An age- and sex-structured HIV epidemiological model: features and applications

D. Low-Beer¹ & R.L. Stoneburner²

An important challenge in modelling the human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS) epidemic is to use the increasing quantity of disease surveillance data to validate estimates and forecasts. Presented is a novel model for forecasting HIV incidence by age and sex and among sentinel groups for which data are available. This approach permits a closer relationship between forecasting and surveillance activities, and more accurate estimates validated to data. As inputs the model uses an estimate of the HIV prevalence, country demographic data, and a profile of the sexual risk of HIV infection by age, to project HIV incidence, prevalence, number of AIDS cases and population. The following examples of the use of the model are given: forecasting HIV incidence in East Africa, by age, sex, and among pregnant women; 3–5-year forecasts of HIV incidence; modelling mixed risk behaviour HIV epidemics in South-east Asia; demographic indicators; and targeting a preventive vaccine by age group.

Introduction

Increasingly human immunodeficiency virus (HIV) and acquired immunodeficiency syndrome (AIDS) surveillance data, by time, sex and age are becoming available. An important challenge is to develop methods to combine forecasting and surveillance activities to use such data effectively since this may improve the validity of projections and guide the way interventions are targeted.

Previous HIV models have used data ranging from a single HIV prevalence estimate to a wealth of biological and behavioural parameters (1–5). This article describes a novel model which uses simple empirical inputs to forecast the incidence and prevalence of HIV infection, number of AIDS cases and mortality, by age, sex and sentinel group. The model can be used to obtain an HIV infection curve, based on past and present data, which is then projected into the short-term future.

Studies have shown that age and sex structures are useful for evaluating HIV prevalence trends (6, 7), behavioural interventions (8), and for assessing demographic and economic impacts (9, 10). Such an approach also permits a closer link between model outputs and the analysis of disease surveillance data, by age, sex, and cohort.

Presented here are the data required, an overview of the model, and examples of its application.

Modelling and surveillance data

Generally a balance is required between the capabilities of a given model and the amount of data required as inputs. As is the case with the Epi Model developed by Chin & Lwanga (5), the present model emphasizes simple empirical inputs: it is therefore limited to short-term forecasts over 3–5 years.

Previously, the lack of HIV surveillance data meant that forecasts were produced with wide confidence bounds (11). As more surveillance data become available, however, forecasts can be more closely validated. The approach used in our model is to generate forecasts based on available data. The model includes also an age and sex structure, which permits closer validation to and evaluation of disease surveillance trends as they emerge, including the following:

- number of AIDS cases, by age, year, and birth cohort;
- HIV prevalence cross-sectional data, by age and sex; and
- sentinel surveillance trends in pregnant women, army entry cohorts, infants, and adults.

Materials and methods

Overview of basic inputs and structure of the model

HIV/AIDS models can be characterized broadly into two groups: dynamic models of biological and behav-
journal processes; and those which characterize and extrapolate disease data, as discussed below.

**Dynamic models.** Such models, which characterize the disease transmission process and mixing between those who are infectious (infected) and those at risk of infection (susceptible), require biological and behavioural inputs, the values for many of which are known imprecisely. Models of this type have provided mainly qualitative descriptions of HIV spread (1, 2, 10, 11); however, they are needed for modelling intervention of the transmission process and for longer-term projections.

**Estimation models.** Estimation models take no direct consideration of sexual mixing and HIV transmission. Rather, they characterize the HIV infection curve and/or incubation distribution and provide an estimate of the number of individuals in one or more disease states. Curve fitting, extrapolation, and back-calculation procedures have all been used (3–5). At some stage, extrapolation of past and present trends to the future is required. Forecasting is therefore limited to the short term.

The model described in this article is an estimation model, based on an HIV infection curve, by time and age, which is applied to a population structured by age, sex and subgroup. The HIV incidence by age is determined by the HIV curve, in relation to past infection in a given age group and replenishment as younger groups become older.

The HIV incidence by time and age is captured by cohort trends in AIDS/HIV prevalence or mortality, which can be compared with surveillance data (7, 12). The minimum data inputs in our model are an estimate of HIV prevalence, date of onset of infection, distribution of population by age, and sexually transmitted disease (STD) by age incidence (see Table 1). These inputs are derived as described below.

**Estimates of HIV prevalence and of date of epidemic onset.** These inputs are similar to those used in the Epi Model (5), and are used to define a gamma function HIV infection curve, by time and sector. As input, an estimate of HIV prevalence, as an adult total or incidence, is required for a specified year. The estimated HIV prevalences among pregnant women and some other sentinel groups can be used for this purpose since these are converted by the model into the value required.

The start of extensive spread of HIV is defined as an HIV prevalence of least 1% among sentinel groups; for example, STD clinic attendees. Lagged start times between subpopulations can be incorporated. For example, sector 1 (Table 1), which could refer to urban, rural, intravenous drug users, or homosexual subpopulations, has an epidemic onset in 1985, and an 11-year period of growth in HIV incidence. This defines the gamma function curve of HIV infection, which reaches a 5% prevalence in 1993.

**Demographic data.** The model requires data on population by age for any single year, obtained by survey or census. Data on fertility and mortality by age are also required, as well as the population growth rate. For this purpose either actual data from a country or default settings, for example, Coale–Demeney model life-tables, can be used (13, 14).

**Natural history data.** Annual progression rates from HIV infection to AIDS and death can be defined in a similar manner to the Epi Model, or using a median incubation period distributed according to a Weibull function (15, 16):

\[ A_{i+n} = I_i \cdot \exp\left[-yn^c\right] \]

where \( A_{i+n} \) is the incidence of AIDS from \( i \) infections \( n \) years later, and \( c \) and \( y \) are constants. Child progression rates from paediatric infection are set separately, with a median default value of 2 years. Otherwise, progression rates do not vary by age, but can be changed by subgroup.

**Age profile of risk of HIV infection.** This is the age distribution of HIV incidence in a fully susceptible population.
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population, defined by a surrogate for sexual risk of infection such as STD incidence by age. The age distribution can be defined from values for the youngest, peak, and oldest age of sexual risk of HIV infection \((a_1, a_2, a_3, \text{resp.})\), and the parameters \(m_1\) and \(m_2\), to fit a Pearson type 1 curve (17):

\[
S_\alpha = S_p \left[ 1 + \left( \frac{a_1 - a_2}{a_2 - a_1} \right) \right]^{-m_1} \times \left( 1 - \left( \frac{a_1 - a_2}{a_3 - a_1} \right) \right)^{-m_2}
\]

Independent values of \(m_1\) and \(m_2\) are used either side of the mode value, \(S_\alpha\), to fit accurately the up- and downslope of the curve to the data.

Structure of the model

As described above the model derives HIV incidence from a gamma function curve of HIV infection, the age profile, and the population defined in each age group and year. Subsequently, it models the natural history of HIV infection to AIDS and death, and provides background demographics on fertility, mortality, and aging. A more detailed description of the model is presented elsewhere (12), but its major features are given below.

Time dependency. A fundamental assumption in the Epi Model was that the cumulative HIV incidence followed an S-shaped curve, characteristic of a single-source epidemic with person-to-person transmission and homogeneous mixing (5, 18). Our model uses a gamma function curve, similar to the Epi Model:

\[
Y_\alpha = t^{(p-1)} e^{-t} / (p-1)!
\]

The value of \(p\) (default = 5) describes the steepness of the curve at time \(t\) since onset of extensive HIV spread. The gamma function curve of HIV infections provides a good empirical fit to reported AIDS cases in many countries (5). However, it is most effective in describing the epidemic growth phase until the HIV epidemic peaks. The long right-hand tail of the gamma function curve is less valid. In our model the gamma function curve is therefore used during the period of growth in HIV incidence, which is subsequently defined as stable or linearly increasing or decreasing. There are three further differences between our model and the Epi Model:

- In our model the curve is applied independently to up to six subgroups, hence the total HIV infections may not follow a gamma function.
- Infection rates are applied to a population whose size is changing over time.

- Younger cohorts age into the epidemic after onset, renewing the susceptibles as the HIV infection curve stabilizes.

Age dependency. Initially, in a susceptible population, HIV incidence is distributed according to the age profile of those at risk. This profile is then transformed, since a proportion of those at risk are already infected, and new individuals age into risk through demographic renewal. In our model the age dependency is calculated using the following expression:

\[
S_\alpha \cdot N_\alpha \left[ 1 - \left( \beta \sum_{x=a}^{t} I_{(\alpha-x)}(t-x) \right) \right]
\]

with the limits \(S_\alpha \geq \sum_{x=a}^{t} I_{(\alpha-x)}(t-x)\) and \(x < t; x < a\)

where \(S_\alpha\) is the risk rate at age \(a\), \(N_\alpha\) the population size, and \(I_{(\alpha-x)}(t-x)\) the cohort HIV incidence \(x\) years ago. The replacement rate of the risk population is given by \(\beta\), which can be thought of as the probability that individuals at risk were also at risk younger ages (0 \(\leq c \leq 1\)). The version of the model described in this article is for \(\beta = 0.95\); the population at risk is therefore saturated by previous infection, with little replacement. HIV incidence is not simply generated temporally and distributed by age according to \(S_\alpha\); rather it varies with population size, \(N_\alpha\), and past HIV incidence in the cohort concerned.

Demographic and paediatric infections. The model simulates fertility, non-AIDS and AIDS mortality, and aging, assuming stable age-specific fertility and non-AIDS mortality, by time. However, total new births and deaths can be defined at a stable, linearly increasing or decreasing rate. The HIV prevalence in newborn children is given by the following expression:

\[
Y_{\alpha t} = \sum_{a=0}^{\infty} f_a \cdot Y_{\alpha a} \left[ 1 - \epsilon \right]
\]

where \(\epsilon\) is the fraction of children born to HIV +ve mothers who remain uninfected, and \(f_a\) the age-specific fertility. The default mother-to-child transmission rate (1 - \(\epsilon\)) is 30%, but can be altered to reflect postulated differences by region (19).

Population subgroups. To forecast mixed risk-group epidemics and differences, for example, between rural and urban populations, the model permits up to six subgroups to be defined. Demographics, lags between the start of epidemics, prevalence estimates, and age profiles can be defined separately by subgroup. These are then combined in a global tem-
plate, which ensures internal consistency, e.g. that population subtotals sum up to the country population total. Both overall and group-specific outputs are permitted.

HIV Infection in sentinel surveillance groups. HIV and AIDS trends can also be obtained as outputs for simulated sentinel groups, for comparison with army entry cohort and antenatal clinic data. The prevalence of HIV infection in antenatal clinics, \( Y_{anc} \), is simulated as the product of age-specific, fertility, \( f_a \), and HIV prevalence by age summed over all age groups, as follows:

\[
Y_{anc} = \sum_{a=0} \left( N_a \cdot Y_a \cdot f_a \right) / \sum_{a=0} \left( N_a \cdot f_a \right)
\]

Interventions. A limitation of estimation models is that intervention of the transmission process cannot be modelled directly; however, the overall reduction in HIV incidence can be estimated. In our model HIV incidence is reduced from the baseline value to estimate the level at which there is a fit with trends in the data. Since the baseline uses independent data (e.g. an HIV prevalence estimation, population and STD data), a fit-and-adjust method is not used. Behavioural interventions are defined by the starting year, period of introduction, and the age groups targeted. Reductions in HIV incidence compared with that at baseline are simulated to interpret sentinel trends, as has been carried out, for example, for army entry cohorts aged 21 years in Thailand (20). For potential vaccine interventions the following are defined: efficacy, coverage, period of introduction, and age groups targeted. Coverage is increased gradually, and vaccinated groups are protected as their HIV risk changes with age. The direct reduction in HIV incidence and the number of vaccines required by age and time are calculated.

Results

The examples below illustrate the wide-ranging applications of the model as well as its use in interpreting national HIV and AIDS surveillance data.

East African HIV epidemic

The simplest application of the model is illustrated using the example of a national HIV epidemic in East Africa. A single group heterosexual epidemic, divided into males and females, is modelled. A full description of an application for surveillance data from East Africa is presented elsewhere (12). The following data were used: the 1991 Uganda census; HIV point prevalence from the 1988 national Ugandan serosurvey of 15% of the population; and the risk profile, by age, from STD rates of a survey in Kampala (21).

Model outputs were validated to AIDS surveillance data by birth cohort and HIV prevalence, by age, from a national survey and the following assumptions tested: a 7-year median incubation period; the risk profile, by age, from STD rates; extensive spread beginning in 1980; and a 5-year period of growth in HIV incidence. The Pearson correlation \( r > 0.9 \) of the model output with birth cohort data was greater than that obtained using sensitivity analyses which varied the incubation period, risk profile, and period of growth (12). Independent empirical data on HIV prevalence, STDs and population are used in the model, thus avoiding an adjustment-and-fit approach.

Fig. 1 shows model outputs for HIV prevalence, incidence and number of AIDS cases, by time, age, and sentinel group. Based on available data, the HIV incidence built up markedly before 1985, with a subsequent age shift to younger groups (12). The projected HIV prevalences among pregnant women suggest that there may be declines in the longer term. The forecasts are illustrative and require an assumption to be made as to whether cohorts entering the epidemic at later stages have the same, increased, or decreased incidences as those before them (shown also are the baseline and reduced incidence scenarios).

Mixed risk-group HIV epidemic

The second example illustrates the extension of the model to include up to six subgroups. Separate epidemic curves and population characteristics are defined for each group. Illustrated are simulations of a South-east Asian HIV epidemic, with input data from Thailand divided into the following subgroups: intravenous drug users; sex workers (indirect and direct); males and females in the northern region of the country; and those in the rest of the country. The following data were used: 1993 United Nations population estimates (22); non-AIDS mortality from the Coale–Demeny–North life-table (level 21); point HIV prevalence, by sector, from 1993 sentinel data (20); estimates of subpopulation sizes from the AIDS control programme; and the date of onset of epidemics staggered between groups from 1986 to 1989.

Fig. 2 shows model outputs of HIV prevalence by sector as well as those for simulated sentinel groups compared to sentinel surveillance trends. The output suggests that the baseline model is valid, although some differences in trends remain; for exam-
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Fig. 1. Model output for an East African HIV epidemic. a) HIV prevalence, incidence and AIDS cases by year. The broken curve shows the HIV prevalence for an incidence reduction of 3% per year from 1988. b) Distribution of HIV incidence, by age, 5 years and 12 years after onset of the epidemic. c) Simulation of trends among pregnant women: fertility-weighted HIV prevalence, by year.

Demographic impacts

An HIV model by age and sex also enables outputs to be obtained for demographic indicators and the impact of HIV. The model simulates a comparison population without AIDS, thereby permitting changes in mortality, fertility and population growth due to AIDS to be monitored. This example is based on the simulation of the East African HIV epidemic discussed above, with population, mortality, and fertility data defined by the 1991 Ugandan census.

Fig. 3 shows the national population pyramid with deficits due to AIDS, by age, for 1997. The model shows the emergence of the demographic im-

ple, those due to effective interventions. A baseline curve of HIV infection by age was developed for time-valid data, and regional trends which diverged from this were interpreted. Assumptions about the reduction in incidence among specific groups due to interventions, e.g. vaccine or behaviour modification, can be made for purposes of comparison with the baseline. The incidence is reduced from the baseline scenario, and the model output fits closely to army cohort data in the north, south, and overall in the country. These scenarios have been used, for example, to interpret the observed declines in HIV prevalence in army entry cohorts in northern Thailand (23).
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Fig. 2. Model output for a mixed risk group epidemic in Thailand. a) HIV prevalence by sector of model and year (IDUs = intravenous drug users). b) HIV prevalence among army entry cohorts by region of Thailand and year (model output compared to data). c) Model output compared to sentinel trends in different groups and parts of Thailand (ANC = antenatal clinic).

Impact of AIDS by the late 1990s, although population growth was sustained at just under 3% per annum. Also shown are modelled population deficits in an extreme situation with a mean HIV prevalence of 40%. Such a population pyramid may be characteristic of small communities severely affected by AIDS mortality, with a deficit in fertility affecting those aged 0–9 years as much as direct paediatric mortality. Overall population growth is maintained at just above unity, even in this extreme situation. An age- and sex-structured model can also be used to calculate changes in life expectancy.

Age-targeting of vaccines

The final example uses the East African HIV epidemic to investigate the targeting of a potential preventive vaccine. In the model the vaccine is
Fig. 3. Demographic Impact of HIV in an East African country. a) Population by age and sex modelled with and without the impact of AIDS by 1997 at the national level. b) A severe epidemic with HIV prevalence, by age and sex (top) and population by age and sex modelled with and without the impact of AIDS (bottom).

Fig. 4. Modelled direct reduction in population HIV incidence, by year, due to a preventative vaccine (efficacy, 60%) given to various age groups at different coverage levels, and introduced from the year 2000 over 5 years.

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reflecting variations by age group, e.g. better coverage of school attendees and pregnant women. The vaccine is introduced gradually and increased to full coverage over 5 years, with cohorts during this window period aging with partial coverage.

Fig. 4 shows that targeting the 10–14-year age group has the greatest impact, reducing 23% of the population HIV incidence after 10 years at 50% coverage; a similar intervention involving 20–30-year-olds also took 10 years to reduce the population incidence by this amount — most of the reduction being achieved during the first few years, however. Vaccinating 20–30-year-olds would therefore be more appropriate at the start of an epidemic, particularly if the HIV incidence is greater during the first 5–10 years (12).

The model also enables monitoring of the number of vaccines required by year for different targeting strategies. Against the background of an increasing population distributed according to the 1991 Uganda census, the logistics of such an intervention would require 2.51 million vaccines among 10–14-year-olds and 2.89 million among 20–30-year-olds to achieve 50% coverage. To reach full coverage in 2–3 years, many more vaccines per year would be required initially. After the initial programme, a much lower number of vaccines (400000) would be required annually to maintain 50% cover, increasing slightly with time due to population growth.

targeted at the age groups 10–14 years and 20–30 years in a demographically expanding population. The vaccine is introduced in the year 2000 and its efficacy is estimated at 60%. Coverage is 25–75%,
Conclusions

There have been many attempts to project the AIDS epidemic, at various levels of complexity (2, 4, 5, 16). A balance is normally required between the time horizon, sophistication of forecasting, and ability to use routine surveillance data. A United Nations workshop, where the models discussed used uniform input parameters, proved useful, but the quantitative results obtained differed widely (11). Until dynamic models are developed further, models are also needed which define the underlying HIV infection curve by time, age, sex and subgroup compared with available data. Despite the limitations of such models, they have been applied in a wide range of situations.

Accurate estimates and forecasts are important for planning responses to the HIV epidemic (24) and interpreting changing trends. By including an age and sex structure the present model permits tighter validation to data and use in a wider range of applications, including those shown below.

• Forecasts, validated to data, by age, sex, and birth cohort.
• Evaluation of HIV prevalence and incidence trends in sentinel groups.
• Inclusion of demographic impacts and the population growth that fuels infection.
• Forecasts of national trends and up to six subpopulations.

The model retains the emphasis on simple empirical inputs, as used in the Épi Model (5) — an HIV prevalence estimate, a population survey, and STD data by age – and also shares some of its limitations: it does not model the dynamic aspects of sexual mixing and transmission, and should be used for short-term forecasts of 3–5 years.

The approach is dependent on the continuity of HIV and AIDS surveillance. In many ways AIDS data are exceptional, with approximately 1 million AIDS cases having been reported from over 190 countries, and HIV prevalence studies over time having been carried out for many sentinel groups. Nevertheless, the global nature of AIDS and the recent establishment of surveillance present important limitations. Reporting completeness varies by time and between countries, from under 10% to over 80%. When the sources of bias are appreciated, and the data disaggregated by age and subgroup, important trends related to the epidemic can be distinguished (12, 25). In particular, surveillance efforts need to be sustained, since continuity in data availability is one of the most important attributes of surveillance.

The model we have described has been used in Thailand and Uganda, and further applications are planned to test its validity for the HIV epidemics in Brazil, the United Kingdom, and USA. It has already assisted in interpreting the HIV trends among pregnant women in Uganda, the declining HIV prevalence in army cohorts in Thailand, and life expectancy and demographic indicators validated to HIV data. Since the model is not dynamic, however, the HIV infection curve for 3–5-year forecasts should continually be adjusted as surveillance data emerge. The model therefore has many of the strengths and limitations of previous simpler models, but since it is age- and sex-structured it can be used for wider applications and more closely with surveillance data.

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Résumé

Un modèle épidémiologique du VIH structuré par âge et par sexe: caractéristiques et applications

L'un des principaux problèmes que pose la modélisation du VIH réside dans l'utilisation d'une quantité de plus en plus grande de données de surveillance pour valider les estimations et prévisions. Cet article présente un nouveau modèle de prévision de l'incidence du VIH par âge et par sexe ainsi que dans des groupes sentinelles, par exemple les femmes enceintes, pour lesquels on dispose de données. Ce modèle permet de relier plus étroitement les activités de prévision et de surveillance et d'obtenir des estimations plus exactes validées par rapport aux données. Il utilise une estimation de la prévalence du VIH, des données démographiques et un profil de risque sexuel par âge, afin d'établir des projections de l'incidence du VIH et de sa prévalence, du nombre des cas de SIDA et de la population. Les caractéristiques du modèle sont décrites, avec les données nécessaires et les hypothèses démographiques et pathologiques retenues. L'article illustre l'utilisation du modèle, par exemple pour les prévisions à 3–5 ans de l'incidence du VIH en Afrique orientale par âge, par sexe et chez les femmes enceintes; la modélisation des épidémies de VIH dues à divers comportements à risque en Asie du Sud-Est; les prévisions concernant l'impact du VIH sur les indicateurs démographiques; et le ciblage d'un vaccin préventif selon le groupe d'âge.
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References


