABC-3TC-DTG and 3.9% (66/170-3) on AZT-3TC-DTG. Among the DTG cohort, 13.6% (231/1703) were new ART initiations, 63.2% (1077/1703) were shifted from a NNRTI regimen, and 23.2% (395/1703) were shifted from a PI regimen.

Outcomes revealed no severe drug toxicity and no discontinuations of DTG, with 98.3% (1674/1703) remaining active in COE care and 1.7% (29/1703) transferred out. Multi-month prescriptions were used in 73.6% (1254/1703) of DTG patients. At the end of the study period, 92.4% (1002/1084) of patients on DTG with documented VL were suppressed, compared to 86.4% (1257/1455) of those with VLs prior to DTG. Among those with pre- and post-DTG VLs (n=908), 85.6% (149/174) of previously unsuppressed became suppressed, and 94.6% (694/734) of previously suppressed remained suppressed.

Conclusion: DTG was well tolerated and highly effective in our clinically diverse cohort of CALHIV, and it use resulted viral suppression for many previously unsuppressed CALHIV. These results encourage widespread use of DTG among eligible CALHIV, especially those who remain unsuppressed on their current regimens.

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Successful Scale- Up of Optimal Antiretroviral Regimens and Improvement in Viral Suppression for Children and Adolescents Living with HIV Amidst COVID 19 Pandemic In Kenya

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Background: Emergence of COVID-19 in mid-March 2020 posed unprecedented challenges in provision of services to children and adolescents 0-19 year living with HIV (CALHIV) in Kenya. There were several adaptations including: reduced clinic visits, virtual adherence support and re-alignment of clinic appointments with treatment monitoring. The country rolled out phase 2 of CALHIV transition on Efavirenz (EFV)-based regimens to dolutegravir-based (DTG) antiretroviral therapy (ART) in May 2020. We report progress in optimization and viral suppression among CALHIV before COVID-19 and 9 months into the pandemic.

Methods: We analyzed data from 1037 sites with electronic medical records in the national HIV data warehouse from 41 counties. We defined baseline period as January to March 2020 and end line as September to December 2020. Outcome variables of interest were number of children transitioned to DTG-based ART, children receiving ≥3-month clinic appointments, viral load coverage (VLC) and viral load suppression (VLS). We compared outcome measures at baseline and end line and tested for significance using chi-square tests.

Results: Of the 58395 CALHIV, 47384 (81.1%) were eligible for optimization to DTG based ART . Median age was 13 (interquartile range 9-16) years and 52.0% were female. Children on DTG-based ART improved from 29.9% at baseline to 65.3%, p<0.0001. At end line, DTG uptake was higher among older adolescents, 50.3%, 67.5% and 69.3% for ages 5-9, 10-14 and 15-18 years respectively, p<0.0001. There was no difference in DTG uptake by sex, 65.0% in females and 65.5% in males, p=0.236. Children on ≥3-month clinic appointments improved from 33.4% at baseline to 46.0%, p<0.0001. VLC improved from 88.2% to 89.6%, p<0.0001 and VLS from 82.8% to 88.2%, p<0.0001 from baseline to end line. At end line, VLS was varied by regimen patients on DTG (92.1%) efavirenz (80.2%), nevirapine (87.1%) and other regimens (79.3%).

Conclusion: Kenya achieved significant progress in ARV optimization and improvement in VLS following implementation of COVID 19 adaptation interventions. Results confirm that with a combination of measures it is possible to improve performance and sustain CALHIV program gains amidst the pandemic.

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Challenges in the effective treatment of infant HIV undermine the potential impact of birth testing and neonatal ART: preliminary results from the LIFE trial in Mozambique and Tanzania

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Background: Neonatal antiretroviral therapy (ART) has been shown to minimize viral reservoirs and facilitate early virologic suppression in controlled research studies. But results from birth point-of-care nucleic acid testing (POC-NAT) and neonatal ART from routine public sector conditions in sub-Saharan African (SSA) countries are lacking.

Methods: The LIFE study is an ongoing trial comparing prevention of mother to child transmission (PMTCT) and infant ART outcomes between health facilities in Mozambique and Tanzania that are either performing POC-NAT in HIV-exposed infants (HEI) at birth with immediate linkage to ART for positives (Arm A), or following the traditional early infant diagnosis algorithm with first POC-NAT at 1 month (Arm B). HEI in Arm B have a dried blood spot (DBS) collected at birth for later conventional DNA-PCR testing.

The neonatal ART regimen for Arm A is zidovudine (AZT), lamivudine (3TC), and nevirapine (NVP) syrups from birth until 1 month and 3kg weight, after which patients are transitioned to abacavir+lamivudine (ABC/3TC) fixed-dose dispersible tabs with lopinavir/ritonavir (LPVr), preferentially in granule formulation. In Arm B, all HEI initiate prophylaxis with NVP and/or AZT, with those testing positive at follow-up visits initiating ABC/3TC+LPVr. Positive infants have viral load (VL) performed at scheduled study visits at 0, 1, 3, 6, 12, and 18 months of age via the Abbott mPIMA® POC platform that has lower and upper limits of detection of 800 and 1,000,000 copies/mL.

Results: Preliminary results are presented from a subset of infants who were positive at birth (POC-NAT positive at birth for Arm A, and POC-NAT positive at 1 month with birth DBS DNA-PCR positive for Arm B). To date 53 infants were born positive, 35 (66.0%) in Arm A and 18 (34.0%) in Arm B. After 3 months on ART, 38.1% (8/21) of infants in Arm A were virologically suppressed (<1000 copies/mL). At the 6-month visit, 21.4% (3/14) in Arm A (6 months on ART), and 11.1% (1/9) in Arm B (5 months on ART) were suppressed, p=0.483. In patients not suppressed at 6 months, 27.3% (3/11) and 50.0% (4/8) had VL >1,000,000 copies/mL in Arms A and B, respectively, p=0.297. And at the 12-month visit, 60.0% (3/5) in Arm A and 0% (0/4) in Arm B were suppressed, p=0.119.

Conclusions: These preliminary findings show the potential impact of birth POC-NAT and neonatal ART with non-significant but higher virologic suppression rates in Arm A. However, results also highlight the challenges countries in SSA face in effective infant HIV treatment with very low overall virologic suppression rates in both study arms. Birth POC-NAT and neonatal ART do not resolve the underlying psychosocial issues that, for many families, contributed to failed PMTCT and negatively impact infant ART adherence. Nor do they address the difficulty seen across national programs in SSA in treating infants >1-month of age with LPVr-based ART. The impact of birth POC-NAT and neonatal ART may be greater with improved adherence support for caregivers and the upcoming introduction of once-daily dolutegravir-based ART to improve ongoing post-natal infant treatment.

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Adolescent and caregiver perspectives on an enhanced adherence counseling intervention for youth with suspected HIV treatment failure in Kenya

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Background: Addressing the myriad of barriers to effective HIV management among children and adolescents living with HIV (CALHIV) is critical to improving patient care and outcomes. We aimed to describe barriers to ART adherence and perceptions and experiences of enhanced adherence counseling (EAC) sessions.

Methods: Sixteen focus group discussions (FGD) were conducted in five study sites in Homa Bay and Turkana counties, between August and October 2019. FGD were held among adolescents aged 12-19 years, and caregivers of children 0-9 years with viral load [VL] >1,000 c/ml after ≥ 6 months on ART, who had received ≥1 EAC session. Five FGD were conducted each for adolescents 12-14 years (n=39) and 15-19 years (n=36); caregivers (n=36) participated in six FGD. Audio recordings were transcribed and translated from Kiswahili/Dholuo into English and coded using MAXQDA (2020) software. Data were thematically analyzed by participant group.

Results: Of 75 adolescents, mean age was 14.2 years (standard deviation [SD]: 2); 34 (45%) were female. Caregiver mean age was 39 years (SD: 11.6); 32 (89%) were female. Common adolescent barriers to adherence included routine activities (school, chores, travel) that prevented timely ART taking and caregiver conflict or lack of support. Stigma also negatively affected adherence, resulting in fear of drug-taking in public and being seen attending HIV clinic. Frequently named barriers to child adherence by caregivers included family conflict and stigma/peer pressure. Caregivers and adolescents felt EAC was generally effective at improving adherence by helping to counteract stigma and correcting behaviors like drug discontinuation when feeling healthy. Reasons for not completing all EAC sessions included poor treatment by providers, visit frequency and length, and repetitive content. Suggestions for improvement included friendlier provider attitudes, avoiding blame for unsuppressed VL, and addressing travel-related challenges (e.g., hold sessions at home/by phone).

Conclusions: Participants perceived EAC as useful in addressing adherence, though they made recommendations for improvement. Barriers to achieving optimal adherence could be addressed more fully in EAC and HIV programming more broadly for CALHIV. Responsive strategies may include fewer clinic-based visits to address transport challenges and stigma, continual reassessment of treatment plans to ensure drug-taking times align with schedules, and additional adolescent-focused provider training and sensitization.

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Adherence to Antiretroviral Therapy among Children Living with HIV in North-Central Nigeria: a Qualitative Evaluation of Barriers and Facilitators among Caregivers

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Background: In 2020, there were nearly 55,000 under-15 children living with HIV (CLHIV) receiving antiretroviral therapy (ART) in Nigeria. Despite advances in treatment access, challenges persist in achieving adherence and viral suppression among CLHIV. The IAS/CIPHER-funded Caregiver Peer Support (CaPS) study evaluated barriers and facilitators in ART adherence for CLHIV.

Materials and Methods: Between September and October 2020, focus group discussions (FGDs) and key informant interviews (KIIs) were conducted among caregivers of zero to 10 year-old CLHIV. Primary caregivers lived with their CLHIV and were chiefly responsible for drug administration and clinic appointments. Secondary caregivers assisted and/or served as "backups" for primary caregivers. Exemplary caregivers had CLHIV who were virally suppressed and had exceptional adherence and retention-in-care.
Caregivers were recruited from three secondary health facilities in the Federal Capital Territory. All interviews were audiotaped, transcribed verbatim and manually analyzed using a Grounded Theory approach.

Results: We interviewed 26 primary, 19 secondary, and 4 exemplary CLHIV caregivers via five FGDs and four KIIs; 78% (38) caregivers were female, and of these, 82 % (31) were biological mothers.

Barriers to adherence:
- Children had challenges with large size and bitter taste of some ART pills.
  - "She complains that the tablets are too big"
  - "When she wants to take the medicine, she might throw it up because she says it's bitter for her".
- ART side effects
  - "If she takes the drug, she'll be having dizziness and nightmares".
- Uncooperative CLHIV
  - "If I give him the drug he will hide it, throw it in the corner or throw it in the toilet".
- Caregivers' busy schedules affect close monitoring of CLHIV adherence
  - "At times I come back around 9 pm and the boy takes the drugs around 7pm, I don't know whether he takes the drugs or not".

Facilitators of adherence:
- Crushing tablets: "My daughter doesn't swallow medicine, so I have to grind the medicine."
- Enticements: "Sometimes, I buy his favorite thing that he likes to eat before he'll even take the drugs."
- Co-scheduling drug administration for child and caregiver: "I administer the (child's) drug at the time I'm taking my own (ART)";
- Direct observation: "I'll stand in front of her, so she won't throw it away"
- Masking drug taste: "I'll put it inside thick pap on a spoon, so that it won't touch her mouth."
- Reminders: "I set the time; once it's 7, the alarm will just ring, and I'll know it's time to take the drugs"
- Extra help: "I have somebody…that even if I'm not around, the person will give that child the drug."

Conclusions: Factors affecting CLHIV ART adherence exist in several areas including at child, drug, caregiver, and external levels.
ART tolerability, minimal side effects, and child-friendly formulations are critical considerations for addressing barriers to adherence. Extra help from trained, tailored peer support for caregivers has potential for improving CLHIV adherence and attainment of viral suppression, through caregiver mentoring, experience-sharing and adoption of best practices.

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Viral Load Coverage and Suppression Around COVID-19: Eswatini

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Background: Programming for HIV-positive clients centers on achieving viral suppression. During the SARS-COV 2 pandemic, Baylor Eswatini has restructured normal programing for a majority pediatric patient population and changed prescribing practices to protect our patients and staff. These adaptations include: 6-month refills, fast tracking, virtual teen clubs, and community ART delivery. Here we compare viral load (VL) coverage and suppression among all clients before the pandemic and one year later to assess the impact of the pandemic on VL coverage and suppression.

Methods: A retrospective cross sectional chart review was performed for clients at 3 clinical sites on Feb 1, 2020 (Pre-pandemic) and Feb 1, 2021 (during pandemic). Inclusion criteria were: clients on ART for at least 6 months and "active" status in the EMR (i.e., not LTFU, deceased, transferred out). VL coverage was defined as having a VL result within 12 months of each period (Feb 1, 2020 and Feb 1, 2021). VL suppression was defined as having a VL result <1000 copies/mL. VL coverage and VL suppression, both conditional (conditional on having an active viral load) and unconditional (including those who do not have an active viral load but should), were compared from 2020 and 2021, and data was disaggregated by gender and age groups. For analysis, Chi Square test was used for unpaired data, and McNemar's Chi Square test was used for paired data.

Results: 5360 clients were active on Feb 1, 2020, and 5213 were active on Feb 1, 2021. In 2020, VL coverage was 95.4%, with 93.2% of those virally suppressed (conditional suppression) and 88.9% of total eligible population virally suppressed (unconditional suppression). In 2021, viral load coverage was 93.9% with 94.8% of those virally suppressed (conditional suppression) and 89% of total eligible population virally suppressed (unconditional suppression).
4,996 clients (2,155 female, 2,841 male) were active at both time points in 2020 and 2021, and 71.5% were less than 25 years of age in 2020. At the 2020 time point, 93.7% were suppressed. At the 2021 time point, 95.2% were suppressed ($p<0.0001$). When disaggregated by gender, improvement in viral suppression from 2020 to 2021 was statistically significant for females ($p<0.0001$) and for the 15-20yo age group ($p=0.035$).

Conclusion: Despite significant disruptions with routine health care delivery due to the pandemic, including drug stock outs, Baylor Eswatini quickly pivoted to maintain excellent VL coverage and suppression. We expected to see a lower rate of viral load suppression, however, clients are doing well – especially the females and teenagers. Viral load coverage decreased slightly, as might be expected, but in those who were able to have viral loads within the year, their suppression rate improved. There are many factors that have affected clients and health delivery during the pandemic, but this data shows that differentiated service delivery models are not detrimental to viral suppression and in fact, may be better for patient outcomes. It also suggests that our adolescent girl and young women focused programming may have helped to maintain viral suppression in this population.

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The Baylor International Pediatric AIDS Initiative (BIPAI) Network's progress towards the second and third UNAIDS 95-95-95 goals among CALHIV receiving care in pediatric HIV centers in six countries in sub-Saharan Africa.

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Background: The UNAIDS 95-95-95 targets for people living with HIV (PLHIV) – 95% knowing their HIV status, 95% initiating ART, and 95% virally suppressed – are an important and ambitious goal for curbing the HIV epidemic and providing excellent care for PLHIV. Children and adolescents living with HIV (CALHIV) face unique challenges that require tailored care to meet the 95-95-95 targets. However, little is known on the progress of CALHIV towards these goals. To address this gap, we analyzed the BIPAI Network progress towards the second and third 95 targets among the seven HIV centres of excellence (COEs) across six countries in sub-Saharan Africa (SSA).

Materials and Methods: We extracted data retrospectively from the standardized electronic medical record used at seven COEs from January 1, 2014 (the year the UNAIDS targets were announced) to December 31, 2019 at the following BIPAI Network countries: Botswana, Eswatini, Lesotho, Malawi, Uganda, and Tanzania (Mbeya and Mwanza). Viral suppression was defined as viral load (VL) less than 1000 copies/mL, and undetectable was defined as VL<400cp/mL.

Results: Between 2014 and 2019, the average number of active CALHIV receiving care annually across the COEs was 23,896. During this period, achievement of the 2nd 95 improved from 95.0% (21990/23154) to 97.1% (22867/23560). Documentation of VL testing and results increased from 43.3% (8152/18627) in 2014 to 77.5% (13652/17605) in 2019 . Among those with VL results, progress towards the 3rd 95 increased from 80.1% (6369/7954) to 88.8% (12175/13710), and the percentage of undetectable VL increased from 77.8% (6191/7954) to 85.5% (11728/13710) during this period.

All seven COE sites also experienced upward trends in these achievements. There was slight heteogeneity of performance between COE sites. The Botswana (97-99%, 91-93%), Eswatini (91-99%, 77-89%), Lesotho (98-99%, 81-92%), and Uganda (99-100%, 76-88%) COEs performed slighter above the network average in the second and third 95 acheivements, while Malawi (86-92%, 74-84%) and Tanzania (Mbeya 97-98%, 50-86%; Mwanza 90-95%, 47-93%) performed slightly below the network average between 2014-2019.

Conclusion: We present one of the first analysis of the progress towards the second and third UNAIDS 95-95-95 targets among a large cohort of CALHIV in six countries in SSA. Between 2014 and 2019, upward trends were seen across the BIPAI network in progress towards both the 2nd and 3rd 95 goals, likely reflecting the Network's ability to adapt and implement best practices and new guidelines timely. While >95% of CALHIV were initiated on ART, gaps remain to achieving the 3rd 95 in this cohort. Additional analysis of this cohort is needed to identify best practices and drivers of success, as well as major barriers, to achieving the 2nd and 3rd 95 targets in CALHIV.

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What are the drivers of improved viral suppression among HIV infected children (0-14 years)? Results from the national data warehouse in Kenya 2020

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Background: Of the estimated 105,000 children living with HIV (CALHIV) in Kenya, 68,611 are currently on antiretroviral therapy (ART). Although viral suppression (VS) is lower in children compared to adults; there has been a 25% increase in VS among CALHIV from 2016 to 2020. We investigated the drivers of improved VS among CALHIV in Kenya.

Methods: Using the national HIV data warehouse, we sampled 81 nationally representative HIV clinics in 41 of 47 counties through stratified random sampling. Stratification was based on counties and facility volume, with high volume being ≥100 active CALHIV. VS was defined as viral load (VL) <1000 copies/milliliter. After bivariate analysis, multilevel mixed effects logistic regression modeling was used to control for confounding variables and random effects at county and facilities.

Results: Of the 6,559 CALHIV, 5,319 (81.1%) had valid VL. Median age was 11 (interquartile range (IQR) 7-13) years and males were 3,242(49.4%). Overall VS was 86.1% with 19 (23.5%) clinics having VS >90% (range 38.5% - 100%). Children 5-9 years were twice as likely to be suppressed compared to <5 years, adjusted odds ratio (aOR) 2.0(95% confidence interval [CI] 1.20 - 3.16, p=0.007. Every extra year on ART improved the odds of VS by 10% (aOR 1.1, 95%CI (1.01-1.1), p=0.012). Children on dolutegravir had a 3-fold odds of VS, aOR 3.2, 95%CI (2.15-4.61) compared to those on efavirenz, p<0.0001. Documented satisfactory adherence was associated with nearly 5 times more likely to be suppressed compared to unsatisfactory adherence, aOR 4.9, 95%CI (2.37-10.11), p<0.0001. CALHIV with initial VS after ART initiation were 3 times more likely to be suppressed, aOR 3.1 95% CI (2.42-4.04) p<0.0001. Tertiary facilities had better VS than health centres, aOR 1.9, 95% CI (1.03-3.43) p=0.04. There were no differences in VS by sex, orphan status, treatment supporter, age at ART start and baseline CD4 (p>0.05).

Conclusion: Older children, longer duration of ART use, being enrolled in a tertiary level facility, being dolutegravir-based regimen and satisfactory adherence are key drivers of high VS among CALHIV. Strategies are needed to improve VS among younger CALHIV < 5 years.

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Low Viral Suppression among Children < 3 Years Old On Two Protease Inhibitor Formulations In Kenya, 2015-2019

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Background: Kenya's preferred first-line antiretroviral therapy (ART) for HIV-infected children aged 0-3 years is a protease inhibitor (PI) based regimens specifically Lopinavir/Ritonavir (LPV/r). Children 0-3 years are either given LPV/r syrup or pellets. There has been substantial scale-up of use of LPV/r pellets, which are heat-stable. We report scale-up of LPVr pellets and viral load suppression rates among children 0-3 years on LPV/r syrup amd pellets from 2015 to 2019.

Methods: We analyzed routine HIV program data from 4 CDC implementing partners in supported sites providing ART for children aged 0-3years from 2015-2019. We described the distribution of data for continuous variables using interquartile ranges (IQR) and categorical variables using proportions. We used Pearson's chi-squared statistics to test for independence of proportions and the extended Cochran-Mantel-Haenszel stratified test of association to test for trends of rates over time.

Results: Over the five years, 1446 children were newly initiated on a PI-based ART regimen and had complete data for both initial and current ART. Males were 45%, and the median age at enrollment was 1.01 years(IQR was 0.43-1.79). At baseline, 150 and 1296 children were initiated on pellets and Syrup formulations respectively.The use of LPVr pellets as an initial regimen improved from 2.1% in 2015 to 24.3% in 2019, p<0.001, while the use of pellets as a current regimen improved from 29.1% in 2015 to 53.0% in 2019, p<0.001. Over a third (38.0%), of children started on LPV/r syrup at baseline were switched to LPVr pellets. Overall viral load suppression (VLS) was 64.6%; VLS among those on syrup was higher at 65.6% compared to those on pellets 50.94% p=0.032.

Conclusions: There has been moderate scale-up of LPVr pellets use among children. However, younger children < 3 years have sub-optimal VLS regardless of LPV/r pellets or syrup use. Findings call for use of optimal regimens and strengthening key interventions and strategies such as enhanced adherence counseling and psychosocial support for caregivers to improve VLS in younger childrenwhich are easier to administer and more palatable for this age group.

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Intensified technical assistance on multi-month dispensing of antiretroviral therapy to children and adolescents living with HIV resulted in achievement of the 85% PEPFAR benchmark in Nigeria

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Background: The PEPFAR/USAID-funded Strengthening Integrated Delivery of HIV/AIDS Services Project supports initiation of, adherence to, and retention on antiretroviral treatment (ART) among people living with HIV in Akwa Ibom and Cross Rivers states in Nigeria. To provide more client-centered care, the project decentralized ART refills and implemented multi-month dispensing (MMD) to improve access, reduce the frequency of ART drug pick-up, and improve clinical outcomes, particularly among children and adolescents living with HIV (C&ALHIV) ages 18 and younger. By December 2019, 23% of the C&ALHIV currently on treatment were receiving three or more months of ART per refill through MMD. Following the onset of the COVID-19 pandemic, in March 2020, the government expanded the MMD eligibility criteria to include all ART clients and recommended fast-tracking MMD to minimize client visits to health facilities.

Materials and Methods: Technical assistance was provided using a data-driven approach that included weekly data analysis and review, site prioritization, mentoring health care providers, line listing C&ALHIV eligible to receive MMD, rolling out the pediatric regimen calculator, providing optimized pediatric regimens, and enrolling C&ALHIV into community ART distribution models. We present progress in MMD implementation at baseline (December 2019) and endline (December 2020) from 36 high-volume facilities.

Results: The proportion of C&ALHIV receiving MMD increased from 23% (620/2,647) at baseline to 86% (3,799/4,423) at endline, thereby exceeding the PEPFAR global benchmark of 85%. As of December 2020, 50% of the C&ALHIV were receiving 3–5-MMD, while 36% were on 6-MMD due to stock limitations. In December 2019, 17% to 28% of the C&ALHIV in each age group were receiving MMD. In December 2020, MMD had reached 99% among adolescents (ages 15–18 years), 94% among those ages 10–14 years, 75% in ages 5–9 years, and 65% in ages 2–4 years. When comparing baseline to endline, the proportion of sites reporting less than 85% of C&ALHIV on MMD reduced from 100% to 30%, and the proportion of C&ALHIV on an optimized pediatric regimen increased from 58% to 79% following phaseout of non-optimized pediatric antiretroviral (ARV) medications. By December 2020, 89% of C&ALHIV enrolled in community ART groups (CAGs) were on MMD.

Conclusions: MMD is feasible among C&ALHIV. Several factors contributed to the positive results in Nigeria. Expansion of the eligibility criteria during COVID-19 facilitated MMD rollout. The technical assistance provided, contributed to the increase in the percentage of C&ALHIV on MMD. Line listing C&ALHIV for MMD was key to identifying the eligible C&ALHIV and tracking progress. Regular stock monitoring and the availability of pediatric ART regimens facilitated the transition to MMD. Finally, CAGs represented the ideal platform for MMD rollout. Going forward, efforts should focus on addressing the low uptake of 6-MMD related to stock limitations, as well as synchronizing ARV refill pick-up and sample collection for viral load testing.

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"I now always go out to play": Evaluating the impact of the New Horizons Initiative for third-line HIV treatment for pediatric patients in Kenya, Uganda and Zambia.

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Paediatric antiretroviral treatment (ART) failure has adverse consequences for children and adolescents living with HIV and remains a challenge with more cases reported in Africa than other regions worldwide. Established in 2014, The New Horizons Advancing Pediatric HIV Care Collaborative (NHC) programme involves the donation of PREZISTA® (darunavir) and/or INTELENCE® (etravirine) to eligible national HIV programmes in African countries, and building the capacity of healthcare workers to identify and manage children, adolescents and young people failing anti-retroviral therapy.
This qualitative study is an evaluation of the processes and impact of the NHC programme in Kenya, Uganda and Zambia. The purpose of the study was to evaluate the programme in order to assess its value to beneficiaries and other stakeholders; and to inform programme changes and decisions about its future.

Material and Methods: Interviews were conducted with programme partners and representatives from the Ministry of Health in all three countries, including those responsible for HIV directorates and pediatric HIV care.
Six study sites were selected to include a mix of urban and rural areas, and both privately funded clinics and public hospitals. Healthcare workers and patients from these sites were identified and approached to participate in the study.
Individual interviews were conducted with 22 caregivers of children receiving medicines from the programme, and with 10 adolescent patients to understand first-hand the impact on their lives. Six focus group discussions were conducted with a total of 38 healthcare workers, to understand their experiences.
Data was analysed thematically to investigate the effectiveness, relevance, efficiency and sustainability of the programme.
Study limitations included some adjustments to the data collection methods due to the Covid-19 pandemic, the small sample size and the self-reported nature of the data.

Results: The evaluation found that the programme had a positive impact on the lives of patients and families in a range of areas, including improved health outcomes, better mental health and addressing stigma.
It also had several benefits for health systems, including building capacity and allowing for the collection of useful data on third-line pediatric treatment. The programme also had an impact on third-line guidelines and multidisciplinary committees for pediatrics. Healthcare workers rated the training content and tools highly, and reported improved confidence in their ability to identify and manage patients failing on previous regimens.
A number of programme challenges were identified; including relationships with governments, shortages of medicines in-country, complex treatment formulations, and the high cost and time of drug-resistance testing, currently a requirement prior to switching patients to third-line treatment.
The study concluded that the programme had been highly effective in bringing third-line treatment to patients failing on other regimens. It was recognised as being relevant, timely and life-saving by patients, healthcare workers and Ministries of Health.
All evaluation participants believed that the programme should be continued and expanded. Its efficiency could be improved through expanding training, addressing supply chain issues, and improving record-keeping and relationships with government partners.
The programme's sustainability depends on its expansion, and addressing some of the issues raised in the evaluation.

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Efficacy, Safety and Tolerability of Guideline-Recommended ARVs from Pediatric Clinical Trials: A Systematic Review

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Background: Pediatric guidelines now recommend INSTIs as the preferred core agent (CA) class in pediatric ART.

To our knowledge there are no comprehensive reviews summarizing treatment outcomes from trials in children living with HIV (CLHIV). We conducted this systematic literature review (SLR) to provide an overview of clinical trial (CT) evidence for guideline-recommended ARTs in CLHIV.

Methods: Searches conducted on 30.06.2020 using Embase, Medline and Medline In-Process, the Cochrane Library and key pediatric conferences. We identified CTs of guideline-recommended ARVs (preferred and alternative) in CLHIV aged ≥4 weeks to ≤18 years, in treatment-naive (TN) and treatment-experienced (TE) populations published from 2010. Outcomes of interest included efficacy, safety and tolerability. PRISMA guidelines were followed. Qualitative synthesis was undertaken (no statistical analyses conducted).

Results: The searches identified 4,609 records. Fifty-five publications from 31 CTs met the inclusion criteria. Herein 'n' refers to number of studies.

Included studies were single-arm (n=15; 48%), 12 randomized (39%) and 4 non-randomized (13%). Thirteen studies enrolled >100 CLHIV. Participants were recruited multinationally (n=21), in South Africa (n=3), Thailand (n=3), Uganda (n=1), Kenya (n=1), and country not reported (NR; n=2).

Baseline treatment status: TN: n=11, TE: n=10 (stable switch: n=7; virologically failing therapy: n=3), TN+TE: n=9 (TE population: stable switch: n=3; virologically failing therapy: n=3, NR: n=3).

Baseline characteristics (ranges): median age: 3.8 months-16 years; female: 25–78%; median weight: 4.3–52.2 kg; mean CD4%: 11.7–40.4%; median viral load (VL): 2.08–5.9 log10 c/mL.

Treatments included 3-drug regimens. CAs studied: PIs (n=10, 32%), NNRTIs (n=6, 19%), INSTIs (n=7, 23%), PIs/NNRTIs (n=8, 26%).

Viral suppression rates (VSR) varied (w24: 47–100%; w48: 27–98%) depending on timepoints, thresholds and outcome definitions. The highest VSR were reported in studies recruiting TN or TE CLHIV with baseline viral suppression. Within this group, high VSR were observed at w24 regardless of CA.

At w48, trials of INSTI- and DRV/r-based regimens were associated with higher VSR (≥90%) than LPV/r (67–73%) and RPV (72%). In TE CLHIV non-suppressed at baseline, INSTI-based regimens reported higher VSRs than PIs or NNRTIs (w24 [w48]: DTG: NR [61–74%], RAL: 54–66% [74%], ETV: 52–57% [53–70%], ATV/r: 47–65% [43–60%]).

All-cause discontinuation (ACD) rates were generally lower in CLHIV receiving INSTIs (0–26%) vs. other CA (0–50%) in overall populations. ACD rates were observed to be higher in CLHIV receiving RAL (w48: 12.5%) vs. other INSTIs (w32: DTG = 3.3%; w48: BIC = 0% and EVG/c = 0%) and were more frequent among teenagers/young adults.

SAE rates were lower for INSTI-based regimens (5–14.6%) vs. other CA (0–33%).

Studies of unboosted-INSTIs (DTG, BIC, RAL) and DRV/r reported 0% discontinuations due to AE (DcAE) at w48. Higher rates of DcAEs were reported in studies of other CAs: boosted INIs – EVG/c: 4%; PIs – LPV/r: 0.8–7.1%; ATV/r: 7.0%; NNRTIs – RPV: 3%; ETV: 7.9%.

Conclusions: These findings support INSTI-based regimens as preferred in pediatric guidelines. Due to heterogeneity between trials, cross-study comparisons should be undertaken only with caution, considering potential bias influencing study results.

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MMD in children: Game-changer at no cost

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Background: To reach the 95-95-95 goals, differentiated approach to care is necessary. Differentiated service deliveries (DSD) is an approach with a client-centered focus to adapt HIV services to adequately meet the needs of people living with HIV, reduce the number of visits to the health facilities and also reducing the workload of health providers. Multi-month prescription (MMP) and dispensation (MMD) in stable HIV patients is one of the most succesful DSD models. Nevertheless, progress to apply this DSD on children has been slower than in adults, rendering challenges in being able to space consultations. According to UNICEF, the COVID-19 pandemic has significantly affected children in terms of paediatric ARV coverage and viral load testing and it has also affected the supply chain of ARV drugs and other supplies, and the redeployment of health providers. WHO⁄UNICEF encourages the use of MMD in children to mitigate HIV treatment disruptions.

Materials and methods: In 2020, Paediatric-Adolescent Treatment Africa (PATA), a network of frontline health providers, conducted cross-sectional surveys with 243 health providers from 15 sub-Saharan African countries in Southern, Eastern, Western and Central Africa to assess the implementation of MMD for infants and children and to evaluate the impact of the COVID-19 pandemic in the implementation of MMD. Data were analyzed using descriptive statistics to describe central tendencies.

Results: Most (88%) health facilities were located in urban or peri-urban areas. Almost all (99%) of the health providers surveyed were familiar with the implementation of MMD in children. The eligibility criteria to enroll children in DSD varied across geographical region. A total of 44% of health providers reported eligibility criteria to enroll according to the WHO guidelines. However, 22% indicated that infants and younger children are not eligibile without clarifying the age of eligibility, and a further 12% responded that all children on DTG or EFV-containing regimen are eligible, but those that are on LPV are not. Detailed analysis of the challenges to implement MMD in children revealed that regimen changes were the biggest issue in enrolling children in this model, followed by inability to assess stability due to delayed viral load turnaroud or the unavailability of viral load testing, drug stock outs or shortages, and lastly, the lack of SOPs to determine eligibility to enrollment.

Conclusions: Although transition from monthly to multi-month dispensing of ART in children have good health outcomes, important constraints related to drug stock-outs and lack of viral load testing to determine eligibility continue to be obstacles to the implement this model. At health facility level, health providers need to be trained to determine eligility in line with WHO guidelines for MMD to increase the number of infants and children to be enrolled.

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Optimizing index testing of biological children of parents and siblings of children in care: Lesson learned from the ELMA project in Cote d'Ivoire

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Background: in Cote d'Ivoire through December 2019, only 47% of children and adolescents living with HIV (CALHIV) have been diagnosed, with 36% of CALHIV initiated on ART. To improve progress toward 95-95-95 for children and adolescents, EGPAF and the Cote d'Ivoire National AIDS Control Program provided support to three pilot sites to optimize index testing of biological contacts aged 0-19 years.

Methods: Three high-volume sites with low rate of HIV diagnosis in children (from 47% to 67%) were selected in Abidjan. We established a listing of all biological contacts aged 0-19 years with unknown HIV status from active adult female on ART, children and adolescents on ART and deceased clients. Lay counselors performed HIV testing of contacts/siblings with unknown HIV status in health facilities or in communities. Data were aggregated and analyzed to describe the cascade of index testing of biological contacts of targeted population.

Results: A total of 3,961 files were screened from 3,482 active adult female clients, 197 deceased clients and 282 active children/ adolescents. Of clients, 3,860 children and adolescents contacts were elicited with 3505 (91%) from active adult female clients, 252 (6%) from active children/adolescents and 103 (3%) from deceased. Of those, 1,271 (33%) had unknown HIV status which was distributed respectively as 32%, 50% and 20% in each type of index. 85% (1076/1271) were tested with low rate 43% among line listing of deceased: 70% (758/1076) were tested in community settings; three (0.3%) identified HIV-positive (all line listing of active adult female clients) including one in each of the following aged groups: 5-9, 10-14 and 15-19. All HIV-positive clients were linked to ART. Of the 1271, 195 were not tested for the following reasons: 23 refusals, 71 non-residents in Abidjan, 23 residents outside the country, 20 promised to come with children but never showed, 18 unreachable.

Conclusions: Active monitoring of the testing of biological contacts/siblings (children and adolescents) is important to avoid missed opportunities. Apply strategy to deceased clients is not useful but relevant to age group 15-19 where positive clients were identified

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Reaching undiagnosed children living with HIV through index testing in Homa Bay, Kenya

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Background: Gaps in knowledge of HIV status among children living with HIV (CLHIV) results in delayed initiation of life-saving treatment and poor health outcomes. Identification of CLHIV through index testing of biological children or siblings of ART clients can increase pediatric case finding. We assessed outcomes of pediatric index testing in Homa Bay County, Kenya.

Methods: We conducted a cross-sectional analysis of routinely collected index testing data in eight high volume health facilities in seven sub-counties. Data were abstracted from standardized registers for ART clients (index clients) enrolled in care in March–June 2020, or who died in 2018–2020, and had biological contacts aged <15 years. Additionally, a random sample of 50 records each (25 from antenatal/postnatal clinic and 25 from HIV clinic) from 5 facilities (250 total) were reviewed to assess the number of index clients who underwent contact line-listing. Variables included cascade outcomes (contacts line-listed, reached, tested) and index/contact characteristics: age, sex, testing entry point, index type (child, sibling), and index time since ART initiation. Data were summarized and logistic regression was used to determine factors associated with cascade outcomes.

Results: In total, 632 index clients (median age: 33 years) were included; 87% were female. Overall, 1,390 contacts were line-listed (median age: 9 years); 51% were female. Overall, 87% (1,205) of line-listed contacts were reached, 77% (928/1,205) were eligible for testing, 99.7% (925/928) were tested and 0.9% (8/925) had an HIV-positive result; all were linked to treatment. Of the 250 index client records abstracted to assess line-listing coverage, 95% were female and median age was 32 years; 69% (173/250) had no documented line-listing. After adjusting for clustering and controlling for other factors, none of the index characteristics assessed were significantly associated with having completed line listing, or having contacts reached or tested.

Conclusions: To optimize index testing strategies for children, line listing of all ART clients should be standardized in practice and a multi-pronged approach used to ensure all children of unknown status are identified and tested. COVID-19 restrictions prevented community-based HIV testing during this period, which may help to explain why 13% of the children line-listed were not reached for testing.

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Impact of a brief community health worker-administered index case testing screening tool on pediatric HIV case identification: early results from Malawi

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Background: Remarkable progress has been made in improving access to ART in Malawi with nearly 100% of pregnant/lactating women living with HIV (WLHIV) in Malawi receiving treatment, however, only 68% of children living with HIV (CLHIV) are receiving ART. This treatment gap between mothers and children signifies a critical missed opportunity to identify CLHIV and link them to care. Index Case Testing (ICT) is a WHO-endorsed model for identifying CLHIV. A contributor to suboptimal ICT implementation is the lack of methods to systematically track HIV status of children of WLHIV. We evaluated the impact of a brief, community health worker-administered screening tool on WLHIV screened for ICT, pediatric HIV testing, and CLHIV identified.

Methods: The brief (<5 minutes) ICT screening tool assesses HIV testing status of children of WLHIV at ART clinic visits. Data captured includes number of children 0-19 years, children's names, ages, and HIV status. Completed tools are attached to mother's ART record for review at subsequent visits. WLHIV attending clinics in 118 health facilities in Malawi were screened from 1 October to 31 December 2020. De-identified program data from ICT registers were used to determine WLHIV screened, children tested, and CLHIV identified. Results were compared to pediatric testing and case identification over the same period in 2019. A single sample t-test was used to test differences in mean number of women screened. Paired t-tests were used to test differences in mean number of children tested and CLHIV identified.

Results: The number of women screened, children tested, and CLHIV identified increased in the period of ICT tool implementation. Total women screened increased 49% from 12,350 in 2019 to 18,342 in 2020, total pediatric clients tested increased 63% from 2,500 in 2019 to 4,075 in 2020, and the total number of pediatric clients tested HIV-positive increased 58% from 78 to 123 clients. Testing yield declined from 3.1% to 3.0%. Mean number of WLHIV screened weekly was rose from 50 (2019) to 1411 (2020) (p-value=0.042). Mean number of children tested weekly was 319 in 2020 compared to 192 in 2019 (p-value=0.018). In 2020, mean number CLHIV identified weekly was ten compared to six in 2019 (p-value=0.059). In both periods, ~3% of children tested HIV-positive.

Conclusions: Systematic documentation of children's ICT status using a brief ICT screening tool is a useful approach to identify untested children of WLHIV. Further examination of characteristics of WLHIV with untested children may inform programmatic interventions to identify more CLHIV.

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An Evaluation of Family Index Testing amongst Biological Children of People Living with HIV in Nigeria

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Background: HIV case-finding among children is a significant challenge in Nigeria. Of the estimated 150, 000 children aged 0 – 14 years and 110, 000 adolescents aged 10 -19 years living with HIV in Nigeria, only 36% and 40% respectively are on treatment.
PEPFAR recommends family index testing (FIT) as a targeted strategy for improving case finding in children. FIT entails HIV testing for all biological children of people living with HIV (PLHIV).
The Pediatric Program at the Institute of Human Virology Nigeria (IHVN) conducted a program evaluation to determine the proportion of biological children of PLHIV in its network of health facilities that were not yet tested for HIV.

Methods: The evaluation was conducted between September and October 2020 at eight randomly-selected high-burden sites across four states-Rivers, Federal Capital Territory, Nasarawa, and Katsina. A sample of adult PLHIV ≥ 18 years old with living biological children aged 0 – 19 years were randomly selected per site. Sample sizes were proportionally determined based on the number of adults enrolled on ART at each site. The PLHIV were interviewed via phone calls; those with at least one untested child were invited to either bring their child(ren) to the facility for HIV testing, or given the option of home-based testing by a healthcare worker. Children under 18 months old were referred for DNA PCR testing if their rapid test was positive.

Results: In total, 803 eligible adult PLHIV were interviewed (67% female). Of the 1, 732 children and adolescents elicited, 63% (1,083) had a known HIV status, with 6% (67) identified as "known HIV-positive".
Age at HIV diagnosis could be remembered for only 82% (55/67) of known positives, and indicated that 62%, 27%, 9% and 2% of these children were diagnosed at 0 – 4, 5 – 9, 10 -14, 15 – 19 years of age, respectively.
Ninety-two percent (597/649) of children with unknown HIV status were eventually tested, with a yield of 1.7% (10/597) HIV-positive.
Of children newly-identified positive, 30% , 0%, 30% and 40% were identified from the 0 -4, 5- 9, 10 -14 and 15 – 19 year age bands, respectively.

Conclusion: Significant progress has been made in scaling up FIT in Nigeria, however, a third of the biological children of adult PLHIV in our evaluation had unknown HIV status. Intensified and further coordinated efforts across Adult, PMTCT, Vulnerable Children and other community-based programs are needed to reach and test eligible children at both facility and community-level. Children in all age bands should remain prioritized for FIT.

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High incidence of severe Respiratory Syncytial Virus' infection among HIV-exposed uninfected infants

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Introduction: Respiratory syncytial virus (RSV) is the most common cause of respiratory viral infections in children worldwide. The risk factors for severe RSV infections are young age, premature birth, underlying cardiac and pulmonary pathologies and immunodeficiency. Children who are HIV exposed and uninfected (CHEU) are known as susceptible to infections in early life. The burden of RSV in this population has been demonstrated in developing countries but poorly studied in high-income countries. The aim of our study is to evaluate the excess risk of hospitalizations linked to RSV in CHEU born in Belgium.

Methods: Between December 2010 and November 2013, 130 HIV-infected and 120 uninfected pregnant women were recruited at Saint-Pierre Hospital, Brussels. Their children were followed up until the age of 1 year, with record of all hospitalizations. Levels of RSV antibodies were measured at 6 months of age to define the rate of RSV infection.

Results: During the study period, 46 hospitalizations for infections including 11 for RSV infections occurred in 37 infants. All hospitalizations occurred before the age of 6 months. Despite similar rate of RSV seroconversion at 6 months of life, the RSV hospitalizations' incidence was 8.7 times higher in CHEU compared to children who are HIV unexposed (CHU) (IR= 7.9 per 100 person-years in CHEU vs 0.9 per 100 person-years in CHU). Risks factors significantly associated with hospitalization for RSV infection in CHEU were initiation of maternal ART during pregnancy (adjusted odds ratio [OR] = 5.9; 95% CI 1.3-25,0) and having one or more sibling living in the same household (OR= 10.1 95% CI 1,0-98,9).

Conclusion: Our study demonstrates that despite similar exposure to RSV, CHEU born in a high-income country show excess hospitalization risk of hospitalization for RSV infection. Because of their vulnerability to severe RSV infection among others infections, CHEU should be closely followed up and may be future target for preventative measures including immunization against RSV.

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Advanced HIV disease among pregnant women at antenatal care enrolment in Southern Mozambique

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Introduction: Advanced HIV Disease (AHD) at antenatal care (ANC) enrolment is a critical precursor to poor pregnancy and perinatal outcomes. We sought to assess the proportion of women attending the ANC in an advanced stage of HIV infection, how long immune-suppressive changes persisted and the impact of HAD on pregnancy and perinatal outcomes in rural Southern Mozambique.

Methods: This was an observational cohort study including a total of 2458 pregnant women living with HIV which had their first ANC visit at the Manhiça District Hospital between 2015 and 2020. We analysed data of 36 months follow-up for the women and of one month for their born children. AHD was defined as CD4 cell count <200 cells/µl or WHO clinical stage III-IV at ANC enrolment. A difference in CD4 count of 25 cells/µl between two measurements performed at an interval of about 6 months was considered clinically significant. Logistic regression was performed to evaluate variables associated with CD4 count decrease 6 months after ANC enrolment.

Results: Over the 5-years study period, 14.2% pregnant women presented with AHD at ANC enrolment, 2% being severely immunosuppressed (CD4<50cells/mm3). The proportion of AHD increased with age, reaching 52% in women between 25 and 35 years old and decreased after 35 years of age (p<0.001). Tuberculosis was the only opportunistic disease detected in women with AHD. Seventy-six percent (75%) of AHD were on antiretroviral treatment (ART) before ANC enrolment. Following national guideline, all HIV pregnant women with no art ART at the ANC enrolment initiated treatment during pregnancy. The majority of the women were still on ART at delivery (97%) and at one month child age (99%). Six months after ANC enrolment coinciding with the delivery or immediate postpartum period, 13.4% of women had a decreased CD4 count, 43.5% had no change in CD4 counts and 43.1% had improved CD4 count. Mean CD4 count decrease was -113.5 cells/µl (95%CI: -185.0;-41.9) and -339.9 cells/µl (95%CI: -516.5; -163.3) in women with HAD and without HAD, respectively. Independent risk factors for CD4 counts decrease were age group 20-24 years (OR=2.19, 95%CI= 1.13-4.28; P=0.021) and WHO stage IV (OR=9.76, 95%CI= 2.94-32.43; P<0.001) at ANC enrolment. No significant differences were observed between HAD and no HAD women regarding the frequency of prematurity (p=0.187), child birth weight (P=0.079), child birth defect (P=0.265) and child HIV status at one month age (P =0.139).

Conclusion: There are still a considerable number of women with advanced HIV disease at ANC enrolment. Earlier HIV diagnosis targeting childbearing women, prompt linkage to HIV care and close monitoring after ART initiation are all strategies urgently needed in this vulnerable group of the population. Since, when ART are available, the effects of advanced HIV disease on pregnancy and immediate perinatal outcomes are attenuated.

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Missed opportunities for prevention of vertical HIV transmission and early infant antiretroviral treatment in Eswatini

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Background: While progress has been made in reducing transmission of HIV from mother to child, these gains have fallen short of global targets. Further, only half of HIV-exposed infants globally are tested for HIV by 8 weeks of age, and fewer than half of children living with HIV <5 years of age are receiving antiretroviral therapy (ART) in a majority of UNAIDS priority countries. To assess potential gaps in maternal and infant HIV services in the Kingdom of Eswatini, we reviewed routinely-collected data for all infants diagnosed with HIV, and their mothers, during an 11-month period in 2016.

Materials and Methods: Data were compiled under a Ministry of Health-led pilot of an HIV case surveillance system, supported by ICAP at Columbia University with funding from the US Centers for Disease Control and Prevention. For all infants testing HIV-positive by DNA PCR throughout Eswatini during February-December 2016, initial case data was exported from the national laboratory information system into a surveillance database. Additional data on HIV services and outcomes were abstracted from facility-based health records through August 2017.

Results: A total of 275 infants were diagnosed with HIV during the period. Roughly half of mothers (140, 51%) were diagnosed with HIV before delivery, 49 (18%) after delivery, and 86 (31%) had missing information on timing of HIV diagnosis. A total of 172 (63%) mothers were documented as having initiated ART; 123 (72%) had information on date of initiation available, with initiation occurring a median of 59 days before delivery (IQR: 206 days before-127 days after). Among these 123 women, 28 (23%) initiated ART before pregnancy; 24 (20%) in the first or second trimester; 23 (19%) in the third trimester; 38 (31%) during the first year after delivery; and 10 (8%) more than 1-year after delivery. The median time of infant HIV diagnosis was 65 days after delivery; 152 (55%) infants were diagnosed by 12 weeks and r 84 (31%) by 12 months. Among the 185 (67%) infants documented to have initiated ART, 179 (97%) had information on date of ART initiation; 10 (6%) initiated ART within 2 weeks of their first HIV-positive test, 48 (27%) between 14-30 days after testing, 65 (36%) between 31-60 days, 22 (12%) between 61-90 days, 27 (15%) between 91 days-6 months, and 7 (4%) >6 months after testing. By the end of the data abstraction period, 22 (8%) infants had died; among the subset of infants who initiated ART, 162 (88%) were active on treatment, 13 (7%) were lost to follow-up, and 9 (5%) had died.

Conclusions: Our findings highlight historical gaps in ART coverage and suggest a high frequency of later-than-optimal initiation of ART among pregnant and postpartum women, as well as among infants diagnosed with HIV. In addition, the data suggest transmission during breastfeeding, reflecting a critical role for pre-exposure prophylaxis services. These results also reflect key data gaps in routine health services that must be filled to better understand and address vertical transmission risks and early infant HIV diagnosis and treatment.

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The impact of a couple-based intervention on one-year viral suppression among HIV-infected pregnant women and their male partners in Malawi: A Randomized Controlled Trial

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Background: Couple-based approaches have an impact on infant outcomes, and may also improve HIV treatment outcomes for HIV-infected pregnant women and their male partners. This hypothesis requires testing in a clinical trial with long-term outcomes.

Methods: A randomized controlled trial was conducted among 500 HIV-infected pregnant women (indexes) and their male sexual partners (partners) attending antenatal care at Bwaila District Hospital in Lilongwe, Malawi from 2017-2019. Indexes were randomized 1:1 to either the standard of care (SOC) or a couple-based behavioral intervention (BI) and followed for one year. The BI offered 1) provider-assisted partner notification; 2) enhanced couple counseling and testing at baseline and six months; and 3) an option for male partner ART pick-up. Index viral suppression (<1000 copies/ml), partner testing, and partner viral suppression were ascertained one year after index enrollment. Risk differences (RD) and 95% confidence intervals (CIs) comparing the BI and SOC arms were calculated using intention-to-treat and complete case analysis. Post-hoc analyses of female viral suppression explored modification by marital/cohabitation status and recent history of intimate partner violence (IPV).

Results: Nearly all indexes were married or cohabiting (93.3%) and reported no recent physical IPV (91.8%). Eighty-one percent had a final study visit and 90.6% provided a one-year viral load measure. Among indexes, viral suppression was 81.5% in the SOC arm and 88.0% in the BI arm. A trend towards greater index viral suppression in the BI arm was observed in intention-to-treat (RD: 6.8, CI: -1.7, 15.3, p=0.1) and complete case analysis (RD 6.6, CI: -0.8, 14.0, p=0.08) (Table 1). A positive intervention effect was observed among indexes who were married/cohabiting (RD: 8.1%, CI: 0.2, 16.0, p=0.05), but not among those who were not (RD: -4.7%, CI: -25.9, 16.4, p=0.7) and among indexes without recent IPV (RD: 7.7%, CI: 0.0, 15.4), but not among those with recent IPV (RD: -9.6%, CI: -41.6, 22.3).

Male partner HIV testing was higher in the BI arm (72.2%) than the SOC arm (57.1%) (RD: 15.1%, CI: 4.7%, 25.5%, p=0.01). Among HIV-infected male partners, there was a trend towards greater one-year viral suppression among men in the BI arm (73.6%) than among men in the SOC arm (58.5%) (RD: 15.1%, -1.6%, 31.8%, p=0.08).

Conclusions: Couple-based approaches enhance viral suppression among married/cohabiting pregnant women without IPV. These approaches also increase male partner testing and may enhance viral suppression among male partners. In certain antenatal subgroups, couple-based approaches could have important impacts on maternal, male partner, and ultimately infant outcomes.

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Transitioning integrated antenatal PrEP delivery from research projects to routine clinic staff at 16 clinics in Western Kenya

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Background: The World Health Organization (WHO) recommends pre-exposure prophylaxis (PrEP) for pregnant and postpartum women at high risk for HIV acquisition. PrEP studies among Kenyan pregnant and postpartum women have found high PrEP acceptance within routine maternal and child health (MCH) settings. Transitioning demonstration projects from dedicated research teams to routine clinic staff not employed by studies is a common challenge in scale up and sustainability.

Methods: Following a cluster randomized trial (NCT03070600) comparing approaches for PrEP delivery to pregnant and postpartum women, we documented the active transition process from research teams to routine clinic staff. We utilized the WHO Health Systems Building Blocks Framework to actively transition care and qualitatively summarized the process through debrief checklists and matrices with study staff.

Results: At 16 health facilities in Western Kenya that transitioned from research to routine clinic team delivery of antenatal PrEP in 2020-2021, all 16 successfully continued PrEP delivery for pregnant and postpartum women. The unique contexts at each clinic influenced heterogeneous solutions to how PrEP was successfully continued; at 6, PrEP delivery shifted to HIV care clinics, while at 10 PrEP remained integrated within MCH clinics.

At all facilities, active transfer of medical commodities and tracking systems (PrEP medication, HIV testing kits, health records and registers) and transition of MCH PrEP users from research to routine health staff providers were successful with few noted challenges. Some facilities actively introduced MCH clients to HIV care clinics while others made a passive referral. Processes for ordering PrEP commodities were heterogeneous across facilities through existing procurement mechanisms, but were not impacted by departing study staff.

Challenges arose around how existing health workforce absorbed new PrEP provision duties, adding to already overloaded responsibility lists. Many facilities identified a new PrEP point person to be mentored by departing research staff, typically the nurse in charge of preventing mother-to-child transmission of HIV. At facilities with donor-supported HIV implementing partners (N=11), implementing partner staff generally assumed PrEP delivery roles.

Conclusions: Transitioning PrEP delivery from research to routine clinic teams was successful and yielded heterogeneous solutions to match local context. Health workforce burden remains a challenge.

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Health systems-level barriers and strategies for improved PrEP delivery for pregnant and postpartum women in Western Kenya

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Background: Pre-exposure prophylaxis (PrEP) is recommended for pregnant and postpartum women at high risk of HIV acquisition within maternal child health (MCH) systems. Identifying health system barriers to PrEP delivery and strategies to overcome barriers could optimize PrEP delivery within MCH systems.

Methods: We recruited health care workers (HCW) with experience delivering PrEP within MCH clinics in two large-scale projects in western Kenya (>25,000 MCH clients offered PrEP at 36 sites). Two surveys (a self-administered and a phone survey) were used to assess barriers to PrEP delivery (using a 5 point Likert scale ranging from 1 – no impact to 5 – very strong impact, summarized with mean scores) and strategies to overcome barriers, based on previous qualitative work grounded in the Consolidated Framework for Implementation Research.

Results: Among 171 HCW recruited, 146 completed the electronic survey and 126 the phone survey. Most (55%) were nurses, female (64%), had PrEP training specific to MCH (73%), and 2.4 years (IQR: 1.5, 3.3) providing PrEP.

The strongest reported barriers to PrEP delivery were insufficient number of providers (3.1) and inadequate training among MCH and HIV testing providers (3.0 and 2.8); insufficient physical PrEP services space (3.0); increased volume of patients (2.8); documentation burden (2.7); perceived uncooperative clients (2.6); and time needed to provide care (2.5). Less impactful barriers included stockouts of PrEP drugs (2.2) and documents (1.9); increased HIV testing (2.3); multiple implementing partners with competing priorities (2.1); and clients with challenges in language (2.0).

Strategies most frequently reported to have been tried and improved delivery included dispensing PrEP in MCH (79%); fast-tracking PrEP clients at MCH (76%), pharmacy (64%), or lab (58%); delivering PrEP education in waiting bays (72%) or other locations (51%); providing communication aids (63%); dedicating space for PrEP (52%); and task-shifting PrEP counseling (60%) and risk assessment (54%) from nurses to HIV testing services providers.

Conclusions: Common barriers to service provision—including client-to-provider ratios, space, and documentation—hinder PrEP delivery. Strategies for co-location, fast-tracking, training, and task-shifting are useful for integrating PrEP provision within MCH care.

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Pregnancy and birth outcomes among young women living with perinatally acquired HIV in Thailand and Vietnam

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Background: As children with perinatally acquired HIV in the Asia-Pacific region age into young adulthood, data on reproductive health outcomes become increasingly important, but remain scarce. We conducted a retrospective multi-center cohort study to investigate pregnancy frequency and characteristics, delivery and infant outcomes among young women with perinatally acquired HIV (YWPHIV).

Materials and Methods: The analysis included YWPHIV aged 15 to <24 years in follow-up for HIV treatment and care at any time between January 2013 and December 2018 at participating TREAT Asia Pediatric HIV Observational Database (TApHOD) sites in Thailand (4 sites) and Vietnam (2 sites). The incidence rate of pregnancy was calculated using all YWPHIV aged 15 to <24 years in follow-up between 2013 to 2018 as the denominator population at risk. Characteristics at pregnancy and birth outcomes were described.

Results: Among 670 YWPHIV, median age was 15.0 years (interquartile range [IQR] 15-17.1) and median follow-up during the study period was 2.69 years (IQR 1.09-5.11). There were 52 (7.8%) pregnancies among 52 YWPHIV after 2089 total person-years, for an incidence of 2.49 (1.90-3.27) per 100 person-years; 41 (79%) occurred between 15-19 years of age and three of 50(6.0%) reported were second pregnancies. Before pregnancy, all these 52 YWPHIV were on cART for a median time of 9.8 years (IQR 7.3-12.4). Fourteen out of 44 (32%) ever experienced CDC category C events. During pregnancy, the median CD4 cell count was 521 cells/ul (IQR 213-760), and 9.1% (4/44) had CD4 cell counts less than 200 cells/ul; 24% (9/38) had HIV RNA >400 copies/ml; 9.8% (4/41) had mild to moderate anemia (hemoglobin 7 to <11mg/dL) and 75% (39/52) were on cART for at least 3 months, including 19 NNRTI-based regimens, 18 PI-based regimens, and 2 other regimens (none with integrase inhibitors). Of 51 pregnancies with available outcomes, 46 (90%) resulted in live singleton births and 5 (9.8%) in abortions. Of infants with available data, 29% (12/42) were reported to be low birth weight (<2,500gm), 3.9% (1/26) had birth asphyxia, and none (0/41) were breastfed. One infant (1/33, 3.0%) was diagnosed with HIV infection.

Conclusions: Among the YWPHIV in our cohort, 8% became pregnant and almost all went to delivery, but low birth weight was common. Most pregnancies occurred in late adolescence, which raises concerns about the long-term social stability of the mother-infant pair. Efforts to strengthen reproductive health education, including contraception and prevention of mother-to-child HIV transmission interventions, are needed for adolescents with perinatally acquired HIV as they transition to young adults.

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Vaginal microbiota, genital inflammation and extracellular matrix remodelling collagenase: MMP-9 in pregnant women with HIV, a potential mechanism for excess preterm birth?

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Background: Pregnant women living with HIV infection (PWLWH) have elevated rates of preterm birth (PTB) in which HIV and cART are implicated. PWLWH also have a high prevalence of adverse vaginal microbiota, which associate with genital tract inflammation. The mechanism underlying PTB in PWLWH has yet to be elucidated. Here we present the first data on genital tract extracellular matrix modifying endopeptidase: matrix metalloproteinase-9 (MMP-9), an important collagenase in the labour cascade, and how it correlates with local inflammation and vaginal bacteria composition in PWLWH.

Material and Methods: Cervical vaginal fluid (CVF) and high vaginal swabs (HVS) were obtained from pregnant women with and without HIV at three time points over the second and third trimester from eleven sites in the London PTB Study Network 2013-2017. CVF was collected by a menstrual soft cup. Maternal characteristics, cART exposure, immuno-virologic parameters and pregnancy outcome were recorded. Concentrations of MMP-9 and ten cytokines in CVF were measured using ELISA and chemiluminescent multiplex immunoassays. Vaginal microbiota composition was determined using 16s RNA gene metataxanomic sequencing of HVS. MMP-9 and cytokine concentrations were compared by HIV status, cART exposure (timing and class) and by prematurity with Independent T tests. The relationship between MMP-9 and individual cytokines and relative abundance of bacterial genera was explored with Spearman's correlation in PWLWH. All analyses were performed in SPSS.

Results: CVF was available for 50 PWLWH (107 samples) and 12 HIV uninfected pregnant women (20 samples) between gestation weeks 12-38. Thirty-six PWLWH conceived on cART and fourteen initiated post conception. There were five and one PTB outcomes in pregnant women with and without HIV respectively. PWLWH had a higher mean concentrations of MMP-9 in the second trimester ($p=0.001$) and higher concentrations of IL-1-beta and IL-8 in both second and third trimesters ($p<0.03$) compared with uninfected pregnant women. No statistical differences in MMP-9 in PWLWH were observed by cART timing or class. In PWLWH MMP-9 positively correlated with all measured genital cytokines ($p<0.02$) with the strongest correlations observed for IL-1B ($r=0.78$), IL-6 ($r=0.59$), IL-8 ($r=0.72$) and TNF-alpha ($r=0.59$) $p<0.0001$. Mean abundance of adverse anaerobic pathobionts correlated positively with MMP-9 ($p<0.004$): Atopobium ($r=0.41$), Gardnerella ($r=0.39$), and Prevotella genera ($r=0.32$). Conversely mean proportion of Lactobacillus genera negatively correlated with MMP-9 ($r= -0.50$, $p<0.0001$). There was no difference in MMP-9 by prematurity in this small sample size.

Conclusions: Matrix metalloproteinases are postulated to be induced downstream of the innate response to ascending genital infection and to be key in preparing the reproductive tract for imminent labour: lowering membrane rupture threshold and remodeling the cervix. Here we show strong correlations of MMP-9 to genital inflammation and adverse bacterial genera indicating this pathway warrants further investigation in understanding the mechanisms behind excess PTB risk in PWLWH.

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Early antiretroviral therapy exposure associated risk of developmental disorder by school-aged and adolescent years among HIV-exposed uninfected children from Uganda

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Background: We examine the hypothesis that in-utero/peripartum antiretroviral (IPA) exposure may increase the likelihood of developmental disorders – i.e., attention deficit and hyperactivity disorder (ADHD), autism spectrum disorder (ASD) and functional impairment (FI) among 250 children HIV-exposed uninfected (CHEU) of pregnant women living with HIV compared to 250 children HIV unexposed and uninfected (CHUU) at 6-18 years old.

Methodology: Children and their primary caregivers were enrolled and followed for 12 months. HIV-exposed children's IPA exposure-type was objectively established via medical records and categorized as: no IPA, single-dose nevirapine with/without zidovudine (sdNVP±AZT), sdNVP+AZT+Lamivudine (3TC), or combination ART (cART). Developmental disorders were assessed at months 0, 6 and 12 per caregiver response to standardized questions from the third edition of Behavioral Assessment System for Children (BASC-3). Multivariable linear regression models estimated standardized mean difference (SMD) with 95% confidence intervals (95%CI) according to IPA exposure-type and developmental stage – i.e., pre-adolescent (6–10) vs. adolescent (11–18) years, for IPA exposed CHEU relative to CHUU/CHEU without IPA exposure in Statistical Analysis Software (v.9.4) with adjustment for caregiver socio-demographic and psychosocial factors.

Results: Among CHEU 35, 48, 52 and 109 were respectively exposed to sdnvp+AZT, sdNVP+AZT+3TC, cART and no IPA in peripartum period. ADHD, ASD and FI scores were similar for CHEU with cART exposure (SMD: -0.05 to 0.05 95%CI: -0.37,0.39) whereas sdnvp+AZT+3TC exposure predicted elevated ADHD, ASD probability and FI (SMD:0.27 to 0.34, 95%CI:0.02,1.60) scores at 6-18 year old relative to CHUU/CHEU without IPA exposure. Association between peripartum sdnvp+AZT and developmental disorder scores differed for by pre-adolescents compared to adolescents. On the one hand, sdnvp+AZT was associated with trend of lower ASD (SMD=-0.66, 95%CI:-1.13,0.19) and FI (SMD=-0.58; 95%CI:-1.26,0.09) probability among children 6-10 years old. On the other hand, peripartum sdnvp+AZT was associated with trend of higher ASD (SMD=0.24, 95%CI:-0.09,0.58) and FI (SMD=0.35; 95%CI:-0.05,0.74) probability among adolescents 11–18 years of old.

Conclusion: These data provide reassuring evidence that cART exposure in the peripartum period was not adversely associated with developmental disorder probability scores in late childhood and adolescent years. However, peripartum sdnvp+AZT+3TC predicted moderate elevation in developmental disorder probability and functional limitation at 6 – 18 years of life. Monitoring relative rate of various developmental disorder among ART exposed CHEU is important for clearer understanding of developmental trajectory in this population.

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Risk factors for hospitalization among children who were HIV exposed and uninfected (cHEU) in Montreal, Canada

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Background: While a number of studies have demonstrated increased risk of morbidity and mortality among cHEU in resource-limited settings, the specific causes of this, and the role of underlying socio-economic factors, including access to care, remain unclear. The objective of this study was to determine risk factors for hospitalization among cHEU living in a well-resourced setting with universal health care coverage.

Methods: Longitudinal cohort study linking patient level data from the Centre maternel et infantile sur le SIDA (CMIS) cohort (1988-2015) to provincial (Quebec) administrative data from the Régie de l'assurance maladie du Québec (RAMQ) (1988-2016), a universal provincial health plan that covers all residents in the province of Quebec through a single patient identifier. Kaplan-Meier curves were constructed to determine risk of hospitalization over time, and risk factors for hospitalization determined using Cox proportional hazards models.

Results: Between Jan 1st 1988 and Dec 31st 2015, 847 children were enrolled in the CMIS cohort; 726 were successfully linked to the RAMQ database. Children ranged in age from 1-25 years at the end of the follow-up period (10.4% between 20-25, 46.5% between 10-20, 26.7% between 5-10, and 16.2% between 1-5 years). A total of 647 hospitalizations were captured (excluding birth hospitalization). Cumulative risk of hospitalization was 29.6% within the first year of life (95% CI 27.9-31.3%), 42.5% in the first 5 years (95% CI 40.6-44.3%), and 48.7% within the first 10 years (95% CI 46.7-50.7%). Significant risk factors for hospitalization on multivariate analysis were gestational age <=37 weeks vs >37 weeks (HR 2.60, 95% CI 1.97-3.42), and detectable (VL>500 copies/ml) vs. undetectable maternal viral load at delivery (1.44, 95% 1.03-2.02), after adjusting for maternal age, race, CD4 count at delivery, class of antiretrovirals used during pregnancy, and year of birth.

Conclusions: In this cohort of cHEU from the province of Quebec, significant risk factors for hospitalization included prematurity and detectable maternal viral load at time of delivery. Further work needs to be done to understand risk factors for elevated maternal viral load at the time of delivery, and potential long-term effects on cHEU health.

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Feeding practices and cost of diet of six-month-old HIV-exposed-uninfected compared to HIV-unexposed-uninfected infants in South-West Tshwane, South Africa

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Background: The growing population of HIV-exposed-uninfected (HEU) children are known to be at risk of poor nutritional status and suboptimal growth, with biological risk factors implicated, yet the cost to families of feeding infants is often overlooked. This study compared the infant feeding practices and cost of macronutrient intake of HEU vs HIV-unexposed-uninfected (HUU) 6-months-old infants in a peri-urban community in South Africa.

Methods: This cross-sectional descriptive study formed part of the bigger Siyakhula study, which recruits low-risk pregnant HIV-infected and HIV-uninfected women in the Tshwane District of South Africa for longitudinal follows-up HEU and HUU children for two years. The present study enrolled 101 children who turned 6-months from October 2018 – May 2020 (HEU (n=46); HUU (n=55)). The structured questionnaire based on World Health Organization questionnaires was used to gather breastfeeding data. A single 24-hour recall and FoodFinder™ program version 3 was used for meal analysis. Cost of macronutrients analysis involved matching supermarket food prices (converted to price per 100g of food item), collected during store visits in 2019, and macronutrient intake per food item.

Results: Mothers of HEU children had lower household income (P<0.01) and educational attainment (P=0.03). The infant feeding practices differed between HEU vs HUU infants (P=0.05): exclusive breastfeeding (50.0% vs 34.0%) and mixed feeding (38.1% vs 64.2%). Common complementary foods included commercial infant cereals (48.7% vs 70.9%; P=0.04); fruits and vegetables (33.3% vs 15.7%; P=0.05) and maize meal porridge (25.6% vs 15.7%; P=0.24) for HEU and HUU children, respectively. The mean daily cost of diet, in terms of macronutrients, of HEU vs HUU children was ZAR8.55±7.35 vs ZAR10.97±7.92; (P=0.10). There were non-significant differences found regarding protein, fat and carbohydrate intakes (P>0.05) and their costs per daily intake (P>0.05), between HEU and HUU children.

Conclusion: South African children are introduced to complementary feeds earlier than recommended in infant feeding guidelines due to suboptimal exclusive breastfeeding practices, incurring unnecessary cost to caregivers. This may lead to diets low in macronutrient content due to financial constraints. Differences exist in feeding practices of HEU and HUU infants. More sustained effort is required to support and promote exclusive breastfeeding, irrespective of maternal HIV status.

Keywords: Cost of diet, nutrient intake, HIV-exposed-uninfected infants, HIV-unexposed-uninfected infants, South Africa

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The effect of HIV and latent Tuberculosis infection during pregnancy on infant immune development

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Background: In utero exposure to maternal HIV infection may impact the infant's ability to develop or retain immunological memory, even in the absence of vertical HIV acquisition. The additional effect of maternal latent tuberculosis (TB) status on immune development is not known.

Material and Methods: We acquired cryopreserved infant PBMC samples from the IMPAACT P1078 study and performed immunophenotyping on 20 HIV-exposed uninfected infants born to HIV+ mothers with (n=10) or without (n=10) latent TB infection (LTBI) as determined by Interferon-gamma release assay (IGRA) during the 2nd or 3rd trimester. Infant samples were obtained at 12 and 44 weeks of life. Immunophenotyping was performed using 28-color flow cytometry and the Cytek Aurora for identification of T cells, B cells, natural killer (NK) cells, and myeloid cells (monocytes, macrophages, and dendritic cells (DC)). Statistical analysis was performed to assess immune development from 12 to 44 weeks (paired students T-test) as well as to compare immune phenotypes between infants from IGRA+ vs. IGRA- mothers (Mann-Whitney U-test). Additionally, plasma samples at study entry from 76 mothers were assessed for inflammatory biomarkers using OLINK Inflammatory panel of 95 proteins and statistical comparisons were made between IGRA+ (n=38) and IGRA- (n=38) groups.

Results: Out of 830 parameters analyzed, statistically significant differences ($p<0.05$) were discovered in paired analysis between samples of infants at 12 and 44 weeks. Frequencies of gamma delta (GD) T cells, CD4 and CD8 T Effector and Effector memory, CXCR5+ CD4 T cells, and CD27+ B cells increased in all infants with age. Frequencies of T cells expressing CD38 and HLADR as well as IgM+, IgD+, and naive B cells decreased in all infants. CD2 expression on NK cells and DC subsets also increased with age in all infants. The myeloid population had the most differences between infants from IGRA+ and IGRA- mothers including decreased expression of CD86 and CD36 on total monocytes at 12 weeks and higher PDL1 and CX3CR1 expression on total monocytes at 44 weeks in infants from IGRA+ mothers. Maternal plasma samples from IGRA+ women showed higher levels of inflammatory proteins including IL18R1, TNSF14, CXCL9, EN-RAGE ($p<0.05$) while PDL1 and IL8 showed trends of higher levels ($p=0.052$ and 0.065, respectively).

Conclusions: Our results indicate that immune development from the perspective of immune cell distribution in blood is not drastically altered due to maternal LTBI however monocytes in infants from IGRA+ mothers may have higher levels of activation due to the maternal milieu of chronic stimulation from LTBI.

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The Effects of Perinatal HIV Exposure on Hearing in Children

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Background: The weakened immune system from human immunodeficiency virus (HIV) mother-to-child transmission often results in opportunistic infections, such as middle ear pathologies and subsequently, hearing loss. Researchers have shown that children with perinatally acquired HIV (CPHIV) are at higher risk for hearing loss compared to both children with perinatal HIV exposure but uninfected (CPHEU) and HIV-unexposed children (CHU). CPHIV with a CDC Class C diagnosis are twice as likely to have hearing loss compared to lesser CDC HIV classifications. The purpose of this study is to evaluate hearing measures from South African children who are participating in the Auditory Research in Children with HIV: Cape Town (ARCH: Cape Town) study. ARCH: Cape Town is an ongoing study with the purpose of examining the effects of PHIV and antiretroviral therapies (ART) on components of the auditory system, from the periphery to the auditory cortex.

Methods: The hearing examination consisted of: otoscopy; tympanometry and ipsilateral acoustic reflexes at 1 kHz; and pure-tone air-conduction thresholds at octave frequencies from 0.25 through 8 kHz, in both ears. Pure-tone thresholds were completed while the child was sitting in a sound-treated room. Hearing loss was defined as a worse ear pure-tone average (PTA) of 0.5, 1, 2, and 4 kHz ≥ 15 dB. Linear regression models were used to evaluate the association between HIV status and middle ear outcomes and PTA. Models were conducted separately for each ear.

Results: Currently, 233 children have hearing measures: 103 CPHIV (58 girls); 49 CPHEU (20 girls); and 81 CHU (40 girls). All children were assessed between 11-14 years of age, and the mean ages for all three groups of children were approximately 11.5 years. For both left and right ears, middle ear outcomes were similar for the three groups of children. Both CPHIV and CPHEU had higher mean worse ear PTAs compared to CHU, but the difference was only 1-2 decibels (dB) and not statistically significant. Both groups, CPHIV and CPHEU, had higher, but not statistically significant, proportions of hearing loss (9% and 14%, respectively) compared to CHU (6%). Among CPHIV, those with greater HIV disease severity (i.e., lower Nadir CD4 counts, higher peak HIV RNA viral loads, and CDC Class C diagnosis) did not have poorer hearing outcomes compared to children with lesser HIV disease severity.

Conclusions: Although CPHIV may be more susceptible to middle ear pathologies, data from the current study do not support that; CPHIV had similar middle ear measures compared to both CPHEU and CHU. Both CPHIV and CPHEU groups had slightly higher proportions of hearing loss compared to CHU. At this time, it is not known what aspects of HIV exposure or HIV infection are the underlying cause for these higher proportions.

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High adherence to pre-exposure prophylaxis in young men who have sex with men aged 16-24 years based on tenofovir diphosphate levels in Thailand

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Background: Although pre-exposure prophylaxis (PrEP) use in adolescents and young adults (AYA) is approved, adherence remains challenging. We look at HIV protection benefit achieved from PrEP use in HIV at risk young men who have sex with men (YMSM) in Thailand.

Materials and Methods: YMSM aged 16-24 years were provided free daily oral tenofovir disoproxil fumerate/emtricitabine at youth-friendly clinics. Participants were randomized to receive youth-friendly services (YFS) or YFS plus P3T (Prepared, Protected, emPowered Thailand), a mobile phone application supporting PrEP adherence. The P3T app, adapted from the US version (P3) utilizes social-networking, game-based elements and evidence-based features, including two-weekly in-app adherence counselling. Clinic visits occurred at baseline, months 1, 3 and 6 for HIV testing, PrEP dispensation, questionnaire completion and risk reduction counselling. Dried blood spots were collected for tenofovir diphosphate (TFV-DP) to quantify PrEP adherence levels at months 3 and 6. Behavioral risk data were summarized into 3-month blocks of HIV risk acquisition to assess HIV protection by PrEP (good adherence and HIV protected >700 femtomoles (fmol) per punch, 350-699 fmol/punch moderate adherence, <350 fmol/punch poor adherence) and/or consistent condom use.

Results: Between June 2020 and January 2021, 60 YMSM were initiated on PrEP. Median (IQR) age was 20 (21-22). At baseline, self-reports for STIs was 10% and inconsistent condom use 79% for the preceding 3 months. Retention at months 3 and 6 were 91.5% and 91.9% respectively. A total of 91 TFV-DP samples were collected (52 at month 3 and 39 at month 6). Seventy-nine HIV risk acquisition blocks were available for analysis. Of these, 70 reported sexual activity, of which 46 (65.7%) were protected with PrEP only, 11 (15.7%) with PrEP and condom use, 3 (4.3%) with condoms only and 10 (14.3%) were not protected. Of the 35 YMSM with available TFV-DP levels at both visits, 31 (88.6%) were protected at month 3 and of these 24 (77.4%) remained protected at month 6. No associations were seen between users ages ≤20 years and >20 years and good PrEP adherence (p=0.6 and p=0.7 at months 3 and 6 respectively). No HIV seroconversions occurred in the 23 person-years of follow-up completed.

Conclusions: YMSM in our study demonstrated high rates of inconsistent condom use. However, they were mostly adherent to PrEP and no HIV seroconversions were seen. Continual PrEP adherence and risk reduction counselling, STI screening and treatment are essential components of AYA PrEP programs to minimize HIV transmission and acquisition risk.

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Self-testing HIV positive and linking to treatment: A tale of resilience and fortitude among adolescent girls and young women in Zambia

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Background: Zambia is scaling up HIV self-testing (HIVST) to increase the number of people aware of their HIV status. We conducted an exploratory qualitative study among adolescent girls and young women (AGYW) testing HIV-positive via HIVST to fill the evidence gap on post-HIVST linkage to treatment among this group.

Methods: From January to July 2019, AGYW (16-24 years) were recruited from three communities in Lusaka, Zambia. Eligible and consenting AGYW were given a HIVST kit, requested to test within two weeks and informed that if they tested positive, they should seek confirmatory testing at their local clinic and return to the research team for an in-depth interview (IDI) within 4 weeks. Participants who did not return were tracked via phone calls and home visits. IDIs were audio recorded and transcribed. Interpretive phenomenological analysis was used to understand internal and experiential processes that informed AGYW's decision to link to treatment, which we defined as confirmatory testing and antiretroviral therapy (ART) initiation.

Findings: Of the 536 AGYW who received an HIVST kit, 16 self-reported a positive HIV result, of whom 12 completed an IDI. Of these 12 AGYW, nine had undergone confirmatory testing at a clinic, of whom, six reported having initiated ART at the time of interview. Perceived risk for HIV infection as a result of high-risk sexual behaviours motivated AGYW to self-test. All participants grappled with serious negative feelings including denial, frustration and loneliness upon self-testing HIV positive. Having easy access to ART services along with supportive mothers, peers and counsellors helped some AGYW to navigate these feelings and swiftly initiate ART. Those who reported delaying confirmatory testing and/or ART initiation had not yet accepted their 'new self,' one associated with fears of premature death, wasting, failed aspirations for marriage and intimate relationships and stigmatization by community members.

Conclusion: Our study suggests that the Test and Treat policy favours early ART initiation among AGYW self-testing positive. Counselling and other social support services can help AGYW who self-test HIV positive to navigate the socio-psychological and structural barriers they face when deciding on when and whether to access confirmatory testing and ART initiation.

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A Qualitative Examination of the Impacts of Perceived Stigma on the Mental Health of Adolescents Living with HIV in Western Kenya

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Introduction: Adolescents represent a critical population of people living with HIV, accounting for more than half of new HIV infections in sub-Saharan Africa. Adolescents living with HIV (ALWH) face myriad difficulties in controlling HIV, including anti-HIV stigma, that may lead to or exacerbate mental health challenges already common among people living with chronic diseases. However, the relationship between mental health challenges and the fear of discrimination because of one's status, known as perceived stigma, remains unclear. This study sought to investigate mental health-related experiences of ALWH in western Kenya within the context of perceived stigma.

Methods: We conducted a qualitative evaluation of the impact of perceived stigma on the mental health and social relationships of ALWH. Semi-structured interviews utilizing cognitive interviewing techniques were used to probe key domains of mental health, anti-HIV stigma, and the development of peer relationships. Forty-six ALWH aged 14-19 years, aware of their HIV status, on ART, and enrolled at either one urban or peri-urban HIV clinic in Western Kenya were included in this study. Interviews were conducted in Kiswahili, English, or both, 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. A software program (Dedoose, SocioCultural Research Consultants, LLC) was used to conduct analyses.

Results: Participants described a range of emotions in connection with their HIV status, including feelings of sadness, racing/intrusive thoughts, and suicidal ideation. Although diagnosis of specific mental health conditions such as anxiety and depression was not undertaken, the emotions described by participants demonstrate key features of these challenges. While some connected these emotions to previous life experiences – especially the discovery of their own HIV status – many reported ongoing concerns, including perceived stigma, that manifest as challenges with activities of daily living: attending school, forming friendships, and pursuing romantic relationships. The majority of our participants described a relationship between living with HIV and feelings of isolation, identifying their HIV status as a barrier to social relationships and involvement in activities they enjoy. They further reported secrecy and purposeful non-disclosure as their primary protective measures against stigmatization and secondary isolation. When asked to contemplate disclosing their status and secondary impacts, many reported fears of "vengeful disclosure" – anticipating their status being weaponized against them by friends or romantic partners. Our findings show that perceived stigma and social isolation have reciprocal and perpetuating effects on one another that contribute to feelings consistent with major mental health diagnoses.

Conclusions: Our results demonstrate that perceived stigma elicits a fear response leading to secrecy and feelings of social isolation. This lack of social support, whether realized or perceived, leads to poor mental health outcomes, demonstrating the importance of peer support opportunities for ALWH. Furthermore, it is clear that our participants are considering the perceived negative impacts of disclosure frequently when making decisions about their personal lives and health care. Therefore, it is critical that interventions targeting this group be modeled with the consideration of adolescent's fears and desires in mind.

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Mental Health Outcomes of an HIV-Prevention Program for South African Adolescent Girls and Young Women and their Female Caregivers

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Background: Estimates of mental health problems in South African youth range from 15% - 41%, with higher rates in adolescent girls and young women (AGYW) than their male peers. Mental health distress intersects with sexual and reproductive health (SRH), including HIV prevention and care. Interventions to reduce HIV-risk behavior and improve prevention uptake (e.g., PrEP) would benefit from co-occurring mental health services, but the need in South Africa far outweighs access, availability, and adolescent-friendly approaches. Female caregivers influence youth SRH and mental health but are a largely untapped resource in HIV-prevention efforts for South African AGYW. Informed Motivated Aware and Responsible Adolescents and Adults (IMARA), an evidence-based mother-daughter HIV-prevention program evaluated in the United States was tailored for South Africa (IMARA-SA) and pilot tested in a 2-arm study. We present preliminary findings on AGYW anxiety, depression, and trauma.

Material and Methods: AGYW and their female caregivers (FC) were recruited through street outreach in Klipfontein/Mitchells Plain and neighboring areas. AGYW-FC dyads were randomized to one of two psychosocial group-based programs matched in time: IMARA-SA or a health promotion control. AGYW and FC separately completed surveys at baseline and follow-up (6-10 months post). AGYW reported their anxiety symptoms on the GAD-7, depressive symptoms on the PHQ-9, and trauma symptoms on the PTSD-5. The GAD-7 and PHQ-9 have strong psychometric properties across cultures and in this study (α=.85 and .78, respectively). Given the presence of skewed and sparse data, we examined intervention effects using zero-inflated negative binomial regression for anxiety (treated as a binary variable) and multinomial logistic regression for depression (treated as a categorical variable). We used logistic regression for PTSD (treated as a binary variable).

Results: Sixty AGYW (mean age=17.1, range=15-19 years) were enrolled (30 per arm). Group comparisons confirmed that AGYW were balanced across treatment groups on baseline demographic characteristics and mental health variables with two exceptions: AGYW randomized to IMARA-SA had higher depression scores (mean=9.4, SD=6.33) than the control group (mean=6.3, SD=5.32) (p=0.04) and a greater proportion screened positive for PTSD (40%) compared to controls (17%) (p=.07). Controlling for baseline mental health scores, AGYW who received IMARA-SA had significantly fewer anxiety symptoms at follow-up compared to controls (adjusted incidence rate ratio for count model= 0.54, 95% CI= 0.29-0.99, p=0.05) and they were less likely to have depressive symptoms (scores of 1-9) relative to no symptoms (scores of 0) (relative risk ratio= 0.22, 95% CI= 0.05, 0.95, p=0.04). AGYW in the IMARA-SA condition were less likely than controls to report symptoms of PTSD relative to no symptoms at follow-up, but this difference did not reach statistical significance.

Conclusions: South Africa has the highest burden of HIV infection worldwide, and AGYW are among those at greatest risk for new infections. Mental health is implicated in risky sexual behavior and HIV acquisition, and reducing emotional distress may mitigate exposure to HIV. This pilot study offers promising findings for the mental health impact of an evidence-based culturally tailored SRH and mental health program for AGYW and their FC.

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"Who am I going to stay with? Who will accept me?" – A qualitative study of family-level factors underlying disengagement from HIV care among Kenyan adolescents

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Background: Adolescents living with HIV (ALHIV, ages 10-19) have lower retention in care compared to other age groups. Adolescents rely on family support in their transition to autonomy. We investigated family-level factors underlying disengagement from HIV care among adolescents who were lost to program (LTP).

Methods: Semi-structured interviews were performed with ALHIV LTP, their caregivers, and healthcare workers (HCW) in the Academic Model Providing Access to Healthcare (AMPATH) program in western Kenya, from 2018-2020. Criteria for ALHIV LTP were ≥1 visit within the 18 months prior to data collection at one of two clinical sites and nonattendance ≥60 days following their last scheduled appointment. HCW were recruited from 10 clinics. Transcripts were coded using an adapted socioecological model, and family-level factors underlying disengagement were elucidated through thematic analysis.

Results: Interviews included 42 ALHIV LTP, 32 caregivers, and 28 HCW. ALHIV were 67% orphaned, 62% female, 60% food-insecure, and average age 17.0 (range 12.9-20.9). Family-level factors were central to disengagement. Orphaned ALHIV experienced challenges when new caregivers or unstable living situations limited support for HIV care. These challenges were compounded by anticipated stigma ("Who am I going to stay with? Who will accept me?"); resultant non-disclosure of HIV status to household members ("I feared telling people at home; I hid it completely"); enacted stigma in the household, with overwhelming effects on adolescents ("If we are at the table eating, they should not discriminate against him. Let us just sit all of us together"); or experiences of multiple forms of trauma. These challenges directly undermined HIV care engagement. Some caregivers lacked finances or social support to facilitate care. Others did not feel equipped to support adolescent engagement or adherence. Regarding facilitators to re-engagement, participants described roles for household disclosure ("Since they know, at least I have the courage I can come"); and supportive caregivers, especially those also living with HIV ("We understand her situation, and we do things as a team").

Conclusions: Family support is integral to adolescent retention in HIV care. Interventions targeting household relationships, disclosure, HIV stigma, and care resources may promote adolescent retention.

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A Group-Based Mental Health Intervention for Youth Living with HIV in Northern Tanzania: Secondary Analyses of a Pilot Trial

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Introduction: Youth Living with HIV (YLWH) face numerous psychosocial stressors that impact mental health and HIV outcomes. YLWH are vulnerable to poor HIV outcomes due to incomplete adherence to ART in the context of stigma, poverty, mental health challenges, and decreased hope for future. Few mental health interventions have been developed to improve HIV and mental health outcomes for YLWH.

Material and Methods: Sauti ya Vijana (SYV; "The Voice of Youth") is a group-based mental health and life skills intervention developed with YLWH to address the complex psychosocial and mental health needs described by Tanzanian YLWH during formative research. SYV sessions were based on existing evidence-based treatment models—including components of cognitive behavioral therapy, interpersonal psychotherapy, and motivational interviewing—designed to improve coping skills, resilience, social support, and hope for future as a pathway to improved adherence and virologic suppression. SYV was comprised of ten 90-minute group-based sessions (two that incorporated caregivers) and two individual sessions with group leaders. The intervention was delivered by six young adults ages 23-30 affected by and/or living with HIV. YLWH ages 12-24 years were recruited from two adolescent clinics in Moshi, Tanzania. Participants included in this analysis were initially randomized to standard of care (SOC) and received the intervention in crossover waves approximately two to three years post-enrollment. Outcomes included HIV-RNA, self-reported mental health measures (PHQ-9, SDQ, and UCLA PTSD Reaction Index), and self-reported HIV measures (stigma and adherence) that were measured at enrollment, pre-intervention, and post-intervention time points. Participants were included in the final analysis if they had data for all three time points.

Results: 21 crossover participants (n=13 males; n=8 females) with a mean age of 20.5 years were included in the final analysis. At enrollment, 15% of participants had symptoms of moderate to severe depression (PHQ9 >10), but none met this threshold pre- nor post-intervention. Mean scores of all self-reported mental health questionnaires were in an asymptomatic range both pre- and post-intervention. Stigma scores and self-reported adherence remained essentially unchanged pre- to post-intervention. There was a 10% increase in participants who were virologically suppressed (HIV RNA >400 copies/mL) post-intervention (81%, N=17) compared to pre-intervention (71%, N=15); participants with virologic failure pre-intervention who became virologically suppressed post-intervention were on the same protease-inhibitor based regimen (ATV/r or LPV/r).

Conclusions: Findings from this crossover group match the findings from the randomized pilot trial that found a 10% increase in virologic suppression pre- to post-intervention in the intervention arm compared to SOC, providing additional support that SYV holds promise to improve HIV outcomes for YLWH.

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Influence of HO-1 Genotype on Neurocognitive Functioning among Adolescents with Perinatally Acquired HIV

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Background: Neurocognitive impairment (NCI) is prevalent among adolescents with perinatally acquired HIV (PHIV), even those virally suppressed. The mechanisms of NCI in PHIV are not fully understood, though chronic inflammation may contribute. Heme oxygenase-1 (HO-1) is a cytoprotective enzyme that limits oxidative stress, inflammation, and cellular injury. An HO-1 genetic polymorphism (a dinucleotide (GT)n repeat length promoter variation) modulates HO-1 transcription. Short (S) HO-1 (GT)n repeat alleles – compared to medium (M) and long (L) – are associated with better outcomes in inflammatory and oxidative stress-associated diseases. HIV-infected adults with at least one S allele have shown decreased risk for HIV-NCI. To date, associations between the HO-1 (GT)n allele genotype and NCI have not been examined in adolescents with PHIV or in Africa. This study examined associations with the HO-1 (GT)n allele genotype and neurocognitive test performance among Ugandan adolescents with PHIV.

Methods: Twenty-eight virally suppressed adolescents with PHIV attending the Joint Clinical Research Centre in Kampala, Uganda (Mean age: 15.18 years (SD = 2.07); 46% female; Mean education 7.57 years (SD = 2.35), completed 12 neurocognitive tests assessing six neurocognitive domains (processing speed, working memory, executive functions, learning, memory, and motor speed). HO-1 (GT)n allele genotypes were determined by PCR of the (GT)n repeat region, followed by fragment size determination on a capillary sequencer in DNA extracted from blood samples. Allele designations were assigned by number of (GT)n repeats: S <27, M 27-34, or L >34 repeats. General linear regression examined associations between test performance and genotypes. ANOVA examined performance differences between all genotypes.

Results: Genotype distribution was: 11% (n=3) SS; 14% (n=4) SL; 14% (n=4) MM; 46% (n=13) ML; and 14% (n=4) LL – none had SM. Controlling for age, sex, and education, no differences in mean test performance between those with an S allele to those without one were found. However, those with an S allele appeared to perform better in simple processing speed compared to those without one (Trail Making 3, p = 0.05). Participants with two S alleles (SS) performed worse in complex processing speed (Visual Discrimination 2, p = 0.01) and executive functioning (Trail Making 2, p = 0.02) compared to all other genotypes.

Conclusions: This is the first study describing the association of the HO-1 (GT)n allele genotype and neurocognitive test performance among adolescents with PHIV and in Africa. Surprisingly, the presence of an S allele was not associated with better test performance. In contrast to adults with HIV, the SS genotype associated with significantly worse performance in executive functioning and complex processing speed. An S allele drives higher inducibility of HO-1 expression and is associated with reduced HIV-NCI risk in adults, suggesting that other factors may influence HO-1 genotype effects in adolescents vs. adults. However, the small sample size and criteria for NCI diagnoses differ between studies. Larger studies could define how the HO-1 (GT)n allele genotype and therapeutic targeting of HO-1 may modulate NCI risk in adolescents with PHIV, particularly in a hyperendemic setting like Uganda.

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"You guide them but ultimately they make decisions": Stakeholder insights about adolescent consent for HIV care and research in Kenya

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Background: Adolescents represent a growing percentage of people living with HIV, but are under-represented in HIV care and research. Requirements for parental/guardian permission pose a significant barrier to engaging adolescents. Key stakeholders involved in HIV-related policy development and implementation can identify strategies for improving adolescent participation, and thus clinical outcomes.

Methods: We conducted semi-structured individual interviews (IDIs) with 16 stakeholders with expertise in ethical, legal, and social issues (ELSI) in Kenya. IDIs were conducted in English by Kenyan social scientists, audio recorded, and transcribed verbatim. Thematic analysis elucidated common themes around adolescent decision-making, autonomy, relationships, and changing societal views regarding adolescent involvement in HIV care and research.

Results: ELSI stakeholders included IRB/ERC members (N=3), lawyers (N=3), policymakers (N=6), and school administrators (N=4). Participants identified three major themes related to adolescent decision-making and consent practices. First, participants noted that decision-making regarding independent consent is closely tied to judgments of adolescent capacity for appropriately considering risk and understanding consequences. Almost all indicated that age is a poor proxy for independent decision-making and described the importance of incorporating context, risk/benefit ratios, and maturity. Second, participants also recognized the role of parents and other trusted individuals in empowering and involving adolescents in early decision-making. By sharing how decisions are made, and including adolescent opinions in decision processes, adolescents gradually gain ownership over their health and lives, improving their confidence and ability to make informed decisions. Third, participants recognized that adolescent culture is affected by increased access to technologies and globalization, giving adolescents access to more information and causing adolescents to mature faster than previous generations. Thus, participants recommended that policies around adolescent involvement in decisions should be frequently evaluated and adapted to accommodate evolving societal views about adolescent autonomy.

Conclusion: Policies and guidelines around consent practices involving adolescents could be revised to consider the type of decision, level of risk, and maturity of the adolescent, rather than just age. Caregivers and other adults may need support on how to empower adolescents and increase their involvement in decision-making. Revising guidelines and supporting caregivers could promote more equitable and representative participation of adolescents in HIV care and research.

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Optimizing HIV and sexual and reproductive health care for adolescent girls and young women in Zambia: Qualitative findings from interviews and focus group discussions

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Background: Zambia remains one of the countries most affected by HIV in the world, and adolescent girls and young women (AGYW) have a disproportionately high incidence. Youth-friendly health care delivery models are needed to address the complex health care needs of AGYW. The aim of this study is to explore the lived experiences of AGYW seeking comprehensive HIV and sexual and reproductive health care and to elicit their preferences about the types of health services they want and how they can be delivered.

Material and Methods: We conducted in-depth interviews and focus group discussions in Lusaka, Zambia among 69 AGYW aged 10-20 who were HIV-negative or of unknown status and 40 AGYW aged 16-24 living with HIV. The data were coded through deductive and inductive processes and analyzed thematically using modified World Health Organization (WHO) dimensions of quality for youth-friendly services. This study received ethical approvals by local and institutional IRBs.

Results: Attributes identified for a youth-friendly health care delivery model included 1) having a one-stop location with bundled, integrated services applicable to AGYW that includes HIV and SRH services, advice on healthy living and disease prevention; 2) ability to promptly access services with flexibility around other commitments, such as school; 3) provision of services in a private location (preference for clinic dedicated just for girls) with assurances of confidentiality at all points of contact with clinic staff and providers; 4) friendly staff that respect and empower all AGYW; and 5) knowledgeable providers (including staff, counsellors, and youth program leaders) that encourage sustained AGYW engagement to improve health outcomes over time. Zambian AGYW also expressed interest in receiving the HPV vaccination alongside HIV services and the desire for educational and clinic resources on cervical cancer screening and prevention.

Conclusions: Youth-friendly, integrated care delivery models that incorporate AGYW preferences may help to optimize linkages to care, encourage increased engagement by AGYW across the HIV prevention and care continuum, and improve outcomes among vulnerable AGYW. Furthermore, women in sub-Saharan Africa face a dual burden of HIV and cervical cancer and increasing access to HPV vaccination within integrated care delivery programs offers an opportunity to substantially reduce mortality and morbidity.

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Influences on Healthcare Worker Acceptability, Feasibility and Sustainability of an Adolescent Transition Package in Kenya

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Introduction: Successfully preparing and transitioning adolescents living with HIV (ALHIV) from pediatric to adult care is critical for ensuring adherence and retention in care. We developed and implemented an Adolescent Transition Package (ATP), which combines HIV disclosure and transition tools, in 10 clinics in Kenya as part of a cluster randomized clinical trial. Understanding healthcare worker (HCW) experiences with implementation of the ATP can identify influences on acceptability and feasibility that inform future scale-up and scale out of the ATP intervention.

Methods: Guided by the Consolidated Framework for Implementation Research (CFIR), we conducted 10 semi-structured focus group discussions (FGDs) (one per clinic) with 76 HCWs to evaluate factors influencing ATP implementation. FGDs were recorded and transcribed verbatim. An analysis of FGD debrief reports and a subset of full transcripts was conducted to identify key influences on implementation.

Results: HCWs believed the ATP intervention was acceptable, feasible and improved the transition process for HCWs and ALHIV. HCWs described how ATP tools met the needs of adolescents, and resulted in improved viral suppression, ART adherence, and retention. The ATP provided a relative advantage when compared to existing tools because it was 1) systematic and provided a step-by-step guide, 2) simple and easy for any provider, including peer educators, to use, and 3) comprehensive, covering both medical and psychological components. The Taking Charge booklet was the most valuable component, providing relevant content in multiple languages and including well-liked illustrations. Feasibility and acceptability were enhanced through systematic study-facilitated adaptations including designated roles for staff and group delivery of book chapters, through which HCWs optimized delivery within their clinic. Flexibility in ATP tools enabled HCWs to expand use to include adolescents and pregnant women outside the study. This underscores broad acceptability and potential for scalability of the intervention. While HCWs were enthusiastic about continuing and scaling implementation post-trial, barriers to perceived sustainability included HCW time and workload.

Conclusion: The ATP intervention improved HCW experiences with preparing ALHIV to transition to adult care. Strategies that support intervention scale-up should address identified barriers to implementation, and incorporate new ways to enhance ATP reach and versatility

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Telehealth and transition: Factors affecting telehealth and engagement in care during health care transition of adolescents and young adults with HIV during the COVID-19 pandemic

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Background: Approximately 5 million young adults (ages 15-24) are living with HIV (YALWH) globally, most of whom will transition to adult HIV care in the next decade. Only about 40-50% YALWH are engaged in care 12 months after transition. YALWH who do not engage in HIV care impact their own health as well as create a public health challenge. When COVID-19 began affecting those in the US, HIV care providers quickly shifted to utilizing telehealth services. The purpose of this study was to examine the relationship between health care transition status, mode of HIV acquisition, demographic factors, HIV stigma, mental health, and telehealth use with engagement in care (HIV RNA PCR, number of visits, and adherence self-report) in YALWH (ages 18-30) during the COVID-19 pandemic.

Method: A quantitative cross-sectional, analytic observational study was completed. Questionnaires included assessments on HIV self-perceived stigma, mental health, and HIV medication adherence. HIV RNA PCRs and the number and types of visits were collected for 8 months before and after the COVID-19 pandemic began in Colorado (operationalized as March 15, 2020). Pre-COVID-19 was 7/15/2019 to 3/14/2020 and post-COVID-19 was 3/15/2020 to 11/15/2020. Data were analyzed using a series of linear and logistic regressions.

Results: Participants (N = 109) were 59.6% male and 51.4% white. There were 60.6% with situationally acquired HIV (SHIV) and 57.8% were post-transition. Those who were post-transition ($p < 0.009$), had SHIV ($p < 0.021$), and who had at least one telehealth visit ($p < 0.001$) were more likely to be undetectable by HIV RNA PCR. Those who were post-transition ($p < 0.009$), had SHIV ($p < 0.04$), or had at least one telehealth visit ($p < .001$) were more likely to be undetectable pre-COVID-19. There was a negative relationship with HIV RNA PCRs and telehealth use ($p < .001$). Those with at least one telehealth visit were more likely to be undetectable post-COVID-19 ($p = 0.002$).Those who were post-transition had lower total visits ($p = 0.042$), and lower total telehealth visits ($p = 0.037$). Those who had at least one telehealth visit had more total visits ($p = 0.042$) and more telehealth visits post-COVID-19 ($p < .001$). No significant relationships existed between the variables and adherence self-report. While the average number of visits declined post-COVID-19, the average number of telehealth visits increased.

Discussion: When COVID-19 hit, there was a rapid increase in telehealth use. The successful uptake of telehealth demonstrated the ability of patients and their health care providers to be flexible in how they provide and access care. Telehealth is an effective way of providing care and could be an innovative means of supporting YALWH during transition. Engaging in telehealth may support improved adherence to medication and increased number of visits leading to HIV viral suppression. YALWH experience stigma, anxiety, and face challenges unique to living with HIV so their health care demands a high level of sensitivity, and telehealth care may be a useful tool to support engagement in care during transition from adolescent to adult care.

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Timely pediatric regimen optimization at health facilities in Malawi is achievable despite COVID-19 pandemic restrictions with use of a virtual pediatric optimization toolkit and dedicated family ART clinic days

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Background: Pediatric ART coverage in Malawi has dramatically improved, however viral load suppression (VLS) among children remains suboptimal. New pediatric ART regimens provide hope for improved VLS. Despite Malawi's early establishment of a robust pediatric optimization policy, implementation was complex with multiple pediatric weight based regimens including use of LPV/r granules and complicated further by COVID-19 pandemic movement restrictions suspending in-person training and supervision.

Description: To facilitate transition to optimized pediatric ART regimens despite COVID restrictions, we 1) created and disseminated a virtual pediatric optimization toolkit (V-POT) consisting of a case based asynchronous self-study for clinical mentors, a decision-making tool to guide regimen transition, and an educational video for guardians on LPV/r granule administration, and 2) established family ART days to facilitate phone consultation by experienced clinical mentors and encourage guardian peer support. V-POT was disseminated to clinical and lay health staff via email and WhatsApp. Using V-POT's decision-making tool, facility-based providers recorded a child's ART regimen, weight, and latest viral load result, and clinical action guidance was provided by phone with experienced mentors. V-POT was implemented at 120 health facilities from April - December 2020.

Lessons learned: With delivery of V-POT, children receiving optimized ART regimens increased from 29% in December 2019 to 93% by December 2020. V-POT was easily implemented with good uptake and allowed identification and consultation of complex cases.

Conclusion/next steps: Use of a virtual package of support and family ART clinics facilitated mentorship resulting in timely regimen transition for children in Malawi despite limited in person support related to COVID-19. Next steps include adaptation of V-POT to facilitate continued VLS monitoring post-regimen optimization, as well as use for the DTG transition for children <20kg. V-POT can be adapted to different clinical topics to address other complex management decisions.

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The impact of the COVID-19 pandemic on uptake of multi-month dispensing (MMD) of Antiretroviral Therapy (ART) for children living with HIV (CLHIV): A multicountry analysis

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Introduction: Uptake of multi-month dispensing (MMD) of antiretroviral therapy (ART) for stable children (<15 years old (y/o)) living with HIV (CLHIV) varied widely across countries prior to the COVID-19 pandemic. COVID-19 prompted efforts to rapidly decongest health facilities to prevent transmission. This analysis updates a 2020 International Pediatrics Workshop oral presentation on MMD services changes for CLHIV during COVID-19.

Methods: MMD uptake among CLHIV in 12 USAID/PEPFAR-supported countries from October 1, 2019 to September 30, 2020 (Fiscal Year 20 quarter (Q) 1 to Q4) was analyzed using implementing partner and program data. Q1 and Q2 data was averaged (Q1/2) to represent pre-COVID-19 results; Q3 and Q4 data represented results during quarters with COVID-19-related-restrictions. Chi-square tests compared results from pre-COVID-19 to during COVID-19 (Q1/2 to Q3; Q1/2 to Q4), and compared changes during COVID-19 (Q3 to Q4). MMD was defined as dispensing ART at intervals of <3 months (<3MMD), 3-5 months (3-5MMD), or ≧6 months (6MMD).

Results and Discussion: From Q1/2 to Q4, the total number of CLHIV on treatment increased from 178,820 to 185,357. The percentage of CLHIV receiving any MMD (3-5MMD or 6MMD) increased from 36.9% (Q1/2) to 54.8% (Q4). The percentage of CLHIV receiving <3MMD decreased from 63.1% (Q1/2) to 45.2% (Q4). The 3-5MMD coverage increased from 34.2% (Q1/2) to 47.6% (Q3); despite a slight decrease to 45.9% in Q4 there remained an overall increase from Q1/2 to Q4. The percentage of CLHIV receiving 6MMD increased steadily from 2.7% in Q1/2 to 6.1% in Q3 to 9.0% in Q4. All changes from Q1/2 to Q3 and Q4, and Q3 to Q4 were statistically significant (p<0.001).

Conclusions: MMD uptake among CLHIV on ART increased significantly during the COVID-19 pandemic. Continued expansion of MMD policies and uptake, even as COVID-19-related restrictions relax, will strengthen access to ART for CLHIV.

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Effect of the COVID-19 Pandemic on Adolescents Living with HIV in Kenya

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Background: The COVID-19 pandemic prompted global restrictions to limit the spread of SARS-CoV-2, including social distancing, stay-at-home orders, and travel bans. The impact of these public health mitigation measures on adolescents living with HIV (ALWH), who are already at risk of disengagement from the clinical system, virological failure, and poor clinical outcomes, are largely unknown and can inform interventions.

Methods: We conducted a prospective survey evaluation with ALWH aged 9-25, receiving HIV care at the Academic Model Providing Access to Health Care (AMPATH) in Western Kenya and enrolled in a cohort study evaluating viral failure and drug resistance in this population. Surveys were conducted either in-person during clinic visits or over the phone, depending on COVID-19 restrictions, every two months for one year, and assessed COVID-19 knowledge and the impact of the pandemic on ART adherence, mental health, and socioeconomic well-being. Here, we report the baseline assessments for a subset of the ALWH cohort.

Results: Baseline assessments for 192 participants (mean age 18 years, 53% female) were completed between February 2020 and February 2021. All participants had heard of COVID-19, and the majority understood that anyone could be infected (n=179, 93%) and that a vaccine had been developed and was available (n=99, 52%). Participants identified fever (n=112, 58%), cough (n=124, 65%), and headache (n=71, 37%) as the main symptoms of COVID-19. Many participants also understood that they should contact a healthcare facility (n=180, 94%) and/or isolate from others (n=126, 66%) if they have symptoms. Participants reported leaving their homes for food (n=166, 87%) and/or medical care (n=183, 95%), and reported wearing a face mask (n=173, 90%) or practicing social distancing (n=73, 38%). Participants (n=153, 80%) did not have concerns about staying healthy during the pandemic. However, 46 participants (24%) reported concerns about running out of HIV medications, with 10% skipping doses due to these concerns. Moreover, a number of ALWH reported a loss of income (n=8, 29%), atypical food insecurity (n=64, 33%), and mental health challenges (n=6, 3%) during the pandemic. The majority of participants continued to stay at their usual residence (n= 156, 81%) during the pandemic. Despite school closures through early 2021, participants reported currently being enrolled (n=168, 88%), of which 95% reported experiencing no impact on their studies . The minority of participants (3%) reported continuing schoolwork without attending in-person classes, and 2% reported no longer completing schoolwork.

Conclusion: Participants demonstrated COVID-19 literacy and reported concerns about food insecurity, financial difficulties, medication availability and ART adherence. Despite school closures, participants reported minimal disruptions to their education, and some disruptions in employment, income, and accessing medical care. These early findings highlight opportunities to support vulnerable ALWH and demonstrate the need for continued research on these difficulties and opportunities.

Keywords: COVID-19, HIV, adolescents, Kenya

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Access to UK healthcare and viral control in adolescents and young adults living with perinatal HIV throughout 1 year of the SARS-CoV-2 pandemic.

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Background: The 2020 SARS-CoV-2 pandemic lead to UK-wide lockdown measures, with NHS England issuing guidance suspending outpatient care bar essential appointments, moving to remote consultations for stable patients. We explored the impact of the pandemic on clinical and virological outcomes for adolescents and young adults living with perinatally acquired HIV infection (YAPaHIV). Face-to-Face (F2F) appointments continued for vulnerable patients, with remote consultations and medication postage for stable patients. Viral load (VL) monitoring occurred at F2F and routine clinic appointments coinciding with 2 periods of lockdown easing.

Methods: A retrospective single-centre cohort analysis of YAPaHIV with data compared between; Period 1(P1) twelve months before the first national lockdown- 23rd March 2019-23rd March 2020, period 2(P2) twelve months of varied pandemic restrictions- 24th March-24th March 2021. Data analysed included age, ethnicity, sex, HIV VL, CD4 count, clinical events and appointment frequency/modality. Primary outcome was the proportion with suppressed VL<200 copies/ml by study period with secondary outcomes describing appointment frequency/modality and hospitalisations. Routine testing for SARS-CoV-2 was not available in the clinic.

Results: Of177 YAPaHIV: 56% were female, 86.9% were black, median age at lockdown 23 years (IQR 21-27). 1 individual was lost to follow up in P2 and excluded from subsequent analysis.

Primary outcome: 147/176 (83.5%) had a suppressed VL in P1 compared with 156/176 (88.6%) in P2. Of 147 YA with a suppressed VL in period 1, 8/147 (5.4%) experienced virological failure in P2; median VL 533 c/ml (IQR 248-14032). Of 29 YAPaHIV with detectable VL in P1 (median VL 3200 c/ml [IQR 925-36500]), 17/29 (59%) achieved viral suppression in P2. For twenty individuals with virological failure in P2 median VL was 911 (IQR 317-52300). Prior to lockdown 15/176 (8.5%) had a CD4 count<200 cells/uL (median 80 [IQR 38-128]), four reconstituting to >200 cells/uL in P2. Three individuals with established poor adherence CD4 counts fell below 200 in P2. 4/25 tested were diagnosed with SARS-CoV-2 by PCR (2), serology (2).

Of 712 appointments in P1; 624 (87.7%) were F2F, 75 (10.5%) telephone and 13 (1.8%) other. Of 541 appointments in P2; 386 (71.3%) were F2F, 141 (26.1%) telephone and 14 (2.6%) other. Average appointments per patient per annum; 4.05 P1 and 3.07 P2 with F2F 3.55 and 2.19 respectively. 12 admissions occurred; 9 in P1; pneumonia (2), HIV wasting (2), symptomatic HIV viral rebound (1), progressive multifocal leukoencephalopathy (3) and cryptococcal meningitis (1). Three in P2; Campylobacter gastroenteritis (1), paracetamol overdose (1) and hepatitis (1). 16 pregnancies reported by 12 women over P1/2 resulted in; miscarriage (2), elective termination (5) live birth- HIV uninfected (5) and ongoing pregnancy (4).

Conclusion: Flexibility in maintaining F2F appointments for vulnerable patients, whilst providing remote consultation for stable patients, maintained very high levels of retention in care and viral suppression in a youth PaHIV cohort despite pandemic restrictions, and an overall reduction in appointment frequency.

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Supporting Access to HIV Prevention and Care for Children and Youth during the COVID-19 Pandemic with Telemedicine and Rideshare

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Background: Telemedicine and rideshare services for clinic and laboratory visits for children and youth at risk for and living with HIV were scaled-up in response to the COVID-19 pandemic at Special Immunology Services (SIS) in Children's National Hospital, Washington, DC. We evaluated the effect of telemedicine and rideshare on retention in care and related health outcomes among patients in care at SIS, and measured the impact of the pandemic on visit completion.

Material and Methods: Data (demographics, rideshare utilization information, visit and laboratory information, HIV RNA viral load (VL) and CD4 test results) was collected from electronic medical records of patients aged 0-24 years who received HIV preventative care and treatment in SIS. Using chi-squared tests and Wilcoxon rank sum tests, we compared demographic, rideshare, visits and laboratory data of patients who scheduled telemedicine at least once (telemedicine) versus those who never scheduled telemedicine (no-telemedicine). We compared the number of scheduled and completed clinic visits before the pandemic (April-September 2019) with those during the pandemic (April-September 2020) using paired t-tests.

Results: During the pandemic, we analyzed 260 patients (median age 15.5 years, 88.9% Black, 50.4% male), of whom 51.5% used telemedicine, and 15.8% used rideshare. The majority (68.5%) were living with HIV (78.7% perinatally infected), followed by HIV-exposed infants (HEIs, 29.2%) and patients receiving pre-exposure or post-exposure prophylaxis (2.3%). Telemedicine patients were significantly older (median 17.9 years; IQR 14.9, 20.4) compared to no-telemedicine patients (median 1.7 years; IQR 0.4, 16.3; p<0.0001). Most telemedicine patients were children and youth living with HIV (93.3%), whereas 54.8% of no-telemedicine patients were HEIs (p<0.0001), reflecting our efforts to see HEIs in-person to provide maternal support and counseling. Telemedicine patients scheduled more visits (251 versus 181, p<0.0001) compared to no-telemedicine patients. A total of 432 visits were scheduled by all patients, the majority of which were completed (combined in-person and telemedicine visits, 83.3%; telemedicine visits only, 83.0%; in-person visits only, 83.6%). Laboratory testing rates (80.6% versus 99.4%, p<0.0001) were less in telemedicine versus no-telemedicine patients. During the pandemic, most children and youth with HIV were virologically suppressed (81.0% with HIV RNA <200 copies/mL). The number of completed visits was similar before and during the pandemic (438 versus 360; p=0.2498) whereas visits before the pandemic were completed at lower rates compared with visits during the pandemic (78.1% versus 83.3%; p=0.0394).

Conclusion: During the COVID-19 pandemic, most children and youth with HIV in our study remained virologically suppressed. We report high rates of visit completion while offering a combination of in-person and telemedicine visits supported by rideshare services during the COVID-19 pandemic among children and youth in metropolitan DC. In view of decreased in-person visits, telemedicine combined with rideshare support was effective in ensuring uninterrupted access to HIV prevention and care among children and youth at risk for and living with HIV. We have now incorporated telemedicine and rideshare within our package of routine HIV prevention and care services beyond the pandemic.

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Differences in SARS-CoV-2 specific antibody production among adults vs. children living with HIV

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Background: Understanding the immunological response to SARS-CoV-2 infection among people living with HIV (PLWH) will be essential to controlling the pandemic in HIV endemic areas. However, there is limited data on SARS-CoV-2 immunity among PLWH. At the same time, clear differences have emerged with respect to the clinical manifestations and severity of the disease in children vs. adults, though the immunological mechanisms are not well described. The objective of this article was to compare the humoral immune response to SARS-CoV-2 infection among adults living with HIV (ALWH) vs. their children, and that observed in adults and children without HIV infection.

Methods: Sub-study of an ongoing, longitudinal, prospective cohort study (COVID-19 Family Study) of children and their parents with SARS-CoV-2 infection at the CHU Sainte-Justine in Montreal, Canada (August 2020-ongoing). Children <18 years old with SARS-CoV-2 infection (i.e. index cases) were identified through the COVID-19 clinic registry, and were offered enrollment alongside their parents. Children living with HIV (CLWH) followed at CHU Sainte-Justine and their parents were eligible for inclusion. Serological testing was done between 4-6 months following the index cases's positive tests using the Diasorin (Liaison XL) assay against SARS-CoV-2 spike protein receptor binding (S1) and fusion (S2), with a mean antibody threshold of 15 AU/ml considered seropositive. Only individuals with a positive SARS-CoV-2 PCR at the time of their COVID-19 diagnosis were included in this analysis.

Results: 51 families were recruited to date, with complete results available for 19 adults and 25 children, including 5 ALWH(median age 46, range 32-50 years) and 7 children affected by HIV (median age 7.8 years, range 1-13 years) including 2 children living with HIV, and 5 HIV exposed and uninfected children. SARS-CoV-2 antibody titers were measured at a mean of 135 days (±81) in adults, and 139 (±49) days in children. Only 20% of ALWH (1/5) were considered seropositive (mean antibody threshold above 15 AU/ml), vs. 92% (13/14) of adults without HIV, p=0.02; median antibody titers were lower in ALWH than adults without HIV (11.8, IQR 7.3-13.8, vs. 48.8, IQR 28-108), p=0.06). All PLWH were on antiretroviral therapy, 3/4adults and 2/2 children with available viral loads were undetectable; median CD4 T cell counts among adults was 687 (IQR 603-844 cells/mm3). In contrast, all HIV affected children (7/7) (100%) were SARS-CoV-2 seropositive, with median antibody titer significantly higher than their parents (median 57.7, IQR 50-130 vs. 11.8, IQR 7.3-13.8) p= 0.06). Among the 14 adults and 18 children without HIV infection, antibody titers were again higher in children vs. adults (median 92.1, IQR 27-108 vs. 44.5, IQR 13.8-121, p=0.61), though the majority of individuals in both groups were SARS-CoV-2 seropositive (13/18, 72% children vs 12/14, 85% adults).

Conclusion: These results suggest that antibody production to the SARS-CoV-2 spike protein may be decreased among ALWH compared to the general population of adults, although children appear to have more robust antibody production than their parents. Further work needs to be done to understand the immunological response to infection, and vaccination, to SARS-CoV-2 among PLWH.

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SARS CoV-2 infection and Seroprevalence in HIV-infected adolescents

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Background: Due to the vulnerability of their immune system, data on the frequency and associated co-morbidity of COVID-19 in HIV infected populations is of utmost importance.

Methods: The study was a Prospective, Observational Study. Sixty-four HIV-1 infected adolescents (median age 20 years old) were enrolled between August to December 2020 at the University of Miami Miller School of Medicine. A self-reporting questionnaire was administered at the entry visit to gather information about their health status and COVID-19related symptoms pre-enrollment. All participants were screened at entry for active SARS CoV-2 infection via nasal-pharyngeal swab-based PCR (Labcore) and for SARS CoV-2 specific antibodies using both Laminar Flow (Confirm Biosciences) and an in-house SARS CoV-2 Receptor Binding Domain of Spike protein ELISA. Participants that were positive by either PCR or serology were followed up at 1- and 3-months post entry and their serum was collected and used to study longitudinal changes in their IgG and IgM titers.

Results: Participants reported no COVID-19 symptoms except one participant who described a temporary loss of sense of smell or taste. Using a combination of PCR, lateral flow and ELISA testing we evaluated the seroprevalence of SARS CoV-2 in our cohort. We found that HIV+ adolescents had higher SARS CoV-2 seroprevalence (25%, N=16 out of 64) when compared to the healthy population in the same time period (August-December 2020) and matching for age group (range 5% to 15%). Interestingly, only 2 out of the 16 positive participants were positive by PCR while the remaining 14 were positive by lateral flow and ELISA. Overall, we concluded that the majority of the SARS CoV-2+ HIV+ participants in our cohort were exposed to the virus before entering this study and had asymptomatic COVID-19.
Of note, we observed a significant loss of IgG titer in the 3 months follow up determined by ELISA in the majority (N=11) of the SARS CoV-2 positive HIV+ adolescents.

Conclusion: The seroprevalence of SARS CoV-2 in HIV+ adolescents was higher than most reported rates from testing of the general population. The longevity of antibodies against SARS CoV-2 is still an open question and it is of special importance in at-high-risk population such as the HIV infected individuals. The observed significant loss of antibodies needs to be characterized in better detail. We suggest that studies specifically designed to understand the persistence of IgG antibodies and their neutralizing ability should include HIV+ individuals including young adults.

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Health care worker experiences with COVID-19 in Kenya: personal protective equipment availability and service disruption for PrEP delivery for pregnant and postpartum women

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Background: COVID-19 has disrupted healthcare services delivery globally. Limited data exist about personal protective equipment (PPE) availability for health care workers (HCW) and perceptions of COVID-19 service disruption in low-resource settings.

Methods: The ongoing PrEPARE study invited HCW with experience delivering pre-exposure prophylaxis (PrEP) to pregnant and postpartum women in western Kenya to complete a self-administered electronic survey about the impact of COVID-19 on PPE availability and service delivery between October 2020 and March 2021. We used the Healthcare Worker Exposure Response & Outcomes (HERO) Registry Protective Equipment Survey to assess PPE availability and re-use. HCW reported perceptions of client volume changes and time spent doing various activities using a 5-point Likert scale ranging from large decreases through large increases.

Results: Of 126 HCW enrolled to date, 57 (45%) were performing clinical duties during COVID-19 and completed this survey, of whom 19 (33%) were nurses, 13 (23%) clinical officers, 7 (12%) nurse counsellors and 4 (7%) were social workers. Of these, 41 (72%) were female, 20 (35%) worked in both Maternal and Child Health (MCH) and Family Planning clinics, 17 (30%) in MCH clinics, 15 (26%) in HIV care clinics, and 1 (2%) in youth friendly clinics.

Among those performing clinical duties, HCW reported challenges procuring PPE; 55% reported challenges getting surgical masks, 86% getting respiratory masks, 82% getting face shields/goggles, 82% getting gowns, 37% getting disinfectants, 28% getting soap, and 29% getting gloves. Among HCW with patient contact, 58% reported reusing the same mask with every patient, and 14% with most patients, due to PPE shortages, when they would have otherwise used a new mask.

HCW reported reduced volume of women seeking services due to COVID-19; nearly two thirds reported decreases in antenatal (65%) and postnatal clients (67%), and 60% reported decreases in new PrEP clients and 61% reported decreases in PrEP refill clients. HCW experiences were mixed regarding time spent serving clients and client wait time, with comparable numbers reporting increases, decreases, and no change. HCW reported changes in how their time was spent; 81% spent more time disinfecting spaces between clients, 73% reported increases in number of hours spent attending to clients, and 51% reported providing more psychosocial care.

Conclusions: HCW reported a dual burden of PPE shortages, limiting their own protection during the pandemic, alongside increased burden in meeting the psychosocial needs of their clients.

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Gaps in knowledge about COVID-19 in adolescents and young people in Sofala and Tete

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Introduction: CUAMM has been working on HIV and adolescent projects in Beira City for over 15 years; and more recently, with support from UNICEF Mozambique, efforts have been increased through "Combating HIV among adolescent girls: increasing access to and adherence to HIV-related services and follow-up for adolescent girls at the community level in the city of Beira, with inclusion MHPSS "intervention
Since the end of March 2020, the Ministry of Health has started implementing various strategies to combat the COVID-19 pandemic. Adolescent and youth friendly services continue to provide health care, but those on antiretroviral treatment receive medications on a quarterly basis. However, assistance from users to health units is reduced. To evaluate the knowledge and awareness of COVID-19, a survey is carried out among users of services that are friendly to adolescents and young people.

Methods: A descriptive and cross-sectional study was carried out in April and May 2020 in ten adolescent-friendly services in the provinces of Sofala and Tete. The eligible population included users with a record of telephone contacts. A questionnaire with sociodemographic variables was administered, via telephone, on COVID-19 knowledge and preventive measures and for those HIV-positive, questions related to antiretroviral treatment. In the statistical analysis, the corrected Fisher's test and the Graph Pad Prism package, version 8.0, were used.

Results and discussion: 2170 adolescents and young people were interviewed, 1580 from Tete province and 590 from Sofala. Only 25% (543) adolescents and young people had a high level of knowledge about COVID-19. In the multivariate analysis, the significant predictors were female (OR = 1.47; 95% CI 1.23–2.89), having a house with a different roof from the straw roof (OR = 1.85; 95% CI 1, 02-2.95) and HIV seropositivity (OR = 1.56; 95% CI 1.36-2.87). The results agree with other similar studies in Africa.

Conclusion: The study describes an important and relevant knowledge gap in adolescents and young people before COVID-19 and draws attention to dedicate efforts to involve the population aged 10 to 24 in raising awareness in the face of the pandemic.
Doctors with Africa CUAMM in close programmatic-strategic collaboration with UNICEF Mozambique works to intervene in the structural fragility of the health system, as well as in the socio-cultural determinants highlighted and documented through this study. In particular, fragile categories such as HIV + pregnant teenagers must be able to receive quality health information in order to protect their pregnancy in order to ensure that they do not infect the fetus and protect it from other infections that are dangerous to their health. , for the unborn child and the whole community.

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Dolutegravir-Based ART is Superior to Standard of Care in Young Children Living With HIV

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Background: ODYSSEY, a multi-country randomised trial, demonstrated superior treatment efficacy for dolutegravir (DTG) plus two NRTIs versus standard-of-care (SOC) in 707 children ≥14kg (median age 12 years) starting first- or second-line ART. We report results for an additional cohort of 85 children <14kg, who completed 96 weeks follow-up on 28th June 2021.

Methods: The primary outcome is a Kaplan-Meier (K-M) estimated proportion of treatment failure defined as confirmed viral load (VL) ≥400c/mL after week 36, lack of virological response by 24 weeks with ART switch for failure, death, or new/recurrent WHO 4 or severe WHO 3 event by 96 weeks. Bayesian estimation was pre-specified as the primary analysis of participants <14kg, incorporating evidence obtained from the ≥14kg participants as a prior distribution, with relative weight 78%, based on clinical opinion elicited before availability of results for children ≥14kg.

Results: 85 children <14kg were randomised (Uganda 43, Zimbabwe 22, South Africa 20); 42 to DTG and 43 to SOC. Median (range) age was 1.4 years (0.1-5.9); 23 were 3-<6kg, 40 were 6-<10kg and 22 were 10-<14kg. 72 children started first-line (29/37 PI-based among SOC); 13 second-line (3/6 PI-, 2 raltegravir- and 1 nevirapine-based among SOC). Median (IQR) follow-up was 120 (97-132) weeks; 5 (6%) children were lost to follow-up. 11 children in the DTG arm had treatment failure by 96 weeks (K-M estimated proportion 28%) vs 21 (48%) SOC; 8 vs. 16 failures were virological. 8 (25%) DTG vs 17 (46%) SOC failed on first line; 3 (48%) vs 4 (60%) failed on second-line. The Bayesian estimated difference in treatment failure (DTG-SOC) in participants <14kg was -11% (95% CI -19%, -2%; P=0.02). A standalone analysis of the <14kg cohort provided an estimated difference in treatment failure of -20% (95% CI -38%, -1%; P=0.04). At 96 weeks, 77% of children in the DTG arm had VL<50c/mL compared with 50% in SOC (P=0.02); corresponding proportions with VL<400c/mL were 91% vs. 71% (P=0.03). There were 15 SAEs (11 children) in the DTG arm versus 19 (11 children) in SOC (P=0.92, comparing children), including 2 versus 4 deaths; 36 (19 children) had grade ≥3 adverse events in DTG vs 34 (21 children) in SOC (p=0.79). In the DTG arm, 41/42 children remained on DTG at last visit, with no changes to NRTI backbone; 1 child in DTG stopped ART 3 weeks post enrolment and withdrew 2 weeks later. In the SOC arm, 37/43 children remained on their initial treatment regimen at last visit; changes included 4 children who switched ART due to treatment failure.

Conclusions: DTG-based ART was superior to SOC (predominantly PI-based) in young children starting first or second-line, judged on treatment failure by 96 weeks. The treatment benefit for DTG in the <14kg cohort was consistent with that observed in children enrolled ≥14kg. There were no safety concerns on DTG. These results strongly support WHO guidelines recommending DTG-based regimens for young children and provide impetus for rapid procurement of dispersible dolutegravir.