HIV Modelling Consortium

Models for Program Planning Reference Group Meeting

Etc. Venues Marble Arch, Garfield House, London

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Meeting Summary Report

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HIV Modelling Consortium

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Objectives of the HIV Modelling Consortium

The HIV Modelling Consortium (HIVMC) aims to improve scientific support for decision making through the co-ordination of a wide-range of research activities in mathematical modelling of the HIV epidemic. This project is currently funded by the Bill & Melinda Gates Foundation through a grant to Imperial College London.

The Consortium's key objectives are to:

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

A Steering Committee of leaders in HIV program and policy directs the focus of the work of the consortium. Further information on the HIV Modelling Consortium is available in a standard briefing document and information about other work packages undertaken by the HIV Modelling Consortium is available at the website www.hivmodelling.org

Background of the Models for Program Planning Reference Group

The HIVMC hosted a workshop on "Allocative Efficiency Tools & Methods to Support Country HIV Programme Budget Allocation" in Vancouver in 2015 (see link to the Workshop Summary Report), as advised by the HIV Allocative Efficiency and Programme Effectiveness Working Group. The latter is a technical working group of the global HIV Economics Working Group (ERG) that is co-convened by the World Bank and UNAIDS. The aim of this workshop was to provide a platform for three widely-used modelling tools to be presented and discussed, to help the HIV modelling community better understand the technical characteristics, applications and policy questions that can be answered with each of these models. The models included Goals (part of the SPECTRUM software suite), AIDS Epidemic Model (AEM) and OPTIMA.

Following this workshop, the HIVMC had been approached by the modelling groups involved and other parties to expand the work and constitute a reference group that would create a forum in which current methods and modelling can be discussed and reviewed, with the aim to strengthen the whole field and the tools available to countries. This group was later named as the Models for Program Planning (MPP) Reference Group, currently housed within the HIVMC.

The organisational structure of MPP Reference Group is built upon that of the HIVMC: it is managed by the Secretariat, based in the Department of Infectious Disease Epidemiology at Imperial College London (ICL). The Secretariat is directed by Prof Timothy Hallett and Dr Sabrina Lamour as Project Manager for MPP Reference Group. In addition, the Key Partners that are members of MPP Reference Group Secretariat include Paul Revill and Prof Mark Sculpher (University of York), Prof Joshua Salomon (Harvard T.H. Chan School of Public Health), and Prof Andrew Philips (University College London).

The Secretariat is responsible for organising biannual general meetings, facilitating discussions and collaborations between HIV modelling groups, generating subsequent meeting reports, and identifying consensus points and further recommendations. They take on the role of overall chair and at each meeting. A Co-Chair would also be appointed (from among the Key Partners) for each meeting, with special expertise in that particular topic to oversee the activities.

In addition to the Secretariat, there are currently core members of MPP Reference Group, constituted of key model developers from the aforementioned Vancouver Allocative Efficiency workshop, namely Mr John Stover (Avenir Health, Goals), Prof David Wilson (Burnet Institute, OPTIMA) and Dr Tim Brown (East-West Center, AEM). Additional participants working within the field are welcome to

contribute to the MPP Reference Group, which includes a large number of *ad hoc* members who may participate on a meeting-by-meeting basis and contribute with their particular expertise.

All activities are overseen by the MPP Reference Group Steering Committee who are responsible for the executive decisions of the group. Their responsibilities include giving direction with regards to group's priority research and/or policy questions that need addressing (via the Secretariat), commissioning of any sub-contracts, aiding in the development of the structure of the biannual meetings, and providing additional guidance on relevant research. The Steering Committee is currently composed of the following members:

- Iris Semini, UNAIDS, Switzerland
- Taoufik Bakkali, UNAIDS, Switzerland
- Prof Allyala Nandakumar, United States Agency for International Development (USAID), USA
- Dr David Wilson, The World Bank, USA
- Michelle Morrison, Bill & Melinda Gates Foundation (BMGF), USA
- Dr Peter Ghys, The Joint United Nations Programme on HIV/AIDS (UNAIDS), Switzerland
- Dr Nalinee Sangrujee, U.S. Centers for Disease Control and Prevention (CDC), USA
- Regina Ombam, National AIDS Control Council (NACC), Kenya
- Edward Kataika, East Central and Southern Africa Health Community (ECSA-HC), Tanzania

Meeting Objectives

This meeting represented the first official assembly of the MPP Reference Group, with the intention to review the characteristics of a variety of HIV intervention models, including the three used routinely in program planning and other relevant academic models. The objective was to increase the HIV modelling community's understanding of the different models and encourage collaborative discussions, to improve the development of their tools. The model characteristics examined in this meeting in particular included the representation and incorporation of sexual risk behaviour and behaviour change interventions, of anti-retroviral therapy (ART) and care cascade interventions, and of epidemiological parameters.

Meeting Outline

The meeting provided an opportunity for the model developers to present an overview of each of their tools and compare their different approaches with regards to the session topics. In addition to the modelling developers, participants also included program planners, epidemiologists and behavioural scientists, to be able to address a wide range of perspectives from different stake-holders.
The meeting was divided into the following session topics over two days:

- Session 1 – Representation of Sexual Behaviour and Behavioural Change Interventions in Models
- Session 2 – Representation of ART and Cascade Interventions in Models
- Session 3 – Representation of Epidemiological Parameters in Models
- Malawi Workshop Update — Use of Modelling and Health Economics in Resource Allocation Decisions

Descriptions of the different models have been summarised in tables in the next section. Discussion points and recommendations specific for each session are outlined individually in the Session Summaries sections, whereas those common across sessions have been summarised under General Recommendations, which also include plans for the next meeting. Additionally, a complete agenda of the meeting and list of participants can be found in the Appendix of this report.

Overview of HIV Program Planning Models

A total of 9 models were presented at this meeting: a short description of each model is listed below in Table 1, whereas Table 2 describes their different approaches to the session topics. Further comparisons between Goals, OPTIMA and AEM can also be found in the Vancouver 2015 Meeting Report.[1]

Table 1. Overview of Presented HIV Models

Model Name	Presenters	Affiliation	Description	Further Information
Goals (in SPECTRUM)	John Stover Lori Bollinger	Avenir Health	Deterministic, compartment model that simulates an HIV epidemic and the cost and impact of interventions intended to change current trends. Goals contains defined risk groups and interventions. Default assumptions are provided for epi parameters, interventions effectiveness, and unit costs. The model is intended to support the development of strategic plans and investment case analyses.	[2] The model and manual are available for download at AvenirHealth.org
OPTIMA	David Wilson Robyn Stuart	OPTIMA	Deterministic, compartmental model with flexible definitions for populations and interventions representative of the local epidemic context, featuring optimisation and scenario analysis	[3] The manual and further information is available at optimamodel.com
AEM	Tim Brown	East-West Center	A deterministic model suited for concentrated epidemics which allows some flexibility in including key populations and interventions and allows adjustments of transmission probabilities and cofactors to fit observed prevalence trends	[4] tim@wiliki.eng.hawaii.edu
HIV Synthesis Model	Andrew Philips	UCL	Individual-based model of heterosexual transmission in context of sub Saharan Africa, updating in 3 month intervals. Partners sampled from distribution of partnerships, taking account of HIV prevalence and viral load in HIV+ people. Not a full network model. Variables simulated include all long and short term condomless sex partners, HIV tests, CD4 count, viral load, use of specific drugs, drug resistance and adherence, risk of AIDS, death	[5,6,7] andrew.phillips@ucl.ac.uk
IDM	David Klein	IDM	Stochastic, individual-based modelling framework that brings together assumptions about network, biology, and health care for HIV, using configurable parameters	[8,9,10] Model documentation on idmod.org Source code on GitHub.com
PopART	Michael Pickles Ann Cori	ICL	Individual-based metapopulation model of open and growing heterosexual population aged 14+ (developed for HPTN-071/PopART trial). Model simulates extended time period and can be calibrated according to HIV prevalence (by age/gender), HIV incidence, ART coverage, knowledge of serostatus, epidemic doubling time. Model uses HPTN-071 baseline population cohort survey data and literature for calibration	Model will be made open source, with full documentation, in the near future m.pickles@imperial.ac.uk
Kenya County & Pan-African Model	Sarah-Jane Anderson Jessica McGillen	ICL	Compartmental deterministic models tailored to reflect the epidemiological characteristics and intensity of the existing response in subnational regions (geographically specific)	[11,12] sarah-jane.anderson@imperial.ac.uk j.mcgillen@imperial.ac.uk
Care Cascade	Jack Olney	ICL	Individual-based model describing the HIV epidemic and the experiences of care among HIV-infected adults in Kenya. The model simulates 12 interventions acting on various aspects of care individually and in combination to identify strategies to improve patient outcomes cost-effectively	[13] jack.olney11@imperial.ac.uk
US MSM Model	Kate Mitchell	ICL	Deterministic compartmental model of HIV transmission and treatment amongst MSM in the USA, designed to be used to assess the impact of the HPTN-078 trial	[14] kate.mitchell@imperial.ac.uk

Abbreviations: HIV+; infected with HIV; ICL, Imperial College London; IDM, Institute for Disease Modelling; MSM, men who have sex with men; UCL, University College London

Table 2. Comparison of Models' Characteristics in the Representation of Behavioural and Care Cascade Interventions and Representation of Epidemiological Parameters

Model Name	Sexual Behaviour and Behavioural Change Interventions	Care Cascade Representation and Interventions	List of Epidemiological Parameters
GOALS	Goals uses an Impact matrix that summarizes the available literature to describe the impact of 13 behaviour change interventions on key behaviours (condom use, no. of partners, age at first sex, needle sharing). Studies are first assigned a quality score and only those exceeding a defined quality level are included Upper and lower quartile versions of the matrix contribute to estimating the uncertainty in the outputs Users can change the default values	ART included as single programme intervention ART is provided to eligible individuals according to selected criteria such as CD4 cell count or population group. The model does not include the full cascade but does include viral suppression, second line treatment, and drop-out. We expect to have the full cascade, including interventions, by the end of 2016	Model fit to historical prevalence trends, (from AIM and surveillance and survey data) Variable parameters include • r (probability of transmission per act), F->M • Multipliers on r (M->F, STI, MSM, primary infection, symptomatic stage • Effectiveness of • ART, condom use, VMMC • Past trends in condom use and STI prevalence
OPTIMA	Users supply context-specific sexual behaviour data for population groups, including frequency of casual, regular, commercial acts, condom usage and circumcision rates These variables are used in an epidemic model to create estimates of new HIV infections due to sexual activity. If country-specific sexual behaviour data are not available, regional default values may be used Scenario analysis allows users to either directly modify behavioural parameters, or to modify program coverage or funding levels. Multiple overlapping interventions that target the same parameter can be flexibly defined to interact with other programs in different ways	Populations are subdivided into compartments based on their CD4 count and where they are, or fall, in the ART cascade Individuals are categorised as susceptible, undiagnosed, diagnosed and untreated, or treated If data is available, the cascade can be extended to include extra components, such as linkage to care Interventions are generalisable and can target various cascade parameters	Default biological parameters (that the user can overwrite) include: • HIV health state progression rates • death rates (background/HIV) • sexual/injection/pregnancy transmission • condom/circumcision efficacies User-specified behavioural parameters include: • no. of sexual partners/acts by type of partnership (regular/casual/commercial) • birth rates • condom-usage/circumcision probabilities • PMTCT treatment rates • injecting drug-usage variables • HIV testing rates

AEM	A behaviour-based process model that simulates transmission dynamics in concentrated epidemics based on sexual and injecting behavioural trends provided by the user
	Intervention Workbook focused on high-impact interventions targeting key populations (e.g. sex work, needle sharing, etc.)
	Allows scenario creation with different program mixes, levels of effectiveness & coverage
		ART included as single programme intervention
		Model uses the Spectrum CD4 model with ART tracked separately for each sub-population
		ART is provided to eligible individuals according to selected criteria such as CD4 cell count or population group
		Components of the cascade such as diagnosis, treatment failure, second line of treatment and viral suppression are not explicitly included at present
			• Start years – IDU, heterosexual, MSM
			• Transmission probabilities (single act):
			  ○ Hetero vaginal M->F and F->M
			  ○ Anal sex (receptive/insertive)
			  ○ single needlestick
			• Cofactors:
			  ○ STI for men and women
			  ○ STI for receptive/insertive anal sex
			  ○ Reduction in transmission with circumcision

			○ Increase in transmission during PHI • Parameters dynamically adjustable to display "tune" epidemic as desired
HIV Synthesis Model	Model includes condomless sex partners only, not all sex partners Sexual behaviour parameters sampled as part of model calibration using ABC approach	Care cascade is modelled explicitly, in terms of diagnosis status, whether ever linked to care, whether currently in care, whether currently on ART, current adherence, current underlying and measured viral load and CD4 count (if measured), effects of lack of adherence and discontinuation of ART on resistance. Cascade interventions can be modelled if specified in terms of effects on one or more of these	Viral load / primary infection status of each infected new partner is obtained by sampling from distribution of viral load in short term partnerships formed by HIV + people, accounting for gender age mixing Transmission rate depends on this status Viral load and primary infection status of HIV+ partners determined by: short term partners - sampling from distribution of viral load in HIV+ population having condomless sex; long term partners – tracked status of the partner. Probability of HIV acquisition given an HIV+ partner also depends on • circumcision (0.5-fold) • use of PrEP (effect depends on adherence) • male to female vs female to male (1.5/2 fold) • current STI present (3 fold)
IDM	Heterosexual relationships divided into 4 configurable types (transitory, informal, marital or commercial), each of which categorised into 3 risk groups (membership for each group dynamic by age, year, and gender) Model includes several factors, e.g. birthday, HIV status, condom usage, duration, etc.	ART and cascade modelled in configurable "building blocks" Architecture allows individual decisions, delays, and interventions to vary parametrically and structurally in space, time, gender, age, disease status, and more Full user configurability	Stage-based transmission with co-factors • Acute, latent, AIDS • ART, ramps down slowly • Individual-heterogeneity • Gender-based, by age Other factors include circumcision, other STIs, condom use, and PrEP/vaccine (may be modelled with time-varying vaccine-like efficacy with boosting and waning)
PopART	Model based on heterosexual population with partnership formation/breakup and 3 sexual risk groups with assortative mixing by age/risk Partnership duration drawn from a Gamma distribution Reduced partner formation or coital frequency, and increased condom use can be incorporated as interventions if data is available to parameterise these changes	HIV testing is modelled through two channels: a background level of testing and an annual testing process, representing clinic and home-based testing channels. Individuals who test positive enter the care cascade, represented by states: in care but not eligible for ART, awaiting ART initiation, early ART, on ART and virally suppressed, on ART and not virally suppressed, and dropped out of care Interventions can be either captured through parameterization (intensification of existing services) or through additional annual testing (as for PopART)	Baseline transmission probability modified by early infection, CD4 stage, set-point viral load, ART (early ART, long-term ART virally suppressed/unsuppressed), circumcision (medical and traditional have different effectiveness in reducing susceptibility) All parameters in the model can be either fixed or adjusted very simply

Kenya & Pan-African Model	Incorporates both heterosexual and homosexual transmission in the population Several interventions included, including behaviour change communication, treatment scale up, VMMC, and PrEP These can be targeted to different risk groups or locations specifically. Coverage levels and efficacy are predefined	Simple representation of ART programmes with two routes to treatment; (1) 'Late ART' which is treatment for clinical need and (2) 'Early ART which is active outreach to find positive individuals and engage them in care prior to clinical need	Model is fit to prevalence data (national surveys and ANC surveillance), ART coverage data and circumcision levels Transmission is modelled per partnership. Different partnership types are assumed to be associated with a different probability of transmission, according to the partnership type, infection state, intervention status and risk groups of the groups mixing
Care Cascade	Model determines new infections through deriving a transmission probability and weighting infected individuals by their relative infectivity.	Cascade captured by describing all possible routes through care for infected individuals from HIV-testing, linkage, pre-ART retention, ART initiation and long-term viral suppression Model simulates 12 interventions acting on care, ranging from, home-based counselling and testing, linkage interventions, point-of-care CD4 testing, outreach interventions and immediate ART and adherence interventions Impact is assessed through calculating DALYs averted relative to a baseline scenario (in the absence of any interventions) between 2010 and 2030. The additional cost of care (relative to baseline) is also assessed in the same time-frame	New infections prior to 2002 are driven entirely by Spectrum estimates In 2002, a fixed transmission probability is calculated by summing the weighted infectiousness of all HIV-positive individuals. This probability is used from 2002 onwards and interventions can indirectly impact incidence through altering the distribution of infectious individuals in care
US MSM Model	Homosexual HIV transmission - different age and race groups have different numbers of main, casual and commercial partnerships per year, with different levels of condom use associated with each partnership type Behaviour change interventions affecting partner numbers or condom use can be incorporated by changing the mean number of partners or average condom use parameters	Detailed explicit care cascade, separate states for those never routinely testing for HIV, those undiagnosed, diagnosed, in care, on ART, dropped out of ART Interventions assessed: increases in HIV testing rates, linkage to care, retention in care, ART initiation, retention on ART, through increasing/decreasing transition rates	Risk of infection per anal sex act varied in fitting, force of infection also incorporates level & efficacy of condom use and of male circumcision, relative infectiousness by HIV disease state (acute, current CD4 strata, set-point viral load strata), ART status (unsuppressed/suppressed), PrEP status

Abbreviations as for Table 1 and including: ABC, Approximate Bayesian Computation; AIM, AIDS Impact Model (Avenir Health); ART, anti-retroviral treatment; F, female; Hetero, heterosexual; IDU, injecting drug users; M, male; STI, sexually transmitted infections; PHI, primary HIV infection; PrEP, pre-exposure prophylaxis; r, probability of HIV transmission per act; VMMC, voluntary medical male circumcision

Session Summaries and Recommendations

Session 1 — Representation of Sexual Behaviour and Behavioural Change Interventions in Models (Day 1)

Summary

Mike Sweat and Kevin O'Reilly (University of South Carolina), the session chairs, began providing a summary of their epidemiological expertise and research on conducting meta-analyses and systematic reviews to assess the impacts of various behavioural change interventions on prevention of HIV infections. They have since accumulated a repository of information for published behavioural studies (set primarily in low- and middle-income countries), and will work with the HIV Modelling Consortium on developing a project to support use of these data with modellers. They raised concerns that current HIV program planning models appear to lack much of the complexity for behavioural interventions and wished that further efforts were given on additional parameters, such as the duration of the intervention, the demographic target population, the effectiveness/quality and effect on both an individual level and scaled up to a population, the order of interventions if multiple interventions are being administered, and the "decay" of the intervention (i.e. the initial beneficial effect of an intervention is not sustained once the intervention has been implemented and wanes over time). Another point that was highlighted was the fact that unlike biomedical interventions (e.g. usage of ART or contraception), behavioural interventions take much longer to be fully adopted within a population, which may only result in relatively small short term effects yet potentially much more significant cumulative effects in the long-term, a factor that required further investigation.

The chairs subsequently demonstrated a number of challenging issues they faced when examining and working with behavioural data, which opened up the discussions to the variety challenges experienced by modellers with incorporating behavioural data and interventions into their models. The limitations with behavioural intervention data were often reiterated and expanded upon throughout the session; the main discussion points have been summarised below:

- Compared with treatment or biomedical interventions, a relatively limited number of studies currently exist for behavioural interventions
- Many of the results from these behavioural studies are not published or are not publically available and would need to be specifically requested (e.g. national/subnational program data)
- The behavioural data that is available is often suboptimal, e.g. incomplete not well described (particularly in program data) and/or not well-validated
- Limited data validation can result in potential bias and some mistrust of data by researchers (e.g. when incorporating results which heavily reliant on self-reporting)
- There is a strong heterogeneity in the results from behavioural studies, which itself is not well understood
- Multiple definitions of parameters in behavioural (and biomedical) interventions, owing largely to modellers independently defining these, which in turn can be interpreted with different outcomes

Each modelling team provided a short introduction of their models in this session, summarised in Table 1. Each introduction was followed by a presentation and discussions surround the different incorporation of sexual behaviour and behavioural change interventions in each model, described in Table 2. A large number of differences was observed between the models, both in the representation of sexual behaviour (e.g. EMOD and PopART only modelled heterosexual transmission whilst Kate Mitchell's model looked specifically at homosexual transmission) and in the way behavioural interventions were both incorporated and assessed (e.g. looking effects on condom use vs. overall effect on transmission, etc.).

Further discussions arose regarding the need from modellers for more guidance by program planners and policy-makers, to specify their requirements from modellers, especially regarding the level of

granularity that is required for interventions — a topic that was frequently visited throughout the meeting (see General Recommendations Section of the report).

Another discussion point raised by Mike Sweat was the potential use and benefits of synthetic data, in contrast to actual observed data, given the aforementioned limitations. However, several reservations were made of use of synthetic data, expressed by many modellers and epidemiologists. Graham Medley stated that synthetic data does not address the complexity of real data, including potential correlations within the data for each country. Tim Brown also added that the synthetic data may mask underlying links within the data. Mead Over (Center for Global Development) raised concern that the relationships that could potentially be found within synthetic data could be highly subjected to bias, depending on what modellers put into the data to begin with. Nevertheless, Josh Salomon pointed out that synthetic data may prove highly useful for in depth direct model comparisons by providing the same data starting point for the models, a point which was generally agreed upon.

The session was closed by concluding remarks by their chairs, acknowledging the strong interest and appreciation for behavioural data by the modellers. This was followed by a review of recommendations agreed amongst the participants to help tackle the challenges with behavioural data and interventions, outlined below.

Recommendations

- An agreement was made amongst the modelling community that more effort should be made for increased access to data resources, and for better usage of current data available. This includes efforts to integrate data from other resources, e.g. the International Bibliography of the Social Sciences (IBSS) data, clinical trial data from country teams, subnational/national program data, unpublished work, etc.
- A commitment amongst modellers to work closely with behavioural scientist experts and epidemiologists to compare and review induced assumptions for interventions, and to review these
- Further discourse required between modellers, behavioural scientists and epidemiologists to lay-out concrete definitions and/or guidelines for behavioural parameters, including inputs, population targets, metrics of success, duration of interventions, etc. to help standardize methods across the multiple models
- An increase in partnerships between modellers and other research groups who have access to intervention data was agreed, to facilitate data sharing. In particular, the MPP Reference group should seek to augment collaboration with the ALPHA Network (hosted by the London School of Hygiene and Tropical Medicine, LSHTM), who can provide data on a wide range of interventions (including behavioural) across several countries.
- **Action Points**
    - All modellers who are modelling interventions that have their effect via changes in numbers of partners or condom use should create an “impact matrix” (similar to GOALS) listing all their behavioural parameters, for clearer comparison between models (John Stover’s suggestion)
    - Emma Slaymaker (ALPHA Network, LSHTM) has agreed to propose a list of measures that can be analysed with the ALPHA network data and disseminate to all modelling groups present at the meeting. In turn, they will provide feedback to prioritise which datasets they would be most interested in to use, to help ALPHA network provide data to modellers in a “user-friendly” format
    - Mike Sweat and Kevin O’Reilly have agreed to work with HIVMC to make their repository of data and meta-analyses of behavioural data more accessible to modellers

Session 2 — Representation of ART and Cascade Interventions in Models (Day 2)

Summary

Joshua Salomon (session chair) gave a summary of the challenges faced by modelling interventions in general, including the discrepancies in measures of outcomes and definitions, the varying levels of precision for interventions, and the variety of the different technologies and modelling tools. He agreed that whilst generally there appears to be a higher level of attention and/or priority given to the treatment interventions in model, as opposed to behavioural or prevention intervention, more could still be done to improve the heterogeneity in modelling treatment (and care cascade) interventions.

Each modelling team presented their representation of ART, care cascade and cascade interventions in their models, as summarised in Table 2. The majority of differences between the models concerned the layers of granularity added for the interventions: OPTIMA and Jack Olney's modelling approaches sweep across a large number of very specific interventions, whilst others looked at a coarser level on the relative effect of implementing certain changes in the care cascade. This raised discussions concerning the level of granularity that is required by and/or useful to program planners (further outlined in the General Recommendations Section of this report), as well as comparing methods to best evaluate the impact of individual vs. a combination of interventions. It was also noted that whilst most models include CD4 count as an output, not all include viral load yet and its incorporation is underway in many models.

Another key difference between the models was the use of 90-90-90 target, set by UNAIDS in 2014n namely that by 2020, *"90% of all people living with HIV will know their HIV status, 90% of all people with diagnosed HIV infection will receive sustained antiretroviral therapy, and that 90% of all people receiving antiretroviral therapy will have viral suppression".*[15] Discussions arose as to how meaningful this target actually was, and Paul Revill suggested that alternative target, such as the number of disability-adjusted life years (DALY's) averted, which may be more appropriate and tangible to program planners. However, feedback from Regina Ombam (NACC, Kenya) and John Stover suggested that the 90-90-90 target is important and regularly used by program planners, even if that target may appear arbitrary or overly ambitious.

A concern raised amongst many participants was the issue of finding data to inform realistic representation of the population who had taking ART but then dropped out of care (for reasons yet to be ascertained), particularly in the difficulty in quantifying the number of drop-outs. It was agreed that further efforts should be made to describe this population group. Such investigations would aid in the impact assessment of adherence interventions, and could potentially further research on human health care-seeking behavioural patterns, within endemic populations.

Recommendations

- An agreement amongst modellers was that that the incorporation of the care cascade (including measures of both CD4 counts and viral load) in current program planning models was important and is already underway in many models. Further discussions on sharing resources would benefit the way in which these models currently represent the care cascade
- There is demand for incorporation of the care cascade in order to explore patient monitoring strategies, and to better describe the population of people who have been treated with ART yet then drop-out from care
- Michael Pickles (ICL) and Andrew Phillips suggested modellers should make efforts to access data from population surveys in order to inform on the proportion of ART experienced people who are currently off ART and help calibrate models to drop out rates
- **Action Point**
    - Nathan Ford (WHO) to update the group when a new review article on adherence interventions is finalised

Session 3 —Representation of Epidemiological Parameters in Models and Transmission Risks (Day 2)

Summary

Marie-Claude Boily (ICL) presented preliminary results[1] from systematic reviews and meta-analyses of observational studies on the risk of HIV transmission, estimated by gender, setting (high- *vs.* low-income countries), type of sex act, stage of infection, and other co-factors (compared with results published in 2009).[16] The results showed that in contrast to high-income countries, the probability of HIV transmission was dramatically increased in low-income countries, and that within the latter, the highest transmission risks were from female to males. The risk also was higher for anal sex acts than for vaginal, particularly for receptive anal intercourse.

The risks of a large variety of additional co-factors that alter transmission or acquisition of infection were presented. Those that have been shown to reduce transmission/acquisition include the use of ART, condom use, and voluntary medical male circumcision (VMMC) — categorised separately from traditional male circumcision, which was found to have no significant protective effect in their studies. Other co-factors which were found to increase risk included co-infection with viral and non-viral sexually transmitted infections (STI's), and non-STI infections (e.g. malaria), whilst others did not appear to significantly alter risk of transmission but may affect acquisition, e.g. pregnancy. One of the issues highlighted by Marie Claude Boily was the difficulties in analysing the effect of multiple co-factors at once, and determining their individual contribution towards transmission.

This was followed by Steve Bellan (University of Texas), who presented their latest analyses on estimating infectivity during the acute (early) phase of HIV infection, using two approaches. The first method was to use viral load trajectories and viral load–infectivity relationships to estimate infectivity trajectories over the course of infection, where they found that their estimates are significantly lower than previously published results. Their second approach was to reanalyse data from the Rakai study (which represents the only study where acute phase infectivity had been directly measured, retrospectively, based on group of serodiscordant heterosexual couples in Rakai, Uganda).

Their model was designed simulate HIV infection and transmission within couples to the Rakai data and estimate the relative hazard of transmission during the acute phase versus the chronic phase. In line with their first approach, the second method also produced significantly lower estimates than published with previous authors.[17,18]. Steve Bellan demonstrated that this disparity between their results and earlier estimates may be due to the lack of accounting for the heterogeneity in susceptibility and infectivity of the couples in the Rakai study, and that the fact that the original authors may have disproportionally excluded low-risk chronically-infected couples from their final analyses, resulting in an overestimation of overall transmission risk. Consequently, he stated that these findings implicate that the elevated acute-phase infectivity may not be as considerable as previously thought, and that treatment inventions such as the scale-up-ART, may potentially have more beneficial effect on prevention of transmission than originally anticipated.

Discussions followed as to how important the variability of viral load has on transmission yet Steve Bellan stated that the heterogeneity of other co-factors, such as coital frequency and others mentioned previously by Marie-Claude Boily, would contribute much greater than differences in viral load. Another point raised by Steve Bellan was that current transmission data are largely based on serodiscordant low-risk couples, thus potentially introducing further selection bias in transmission analyses. Jeff Eaton expanded this issue and stated that currently much focus exists on the heterogeneity of infectivity, but that of susceptibility of infection also needs to be further addressed.

Following these discussions, the different modelling teams presented representation of various epidemiological parameters which have been summarised in Table 2, which were generally in agreement with one another. Questions were raised on the level of uncertainty required to parameterise in each model and whether to include transmission parameters as fixed or free

[1] Further analyses are underway and are planned to be published in the near future.

parameters, and what distribution to use. No consensus had been reached, owing to the variety of approaches used between modellers, e.g. in some models such as OPTIMA, the transmission rate incorporates more than just the biological transmission rate and is treated as a free parameter, to enable fitting to data.

Recommendations

- It was agreed that modellers should continue to maintain awareness of emerging data and in different ways in which transmission is modelled in the various models. This will help in interpreting any differences in model outputs when applied in similar settings
- There was an agreement for the need for more data than the Rakai data to improve estimates of transmission. One possible useful source is the ALPHA network data and calibration of models to the data from one or more of these sites could be very informative

Malawi Workshop Update — Use of Modelling and Health Economics in Resource Allocation Decisions (Day 2)

Shortly before Session 2, an additional update was given by Paul Revill, about the 3-day Workshop on the value of using modelling and health economics to support resource allocation decisions that was held in Malawi in June 2016 (see Workshop Summary Report for further details).[19] The workshop included a group of economists, decision makers, and modelling groups, including representatives from Avenir Health, Optima and HIV Synthesis teams.

One of the main discussion points from the workshop was the acknowledgement that the allocation of resources on HIV programs sit within the wider context of the Malawi healthcare system, which itself is under multiple (financial and other physical) constraints. Consequently, drawing upon further resources to benefit anti-HIV causes could pose larger implications, and potentially negative consequences, on the general healthcare of the population. Paul Revill suggested that current models are heavily involved with fulfilling the requirements of the HIV funders, but more efforts are needed to champion the program planners, including the need for continual discourse with decision makers and country teams.

Mead Over continued by urging the need for models to capture the not only the cost and resource contractions of countries into models, but also the time constraints, to better reflect the duration of intervention programmes (e.g. over 5 years). Furthermore, Nathan Ford added that it is important to also consider the timings of such meetings/workshops and link these to the timelines of local/international programmes, e.g. before the preparation of national guidelines, so that outcomes form such workshops may help direct the decision-making processes, a point that was generally agreed upon.

A comparison between cost-effectiveness of interventions in OPTIMA, GOALS and HIV synthesis models had been undertaken during the Malawi workshop, which had produced contrasting results between the models. This finding gave rise to further discussions during the current meeting for the need to do further comparisons between models using “real data” to better understand the models, a point that already been raised in the first meeting session.

Recommendation

- It was generally agreed that it was important to incorporate the resource constraints currently faced by healthcare systems into their program planning models, to better reflect the reality of low-income and middle-income settings

General Recommendations

Input from Program Planners and Policy Makers on Modelling Interventions

Strong expression of interest from the modelling community for further guidance from program planners and policy-makers, to specify their requirements from modellers, including the level of precision (granularity) which is required for interventions and any additional considerations. Their feedback has been summarised below:

- Regina Ombam (NACC, Kenya) and Nalinee Sangrujee (CDC) both stated that interventions are generally assessed from a top-level perspective, as opposed to detailed specific interventions. Thus further efforts should be made on looking at general intervention effects in models, which should ideally also include the capability of targeting subpopulations and geographical locations
- Regina Ombam described that their focus is largely keen on outputs with greatest impact on population health, to facilitate prioritisation of interventions
- Paul Revill and Mead Over (see previous Malawi workshop Update section) suggested that the complexity of health resources, financial and time constraints of endemic countries should be factored into the models, for more realistic recommendations of interventions
- Regina Ombam and Nathan Ford described that greater uncertainty currently lie with planning prevention interventions, compared with treatment, which are better described in models. Nathan Ford continued that in a "post-ART era", prevention interventions are becoming increasingly important as treatment becomes more standardised, and thus further efforts need to be made in describing preventions in models to better inform program planners
- An additional suggestion from James Hargreaves was to apply a more epidemiological approach to choosing/optimising interventions incorporated in models, particularly for prevention and/or behavioural interventions, namely:
    - Is there enough supply?
    - Is the demand there?
    - Is there a better way to use the same intervention?
    - This suggestion is based on the idea of the Prevention Cascade[20] and as more data is collected along these dimensions, it may be possible for models to incorporate these data directly

Outlook for the next MPP Reference Group Meeting

The next general MPP Reference Group meeting shall be on the different costing approaches of the scale-up of interventions by the models, ideally using specific examples (e.g. in treatment and circumcision).

The meeting is planned towards the end of 2016/early 2017 and should ideally be held in a high burden country, with greater efforts to be made incorporating more program planners and other decision-makers at the meeting, to gain a better understanding of their needs and tailor models to be more realistic.

- Program planners, as well as donors, policy-makers in additional to country team members, should be invited to participate, to include their input in the modelling processes and thus better specify measuring inputs and outputs that program planners need from modellers
- The date of the meeting should try to accommodate for timings of national guidelines and/or plans for other intervention programs
- Josh Salomon suggested a systematic review of costs of the care cascade, with efforts to include unpublished data and program data alongside literature

- Nalinee Sangrujee to present a list of how much PEPFAR have spent on a variety of treatment and prevention interventions and locations/countries, as an example to help guide modellers on how to factor in cost
- Mead Over to present findings of his cost function analysis work
- Data that are arisen from country level work from all groups would ideally be shared and scrutinized and compared with other estimates
- Global Health Costing Consortium to be heavily involved to discuss their future work. That group looks to the MPP Reference Group for input into the design of the costing models they will develop, including work currently ongoing by many modelling teams within MPP Reference Group

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Appendix

The **Meeting Agenda** and **List of Participants** can be found on the subsequent pages.

HIV Modelling Consortium

Meeting Agenda

Models for Program Planning Reference Group Meeting,

Tuesday 12th July – Wednesday 13th July, Etc. Venues Marble Arch, Garfield House, London

Day 1: Tuesday 12th July, 2016

Time	Topic	Facilitator/Speaker
08:45	Opening Remarks	Timothy Hallett
Session 1: The Representation of Sexual Behaviour and Behaviour Change Interventions in the Model Chairs: Keith O'Reilly, Michael Sweat and Timothy Hallett		
09:00	Overview of Session 1	Kevin O'Reilly Michael Sweat
09:30	**Evidence Project Presentation:** • Who we are (systematic reviews, HIV interventions, LMICs) • Key Issues - behavioural data in our syntheses – timing, targeting, duration, coverage, sequencing, and cumulative impacts	Kevin O'Reilly Michael Sweat
10:00	**How is behavioural data incorporated into the model structure, parameters, data sources and analysis?** All modellers/modelling groups are invited to present details of their model (10 minutes for each group, 5 minutes for discussion)	All Modellers
10:30	*Break*	
10:45	**How is behavioural data incorporated into the model structure, parameters, data sources and analysis? (continued)**	All Modellers
11:30	Group Discussion	All
12:00	*Lunch*	
13:00	**Discussion I: Model structure** • Agent-based vs. compartmental models • Risk groups What is the "behavioural" component of a model?	Kevin O'Reilly Michael Sweat Timothy Hallett
14:00	**Discussion II: Parameters and data sources** • Data on behavioural parameters (epi) vs. behavioural interventions (impact) • What data exist/how do you get data • Specificity and heterogeneity • Need for synthetic databases/new data collection	Kevin O'Reilly Michael Sweat Timothy Hallett
14:30	*Break*	

15:00	**Discussion III: Analysis** • Cumulative effects of interventions • Combinations of interventions Optimization	Kevin O'Reilly Michael Sweat Timothy Hallett
15:30	Group Discussion	
16:00	Next Steps, Key Outcomes and Recommendations	Keith O'Reilly Michael Sweat
17:00	*Close of Day 1*	

Day 2: Wednesday 13th July

Time	**Topic**	**Facilitator/Speaker**
08:45	Malawi Workshop Update: Exploring the use and value of modelling in health economics in guiding programme decisions in Malawi	Paul Revill
Session 2: The Representation of Antiretroviral Therapy (ART) and Cascade Interventions in the Model **Chair: Josh Salomon**		
09:00	Overview of Session 2	Joshua Salomon
09:15	**Modellers, Part I: How do models capture ART and cascade?** All modelling groups are invited to describe the following (5 minutes for each group, 5 minutes for discussion): • The structure and parameterization of the model regarding the representation of ART effects on transitions between health states outcomes. • Additional model structure and parameterization to capture transitions through the cascade (i.e. does the model distinguish between unknown and known infection status, linked vs. unlinked to care, etc.) What are the main sources of evidence to support these modelling choices?	All Modellers
10:15	Group Discussion	All
10:45	*Break*	
11:00	**Modellers, Part II: How do models capture interventions along the cascade, including aspects of scale up and implementation?** All modelling groups are invited to describe the following (5 minutes for each group, 5 minutes for discussion): Are interventions explicitly captured through model structure and/or parameterization? • Which types of interventions can be accommodated? • What are the main sources of evidence to support the modelling choices?	All Modellers

11:30	**Group Discussion** • Available data on cascade intervention effects • Data on coverage levels across countries • How do/should models handle contextual factors that mediate intervention effects (e.g. health system capacity, quality, etc.) • Priorities for methods advances • Priorities for data collection / collation	All
13:00	*Lunch*	
Session 3: The Representation of Epidemiological Parameters in the Model **Chair: Andrew Phillips**		
14:00	Overview of Session 3	Andrew Phillips
14:15	Summary of what we know about HIV transmission per contact/ per partner effects of ART, gender of HIV+ and HIV- partner, primary infection, concomitant STIs, circumcision, other co-factors	Marie-Claude Boily
14:45	**How is HIV transmission and factors modifying this incorporated into the model structure, parameters, data sources and analysis?** All modellers/modelling groups are invited to present details of their model (5 minutes for each group, 5 minutes for discussion)	All Modellers
15:45	*Break*	
16:00	**Group discussion** • Pros and cons of the different approaches to model transmission. What are our concerns and recommendations for improvements? • Allowing transmission parameter values to vary as part of calibration process • Primary HIV infection: whether we think transmission during primary infection is adequately captured for most prevention questions (not only ART as prevention) - what predictions can/do the models make about the proportion of new infections arising from a person in primary infection? (5 minutes) What further data are needed? • Is there a role for a model comparison in order to really understand whether different models are drawing importantly different conclusions? – if so, what should it look like • Recommended ranges for the key parameter values (transmission per act, primary stage, STI, etc.)	All Steve Bellan
17:00	***Meeting Close***	

Models for Programme Planning
Reference Group Meeting
Tuesday 12th July – Wednesday 13th July, London UK

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(Continues on next page)

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