The HIV Modelling Consortium

Report for Topic Meeting One

Title: ***Sources of Infections and National Intervention Impact Projections***
Date: 28-29th April, 2011
Location: Montreux, Switzerland

Aim: *To Review Current Methods for Estimating Sources of Infections in Generalized Epidemics in Africa (mostly) and Evaluate Implications For Projections of Intervention Impact.*

About the HIV Modelling Consortium:

The HIV Modelling Consortium aims to help improve scientific support for decision making by co-coordinating a wide range of research activities in mathematical modelling of the HIV epidemic. This involves:

- Identifying questions that demand mathematical modelling input and identifying new modelling results that may require further validation.
- Facilitating sharing of information, modelling techniques, data and expertise between research groups.
- Providing a forum for rigorous review of new mathematical modelling research and tools.
- Providing funding through sub-contracts to commission research to address those needs.

A steering committee of leaders in HIV programme and policy directs the focus of the work of the consortium. The HIV Modelling Consortium is funded by the Bill & Melinda Gates Foundation through a grant to Imperial College London. Further information on the HIV Modelling Consortium is available in a standard briefing document.

The first topics that the consortium addressed were methods for estimating the sources of HIV infection in a population and comparisons of model projections of intervention impact.

Background to the Topic:

To help optimize the allocation of resources in HIV prevention programmes, the UNAIDS/ World Bank initiative 'Know Your Epidemic – Know Your Response' has been designed to facilitate programme managers to examine the sources of HIV infections in a country, which can then be used to guide prevention programme and data collection priorities. The method for estimating sources of infection is the 'Modes of Transmission' model, a spreadsheet-based tool that uses inputs on the numbers of individuals in particular risk groups (sex workers, clients of sex workers, those with casual partnerships, etc.), HIV prevalence and behaviours among the groups and transmission risk associated with the behaviours to project the number of new infections in each group in the next year. This model been applied in several countries but questions have been raised about the accuracy of results. The HIV Modelling Consortium convened a meeting of expert epidemiologists, demographers, mathematical modellers and programme implemeneters to review methods for estimating sources of HIV infections. A secondary aim was to understand how the assumptions other models make about the sources of HIV infection in populations influences the projections they make about the impact of different interventions.

Organization of the Meeting:

The meeting, held over two days in Montreux, Switzerland, began with a session to introduce the aims of the HIV Modelling Consortium and to describe how participation in the consortium would be structured. The rest of morning session on day one was spent reviewing the need for estimates of sources of infection, how the existing models generate estimates and how that information is used. A critique of the existing methods was presented at the start of the afternoon session followed by presentations of current plans to strengthen the model and other new work that has examined different modelling approaches.

The first session of the second day included a brief discussion of policy instruments in models and then focused on the GOALS model (produced by the *Futures Institute*). The next session reviewed a set of five other models that have been used to represent the HIV epidemic in South Africa and estimate the impact of particular interventions. In a final session, the team of modellers from Intellectual Ventures introduced their approach to build new software that enables detailed microsimulation modelling of HIV transmission and within-host dynamics.

The full agenda is provided as an appendix.

Key Discussion Points:

All presentations made during the meeting are available on-line (links are provided in the copy of the agenda in the appendix). Brief remarks about the commentary made during the presentations and in the discussions are provided here.

- Modelling Consortium Process Issues

This was the first meeting of the modelling consortium and the aims of the project and the processes for being involved were described and discussed. The secretariat presented the proposed governance structure of the HIV modelling consortium (appendix). There was broad agreement in overall approach. Some raised that the sharing of model source-code was a substantial endeavour, which would require funding support – and it was agreed that this could be done through the modelling consortium. It was noted that in other fields, norms dictate a freer mode of sharing and communication of methods and results, and it was highlighted that the consortium project is intended to move the HIV modelling field closer to those practices. It was agreed that participants at the meeting would sign a simple confidentially agreement that formalised the usual agreements at similar meetings for publication and sharing without permissions, and was intended to increase the confidence of participants in presenting unpublished or preliminary work. The findings from an exercise to survey the range of HIV modelling activities were presented, which showed more than 50 groups actively engaged in HIV modelling world-wide. The majority of groups reported producing work with an intended audience of policy-makers and half expressing willingness to share modelling methods and code.

- Methods for Estimating Sources of Infections

Members of the steering committee made presentations explaining why this topic was chosen for consideration by the modelling consortium. There is a need for ‘real time, actionable’ information in running HIV programmes that could enable an optimized match between sources of infections and intervention effort. However, cases were cited where existing modelling studies have suggested a spurious precision in such estimates, produced

results that some have suggested are inconsistent with other epidemiological and qualitative findings (e.g. high proportion of infections due to low risk behaviour in concentrated epidemics) and where modelling has seemed unnecessary given the apparent clarity of empirical observations.

The methods used in the first generation of the 'Modes of Transmission' (MoT) model, used by UNAIDS, were described. In essence, it is a spreadsheet-based tool that uses inputs on the numbers of individuals in particular risk groups, HIV prevalence and behaviours among the groups and the transmission probability associated with the behaviours to project the number of new infections in each group in the next year. It was emphasised by multiple speakers and participants that the initial aim of the model was to identify gaps in the data and raise awareness of the potential role of particular groups that had not received sufficient attention.

The model has been applied, as part of the 'Know Your Epidemic, Know Your Response' project, in 9 Southern/Eastern African countries and 6 West African countries. In some cases, there have been formal comparisons of results to the Asian Epidemic Model, which has shown some degree of discrepancy. For calibration of the model to a particular setting, reported behaviour data is input and the overall transmission rate of HIV is scaled in an *ad hoc* way to produce a total incidence consistent with official national estimates. Also, the results of the models have, in some cases, been compared to independent data (e.g. case notifications) and to independent epidemiological assessments (qualitative and based on expert opinion). In some cases, UNAIDS epidemiological experts have recommended a country not publish the results of a modes of transmission exercise because insufficient data were available, although in some instances analysis have proceeded in spite of this caution. A procedure has been developed for assessing uncertainty associated with model input parameters by independently sampling values from pre-specified ranges for key input parameters. The total size of the population and HIV prevalence in the whole population is maintained by adjusting the size and HIV prevalence in the low risk group as necessary. It was noted that this method may not fully capture uncertainty in estimates of sources of infections due to systematic biases in reported behaviours, un-modelled correlation between parameters, the lack of manipulation in the model's structural assumptions, and the method of adjusting the sizes of the low risk groups, which have been some of the parameters most susceptible to criticism in reviews of MoT results.

Further data were presented from specific applications of the modelling approach to data

in West Africa. Several different dynamic models of the epidemic in West Africa were shown to produce similar (high) estimates for the 'population attributable fraction' of sex work, which builds confidence that this is truly the main driver of the epidemic in that region.

Examples were then presented of where some believe that results of previous MoT work have been counter-productive. In Lesotho, the model indicates a high proportion of new infections occurring among low risk couples, a result which may have contributed to further investment in testing and counselling; in Uganda National AIDS commission report that "marriage is the biggest risk factor for HIV" which lead to an increase in attention to those in stable sero-discordant couples, which were suggested to be an 'epidemiological dead-end'; in Swaziland, lack of adequate to complete the MoT exercise prompted a survey to be commissioned to sample 300 MSM, IDU, but researchers had difficulty even finding sufficient numbers in the population to reach the desired sample size, questioning the necessity of a mathematical model for assessing the contribution of these groups to the generalised epidemic. These comments prompted substantial discussion. It was suggested that new infections in "stable couples" are not dead-ends (epidemiological less important since they would not lead to further transmission) because they couples split up, and could form new external partnerships. The linkage between MoT results and specific policy recommendations was also queried (e.g. if a high proportion of transmission in low risk couples, why is the intervention testing and counselling rather than circumcision?). Many commented again that this model was meant to help analysts think about data, rather than as a basis for major policy decisions.

Prior to the meeting, experts that had been critical of the results of the MoT modelling had been contacted to record their comments and suggestions. Although there was a great deal of support for high-level concept ('knowing the epidemic and response'), there were concerns about the potential for misleading results to push programme decisions "further off course". There were five main areas of concern:

i. headline results did not seem consistent with other epidemiological data (in particular, a small proportion of new infections seem to be attributed to groups with multiple sexual partners);
ii. the model paradigm was misinterpreted (the model estimates the group in which new infections will occur in the short-term, rather than the groups responsible for driving the epidemic);
iii. the model representation of risk structure is highly simplified and may not fully

capture true variations in behaviours, multiple risk behaviour or other behaviours thought to be important for HIV transmission;

iv. the data used to parametrise the model relies heavily on self-reported behaviour data (especially from Demographic and Health surveys) which, due to biases, could lead to misleading results;
v. the way in which results have been visualized and presented was thought to portray an artificial sense of precision given the substantial uncertainties in the data.

In response to these comments, multiple suggestions were made for possible improvements: a new paper explaining strengths and weakness of current methods and outlining how model results should be used in programme planning; clearer rules for minimum data requirements, calibration and checking; and strengthened uncertainty analysis. The possibilities of relaxing an initial criterion that a single model be used in all places was discussed, and this would allow models to be developed that are tailored to specific settings taking into account the questions being asked and data availability. Alternatively, different models could be developed by sets of epidemic type, for example following a classification based on indicators such as HIV and STI prevalence rates, circumcision level, current range of interventions in place. One suggested approach for developing new models was to first complete a full systematic review of epidemiological indicators and use clustering methods, such as latent-class analysis, for identifying and classifying key characteristics of epidemics. Another suggestion, which attracted support when raised, was estimating the distribution of infections in a population (with a generalized epidemic) according to life-course stages (age, location, marital-status etc). This would have the advantage of clarifying the distinction between the question of 'among whom' are infections occurring (which the model can answer) and 'which types of risk behaviour drive transmission' (which the model is less well suited to answer), and for defining the epidemic in terms of identifiable and targetable groups rather than based on often hidden characteristics such as 'multiple partnerships'. It was also proposed that, besides dissecting the population along demographic lines, the population could be further divided according to how they could be accessed through intervention: examples of 'access channels' would include attendance in antenatal clinics, attendance to STI clinics, availability to household contact etc.

Work was then presented that the made a comparison between the results of a static 'MoT'-like model making projections one year into the future and an analogous dynamical model that represented infectious transmission of HIV over time. This was used to explore whether the annual distribution of new HIV infections estimated by the static model accurately identify 'epidemic drivers' (the groups and their behaviours that contribute

to sustaining the epidemic). The answer depends on the type of epidemic (generalized or concentrated) and on epidemic phase (early, growth phase or late phase) and, overall, static models can fail to identify the contribution of high risk groups to the onward spread of epidemics. The implication is that a portfolio of interventions decided on the basis of static models could be sub-optimal over the long-term. This raised the question of the time-horizon over which decisions should be optimized (influenced by the discount rate) and also that the appropriate choice of model structure (and the need for a model to capture long-term effects) will depend on that time-horizon.

The influence of assumptions made about the patterns of risk behaviour was then explored in case-studies of the epidemics in Cambodia and Uganda. In both cases, the assumptions of the MoT model were revised in the light of a review of the epidemiological literature in each setting to produce a 'bottom-up' model tailored to each setting. In Cambodia, particular groups were added in the MoT. In Uganda, the 'low risk and casual sex' categories was changed to reflect heterosexual adults, sub-divided by age and sex. In both cases, it was proposed that this analysis could increase the specificity of interventions.

A set of simple demographic model were presented that have used longitudinal data from several cohort studies to estimate patterns of HIV incidence, AIDS-related mortality and ART needs in populations. These models differ from 'infectious disease transmission' models in requiring substantially more data than is available for most populations but they could provide a valuable resource to modellers in providing another way to test and validate model projections and as a data-grounded 'reality check'.

In a final session for discussion of the whole day, discussion generally focussed on whether the challenges with implementation and consumption of the MoT model are principally due to limited and unreliable data or fundamental limitations of the model structure and strategy. The following points were emphasized:

1. There is substantial concern over the reliability of self-reported data on behaviours, which should be properly reflected in models that use those data. The same is true for 'size estimate' of the risk groups, which had received less attention in the discussions up to that point.
2. The taxonomy of risk groups in a population varies from place to place, and so do the 'access channels' (see above). This raises the question of whether the aim should be to have a model that can be used everywhere or instead a different model

for each epidemic (or epidemic typology), or detailed modelling for the highest priority countries (given the concentration of new HIV infections in a few countries). It was suggested that there is need to understand the priority for planners between ‘local validation’, ‘simplicity to use’ and ‘universality’ (meaning that it could be used in any population), recognising that it may not be possible to achieve all three criteria at once.

3. There were further calls to use the modelling results as only one part of wider epidemic syntheses work and to find ways that models results could be used carefully. The use of consultants to run the modelling for countries that did not have a background in mathematical modelling could be a limitation, and where experienced modellers have applied the MoT model, the findings have tended to be more fully nuanced and caveatted and integrated into synthesis work.
4. The MoT model should be described and reported as more of a 'process' for investigating an epidemic rather than a tool for producing definitive results for directing resource allocation. Suggestions for reducing the reliance on a single MoT analysis included presenting only qualitative results from the MoT but not actual numbers, or using an MoT like model for quantifying the exposure to HIV but not actual numbers of incident infections. These ideas were viewed as not likely to be popular with consumers, but indicate of how modelling experts believe the model could be effectively utilised.
5. There were further call for model validation work, and it was suggested that the Asian Epidemic Model and a new model by David Wilson could be used for this.
6. There was broad enthusiasm for pursuing work examining how assumptions about hierarchies of risk in population and the static nature of the model influence results.

- Model Projections of Intervention Impact

There was first a discussion of the interaction between policy instruments and mathematical models. It was observed that actual behaviours and events represented in models are, in reality, related to policy instruments through service availability and the propensity of individuals to access services, even though this is not commonly included in model. It was recommended that this be a topic of future discussion in the HIV Modelling Consortium.

The GOALS model, developed by the Futures Institute, has been used by many international agencies and country programme managers to understand how decisions about resource allocation in HIV prevention and treatment can influence impact and costs. The model was originally intended to move those discussions to an explicit and quantitative grounding, and away from 'personal opinions'. The discussion than followed a technical description of the model focused on the Impact Matrix, which specifies the efficacy of particular interventions per unit increase in coverage. The data used to specify that matrix was queried – in particular how outputs and impact were used (the matrix uses reported

behaviours as an impact alongside studies that have HIV incidence end-points) and how types of intervention were classified (because, in reality, the distinction between classes of intervention is less than in the model). Future versions of the model may allow for the impact matrix applied to be manipulated by the user to exclude certain forms of information which could exclude, for instance, studies that were not based on HIV-incidence endpoints. It was noted that the debate about the impact matrix is about the paucity of data rather than the model architecture used. Other comments pointed out that in the model assumptions are made that could lead to depletion of the numbers in the high risk groups as epidemic matures and that the model represents the scaling up of intervention with a linear increase in average 'effectiveness', which might over-estimate the impact of weak interventions compared to model that capture heterogeneity between those that do and do not receive the intervention. There were suggestions about comparing the GOALS model to other models, and this was theme that was later returned to later when work comparing three model's projections of the impact of Chlamydia screening was presented. One example of a major application of the GOALS model was then presented (aids2031). When this work had been presented previously many of the same comments have been made as indicated above. In a detailed discussion following the presentations about GOALS, the following themes were emphasized: (i) the need for model results to have a better handle on uncertainty; (ii) at a fundamental level, have epidemiologists been too timid to point out disparities between states of epidemics and the portfolio of interventions?; (iii) can model be used more productively to make arguments about the value of particular forms of information (e.g. the value of further data collection, an effectiveness trial, and the price of a bad decision etc).

At the beginning of the next session, the exercise comparing chlamydia models were described. This identified the reasons for disparities between model projections were mostly related to assumptions about heterogeneity in risk behaviour, and through a comparison to detailed behavioural and biological data was able to adjudicate on the relative strengths of the models. Several models of the HIV epidemic in South Africa that have been used for projecting intervention impact were then presented. Distinctions and similarities between models were noted. The overall commentary focused on following issues: The difference in the level of detail in the model, with arguments made about the benefit of limiting complex details as much as possible to gain a clear understanding. Population-level heterogeneity in risk behaviours, included in some models but not others, has been shown to be a major determinant of the impact of interventions, including the estimated effect of recent changes in behaviour in South Africa on HIV and, as above, the impact of Chlamydia screening interventions. Model fitting was discussed, with some models having been carefully fitted to

data using sophisticated statistical procedures, others fit 'by eye' and others not fit at all. It was discussed whether a 'good fit' meant the model was validated. Last, there was the question of what metrics included in the models could be 'optimized' in an analysis to find the 'best' set of interventions/decision. It was noted that there are many possible metrics and different modellers have used different ones at different times, but greater research into how those choices influence results will be required.

In the final session, the group from Intellectual Ventures introduced a new modelling project that will aim to produce new software to enable detailed microsimulation models of HIV (and other infectious diseases). A demonstration of a web-based interface to the model and a high-level overview of the architecture of the model were given. The model is currently in development, but future meetings of the HIV modelling consortium will explore the model in much greater detail.

Outcomes:

It was agreed that the following would be the outcomes from the meeting:

1. Two RFAs would be issued to support research into particular aspects of the discussion about sources of HIV infection – the influence of assumption about hierarchies of risk in population (RFA MC 1.1) and the influence of the 'static' nature of the existing modelling tool (RFA MC 1.2).
2. One RFA would be issued to support research comparing the estimated impacts of interventions in two or more different mathematical models (MC 1.3).
3. The Modelling Consortium secretariat would coordinate the drafting of a manuscript discussing the strengths and limitations of the existing 'Modes of Transmission' tool.
4. Secretariat to examine potential for generic methods of estimating sources of infection along life-course categorizations (including age, sex, location, marital status).

The RFAs were issued on 17th May and included in the appendix. The manuscript will be drafted and circulated within 3 months of the consortium meeting.

Next Meeting:

The next meeting of the HIV Modelling Consortium will be planned for September/October, with a topic to be decided by the steering committee in July.

Appendices:

1. Meeting agenda with link to posted presented files.
2. List of participants.
3. Request for funding applications issue: available here.
4. Finalized governance structure document: available here.

The HIV Modelling Consortium

Topic Meeting One: Sources of Infections and National Intervention Impact Projections
Date: 28-29th April, 2011
Location: Montreux, Switzerland

Aim: To Review Current Methods For Estimating Sources of Infections in Generalized Epidemics in Africa (mostly) And Evaluate Implications For Projections Of Intervention Impact.

27th April

19.00-20.30 ***Welcome Reception:*** Bar and Terrace.

Day One: 28th April

Part I: Current methods/model/information about sources of infection.

Chair: Geoff Garnett.

9:00-9.15 Introductions & Description of the Modelling Consortium -- Geoff Garnett

9.15-9.45 Data / Model Sharing Discussion -- Tim Hallett

9.45-10.00 What Decision-Makers Need to Know About Epidemics -- Rifat Atun & David Wilson

10.00-10.25 The 'Original' Modes of Transmission Spreadsheet -- Peter White

10.25-10.50 UNAIDS' Know Your Epidemic Program: Process and Results -- Eleanor Gouws.

10.50-11.05 Coffee.

11.05-12.25 Detailed Country-specific Methods and Results of 'MoT' Analysis

West Africa: Catherine Lowndes (~20 mins)
Benin: Marie-Claude Boily (~20 mins)
Western and Southern African Countries and Implications of Results on Decision Making: Marelize Gorgens (~20 mins)
South Africa: Alex Welte (~20 mins)

12.25-13:00 Discussion

13.00-14.00 Lunch

14.00-14.20 Perceived Strengths and Limitations of Current Approach By Others -- Tim Hallett

14.20-14:35 Influence of Model Structure and Calibration on MoT estimates -- Sharmistha Mishra

14:35-14.50 The Influence of Model Assumptions in the MoT: Uganda and Cambodia as Case Studies- Anna Foss

14:50-15.10 Proposed updates / recent additions to MoT -- John Stover

15.10-15.25 Other Ideas: Demographic / “Life course” Approaches - Basia Zaba

15.25-15.40 Coffee.

15:40-17:00 Structured Discussion (lead by Chair).

Brain-storm for potential way forward: (i) short-term updates to model; (ii) longer-term changes ; (iii) further data needs.

17:00 Close.

20.00-22.00 Dinner

Day Two: 29th April

Part II: Model Projections of Intervention Impact

Chair: Geoff Garnett.

9:00-9:05 Introduction To “Impact Modelling” -- Geoff Garnett

9:05-9:25 Policy Instruments and Individual Behaviour in Models -- Mead Over

9.25-9.40 Discussion.

9.40-10.05 “Under the hood” methods in GOALS (structure and parameters) and calibration and projections for South Africa -- John Stover

10.05-10.20 Projections for impact of intervention packages in *aids2031* And Summary of Feedback Received-- Kelsey Case

10:20-10:35 Coffee.

10:35-10:50 Formal model comparison work in chlamydia interventions -- Nicola Low

10:50-12:30 Landscape of models for South Africa Estimating Impact of Interventions:
Leigh Johnson (~20 mins)
Nicholas Bacaer / Carel Pretorius (~20 mins)
Brian Williams (~20 mins)
Bertran Auvert (~20 mins)
Till Barnighausen (~20 mins)

12:30-13:00 Open source microsimulation code - Philip Eckhoff

13:00-13:30 Discussion of potential work to be undertaken over next 12 months and expressions of interest.

13:30 Close

13.30-14.30 Lunch (Buffet)

Imperial College London

The HIV Modelling Consortium

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Date: 28-29th April, 2011
Location: Montreux, Switzerland

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