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## Technical Discussion on TB-HIV Modelling in Spectrum

Short report and recommendations from a meeting of  
the UNAIDS Reference Group on Estimates, Modelling  
and Projections held in Geneva, Switzerland,  
6 December 2012

### SHORT REPORT & RECOMMENDATIONS



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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](http://www.epidem.org)) based at Imperial College London. Participants of the meeting are listed at the end of this document.

Kelsey Case, December 2012

## Introduction

The Joint United Nations Programme on HIV/AIDS (UNAIDS) *Reference Group on Estimates, Modelling and Projections* exists to provide impartial scientific advice to UNAIDS, the World Health Organization (WHO) and other partner organisations on global estimates and projections of the prevalence, incidence and impact of HIV/AIDS. The Reference Group acts as an 'open cohort' of epidemiologists, demographers, statisticians, and public health experts. It is able to provide timely advice and also address ongoing concerns through both *ad hoc* and regular meetings. The group is co-ordinated by a secretariat based in the Department of Infectious Disease Epidemiology, Imperial College London.

### *Aim of the meeting*

To review and discuss the UNAIDS and WHO processes for estimating HIV and tuberculosis, the different modelling approaches used, the current and future work planned and the potential utility of an HIV-TB module in Spectrum.

### *Approach*

The meeting featured presentations combined with group discussion to generate consensus recommendations. The meeting agenda is included in Appendix I and the list of participants is included in Appendix II.

The recommendations drafted at Reference Group meetings give UNAIDS and WHO guidance on how best to produce estimates of HIV/AIDS, provides an opportunity to review current approaches and also helps to identify information needs (earlier reports are published on the Reference Group website [www.epidem.org](http://www.epidem.org)). This transparent process aims to allow the statistics and reports published by UNAIDS and WHO to be informed by impartial, scientific peer review.

## **UNAIDS process for HIV/AIDS estimates and evolving needs**

The process of UNAIDS estimates began as a global and regional exercise and transitioned to become a country-specific endeavour. Since 1998, UNAIDS has worked with countries to provide technical guidance and support to produce estimates and projections of HIV/AIDS in a two-year cycle. The methods and tools used to produce these estimates continually evolve as more data become available and new knowledge is obtained. The next cycle of estimation will begin in early 2013 with a series of regional workshops from March through June. Countries will use Spectrum 2013 to generate estimates and projections of HIV prevalence, people living with HIV, HIV in children, HIV-related deaths, need for ART and PMTCT (and coverage), among other indicators. In high HIV-burden areas, countries are increasingly requesting estimates of tuberculosis (TB) mortality among people living with HIV.

In 2013, there will be a mid-term review of the progress towards achieving the commitments set forth in the 2011 UN Political Declaration which is a joint partnership. The 5<sup>th</sup> target of the Declaration is to reduce TB deaths by 50% in those living with HIV by 2015. UNAIDS does not currently estimate TB-related indicators. For the Millennium Development Goals, there is also a need to identify countries that are falling behind on their TB-related targets, but without country-level estimates, this cannot be done. Additionally, estimates of TB mortality and other epidemiological indicators are needed for advocacy for impact assessment and to provide better planning for services.

## **WHO process for estimates of the burden of TB and TB-HIV and TB-HIV mortality**

Since 2009, WHO has conducted workshops in over 100 countries to assess the data available for TB, the surveillance systems, the beliefs about plausible range of incidence and help countries to develop a plan for monitoring and evaluation. There remains a need for monitoring at the country level and coordinated efforts to capture routine data from HIV cohorts for both incidence and mortality of TB.

Indicators of the burden of TB are problematic as a result of the data available. While there is testing in children that measures infection, the findings are very difficult to extrapolate to adults. Direct measures of incidence are impractical because TB is a rare event in most settings and the sample sizes needed are too large to be feasible for direct measurement. Incidence is best documented through high quality surveillance, but the estimates are uncertain due to both under-reporting and under-diagnosis. In most high-burden countries, incidence is not directly measured. Only a very small number of countries conduct prevalence surveys. The majority of data available comes from vital registration (VR) which is useful for generating estimates in people who do not have HIV; however, these data are missing for most high-burden countries. For people infected with HIV, VR data are predominantly coded as death due to HIV. In sub-Saharan Africa, very few countries have strong VR data. In order to estimate TB incidence in those with HIV, TB surveillance in people living with HIV (PLHIV) is used as the informative data source. TB-HIV incidence is calculated by imputing missing data on HIV prevalence in those with TB and then multiplying HIV prevalence in those with

TB by TB incidence. Imputation is done using HIV prevalence estimates; however, it is difficult to define the relationship between the coverage of HIV testing and HIV prevalence in those with TB. A simple, linear model (with a time lag) is used to predict HIV in those with TB from HIV in the general population.

For estimates of TB-HIV mortality, the data sources used to inform include cohort studies and autopsy studies. Since 2005, WHO has used a Bayesian approach where the likelihood is calculated using incidence multiplied by the case fatality rate. At the regional and global level, these estimates are then “squeezed” to fit into the overall mortality envelope to ensure that there are not more TB-associated AIDS deaths than total AIDS deaths. The amount of the “squeeze” is determined from autopsy study results in 10 African countries which identified that 37% (range 32-45%) of AIDS deaths had TB as the contributory cause.

### **The Spectrum TB Impact Model**

The Spectrum model for estimating TB incidence by HIV status combines the information available in Spectrum (including the detailed demographic data, national projections of HIV infection including HIV infection and treatment by CD4 count) and information from the WHO Stop TB database to generate estimates of TB incidence disaggregated by defined CD4 category. A regression method is used to estimate the relative risk for TB incidence across the CD4 categories used in Spectrum. Case fatality rates are then applied to estimate TB mortality. Additional model features include the estimation of the rate of multi-drug resistant TB, the calculation of diagnostic and management costs (which can be calculated by linking to the costing module), and the ability to explore the impact of interventions.

### **TB Modelling and Analysis Consortium (TB Mac)**

The aim of the TB Modelling and Analysis Consortium (TB Mac) is to improve global TB control by coordinating and promoting mathematical modelling and other quantitative research to support evidence-based policy making and implementation. The main objectives focus on reviewing the priority research questions that require mathematical modelling and quantitative research, achieving consensus on current knowledge, knowledge gaps and the methodological standards and best practice for decision-making in order to achieve TB control, and then widely disseminating this information. For 2012-13, the main focus is on impact and the following three priority modelling questions were identified:

1. Optimising TB control in populations with high HIV prevalence
2. Impact and cost-effectiveness of current and future diagnostics for TB
3. Rational introduction of new drugs

TB Mac has funding to support small modelling activities and may be a useful mechanism for bringing together experts to review methodology and modelling approaches, to conduct analyses and to review data sources. In the future, TB Mac may also have the potential to provide secretariat support, similar to the functioning of the UNAIDS Reference Group, for annual review of TB-modelling tools and country-level estimates.

# Recommendations

## Consensus recommendation:

**Groups involved in estimating HIV and TB will work collaboratively to work on estimates of HIV-TB mortality and other related epidemiological quantities.**

In order to support the consensus recommendation, the following recommendations were defined:

- Use the opportunity of the start of the two-year UNAIDS Estimates workshops to move forward with TB-HIV modelling in Spectrum 2013 at the African regional workshops.  
*Follow-up: UNAIDS Reference Group to organise a technical review meeting in January 2013*  
*Follow-up: UNAIDS & WHO to coordinate workshops, March 2013*
- Convene a technical meeting, bringing together epidemiologists, statisticians, mathematical modellers, and other technical experts to review and refine the proposed methodology for TB-HIV modelling in Spectrum.  
*Follow-up: UNAIDS Reference Group Secretariat to organise for January 11, 2013*
- Provide a full description of the model and methodology to circulate for review.  
*Follow-up: Carel Pretorius, Dec 2012*
- Identify the key technical specifications needed for robust estimation of TB mortality and other related epidemiological quantities in high HIV-burden settings, according to WHO TB staff and expert TB epidemiologists (in advance of the meeting in January). Implement modifications to the approach in Spectrum (following the meeting in January) in order for the methodology to be ready for initial release in March 2013.  
*Follow-up: UNAIDS Reference Group Secretariat to circulate technical specification of model to invite meeting participants to critique and respond to specific questions about the appropriateness of particular aspects of the model, Dec 2012*
- Incorporate TB experts as facilitators during the pilot-testing at the African regional workshops to provide technical support, review the data available and the preliminary results and to liaise with the country working groups.  
*Follow-up: WHO to identify 1-2 facilitators for participation in the March 2013 workshops*
- In the January Reference Group meeting, discuss the potential for TB Mac to take a role in the longer-term review and refinements of methods in TB estimation.  
*Follow-up: UNAIDS Reference Group meeting in Geneva, January 2013*

## Appendix I: Meeting Agenda

### Technical Discussion, TB-HIV Modelling in Spectrum 2013

Geneva, 6 December 2012

**Venue:** UNAIDS, room D46031, **9:00-12:00**

**Co-chairs:** Tim Hallett and Richard White

#### Agenda:

- 1) UNAIDS process for HIV/AIDS estimates and evolving needs (*Karen Stanecki/Peter Ghys 20/10 min*)
- 2) WHO process for TB and TB/HIV estimates and WHO modelling of mortality among HIV-TB (*Philippe Glaziou, 30/15 min*)
- 3) Spectrum model for modelling national HIV epidemics, with specific focus on number of TB patients eligible for ART and estimates of HIV/TB mortality (*John Stover/Carel Pretorius, 20/10 min*)
- 4) Discussion: (*Group, 45 min*)
  - a. Is there value in having countries or a sub-set of countries produce TB/HIV-related estimates?
  - b. What changes need to be made to the model(s) before they can be used by countries?
  - c. If/when models are ready, what is the best way to pilot their use by country users?
    - East and Southern Africa HIV estimation workshops?
    - Separate pilot workshop for country TB epidemiologists?
    - Additional suggestions?
- 5) Discussion: TB Mac to update regarding current and future work plans (*Richard White, 15/10 min*)

## Appendix II: List of Participants

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