Improving and validating estimates of AIDS deaths

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

Bern, Switzerland, 17-18 September 2018

REPORT & RECOMMENDATIONS

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

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

Kelsey Case, October 2018

Abbreviations

AIM	AIDS Impact Model
ART	Antiretroviral therapy
ART-CC	Antiretroviral Therapy Cohort Collaboration
CSAVR	Case Surveillance and Vital Registration tool
ECDC	European Centre for Disease Prevention and Control
EPP	Estimation and Projection Package
IHME	Institute for Health Metrics and Evaluation
LTFU	Loss to follow-up
PEPFAR	US President's Emergency Plan for AIDS Relief
PHIA	Population-based HIV Impact Assessment
TESSy	The European Surveillance System
UNAIDS	Joint United Nations Programme on HIV/AIDS
WHO	World Health Organization

Background

UNAIDS Reference Group

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 managed at Imperial College London and the University of Cape Town.

Work at UNAIDS Reference Group has been organised broadly into tracks:

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

Meeting Objectives

The number and trends in AIDS deaths are a key indicator for the impact of the AIDS epidemic and the impact of the HIV response, and a core output of the UNAIDS Estimates. Estimates of AIDS deaths are the outcome of several interacting model processes including estimates of earlier HIV incidence trends, model structure and parameter values for HIV natural history (CD4 progression and mortality by CD4), model inputs for the numbers of men and women receiving ART, model structure and assumptions determining the allocation of ART and parameter values for mortality rates on ART.

There have been substantial improvements to estimates of AIDS mortality in recent years. Even so, model estimates in many settings struggle to reconcile observed data about AIDS mortality from vital registration and other sources. Moreover, new data are increasingly emerging and modelling methods and estimates should be responsive such as country-specific data about survival of ART patients from surveillance studies, routine patient data about deaths to those on ART, and all-cause mortality data from vital registration.

Reconciling and improving model estimates of AIDS deaths should consider each of the components of AIDS death estimates including incidence estimates, disease progression and mortality for those untreated, allocation of ART, and mortality for those receiving ART. The objectives of this meeting were to come to consensus recommendations for:

- Interpretation and utilization of AIDS cause of death data from vital registration.
- Parameter estimates for AIDS mortality amongst persons on ART.
- Assumptions about patterns of ART initiation and mortality amongst untreated persons in the ART era.

Outline

The UNAIDS Reference Group held its thematic meeting on on *Improving and validating estimates of AIDS deaths* at the Institute for Social and Preventive Medicine, University of Bern in Bern, Switzerland, 18-19 September 2018. The meeting featured presentations and group discussion to generate consensus recommendations. The programme was divided into the following sessions:

1. Reconciling model estimates with reported AIDS deaths in high income countries
2. Estimates of AIDS mortality data in other concentrated epidemic settings
3. Case studies of mortality data in sub-Saharan Africa

This report presents a summary of the meeting presentations and discussions. The presentations are available to UNAIDS Reference Group members at www.epidem.org (non-members, please contact the Secretariat. 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.

Session 1: Reconciling model estimates with reported AIDS deaths in high-income countries

With default model and parameter assumptions, Spectrum estimates a greater number of AIDS deaths compared to the number of AIDS deaths reported in high quality vital registration in western Europe. The objectives of this session were to review cause of death data in countries with high quality vital registration systems, to review mortality amongst those on ART from patient cohorts, and assumptions for patterns of ART initiation and mortality among untreated adults, and to consider approaches to reconciling and calibrating mortality to reported AIDS deaths.

AIDS vital registration data

The case surveillance and vital registration (CSAVR) tool in Spectrum allows for AIDS deaths data from vital registration to directly inform model fitting. Most countries using this tool input raw AIDS deaths, as opposed to adjusted estimates of AIDS deaths corrected for incompleteness and misclassification. Both the World Health Organization (WHO) and Institute for Health Metrics and Evaluation (IHME) produce estimates of AIDS-related deaths adjusted for misclassification and provide quality indicators for the vital registration data in each country. The estimated AIDS deaths from IHME and WHO are 10-20% higher than raw AIDS deaths from vital registration, the level of difference varies from country to country related to the completeness and quality of vital registration. It was agreed that countries with high quality vital registration and cause of death statistics should input estimates of AIDS deaths, adjusted for miscoding and completeness, into CSAVR, and that final UNAIDS estimates of AIDS mortality should reflect these adjusted estimates in countries with high quality vital registration.

The European Centre for Disease Prevention and Control (ECDC) highlighted that AIDS-related deaths and deaths among PLHIV are under-represented in case surveillance in Europe. The European Surveillance System (TESSy) is a repository for HIV case surveillance data for 55 countries in Europe and Central Asia. However, this data system only captures deaths among those diagnosed and there is substantial underreporting with TESSy capturing only one-third of the AIDS deaths reported by Eurostat. Migration is also a key issue in this region with models currently unable to appropriately adjust for both in- and out-migration.

Mortality in European cohorts compared to Spectrum

The Antiretroviral Therapy Cohort Collaboration (ART-CC) curate data about cohorts of adults who initiate ART in Europe and North America. An analysis of the European data from 2000-2015 indicates there remains a substantial difference in mortality on ART in the first year compared to subsequent years on ART, even in the universal ART era. Country-specific analyses of ART-CC data compared to Spectrum find the crude all-cause mortality in ART-CC illustrate higher observed mortality in the historical period, but similar or lower mortality in the more recent period. Country-specific comparison of the proportion of deaths due to AIDS found lower proportion of deaths due to AIDS in ART-CC compared to Spectrum for all countries, with Spectrum estimates generally outside the ART-CC confidence intervals. Note that loss to follow-up (LTFU) remains a key issue with the ART-CC data and while AIDS deaths have declined over time, the proportion of deaths unknown or unclassifiable has increased (39% in the most recent data period). However, even if all unknown were assumed to be AIDS deaths, the ART-CC proportion of deaths due to AIDS would still not reach Spectrum estimates.

In the Netherlands, the AIDS Therapy Evaluation in the Netherlands (ATHENA) cohort is a national observational cohort open to all PLHIV in HIV treatment centres. Comparison of the total number of

deaths with Spectrum estimates illustrates agreement in the historical period, but the number of deaths increases more rapidly in Spectrum compared to the observed data in the ART era. AIDS-related deaths in Spectrum are substantially higher compared to the ATHENA cohort; however, all-cause mortality is much lower in Spectrum albeit with a similar upward trend. Analysis of mortality by ART status finds that Spectrum underestimates mortality amongst those on ART compared to cohort data. The AIDS-related deaths of those on ART are similar, but Spectrum non-AIDS deaths are much lower (but exhibit a similar trend). For those not on ART, Spectrum estimates are higher than the cohort data in the recent period.

Approaches to reconcile mortality estimates with available data

Both HIV natural history progression parameters and the assumed patterns of ART allocation by CD4 category have a substantial effect on estimates of AIDS deaths in Spectrum. ART initiation and non-ART mortality can be adjusted in Spectrum to better match national data. ART is currently distributed in Spectrum based on an average of those who are eligible and those who need it for survival (i.e. those with low CD4 counts). The current allocation assumptions are fairly representative of the minimum data available for validation. However, the early adoption of high treatment thresholds (e.g. eligibility with CD4<500 or 'treat all' policies) can result in increased estimates of AIDS deaths as allocation patterns are redistributed across eligible CD4 categories, taking treatment slots away from those with lower CD4 counts. Countries in western and central Europe have identified that Spectrum estimates of mortality among HIV positive persons on ART are too high. For the 2018 Estimates, many countries subsequently altered the default ART allocation patterns to assume ART allocation occurred first to people in the lowest CD4 categories, to reduce on-ART mortality. This approach could be introduced as new option for ART allocation in Spectrum. It was discussed that this option would only make sense for settings with a high HIV diagnosis rate. To address elevated non-ART mortality, zero mortality for those off ART above a cut-off threshold (i.e. CD4 >100) could be implemented in Spectrum. At present, this type of approach is the only way to reconcile the very low mortality observed in countries like France, for example.

Leigh Johnson investigated the use of an alternative approach which corrects for the bias that may arise if mortality rates in treated and untreated individuals are assumed independent of ART initiation rates. This is a simple approach which accounts for the fact that the sickest individuals will start ART when there is low ART initiation, while at high rates of ART initiation, all eligible individuals will likely have a similar probability of starting ART. The Thembisa model was fit to recorded death data in South Africa and the rate of mortality at CD4 counts below 200 was assumed to depend on the rate of ART initiation. The results illustrate a significant improvement in the model fit to South African data when the effect of ART initiation on mortality is included.

Finally, Ben Lambert presented ongoing work modelling CD4 progression to AIDS before death. This approach extends the previous work conducted by Tara Mangal and may become an option to replace the current CD4 progression model in Spectrum. He used a continuous-time hidden Markov model incorporating an AIDS compartment to allow for asymptomatic individuals with a low CD4 count, and to allow for selection of symptomatic individuals onto ART. The latter changes the dynamics of ART initiation (and will explain higher mortality at higher CD4 counts). This approach may be able to improve estimates of mortality amongst persons not on ART by mechanistically capturing HIV diagnosis and late ART initiation upon AIDS diagnosis. This work is ongoing.

Session 2: Estimates of AIDS mortality in other concentrated epidemic settings

The objectives of this session were to review data to update model parameters for mortality on ART using the most current cohort data, to assess the need to model changes in mortality on ART for durations greater than one year, and to generate recommendations for adjustments for loss to follow-up.

Mortality after ART initiation from IeDEA data

The International Epidemiology Databases to Evaluate AIDS (IeDEA) is a multi-regional collaboration of ART programmes. Data from IeDEA are used to inform the assumptions for mortality on ART in Spectrum, including adjustments to account for those LTFU. Data from 2009-2014 were used to inform the current Spectrum assumptions. There is now a need for an updated analysis. The following questions were raised:

Does Spectrum over-estimate mortality at higher CD4 counts? The current model parameters were based on IeDEA data collected prior to the widespread adoption of universal ART. Mortality at higher CD4 counts may be over-estimated if the minimal data available at that time are biased, reflecting a sub-set of sick individuals eligible for ART based on clinical criteria.

Should the rates of mortality on ART decline over time in Spectrum? The current ART mortality patterns in Spectrum assume that mortality rates following ART initiation are constant over time conditional on age, sex, baseline CD4, and duration on ART. However, studies have shown mortality rates decline over time, even after controlling for temporal changes in baseline CD4 count and treatment duration. Data from IeDEA also illustrate a decline and it was agreed trends in mortality on ART over time should be updated in Spectrum.

How should mortality on ART be adjusted to account for lost to follow-up? Currently in Spectrum, correction factors which account for the outcomes of those LTFU identified from tracing studies in East and South Africa are applied to all other regions, including concentrated epidemic settings. It was agreed this assumption is inappropriate in concentrated epidemic settings with active follow-up and linkage to vital registration systems as these assumptions will likely over-estimate mortality.

Mortality data from Brazil and China

Brazil has a robust, long standing surveillance system which can track individual patients through different steps of the treatment cascade. Compared to Spectrum, ART programme data suggested lower mortality on ART for 0-6 and 6-12 months, with agreement after one year on ART. Over time, the Spectrum mortality estimates are lower than the Brazil data pre-2015, then fairly aligned from 2015.

China also has substantial data from surveillance systems. China has used the available data to modify the rates of CD4 progression in Spectrum. Notably, they find that all-cause mortality amongst HIV-positive individuals in China is higher than Spectrum defaults.

Session 3: Case studies of mortality data in sub-Saharan Africa

The objectives of this session were to review mortality data from country and survey data in sub-Saharan Africa and generate recommendations for assumptions of mortality on ART and adjustments for loss to follow-up.

Adjusting mortality to account for those lost to follow-up

Frédérique Chammartin, et al. conducted a systematic review and meta-analysis of the outcomes of patients LTFU from ART programmes in sub-Saharan Africa (https://doi.org/10.1093/cid/ciy347). Individual patient data from eight countries in three regions in Africa contributed to this analysis. The authors found the reported proportion of patients LTFU who had died decreased over time while silent transfer and cessation of ART increased over time. While there is still a substantial proportion of those LTFU who are dying (20%), most deaths happen very shortly after last clinic visit thus should be counted as mortality to those on ART. Mortality amongst those LTFU was much higher than mortality of those on ART, and was associated with male sex, advanced disease and shorter duration on ART.

Leigh Johnson presented an imputation approach to adjust Spectrum estimates of mortality on ART using the Chammartin, et al. meta-analysis results. It was noted the data included in the analysis are now outdated (most recent data are from 2010), and that new patient tracing data will be available in 2019. There is also no representation from West Africa. A substantial proportion of individuals were not traceable, thus there is the potential for bias, but it is not clear in what direction. Adjusting the regional patterns of mortality on ART results in substantial increases in mortality (and re-ranking), notably for West and Central Africa. The effects of baseline CD4 at ART initiation are also stronger than previously estimated. The results indicate declining mortality as CD4 increases and time since ART initiation increases. Mortality differs substantially at >12 months ART durations. A strong effect by age was not observed, which was surprising; however, it was noted a strong age effect was also not observed in the ALPHA network data. It was recommended to use ALPHA network data for validation.

Constantin Yiannoutsos and colleagues are working to develop new modelling approaches which capture the entire process of disengagement from care, including reengagement. This work is currently focussed on estimating where return to care occurs (i.e. which CD4 category) after disengagement. The overall aim of this work is to be able to estimate where patients are in the cascade at any point in time.

PEPFAR is introducing a new treatment indicator in their programmes (TX_ML) – *the number of patients on ART with no clinical contact in at least 3 months since last expected contact*. This indicator will be reported at the facility level, semi-annually, and include patient outcomes (by age and sex) indicating undocumented transfer, traced (unable to locate), did not trace, or death. Cause of death is a new optional indicator being introduced. The group discussed it would be ideal to use a consistent time period to define those LTFU (i.e. 3 months) for effective analysis and comparison of the data obtained. It was cautioned this new data collection is a substantial amount of work for programmes.

Mortality from country case studies and survey data compared to Spectrum estimates

Malawi collects of routine programme data from all 744 ART sites, audited quarterly. These data were compared with estimates of mortality from Spectrum. For mortality on ART, Spectrum underestimates mortality in early years compared to programme data. In later years, the Spectrum estimates are in alignment for mortality during the first year on ART, but Spectrum may overestimate mortality on ART

2+ years compared to programme data. The Malawi data show mortality continuing to decline 2+ years on ART, which is not currently captured in Spectrum. For mortality not on ART, the Spectrum estimates of AIDS deaths are very high and require further investigation, though validation is challenging due to lack of direct data on AIDS deaths among untreated adults in Malawi and similar settings.

South Africa has the highest rates of vital registration in sub-Saharan Africa with over 90% of adult deaths recorded. Mortality from vital registration is not currently used to inform model fitting in Spectrum in generalised epidemic settings but is used in the Thembisa model to produce estimates for South Africa. Leigh Johnson used the Thembisa model calibrated to age-specific HIV prevalence and mortality data, compared with estimates obtained from the model calibrated only to prevalence, to illustrate excluding mortality data from model calibration results in substantial overestimation of AIDS mortality in South Africa.

The Spectrum model for South Africa has been modified (adjustment of survival assumptions) to better align with the estimates obtained from the Thembisa model. While the estimates for the overall number of annual AIDS deaths are now in agreement, the Spectrum mortality estimates are much lower for those on ART and are higher in ART-naïve adults (in more recent period) compared to Thembisa. When using default Spectrum model parameters that are used in other SSA countries, Spectrum predicts about 20% greater AIDS deaths in recent years than Thembisa. It was recommended to further compare the CD4 distributions of those starting on ART.

The Population-based HIV Impact Assessment (PHIA) surveys capture CD4 data for the untreated population. The CD4 distribution of those not on ART in Spectrum compared to data from the PHIA surveys illustrate a much higher proportion at CD4 counts >350, and a much lower proportion at CD4 counts <200 in Spectrum compared to PHIA data. This finding was consistent across all surveys.

Key Recommendations

UNAIDS Reference Group on Estimates, Modelling and Projections

Thematic Meeting 2: Improving and Validating Estimates of AIDS Deaths

17-18 September 2018, Bern, Switzerland

Recommendation/Action Item	Lead Person(s)	Proposed timeline
Session 1: Reconciling model estimates with reported AIDS deaths in high income countries • Cause of death data in countries with high quality vital registration • Evidence and interpretation of mortality among ART patient cohorts • Assumptions about patterns of ART initiation and mortality among untreated adults • Approaches to reconciling and calibrating mortality to reported AIDS deaths		
AIDS vital registration data		
• In countries with high quality vital registration and cause of death statistics, estimates for AIDS deaths should reflect levels and trends in AIDS deaths from VR adjusted for miscoding and completeness.		
– Define set of countries & criteria: minimally 47 countries where WHO and GBD agree VR data are high quality. Explore additional countries	UNAIDS	10/2018
– Improve communication and understanding of adjustment approaches.	UNAIDS, WHO, IHME	2018-2019
• Review adjustment approaches used by WHO and GBD; compare adjusted results across countries, further investigation into countries with substantial differences	UNAIDS, WHO, IHME	10-11/2018
• In countries with lower quality VR data, consider implications of fitting HIV epidemic estimates to modelled AIDS deaths – example countries for testing: Lebanon, Argentina	UNAIDS	10-11/2018
– Develop approach to ensure Spectrum exactly matches or closely reflects input AIDS deaths for countries with high quality VR.	Avenir Health	10-11/2018
• Test for countries with high-quality mortality data	Secretariat, UNAIDS, Avenir Health	11/2018
• Estimates of total deaths to PLHIV should reflect excess mortality due to other causes.		
– Consider commissioing systematic review & meta-analysis of relative non-AIDS mortality among PLHIV compared to HIV-negative adults.	Ref Group Secretariat	2019
– Further analysis of ART-CC & NA-ACCORD	Adam Trickey, Margaret May	2019
– Total mortality estimates by post-stratifying ART-CC mx rates using ECDC case surveillance distributions.	Adam Trickey, Margaret May, ECDC	2019
– Enable countries to directly input and utilize total deaths to PLHIV in settings where this is reliably known.	Avenir Health	2019
– Develop approach to account for international migration in estimates of PLHIV.	ECDC, UNAIDS, Reference Group	2019
• Mortality at CD4 >100 in Spectrum appear too high.		
– Addressing requires reassessment of natural history model.		
– 'Set to 0 adjustment': explore drawing mx rate onto ART [late diagnosis & initiation] instead of setting to 0	John Stover, Josh Salomon	09-10/2018
– Recommend further development of structural model changes to explicitly model progression to AIDS and symptom-based diagnosis and treatment.	Ben Lambert, Jeff Eaton, Tara Mangal	2019

Session 2: Estimates of AIDS mortality data in other concentrated epidemic settings • Update model parameters about mortality on ART using most current ART cohort data. • Assess need to model changes in mortality on ART for durations >1 year. • Recommendations about LTFU adjustments for other regions: Latin America, Asia • Assumptions about patterns of ART initiation and non-ART mortality		
ART mortality in concentrated epidemic settings		
• Update default Spectrum parameter estimates to reflect new IeDEA analysis. – No adjustment factors for LTFU in Latin America, North America and Asia Pacific because all cohorts include VR linkage or active follow-up	Leigh Johnson, John Stover	09-10/2018
• Compare IeDEA & Brazil programme data estimates	Leigh Johnson, Tara Mangal, Ana Roberta Pascom	10/2018
• Pooled analysis of Latin America, North America and Asia Pacific region cohorts w/ region effect. – Differences small relative to heterogeneity across cohorts	Leigh Johnson Leigh Johnson, Adam Trickey	11/2018 10/2018
• Incorporate trends in ART mortality over time. – Harmonize specifications across regions (ART-CC and IeDEA)	Reference Group Secretariat	2019
• Consider how to formally use heterogeneity		
Session 3: Case studies of mortality data in sub-Saharan Africa • Recommendations for mortality on ART assumptions and LTFU adjustments		
Mortality on ART in Spectrum		
• Recommend adoption of imputation model for death amongst persons LTFU based on individual patient meta-analysis of tracing studies. – Update imputation model to include more recent tracing data from CIDERZ in Zambia – Provisionally run results through Spectrum and review results – Comparison with ALPHA data – Review literature for more recently available datasets	Leigh Johnson Leigh Johnson Avenir Health Leigh Johnson, Emma Slaymaker ISPM	10/2018 10/2018 10/2018 2019 2019
• Strong evidence of continued declining in mortality on ART 1, 2, 3+ years. – Explore magnitude of effect on Spectrum estimates.	Leigh Johnson, John Stover	2019
• Pool central and west: estimate 3 regions (southern – non RSA)	Leigh Johnson	10/2018
• Continue to follow progress of modelling disengagement	Imperial Secretariat, Constantin Y	2019
• Malawi & South Africa: Spectrum deaths on ART lower than programme data (early years) / Thembisa – Revisit comparison after implementing mortality rates from new analysis of IeDEA cohort data – Compare CD4 at initiation distributions between Spectrum and programme data	Leigh Johnson Andreas Jahn, John Stover	2019

• Explore Bayesian evidence synthesis of CD4 distribution (previously calibrated with KAIS and UAIS) – Update with new PHIA distribution ✓ Compare with ALPHA	John Stover	2018
– CD4 distribution at ART initiation (IeDEA / MeSH analysis)	Assemble group	2019
– Evidence from seroconverter cohorts	Jeff Eaton, Ben Lambert	2019
• Identify overlaps to compare new PEPFAR indicators with research tracing studies	Leigh Johnson, ISPM, Secretariat, PEPFAR	2019

Appendix I: List of Participants

Name	Affiliation
Leigh Johnson	University of Cape Town
Jeff Eaton	Imperial College London
Kelsey Case	Imperial College London
Tara Mangal	Imperial College London
Ben Lambert	Imperial College London
Josh Salomon	Stanford University
Mary Mahy	UNAIDS
Kim Marsh	UNAIDS
Peter Ghys	UNAIDS
Ian Wanyeki	UNAIDS
Anna Wadhwani	UNAIDS
John Stover	Avenir Health
Guy Mahiane	Avenir Health
Robert Glaubius	Avenir Health
Tim Brown	East-West Center
Irum Zaidi	OGAC
Ray Shiraishi	CDC
Tim Fowler	US Census Bureau
Emma Slaymaker	LSHTM
Adam Trickey	Bristol University
Margaret May	Bristol University
Constantin Yiannoutsos	Indiana University
Matthias Egger	ISPM, Bern
Nina Anderegg	ISPM, Bern
Chantal Quinten	ECDC
Anastasia Pharris	ECDC
Ard van Sighem	Stitching HIV Monitoring
Andreas Jahn	I-Tech / Malawi DHA
Ana Roberta Pascom	Brazil MOH
Sasi Jonnalagadda	CDC
Michelle Morrison	BMGF
Charles Holmes	Georgetown

Remote participants:

Hmwe Kyu	*IHME*
Fan Lyu	*China CDC*
Wei Guo	*UNAIDS*
Le Bao	*Penn State*
Giorgos Bakoyannis	*Indiana University*

Appendix II: Agenda

UNAIDS Reference Group on Estimates, Modelling and Projections

Improving and Validating Estimates of AIDS Deaths

17-18 September 2018, Bern, Switzerland

AGENDA

Day 1, Monday 17 September 2018

Time	Duration (min)	Topic	Presenter(s)/ Lead Discussant
900	20	Meeting opening • Welcome and introductions • Meeting objectives and overview	Peter Ghys, UNAIDS Jeff Eaton, Imperial
Session 1: Reconciling model estimates with reported AIDS deaths to in high income countries Chaired by Josh Salomon Objectives • Review cause of death data in countries with high quality vital registration • Review evidence and interpretation of mortality among ART patient cohorts • Review assumptions about patterns of ART initiation and mortality among untreated adults • Consider approaches to reconciling and calibrating mortality to reported AIDS deaths			
920	80	Overview of key issues - Review AIDS mortality in VR settings - Discrepancies between Spectrum and available death registration - Review of AIDS cause of death assignment rules, tools, and interpretation - Current interpretation of cohort data excess mortality Surveillance systems in Europe and priority questions in the EU region Mortality among ART-CC cohorts - Patterns of mortality by age, sex, baseline CD4, ART duration, and time - Country-specific comparisons of ART-CC with Spectrum / VR discrepancies - COD among ART-CC cohort vs. Spectrum Mortality and COD among HIV+ persons by ART experience in the Netherlands Trends in AIDS as COD among multiple COD data	Kim Marsh, UNAIDS Anna Wadhwani, UNAIDS Anastasia Pharris/Chantal Quinten, ECDC Adam Trickey, Margaret May, Univ of Bristol Ard van Sighem, Stitching HIV Monitoring Institute Hmwe Kyu, IHME
1040	20	Coffee	

1100	60	Modelling approaches to reconciling and fitting mortality to reported AIDS deaths • Adjusting pattern of ART initiation, ART coverage, and non-AIDS mortality by CD4 • Heuristic adjustments to non-ART mortality related to ART coverage • Mechanistic modelling of progression to AIDS	John Stover, Avenir Health Leigh Johnson, Univ of Cape Town Ben Lambert, Imperial
1200	60	Session 1 discussion & recommendations: *- Interpretation of AIDS COD data* *- Assumptions for mortality* *- Assumptions for ART initiation / non-ART mortality*	Led by Chair
1300	60	Lunch break	
Session 2: Estimates of AIDS mortality data in other concentrated epidemic settings (chaired by Jeff Eaton) Objectives • Update model parameters about mortality on ART using most current ART cohort data. • Assess need to model changes in mortality on ART for durations >1 year. • Recommendations about LTFU adjustments for other regions: Latin America, Asia • Assumptions about patterns of ART initiation and non-ART mortality			
1400	35	Mortality following ART initiation in Latin America, North America, and Asia regions • Analysis of IeDEA collaboration cohorts. • Assumptions about mortality under-ascertainment. • Heterogeneity across cohorts and countries	Leigh Johnson, Univ of Cape Town
1435	55	Evidence from national HIV programme data: • Overview of surveillance system (HIV and vital registration COD) • Evidence about AIDS COD from vital registration vs. AIDS reporting • Trends in AIDS deaths & comparisons to Spectrum • Mortality following ART initiation by age, sex, baseline CD4, ART duration, and time – comparisons to current Spectrum parameters.	Brazil: Ana Roberta Pascom, MoH and Tara Mangal, Imperial China: Lv Fan, China CDC and Le Bao, Penn State
1530	30	Coffee break	
1600	60	**Discussion and recommendations** - *Parameter assumptions for mortality on ART (including under ascertainment)* - *Assumptions about ART allocation/initiation*	

		- *Interpretation and fitting to AIDS COD data*	
1700	15	Wrap-up and close	
1715		End of Day 1	

Day 2, Tuesday, 18 September 2018

Time	**Duration (min)**	**Topic**	**Presenter(s)/ Lead Discussant**
0830	10	Introduction to Day 2	Jeff Eaton, Imperial
Session 3: Case studies of mortality data in sub-Saharan Africa (chaired by Josh Salomon) Objectives • Review mortality data from countries in SSA • Generate recommendations for mortality on ART assumptions and LTFU adjustments			
0840	80	Adjustments for mortality among LTFU: • Meta-analysis and IPW meta-analysis • Proposed incorporation into modelled estimates for SSA Analyses of mortality on ART: • Time trends in mortality on ART • Evidence for mortality changes >1 year on ART and implications for AIDS deaths trends. • Heterogeneity (random effects) • Mortality among persons initiating at high CD4 in new guidelines era (<500, all) Update on modelling disengagement from care	Matthias Egger/Nina Anderegg, ISPM IeDEA: Leigh Johnson, Univ of Cape Town IeDEA: Leigh Johnson, Univ of Cape Town Constantin Yiannoutsos, Indiana University
1000	20	Coffee	
1020	80	Mortality data from countries in SSA • Malawi (programme data compared with Spectrum) • South Africa case study New PEPFAR MER indicators for mortality and LTFU CD4 distribution among untreated adults – evidence from PHIA surveys	Andreas Jahn, I-TECH, MoH Leigh Johnson, Univ of Cape Town Irum Zaidi, OGAC Sasi Jonnalagadda, CDC Elvin Geng, UCSF and

		Opportunities and challenges of local AIDS mortality estimation in SSA	Charles Holmes, Georgetown
1140	60	Session 3 discussion & recommendations - *Assumptions for mortality on ART in SSA settings* - *Assumptions for non-ART mortality and patterns of ART initiation in SSA* - *Research agenda for incorporating mortality data*	Led by Chair
1240	20	Summary of final recommendations, action points	Jeff Eaton, Imperial
1300	–	Close of mortality meeting	