The future of the HIV pandemic

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Abstract The emerging HIV epidemics in countries of Asia and Eastern Europe will contribute significantly to the future of the HIV pandemic. Forecasts of the scale of these epidemics are subject to massive uncertainty, however, mainly because of the sensitivity of predictions to small alterations in parameters that are difficult to estimate. In most of these countries, HIV is currently concentrated among vulnerable populations such as injecting drug users, sex workers and their clients, or men who have sex with men. This distribution suggests an alternative to disease forecasting based on the techniques of risk assessment routinely used by environmental epidemiologists. Exposure mapping, dose–response curves and the concept of acceptable risk are some of the tools that may be useful for HIV risk management. This approach is illustrated by a description of exposure in Indonesia and an assessment of currently accepted risk of death for different causes including HIV in the Russian Federation. Although inappropriate for forecasts of heterosexual HIV transmission, mathematical models are shown to be useful for making qualitative predictions about the relative importance of different behaviours for the spread of HIV over time and for interpreting observed trends in HIV prevalence from sentinel surveillance sites.

Keywords HIV infections/epidemiology; Disease outbreaks; Forecasting; Risk assessment/methods; Models, Theoretical (*source: MeSH, NLM*).

Mots clés Infection à VIH/épidémiologie; Epidémie; Prévision; Evaluation risque/méthodes; Modèle théorique (*source: MeSH, INSERM*).

Palabras clave Infecciones por VIH/epidemiología; Brotes de enfermedades; Predicción; Medición de riesgo/métodos; Modelos teóricos (*fuente: DeCS, BIREME*).

Arabic

Bulletin of the World Health Organization 2005;83:378-383.

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The “next wave”?

Recent predictions of a catastrophic “next wave” of the HIV pandemic in the populous countries of Asia and Eastern Europe (*1*, *2*) are a cause of controversy within international development agencies and have been condemned by some of the national governments concerned (*3*). The predictions suggest that prevalent HIV infections in China, India and the Russian Federation alone could reach between 35 million and 68 million in 2010, compared with the current global total of 38 million estimated by the Joint United Nations Programme on HIV/AIDS (UNAIDS) and WHO (*4*). Undoubtedly the drug-using and sexual behaviours that transmit HIV are increasing in these countries (*5*), and numbers of newly diagnosed HIV infections have surged in recent years (*4*). However, next-wave scenarios are contingent on a generalized heterosexual spread occurring on a scale similar to that seen in sub-Saharan Africa. Is this possible?

While many studies have shown the correlation between an individual’s sexual behaviour and infection with HIV, there is little evidence for population-level measures that can explain differences in adult HIV prevalence (*6–8*). This lies at the heart of the difficulty in forecasting the scale of heterosexual HIV epidemics, because no measures of sexual behaviour in the population have been identified as accurate predictors of the size of an epidemic. Current forecasts therefore have to rely on scenarios proposed by experts using Delphi or similar techniques or on mathematical models. Models that attempt to forecast the size of a heterosexual HIV epidemic tend to be based either on fitting epidemic curves to available prevalence data and extrapolating (*9*) or on mathematical descriptions of sexual behaviour and the associated transmission of HIV (*10*). There is a massive level of uncertainty in such forecasts (*5*). Thus, while next-wave scenarios can be deemed unlikely or derived through applying a worst-case scenario systematically (*11*), they can only ever be disproved after the event. It is the role of UNAIDS, WHO and the scientific community to make clear what can and cannot be said about the future of the HIV pandemic. If accurate forecasts are so problematic, is there an alternative approach that can be adopted?

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Ref. No. **04-011684**
(*Submitted: 19 January 2004 – Final revised version received: 21 May 2004 – Accepted: 24 May 2004*)

Distinct epidemics

In most countries of Asia and Eastern Europe, in contrast to sub-Saharan Africa, HIV currently remains concentrated within identifiable vulnerable populations such as injecting drug users and their sex partners, men who have sex with men, and sex workers and their clients. In many of these countries it has been possible to estimate the size of these populations, using data from surveys and censuses or indirect estimates based on multiplier or capture–recapture techniques (*12*). HIV prevalence estimates from sentinel surveillance sites among these populations can then be multiplied by population size to estimate the number of people infected with HIV. UNAIDS and WHO have developed software and held training workshops worldwide to assist national AIDS programme staff and others in the implementation of this approach (*13*) (see Table 1 for an example from Indonesia).

Once HIV reaches vulnerable populations where condom use is inconsistent or needle sharing is common, epidemics are usually inevitable (*14*). Ignoring the possibility of heterosexual HIV transmission in the wider adult population, it is possible to explore the effect of different assumptions about the peak prevalence and timing of HIV epidemics among vulnerable populations on future epidemic size. Assumed peak prevalence levels can be informed by comparison with long exposed populations from the same or neighbouring countries. Using this approach, it has been estimated that the epidemics in Eastern Europe and Asia are likely to add about 21 million infections to the HIV pandemic by 2010 if there is not a rapid and expanded response (*15*). Thus, even without a generalized heterosexual epidemic, the need for action is clear.

Risk assessment

The concentrated nature of the HIV epidemics in most Asian and Eastern European countries suggests the utility of a novel approach to the management of HIV in these countries. The techniques of risk assessment, routinely used by environmental epidemiologists, can be used to map exposure to HIV. Behavioural surveillance can identify the high risk behaviours that transmit HIV and can be used to map the distribution of vulnerable populations within a country (*16*). The need for mapping emerges from the heterogeneous distribution of risk behaviours and hence HIV within countries. For example, in India, injecting drug use is concentrated in the north-east of the country and in urban centres such as Chennai, Delhi and Mumbai, where HIV transmission associated with needle sharing has led to significant epidemics of HIV (*17*, *18*). These maps may be supplemented by surveillance of HIV-related knowledge and of biological markers of risk, such as the sexually transmitted infections that facilitate HIV transmission (e.g. herpes simplex virus type-2), or bloodborne infections such as hepatitis C. Procedures for the estimation of the size of the vulnerable populations can then define the magnitude of exposure to HIV by the different transmission routes in different parts of the country (*12*).

A key step in risk assessment is to identify what is an acceptable risk. In the United Kingdom, for example, the Health and Safety Executive considers a one-in-a-million excess risk of death per year from environmental pollutants as the level of acceptable risk at which no further improvement in safety needs to be made (*19*). It is often illuminating to compare policy on acceptable risk with currently accepted risk revealed in morbidity and mortality statistics. For example, using estimates of cause-specific death rates (*20*) and HIV case reports (*21*), it is possible to estimate the average time it takes a 15–24-year-old living in the Russian Federation to acquire a one-in-a-million chance of death from specific causes (Table 2). The accepted risk of death from AIDS revealed by these statistics should highlight the need for HIV prevention strategies to bring the accepted risk in line with what is considered acceptable. In reality, this average masks a great deal of heterogeneity in risk. Moral judgements tend to be made about the culpability of those becoming infected with HIV, and the concept of acceptable risk for these people implicitly revised.

Effective surveillance of vulnerable populations identifies prevalent HIV infections. However, the incidence of new HIV infections can show a markedly different pattern. For example, in 2002 in Indonesia, although prevalent infections were equally distributed between injecting drug users, and sex workers and their clients (Table 1), the majority of incident infections were among injecting drug users (*22*). Patterns of incidence for a given year can be crudely estimated from simple measures of risk behaviour without the need for a complex dynamic model. For example, the average number of visits to different sex workers reported by male clients (e.g. x per year), together with the probability of HIV transmission per sex worker visited (P), and HIV prevalence among sex workers (y), can give an estimate of the expected number of new infections among clients that year $\approx N - N(1-Py)^x$, where N is the number of clients. Simple estimates of expected incidence based on similar

Table 1. **Estimates of the size and HIV prevalence of selected vulnerable populations in Indonesia, 2002**

Vulnerable population	Population size (range)		HIV prevalence (range) %		No. infected with HIV/AIDS (range[a])	
Injecting drug users (IDUs)	160 000	(124 000–196 000)	27.0	(19.2–34.4)	42 700	(27 300–58 200)
Non-IDU sex partners of IDUs	121 000	(94 000–149 000)	9.0	(6.4–11.5)	10 800	(6 900–14 700)
Sex workers	233 000	(193 000–273 000)	4.0	(2.0–5.2)	8 400	(4 400–12 400)
Clients of sex workers	8 222 000	(6 859 000–9 585 000)	0.4	(0.2–0.6)	32 900	(15 600–50 200)
Prisoners	74 000	(74 000–74 000)	12.0	(8.6–15.4)	8 800	(6 400–11 300)
Men who have sex with men	1 150 000	(575 000–1 725 000)	1.0	(0.4–1.3)	10 000	(2 600–17 400)
Total[b]					**113 700**	**(88 600–138 800)**

Source: adapted from *33*.
[a] Calculated using the delta method assuming all estimates are independent of one another.
[b] Excludes some vulnerable populations.

Table 2. **Length of time necessary to accumulate a 1:1 000 000 chance of death from selected causes for a person aged 15–24 years living in the Russian Federation**

Cause	Time
AIDS[a]	1.6–6.4 hours
Motor vehicle accident[b]	1.4 days
Homicide	1.9 days
AIDS (sexual transmission)[a, c]	2.5–9.9 days
Accidental poisoning other than by alcohol	2.8 days
Accidental drowning	3.3 days
Accidental poisoning by alcohol	11.6 days
Accidental fall	16.2 days

[a] Lower confidence bounds based on HIV case reports in 2001 adjusted for underreporting using a multiplier of 4 from UNAIDS prevalence estimates, and upper bounds based on unadjusted case reports. Death is assumed to occur on average 10 years after first diagnosis, with future health outcomes discounted at 5%.

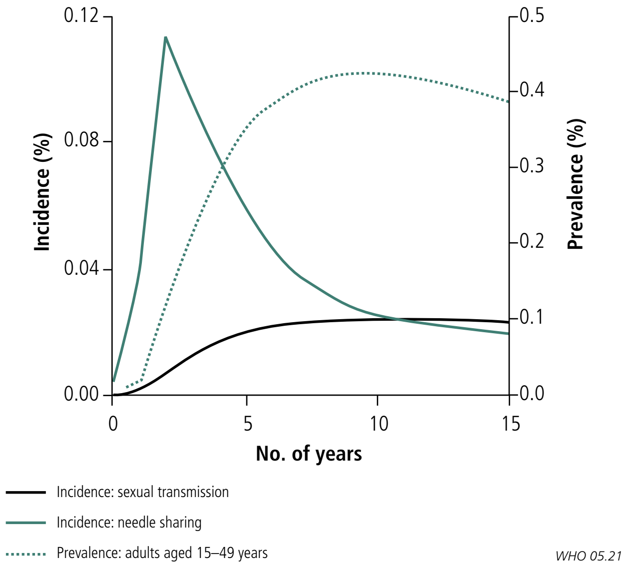
[b] Data for causes other than AIDS are based on age-standardized mortality rates for 1998.

[c] Sexual transmission confirmed. This may underestimate actual levels of sexual transmission.

calculations for different vulnerable groups can act as a useful guide for HIV prevention (*22*). Interventions that focus on HIV prevention among vulnerable populations have been found in the past to be both effective and cost-effective, even where HIV transmission has become more generalized (*23*, *24*).

The relationship between simple measures of risk behaviour and HIV incidence is analogous to the dose–response relationship central to the assessment of health risks in environmental epidemiology. Dose–response relationships need to account for the timing of health outcomes, and this is especially important for infectious diseases with long incubation and infectious periods. The relationship is simplified by focusing on HIV status rather than on health outcomes, and it is possible that measures of risk at the population level can be linked to HIV prevalence some years later. For vulnerable populations the relationship may be reasonably well defined, since high prevalence of unsafe behaviour such as needle sharing typically results in rapid HIV transmission and an epidemic that saturates at high prevalence. Of course, policy-makers are also (and often solely) concerned with risk of HIV to the wider adult population. In sub-Saharan Africa there is evidence, albeit limited, that living in a community with a certain risk profile — economically active, mobile population, many female bar workers, close to a large town — increases an individual's risk of infection over and above his or her own sexual behaviour (*8*). In Asia and Eastern Europe, although analogous research has not been carried out, models suggest that adults living where injecting drug use and sex work are common are at a higher risk of infection irrespective of their own sexual behaviour (*5*). Thus, risk in the general population is likely to be correlated with risk in other groups as well as with patterns of sexual behaviour. Epidemiological theory suggests a threshold relationship, such that below a certain level of sexual activity in the population the risk may be minimal (*25*). This contrasts with linear relationships seen, for example, between risks of ischaemic heart disease and blood pressure, cholesterol or obesity (*26*). As noted earlier, however, this relationship is not well understood, and therefore dose–response curves for the general adult population will be poorly defined. Furthermore, as the time frame expands, the problems inherent in forecasts of HIV prevalence will return. What role, then, can be played by transmission dynamic models?

Fig. 1. **Results of a deterministic model that show a high incidence of HIV attributable to sexual transmission compared with needle sharing, even for an epidemic that remains largely concentrated among injecting drug users (adult prevalence remains below 0.5%).** The model and parameter estimates are based on surveys in urban areas of the Russian Federation where 1% of the adult population (15–49 years of age) is thought to inject drugs (*5*). The parameter for the mean rate of sexual partner change in the adult population was chosen to ensure heterosexual HIV transmission in the adult population remains low



The role of dynamic models

Mathematical models of HIV transmission are useful for exploring the relationship between risk behaviour — including that of vulnerable populations such as sex workers — and risk of infection in the wider population. Many models have been published illustrating the importance, for instance, of numbers of sex partners, rates of needle sharing, transmission probabilities, heterogeneities in their values and the mixing between different groups (*5*, *27*, *28*). The difficulty of accurately measuring these key variables means that such models are better suited to generating qualitative rather than quantitative predictions. Such qualitative predictions can be compared with observed surveillance data indicating whether gross changes in the epidemiology of HIV are under way. For example, following an epidemic of HIV among injecting drug users, a model based on behavioural data from urban areas of the Russian Federation predicts significant sexual transmission among drug users and also to others through both commercial and noncommercial sex (Fig. 1). Although models are unable to predict the final extent of this sexual transmission, they highlight the importance of preventing sexual transmission among injecting drug users as well as among their non-injecting partners.

Comparison of qualitative model predictions with sentinel surveillance HIV prevalence data and, where available, behavioural data makes clear where changes in patterns of exposure — and therefore prevention — must be occurring.

This can also highlight significant gaps in surveillance systems. For example, simple models of HIV transmission among sex workers or injecting drug users estimate significant HIV prevalence among individuals who have stopped sex work or injecting drug use and are therefore no longer considered vulnerable. In the case of female sex workers, their infections may be detected at antenatal clinic surveillance sites if they become pregnant, but men who cease injecting drug use will not be picked up by most surveillance systems and may represent an overlooked source of prevalent and incident HIV infections.

Mathematical models are also essential to estimating the likely impact of behavioural change resulting from interventions on the incidence of HIV. This may be particularly important when transferring a successful intervention from one location to another where the epidemiological context may differ (*29*). In the past, models of HIV transmission have been used to highlight the importance of good intervention coverage and the efficiency gained by targeting vulnerable populations (*30*). Ongoing behavioural surveillance as part of a risk assessment framework can help track trends in behaviour and identify effective and ineffective programmes. The integrated analysis of behavioural and biological surveillance data can provide a compelling argument for the success of national programmes (*31*).

Conclusion

The risk assessment approach described in this paper offers an alternative to scaremongering based on uncertain forecasts. *The world health report 2002* has advocated bringing risk assessment into the heart of decisions about the allocation of resources in reducing the global burden of disease (*32*). A focus on risk may also help an effective response to the ongoing HIV pandemic. ■

Competing interests: none declared.

Résumé

L'avenir de la pandémie de VIH

Les épidémies de VIH qui se développent dans les pays d'Asie et d'Europe de l'Est contribueront de manière importante à l'évolution future de la pandémie de VIH. Les prévisions concernant l'ampleur de ces épidémies comportent cependant d'immenses incertitudes, en raison principalement de la sensibilité des prédictions à de faibles variations de paramètres difficiles à estimer. Dans la plupart des pays, les cas de VIH se concentrent actuellement parmi les populations vulnérables telles que les toxicomanes par voie intraveineuse, les professionnels du sexe et leurs clients, ou encore parmi les hommes ayant des relations sexuelles avec d'autres hommes. Cette répartition incite à recourir à une autre solution que les prévisions concernant la maladie obtenues par les techniques d'évaluation des risques habituellement appliquées par les épidémiologistes de l'environnement. La cartographie des expositions, les courbes dose-réponse et le concept de risque acceptable sont quelques-uns des outils pouvant servir à la gestion du risque VIH. Cette démarche est illustrée par une description de l'exposition en Indonésie et par une évaluation du risque de décès actuellement admis pour différentes causes, y compris le VIH, dans la Fédération de Russie. Bien que les modèles mathématiques ne se prêtent pas aux prévisions concernant la transmission du VIH par voie hétérosexuelle, leur utilité a été démontrée dans la réalisation de prévisions qualitatives sur l'importance relative de différents comportements dans la propagation du VIH au cours du temps et dans l'interprétation des tendances observées pour la prévalence du VIH à partir des sites de surveillance sentinelles.

Resumen

El futuro de la pandemia de VIH

Las nuevas epidemias de VIH que se han declarado en países de Asia y Europa Oriental tendrán importantes repercusiones en el futuro de la pandemia de VIH. No obstante, las previsiones con respecto a la magnitud de estas epidemias son inciertas, sobre todo por su sensibilidad a pequeños cambios en parámetros que son difíciles de estimar. Actualmente, en la mayoría de estos países, el VIH se concentra en las poblaciones vulnerables, como los consumidores de drogas inyectables, los trabajadores sexuales y sus clientes, o los hombres que tienen relaciones homosexuales. Esta distribución sugiere una alternativa a las previsiones de la enfermedad basadas en las técnicas de evaluación de riesgos que utilizan habitualmente los epidemiólogos ambientales. El marco de la exposición, las curvas dosis-respuesta y el concepto de riesgo aceptable son algunos de los instrumentos que pueden ayudar a gestionar los riesgos de infección por VIH. Este enfoque se ilustra mediante una descripción de la exposición al virus en Indonesia y una evaluación del riesgo aceptable de muerte en la Federación de Rusia por distintas causas, entre ellas el VIH. Aunque son poco apropiados para realizar previsiones sobre la transmisión del VIH entre los heterosexuales, se ha demostrado que los modelos matemáticos sirven para hacer predicciones cualitativas sobre la importancia relativa de los distintos comportamientos en la propagación del virus a lo largo del tiempo, así como para interpretar las tendencias observadas en la prevalencia del VIH a partir de los lugares donde se lleva a cabo una vigilancia centinela.

Arabic

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Commentary

New approaches to effectively programming HIV/AIDS prevention resources

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In the above article, Grassly & Garnett propose the use of tools based on risk assessment techniques to explore the likely future course of the HIV epidemic in Asia and Eastern Europe. They argue that current approaches involving epidemiological modelling are less useful in emerging epidemics than in mature ones because the uncertainty in key model parameters can lead to huge variations in projections of future trends. As an alternative, the authors propose risk assessment approaches such as surveillance of high-risk behaviours, mapping the geographical distribution of high-risk behaviours, simple transmission models to identify the major sources of new infections, considerations of dose–response relationships to identify when key thresholds may be approached, and the use of dynamic models to indicate how research on the effectiveness of interventions in one location may be used to assess the likely effects in a different context.

These risk assessment approaches are actually not useful for quantitative forecasting, as the authors admit, since they are subject to many of the same limitations as other approaches when it comes to projecting into the future. These approaches can be very useful, however, in providing qualitative programme guidance, indicating where programmes should be focusing their efforts in order to reduce the chances of rapid expansion of the epidemic. The use of simple transmission models with surveillance data can show the source of most new infections: it might be injecting drug use in the Russian Federation, sex between men in Central America, commercial sex in South African mining communities, casual sex in Botswana, or sex between spouses in Uganda. Once the key sources of new infections are understood, programmes can focus efforts in those areas (*1*). Mapping the geographical distribution of high-risk behaviours can indicate the epidemic "hot spots" where intensive prevention efforts can be most effective (*2*). The use of dynamic models of intervention effects can indicate whether prevention successes elsewhere (such as the 100% condom use policy in brothels in Bangkok or the syndromic management of sexually transmitted infections in Mwanza) are likely to be similarly effective in other settings or not (*3*). The use of these simple tools can help programmes to plan how to allocate their resources most effectively in order to contain the epidemic and reduce the risk of concentrated epidemics becoming generalized in the future.

Most countries developed five-year HIV/AIDS strategic plans in or around 2000 at the urging of UNAIDS and major donors. These plans represented an advance from the previous practice of medium-term workplans. However, very few of them took advantage of all the information available to them to strategically focus their efforts where they would do the most good. Another round of strategic plans will be developed soon in many countries. Greater use of techniques such as those described in this paper could help to ensure that the expanded resources now available are used wisely and result in greater success against the HIV/AIDS epidemic than has been seen so far. ■

Competing interests: none declared.

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Ref. No. **04-016790**