Consolidating data and estimation tools for next-generation models

Report and recommendations from a meeting of the UNAIDS Reference Group on Estimates, Modelling, and Projections
21-24th April 2020

REPORT & RECOMMENDATIONS

UNAIDS
JOINT UNITED NATIONS PROGRAMME ON HIV/AIDS
UNHCR UNICEF WFP UNDP UNFPA UNODC ILO UNESCO WHO WORLD BANK

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, April 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 *Consolidating data and estimation tools for next-generation models* from 21-24th April 2020. The meeting featured presentations and group discussion to generate consensus recommendations. The programme was divided into the following sessions:

1. Spectrum updates
2. Next generation models
3. Natural history model
4. Voluntary Male Medical Circumcision
5. Evidence on age-patterns of incidence and transmission in sub-Saharan Africa
6. Age patterns of transmission: model based approaches
7. Harmonising data inputs and codebases for next generation models

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, provide an opportunity to review current approaches, and help to identify the data needed to further improve the 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.

Meeting Objectives

The global HIV epidemic and the data through which to understand it are continually evolving. Recent developments in HIV estimation tools have been marked by increasing granularity and diversity of data about the epidemic, and the multitude of indicators required to guide the HIV response. This has resulted in a proliferation of specific tools to meet the continually evolving needs for HIV policy in particular settings for particular types of data.

At the same time, the longstanding segmentations of the global HIV epidemic based on epidemiologic profile, types of data, or technical and policy needs are becoming increasingly artificial. Utilisation of these data sources by the UNAIDS-supported models to estimate HIV epidemics is, at present, fragmented across several bespoke tools. This fragmentation forces unsatisfactory decisions between using one data source or another, but frequently not all available data and epidemiologic information holistically to understand and respond to the HIV epidemic.

Key objectives for the Spring 2020 meeting of the UNAIDS Reference Group were to reach recommendations about:

1) Key features of future HIV estimation tools, including required output indicators, stratifications thereof, and required and supported input data sources;
2) Create a work plan of modular developments that will culminate in a cohesive set of tools fulfilling the consensus feature specification; and
3) Determine priorities and objectives for development and implementation during 2020-21 Reference Group period.

Session 1: Reviewing 2020 UNAIDS estimates

Every year, UNAIDS supports countries to develop updated national HIV estimates using Spectrum and related modelling tools. The estimates process starts in December. Data and estimates are reviewed and developed by national HIV estimates teams with support from UNAIDS Strategic Information advisors over the period December through April. Upon completion, ministerial approval is sought for publication of final estimates in the UNAIDS global report in July.

The first session of the meeting reviewed key updates, progress, challenges, and priority short-term developments for the modelling tools supported by UNAIDS for the 2020 global HIV estimates process. Feedback on the estimates process, challenges identified, and requests from users are key inputs guiding the work and priorities of the UNAIDS Reference Group.

1.1 Global estimates

Mary Mahy provided an overview of the ongoing 2020 process, through which 170 national estimates teams are supported by UNAIDS to create annual estimates. The

COVID-19 pandemic and the demand it has placed on Ministries of Health and in-country epidemiologists has reduced capacity of countries to engage with finalizing UNAIDS estimates, resulting in a projected 57 countries, at the time of the meeting, which may not finalize estimates for publication this year, a higher number than previous years. Few methodological changes have been made to the generalised epidemic estimation models for the 2020 process, and accordingly little change is expected in global estimates of new infections, PLHIV, or AIDS deaths compared to 2019 estimates.

1.2 Asia-Pacific estimates

Similar to global estimates, estimates of PLHIV, new infections, and AIDS deaths are anticipated to be similar to 2019 estimates as no methodological changes have been made to the AIDS Epidemic Model or EPP in concentrated epidemics, the two most used models in the region. Country teams have noted that they do not expect marked increases in ART coverage towards 2020 or 2025 due to resource and health system constraints. As noted by Sabin in the Autumn 2019 Reference Group meeting (Session 8 I [1]), the robustness of paediatric HIV estimates in the Asia-Pacific region remains of concern, with low quality and quantity of surveillance data for pregnant women and sparse direct data to validate paediatric HIV estimates.

1.3 Shiny90: estimating knowledge of status

In 2020, 43 countries used the Shiny90 model to produce estimates of the proportion of adults aware of their HIV status (20 in Eastern and Southern Africa, and 23 in Western and Central Africa), of which 28 supplied programmatic testing data in addition to the necessary survey data – in increase of 5 on the previous year. Wanyeki and Mahy both raised process challenges surrounding model workflow in which countries iteratively update their Spectrum and EPP files, and can fail to re-run Shiny90 or Spectrum uncertainty analysis, resulting in inconsistent estimates of the first 90 and overall PLHIV.

Estimates of knowledge of status across sub-Saharan Africa were presented by Katia Giguère. Twelve countries and the region of Southern Africa were projected to attain the first 90 target by 2020 (Fig 1). Men and younger age groups have lower knowledge of status. The group with the largest absolute number of PLHIV who were undiagnosed was men aged 35-49.

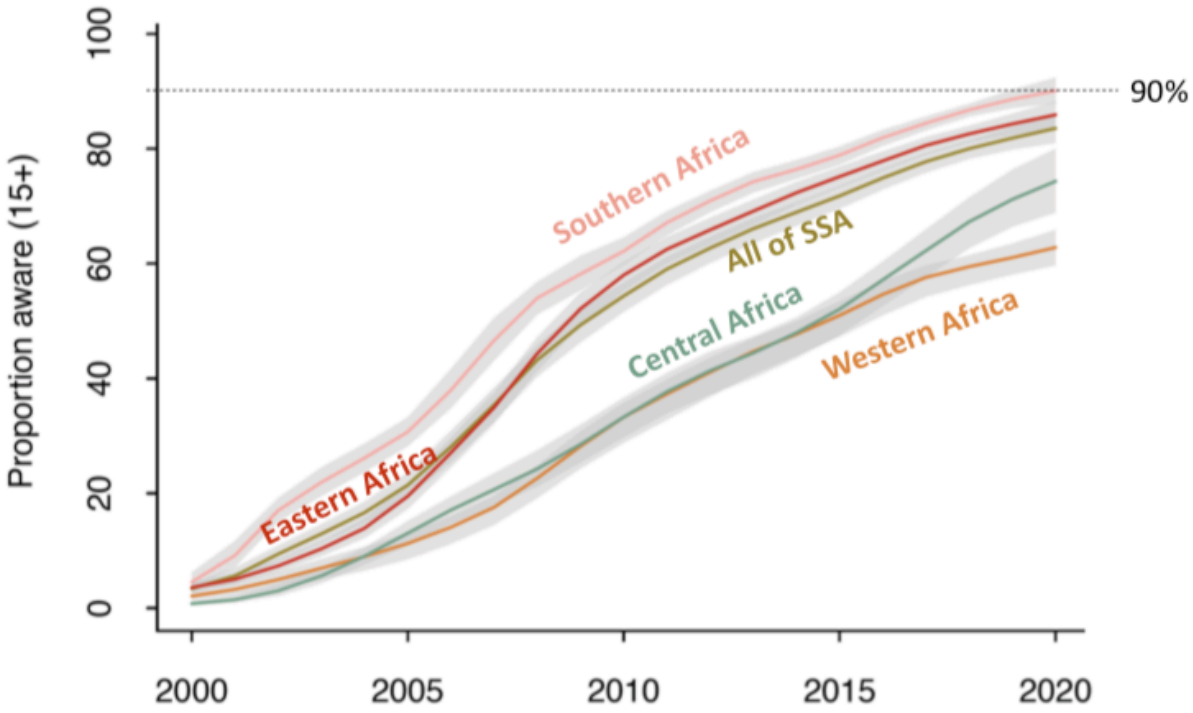


Figure 1: Regional attainment of the first 90 – knowledge of status – in sub-Saharan Africa.

Arnaud Godin presented predictions for the proportion who were infected with HIV in the past six months out of all persons tested for HIV and HIV positive persons tested for HIV. Results were based on Shiny90 model results for Malawi, Mozambique and Cote d'Ivoire. These results may be compared to data from surveillance of HIV recent infection amongst new HIV diagnoses. In particular, this analysis provides guidance on whether HIV tests or all positive HIV tests should be used as the denominator for recent infection surveillance indicators. When using all HIV tests as the denominator, the proportion recently infected was decreasing and/or changes in testing strategy are reaching lower risk individuals; when using positive HIV tests as the denominator, the proportion of people with recent infection is increasing over time but the patterns are difficult to interpret. Further development of this work will support inclusion of recent HIV testing surveillance data into future versions of the Shiny90 model for estimating HIV testing and diagnosis rates and the EPP model for estimating HIV incidence trends.

Shiny90 relies on self-reported testing histories in surveys, Yiqing Xia presented analysis of household survey data to evaluate the accuracy of self-reported HIV testing history status. ART metabolite data from Population Health Impact Assessment (PHIA) surveys is used to empirically derive the sensitivity of self-reported testing behaviour in on-ART individuals, and estimated in off-ART individuals. A prior on the non-disclosure ratio between off-ART and on-ART individuals is derived from Mozambique data. Empirically derived sensitivity is high in on-ART individuals, with lower sensitivity in women, and the analysis finds that adjusting for self-reporting bias in survey data has little impact on the proportion of those ever tested.

Mathieu Maheu-Giroux outlined proposals for future developments of the Shiny90 model focused on increasing the granularity and stratification of estimates and reflecting evolution of HIV testing strategies. These included:

- Stratification of HIV testing rates by different testing modalities.
- Incorporating HIV self-testing and the consequences of HIV self-testing on presentation for provider-based testing HIV testing services.
- Data about HIV recent infection testing surveillance.
- Stratification of HIV testing and knowledge of status by key population group.

1.4 Naomi: district-level HIV estimation in SSA

Naomi is a district-level HIV estimation model used for the first time during the 2020 estimates process by 20 countries across sub-Saharan Africa. The model workflow and interface were well received by country estimates teams, particularly elements relating to data visualisation and validation. Data challenges encountered during model development and use were finalising geographic administrative boundaries and populations stratified by age, sex, and district. Identifying and remedying programmatic data quality issues within the thousands of individual data elements consumed by the model was a particular challenge. Further tools to review programmatic data quality are a high development priority for 2021 estimates.

Additional model development during the estimates development process and responsive to particular challenges encountered with HIV programme data were:

- Time varying cross-district ART attendance
- Allowing model input of ART programme data at admin-1 level
- Additional constraints were placed on District level incidence, with incidence being derived from ART coverage and prevalence, removing district-level random effects on incidence informed by PHIA recency data.

Priorities for Naomi development towards the 2021 estimates are:

- Critical review of Naomi model and process, including technical, user, and consumer input
- A manuscript detailing the estimation methodology
- Improving workflows surrounding extracting, reviewing, cleaning, and validation model inputs and outputs
- Integrating with the AIDS Data Repository
- Technical development:
    - Improve robustness to varying consistency and temporal trends in programmatic data
    - Choice of data inclusion and model options
    - Include PMTCT need and coverage as district level outputs

Meeting discussion identified additional requests and priorities:

- Request by model users for district level estimates of the first and third 90.
- Guidance about policy and programme planning utlitily of separate indicators of the number of residents on ART and the number receiving ART at health

facilities in particular districts. The Reference Group should engage national target setters and programme managers on how to improve the model outputs best to suit their needs.
- More flexible options and transparency about model calibration to Spectrum results.

1.5 CSAVR

The CSAVR tool is a model within Spectrum for estimating HIV incidence trends from case surveillance vital registration data. Forty three countries used CSAVR in the 2020 estimates process, including four new countries in Eastern Europe and Central Asia. Model changes from 2019 include:

- Model calibration using age and sex disaggregated data about new HIV diagnosis and AIDS deaths.
- Removed fitting to CD4 count at diagnosis.
- Increased flexibility of model specifications for HIV diagnosis trend and incidence trend.

It was noted that:

- Without fitting to CD4 count at diagnosis, the mortality data are critical to model fitting, which poses a problem in countries with poor mortality data quality (e.g. many in Middle East & North Africa);
- CSAVR should include estimates of time from infection to diagnosis without which the interpretation of fits to new diagnoses data is difficult;
- European countries do not have data on previously diagnosed migrants stratified by age and sex and a method is needed to add previously diagnosed PLHIV; and
- Improvements to the interface could aid country teams in interpreting CSAVR results, possibly to include:
    - Ability to “Fit all” models as in EPP
    - Ability to compare models
    - Add back in total PLHIV numbers as a trend in the proportion of PLHIV who know their status
    - Add in time from infection to diagnosis

CSAVR is now available as an R package, well suited to batch processing of model options or countries. The R implementation is around 10 times faster than CSAVR within Spectrum. Ongoing model development includes:

- Fitting to key population stratified data (further stratified by sex where appropriate), using population proportion size estimates, new diagnoses, AIDS deaths, and turnover rates as model inputs;
- Including multiple data sources for a given population;
- Accounting for uncertainty in surveillance data; and
- Reintroducing fitting to CD4 count at diagnosis.

The UNAIDS Reference Group will convene a separate meeting in May or June 2020 focused on technical review of the CSAVR model, model validation, and proposed future development.

1.6 Paediatric estimates

There were minimal changes to the paediatric HIV sub-model within Spectrum for the 2020 HIV estimates. Two small updates for the 2020 estimates were:

- updating the breastfeeding dropout rates (1.2%/month for the first 12 months and 0.7%/month thereafter) and
- breastfeeding duration from survey data as presented at the Autumn 2019 Reference Group meeting.

The changes caused small historical increases in CLHIV compared to 2019 estimates, with minimal change in recent years.

Several updates to the paediatric model are proposed for development in the 2021 estimates and will be discussed in detail at the upcoming Autumn 2020 Paediatric Reference Group meeting. In brief, these are updates to:

- Assumptions of on-ART mortality
- Assumptions of transition from CD4% to CD4 count categories at 5 years of age
- CD4 progression in off-ART older children
- Trends in age and CD4 distribution at ART initiation
- Mortality in adolescents by time of infection
- Loss to follow up amongst pregnant and breastfeeding women
- ART dropout and reengagement

Further potential model development includes the use of additional sources of paediatric data for either model calibration or validation (e.g. PEPFAR and CIPHER programmatic data, HIV testing data, proportion of HIV+ pregnant women already on ART at 1st ANC, and CHAMPS mortality data), estimation of the first 90, adjustment to AIDS mortality rates based on treatment coverage as implemented in the adult model, and simplification of CD4 and timing of transmission compartmentalisation.

Session 2: Next generation models

Evolution of surveillance systems and data availability has led to a proliferation of modelling approaches used for specific components of the UNAIDS HIV estimates process:

- Incidence estimation tools – EPP, CSAVR, AEM
- Tools for specific programmatic indicators – Shiny90 for knowledge of status, DMPPT2 for medical male circumcision
- Granular estimation tools – Incidence Patterns Model by subpopulation group, Naomi by district
- Intervention impact evaluation – Goals and Optima

As the historical delineation between epidemic types becomes increasingly blurred, there is a need for harmonised future models to:

- Consume case surveillance, survey, and programme data;
- Incorporate key populations in all epidemic settings
- Interface smoothly with country health information systems, both for pulling input data and pushing estimates back to systems
- Interface better with estimates for maternal health, TB, and malaria.

Jeff Eaton proposed focusing development towards two harmonised epidemic estimation tools:

1) A national level model that represents:
    a. The entire epidemic history with a medium range projection;
    b. A mechanistic representation of transmission dynamics including key interventions;
    c. Estimation of historical impact of key HIV interventions and short-term projection of intervention impact.

2) A subnational model with recent trends (e.g. since 2010) and short 3-5 year projections, focused on programmatic planning and allocation purposes.

Four work streams were proposed for priority development over the next two years towards the goal of harmonising existing modelling approaches:

1) Integration of existing concentrated epidemic tools for case surveillance data (CSAVR), survey and prevalence data (EPP), and transmission (AEM) into a single estimation tool.

2) Incorporation of sexual mixing and interventions in the generalised epidemic EPP model.

3) 'Disaggregation' of national level infections and transmission by key population groups in sub-Saharan Africa.

4) Unification of data and codebases for existing tools.

Key points from discussion of recommendations

Two epidemic models for national and subnational estimation needs:

- There was general consensus about pragmatic need for separate modelling approaches for national and subnational approaches, but many identified that conceptually this leads to several challenges that need careful consideration in implementation.

- Subnational models spanning the full history of the HIV epidemic are not desirable due to data challenges at subnational levels and the existing burden

of reviewing and signing off on subnational estimates for a single year (John Stover).

- Alignment of national and subnational level models that are fit separately is likely impossible. Separate adjustment of prevalence, incidence, and mortality will lead to results of multiple indicators that are not fully internally consistent results (Laura Dwyer-Lindgren).

- Version control becomes challenging with multiple models and multiple flexible options for calibrating models are desirable (Peter Young).

Priority steps:

- Including sexual mixing (both age mixing and heterogenous risk mixing) markedly increases model complexity and will make the results harder to understand and use. Initially including age mixing alone is preferable (John Stover).

- Conversely, it is difficult to consider sexual mixing without including subpopulation transmission dynamics, and age mixing alone may misrepresent transmission dynamics (Leigh Johnson).

- Integration of tools may make them more of a "black box". The Reference Group should consider:
    1) What additional characteristics of the epidemic does the data inform?
    2) Are the data informative about those parameters?

  If the gain is perceived to be limited, then tools should be kept separate rather than integrated (Le Bao).

- Considering the integration of the concentrated epidemic models, Tim Brown recommended first integrating the curve fitting models (EPP and CSAVR), and the transmission dynamic-driven approaches (AEM) at a later stage.

- Age mixing is the primary method by which heterogeneity in interventions is propagated through the EMOD model. Relatively simple age mixing restrictions (e.g. male partners are always older than female partners) can capture key dynamics (Adam Akullian).

3. Natural history model

Rob Glaubius presented an update about 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 (Session 1.6 [1]). 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.

Natural history parameters—the distribution of CD4 at seroconversion, the rate of HIV progression between CD4 category, mortality rates by CD4 category in the absence of ART—were re-estimated better to fit the CD4 distribution in PHIA surveys, initial CD4 distribution following seroconversion, and mortality by CD4 category, while also retaining overall consistency with data about HIV survival by age at infection from general population cohort studies comprising the ALPHA Network (Todd et al. 2007).

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)

Though good fits were obtained to calibration data, after inputting the new parameters into Spectrum, resulting estimates implied a lower distribution of CD4 count at ART initiation compared to empirical estimates of CD4 count at ART initiation from the IeDEA network [2] (Fig. 2). Consequently, due to a higher proportion initiating ART at low CD4 counts, which have high mortality during the first year on ART, new parameters produced a substantial increase in adult AIDS deaths when compared to Spectrum defaults in high burden countries (roughly 20% increase in estimated AIDS deaths in 2019 across 10 SSA countries).

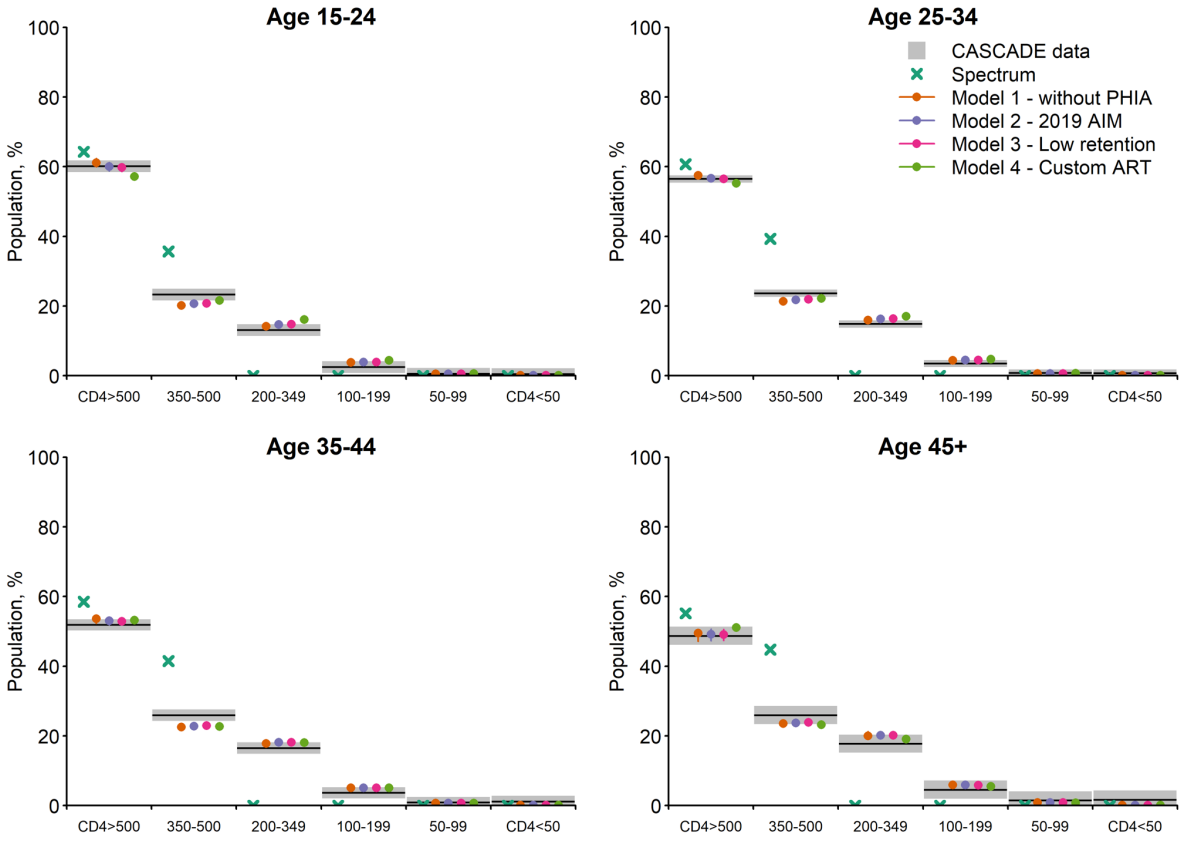


Figure 2: Comparing CD4 count at initiation by age in Spectrum (green) with CASCADE data and four fitted model variants.

Glaubius reported results for four fitted model variants:

1. The natural history model fitted to HIV survival, CD4 distribution at seroconversion, and mortality by CD4 category (without PHIA data).
2. The natural history model fitted to the primary data in (1), and additionally with PHIA data assuming ART retention as in 2019 AIM files
3. The natural history model with PHIA data and assuming modified, lower ART retention compared to 2019 AIM files.
4. As (3) but using CD4 counts at initiation from IeDEA as a direct input to allocate patients to ART.

Variants 1 and 2 resulted in an approximately 20% increase in the estimated number AIDS deaths in 2019. Variant 3 with lower assumed retention on ART resulted in a 50% increase in the estimated number of AIDS deaths. The poor correspondence with CD4 count at ART initiation estimated from IeDEA Network studies was consistent for variants 1, 2, and 3. Variant 4 which enforced consistency with IeDEA Network estimates for CD4 distribution at ART initiation but sacrificed quality of fit to data on CD4 counts amongst PLHIV of ART.

It was questioned whether the extent to which missing data about CD4 count at ART initiation might result in upward bias in the estimated CD4 distribution at ART initiation from the IeDEA Network, which could explain the discrepancy between

Spectrum estimates with revised natural history parameters. The initial response was that the difference was too large to be explainable by missing data based on the levels of missing CD4 counts reported by Anderegg et al., but it was agreed this should be further investigated.

Several additional sources were suggested for further triangulation and validation of model results:

- Baseline data about CD4 distribution amongst untreated PLHIV from recently completed Universal Test and Treat trials in sub-Saharan Africa.
- Empirical estimates of AIDS deaths from South Africa and Thembisa model estimates of AIDS deaths by treatment status.
- Estimates of disease progression and untreated CD4 distributions from the HIV Synthesis microsimulation model, which carefully reconstructs HIV disease progression.

Recommendations

- UNAIDS should aim to adopt revised default natural HIV history parameters proposed by Glaubius for 2021 HIV estimates, subject to further review and validation including:
    - Further analyses proposed by Glaubius.
    - Review of potential magnitude of bias in estimated CD4 distribution at ART initiation that could arise from non-random missing CD4 count observations in IeDEA cohort data.
    - Comparison with baseline CD4 distribution of untreated adults from UTT trial surveys.
    - Comparison with South Africa AIDS deaths data and Thembisa model estimates for South Africa.
    - HIV natural history results from the HIV Synthesis model.

  This change is anticipated to increase current estimates of the number of AIDS deaths by potentially 20%.

4. Voluntary Medical Male Circumcision

Estimates of the coverage and unmet need for medical male circumcision (MMC) are routinely required to guide HIV intervention programming and also to quantify HIV incidence trends and MMC programme impact. Furthermore, integrating estimates of medical circumcision coverage and need into existing HIV estimation tools, better reflecting transmission dynamics in generalised epidemic estimates, is part of the development towards harmonised and integrated models. Consequently, tools are required to estimate national and subnational (e.g. district) coverage of MMC using available survey and MMC programme data as part of the annual HIV estimates process in 15 priority countries in sub-Saharan Africa.

Objectives of this session were to reach recommendations about:

- Appropriate methodology to estimate national and subnational MMC coverage by age and time.
- Incorporation of MMC coverage into estimates of national and subnational HIV incidence trends.

Katharine Kripke presented DMPPT2, a web-basd modelling tool to provides estimates of circumcision and medical circumcision by age, district, and year to guide policy making and programme planning. The model uses a constant 'baseline' rate of circumcision over time estimated from survey data that precedes VMMC programmatic scaleup, on top of which VMMC programme circumcisions are added.

Interpretation of data and estimates of MC coverage can challenging for several reasons:

- Replacement – As VMMC programmes scale up, individuals who may have previously sought out traditional circumcision may instead seek out VMMC. The baseline circumcision rate is no longer constant, and modelled circumcision estimates overestimate the true coverage
- Cross-district service attendance – Individuals may seek circumcision services in a district other than their resident district, which may exaggerate heterogeneity in coverage between districts
- Population – inaccurate age-stratified population denominators may lead to distorted estimates of coverage or implausible absolute target numbers when converting coverage to individuals

Further examination of data quality issues can be found in Kripke et al. 2018 [3].

Model estimates of circumcision coverage at the national level align well with PHIA survey estimates in Malawi, Namibia, Tanzania, Lesotho, and eSwatini. Larger discrepancies may exist at more granular subnational levels. Model estimates overestimate coverage compared to survey data in Uganda and Zimbabwe. It was noted that DMPTT2 does not include a formal representation of uncertainty around coverage estimates, instead using the uncertainty around the baseline circumcision rate.

Luisa Frescura described the process of VMMC data submission to UNAIDS Global AIDS Monitoring. Countries submit the total number of medical circumcisions conducted during the most recent calendar year. Age- and city-disaggregated data are requested to be submitted where available. Data are validated using PEPFAR programme data for the previous calendar year. Key data challenges include incomplete facility reporting within national databases, of note as DMPTT2 requires complete programmatic coverage for its estimates.

Megan Bronson described estimates of medical circumcision derived from PHIA surveys. If circumcision was self-reported as conducted by a doctor, clinical officer, nurse, or midwife, circumcision is classified as medical, with all other options classified as traditional. In a number of countries, however, traditional circumcisers have been trained to carry out medical circumcisions and there is the risk of underestimating the coverage of medical circumcision using the PHIA definition. There is considerable heterogeneity in national and subnational level estimates, both in terms of total circumcision coverage, and the fraction of circumcisions that are medical.

Evidence of baseline replacement was exemplified in age-stratified data in Tanzania, where total circumcision coverage is broadly stable over age whilst non-medical circumcision declines rapidly towards younger age groups. Using recency testing data, PHIA surveys suggest a significantly lower incidence in medically circumcised men aged 15-34, though restricted by small sample size (75 recent infections in men 15-59 across 8 sub-Saharan African countries)

The Local Burden of Disease study used male circumcision at the 5x5km grid level as a covariate to estimate HIV prevalence. The MC model, presented by Michael Cork, was a geostatistical spatiotemporal model which uses survey data to estimate 15-49 MC prevalence at the 5x5km level. The model elucidated subnational heterogeneity, particularly in 14 priority countries in Eastern and Southern Africa and identifies large changes in MC coverage between 2008 and 2016, reflecting programmatic scale up. At this time the model does not produce age-stratified estimates, consume programmatic data, or use additional sociodemographic covariates.

Matt Thomas described a small-area survival analysis model to estimate rates of circumcision by age, province, and time in South Africa. The model synthesised data from five nationally representative household surveys and data about number of MMC conducted reported to the national health information system. A baseline provincial circumcision rate estimated from before programmatic scale up (preceding 2008) is assumed to be constant over time, with an excess programmatic rate component added from 2008 onwards. The model reconciles survey and programmatic data, and captures increasing MMC coverage with spatiotemporal heterogeneity. Future work will look to estimate circumcision rate at the district level,

account for cross-district care seeking, and further examine medical vs non-medical circumcision.

John Stover outlined options and considerations for integrating estimates of MC/MMC coverage into EPP incidence estimation in generalised epidemics. Trial data are conclusive that circumcision is effective at reducing female-to-male acquisition and could be included in EPP's incidence equation akin to the implementation of ART at present. Stover summarised key considerations for integrating male circumcision into EPP:

- **Are the data available?** Yes, survey and program data for 15 countries. However, additional burden to incorporate program data correctly.
- **Is the method feasible?** Yes, impact could be added as another term to the EPP incidence equation.
- **Is the impact significant?** Yes, changes in MC prevalence are large in at least half of the countries.
- **Is it necessary for target setting?** No, targets rely on only on prevalence of MC.
- **Is it necessary for impact estimation?** No, this can be done through other models, just as is done ART.

Accounting for the age distribution of VMMC is important, and will change over time as the population ages and as programmatic targeting shifts to only circumcising ages 15+.

Key points from discussion

Validation of MMC programme data and reconciliation of discrepancies between programme data and survey data was identified as a challenging and likely labour intensive task. Key points from discussion were:

- Country teams will require technical assistance (e.g. as provided in successful applications of DMPPT2) to review and validate programme data at the district level.
- Survey data and programme data can be inconsistent (Peter Young); inconsistencies can be driven by cross-district attendance to districts with funded MMC programmes (Mutsa Mhangara).
- Self-reported circumcision data correlates in Malawi well with empirical observations from STI clinic surveillance (Andreas Jahn); validation studies of self-reported circumcision status in South Africa and Kenya suggest high sensitivity (Katharine Kripke).
- Close collaboration with VMMC country teams is required to reconcile country-specific data discrepancies (Katharine Kripke, Mutsa Mhangara).

There was not consensus about the whether or how male circumcision should be incorporated into national or subnational HIV incidence estimates. Discussion raised several considerations to guide this decisions:

- It is unclear whether the impact of MMC on HIV incidence is large enough, relative to other factors not modelled, to require explicit representation in EPP (Leigh Johnson).
- Other cited evidence from cohort sites suggests large effects of MMC on HIV incidence trends and sex ratios of incidence (Kate Grabowski and Adam Akullian).
- It is essential that any inclusion of MMC in incidence estimates explicitly account for age patterns of circumcision relative to age patterns of HIV risk (Milly Marston) and the differential impact of circumcision on female-to-male and male-to-female transmission (Tim Brown).
- Quantifying the effect of non-medical circumcision on incidence patterns is not necessary because this is implicitly accounted for in baseline incidence estimates from EPP (John Stover).
- HIV incidence trends in EPP are largely inferred from data on pregnant women, with data on men only included in EPP when surveys are conducted. Thus direct effects of MMC on male incidence are only likely to be captured with delay (Jeff Eaton).

Recommendations

Recommendations about estimation of coverage and impact of MMC programmes are organised to three areas for attention identified from the session:

1. A systematic process and technical support are required for validating MMC programme data and reconciling discrepancies across sources.
2. Methodology and tools are needed for systematically estimating circumcision coverage and targets.
3. Further review of evidence is required to reach consensus about approaches for estimation of impact of MMC programmes, including whether MC coverage should be explicitly represented in EPP and Naomi incidence estimates.

Supporting review and validation MMC programme data and coverage estimates:

- MMC teams and HIV estimates teams should undertake a process to validate and reconcile MMC programme data to have the best possible data available for HIV programmatic target setting and potential inputs to impact modelling and incidence estimation.
- Create a tool to export district results from DMPPT2 to Spectrum for inclusion of MMC estimates in the Spectrum to Data Pack process in 2021.
- Estimates of the baseline circumcision coverage (pre MMC) inputs to DMPPT2 should be updated with systematic analysis of survey data through a small-area estimation or Bayesian geostatistical modelling approach.
- A process should be established for incorporating district level PHIA survey data about male circumcision coverage, similar to data about HIV prevalence, ART coverage, and incidence in Naomi model estimates process.

- Partners (including Avenir Health, USAID, UNAIDS, ICPI, CDC, WHO) should engage countries over next two months about transitioning MMC estimation to the HIV estimates process and convening working group to review and validate MMC programme data.
- Technical support should be provided to country MMC and estimates teams over July to January to review and validate MMC programme data.
- HIV estimates workshops in for eastern and southern African countries in 2021 should include a half day session to finalize and complete export estimates workshop in 2021 focused on finalizing and exporting MC coverage estimates for data pack. *(Maybe / TBC?)*

Methodology and tools for synthesising district-level MMC programme and survey data

- A working group of the UNAIDS Reference Group should continue to review modelling approaches for district-level estimation of male circumcision coverage, including Bayesian geostatistical models, small area estimation models, and survival analysis models.
- Analysis and extension to other countries should focus on reviewing data and evidence about:
    - Accessing MMC services in different locations than location of residence, for example influenced by districts where services were initially established.
    - Misreporting of circumcision status in surveys, for example due to social desirability bias.
    - Ability to identify and adjust for inaccurately reported male circumcision programme data.
    - Availability of other data sources to triangulate and improve estimation of male circumcision coverage, such as STI clinic patient records

Estimation of MMC impact and incorporating male circumcision into HIV estimation

The UNAIDS Reference Group should convene a further working group to review:

- Whether the impact of MMC on HIV incidence is likely already captured through estimated HIV incidence trends inferred from household surveys and ANC testing data.
- The anticipated magnitude of effect of explicitly modelling effects of MC on HIV incidence relative to other aspects and uncertainties in incidence estimation.
- Potential model specification for the effect of male circumcision on HIV incidence that adequately captures localized direct effects to men of particular age ranges.
- Whether male circumcision must be explicitly incorporated in future integrated models for HIV estimation, transmission dynamics, and impact assessment.

5. Evidence on age patterns of incidence and transmission in sub-Saharan Africa

HIV interventions are increasingly targeted at particular age and sex groups with high incidence or transmission. This relies heavily on the accuracy of model estimates for these quantities. The objectives for sessions 5 and 6 were to:

- Review empirical evidence about the age patterns of HIV incidence and transmission compared to current model estimates.
- Consider incorporation of HIV transmission dynamics (e.g. sexual debut, sexual behaviour, age mixing) to enhance estimates and projections of age-specific estimates incidence and transmission.

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

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

where $\lambda_{15-49}(t)$ is the HIV incidence rate, $r(t)$ is the average HIV transmission rate by *untreated* HIV positive adults as ρ_{15-49} is the HIV prevalence among adults age 15–49, and α_{15-49} is the ART coverage among adults age 15–49. The parameter ω is the average reduction in population HIV transmission per 1% increase in 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 (e.g. around 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 eastern and southern Africa and western and central Africa (Fig 3). 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 over time, consistent with the assumption of static incidence rate ratios.

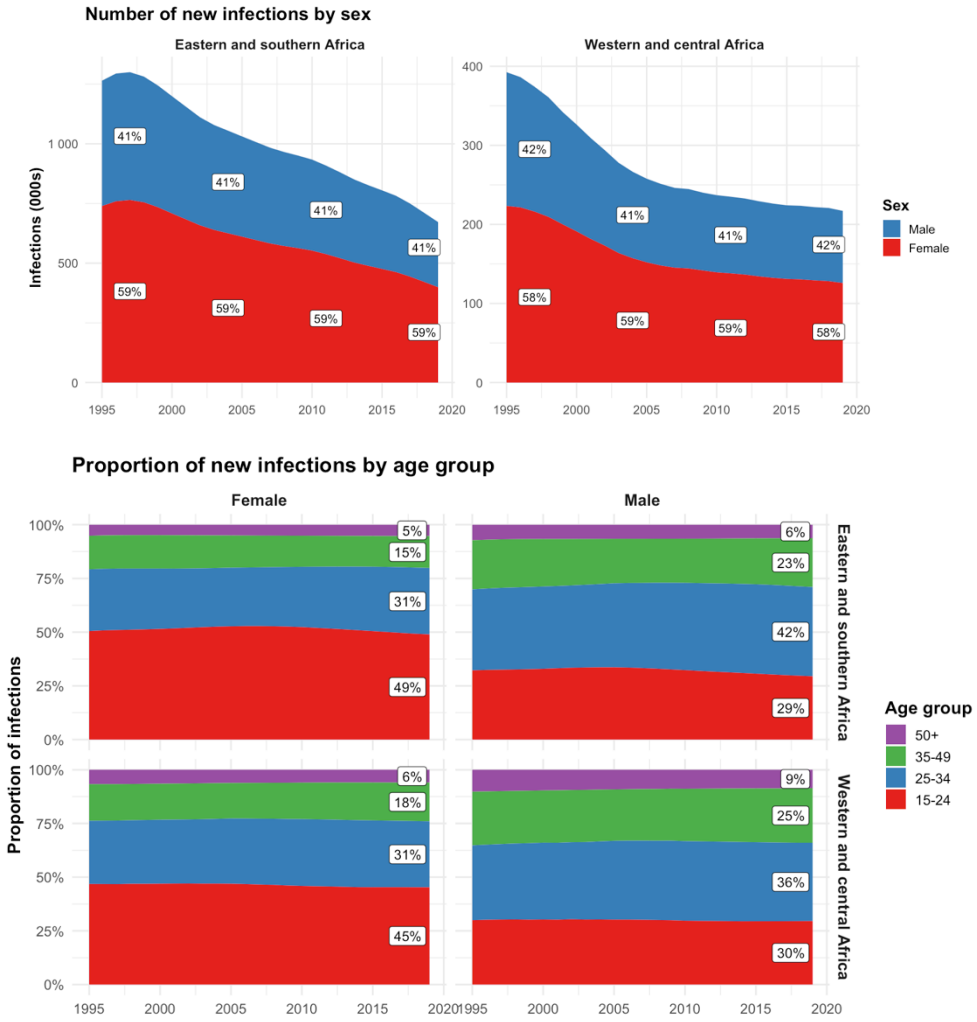


Figure 3: Estimates of the number and distribution of new infections by sex in sub-Saharan Africa (top) and the distribution of new infections by age group (bottom). *Source: UNAIDS 2019 estimates*.

Kate Grabowski reported results of a systematic review of directly observed HIV incidence esitmates in sub-Saharan Africa from 2010-2019. Over 18,000 records were screened, from which 292 articles or reports were included in analysis. Directly observed incidence estimates were available from cohort studies, control arms of randomised control trials, or studies with cross-sectional measures of incidence (Fig 4). High HIV burden settings in eastern and southern were disproportionately represented and 19 SSA countries had no published HIV incidence data since 2010.

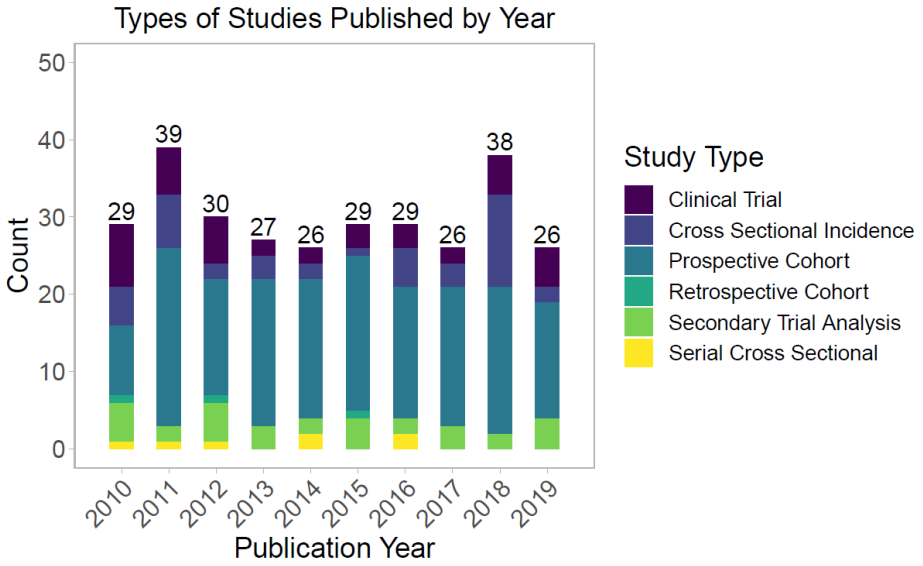


Figure 4: Study types included in systematic review by Grabowski et al. by year of publication

Pooled trend analysis estimated declines in both male and female incidence in Southern Africa from 2005, and in East Africa from 2010 (Fig 5), consistent with UNAIDS estimates. Though only 10 studies included 3 or more measurements of incidence over time, declines were seen in nearly all studies. Incidence data from Western and Central Africa and by risk group were too sparse to inform an incidence trend over time.

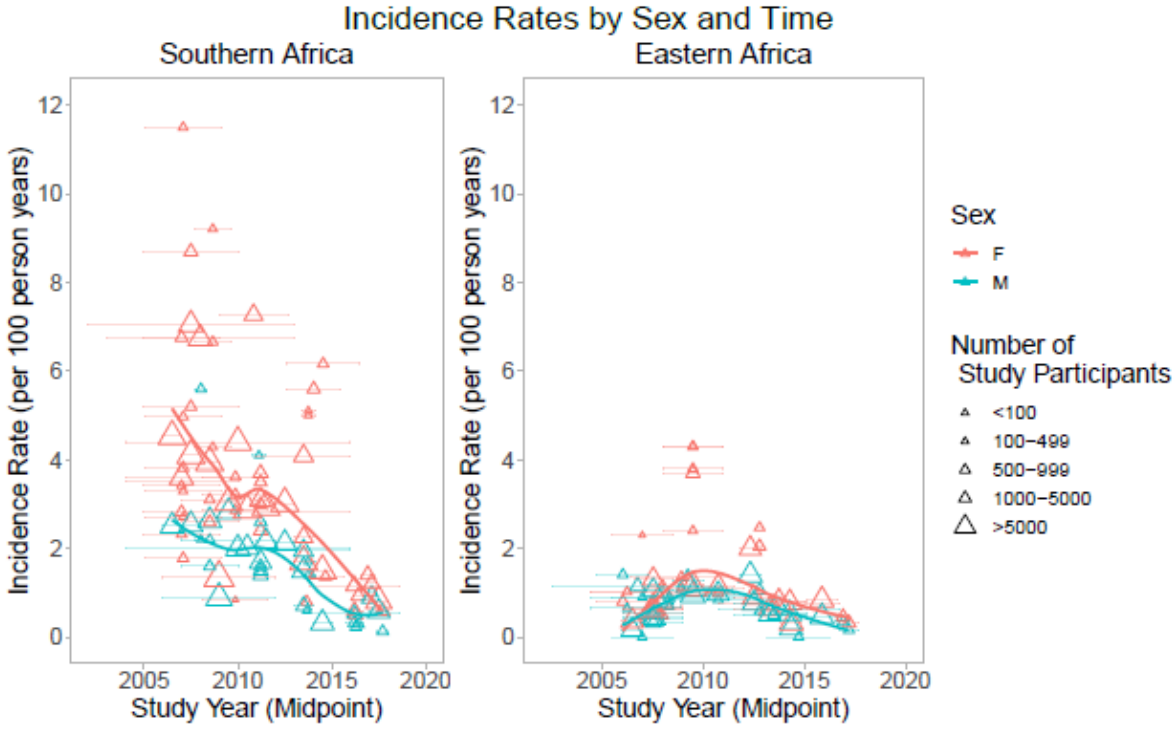


Figure 5: Sex-specific incidence declines in Southern and Eastern Africa

Katie Risher reported estimates of age-specific HIV incidence from jointly modelling mortality and HIV incidence in six population cohort studies collaborating through the ALHPA network. Incidence declined among all age groups in all studies. The timing of decline varied—female incidence in Karonga fell steeply from 2000, whilst in uMkhanyakude in eastern South Africa, incidence only precipitously fell from 2014 (Fig 6). The age distribution of incidence was flatter with older average age at infection in smaller magnitude epidemics with earlier incidence declines—Karonga, Kisesa, Masaka, and Manicaland—compared to Rakai and uMkhanyakude. Roughly 50% of infections across all sites in women occurred between 15-24, whilst around 50% of infections in men were between 20-29. Thus, estimates of the age distribution of HIV infections from population cohort studies were broadly consistent with prevailing UNAIDS estimates.

Estimates for most studies exhibited some increase in the average age of new HIV infection over 2000 to 2017, but changes were relatively minimal. Increases ranged between no increase to 2 years increase. Risher's analysis did not report about the sex ratio of HIV infections over time.

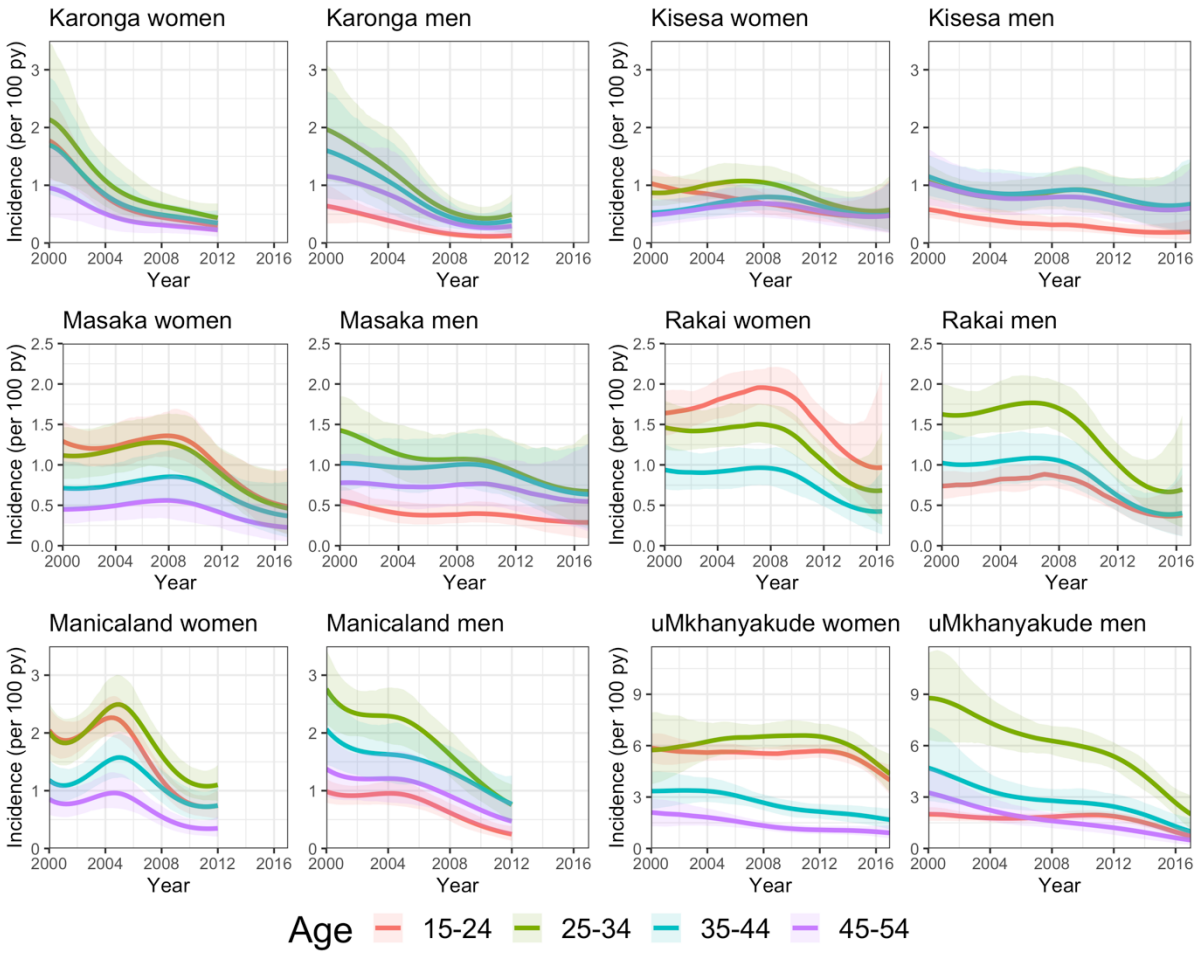


Figure 6: Age-stratified HIV incidence trends among population HIV cohorts in eastern and southern Africa.

Paul Stupp presented cross-sectional estimates of HIV incidence from 13 PHIA surveys estimated through a recent infection testing algorithm including the LAg recent infection assay, viral load, and biomarker-based ARV measurement. Based on this algorithm the false-recency ratio was assumed to be 0 and the mean duration of recent infection was 130 days (except Uganda). Recent HIV infection was detected amongst 82 male and 199 female respondents aged 15-49 across the 13 surveys. Derived annual HIV incidence varied across countries, exceeding 1% in eSwatini and Lesotho. In all countries, female incidence exceeded that in men, though with high variability. Disaggregating country-specific incidence by age results in small sample sizes and trends that are difficult to interpret.

Wolfgang Hladik analysed PHIA survey data about the association between unsuppressed viral load and incidence in the opposite sex. Despite higher ART coverage and viral suppression among women than men, there were an estimated 1-1.5 times more women with unsuppressed HIV infection than men with unsuppressed HIV infection due to the higher overall prevalence of HIV among women than men. Transmission ratios (number of estimated adult HIV transmission per 100 viremic person years) were greater for male-to-female transmission than female-to-male, though with substantial variation across surveys. Total HIV incidence rate was well correlated with population viremia and population prevalence. Correlation was weaker when stratified by sex or expected age mixing pairs. It was noted that correlation between viral load in diagnosed PLHIV or PLHIV on ART and incidence was worse than between VL in all PLHIV and incidence, highlighting the value of sampling undiagnosed PLHIV in surveys rather than only those engaged in programmes.

Maya Peterson, on behalf of the Universal Test and Treat Trials Consortium (UT3C), presented pooled analysis of the relationship between community-level population viremia and HIV incidence rate from four UTT trials [4]. Both HIV incidence, measured over 345,000 person years, and population viremia, measured over 40,000 person years, varied considerably within studies – 0.03 to 3.4% and 3 to 70% respectively. Population viremia was associated with HIV incidence in all UTT trials, with HIV incidence increasing by 0.07% for each 1% increase in viremia in unadjusted analyses. When adjusting for study prevalence, the effect size was smaller, but still significantly associated; HIV incidence increased by 0.12% for each 10% increase in population viremia (Fig 7). Population viremia explains the majority of differences in incidence across trial arms.

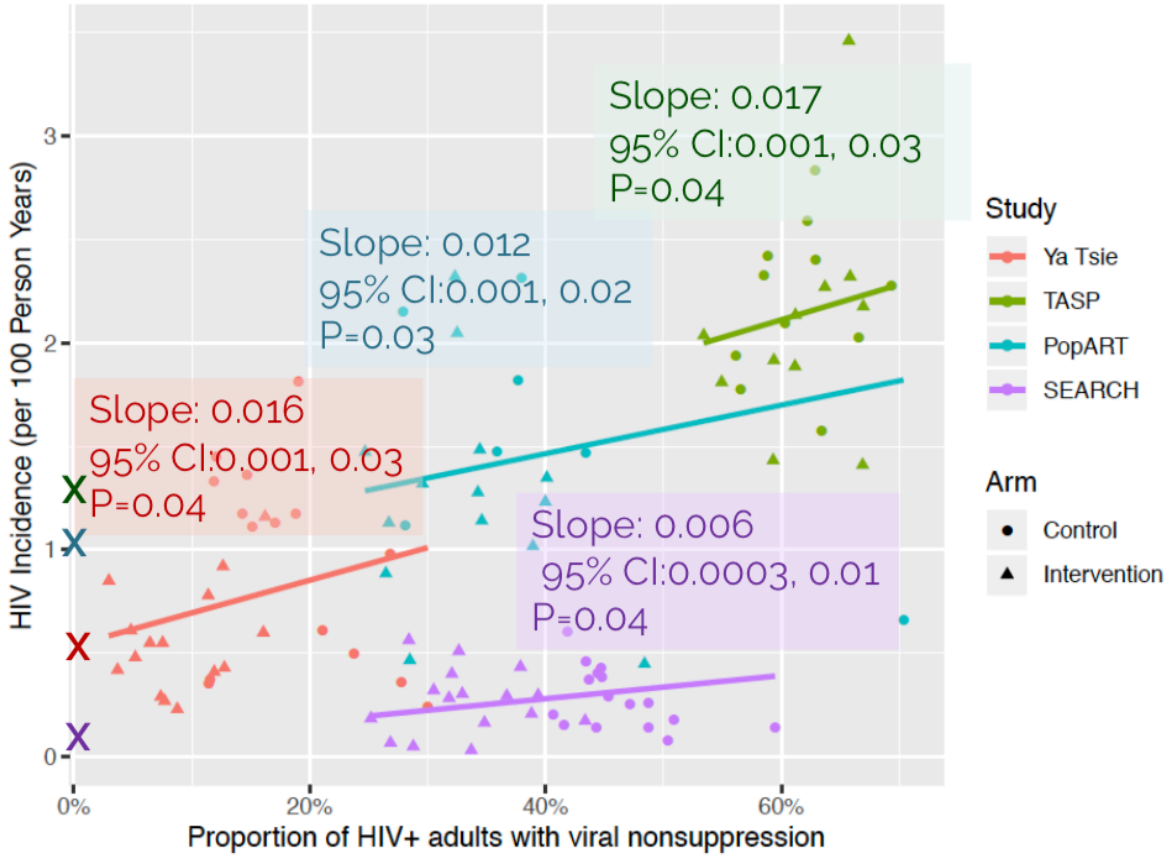


Figure 7: Association between HIV incidence and population viremia in UT3C studies

Will Probert, described two independent methods to estimate age patterns of incidence within the HPTN 071 (PopART) trial – an individual based model calibrated to trial epidemiologic data and reconstructed phylogenetic data. Within the individual based model, sexual behaviour was parameterised to allow for varying heterosexual partnership formation and dissolution, age assortative mixing, sexual risk mixing, and age-specific partnership formation rates. From 8000 sampled next-generation HIV viral sequences phylogenies were reconstructed, and 316 likely transmission pairs identified. Both methods identified peaks in HIV transmission between ages 20-24 in women and between 25-29 for men. The age-specific peak in transmission corresponds well to lower age-specific ART coverage in the opposite sex.

Adam Akullian presented an analysis of data from the Africa Health Research Institute cohort study in KwaZulu-Natal. HIV incidence has recently declined by around 50% for men, and around 35% for women. Seroconversion data indicate little change in age- and sex-specific incidence from 2004 to 2011, with declines thereafter, particularly in young age groups. Men under 30 have experienced significant incidence declines over the past 10 years, with later declines in women under 25 years of age (Fig 8). Several factors were hypothesised to explain differential changes in age- and sex-specific incidence:

- VMMC scale up, with higher uptake in younger men;
- ART scale up, with more uptake in women;

- Larger and earlier declines in population viremia in younger age-groups; and
- Large increases in HIV prevalence in older ages over time

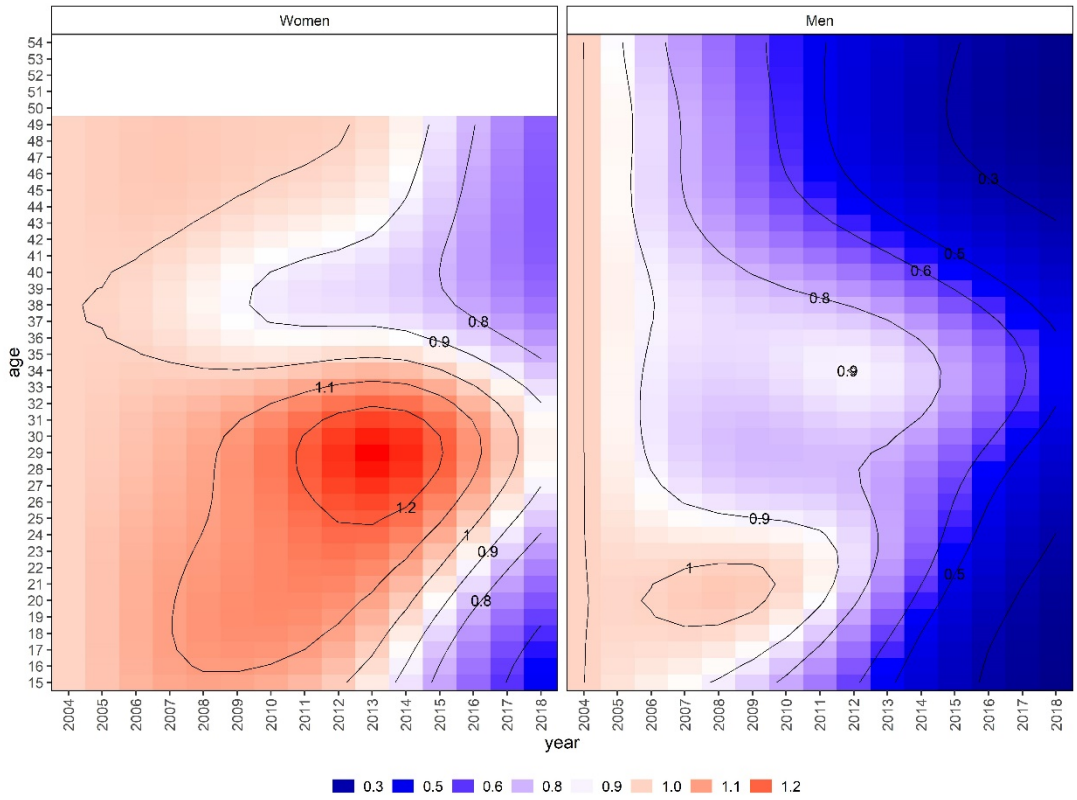


Figure 8: Sex and age specific incidence relative to incidence in 2000 in KwaZulu-Natal cohort site. Image from Akullian et al. CROI 2020

Key points from discussion

Discussion focused on whether age patterns of HIV incidence in UNAIDS Spectrum estimates for SSA were consistent with empirical evidence. Key points included:

- Akullian showed a clear shift in age pattern over time, and Risher showed shifts in some cohort studies. There is no single clear change in age pattern across settings (Leigh Johnson).
- Though decreases in incidence have been observed, there is little evidence for change in age pattern of incidence over time (John Stover)
- The peak in female incidence may have remained the same, but the age distribution of incidence is changing and alternate metrics like the area under the curve should be considered (Adam Akullian).
- Recently reported 2018 Rakai cohort data shows large incidence falls in adolescent girls and young women, with 15-49 incidence now 60% lower in women compared to the pre-ART period (Kate Grabowski) [5]

Session 6: Modelling approaches to age patterns of HIV incidence and transmission

Session 6 focused on reviewing the key transmission dynamics that need to be considered in a parsimonious mathematical modelling approach to capture evolving HIV epidemic dynamics. Three mathematical models were discussed: the Goals-ASM, EPP-ASM+ with sexual mixing, and the Thembisa model for South Africa.

The Goals-ASM model is a mechanistic HIV model within Spectrum that models sexual mixing and HIV transmission by age, but not heterogeneous HIV risk behaviour. Sexual behaviour is parameterised using sexual activity by age, lifetime partner change rate for women, and age differences in sexual partnership. Age differences in sexual partnerships are invariant with respect to the age of partners, informed by stable age differences from survey data over age. Though Goals-ASM fits to the same household serosurvey data and antenatal prevalence data as in AIM/EPP, estimated prevalence and incidence are substantially different in epidemic peak and shape. Goals-ASM estimates an increasing proportion of new infections in older age groups. Additionally, the sex ratio of new infections in Goals-ASM diverges from that in AIM/EPP, with male new infections falling faster than female new infections. This divergence is driven by the combination of VMMC scaleup and higher ART coverage in women.

Kinh Nguyen presented a modified version of EPP-ASM to include sexual debut, change in sexual activity by age, sexual mixing, and partner acquisition. Sexual behaviour parameters were derived from statistical analysis of household survey data about age at first sex, sexual activity in the past year, number of lifetime partners, and age of sexual partners. Across countries women sexual debut earlier and remain more sexually active at younger ages. The rate of sexual partner acquisition varies widely between countries, with the highest partner change rate at young adult ages. The age difference between partners varies across countries, though men are always older than their partners.

Using Malawi as an example, the modified model estimated an epidemic curve that starts earlier and peaks lower than default EPP, and both models fit 15-49 survey prevalence well. Disaggregating serosurvey prevalence by age, the modified model fitted ages 55+ poorly, though all other five year age bands are well fit.

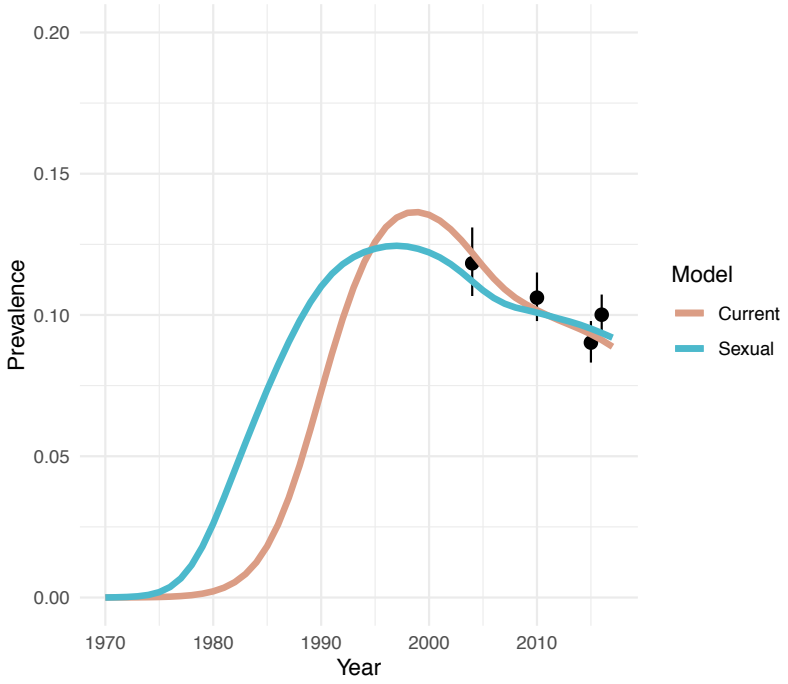


Figure 9: Comparison of prevalence curves fit in EPP with and without sexual behaviour

Using the Thembisa model, Leigh Johnson addressed two questions:

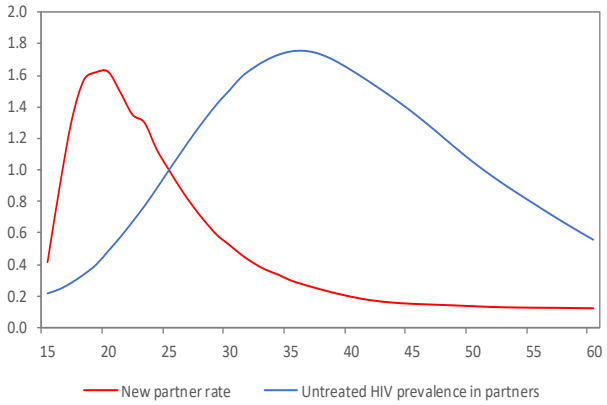
1) How have age patterns of incidence in South Africa changed over time?

Relative to age-specific incidence in 2000, HIV incidence among those under age 45 has declined by around 60%; declines were similar across all ages amongst those under age 45. However, in the older age groups, incidence declines were smaller than in younger age groups, and at the oldest ages incidence has increased relative to 2000. These patterns are similar for both sexes.

Factors contributing to the characteristics of incidence change were:

- Aging effects: As more HIV-positive people survive to older ages, they generate higher HIV incidence at older ages.
- Differences in intervention uptake by age:
    - Condom use is substantially lower at older ages than at younger ages.
    - Similarly for VMMC.
- Interventions may delay the age at HIV acquisition in high-risk individuals (rather than 'prevent' HIV).

2) *Can we approximate the age pattern of HIV incidence with age pattern of partner contact and age pattern of viremia in the opposite sex?*



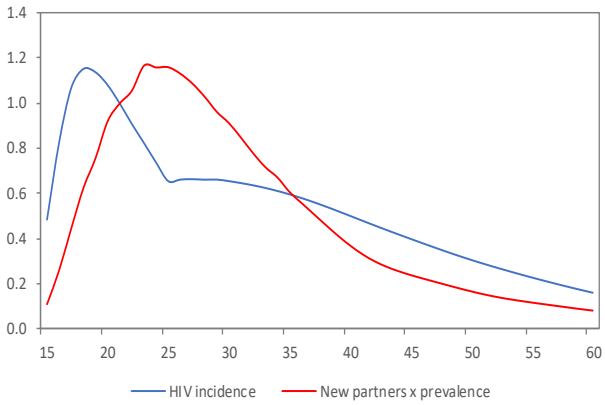


Figure 10 (left): Relative partner contact rate for women standardised to age 25 (red) and untreated HIV prevalence by age in men (blue)
Figure 11 (right): Thembisa estimate of age pattern of incidence for women, standardised to age 21 (blue), approximated age pattern of incidence for women, using the product of the two curves in Fig 10

Fig 10 shows the relative partner contact rate for women and untreated HIV prevalence in their male partners based on age patterns of sexual mixing and untreated prevalence by age for men, both standardised to age 25. Fig 11 shows the female HIV incidence (blue) and the distribution of HIV incidence rate that would be expected if the age pattern of female incidence was proportional to the partner contact rate and untreated prevalence among partners (red, the product of partner rate and prevalence in Fig 10), both standardised to age 21.

The peak age of female HIV infection was younger than predicted by the untreated prevalence among sexual contacts for two reasons:

- The model incorporates a higher risk of HIV acquisition per sex act for women below age 25.
- At young ages, the HIV-negative men are less sexually active than the HIV-positive men (i.e. risk behaviour heterogeneity not taken into account).

Two factors also contributed to higher relative infection at older ages than would be predicted by the age pattern of sexual partners:

- In older women, the number of new sexual partners does not capture the exposure to HIV acquisition because new HIV infections are acquired through previously-established relationships.
- Older untreated men are more likely to be in the more advanced HIV disease stages, with higher HIV infectiousness.

Key points from discussion

1) Should the EPP model in generalised epidemic settings more explicitly represent transmission dynamics in estimates of HIV incidence patterns?

- It is difficult to discern whether empirical changes in sex and age patterns of new infections driven by evolving natural transmission dynamics or by specific intervention scale-up in particular study locations (Jeff Eaton & Leigh Johnson).
- Evidence was strongly suggestive of an increasing sex ratio in new HIV infection, which EPP/Spectrum estimates should aim to capture. The distribution of new infections by age was relatively consistent with Spectrum estimates and evidence was less conclusive about systematic changes (John Stover); sex ratios of infection come into question during estimates process in countries with high ART coverage when programme data about the number of women on ART exceeds model estimates of the number of women living with HIV (Mary Mahy).

2) Should EPP model assumptions about the effect of ART on population incidence, represented by ω in EPP, be revised?
   - Adjusting ω and representing transmission dynamics are linked issues. If EPP moves towards explicitly representing transmission dynamics ω can be set closer to the proportion of those on ART who are virally suppressed (Leigh Johnson).
   - Consider adding a second parameter that permits ω to vary across age or time as a parsimonious approach to capture evolving dynamics (Adam Akullian).

Recommendations

- Evidence about sex ratios of new infections should be more systematically collated to inform updated default assumptions about changes in sex ratio of HIV incidence. This should include consolidation of evidence about sex ratios of incidence from:
  - Grabowski and Joshi et al systematic review.
  - Risher et al. analysis of population cohort data.
  - UT3C pooled analysis of Universal Test and Treat trials.
  - Akullian et al. analysis and modelling of AHRI population cohort data.
  - Thembisa model estimates for South Africa.
  - The Goals-ASM model.
  - Other applicable and readily available transmission dynamic modelling evidence.

- In the Spectrum model, approaches should be explored for establishing a default pattern for changing sex ratio of incidence in the, or dynamically adjusting the sex incidence rate ratio based on sex-specific ART coverage, and potentially male circumcision coverage.

- A working group of the UNAIDS Reference Group should produce a consensus paper describing the EPP model assumptions about the effect of ART scale up on HIV incidence. This should include evidence based on:

    - Further empirical analysis of the relationship between HIV prevalence, treatment coverage and incidence from pooled analysis of UTT trial data and PHIA survey data.
    - Analysis of readily available mathematical modelling outputs about the relationship between ART coverage scale-up and population-wide incidence reductions.

- A working group of the UNAIDS Reference Group should produce a consensus report of key dynamics underpinning changing patterns of new HIV infections, which should be captured in future model development. This should guide features for continued development work on age patterns and transmission dynamics for future implementations of EPP/Spectrum.

Session 7: Data requirements and harmonised codebases for next generation tools

Current estimates tools involve application of several different models that reproduce the same underlying calculations (Spectrum, EPP, CSAVR, Shiny90) and rely on input data from the same sources (household surveys, household censuses and demographic estimates, national HMIS/DHIS). Harmonisation and logical integration of code and data inputs will enhance both maintenance and updating of tools and user experience. However, changes to existing tools entail substantial development effort and disruption for existing users. As such, large changes need be undertaken conservatively, likely over several years.

The objectives for this session are to establish objectives and timelines for harmonisation of:

- Model code bases
- Methodological inference approaches
- User interfaces
- Data inputs to multiple models

Jeff Eaton proposed an approach for development towards harmonisation of data structures and data models for all modelling tools supported by UNAIDS for HIV estimates:

- All data inputs stored in the AIDS Data Repository (ADR) in 'long' format datasets with consistent ID keys and constraints across models.
- All models access datasets via ADR API.
- Where possible, the ADR should archive steps in the data workflow for reproducibility and efficient updating of model inputs.
    - Source data extraction
    - Scripts for transforming data
    - Final model input datasets

Eaton outlined a four stage data extraction and transformation process (Fig 12), noting that user interaction and manual data cleaning may occur at each stage of the process.

Key challenges that need to be addressed include:

- Data need updating annually;
- Data cleaning and editing during modelling process;
    - Inputs may become inconsistent across models
- Upstream data may change
    - Updates to primary survey datasets
    - Revisions and Data Quality Adjustments
- Other changes necessitating data refresh
    - e.g. district boundary changes

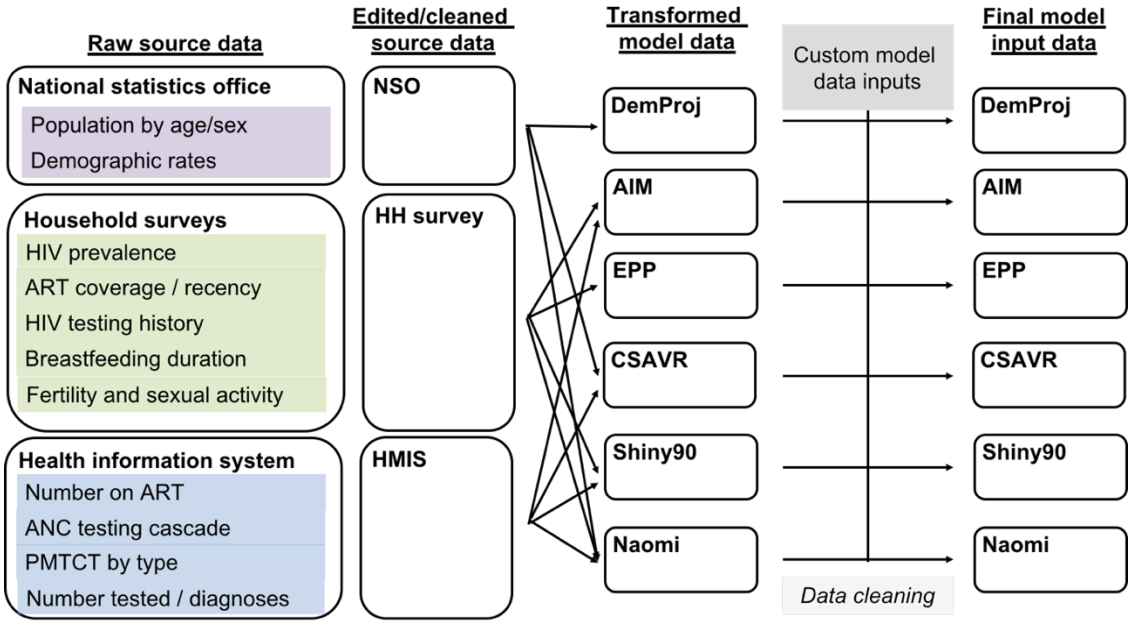


Figure 12: Four stages of data extraction and transformation from raw data to model inputs

In addition to the survey dataset used by the model, accompanying metadata must be also be maintained to allow the survey dataset to be regenerated should, for example, the area hierarchy, survey regions, individual recode, or biomarker datasets change.

The AIDS Data Repository was used to support UNAIDS estimates for the first time in the 2020 process. Country teams were receptive to storing national data within the ADR. The ability to automatically extract and transform programmatic data from DHIS2 was particularly well received. Future development will include:

- User friendly DHIS2 extracting
- Automated model interoperability
- Data versioning and change tracking
- Inputs to UNAIDS estimates package
- Improved access management
- Pre-configured visualisations of data

Accepting raw data from DHIS2, finalised model inputs, and finalised model outputs into the ADR has progressed well, facilitated by clearly defined data structures. The iterative process of data cleaning, review, and validation is harder to capture. Ongoing development of will require:

- Well defined structure to model inputs
- Good model interoperability
- Versioning and change tracking

Bob McKinnon and Robert Puckett gave an update on the development progress of Spectrum and EPP online. The demographic projection module DemProj is operational online, mirroring the interface currently implemented in the desktop version. Additional data visualisation has been included to assist users identify data

input errors. EPP online, also mirroring the existing interface, is now able to fit to surveillance data and will be accessible within a tab from Spectrum online.

John Stover and Andrew Tait described development steps for a common codebases for demographic and HIV simulations, currently replicated across several models. The common simulation codebase needs to:

- Balance the speed requirements of EPP, CSAVR, Naomi, and Shiny90, with the number of calculations required by AIM; and
- Be usable in Delphi, Java, R, and C++.

To ensure the code is usable between platforms and retains fast computation, a C++ library will be developed with a simple API. All arrays will be linearised so that data structures are language agnostic. Around this API, wrappers to support Windows, Linux, and OSX interfaces will be written, and further helper functions for R and Java support. At first instance, the full model stratification in the present implementation of Spectrum will be written into C, and once fidelity is confirmed, model approximations and simplifications for faster computation can be considered.

Development work to convert Spectrum models into C++ has begun. The proposed steps for a given module are:

- Create Delphi DLL
- Test in Spectrum
- Covert to C++
- Test in Spectrum
- Make available to East West Center, Imperial to test with their applications
- Provide to all developers
- Finalise optimised, fully documented code

A prototype implementation of DemProj will be available for review in mid-May and full implementation of DemProj and AIM will be available by July 2020. This will reproduce computations currently implemented by AIM. Following this, code will be adapted for specific computations by other modelling tools and integrated into existing interfaces (EPP, Shiny90, CSAVR).

Rob Ashton presented a workflow to improve documentation and identification of when model or data input changes alter modelled outputs. In the 2020 Naomi estimates, changes to the estimates were difficult to trace back to either model development and/or data inputs changes, and model code debugging was challenging. Continuous integration – running a test suite on every model code update – would reveal model failures, but would not account for changes caused by differing data inputs, nor give an understanding of how the estimates have changed. Instead, a process that is triggered each and every time data in the ADR or model code changes that generates a report would allow country teams and modellers to compare data and model versions – “continuous data integration”.

Key points from discussion

Data inputs and harmonisation

- Models need to record which version of datasets were used (Tim Brown)
- Data flow from Spectrum to the ADR
    - Model metadata – e.g. subnational regions in EPP, or whether to use PHIA incidence in EPP – selected by users in the Spectrum interface needs to be returned and stored in the ADR (Tim Brown)
    - Users need to be able to interactively edit data in Spectrum and other software interfaces. If data are to be stored in ADR, changes need to also be able to be pushed back to (John Stover).
    - API access to write data from Spectrum online to ADR is straightforward, but it is unclear how authentication and permissions would be implemented when using Spectrum desktop.
    - If countries edit input data in Spectrum, in conflict with DHIS2, changes should be automatically detected and users should be encouraged to annotate the edit made to the data. When a subsequent data extraction from DHIS2 is conducted, countries should have the option of either retaining the edited data or overwriting it with the data from DHIS2 (Jeff Eaton).
- Development of tools to assist in data visualiation, validation, and cleaning will be vital for country teams fully to engage with centralising data within the ADR (Mary Mahy, Eby Pascal)
    - Should these tools reside within the ADR or within modelling tools?

Data workflows

- Continuous data integration requires continuous ADR access to all country data which may be difficult to secure (John Stover).
- Dashboards to visualise when and where changes were introduced into the estimates would be useful for UNAIDS and country teams during the estimates process (Mary Mahy, Peter Young, Mutsa Mhangara).
- Multiple changes to estimates within a single year outside of the estimates process would be counterproductive and damaging to the national policymaking process (Mutsa Mhangara, Mary Mahy).
- Countries produce estimates from a set of data inputs that have been cleared for use by national policymakers. These estimates are then “frozen” rather than dynamic as continuous data integration suggests (John Stover).

Recommendations

Data inputs and harmonisation

- The four stage data extraction process outlined by Eaton should be housed within the ADR

- A tool should be developed to assist countries in visualising and validating transformed, cleaned input data for each supported model. This will permit data visualisations at all area and age aggregates.
- Data editing will be retained in Spectrum and when estimates are finalised, a report will be generated that compares the data used in Spectrum with the data pulled in from the ADR. This can be uploaded into the ADR with final estimates.
- The process of accessing harmonised datasets from the AIDS Data Repository for Spectrum will be tested with transformed 5 year age band prevalence data from household surveys used for IRR fitting (data currently contained within AMModData spreadsheet),
- Naomi to access input data directly from ADR through API for 2021 estimates.
- Shiny90 model to access input data direcly from ADR through API for 2021 estimates.
- UNAIDS will convene a working group to define harmonised data models for all UNAIDS supported models (Fjelltop, UNAIDS, Imperial, Avenir, East-West, McGill).

User interfaces

- Development of Spectrum Online and EPP Online to continue by Avenir Health and East West Center.
- The Shiny90 user interface should be integrated into the Spectrum software. Avenir Health will prepare plan for integration of Shiny90 into Spectrum.

Codebase harmonisation

- Prototype code for DemProj to be completed and shared by 10th May 2020.
- Full implementation of DemProj and AIM modules will be available by July. The Secretariat will organize a meeting in July 2020 to coordinate steps for extending code for other model computations and integrating in user interfaces.

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Appendix 1 – Agenda

Day 1: Reviewing 2019/20 UNAIDS estimates and development pathway for next generation models (21st April)

Time	Duration (mins)	Topic	Presenter(s)/ Lead Discussant
15.30	20	Welcome and introductions	Shannon Hader & Peter Ghys
15.50	10	Meeting objectives and overview	Jeff Eaton
Session 1: 2019/2020 UNAIDS estimates process (chaired by Leigh Johnson) • Review the use of UNAIDS supported models in 2019/20 global HIV estimates process. • Identify priority developments for 2020/21 HIV estimates process.			
16.00	25	Review of 2020 estimates process Asia/Pacific estimates	Mary Mahy Keith Sabin
16.25	25	Shiny90 • Application in 2020 estimates • Estimating knowledge of status, incoporating recent infection data, and future model development	Kim Marsh Mathieu Maheu-Giroux
16.50	25	Naomi: estimating indicators at the district level • Application in 2020 estimates • Future model development	Ian Wanyeki Jeff Eaton
17.15	25	CSAVR • Application in 2020 estimates • Future model development	Kim Marsh Guy Mahiane
17.40	25	Paediatric estimates • 2019/20 estimates • Priorities for 2020/21 estimates	Mary Mahy Leigh Johnson
18.05	10	Break	
Session 2: Next generation models (chaired by Josh Solomon) • Reach scoping recommendations for model development within 5 year time horizon including: • Required indicators from HIV estimates. • Required stratifications of indicators. • Data input sources synthesised by tools. • Segmentation of tools across geographic scales, epidemic types, and time horizons. • Scope of purpose for estimation tools.			
18.15	15	Vision for scope and outputs of next generation HIV estimation tools	Peter Ghys
18.30	15	Reference Group development priorities and strategy development pathway	Jeff Eaton
18.45	45	Discussion	
19.30	CLOSE		

Day 2: HIV natural history assumptions and male circumcision in SSA (22nd April)

Session 3: Natural history model (chaired by Jeff Eaton) • Review proposal for updating CD4 progression and mortality parameters. • Assess impact of proposed parameters on estimates.			
15.30	30	Natural history model	Rob Glaubius
16.30	45	Discussion and recommendation	
Session 4: VMMC (chaired by Mary Mahy) Reach recommendations on: • Methodology for estimating MC coverage by age/time at national and subnational level. • Approach to incorporating into estimates process and/or Spectrum software. • Model assumptions to incorporate effects of VMMC on HIV incidence in EPP and Naomi.			
17.15	5	Session overview and objectives	Jeff Eaton
17.20	30	Review of existing data sources, data quality, and estimates; DMPPT2 tool	Katharine Kripke
17.50	10	Break	
18.00	15	PHIA survey evidence on circumcision coverage	Megan Bronson
18.15	15	Mapping male circumcision coverage in SSA	Michael Cork
18.30	15	Modelled-based estimates of MC in South Africa	Matt Thomas
18.45	15	Potential model-based assumptions for EPP	John Stover
19.00	30	Discussion and working group outline	
19.30	CLOSE		

Day 3: Age patterns of HIV incidence and transmission in SSA (23rd April)

Time	Duration	Topic	Presenter(s)/ Lead Discussant
Session 5: Evidence about age patterns of incidence and transmission in SSA (chaired by Leigh Johnson) • Are UNAIDS estimates of age and sex patterns of HIV incidence consistent with directly observed HIV incidence estimates? • Are the age distribution of unsuppressed VL and age distribution of sexual contacts a sufficient model for age patterns of HIV incidence and transmission over time?			
15.30	5	Session overview and objectives	Jeff Eaton
15.35	20	Systematic review of directly observed HIV incidence measures in SSA	Kate Grabowski
16.05	15	Distribution of new infections by age: ALPHA Network	Katie Risher
16.20	15	Age and sex incidence patterns from Population HIV Impact Assessment Surveys	Paul Stupp/Wolfgang Hladik
16.35	15	Population viremia and HIV incidence: UT3C Consortium	Maya Petersen
16.50	15	Age patterns of HIV transmission: PANGEA network	Will Probert
17.05	15	Analysis and modelling of the AHRI population cohort	Adam Akullian
17.20	30	Discussion	
17.45	10	Break	
Session 6: Age patterns of incidence and transmission: model-based approaches (chaired by John Stover) • Should the EPP model in generalized epidemic settings incorporate age dynamics of sexual activity and sexual mixing in estimates of HIV incidence patterns?			
18.00	20	Goals-ASM	Rob Glaubius
18.20	20	EPP-ASM with sexual mixing and debut	Kinh Nyugen
18.40	20	Thembisa	Leigh Johnson
19.00	30	Discussion and working group outline	John Stover
19.30	CLOSE		

Day 4: Harmonisation of data inputs and code bases for HIV estimation tools (24th April)

Session 7: Data requirements and harmonised codebases for next generation tools (chaired by Tim Brown)
• Establish feasibility of and timelines for the harmonisation of:
  • Model code bases
  • Methodological inference approaches
  • User interfaces
  • Data inputs to multiple models			

16.30	30	Harmonisation of data structures and data models	Jeff Eaton
17.00	30	AIDS Data Repository: consolidating input data	Jonathan Berry
17.30	30	Consolidation of user interfaces	John Stover
18.00	10	Break	
18.10	30	Review of supported tools and shared computation	John Stover
18.40	30	Workflow and reproducibility	Rob Ashton
19.10	40	Discussion and working group outline	
19.50	10	Wrap up and recommendations	
20.00	CLOSE		

Appendix 2 – Participant list

Name	Institution
Annette Sohn	amFAR
Guy Mahiane	Avenir Health
John Stover	Avenir Health
Katharine Kripke	Avenir Health
Peter Stegman	Avenir Health
Rob Glaubius	Avenir Health
Geoff Garnett	Bill and Melinda Gates Foundation
Michelle Morrison	Bill and Melinda Gates Foundation
Andrew Tait	Decision Mechanics
Joy Fishel	Demographic Health Surveys Program
Robert Puckett	East West Center
Tim Brown	East West Center
Jonathan Berry	Fjelltop
Mehran Hosseni	The Global Fund to Fight AIDS, Tuberculosis and Malaria
Stephen Delgado	ICAP
Jeff Eaton	Imperial College London
Kelsey Case	Imperial College London
Kinh Nguyen	Imperial College London
Matt Thomas	Imperial College London
Oli Stevens	Imperial College London
Rob Ashton	Imperial College London
Tim Wolock	Imperial College London
Adam Akullian	Institute for Disease Modelling
Deepa Jahagirdar	Institute of Health Metrics and Evaluation
Hmwe Kyu	Institute of Health Metrics and Evaluation
Laura Dwyer-Lindgren	Institute of Health Metrics and Evaluation
Michael Cork	Institute of Health Metrics and Evaluation
Kate Grabowski	Johns Hopkins University
Katie Risher	London School of Hygiene and Tropical Medicine
Milly Marston	London School of Hygiene and Tropical Medicine
Andreas Jahn	Malawi Department of HIV & AIDS
Ipianah Chagoma	Malawi Department of HIV & AIDS
Andrea Ciaranello	Massachusetts General Hospital
Arnaud Godin	McGill University
Katia Giguere	McGill University
Mathieu Maheu-Giroux	McGill University
Peter Kirwan	University of Cambridge
Le Bao	Penn State University
Parviez Hosseni	PEPFAR
Josh Salomon	Stanford University

Wilford Kirungi	Uganda Ministry of Health
Patrick Gerland	UN Population Division
Sara Hertog	UN Population Division
Eby Pascal	UNAIDS
Ian Wanyeki	UNAIDS
Keith Sabin	UNAIDS
Kim Marsh	UNAIDS
Luisa Frescura	UNAIDS
Mary Mahy	UNAIDS
Peter Ghys	UNAIDS
Amala Reddy	UNAIDS
Mary Ann Seday	UNAIDS
Andrew Phillips	University College London
Loveleen Bansi-Matharu	University College London
Maya Peterson	University of California, Berkeley
Leigh Johnson	University of Cape Town
Mary-Ann Davies	University of Cape Town
Reshma Kassanjee	University of Cape Town
Constantin Yiannoutsos	University of Indiana
Giorgos Bakoyannis	University of Indiana
Will Probert	University of Oxford
Richard Gray	University of New South Wales
Dzifa Adjaye Gbewonyo	US Census Bureau
Redouane Betrouni	US Census Bureau
Tim Fowler	US Census Bureau
Abu Abdul Quader	US Centers for Disease Control and Prevention
Megan Bronson	US Centers for Disease Control and Prevention
Carlos Toledo	US Centers for Disease Control and Prevention
Drew Voetsch	US Centers for Disease Control and Prevention
Italia Rolle	US Centers for Disease Control and Prevention
JP Abellera	US Centers for Disease Control and Prevention
Katie Battey	US Centers for Disease Control and Prevention
Laura Porter	US Centers for Disease Control and Prevention
Peter Young	US Centers for Disease Control and Prevention
Ray Shiraishi	US Centers for Disease Control and Prevention
Roma Bhatkoti	US Centers for Disease Control and Prevention
Sasi Jonnalagadda	US Centers for Disease Control and Prevention
Steve Gutreuter	US Centers for Disease Control and Prevention
Stupp, Paul	US Centers for Disease Control and Prevention
Faith Ussery	US Centers for Disease Control and Prevention
Wolfgang Hladik	US Centers for Disease Control and Prevention
Aisha Yansaneh	USAID
Josh Davies	USAID

Mutsa Mhangara	USAID
Valerian Kiggundu	USAID
Vincent Wong	USAID
Laura Heaton	US Census Bureau
Cheryl Johnson	WHO
David Lowrance	WHO
Fabian Ndenzako	WHO
Julia Samuelson	WHO