Modelling Paediatric HIV and the need for ART

Report and recommendations from a meeting of the UNAIDS Reference Group on Estimates, Modelling, and Projections
8 October 2021

REPORT & RECOMMENDATIONS

Index

Abbreviations

AIM	AIDS Impact Model
ANC-RT	Antenatal Clinic Routine Testing
ART	Antiretroviral Therapy
ASM	Age Structured Model
CLHIV	Children Living with HIV
EPP	Estimation and Projection Package
IeDEA	International Epidemiology Databases to Evaluate AIDS
LTFU	Loss to Follow Up
PHIA	Population-based HIV Impact Assessment
PMTCT	Prevention of Mother to Child Transmission
UNAIDS	Joint United Nations Programme on HIV/AIDS
VLS	VL Suppression

The meeting of the UNAIDS Reference Group on Estimates, Modelling, and Projections was organised for UNAIDS by the Secretariat of the Reference Group (www.epidem.org), managed at Imperial College London and the University of Cape Town. Participants of the meeting are listed at the end of this document (Appendix B).
Oli Stevens, October 2021

Background

UNAIDS Reference Group on Estimates, Modelling, and Projections

The Joint United Nations Programme on HIV/AIDS (UNAIDS) relies on impartial scientific advice from international experts in relevant subject areas to provide guidance on how to best calculate estimates and projections of the prevalence, incidence, and impact of HIV/AIDS globally. The UNAIDS Reference Group on Estimates, Modelling, and Projections acts as an 'open cohort' of epidemiologists, demographers, statisticians, and public health experts to provide scientific guidance to UNAIDS and partner organisations on the development and use of the tools used by countries to generate annual HIV estimates, which are the source for UNAIDS Global HIV epidemic estimates. The group is coordinated by a secretariat hosted at Imperial College London and the University of Cape Town. Work of UNAIDS Reference Group has been organised broadly into tracks:

- 'Technical update' work streams: These work streams are oriented to conducting research and providing technical feedback and guidance on specific updates for the suite of tools used for annual UNAIDS estimates, i.e., Spectrum, which includes the AIDS Impact Module (AIM), the Estimation and Projection Package (EPP), and the Case Surveillance and Vital Registration tool (CSAVR).
- 'Thematic' meetings: These meetings are focused on convening new research to catalyse innovation on specific aspects of HIV estimates that require substantial conceptual or methodological developmentMeeting Overview

Outline

The UNAIDS Reference Group held a virtual meeting on *Modelling Paediatric HIV and the need for ART* on 8th October 2021. The meeting featured presentations and group discussion to generate consensus recommendations. The programme was divided into the following sessions:

Session 1: Review of 2021 paediatric methods
Session 2: Paediatric estimates in concentrated epidemics
Session 3: Mother to child transmission

This report presents a summary of the meeting presentations and discussions. The presentations are available to meeting participants (Appendix B) at www.epidem.org (others, please contact the Secretariat via epidem@sun.ac.za). The final recommendations can be found at the end of this report. The recommendations (Appendix A) drafted at these meetings provide UNAIDS with guidance on generating HIV estimates, review current approaches, and identify required data to further improve HIV estimates. The meeting agenda and objectives are shown in Appendix C. Previous meeting reports are available at www.epidem.org. This transparent process aims to allow the statistics and reports published by UNAIDS and partners to be informed by impartial, scientific peer review.www.epidem.org. This transparent process aims to allow the statistics and reports published by UNAIDS and partners to be informed by impartial, scientific peer review.

Session 1: Review of 2021 paediatric methods

Mary Mahy presented the **paediatric estimates from the 2021 UNAIDS Estimates process and summarised challenges encountered by country teams**. Three changes were introduced to the paediatric model for the 2021 estimates:

- Revising the transition categories between CD4% and CD4 count as children living with HIV (CLHIV) transition from age 0-4 years to age 5-14 years,
- Updated estimates of breastfeeding duration among HIV positive women based on revised analysis of household survey data including omitting PHIA surveys with inconsistent skip patterns for breastfeeding data, and
- Updated on mortality rates estimates for children on ART incorporating newly available data from the IeDEA Consortium into on-ART mortality rates.

This resulted in slightly higher historical numbers of new mother-to-child infections, children living with HIV (CLHIV) and AIDS deaths, but minimal change to recent estimates. Spectrum paediatric estimates remained consistent PHIA survey estimates for paediatric HIV prevalence in most countries.

Remaining challenges included ANC data quality in Western and Central Africa, validation of paediatric mortality estimates, and incorporating country-level data on paediatric treatment retention.

Jeff Eaton presented **district-level paediatric estimates from Naomi**. Estimates are calibrated to ART programme data for ages 0-14 and, in countries with PHIA surveys, survey HIV prevalence and ART coverage. This is challenging as data are sparse. There are not data to inform district-level estimates of PMTCT coverage and MTCT rate. To constrain estimates, the district-level CLHIV estimates are linked to the national-level adult-to-paediatric HIV prevalence ratio and ART coverage by age. New paediatric infections at the district-level are calculated by distributing the national-level new infections proportional to district-level adult female prevalence and paediatric population size.

Reshma Kassanjee presented **updates to estimates of paediatric on-ART mortality** from IeDEA Consortium data. The model used to simulate outcomes following loss-to-follow-up (LTFU) has been refined with an improved fit to calibration data. Across sub-Saharan African regions, adjusting for LTFU increases the mortality rate by an average of 50%, with mortality decreasing from 2005 to 2017 between 11% and 90% across regions and ART duration categories.

- Early infant diagnosis data could be used as validation for the Naomi paediatric estimates (Wilford Kirungi, Jeff Eaton)
- Routine HIV testing data in South Africa should be used to explore subnational differences in paediatric testing (Leigh Johnson, Jeff Eaton)

Session 2: Paediatric estimates in concentrated epidemics

Hmwe Kyu presented an overview of a new **NIH R01 project on paediatric HIV estimation** with four key aims:

- Incorporate new data in estimation of MTCT and HIV burden in children aged 0-9
- Estimate new HIV infections in young adolescents
- Quantify the impact of biomedical, behavioural, and structural factors on new HIV infections and mortality in children
- Forecast paediatric HIV epidemic indicators to 2040

The project will extend EPP-ASM to estimate paediatric populations alongside the present adult calculations, and calibrate paediatric estimates to paediatric mortality, treatment, and HIV testing data.

John Stover presented Spectrum editor updates for paediatric estimates in concentrated epidemics. Six countries have input data on nosocomial paediatric HIV infections, which add to CLHIV and infections outside of the typical mother-to-child HIV transmission route. The nosocomial infection editor has been expanded to stratify by five-year age group to more accurately capture the age profile of CLHIV due to nosocomial infections. In some countries a significant proportion of 'new' PLHIV is due to recent migrants who were infected before arriving. A second editor has been added to stratify all HIV-positive in-migrants by age to improve estimates of resident vertical transmission.

Mary Mahy presented a summary of **challenges for estimating paediatric HIV concentrated epidemics**. A key challenge is accurately quantifying need for PMTCT in concentrated epidemic settings. HIV positive women in concentrated epidemics are members of key populations or partners of members of key populations with fertility different to that of women in the general population. Triangulating fertility rates from biobehavioural survey data, paediatric treatment data, or vital registration data has been challenging. Several countries have unrealistic PMTCT coverages (either exceeding 100%, or PMTCT coverage greatly exceeding adult female ART coverage), and cases where paediatric ART coverage exceeds adult ART coverage.

Discussion highlighted several suggestions to triangulate and improve paediatric HIV estimates in concentrated epidemic settings.

- Generally we expect paediatric ART coverage should increase with age (Leigh Johnson). However, Mary Mahy also noted that in the estimates for generalised epidemics there is often lower coverage in the 5–9-year-olds relative to 0-4 and 10-14 in generalised epidemics. There was not consensus about whether this was likely a realistic feature of paediatric ART coverage in these settings or represented implausible estimates.
- Vietnam and Malaysia may have health system data that would assist in validating the number of HIV-positive children (Annette Sohn)

- HIV testing could be included in serosurveys conducted when verifying hepatitis elimination and genetic newborn screening (Annette Sohn, George Siberry)
- Countries with ANC testing data should use the fertility rate ratio adjustment factor in Spectrum (John Stover). However, there was caution that in concentrated epidemics, antenatal HIV testing may be more likely to be prioritised among higher risk women, and therefore not representative of prevalence among all pregnant women.
- Conduct systematic analysis across countries of estimates for ratio of paediatric-to-adult ART coverage and PMTCT coverage-to-female ART coverage to inform thresholds outside which estimates should be reviewed (Mary Mahy, Jeff Eaton)
- Spectrum should display modelled paediatric AIDS deaths with vital registration data as a validation output (Jeff Eaton)

Session 3: Mother to child transmission

Leigh Johnson presented on **challenges with using IeDEA VLS data to stratifying estimates of MTCT rate** by viral load. Routinely collected data on maternal VLS are not yet widely available, and IeDEA data are not suitable as they are not necessarily nationally representative and do not record date of conception or gestation which means it is difficult to ascertain the timing of viral load measurement within a pregnancy.

Discussion of this presentation reinforced the challenges of using VL among pregnant women to model MTCT:

- It is difficult to use viral load data during pregnancy because it does not capture post-partum breastfeeding transmission (Lynne Mofenson)
- A model could accept both viral load and CD4 count (Andrea Ciaranello) but the model complexity would be excessive for data commonly available in most countries (Caitlin Dugdale, Lynne Mofenson)

Lynne Mofenson presented an update on new data about **MTCT rates from 2019-2021**. There were nine new studies with sufficient data to consider including in meta analysis. Considering peripartum transmission in breastfeeding populations, pooled infant HIV prevalence across six studies was 0.61% (0.14% if ART start was before pregnancy, and 1.81% if started during pregnancy). Two studies measured postnatal transmission in breastfeeding populations estimated a risk of HIV transmission of 0.053%/month.

Oli Stevens presented **survey-based adjustments to PMTCT need and new child infections in Mozambique.** Mozambique has reported PMTCT and ANC coverages over 100% since 2016 and sharp declines in ANC-RT HIV prevalence in some provinces. Survey-reported ANC attendance at last pregnancy was used to estimate the number of double-counted ANC visits, which were removed from the ANC-RT HIV prevalence denominator, increasing ANC-RT HIV prevalence. By increasing HIV prevalence in pregnant women, PMTCT coverage was reduced to under 100% in all

provinces without any adjustment to the number of women receiving services. New child infections increased from 13,000 to 17,000 in 2020.

Key points from the discussion were:

- Expand the Mozambique ANC adjustment analysis to countries in West and Central Africa which have ANC and/or PMTCT coverage >100% (Mary Mahy)
- Many countries do not have usable data to quantify trends in HIV prevalence and incidence and there is a need to seek sentinel-type surveillance to monitor the epidemic (Jeff Eaton). The quality of routine ANC data in South Africa has been variable and retaining ANC surveys has been useful (Leigh Johnson)

Appendix A

Recommendations

Recommendation	Lead person(s)	Timeline
Session 1: Reviewing 2021 estimates		
<u>Naomi paediatric estimates</u>		
• Use early infant diagnosis data to triangulate distribution of paediatric new infections	UNAIDS / Jeff Eaton	2022
• Triangulate South Africa estimates with paediatric HIV testing data using similar approaches as Thembisa	Jeff Eaton / Leigh Johnson	2022
<u>Paediatric on-ART mortality</u>		
• No change is recommended to the paediatric on-ART model		
• Future IeDEA analyses should directly estimate smooth rates, pending review of the transition between paediatric and adult on-ART mortality models	Avenir Health / Leigh Johnson / IeDEA	2022 and beyond
Session 2: Paediatric estimates in concentrated epidemics		
<u>Validating estimates</u>		
• Conduct systematic analysis across countries of estimates for ratio of paediatric : adult ART coverage and PMTCT coverage : female ART coverage to inform thresholds outside which estimates should be reviewed	UNAIDS	November 2021
• Where available, countries in concentrated epidemic settings should calibrate fertility rate ratios to routine ANC testing HIV prevalence data	UNAIDS	
• Conduct systematic comparison of concentrated epidemic estimates with and without fitting local FRR adjustment factor	John Stover	2022 Paediatric Reference Group meeting
• Display validation of modelled paediatric AIDS deaths compared vital registration cause of death data. ○ Pre-populate paediatric AIDS deaths validation display with data from either WHO mortality database or GBD adjusted deaths estimates	Avenir Health	November 2021
<u>New data sources</u>		
• Consider including HIV testing as part of existing serosurveillance monitoring hepatitis elimination	UNAIDS	2022 and beyond

• Consider HIV testing dried blood spots collected for genetic newborn screening	UNAIDS	2022 and beyond
• Review data audits conducted to assess MTCT elimination for additional data to triangulate paediatric HIV estimates	WHO	2022
<u>Estimate review</u>		
• Recommend country case studies with strong vital registration and treatment data and discrepant paediatric estimates	UNAIDS	October 2021
• Review data from Malaysia and Vietnam to validate estimates of HIV+ pregnant women	UNAIDS	
Session 3: Mother to child transmission		
• Maternal viral load suppression is not recommended for inclusion within the Spectrum paediatric model at this time due to data quality issues		
• Consider re-estimating peripartum transmission rate if incorporating new data from updated Mofenson review impacts pooled estimate	TBC	November 2021
• Expand ANC adjustment analysis to include: o Western and Central Africa o Demographic surveillance site	Oli Stevens	2022
o Review and triangulate Mozambique case study ANC testing data with ICAP programme data	Fatima Tsouris, Oli Stevens	December 2021
• Consider suggesting countries should use sentinel surveillance if routine data are of poor quality to (1) provide sufficient quality data on ANC HIV prevalence and treatment coverage for monitoring and modelling epidemic trends, and (2) support programme monitoring and evaluation towards the creation of robust routinely collected HIV programme data	UNAIDS	2022 and beyond

Appendix B

Participants

Name	Organisation
Rob Glaubius	Avenir Health
John Stover	Avenir Health
Ray Shiraishi	CDC
Steve Gutreuter	CDC
Fatima Tsiouris	ICAP
Hmwe Kyu	IHME
Oli Stevens	Imperial College London
Rob Ashton	Imperial College London
Jeff Eaton	Imperial College London
Mathieu Maheu-Giroux	McGill University
Andreas Jahn	MoH Malawi
Wilford Kirungi	MoH Uganda
Isaac Taramusi	MoH Zimbabwe
Annette Sohn	amFAR
Aderonke (Solape) Ajiboye	CDC
Caitlin Dugdale	Harvard University
Lynne Mofenson	Independent Consultant
Milly Marston	LSHTM
Andrea Ciaranello	MGH
Rohan Hazra	NIH
Mary-Anne Davies	University of Cape Town
Alison Drake	University of Washington
Athena Pantazis	
Laura Broyles	
Rachel Vreeman	
Deepa Jahagirdar	Stanford University
Josh Salomon	Stanford University
Peter Ghys	UNAIDS
Keith Sabin	UNAIDS
Mary Mahy	UNAIDS
Ian Wanyeki	UNAIDS
Gatien Ekanmian, Gatien	UNAIDS
Taoufik Bakkali	UNAIDS
Mary Ann Seday	UNAIDS
Eby Pascal	UNAIDS
Rangaiyan Gurumurthy	UNAIDS
Stanley Kamocha	UNAIDS
Lev Zohrabyan	UNAIDS

Chibwe Lwamba	UNICEF
Savvy Brar	UNICEF
Reshma Kassanjee	University of Cape Town
Leigh Johnson	University of Cape Town

Appendix C

Agenda

All times are London time (GMT+1)

Time	Duration (mins)	Topic	Presenter(s)/ Lead Discussant
15.30	10	Welcome and introductions	Mary Mahy
15.40	10	Meeting objectives	Leigh Johnson
Session 1: Review of 2021 paediatric methods (chaired by Leigh Johnson)			
15.50	15	Review of 2021 estimates and pending challenges	Mary Mahy
16.05	10	Reviewing Naomi paediatric methods	Jeff Eaton
16.15	10	leDEA estimates of paediatric on-ART mortality • Mortality rates by single year of age	Reshma Kassanjee
16.25	15	Discussion	
Session 2: Paediatric estimates in concentrated epidemics (chaired by Jeff Eaton)			
16.40	10	NIH project development plan	Hmwe Kyu
16.50	10	Spectrum paediatric editors for concentrated epidemics • Immigrant CLHIV by age • Nosocomial infections by age	John Stover
17.00	20	Reconciling mortality and programme data with Spectrum paediatric estimates in concentrated epidemics • Numbers on ART • AIDS deaths	Mary Mahy
17.20	10	Break	
17.30	40	Discussion	
Session 3: Mother to child transmission (chaired by Mary Mahy)			
18.10	15	Viral load suppression in pregnant women	Leigh Johnson
18.25	15	Reviewing transmission probabilities through the DTG transition	Lynne Mofenson
18.40	15	Survey-based adjustments to PMTCT need and ANC clients in Mozambique	Oli Stevens
18.55	20	Discussion	
19.15	10	Recommendations	
19.25	CLOSE		

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