

HIGHLIGHTS FROM INTERNATIONAL WORKSHOP ON HIV PEDIATRICS 2020

16-17 November, 2020

Day 1

Session 1: Global Update

The workshop was opened with a global update on paediatric HIV. Mary Mahy, Epidemiology Team Lead at UNAIDS, provided an overview of the epidemic in infants, children, adolescents and women as well as the impact of COVID-19 on HIV services. She shared recent data from countries reporting to the UNAIDS, UNICEF and WHO HIV services disruption tracker, which showed that declines took place in paediatric treatment, prevention of mother-to-child transmission (PMTCT) and early infant diagnosis (EID) services in most countries during the first half of 2020. PMTCT and EID appear to have returned to pre-pandemic levels but remain below global targets. She stressed that EID remains alarmingly low, and that two out of three undiagnosed children living with HIV are over the age of five years and must therefore be found through intensification of other interventions such as family-based index testing.

The UNAIDS 2020 update was complemented by Martina Penazzato, Paediatric HIV Lead at WHO Headquarters, who dissected the ‘double trouble’ for children caused by the intersection of HIV and COVID-19. She emphasized the need to unpack the direct effects of COVID-19 as well as the indirect effects of the pandemic from disruption of health services, in addition to the widespread secondary socio-economic impacts. HIV testing and viral load monitoring have been the most impacted HIV services, reducing the number of new ART initiations and expanding the existing treatment gap for children. Dr. Penazzato provided examples of mitigation strategies and [innovations](#) implemented by countries, stressing the importance of preparing to implement targeted ‘catch up’ interventions. Efforts to “build back better” should focus on person-centred approaches and placing families at the centre of a comprehensive package of care.

Dan Kuritzkes from Harvard Medical School / Brigham and Women’s Hospital, United States presented on advances in cure research across the lifespan with a focus on the importance of cure research in infants. He outlined the unique features and cure opportunities of perinatal HIV infection as well as the specific research challenges. Dr. Kuritzkes further presented promising findings from the Early Infant Treatment study in Botswana that aimed to limit the establishment of a viral reservoir by immediately initiating ART in infants that in were infected in utero and diagnosed as HIV positive at birth.

Session 2: Oral Abstract Presentations

Pediatric HIV Treatment – Old Drugs, New Drugs

Five presenters shared results from studies on various topics relevant for optimization of paediatric HIV treatment, using newer paediatric formulations and regimens.

- **Theodore Ruel, United States** presented results on 24-week safety, tolerability and efficacy of a five mg dispersible dolutegravir tablet (DTG-DT) paediatric formulation that is being evaluated in IMPAACT P1093. The results showed that a once-daily weight-band dosing of DTG-DT was well-tolerated in children aged four weeks to <six years, with a robust antiviral effect and improvement in CD4 parameters.
- **Rajendra Singh, United States** provided recommendations on paediatric DTG dosing derived from a combined P1093 and ODYSSEY population pharmacokinetic analysis. He noted that the recent Tivicay (dolutegravir, DTG) paediatric regulatory submissions propose WHO weight-band based recommendations for once-daily dosing in children \geq four weeks of age, which was informed by the analysis presented. Using the filmed coated tablet (FCT) and DT formulations, DTG dosing in children age \geq four weeks on an age/weight-band basis was found to provide comparable exposures to those historically observed in adults. Observed pharmacokinetic variability was higher in this paediatric population.
- **Eva Natukunda, United States** presented interim findings from a clinical trial on the safety, pharmacokinetics and efficacy of low-dose elvitegravir, cobicistat, emtricitabine, and tenofovir alafenamide (E/C/F/TAF) fixed dose formulation in virologically suppressed children living with HIV aged \geq two years. The single-tablet regimen (STR) E/C/F/TAF is currently approved for treatment in children age \geq six years and \geq 25 kg. The interim analyses showed that E/C/F/TAF low-dose STR was acceptable in young children, resulting in high virologic suppression.
- **Julient Mwangi, Uganda** presented findings from the LOLIPOP Study on the safety, pharmacokinetics and acceptability of abacavir, lamivudine, and lopinavir/ritonavir (ABC/3TC/LPV/rtv) granules (4-in-1) in children living with HIV (weighing three to 20kg) in Uganda. This first-line paediatric treatment combination has previously not been available for young children in a fixed dose combination. The strawberry-flavoured “4-in-1” granule formulation for children was found to be safe, well-accepted and effective in achieving or maintaining viral suppression amongst children.
- **Jason Bacha, Tanzania** shared trends and gaps from the roll-out of DTG for children and adolescents living with HIV (CALHIV) in 2019 in Tanzania. DTG was found to be well tolerated and effective in clinically diverse cohorts, and its use has shown promise in achieving viral suppression for many previously unsuppressed CALHIV.
- **Ogara Collin, Uganda** shared learnings from an assessment of caregiver acceptability of administering a new 4-in-1 ABC/3TC/LPV/rtv paediatric fixed-dose combination to children living with HIV. The 4-in-1 granule formulation was demonstrated to be highly acceptable by caregivers among all weight-bands compared to the pellets/tablet combination due to factors related to ease of administration, easy storage, appealing flavour, and child’s acceptance.

Diagnosis, Case-Finding, Retention and Viral Suppression in Children Living with HIV

The session included presentations of five different abstracts on HIV screening tools from Uganda and Malawi for outpatient testing of children; a randomized controlled trial comparing viral load point of care versus centralized laboratory testing in Zimbabwe; opportunities to find unidentified children living with HIV through family index testing; and factors associated with late presentation for early infant diagnosis in Kenya.

- **Rhoderick Machekano, United States** presented a simple HIV screening tool, which was validated in community settings and outpatient departments (OPD) in Uganda to target testing of children and adolescents more likely to be living with HIV. Used in OPD, the tool was found to be as efficient as paediatric index testing in Uganda and saved up to two thirds of unnecessary tests.
- **Vinie Kouamou, Zimbabwe** shared findings from a randomized controlled trial comparing viral load point-of-care (POC) versus centralized laboratory testing among children, adolescents and young adults infected with HIV-1 in rural Zimbabwe. POC provided earlier and efficient confirmation of viral load suppression, but with similar results for drug switching.
- **Anna Tallmadge, Malawi** shared results from use of a simple checklist for HIV screening of children between 2-12 years presenting in outpatient departments in Malawi, focusing on their mother's testing history as many of these children may have been 'missed' by PMTCT. Introduction of the screening tool reduced testing volumes by 27 per cent while increasing yields 270 per cent from baseline.
- **Megan Gleason, United States** presented opportunities to find the remaining unidentified children living with HIV through index testing, drawing on PEPFAR programme data and national demographic and health surveys from 23 African countries. The analysis showed that only 38 per cent of women living with HIV were offered family index testing from 2018 to 2020 in the countries studied, representing a missed opportunity to diagnose 513,215 children living with HIV
- **Agnes Langat, Kenya** shared learnings on the factors found associated with late presentation of HIV-infected infants for early infant diagnosis (EID) services in Kenya. Late enrolment into HIV-exposed infants (HEI) services included lack of maternal antenatal care attendance, new maternal HIV diagnosis, lack of maternal prophylaxis, HEI identification in outpatient or inpatient settings, and late infant immunization.

Session 3: Clinical Case Presentations were led by Natella Rakhmanina, Professor of Pediatrics at the George Washington University and Director of HIV Services at Children's National Hospital in Washington, DC, United States, and Sharon Nachman, SUNY Stony Brook, New York, United States. Cases were presented by Vanessa Rouzier, GHESKIO Centers, Haiti/Weill Cornell Center for Global Health (a case of tuberculosis diagnosed in the context of

the COVID-19 epidemic) and Elizabeth Whittaker (a case of multi-system inflammatory syndrome associated with COVID-19). Discussants included Nadia Sam-Agudu, Institute of Human Virology, Nigeria and Thanyawee Puthanakit, Chulalongkorn University Thailand.

Session 4: Undetectable = Untransmittable – Relevance to Breastfeeding

The focus of this session was to share evidence on the implications of undetectable = untransmittable (U=U) on breastfeeding in the context of post-natal prevention of mother-to-child transmission of HIV (PMTCT). Lynne Mofenson, Elizabeth Glaser Pediatric AIDS Foundation, first reviewed the evidence for MTCT in formula-feeding infants of women who started ART pre-conception versus during pregnancy. The data demonstrate that the viral load threshold for undetectability related to MTCT would have to be plasma HIV RNA under 50 copies/mL. For formula-feeding populations, U=U appears to apply if the mother starts ART preconception, achieves and maintains viral load suppression below 50 c/ml prior to pregnancy and through delivery. There are more limited data in breastfeeding populations. Intrapartum transmission cannot be easily distinguished from early breast milk transmission and are assessed together; a few studies have reported on MTCT through age 4-6 weeks (including in utero, intrapartum, and early breastmilk MTCT) stratified by maternal viral load, finding transmission can occur even in women with viral load <50 copies/mL at delivery. Few studies have provided data on final infant infection status at the end of breastfeeding stratified by maternal postpartum viral load, and data on postnatal transmission after age 1 month from women who are on ART preconception and consistently suppressed before and through pregnancy and during breastfeeding are not yet available. Current data suggest there may be some residual risk of postnatal infection after age 1 month even in women with undetectable postnatal viral load, but this risk appears low, under one per cent.

The presentation was followed by a panel discussion with advocates for women living with HIV from Kenya, Canada and the United Kingdom, in which each panellist shared their views on what U=U would mean for mothers living HIV, and the advocacy efforts that would be required to make this a reality for women. The panellists stressed the importance of providing women and peer supporters with evidence-based information that empowers individual decision-making. *“U=U is about choice and decision-making power”* – Fungai Murau, United Kingdom

Day 2

Session 5: Pediatrics

This session included perspectives on HIV disclosure, pre-exposure prophylaxis during pregnancy and breastfeeding, and global gaps and potential solutions for prevention of mother-to-child transmission.

Ann Petru, University of California San Francisco Benioff Children’s Hospital, United States and Regina Oladokun, University of Ibadan, Nigeria discussed the “why, when and how to” of HIV disclosure in the global north and south, highlighting the different approaches and implications depending on socio-economic, cultural and health systems setting. HIV disclosure is an important part of management of children and adults living with HIV and all clinics need to consider having guidelines on how and when it needs to be done and the process documented.

Jilian Pintye, University of Washington Seattle, United States reviewed the “why, what and how” of PrEP in pregnancy and breastfeeding. She presented findings from three connected studies (PRIYA, PrIMA, AGYW) that aim to address implementation science gaps for delivery of PrEP to pregnant women in Kenya. Initial results found high uptake of PrEP among young and adolescent women whose husbands/partners were known to be living with HIV, while low perceived risk of HIV acquisition and pill burden associated with PrEP were among the top reasons for both declining or discontinuing PrEP.

Benjamin Chi, University of North Carolina, United States presented global gaps in PMTCT and potential solutions to eradicate such gaps, which are included in the recent roadmap developed by UNICEF in collaboration with WHO and UNAIDS, [Going the ‘Last Mile’ to EMTCT](#). He described the steps in the roadmap at national level: 1) Developing a consultative process, 2) Determining the most important missed opportunities for PMTCT using the “stacked bar analysis” and identifying programmatic gaps, 3) planning and prioritizing interventions, 4) implementing, monitoring and evaluation. Factors to consider when adopting potential solutions include the strength of evidence and cost-effectiveness.

Session 6: Oral Abstract Presentations

Parallel abstract sessions took place on Adolescents and HIV, Mother to Child Transmission and COVID-19 in children.

Adolescents and HIV

- **Brian Zanoni, United States** presented an abstract on development and validation of the HIV Adolescent Readiness for Transition Scale (HARTS). The HARTS questionnaire is a validated scale that can be used to determine which adolescents may need additional interventions prior to transitioning to adult care to ensure retention in care and viral suppression.
- **Lindsey Reif, United States** presented findings from a randomized controlled trial on point-of-care (POC) viral load testing among adolescents and young adults living with HIV in Haiti. POC viral load testing was efficiently implemented in this low resource setting among adolescents and provided faster time to viral load results and adherence counselling and greater accuracy in ART adherence reporting.
- **Maureen Syowai, Kenya** shared findings on antiretroviral drug transition and adverse event monitoring among adolescents aged 15-19 years. One in every ten adolescents with HIV in Kenya had reported at least one adverse event on treatment; adolescents on

DTG-based ART had higher rates of viral suppression and no serious adverse events compared with those on efavirenz (EFV)-based ART.

- **Sibongile Wusumani, Swaziland** shared lessons from Eswatini on bringing HIV and SRH services closer to adolescent girls and young women through a comprehensive mobile package. It was found that delivery of integrated, friendly, and comprehensive services to these groups outside the health facility during convenient hours was feasible and can increase demand and uptake of services.
- **Joseph Fokam, Cameroon** presented results on archived HIV-1 drug-resistance variants in cellular reservoirs and its determinants among vertically infected adolescents failing ART. About one-third of adolescents with HIV in Cameroon experienced viral failure. Although plasma RNA remains the standard biomarker for detecting drug resistance mutations, about one-quarter of those failing ART had drug resistance detected in cellular compartments (which may be discordant from those found in the plasma RNA compartment).
- **Barbara Laughton, South Africa** shared insights on deficits in fine motor dexterity and auditory working memory in children with HIV starting early ART. Despite early ART in the CHER study and careful clinical management, persistent mild deficits were noted at age 11 years.

Mother to Child Transmission

- **Jillian Pintye, United States** presented a study that evaluated the extent of mother to infant tenofovir (TFV) transfer in utero using weight normalized TFV hair concentrations in mother-neonatal pairs in the United States. The study confirmed that there is in utero transfer and that such transfer is cumulative.
- **Alka Khaitan, United States** presented findings from a comprehensive analysis of 81 plasma biomarkers in a cohort of Kenyan children. Children who were HIV-exposed but uninfected (CHEU) did not exhibit more immune activation biomarkers than their HIV-unexposed (CHU) peers between age 18-36 months. HEU children had higher levels of soluble TIM-2 (an inhibitory immune checkpoint); soluble CD40 (negative regulators of CD49-CD40L interactions); and lower levels of some proinflammatory cytokines, chemokines and growth factors. Thus, the profile of CHEU was more immune suppressive rather than inflammatory.
- **Raji Balasubramanian, United States** shared results from a prospective cohort study on EID in the United States. Time to first positive HIV DNA PCR in infants infected with HIV-1 subtype B was found to be longer in infants exposed to maternal combination ART compared to those receiving single drug regimens. However, it was unaffected by infant ARV regimen.

- **Shu-Nan Jessica Li, Canada** presented a study investigating hospitalizations between 1990 and 2012 in Canada among CHEU, by antenatal ART exposure timing. CHEU experienced increased odds of hospitalization compared to control CHU; most of these hospitalizations occurred in the first month of life, and were intensive care unit admissions, particularly for neonatal abstinence syndrome. Preconception maternal ART tended to lower severity of hospitalizations compared to ART initiated during pregnancy.
- **Faith Moyo, South Africa** described the longitudinal evolution of maternal viral loads during pregnancy and postpartum among women living with HIV in South Africa. Only 63 per cent of pregnant women on ART reached a viral load <50 copies/mL by the time of delivery. Being older (≥ 25 years), having CD4 ≥ 200 cells/mm³ and having viral load <50 copies/mL at baseline were associated with a sustained viral load decline.
- **Alexander Moran, United States:** shared learnings on the role of stigma in PrEP initiation and persistence among HIV-uninfected pregnant women in South Africa. PrEP-related stigma was found to pose as an important barrier to both PrEP uptake and PrEP retention among pregnant and postpartum women at risk of HIV acquisition.

COVID-19 in Children

- **Ariana Traub, United States** presented findings from a multi-country analysis of the impact of COVID-19 on HIV services for children and adolescents living with HIV. PEPFAR's data showed that HIV testing in children living with HIV dropped by 40 per cent in 2020.
- **Cheryl Pikora from Gilead, United States** outlined challenges related to remdesivir pediatric development for SARS-CoV-2 infection. With children making up 10 per cent cumulatively out of the total COVID-19 case load in the United States, Gilead has commenced a study to determine dosing of remdesivir in paediatric patients. Study completion is expected at the beginning of 2021.
- **Nimasha Fernando, United States** presented findings from a multi-country analysis of the impact of COVID-19 on uptake of multi-month dispensing for children living with HIV on antiretroviral therapy. The mean percentage of children living with HIV receiving multi-month dispensing (MMD) through USAID support doubled from Q1 to Q3 in 2020. The majority of children received between three to five months MMD.
- **Alexandra Vrazo, United States** presented a multi-country study on the impact of COVID-19 on HIV services for pregnant and breastfeeding women and their infants. The data showed a decrease in the number of HIV positive women identified at ANC1 while the positivity rate trend remained unchanged. The speaker recommended the following additional adaptations: catch-up campaigns, SMS or phone consults by providers or

peer mothers to support post-partum women, and community-based PBS collection.

- **Isabella Lopez, United States** presented findings from a study on the use of a walk-in HIV and STI testing model for at risk youth ages 13 to 24, and an assessment of the impact of the COVID-19 pandemic on testing services. She presented trends over three years and disruptions caused by COVID-19, showing an average decline in overall

services of 34 per cent between May and September compared with January and February. HIV testing decreased by 13 per cent and STI testing by 33 per cent, while positivity rates remained the same when compared to previous years.

Session 7: COVID-19 in Pediatrics

Lynne Mofenson, Elizabeth Glaser Pediatric AIDS Foundation, provided an overview of the state of the knowledge on SARS-CoV-2 and COVID-19 in children. She highlighted that while reported infections in children remain lower than in adults, there is an increasing trend of infections among children, particularly adolescents. Data remain confounded due to low rates of testing among children due to higher rates of asymptomatic or mild disease. She highlighted that while some studies suggest that younger children (under age 10 years) may be less susceptible to infection, the data do not provide a clear picture on this nor on the ability of children to transmit the virus to others. She presented data demonstrating that despite young age, some outbreaks have been reported in infant and young childcare facilities in the United States and Poland, as well as among older adolescents.

Moherndran Archary, University of KwaZulu Natal, reviewed studies from various settings on COVID-19 in schools and day care settings, discussing how to get children back to school safely as a basic right to education. He weighed the risks and direct/indirect benefits of reopening schools. Studies from Sweden, Australia, Singapore, England and France have not found any major impact on the number of children infected with COVID-19 when schools were reopened with appropriate precautions in place, such as masking, social distancing and frequent handwashing. These studies also suggested that the main mode of transmission was between staff members, emphasising the need to protect staff at risk and develop guidelines for management of COVID-19 in schools.

Daniele De Luca, AP-HP Université Paris Saclay, reviewed the developing evidence on maternal to child transmission of SARS-CoV-2. He noted that while in utero mother-to-child SARS-CoV-2 transmission has been reported, it appears to be extremely rare. More common is transmission occurring in the peripartum or postnatal period, which may reflect horizontal rather than vertical transmission.

Elizabeth Whittaker from Imperial College London presented an overview of the clinical picture of paediatric COVID-19, including the multi-system inflammatory syndrome in children (MISC), as well as the currently available paediatric treatment options. Remdevisir and steroids have been the most common drugs used in children, however, children have largely been excluded

from clinical trials and there is a need for RCTs that include this age group. The safety data are reassuring, but there are currently no efficacy or outcome data on the use of remdesivir or dexamethasone in children.

Anthony Fauci, Director of the National Institute of Allergy and Infectious Diseases, United States presented recent updates on vaccine development and roll-out stages and highlighted how decades of HIV vaccine and treatment work have played an important role in multiple trials of COVID-19 vaccine candidates. He reviewed the lessons learned of doing clinical trials amid an outbreak by integrating clinical research into the epidemic response to Ebola and HIV.



This report was drafted by Rikke Le Kirkegaard, Programme Specialist, UNICEF Headquarters with inputs from Geoffrey Chipungu, HIV/AIDS Specialist, UNICEF Eastern and Southern Africa; Terezah Alwar, Adolescent and HIV Specialist, UNICEF Kenya; and Lynne Mofenson, Sr. Advisor to the Research Programme at Elizabeth Glaser Pediatric AIDS Foundation.