Technical updates for UNAIDS-supported estimation tools

Report and recommendations from a meeting of the UNAIDS Reference Group on Estimates, Modelling, and Projections
5-8th October 2020

REPORT & RECOMMENDATIONS

Abbreviations

ADR	AIDS Data Repository
ANC	Antenatal clinic
ART	Antiretroviral therapy
CDC	US Centers for Disease Control and Prevention
CLHIV	Children living with HIV
EPP	Estimation and Projection Package
IeDEA	International Epidemiology Databases to Evaluate AIDS
PEPFAR	US President's Emergency Plan for AIDS Relief
PHIA	Population-based HIV Impact Assessment
PLHIV	People living with HIV
(P)MTCT	(Prevention of) Mother to Child Transmission
UNAIDS	Joint United Nations Programme on HIV/AIDS
WHO	World Health Organization

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, the University of Cape Town, and Stanford University. Participants of the meeting are listed at the end of this document.

Oli Stevens, October 2020

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, the University of Cape Town, and Stanford University.

Meeting Overview

The UNAIDS Reference Group held its virtual thematic meeting on *Technical updates for UNAIDS-supported estimation tools* from 5-8th October 2020. The meeting featured presentations and group discussion to generate consensus recommendations. The programme was divided into the following sessions:

1. Spectrum updates
2. The AIDS Data Repository and Naomi
3. Natural history model
4. COVID-19 and HIV
5. Key populations in sub-Saharan Africa
6. Medical male circumcision
7. Evolving patterns of HIV incidence
8. Viral load suppression
9. AIDS Epidemic Model
10. CSAVR

This report presents a summary of the meeting presentations and discussions. The presentations are available to meeting participants at www.epidem.org (others, please contact the Secretariat via epidem@imperial.ac.uk). The final recommendations can be found at the end of this report.

The recommendations drafted at these meetings provide UNAIDS with guidance on generating HIV estimates, review current approaches, and identify required data to further improve HIV estimates. 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.

The list of participants and meeting agenda are included in Appendix I and Appendix II, respectively.

Introduction: Overview of UNAIDS Estimates Process and Impacts of COVID-19 on Process

Mary Mahy provided an overview of the 2020 estimates process, through which 170 national estimates teams were supported by UNAIDS to create annual HIV estimates during January to April 2020. Due to competing demands of the COVID-19 pandemic on Ministries of Health and estimates teams, 124 files were submitted. Participation was most reduced among countries from Western Europe and other high-income countries where the impacts of COVID-19 have been most severe. Notable challenges included:

- Teams from from China, India, and Russia do not formally participate in the UNAIDS estimates process
- Ensuring sufficient time to validate input data, particularly at the district level for Naomi
- Data on loss-to-follow-up in HIV treatment is often unavailable
- Estimation tools have become fragmented and the modelling workflow can be difficult for country teams to navigate

The estimates workshops for the 2021 estimates will be held virtually and will be used as an opportunity to improve capacity building tools to assist countries in moving through the estimates process. This will include webinars with facilitators, focused pre-recorded videos for core steps, and improved user manuals.

Session 1: Spectrum updates

An online Naomi results viewer has been developed to visualise district-level results without downloading Spectrum or using the dedicated Naomi web interface. This will assist with disseminating Naomi results to those unfamiliar with Spectrum.

Separate, web hosted, HIV modelling tools—including Shiny90 and Naomi—have been used alongside Spectrum for recent estimates rounds. Feedback from estimates teams indicates this produces a fragmented workflow, and it can be difficult to know when Spectrum needs to be rerun following changes to Shiny90. A flag within Spectrum has been included to indicate to users when this needs to be done.

Development work to consolidate estimation codebases is ongoing. A codebase has been developed in Rust for all adult AIM calculations. Next steps will include increasing the efficiency of the code, reading PJNZ files, and adding additional calculations to be used by EPP and Shiny90. The expected timeline is implementation for the 2022 estimates process.

Development work for Spectrum on the Web is in the final stages. Remaining components are linking to EPP online and the AIDS Data Repository (ADR). Spectrum on the Web will be usable with slow or intermittent internet connections as model calculations are carried out in the cloud, rather than locally. Several new data display editors have been created for Spectrum on the Web, including graphical

displays of programmatic data and progression parameters, and comparison charts of different indicators. Both Spectrum Desktop and Web will be made available for this estimates round, with both platforms supported in parallel for a few years before transitioning to the online platform.

Updates to Shiny90 were presented by Mathieu Maheu-Giroux. Shiny90 will be maintained as a separate web application this year, with past years' HIV testing data to be added to the ADR to streamline the data input pipeline for country estimates teams. New developments for this year are:

- Time from infection to diagnosis, probability of getting tested within one year of infection, and probability of getting tested before reaching a given CD4 threshold will be available as a spreadsheet download through the web application.
- Calculation of uncertainty around the above metrics is computationally intensive, and only point estimates will be made available through the web interface. Uncertainty bounds will be available through the *first90* R package
- Age-specific outputs by five-year age groups up to 50+ will be produced by disaggregating existing age 15+ results
- New HIV infections are to be intercalated throughout the year, transitioning from an end-of-year approach. This is expected to increase knowledge of status by ~2% for tested countries

To mitigate the impact of COVID-19-related service disruption on Shiny90 estimates, countries should be encouraged to input sex-disaggregated programme data (both number of tests and test positivity) as antenatal services may have been less disrupted than other testing modalities. Future model development will include:

- Incorporating HIV self-testing data and data on testing modality
- Key population stratified estimates
- Incorporating the modelling interface within the Spectrum workflow

Key points from discussion

- Consider extending age disaggregated outputs In Shiny90 beyond 50+ to include 50-54, 55-59, 60+ (Eby Pascal)
    - Older surveys may present issues with data sparsity at ages 50+ (Mathieu-Maheu Giroux)
    - This would also require reviewing the approximation in EPP of constant ART coverage in ages 50+ (Jeff Eaton)
- Uncertainty around PLHIV and HIV incidence is not currently accounted for in Shiny90 and uncertainty in Shiny90 estimates is not reflected in Spectrum uncertainty analysis (Jeff Eaton)
- *The effects of COVID-19 and knowledge of status estimates is further discussed below in Session 4*

Session 2: The AIDS Data Repository and Naomi

Twenty-one countries used Naomi to estimate HIV at the district level in the 2020 estimates and a further 18 used Spectrum's district estimates disaggregation tool.

Key requests from the 2020 estimates round was the expansion of Naomi outputs to include PMTCT, AIDS deaths, and knowledge of HIV status. Common challenges were reaching a consensus on district level populations, compiling and validating HIV programme input data on the routine ANC testing and the number on ART, and reconciling Spectrum national estimates with Naomi district level results.

The AIDS Data Repository was used by country estimates teams during the 2020 estimates process as a data store for Naomi district-level input data. Further development has since expanded the ADR's function, including automating importing district-level programme data from DHIS2, consolidating inputs for estimation tools into packages, and archiving final model results.

Rob Ashton presented key changes to the Naomi interface for the 2021 estimates round.

- **Project view** - Users can now manage multiple model runs that can be shared with other registered Naomi users. Future development will allow side by side comparison of results from different model runs
- **ADR integration** – Data stored in the ADR can now be directly imported into Naomi
- **Data display** – Tabular data view and customisable colour scales are now available
- **Separation of calibration from model fitting** – Users can run calibration to Spectrum without refitting the model, aiding sensitivity analyses and understanding the effects of calibration
- **Summary report** – an automatically generated summary report of key indicators will be available for users to download alongside model results.

Naomi model updates were presented by Jeff Eaton, including:

- **Accounting for complex survey design** – standard survey analysis incorporates design-based standard errors. As these are challenging or impossible to calculate in small strata, Naomi currently uses the unweighted observed sample size as the denominator. The Kish effective sample size approximation will be used for the 2021 estimates, accounting for unequal respondent weight.
- **ANC testing cascade** – estimates by five-year age group will be produced by incorporating district level estimates of fertility to the existing internal calculations of age-specific ANC testing cascade
- **Awareness of status** – estimates will be produced by applying the national level proportion aware amongst untreated PLHIV from Shiny90 to district level proportion untreated.
- **Tools for recoding and processing household survey data** – developing an R package to create user-friendly tools for country teams to reproduce finely disaggregated survey datasets.

Key points from discussion

- Can the Spectrum disaggregation tool or Naomi be expanded to produce subnational estimates outside of SSA? (Chibwe Lwamba)

    - The Spectrum disaggregation tool and Naomi are designed for use in generalised epidemics where antenatal prevalence can guide disaggregation. Future development of concentrated epidemic tools guided by case reports and AIDS death data at the subnational level will be required (John Stover/Jeff Eaton)
- Clear guidance is required for users on how to conduct and interpret sensitivity analyses of Naomi model results and model calibration steps (Mary Mahy)
- Age-disaggregated ART coverages at the district level can exceed 100% when calibrating to Spectrum, as cross-district ART reallocation adjusts total numbers on ART for ages 15+. Further examination of calibration methods to Spectrum is required. (Wilford Kirungi/Jeff Eaton)

Session 3: Natural history model

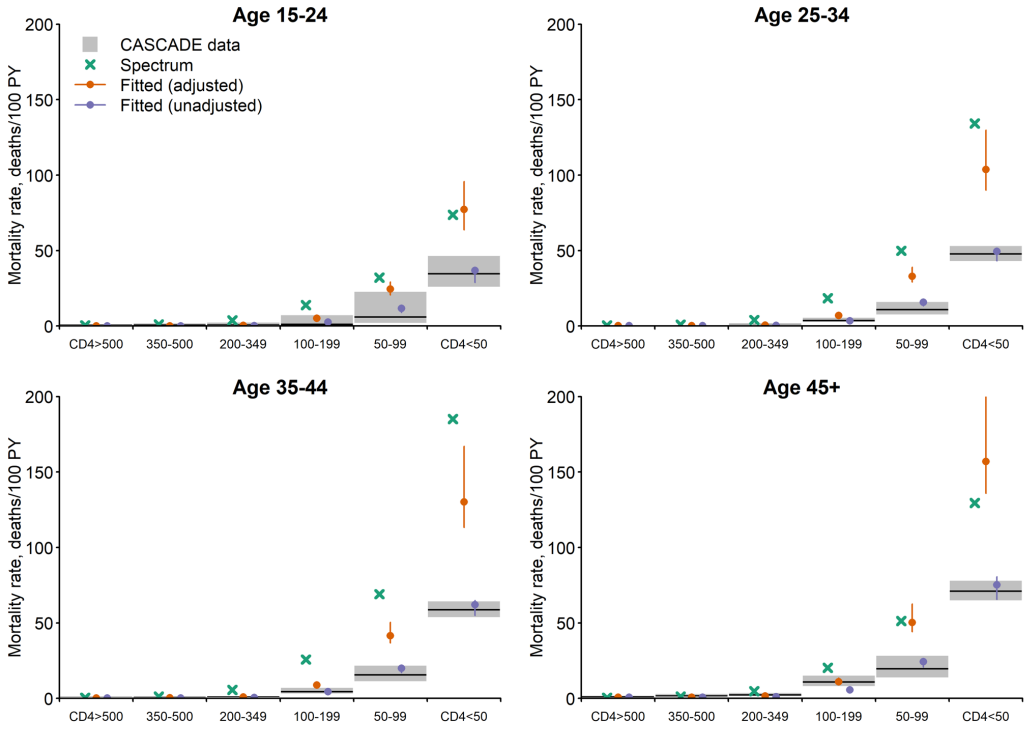
Rob Glaubius presented an update about ongoing analysis of proposed revisions to the Spectrum/AIM assumptions about HIV CD4 progression and mortality in light of new evidence from cross sectional household surveys [1], [2]. Comparison of current national Spectrum results about the CD4 distribution of untreated adults with PHIA survey data indicate a lower proportion of untreated PLHIV with CD4 <200 cells/μL in Spectrum compared to the PHIA surveys and a higher proportion with CD4 >500 cells/μL. Comparison with estimates from the CASCADE collaboration of HIV seroconverter cohorts indicated a lower average CD4 count at HIV seroconversion and lower mortality rates at low CD4 categories than current Spectrum parameters. These observations both imply that untreated PLHIV spend more time at lower CD4 count categories, consistent with observations from PHIA survey data.

Continuous models, stratified by ages 15-24, 25-34, 35-44, 45+, were fit to data about:

- CD4 category at seroconversion (data from CASCADE Collaboration)
- All-cause mortality rates by CD4 category (data from CASCADE Collaboration)
- Survival after seroconversion with untreated HIV (data from ALPHA network)
- CD4 categories among untreated PLHIV (data from PHIA surveys)

Previously examined models aligned well to CASCADE mortality estimates. However, in order to fit survival after seroconversion from the ALPHA network with low HIV-related mortality, rapid CD4 decline was required relative to Spectrum defaults, resulting in a large proportion initiating ART at CD4<50. Validation with ART initiator cohort data suggested that this was implausible. Consequently, a mortality rate ratio (MRR) parameter has been included in model fitting to allow for a systematic difference between mortality experienced by CASCADE participants in high-income settings and those experienced in sub-Saharan Africa. Precedent exists for systematic differences in mortality between settings, with Mangal et al. estimating 2.68 times higher mortality in SSA compared to WCENA [3].

When including the mortality rate ratio parameter, estimated natural history parameters indicated CD4 cell counts at seroconversion are lower than Spectrum defaults, consistent with CASCADE data, and PLHIV progress faster through higher CD4 categories, spending more time in lower CD4 categories. Mortality rates are estimated to be 2.1 times higher than those from CASCADE with HIV-related mortality rates by CD4 count largely lying between Spectrum defaults and CASCADE data (Fig 1 and 2). Fitted estimates of survival after seroconversion are similar to those in Spectrum, the ALPHA data, and survival estimates from CASCADE data [4]. Removing the MRR from model fitting produces longer survival estimates that lie further from ALPHA and CASCADE data, indicating that the MRR adequately captures mortality across settings.



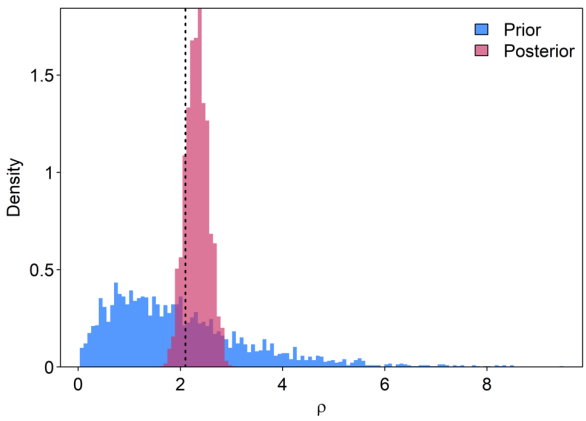


Figure 1 (top): Age-specific mortality rates by CD4 category. The model from which adjusted fitted rates are derived includes the mortality rate ratio parameter, and whilst the model for unadjusted fitted rates does not.
Figure 2 (bottom): Prior and posterior distributions for the mortality rate ratio parameter (Glaubius)

The model estimates ART allocation to be driven by eligibility over mortality (83:17 eligibility:mortality), compared to the Spectrum default of 50:50. This is challenging to interpret as there is an interaction between allocation weight and mortality. Mortality in the fitted estimates is concentrated in lower CD4 counts compared to Spectrum defaults. To approximate default ART initiation rates with fitted mortality rates, an ART allocation weight favouring eligibility is required, as ART initiation based on mortality would lead to little ART initiation at high CD4 counts.

Fitted estimates of CD4 distribution in untreated PLHIV match the PHIA survey data better than those using Spectrum defaults in six of nine countries. Estimates of CD4 distribution at ART initiation with CD4<50 are substantially improved when compared to IeDEA data than in previous versions of the model.

The impact of the fitted natural history model on adult HIV estimates in countries using either EPP-ASM or CSAVR in 2019 is given in Table 1.

	All	EPP-ASM countries	CSAVR countries
Ages 15+			
PLHIV	-4.8%	-5.5%	-1.2%
New infections	-5%	-7.9%	+2.1%
AIDS deaths	+15.3%	+19.8%	-8.3%
Off-ART AIDS deaths	+23.8%	+40.9%	-12.6%
On-ART AIDS deaths	+9.5%	+9.4%	+10.5%

Table 1: Impact of the revised natural history model by indicator and incidence model (Glaubius)

The average effects by model in Table 1 are not reflected in individual countries, where the effects on prevalence, new infections, and mortality are heterogeneous (Fig 3). Data used for incidence estimation, new diagnosis and AIDS deaths in CSAVR, and prevalence in EPP-ASM, may constrain changes in AIDS deaths and HIV prevalence respectively. Small decreases are seen in paediatric prevalence, new infections, and deaths, driven by the decrease in adult new infections.

In summary:

- Fitted parameters suggest more rapid disease progression and lower HIV-related mortality rates compared to Spectrum's current defaults
- Elaborating model to adjust for potential underestimation of mortality in CASCADE data preserves model fit to training data and substantially improves alignment with ART initiator data
- Compared to default inputs, fitted inputs:
    - Decrease estimates of 15+ PLHIV and new HIV infections in 2019 by ~5%
    - Increase adult HIV-related deaths by ~15%, comprised of a 24% increase in off-ART deaths and a 10% increase in on-ART deaths.

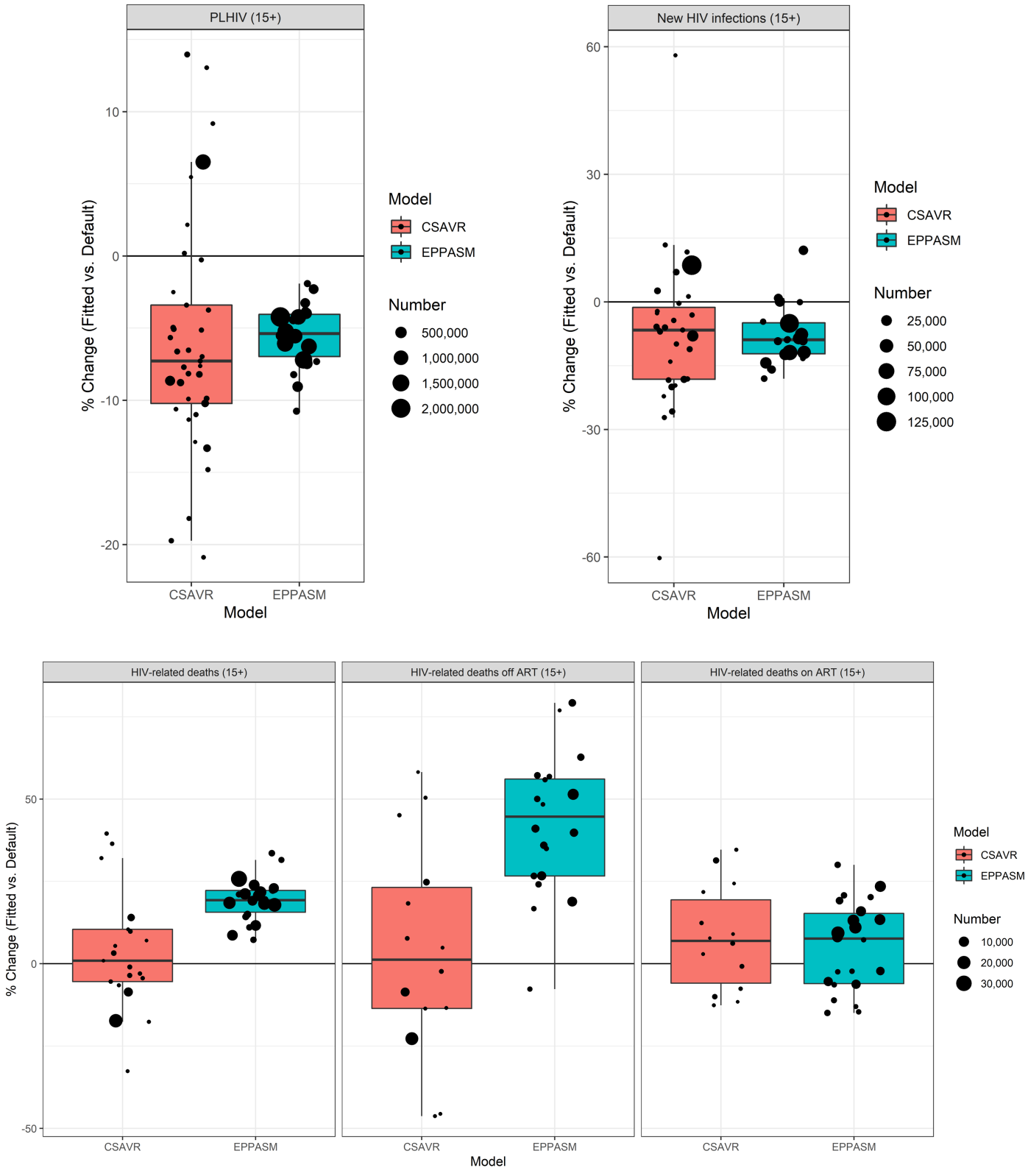


Figure 3: Heterogenous impact of revised natural history model by indicator, incidence model, and country (Glaubius)

Oli Stevens presented a case study of the proposed natural history parameters in South Africa. Estimates of AIDS deaths from Thembisa, calibrated to South Africa's vital registration system, provide a validation opportunity unavailable in other SSA settings. Estimates of AIDS deaths using Spectrum's default natural history model are 44% higher than in Thembisa (-38% and +108% for off- and on-ART deaths respectively). Parameter adjustments were made to the 2020 Spectrum file to ensure AIDS deaths matched those estimated by Thembisa, notably a 30-50% reduction in on-ART mortality compared to Spectrum defaults. When replacing the default natural history model with the fitted parameter set, the discrepancy between Spectrum and Thembisa widens (Total AIDS deaths +82%, off-ART deaths +16%, on-ART deaths +133%).

On ART mortality in Thembisa progressively decreases beyond a year's duration on treatment, the final category in Spectrum. As around half of AIDS deaths on ART are of PLHIV who have been on treatment for >5 years, their experienced mortality is higher in Spectrum than in Thembisa, and this may underlie some of the excess mortality seen in Spectrum.

Key points from discussion

<u>Revised natural history model</u>

- Is the mortality rate ratio adjusting for bias in the Dunn study data (comprising the data for high income countries) or a true difference between regions?
    - The MRR is adjusting for a true difference between regions (Rob Glaubius & Nikos Pantazis)
    - Additional evidence for longer survival in non-SSA settings will be reviewed

<u>South Africa case study</u>

- A direct comparison between the Thembisa and fitted natural history models may help explain differences in AIDS deaths (John Stover & Rob Glaubius)
- Consider a mortality adjustment parameter as implemented in Thembisa at CD4<200 to fit overall mortality (Jeff Eaton)
- Estimates of AIDS deaths are sensitive to the handling of treatment disengagement and dropout (Nikos Pantazis)

Recommendations:

- UNAIDS should adopt the revised, fitted natural history parameters, including:
    - The mortality rate ratio parameter, recognising evidence that indicates different HIV progression and CD4 distribution between regions
    - Updating the ART allocation weight from 50:50 to 83:17 eligibility:mortality
- Review the impact of the fitted parameters in Asia/Pacific estimates
- Conduct a more direct comparison between natural history models in Thembisa and fitted parameter sets

Session 4: COVID-19 and HIV

Kim Marsh presented data from a joint UNAIDS/WHO/UNICEF data collection platform on global disruptions of routine HIV services caused by the COVID-19 pandemic from January-July 2020. Fifty-six of 197 countries submitted HIV testing data, of which 26 reported trend data. Large, sustained decreases in HIV testing services were seen in all countries, with five countries recovering to pre-COVID-19 levels by July 2020. The testing positivity rate remained stable in the 7 countries with positivity data. Antiretroviral treatment services have been less affected: of 22 countries with trend data, only 5 reported declines. As most countries have a three-month LTFU definition, some treatment disruptions caused by lockdowns introduced later in the spring may not be detected in this dataset to July 2020. Declines in treatment initiation are seen in 21 of 22 countries from January to June, and 37 of 50 countries had smaller treatment scaleups than the same period in 2019. Whilst trend data on VLS were only available for nine countries, most showed rebounds following disruption and relatively stable, high viral load suppression estimates consistent with their end-2019 estimates.

John Stover described possible changes to Spectrum/AIM to capture the impacts of COVID-19:

1) **Treatment interruption:** A monthly data editor for numbers on ART can added to Spectrum to be optionally used by countries with significant treatment disruption. Countries with little disruption can continue to use annual inputs.

   The current implementation of ART interruption in Spectrum returns individuals to their initiating CD4 count. Studies in Europe & USA [5]–[9] suggest that after 8 weeks' treatment interruption, 40-73% of CD4 count gain while on treatment is lost & after 48 weeks' interruption 57-80% of CD4 gain is lost, with average CD4 count remaining above 500 (Fig 4). However, these studies selectively recruited those with high CD4 counts, and placed patients back on ART if CD4 decline was too steep. Touloumi et al (2006) [9], using CASCADE data, is likely the most representative of available studies and suggests average CD4 count after 48 week interruption is below 500, but still above count at initiation.

   Placing treatment interrupters one CD4 category higher than their initiating CD4 category produces a CD4 distribution most similar to Touloumi et al. This will also affect historical estimates for countries with non-zero LTFU, but will have a limited impact as 75% of countries have 0% LTFU in Spectrum, and the remainder have low LTFU (1-3%).

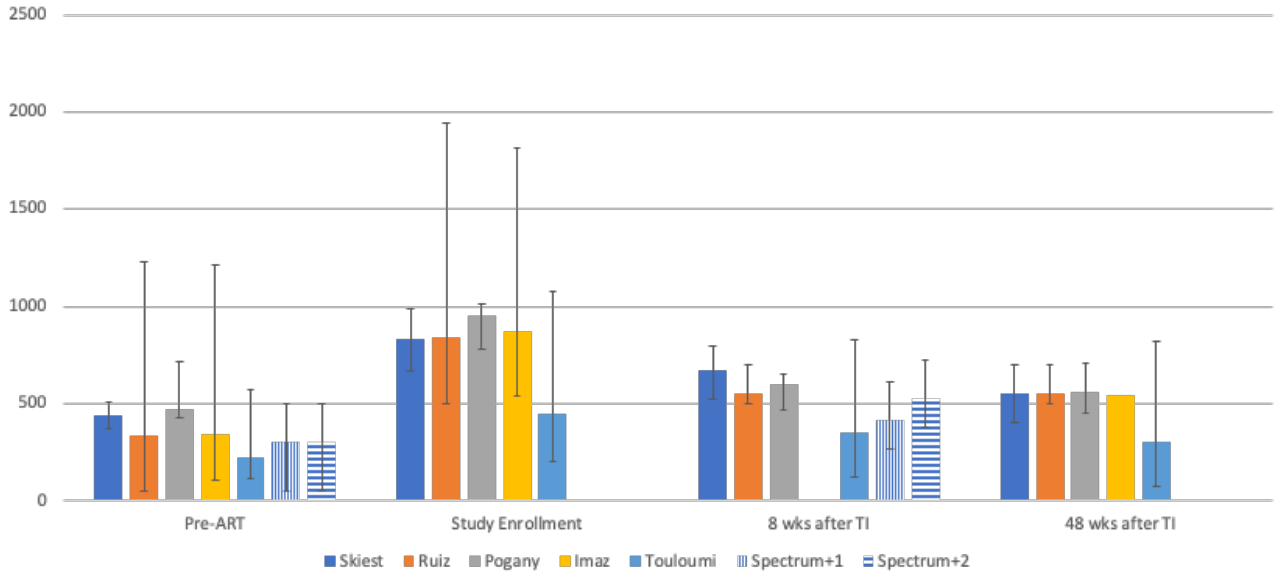


Figure 4: CD4 decline after treatment interruption (Stover)

2) **Increased risk of COVID-19 mortality in PLHIV:** Studies from Western Cape and the UK indicate an approximately two-fold increase in COVID-19 mortality among PLHIV [10], [11]. Based on these studies, the HIV-adjusted COVID-19 mortality rate from South African vital registration data would be 0.13%, resulting in around 10,000 excess COVID-19 deaths in South Africa due to HIV. This should be viewed in context of 70,000 AIDS deaths and 50,000 non-AIDS deaths among PLHIV in South African. Estimated excess COVID-19 deaths due to HIV outside of South Africa are expected to be minimal.

Key points from discussion

- Mortality in ART reinitiators may be overstated if they experience mortality rate of those on ART for <6 months when restarting treatment (Jeff Eaton)
    - A proportion of initiators could be assumed to be reinitatiors, informed by the LTFU rates entered into Spectrum, and the mortality rates for <6 months on ART downward adjusted accordingly (John Stover)
- The six-month treatment interruptions in Touloumi study were most often caused by treatment failure and led to a CD4 count loss of ~100. Placing treatment interrupters one CD4 category higher than their initiating category is a pragmatic recommendation (Nikos Pantazis)

Recommendations

<u>Programme data entry</u>

- A monthly treatment editor should be included in Spectrum. Countries may have treatment by calendar quarter, not by month, and should enter the same value for three consecutive months in the Spectrum monthly editor
- An editor to specify loss to follow up rates by month should be included in Spectrum

Treatment interruption

- PLHIV should be placed in a CD4 category one higher than their initiating category
- Consider adjusting the <6 month on-ART mortality rate downward if there are a large number of persons restarting ART after short disruptions to prevent overstatement of mortality in the first 6 months of ART.

Direct effects of COVID-19 mortality among PLHIV

- Increased risk of severe Covid-19 among PLHIV will have small net effect. Do not adjust mortality among PLHIV for increased risk of severe Covid-19 and death.

Shiny90

- Encourage countries to submit sex disaggregated HTS data.
- Data on service disruption indicate minimal change in test positivity, and expect impact on Shiny90 model calibration to be limited.

Session 5: Key populations in SSA

Keith Sabin presented an overview of the methods used to create estimates for new HIV infections among key population groups in the UNAIDS estimates. Estimates of population size (PSE) vary in quality, quantity, and national representativeness throughout sub-Saharan Africa. Outside of WCENA, only 13 nationally adequate population size estimates are available across all key populations for the period 2001-2017, and none in Eastern or Southern African countries. Population sizes, HIV prevalence, and ART coverage data are most readily available for FSW, followed by MSM, PWID, and TG populations.

Depending on epidemic setting and region, UNAIDS published estimates for new infections by risk behaviour are calculated from one of a) EPP/Spectrum estimates by key population, b) ECDC key population-stratified case reports, or c) applying regional medians where national data are not available. Estimates of incidence, relative risk of acquiring HIV compared to the general population, and new infections of sex partners of key populations can then be calculated. Age disaggregated estimates are available by applying age patterns derived from a limited number of published studies to estimates of new infections.

Key points from discussion

- Estimates from the Incidence Patterns Model, Goals, and Optima may be used for validation and modelled key population estimates completed as part of a national modelling exercise could be used as an input into official estimates (John Stover/Jeff Eaton/Leigh Johnson)
- A streamlined version of biobehavioural surveys – “BBSLite” – is being deployed in Jamaica and Cameroon to inform programme evaluation and epidemiologic surveillance. This lightweight survey may be able to be used routinely in the future (Keith Sabin)

- Key population size estimates within models should be reviewed (Tim Brown/John Stover)
- Models should be used to drive data collection, including data not yet used within the models e.g. modes of transmission in CSAVR case report data, and document the source of inputs (Peter Ghys/Tim Brown/Jeff Eaton)

Session 6: Medical male circumcision

Lycias Zembe presented an overview of the integration of VMMC coverage estimation into the annual UNAIDS estimates process. To date, estimates of district-level VMMC coverage have been created in ten countries through DMPPT2. For the 2021 estimates process, a further five countries will create district-level estimates.

Ongoing challenges included:

- Discrepancies between programmatic data sources
- Limited or outdated survey data
- Missing district-level data

UNAIDS, Avenir Health, and the Interagency Collaboration for Program Improvement (ICPI) have supported countries to collate and validate district-level programme data for input into DMPTT2. Future development will integrate estimation of VMMC coverage into Naomi, and subsequently use VMMC estimates to inform district-level incidence trends.

The data validation process was presented by Katharine Kripke. Most countries have convened relevant stakeholder meetings and are gathering, updating, and validating programme data, which will be stored within the ADR. Common issues included:

- Logistics: connecting HIV estimates teams and VMMC programme teams in country
- Redistricting and discrepancies with district lists
    - Alignment with Naomi area hierarchies
- Disaggregation of VMMC program data by five-year age band
- Location of medical circumcisions and cross-district service attendance
- Replacement of traditional circumcision with VMMCs thereby altering the base circumcision rate used in DMPTT2

An Excel-based data validation tool, presented by Randy Yee, has been used to support countries in visualising and exploring their VMMC programme data. Visualisations of numbers of circumcisions, disaggregated by district, calendar year, and five-year age groups, are available. As programmatic context differs between countries, systematic data quality thresholds have been established. Instead, districts can be sorted by standard deviation such that country teams may identify districts with implausible trends over time.

DMPTT2 uses a constant circumcision prevalence from before programmatic scaleup as a baseline to which medical circumcisions are added. This baseline

prevalence is a direct estimate from DHS data at national level and uniformly applied to all nested districts. For the 2021 estimates process, the national baseline prevalence is to be replaced with district-level modelled estimates of circumcision coverage derived from Cork et al., using estimates from 2008 to represent the pre-programmatic era [2]. District-level estimates from Cork et al. are for ages 15-49, and are distributed to five-year age groups based on the national age pattern of circumcision and the national population age distribution.

DMPTT2 will be retained as a separate web tool for the 2021 estimates round, and produce an outputs file which users will upload to Spectrum. Spectrum will collate estimates from Naomi and DMPTT2 and produce a single CSV file that can be read into the DataPack.

Key points from discussion

- A review of the VMMC estimation exercise will be held for countries to provide feedback on the use of the Excel validation tool and could be considered for use in the validation process for district-level ART and ANC data in Naomi (Mary Mahy/Jeff Eaton)
- DMPTT2 may be retired as a standalone web application and integrated into Naomi for the 2022 estimates process (John Stover/Katharine Kripke/Jeff Eaton)
- Develop data quality metrics for VMMC data and explore adding VMMC data review alongside ART data quality assessments (Peter Ghys)

Session 7: Evolving patterns of HIV incidence

Estimates of the number of new infections by sex and age group in Spectrum arise through a two-step modelling process. First, the total HIV incidence rate among adults age 15-49 is estimated by the EPP model based on the relationship

$$\lambda_{15-49}(t) = r(t) \cdot (\rho_{15-49}(t) \cdot (1 - \omega \cdot \alpha_{15-49}(t))$$

- $\lambda_{15-49}(t)$: HIV incidence rate among age 15-49
- $r(t)$: rate of HIV transmission for untreated age 15-49
- $\rho_{15-49}(t)$: prevalence age 15-49
- $\alpha_{15-49}(t)$: ART coverage age 15-49
- ω: Average reduction in transmission per 1% increase in population ART coverage.

The default value in EPP is $\omega = 0.7$. If all HIV positive adults were equally likely to transmit HIV, a natural choice for ω would be the proportion of treated adults who are virally suppressed (~0.9). The lower value $\omega = 0.7$ is a crude mechanism to capture that PLHIV on ART are on average also less likely to be exposed to HIV transmission, for example due to older age and longer duration of infection.

In the second step, the HIV incidence rate among age 15–49 are distributed to sex and age groups following a pattern of incidence rate ratios. The incidence rate ratios are calibrated for each country so that model estimates are consistent with age/sex-stratified prevalence data from national surveys. The incidence rate ratios are static over time in most countries, informed by analysis showing that time-varying incidence rate ratios did not improve the statistical fit to age-specific prevalence in most countries.

In UNAIDS 2019 estimates for sub-Sahara Africa, the number of new HIV infections has steadily declined in both ESA and WCA. Around 60% of new adult HIV infections were among females and 40% among males. Around half of female infections were estimated to be among age 15–24 years and 30% of male infections were among age 15–24 years. These percentages were relatively constant over time, consistent with the assumption of static incidence rate ratios.

The objectives for the session were a continuation of work presented at the Spring UNAIDS Reference Group meeting, where evidence from observational cohorts, clinical trials, and model-based estimates suggested changing patterns of HIV incidence over time [2]. It was recommended that evidence should collated to answer whether:

1. Current Spectrum estimates for the sex ratio and age distribution of incidence are consistent with empirical and modelling evidence
2. The sex ratio and age distribution of new infections has changed systematically over time
3. MMC has had an impact on HIV incidence up to 2020
4. MMC has affected the sex ratio of HIV incidence

5. The marginal impact of population ART coverage on HIV incidence is correctly specified in EPP (ω parameter)

Jeff Eaton presented a consolidated analysis of empirical data on HIV incidence patterns (ALPHA network, UTTT Consortium, and PHIA surveys) and a comparison with models that explicitly represent transmission dynamics in SSA (Goals-ASM, Optima, HIV Synthesis, and Thembisa). To assess the marginal effects of MMC and ART coverages on patterns of HIV incidence, three scenarios were used:

- **Baseline:** Best calibration to HIV epidemic setting.
- **No ART counterfactual:** No impact of ART on incidence in years 2005, 2010, 2015, and 2020.
- **No MMC counterfactual:** No increase in male circumcision coverage since 2008.

Sex ratio of new infections

Modelled estimates of the sex ratio of new infections show a similar pattern: stable between 2000-2010, and increasing thereafter with more new infections amongst women (Fig 5). In several settings, new infections in women outnumber those in men by more than 2:1 in 2020. Considering ALPHA network data, data in uMkhanyakude cohorts show a clear increase in sex ratio, while the remaining cohort sites have less clear evidence for an increasing proportion of new infections in women. Point estimates of the sex ratio of new infections from PHIA surveys lie above the Spectrum default of 1.5, though uncertainty around sex-stratified incidence rate ratios is large.

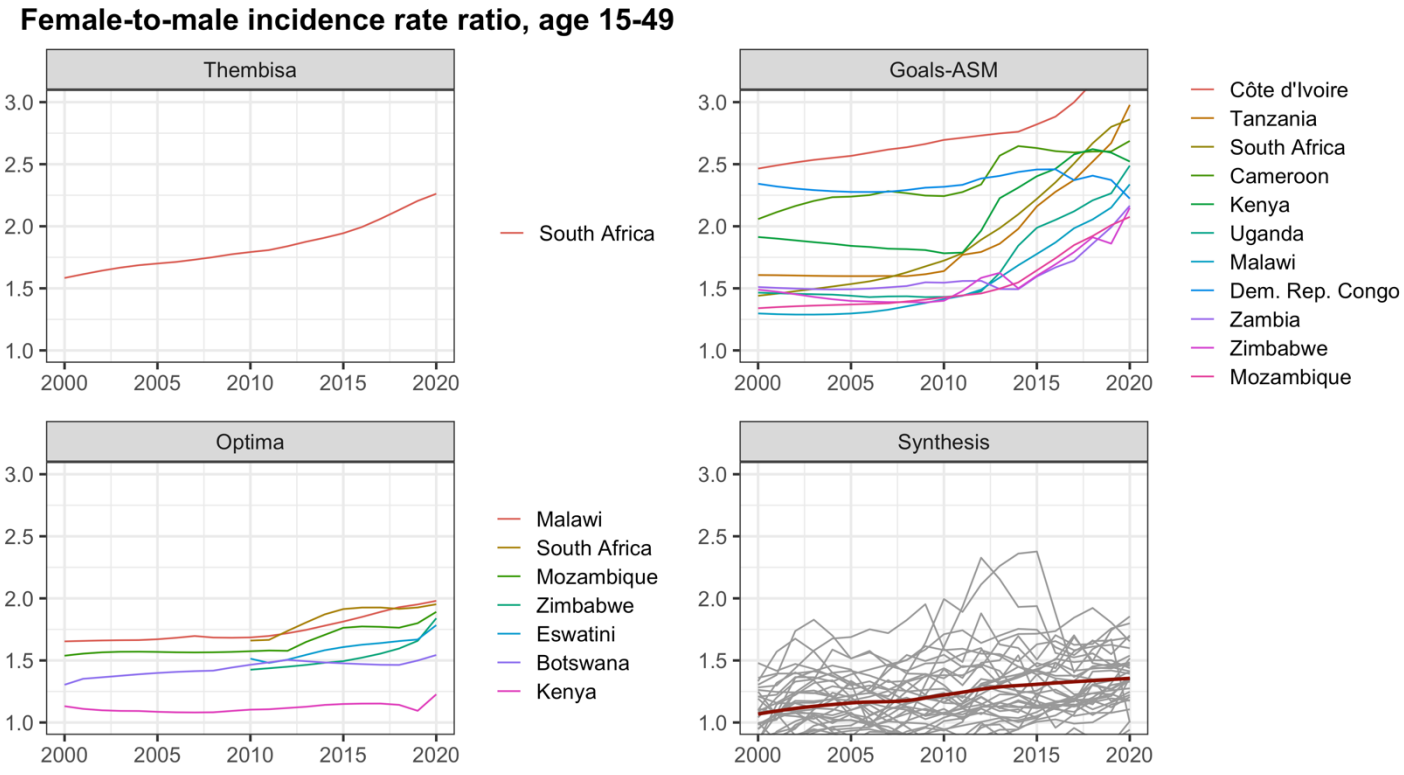


Figure 5: Model-based estimates of female:male sex ratio of new infections (Eaton)

Impact of MMC on HIV incidence trends and sex ratio

MMC counterfactual scenarios in Thembisa and Goals-ASM suggest that VMMC programmatic scale-up has reduced HIV incidence in 2020 by 2-15% in 8 countries. In these scenarios, countries with larger MMC scale-up have experienced larger reductions in 15-49 HIV incidence, and reductions in HIV incidence in men exceed those in women by two-fold. Thembisa estimates that VMMC's differential impact on HIV incidence by sex is responsible for 40% of the increase in female-to-male sex ratio of new infections since 2010. Similar patterns are repeated in Goals-ASM results, with the sex ratio of new infections changing more in countries with larger MMC scaleup.

Marginal effect of ART on HIV incidence

In counterfactual scenarios, models simulated the removal of ART in 2005, 2010, 2015, 2020 by either setting treatment numbers to zero, or setting the effect of ART/VLS on transmission to zero. The average reduction in transmission per 1% increase in population ART coverage (ω) is given by:

$$\omega = \left(1 - \frac{\text{Incidence}}{\text{No ART incidence}}\right) \times \frac{1}{\text{ART coverage}}$$

In 2020, Goals-ASM, Optima, and Thembisa estimate $\omega \approx 0.83$, whilst HIV Synthesis estimates $\omega \approx 0.4$ (Fig 6). Previously it had been suggested that ω may increase over time as universal treatment shifts coverage patterns to younger, more recently infected individuals.

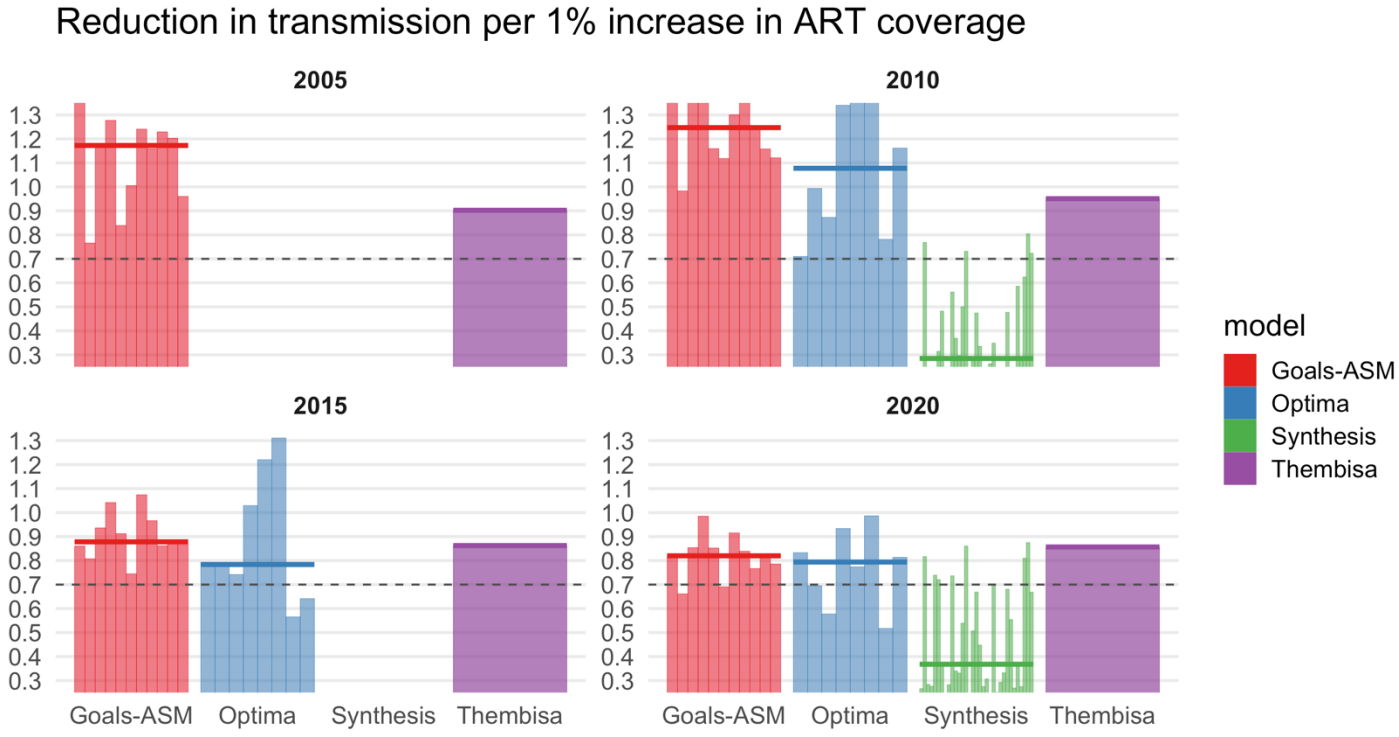


Figure 6: Model-based estimates of the marginal effect of ART on HIV transmission (Eaton)

Peterson et al. estimated the effect of viral nonsuppression on HIV incidence adjusted for prevalence and study site [2]. Community-level UT3C data may be used to estimate ω by reformulating EPP's HIV incidence calculation to a log-linear regression. Assuming VLS amongst those on ART is 90%, the point estimate for ω in UT3C data is 0.62 (0.28-0.79).

Consolidating the model-based estimates of ω, Eaton proposed increasing ω from its current default of 0.7 to 0.78.

Key points from discussion

Sex ratio

- Country-specific sex ratios of new infections could be informed by sex-specific ART coverage and VMMC coverage (Josh Salomon/Jeff Eaton)
- Taking a median change across models from 2010-2020 and applying it universally is preferred for this estimates round (Jeff Eaton/John Stover)
- Close examination of trends is required in Western and Central Africa due to paucity of data (Kate Grabowski)
- There is a need to consider how to project the sex ratio forward in time (Rob Glaubius), with modelled results for 2020-2025 available (Jeff Eaton)
- AIC scores in the IRR fitting tool will indicate whether increasing sex ratios over time produces preferred fits (Rob Glaubius)
- Increasing the sex ratio would lead to a small increase in PMTCT need

Key recommendation: Implement default trend of linear increase in the female-to-male sex ratio of HIV incidence between 2010 to 2020 in generalised epidemics

Marginal effect of ART on HIV incidence

- It is unclear why HIV Synthesis produces a low estimate of ω (Jeff Eaton)
    - HIV Synthesis includes treatment dropout and initiation and the other models' treatment of re-initation may underlie some of this difference (Nikos Pantazis)
- Can ω be fit rather than specified? (Guy Mahiane)
    - Fitting ω may absorb other data quality issues (Jeff Eaton)
    - This was tried five years into the ART era and produced issues with the transmission rate (Tim Brown)
- The proposed change to 0.78 is expected to cause a large decrease in HIV incidence. Incidence trends in AIM would reflect Goals-ASM trends with sharper declines in incidence since the last survey (Jeff Eaton/John Stover)

Key recommendation: Increase ω to 0.8

Effects of MMC on HIV incidence

- The recommended change to the sex ratio of new infections accounts for some of its impact (Jeff Eaton)

- MMC does impact on HIV incidence and should be included in models in future (Jeff Eaton)
- District-level MMC coverage should be included in Naomi to support district level incidence estimates for 2022 estimates (Mary Mahy)

Key recommendation: No changes to EPP or Naomi for this estimates round. Some impact of MMC on incidence dynamics is captured by the recommended change in the sex ratio of incidence.

Session 8: Viral load suppression

Leigh Johnson presented model-based approaches to adjusting reported rates of viral suppression to account for differing reporting thresholds. Previously presented work used IeDEA data from South Africa and proposed a shape parameter of 1.5. This expanded analysis used global IeDEA data from seven regions suggests a shape parameter of 3, when limiting the analysis to programme-years with a lower detection limit of <50 copies/ml. However, this model performs poorly against validation data. Using region-specific shape parameters produces better fits to validation data, suggesting that viral load distribution is not consistent across regions.

Key points from discussion

- Some countries are not using the existing adjustment as they do not recognise their adjusted rates of viral suppression (Kim Marsh)
- What underlies regional differences in shape parameters (Jeff Eaton)
    - If the differences are driven by test turnaround times or assay differences then regional parameters should not be used, but if driven by biological factors (e.g. viral subtype) then they should (John Stover)

Session 9: Asia/Pacific estimates

Tim Brown presented methodological updates to the AIDS Epidemic Model (AEM) following recommendations at the 2019 Reference Group Autumn meeting [1]. Mortality between Spectrum and AEM does not align as Spectrum is age-structured, whilst AEM is not and significant differences exist in background mortality between the models. To produce estimates of HIV prevalence, incidence, and AIDS deaths in Spectrum that match those estimated in AEM, Spectrum mortality parameters are hand-tuned. As this is difficult to justify and hard to understand by country teams, there is a need to bring Spectrum-AEM mortality into alignment.

An Asia-specific background mortality database, with sex and temporal structure, has been implemented. Non-ART mortality reduction with ART scale up and variable on-ART mortality over time, as implemented in Spectrum, have also been included in AEM. Average mortality (off- and on-ART) and HIV progression parameters have been replaced with sex and CD4 specific values, which closes the gap in AIDS deaths between Spectrum and AEM in most tested countries. Harmonising Spectrum

and AEM's treatment of mortality in PWID should align mortality in the remaining countries where PWID transmission dominated in the early years of the epidemic.

The proposed annual workflow for the estimates process is:

- Off-ART, progression, and on-ART mortality equivalents over time will be generated for each country from the latest Spectrum projection
- These will be put in a database to be read by the AEM baseline workbook
- AEM calculations then reflect age-sex structure over time in Spectrum

Regional on-ART mortality rates

Vital registration data from Thailand and Vietnam suggested that the Spectrum on-ART mortality defaults may be too low. A data request was submitted to countries for on-ART AIDS deaths by gender and CD4 count at initiation where available, and data from eight countries were received. Spectrum on-ART mortality defaults appear:

- Low in Myanmar, Thailand, and Vietnam;
- Good in Cambodia and the Philippines, and;
- Difficult to ascertain a pattern in Sri Lanka and Mongolia (though both have low on-ART counts)

Keith Sabin presented a validation exercise to triangulate paediatric estimates in Asia/Pacific. ANC coverage can be low in the region, alongside infrequent HIV testing in antenatal clinics. Countries with high volumes of HIV testing have paediatric estimates similar to case reports, though PMTCT coverage gaps suggest that more paediatric infections should occur than estimated. Future work will look to request data from additional countries and investigate spatial distribution of PMTCT sites

Key points from discussion

AEM model development

- Reviewing the impact of the revised adult natural history model in Asia-Pacific is a priority, and results will be circulated to the Reference Group when available.

On-ART mortality rates

- Spectrum on-ART mortality defaults are derived from IeDEA Asia-Pacific data and it was difficult to capture the heterogeneity in regional rates. Passive tracing may lead to under-enumeration of mortality rates. Country level variation may be required in future mortality estimates (Leigh Johnson)
- Cambodia and the Philippines do not add a LTFU adjustment to their deaths, unlike Myanmar, Thailand and Vietnam. If they did, the programme data in Cambodia and Philippines would be higher than the Spectrum defaults (Wiwat Peerapatanapokin)
- Mortality rates may differ by key population, but reporting of mode of transmission in IeDEA data is poor. Central Asian vital registration systems may be informative (Parviez Hosseini/Leigh Johnson/Keith Sabin)

Session 10: CSAVR

Guy Mahiane presented updates to CSAVR for the 2021 estimates process. The inverse Gaussian likelihood used for new HIV diagnoses and AIDS deaths has been replaced with a gamma distribution, with binomial and multinomial likelihoods used for sex and age distributions, respectively.

Mean CD4 at diagnosis and knowledge of status remained higher than expected, including in the early epidemic. Using the revised natural history model reduced mean CD4 at diagnosis by around 100 and the absolute percentage error (APE) for the proportions diagnosed by CD4 category, though both estimates and error remain high. Out-of-sample validation was conducted on the best fitting model as chosen by AIC by excluding the last three years of data. Out-of-sample coverage remains low, around 50%, under the targeted 95% coverage. Fits to age- and sex- disaggregated data are improved by fitting IRRs and sex ratios of new infections, which in turn improves absolute percentage error by around two- fold, though remaining high.

Rob Glaubius presented interface updates for CSAVR in 2021 estimates. The model fitting screen will be divided into four tabs:

- Model fitting – selection of input data, incidence model options, and visualising ouputs
- Model comparison – comparison of results with all incidence model options
- Validation – viewing full results by sex and incidence model
- Past estimates – compare with last year's estimates as implemented in EPP

Oli Stevens presented a tool to visualise CSAVR HIV mortality inputs by age and sex. Users are recommended to input adjusted HIV deaths data from the Global Burden of Disease Study into CSAVR rather than raw vital registration data. This three-step cleaning process, as previously presented to the Reference Group by Hmwe Kyu [12], recodes garbage cause of death codes and misclassification of proximal causes of death to HIV. As input data do not match national raw vital registration data, this can be a source of confusion for country estimates teams, and this tool will make this redistribution process easier to understand.

Rob Glaubius presented an analysis to update default incidence rate ratios in concentrated epidemics using ART data by age. Age-disaggregated programme data were compared to the on-treatment age distribution outputted by Spectrum. Concentrated epidemic countries using the default incidence rate ratio (IRR) pattern had a younger age distribution in their programme data than Spectrum estimates, whilst those in generalised epidemic settings were better aligned. As generalised epidemic IRRs are fit to household survey data, this may suggest that the default age distribution of incidence in concentrated epidemics is too old. The on-treatment age distribution is highly sensitive to IRR adjustments, with inputs matched best when the median age of infection is age 19 in Madagascar and Nicaragua (Fig 7).

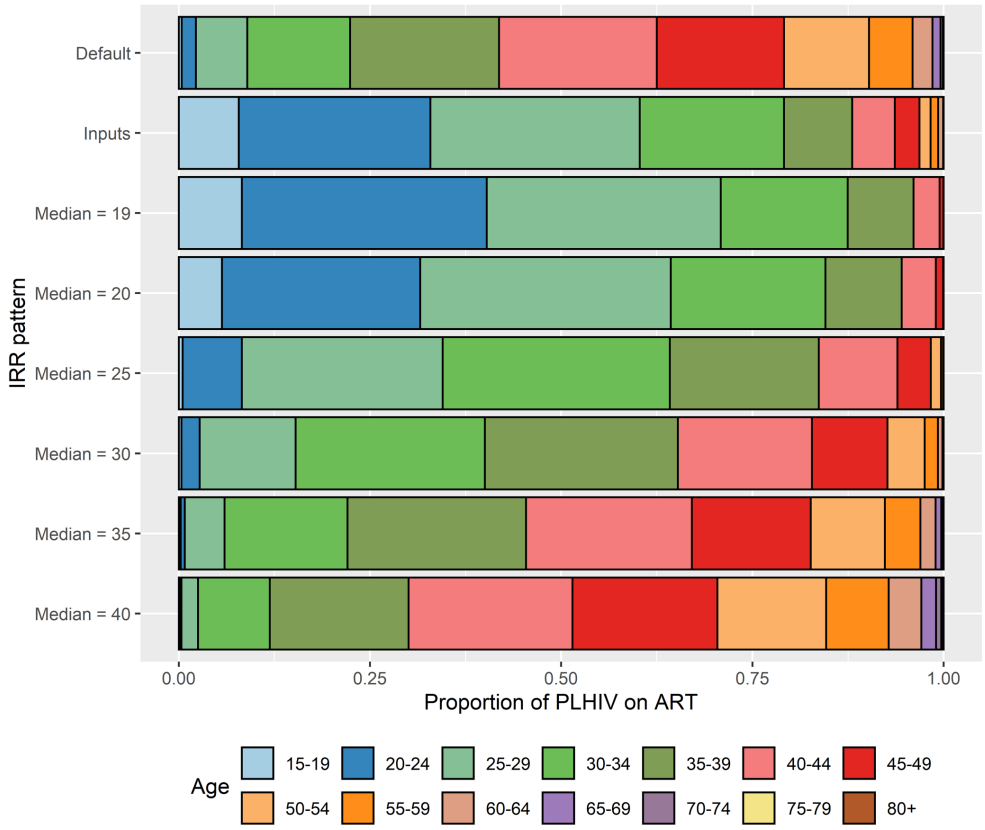


Figure 7: Comparison of ART by age outputs in Spectrum stratified by median age of peak incidence in the incidence rate ratios with age-stratified ART input data

Key points from discussion

CSAVR

- Fitting IRRs slows model fitting by five-fold in R and is expected to be slower in Spectrum (Guy Mahiane)
- If a bias is to exist in TESSy CD4 count at diagnosis data, it will be a downward bias as people with low CD4 counts are less likely to be linked to care (Nikos Pantazis)
- Fitted incidence rate ratios can be validated with age-disaggregated ART programme data (Josh Salomon)
- Calibrating to CD4 count at initiation should be revisited with the new natural history model (Jeff Eaton)

Concentrated epidemic IRRs

- The default IRRs in Spectrum should be revised to reflect this analysis (Jeff Eaton)
- A peak incidence median age of 19 is young for concentrated epidemics, and the IRRs may be absorbing data quality issues in the programme data (John Stover/Rob Glaubius)

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[3] T. D. Mangal and UNAIDS Working Group on CD4 Progression and Mortality Amongst HIV Seroconverters including the CASCADE Collaboration in EuroCoord, “Joint estimation of CD4+ cell progression and survival in untreated individuals with HIV-1 infection.,” *AIDS*, vol. 31, no. 8, pp. 1073–1082, May 2017, doi: 10.1097/QAD.0000000000001437.

[4] CASCADE Collaboration, “Time from HIV-1 seroconversion to AIDS and death before widespread use of highly-active antiretroviral therapy: a collaborative re-analysis. Collaborative Group on AIDS Incubation and HIV Survival including the CASCADE EU Concerted Action. Concerted Actio,” 2000.

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[10] A. M. Geretti *et al.*, “Outcomes of Coronavirus Disease 2019 (COVID-19) Related Hospitalization Among People With Human Immunodeficiency Virus (HIV) in the ISARIC World Health Organization (WHO) Clinical Characterization Protocol (UK): A Prospective Observational Study,” *Clin. Infect. Dis.*, Oct. 2020, doi: 10.1093/cid/ciaa1605.

[11] M.-A. Davies, “HIV and risk of COVID-19 death: a population cohort study from the Western Cape Province, South Africa.,” *medRxiv Prepr. Serv. Heal. Sci.*, Jul. 2020, doi: 10.1101/2020.07.02.20145185.

[12] UNAIDS Reference Group on Estimates Modelling and Projections, “CSAVR technical review and model development,” 2020.

UNAIDS Reference Group on Estimates, Modelling, and Projections
Recommendations I Autumn meeting 2020

Recommendation		Timeline
Session 1: Spectrum updates		
Shiny90		
• Archive HTS data inputs to 2020 estimates round in the ADR for each country	Fjelltop / UNAIDS	2021 estimates
• New outputs available in a spreadsheet download as point estimates only:	Imperial College London / Mathieu Maheu-Giroux	
○ Uncertainty around these indicators will not be available in the interface.		
○ Available to produce by users via 'first90' R package.		
• Outputs to be provided by 5 year age groups up to 50+.		
○ Consider extending five year age groups to 60+ and communicate accuracy of these results to countries.	Mathieu Maheu-Giroux / UNAIDS	
○ EPP-ASM: Review sensitivity of constant ART coverage approximation in age 50+	Jeff Eaton	
• New HIV infections to be intercalated throughout the year to produce mid-year estimates for Spectrum.	Mathieu Maheu-Giroux	
• Encourage countries to submit sex- disaggregated programme data for 2021 estimates round.	UNAIDS	
Session 2: The AIDS Data Repository and Naomi		
Naomi		
• Review methods for Naomi-to-Spectrum calibration to address implausible age-specific ART coverage.	Jeff Eaton	2021 estimates
• Provide clear guidance to countries on how to conduct sensitivity analyses of model options and calibration steps, and their interpretation	UNAIDS / Imperial College London	
Session 3: Spectrum/AIM natural history model		
• Conditional on accepting the fitted estimates, accept mortality rate ratio parameter (mortality ~2 fold higher than Dunn et al. CASCADE estimates).		
○ Review evidence for whether to implement longer survival in WCENA settings. (Incl. Pantazis et al. *PLOS ONE* 2012).	Rob Glaubius	
• Conditional on accepting the fitted estimates, accept ART allocation weight of 83:17 eligibility:mortality ratio.		
• Final recommendation to accept fitted estimates pending on further examination of the South Africa case study:		
○ Investigate discrepancy by: ○ Adjusting default on-ART mortality in Spectrum for long ART durations. ○ Direct comparison of natural history assumptions in Thembisa with fitted parameters.	Rob Glaubius / Oli Stevens	

○ Consider whether adjusting off-ART mortality by ART coverage adjustment may reconcile discrepancies.	Rob Glaubius	
• Review effects of fitted parameters in Asia/Pacific & AEM and validate against vital registration data where available.	Tim Brown	October 2020
• Produce clear and simple explanatory slide decks and videos for countries to understand changes	Rob Glabius / UNAIDS	2021 estimates
Session 4: COVID-19 and HIV		
<u>Programme data entry</u>	Avenir Health	2021 estimates

• Update Spectrum editor to optionally allow monthly treatment inputs.
  • Separate monthly inputs should be available for paediatric and adult ART programme data.
  • Countries with quarterly data to enter the same data for 3 months – to be included in country guidance
	UNAIDS	

Update Spectrum editor to record LTFU by month		
<u>Treatment interruption</u> • Place individuals who interrupt treatment one CD4 category higher than they initiated. This is to be applied only to individuals with ART durations >12 months. • Consider adjusting the <6 month on-ART mortality rate downward if there are a large number of persons restarting ART after short disruptions to prevent overstatement of mortality in the first 6 months of ART.		
<u>Direct effects of COVID-19 on mortality among PLHIV</u> • Increased risk of severe Covid-19 among PLHIV will have small net effect. Do not adjust mortality among PLHIV for increased risk of severe Covid-19 and death.		
<u>Shiny90</u> • Encourage countries to submit sex disaggregated HTS data. • Data on service disruption indicate minimal change in test positivity, and expect impact on Shiny90 model calibration to be limited.		
Session 5: Key populations		
• Systematically compare UNAIDS key population estimates with the Incidence Patterns Model, Goals, Optima, AEM. ○ Consider incorporating modelled outputs conducted as part of national modelling exercise within UNAIDS estimates	UNAIDS	2021
• UNAIDS consultancy to examine size estimates and turnover used within key population models – EPP, AEM, Goals – in addition to existing TOR to collect estimates of population size, prevalence, and the treatment cascade in key populations in SSA	UNAIDS	2021
• Expand facility for key population data collection within models	UNAIDS	2021

• Modes of transmission in CSAVR countries		
• Continue to encourage countries to document input data and develop systematic guidance to create audit trails for input data	UNAIDS	2021 estimates
Session 6: Medical male circumcision		
• Reference Group should review user experience of the MMC data validation tool and consider guidance for other key data	Naomi working group	Spring 2021
• Consider integrating DMPTT2's function within Spectrum/Naomi		2021
• Develop data quality metrics for VMMC data and explore adding VMMC data review alongside ART data quality assessments	UNAIDS	2021
Session 7: Evolving patterns of HIV incidence		
<u>Sex ratio of new infections</u>		
• Implement default trend of linear increase in the female-to-male sex ratio of HIV incidence between 2010 to 2020 in generalised epidemics	Avenir Health	2021 estimates
○ Review modelling and empirical evidence sources to derive a single default pattern across countries	Jeff Eaton	
○ Review simulation model results to guide assumption for period 2020 - 2025; predisposed to be conservative about further change in sex ratio over this period	Jeff Eaton	
○ Review whether default sex ratio improves average model fit to household survey data in EPP / Spectrum IRR fitting	Avenir Health	Spring 2021
• Recommend further examination of recommended changes in WCA as little data are available	Imperial College London	
<u>Omega parameter</u>		
• Recommend increasing omega parameter to 0.8		2021 estimates
• Explore HIV Synthesis results further, including comparison of models' implementation of treatment interruption	Jeff Eaton, Andrew Phillips	
<u>VMMC</u>		
• No changes to EPP/Naomi for 2021 estimates round		
• Incorporate district-level VMMC coverage into Naomi to inform district-level incidence estimation	Jeff Eaton	2022 estimates
Session 8: Viral load suppression		
• Implement region-specific shape parameters for virally suppressed threshold adjustment in Spectrum	Avenir Health	2021 estimates
• Seek more information on what is underlying regional differences	Leigh Johnson	2021

• Seek VLS data from Europe to inform Europe region parameter	Leigh Johnson, Kim Marsh	2021 estimates
Session 9: Asia/Pacific estimates		

AEM development
• Recommend:
  • Align AEM with Spectrum by non-ART mortality reduction with ART scaleup and variable on-ART mortality over time
  • Sex structured Asia-specific background mortality database
  • Replace average mortality and progression parameters with sex- and CD4- specific parameters
  • Align AEM and Spectrum PWID mortality
	Tim Brown/Avenir Health	2021 estimates

• Review outputs with proposed fitted natural history parameters	Tim Brown	October 2020
Regional on-ART mortality rates • No changes for 2021 estimates		
• Countries recommended to upward adjust on-ART mortality rates to achieve good fit to programme data	UNAIDS	2021 estimates
• Multiplier input field to be added to Spectrum advanced parameter editor and implemented in EPP-ASM/Shiny90/CSAVR/AEM	Avenir Health	2021 estimates
• Seek additional data sources to address whether on-ART mortality rates differ by key population		2021
o Modes of transmission data within IeDEA collaboration	Leigh Johnson	
o Central Asian countries with strong vital registration systems and transmission information	Keith Sabin	
Triangulating paediatric estimates • No changes recommended for 2021 estimates		
• Conclude validation exercise by the Asia/Pacific workshops to assist countries in understanding their latest surveillance data	Keith Sabin	2021 estimates
Session 10: CSAVR		
• Recommend using a gamma distribution for new diagnosis and AIDS death likelihood		
• Accept proposed updates to CSAVR interface	Avenir Health	2021 estimates
• Accept HIV/AIDS death reallocation visualisation tool and continue development for this estimates round	Oli Stevens	2021 estimates
• Validate fitted incidence rate ratios with age-disaggregated ART programme data	Guy Mahiane	December 2020
• Test inclusion of CD4 at diagnosis data as calibration data with proposed fitted natural history parameters	Guy Mahiane	November 2020
• Review flexibility and specification of the diagnosis rate model	Guy Mahiane	November 2020

Fitting IRRs in concentrated epidemics

- Continue development work to improve the default IRR patterns in concentrated epidemics — Rob Glaubius

- Automated IRR fitting as in generalised epidemics not recommended for 2021 estimates round

UNAIDS Reference Group on Estimates, Modelling and Projections

Technical updates for UNAIDS-supported estimation tools

5-8th October 2020

All times are GMT+1 (London)

Day 1 | Monday 5th October

Time	Duration (mins)	Topic	Presenter(s)/ Lead Discussant
15.30	20	Welcome and introductions	Peter Ghys
15.50	10	Meeting objectives and overview	Jeff Eaton
16.00	20	2020/21 estimates round: process, workshops, and timelines	Mary Mahy
16.20	10	Discussion	
Session 1: Spectrum updates (chaired by Mary Mahy)			
16.30	20	Spectrum updates - Interface changes and new features ○ Shiny90 invalidation flag - Spectrum on the web - Code harmonisation	John Stover
16.50	15	Shiny90 updates - Interface and outputs - Age-specific results - Additional HTS programme outputs	Jeff Eaton
17.05	20	Discussion	

Session 2: ADR and Naomi (chaired by John Stover)
• Review:
  ○ ADR development and integration with Naomi
  ○ Estimates and workshop process for 2020 estimates
• Reach recommendations on Naomi model and interface development for 2020 estimates round			

17.25	20	Naomi in the 2020/21 estimates round - Expected workshop process - New countries - Data validation and encountered challenges	Ian Wanyeki
17.45	10	Break	
17.55	20	AIDS Data Repository development - Data packages - DHIS2 integration - Data visualisation and validation tools	Jonathan Berry
18.15	15	Discussion	
18.30	20	Naomi interface updates - ADR integration - Model version management - Model output reports	Rob Ashton
18.50	20	Model updates - ANC testing cascade and knowledge of status	Jeff Eaton
19.10	20	Discussion	
19.30	CLOSE		

Day 2 | Tuesday 6th October

Session 3: Natural history model (chaired by Jeff Eaton)
• Review:
  ○ Changes to parameter estimates since UNAIDS Reference Group Spring meeting
  ○ Impact on AIDS deaths by region and treatment status
  ○ CD4 distribution at treatment initiation
  ○ Validation analyses with Thembisa, Spectrum in South Africa, ALPHA data
• Reach recommendation on whether revised parameter estimates should be adopted for 2020/21 estimates			

15.30	45	Natural history model	Rob Glaubius
16.15	45	Discussion	
17.00	5	Break	
Session 4: COVID-19 (chaired by Leigh Johnson) • Approach for accounting for COVID-19 related service disruptions			
17.05	20	Data about HIV service disruptions	Kim Marsh
17.25	30	Proposed adjustments to Spectrum/AIM - Data inputs - Model assumptions - User interface changes - Anticipated impact in SSA and non SSA	John Stover
17.55	30	Discussion	
18.25	5	Break	
Session 5: UNAIDS estimates for key populations in sub-Saharan Africa (chaired by Tim Brown) • Review and make recommendations on existing methods for creating estimates by key population group in sub-Saharan Africa			
18.30	20	Existing approaches to quantifying key population transmission in UNAIDS estimates	Keith Sabin
19.50	40	Discussion & recommendations	
19.30	CLOSE		

Day 3 I Wednesday 7th October

15.30	15	Draft recommendations review	Jeff Eaton
Session 6: Medical male circumcision (chaired by Peter Ghys) • Review: o Proposal to incorporate VMMC estimation within annual UNAIDS estimates, and DMPPT2 within Spectrum o Process to support country estimates teams to validate district level VMMC programme data			
15.45	25	Incorporating VMMC into the UNAIDS estimates process	Lycias Zembe
16.10	25	Validating district-level VMMC programme data	Katharine Kripke Randy Yee
16.35	15	DMPTT2 updates Integration with Spectrum	Katharine Kripke John Stover
16.50	30	Discussion	
17.25	5	Break	
Session 7: Evolving patterns of HIV incidence (chaired by Leigh Johnson) • Do empirical data support: o the default sex ratio of new infections in Spectrum? o EPP's paramterisation of the population-level effect of ART on reducing HIV transmission rate? o Inclusion of MMC within incidence estimation models			
17.25	30	The effect of ART coverage on the HIV transmission rate Evidence on the sex ratio of new infections Impact of MMC on HIV incidence	Jeff Eaton
17.55	20	Assumptions for time-varying sex ratio of new infections in Spectrum	John Stover
18.15	40	Discussion & recommendations	
18.55	5	Break	
Session 8: Viral load suppression (chaired by John Stover) • Review updates to viral suppression adjustments			
19.00	15	Viral load suppression	Leigh Johnson
19.15	15	Discussion	
19.30	CLOSE		

Day 4 | Thursday 8th October

Time	Duration	Topic	Presenter(s)/ Lead Discussant

Session 9: AIDS Epidemic Model (chaired by Jeff Eaton)
• Review AEM technical development:
  ○ Historical mortality discrepancies between AEM and Spectrum
  ○ Updated mortality rates in AEM
  ○ Implementation of the incidence/prevalence adjustment for Asia/Pacific estimates
  ○ Effects of revised natural history model
• Validate Asia/Pacific paediatric estimates
• Identify whether regional on-ART mortality rates require updating			

15.30	45	AEM updates • Mortality and incidence/prevalence adjustment • Effects of revised HIV natural history • Validation of regional on-ART mortality rates in South East Asia	Tim Brown
16.15	15	ANC data & paediatric estimates	Keith Sabin/Annette Sohn
16.30	45	Discussion	
17.15	10	Break	

Session 10: CSAVR (chaired by Josh Salomon)
• Review:
  ○ Likelihood formulation
  ○ Fitting to age/sex stratified data
  ○ Fitting incidence rate ratios
  ○ Early epidemic knowledge of status
  ○ CD4 count at diagnosis
  ○ Effect of revised natural history model
• Inclusion of CD4 count at diagnosis in 2020 estimates			

17.25	45	CSAVR	Guy Mahiane
18.10	10	User interface	Rob Glaubius
18.20	10	Visualising adjusted mortality data	Oli Stevens
18.30	20	Fitting incidence rate ratios to non-survey data	Rob Glaubius
18.50	40	Discussion and recommendations	
19.30	CLOSE		