Understanding the modes of transmission model of new HIV infection and its use in prevention planning

Kelsey K Case, Peter D Ghys, Eleanor Gouws, Jeffrey W Eaton, Annick Borquez, John Stover, Paloma Cuchi, Laith J Abu-Raddad, Geoffrey P Garnett & Timothy B Hallett on behalf of the HIV Modelling Consortium

Abstract The modes of transmission model has been widely used to help decision-makers target measures for preventing human immunodeficiency virus (HIV) infection. The model estimates the number of new HIV infections that will be acquired over the ensuing year by individuals in identified risk groups in a given population using data on the size of the groups, the aggregate risk behaviour in each group, the current prevalence of HIV infection among the sexual or injecting drug partners of individuals in each group, and the probability of HIV transmission associated with different risk behaviours. The strength of the model is its simplicity, which enables data from a variety of sources to be synthesized, resulting in better characterization of HIV epidemics in some settings. However, concerns have been raised about the assumptions underlying the model structure, about limitations in the data available for deriving input parameters and about interpretation and communication of the model results. The aim of this review was to improve the use of the model by reassessing its paradigm, structure and data requirements. We identified key questions to be asked when conducting an analysis and when interpreting the model results and make recommendations for strengthening the model’s application in the future.

Introduction

In the current global financial climate, it is more important than ever that effective resource allocation for the control of human immunodeficiency virus (HIV) infection is based on informed, strategic decision-making. Planning HIV prevention programmes requires up-to-date information on the likely sources of new infections and mathematical modelling provides a framework for understanding epidemic patterns and for highlighting priority areas for prevention. Various models of HIV epidemics, in particular the modes of transmission (MOT) model recommended by the Joint United Nations Programme on HIV/AIDS (UNAIDS), are used to increase understanding and to assist national planning.

When constructing a model, it is important to include adequate detail to address the questions posed. Superfluous detail reduces the transparency of the model and can make it more difficult to estimate model parameters reliably, whereas excluding important details can lead to erroneous conclusions. The MOT model was developed in 2002 and was designed to focus on identifying who is at risk of infection rather than on the broad categorization of the type of epidemic (i.e. low-level, concentrated, generalized or hyperendemic). Its aim was to provide better information for strategic planning of disease prevention.

Unlike models that are region-specific (e.g. the Asian Epidemic Model) or country-specific (e.g. the Actuarial Society of South Africa model, used primarily in South Africa but also in other countries in southern Africa), the MOT model was designed to be easy to use and can be applied in any epidemic setting. It differs from other approaches, such as the Estimation and Projection Package curve-fitting approach embedded within the Spectrum modelling software, which estimates and projects HIV prevalence and incidence from surveillance data and does not aim to take mechanisms of infection into account.

Use of the MOT model at the country level was recommended in 2008 as part of a synthesis process supported by UNAIDS and the World Bank Global HIV/AIDS Monitoring and Evaluation Team in southern and eastern Africa consistent with the UNAIDS “know your epidemic, know your response” strategy. This approach emphasizes the importance of understanding, at the local level, which subpopulations are most at risk of HIV infection and which risk behaviours may facilitate transmission and of using this information to tailor national responses.

When evaluating the performance of a model that is widely used to assist countries in decision-making, it is important to consider the perspective and experience of individuals involved in the modelling process, including those involved in developing and implementing the model, those who rely on the model results for decision-making and the normative agencies that help support the modelling process. In April 2011, the HIV Modelling Consortium (participants are listed in the acknowledgements section) gathered together stakeholders involved in different stages of the modelling process to review both the methods used for estimating sources of HIV infection and the MOT process. The impetus for this manuscript originated from discussions at this meeting; one outcome of the meeting was a manuscript that described the strengths and limitations of the MOT process.

Our intention was to strengthen future use of the MOT model by reviewing its principle features in detail and by summarizing feedback from previous applications. Specifically, we

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aimed to clarify the model paradigm, to review the model structure and data requirements and to propose questions that can be used to guide interpretation of the model results.

**Modes of transmission model**

The MOT model uses information on the current distribution of prevalent infections in a population and assumptions about patterns of risk behaviour within different risk groups to calculate the expected distribution of new adult HIV infections in the following year in terms of the mode of exposure. The inputs to the model, which are based on a comprehensive review of available epidemiological and behavioural information, are:

- the proportion of the adult male and female population that belongs to each of several risk groups, which are precisely defined by each country, including: sex workers and their clients, injecting drug users, men who have sex with men, individuals with multiple heterosexual sex partners in the last year, the spouses of individuals with higher-risk behaviour and individuals in stable heterosexual relationships (i.e. generally married or cohabiting couples with one monogamous heterosexual partner in the last year; these individuals were previously referred to as “low risk”);
- the prevalence of HIV infection and of a generic sexually transmitted infection (STI) within each risk group;
- the average number of sexual or injecting partners per year and the average number of exposures per partner, taking into account the average level of protective behaviour (e.g. condom use or the use of clean needles), for individuals in each risk group;
- the probability of HIV transmission per exposure act in each risk group, taking into account the effect of STIs and the prevalence of male circumcision.

The model estimates the number of new adult HIV infections that will occur over the ensuing year in each risk group from the number of HIV-susceptible individuals, the number of contacts each had with HIV-positive individuals and the probability of HIV transmission associated with each type of contact. Taken together, this provides an estimate of the distribution of new infections in adults according to the population risk structure defined by each country.

By the end of 2012, over 40 countries with a diverse range of HIV epidemics will have completed or begun an MOT analysis (Table 1, available at: http://www.who.int/bulletin/vol90/11-102574). The results of model analyses conducted in sub-Saharan Africa (Fig. 1) show that the majority of new infections were expected to occur in the general heterosexual population, either in serodiscordant couples or as a result of having multiple sexual partners. Although there is substantial uncertainty, the estimated proportion of new infections that occur in men who have sex with men and in injecting drug users in many countries in this region is larger than acknowledged before the advent of the MOT framework.

**Benefits**

The MOT analysis forms part of a multi-stage process that typically includes: (i) a comprehensive review and synthesis of epidemiological and behavioural data; (ii) use of the MOT model to estimate the distribution of new infections; (iii) a review of existing or proposed HIV prevention planning and resource allocation for treatment and prevention; (iv) a comparison of resource allocation and the modelled distribution of sources of infection, and (v) a national stakeholder consensus meeting to discuss the model results and formulate key recommendations. This process provides a framework for countries to interpret and evaluate their data, to assess data availability and quality, and to identify gaps in data collection. It can help consolidate knowledge of the current situation, but can also expose gaps in information about specific risk behaviours. In addi-
tion, the model results could be used to raise awareness for groups that may not previously have received enough attention, to highlight areas for improvement in prevention and to identify areas for further research. Although the concept of the MOT analysis has gained broad support, important questions have been raised about the simplicity of the model, its use of data and how the results are interpreted.

Limitations

The limitations of the MOT model and its assumptions can be divided into three categories relating to the model structure, the data used in the model and the interpretation of the results.

Model structure

The MOT model is a static model representing risk in a single year. It has a simple structure that does not incorporate many of the complexities of HIV epidemiology. It assumes that the populations in each risk group are mutually exclusive and that the risk of infection is homogenous within each group. This means, for example, that all men who have sex with men are assumed to have the same risk of infection. Moreover, the assumption of homogeneity would not capture details such as the clients of sex workers only visiting a particular type of sex worker or an injecting drug user sharing injecting equipment only within a specific cluster. These factors could influence the model results if there are important differences among those classified as belonging to the same risk group. However, the model offers the flexibility to disaggregate a subpopulation if there is enough evidence of heterogeneity in risk and sufficient data are available to characterize the different subgroups within a subpopulation, but generally suitable data are not available.

In the model, individuals must be assigned to a single risk group and are, consequently, assumed to be at risk of infection from only one source. Those at risk of infection from more than one source are classified according to the behaviour associated with the highest probability of HIV transmission. For example, a sex worker who also injects drugs is classified as an injecting drug user. This assumption implies that eliminating that source of risk will avert infection. An analysis that looked at the effect of modifying the model structure to allow for an individual’s risk of infection from more than one source found that assuming a single source could result in overestimating the potential impact of interventions targeting that source. Conversely, the effect of interventions targeting a less risky behaviour could be underestimated if the size of the risk group is underestimated because that behaviour ranks lower in the hierarchy of risk. For example, the model assumes that sex workers who are also injecting drug users and who would be classified as such would not benefit from a successful intervention among sex workers.

The probabilities of HIV transmission for different exposure acts and the parameter used to modify these probabilities when an STI is present are derived from published data, systematic reviews and meta-analyses of observational studies. While these sources represent the best available evidence, they may not capture potential variability of transmission in different geographical settings. Additionally, it is assumed that there is no variation in transmission probability by stage of HIV infection and the model does not allow for modification of the risk of HIV transmission arising from onward transmission within that year. Further, the MOT model assumes that the population is closed and defined by country borders and a defined age range. The estimates obtained are for new HIV infections that arise within a country and do not account for exogenous HIV exposures, which may contribute to a considerable fraction of HIV infections in some countries, in the Middle East and northern Africa, for example. As epidemiology matures, the contribution of older adults, outside the age range of 15 to 49 years that is typically used in the MOT model, to new HIV transmissions may increase. The model can be adapted to incorporate older age groups if data are available.

Data inputs

The MOT model requires detailed, up-to-date information on the size of risk groups and on the prevalence of HIV infection and of other STIs and precise descriptions of sexual behaviour in each risk group. Often this exceeds the data available, particularly when describing hidden or stigmatized populations, but also when describing the general population in countries where national survey data are not available. Standard survey instruments do not collect specific information on the detailed inputs required by the MOT model and most other models, including the average number of sex acts per partnership, injecting behaviour and the prevalence of HIV and STI in each risk group. It is unlikely that all the information needed to characterize a specific group can be obtained from a single study. Instead, estimates are often based on data from several sources that were collected at different times within a prespecified period, typically 5 years, using different study designs.

The quality of the model results depends on the quality of the input data and the MOT model is highly sensitive to the size of subpopulations and to behaviour within risk groups. Although guidelines exist for estimating population size, the methods used are often complex and of uncertain precision, particularly for hidden or hard-to-reach populations such as men who have sex with men in Africa. Consistently defining the risk of HIV infection is not straightforward in certain populations, for example, women who occasionally sell sex in informal settings but do not self-identify as sex workers. These factors contribute to the use of different estimation methods, producing substantially varying population size estimates which could affect the model results.

The patterns of risk behaviour ascribed to high-risk groups may be subject to bias in self-reported mea-
sures of behaviour. National household surveys, such as the Demographic and Health Survey, are often used as a source for sensitive information on, for example, individuals who engage in casual heterosexual sex or the clients of sex workers. Increasing evidence suggests that higher-risk behaviour may be substantially underreported in these surveys.32–34 Other sources of HIV prevalence and behavioural data for hard-to-reach, hidden or stigmatized populations may not be representative. Such data generally come from surveillance or behavioural studies in capital cities or urban centres (often via convenience samples) and may be difficult to extrapolate to national-level estimates.

Nevertheless, it is important to recognize that the MOT model requires fewer data than many dynamic models, which have the same data limitations, but still aims to capture the mechanisms of infection.

Interpreting and communicating results

The major misunderstanding of the model results comes from a misapprehension of the question addressed by the model analysis. The model calculates the estimated distribution of new infections in 1 year; it does not take into account the number of secondary infections that will result from new infections in a risk group. It is important to distinguish between identifying among whom new infections are predicted to occur in the short term, which the model does, and the types of risk behaviour that sustain the epidemic (i.e., the epidemic drivers).31 For example, although a large proportion of new HIV infections may occur among individuals in serodiscordant, stable, monogamous partnerships, the index HIV-positive partners in these couples may have previously acquired the infection through higher-risk behaviour, such as commercial sex. Currently, both partners would be classified as part of the low-risk population, but the essential driver of HIV transmission between the partners is previous sexual contact within commercial sex networks. This is an important distinction, particularly when the model results are used for planning prevention programmes, which may then underallocate resources for prevention in commercial sex settings. Allocating resources for prevention to match the predicted distribution of new infections identified in the MOT analysis implicitly focuses prevention efforts on reducing the risk of acquisition among susceptible individuals. However, in some cases, it may be more effective or efficient to target prevention efforts towards the individuals who contribute most to onward transmission.31

One difficulty with the communication of the results of the MOT model is that concise pie or bar charts (Fig. 1) do not represent uncertainties in input data, which can be substantial. Users of the MOT model can conduct a simple uncertainty analysis based on specifying plausible ranges for key input variables. Then, a large number of parameter combinations from the specified plausibility bounds are independently and uniformly sampled and outputs are calculated for each combination of parameters. During this process, the prevalence of HIV infection in the total population is maintained by adjusting the size of the low-risk group and the prevalence in that group. While this method gives some notion of how uncertainty in input data could affect the model outputs, it does not take into account systematic bias or correlated errors between model inputs. The results can also vary substantially depending on the plausible ranges specified by the user and the use of plausibility ranges for model parameter values does not take account of the intrinsic uncertainty caused by the simplified model structure. In addition, use of the low-risk group as a “catch-all” for maintaining internal consistency neglects the fact that countries with good surveillance of HIV infection in the general population may have more robust data on the low-risk group than on less surveyed, high-risk groups.

Nevertheless, even simple demonstration of how uncertainties in certain model inputs translate into uncertainties in outputs is helpful. Representation of uncertainty is a strength and an important consideration in decision-making. If recommendations do not change when uncertainty is taken into account, decision-makers can have more confidence in the use of the model results. However, if the implications are more ambiguous, decisions about resource allocation based on the model results should reflect this and priority should be given to improving knowledge about parameters that contribute most to uncertainty. Box 1 lists questions that should be considered when conducting an MOT analysis and interpreting the model results. Responses to these questions can help in forming a cautious, nuanced analysis of the model results that will ultimately strengthen its contribution to decision-making.

The way forward

Mathematical modelling can be used to inform health policy and focus decision-making on key issues, for example, in the design and allocation of resources for HIV prevention programmes. However, translating model outputs into policy decisions should be done carefully and within the local context. In addi-
tion, the results need to be interpreted considering the underlying structure of the model, the sensitivity of outputs to variations in model parameters and the potential deficiencies in data quality or availability. Recently, UNAIDS developed a toolkit to help countries assess the availability, completeness and quality of the epidemiological data before application of the MOT model.

Box 2 contains a list of recommendations for improving the use of the MOT model. Viewing the modelling exercise as a process rather than an endpoint and using it as a tool to identify key data needs and to understand which aspects of the data or the model structure affect results will ensure more constructive use of the model. This will enable those advising policy-makers on the basis of modelling to help distinguish between decisions that can be recommended robustly and decisions on which the model is unable to provide clear guidance. A way to increase confidence in the model findings is to test whether the model can be corroborated with other independent data or epidemiological information.

One strength of the MOT model is that it has been designed to acknowledge and evaluate potential sources of infection in a range of settings. In some countries with particularly strong epidemiological surveillance, country-specific models or modified versions of the MOT that expand the model structure to disaggregate subpopulations and incorporate multiple sources of risk may offer a better balance between model complexity and data availability and provide more actionable information, but will require additional effort, expense and time to develop.

Looking at new infections over 1 year may not highlight the underlying factors that drive an epidemic and, if the contribution of high-risk groups to the epidemic is underestimated in static, short-term modelling, then a portfolio of interventions based on these results may be sub-optimal for long-term control.24 Comparing the short-term predictions of the MOT model with dynamic transmission models could suggest how decision-making may have differed if it was based on determinants of long-term epidemic spread. One such comparison, in two distinct epidemics, illustrated how the MOT model can overestimate the contribution of low-risk groups and underestimate the contribution of commercial sex, thereby underestimating the longer-term preventive potential of targeted interventions for commercial sex workers.35

Moving forward, the current MOT process can be strengthened by better understanding of the limitations of the model and the data, by some modifications to the model structure and assumptions, and by careful and considered interpretation and application of its results.

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Resumen

Entender el modelo de los modos de transmisión de las infecciones nuevas por VIH y su uso en los planes de prevención

El modelo de los modos de transmisión se ha empleado de manera generalizada para ayudar a los responsables de la toma de decisiones a dirigir las medidas para la prevención de la infección por el virus de la inmunodeficiencia humana (VIH). El modelo calcula el número de infecciones por VIH nuevas adquiridas durante el año subsiguiente por individuos en grupos de riesgo identificados en una población dada empleando datos acerca del tamaño de los grupos, el comportamiento de riesgo conjunto en cada grupo, la prevalencia actual de la infección por VIH entre las parejas sexuales o personas que comparten jeringuillas para el consumo de drogas de los individuos de cada grupo y la probabilidad de transmisión del VIH asociada a los diferentes comportamientos de riesgo. El punto fuente del modelo es su sencillez, que permite sintetizar datos de fuentes variadas, de lo que resulta una caracterización más exacta de la epidemia del VIH en algunos entornos. No obstante, han surgido dudas acerca de las suposiciones que subyacen a la estructura del modelo, las limitaciones de los datos disponibles para derivar de ellos parámetros de entrada y la interpretación y comunicación de los resultados del modelo. El objeto de este examen fue el de mejorar el uso del modelo volviendo a examinar su paradigma, su estructura y los requisitos de los datos. Identificamos los puntos clave que deben cuestionarse durante la realización de un análisis y la interpretación de los resultados del modelo y formulamos recomendaciones para consolidar la aplicación del modelo en el futuro.

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Table 1. Countries using the modes of transmission model to estimate the source of new HIV infections, by region, 2005–2013

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<tr>
<th>Region and country</th>
<th>Year model analysis completed</th>
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HIV, human immunodeficiency virus.