DEMOGRAPHIC RESEARCH

Research Article

**Inconsistencies in age
profiles of HIV prevalence:
A dynamic model applied to Zambia**

Pauline M. Leclerc

Michel Garenne

Table of Contents

Inconsistencies in age profiles of HIV prevalence:
A dynamic model applied to Zambia

Pauline M. Leclerc [1]

Michel Garenne [2]

Abstract

A two-sex compartmental model of the dynamics of HIV infection was developed and applied to the case of Zambia. Parameters included age specific rates of fertility, mortality, entry into sexual life, number of partners and age of partners. They were all derived from empirical data from Demographic and Health Surveys, and applied by single year of age. The model was unable to fit age and sex patterns of infection observed in 2001. Current knowledge of HIV transmission does not allow fitting the dynamics of HIV epidemics. Further research is needed to understand the dynamics of HIV heterosexual epidemics in Africa.

[1] PhD candidate, Université Paris 6 and Institut Pasteur, Unité d'Epidémiologie des Maladies Emergentes, 25-28 rue du Dr Roux, 75000 Paris Cedex 15, France. E-mail: leclerc@pasteur.fr
[2] Directeur de Recherche, Institut Pasteur, Unité d'Epidémiologie des Maladies Emergentes, 25-28 rue du Dr Roux, 75000 Paris Cedex 15, France. E-mail: mgarenne@pasteur.fr

1. Introduction

Some twenty five years after their onset, HIV/AIDS epidemics are still raging in Africa, whereas they have to a large extent stabilized in developed countries. According to UNAIDS, some 25.8 million Africans were infected in 2004, causing high mortality (2.4 million), with numerous demographic, economic and social consequences (UNAIDS 2005, Zaba, Whiteside and Boerma 2004). However, the dynamics of these HIV epidemics vary considerably between countries, with some remaining little infected, and others where prevalence has been increasing steadily since the first cases (UNAIDS 2006). This heterogeneity does not seem to be attributable to different dates of onset in each country, but rather to a complex compounding of sexual behaviour and biological factors (Buvé, Bishikwado-Nsarhaza, and Mutangadura 2002).

In sub-Saharan Africa, the main route of HIV transmission for adults is heterosexual contact (Sewankambo et al. 1987) and for children, the mother-to-child transmission (ONUSIDA 2006). Little is known about the determinants of the different dynamics, though many factors have been invoked. In their classic studies of HIV risk factors, comparing two cities with high seroprevalence and two cities with low seroprevalence, Buvé et al. (Buvé et al. 2001) found few such factors: the well documented effect of male circumcision was confirmed, as well as the controversial correlation with another sexually transmitted disease, genital herpes infection (HSV-2). Another troublesome feature of HIV epidemics in Africa is its age pattern. In particular, young women tend to become infected very rapidly after their first sexual encounter, and in countries with high levels of HIV infection, female seroprevalence tends to peak around age 25-30, whereas it peaks some 5 to 10 years later for males. This pattern remains partly unexplained, and even in the carefully conducted four-city study authors recognize that available data, especially about women having older sexual partners, do not permit to fully explain it (Glynn et al. 2001).

The aim of this paper is to further explore inconsistencies in current knowledge of HIV transmission in Africa. The approach followed is that of mathematical modelling. The hypothesis underlying this work is the following: understanding the modes of transmission with the proper parameters of HIV transmission should enable one to simulate the dynamics of the epidemic and to reproduce the age patterns of seroprevalence. For this matter, a comprehensive model of transmission in a general population was developed, and applied to the case of Zambia. There were several reasons for selecting Zambia for this study. Firstly, HIV arrived early in Zambia, probably because of its geographical proximity with the central focus of the HIV African epidemic (Republic of Congo, formerly Zaire, and areas surrounding Lake Victoria). Secondly, HIV prevalence has been increasing steadily between 1980 and 2001, a good case for a monotonic increase, quite different from nearby Zaire or

Uganda for instance. Thirdly, and most important, Zambia has conducted in 2001 a detailed Demographic and Health Survey (DHS), which includes all the parameters needed for the model: patterns of fertility, level of mortality, distributions of number and age of sexual partners, and a population based survey of HIV prevalence on a fairly large sample, which provides the empirical data against which testing a variety of hypotheses for the model. According to this survey, HIV seroprevalence among adults age 15-49 was 17% for females and 12% for males, high values even by African standards, and had an age and sex pattern typical of most countries of Southern Africa. The model attempted to fit the dynamics of the HIV epidemic for the 1980-2001 period, monitored by various sentinel sites throughout the country, and the age and sex pattern of HIV seroprevalence observed in 2001. Its structure was similar to models described by Anderson and May (Anderson and May 1991, Anderson et al. 1992). To our knowledge, no compartmental model of this type has so far been able to reproduce current age patterns of prevalence for each sex using empirical data and realistic parameters.

2. Methods

2.1 The simulation model

The model used for simulating the dynamics of the HIV epidemic in Zambia was a straightforward compartmental model. The model had three compartments: (1) not susceptible: persons not infected and who never had sexual intercourse, noted $Z(a,s)$ where (s) stands for sex and (a) for age; (2) susceptible not infected: persons sexually active and not infected, noted $X(a,s)$; and (3) infected with HIV, noted $Y(a,s)$, and death was the absorbing state.

The main focus of the model was on heterosexual transmission of HIV and susceptibility after the first intercourse. However, it was considered more satisfactory, and in some way easier, to have a full scale population model including children and adults in order to have the proper number of susceptibles at each age and time period. Therefore, both heterosexual transmission and vertical transmission were considered the modes of HIV infection.

Transitions were straightforward. Children were born either from HIV- mothers or from HIV+ mothers, according to age specific fertility rates, different for HIV- women ($\beta(a)$) and for HIV+ women ($\beta'(a)$). Infected children are only a fraction, defined by the mother-to-child transmission rate (mtc), of those born to HIV+ mothers, they die from other causes ($\mu(a,s)$) or from HIV/AIDS (α). Non susceptible children are children born to HIV- mothers or those who escape the infection from HIV+ mothers (1-mtc), they

only die from other causes. In adolescent years, persons entered susceptibility with the first intercourse ($\sigma(a,s)$) and became infected proportionately to the force of infection ($\lambda(a,s)$) depending on the number and age of their partners. As children, adults were exposed to the risk of 'natural' death and, if infected, to AIDS mortality. All calculations were done by single year of age from 0 to 90 years, and single calendar year over the 1980-2001 period. All parameters were age and sex specific, though AIDS mortality was assumed constant, but different for adults and for children.

The model could be represented by the following system of differential equations, each variable being defined for age (a) and sex (s):

For children:

$$
\begin{cases}
\dfrac{dY(t)}{dt} = -(\mu + \alpha) \times Y(t) \\[2mm]
\dfrac{dZ(t)}{dt} = -\mu \times Z(t) \\[2mm]
Z_0(t) = \beta \times X_f(t) + (1 - mtc) \times \beta' \times Y_f(t) \\[2mm]
Y_0(t) = \beta' \times mtc \times Y_f(t)
\end{cases}
$$

For adults:

$$
\begin{cases}
\dfrac{dX(t)}{dt} = -(\lambda + \mu) \times X(t) + \sigma \times Z(t) \\[2mm]
\dfrac{dY(t)}{dt} = \lambda \times X(t) - (\mu + \alpha) \times Y(t) \\[2mm]
\dfrac{dZ(t)}{dt} = -(\mu + \sigma) \times Z(t)
\end{cases}
$$

And total population is N(t)= X(t) + Y(t) + Z(t)

2.2 Baseline parameters values

Baseline parameters values are displayed in Table 1. For the simulations, only the heterosexual transmission rate (htr) and the number of partners were changed, all the other parameters remaining constant. The baseline population was a stable population with the same fertility and mortality rates applied to the total population of Zambia in year 1980 (5.6 millions persons). Age-specific death rates were derived from a model life table (United Nations System, General pattern for developing countries) with the same life expectancy (51 years for women and 48 years for men). AIDS mortality (α)

was taken as 0.10 per year for infected adults, and 0.30 per year for infected children, which is consistent with values found in the literature: a mean survival duration from seroconversion to death of 8-10 years for adults (Todd et al. 1997, Mulder et al. 1994, Sewankambo et al. 1994) and a two-year mortality in infected children slightly higher than 50% (Newell, Brahmbhatt and Ghys 2004, Newell et al. 2004). Age specific fertility rates for HIV- women (β) were taken from the Zambia 2001 DHS survey, corresponding to a total fertility rate (TFR) of 6.1 children per woman (Zambia Central Statistical Office 2003). For HIV+ women, fertility rates were discounted by 20% at all ages (Lewis et al. 2004, Zaba and Gregson 1998, Gregson 1994, Ryder et al. 1991). At time t=0, i.e. 1980, one percent of HIV infected people were introduced in the adult population, proportionately to the age and sex specific seroprevalence observed in 2001. At baseline, htr was taken at 0.153 per person per year, a value derived from empirical estimation in discordant couples in Uganda (Carpenter et al. 1999). Zambia being primarily a non-circumcised country, htr was identical for male to female and for female to male, as found in Uganda and Europe (Downs and De Vincenzi 1996, Quinn et al. 2000). Mother-to-child transmission was taken at 0.30, an average value for various surveys (Newell, Brahmbhatt and Ghys 2004, Dabis and Ekpini 2002).

Table 1:   Model parameters: notations, values and sources

Parameter	Notation	Value	Source
Fertility	β(a)	TFR= 6.1	DHS survey
	β'(a)	0.8×β(a)	Lewis et al. 2004
Natural Mortality	μ(a,s)	e°= 48 (M), 51 (F)	Model life table
AIDS Mortality	α	10%/year for adults	Todd et al. 1997
		30%/year for children	Newell et al. 2004
Age at first intercourse	σ(a,s)	Median age =	DHS surveys
		15.7 (M), 16.3 (F)	
Partners age	a'(a,s)	Mean gap ~ 7 years	DHS surveys
Annual number of partners	k(a,s)	Mean= 1.25 (M), 0.87 (F)	DHS surveys
Heterosexual transmission rate	htr	0.153/py	Carpenter et al. 1999
Mother-to-child transmission	mtc	30%	Dabis et Epkini. 2002

Note: see text for details. Rates and other parameters were provided by single year of age, with the exception of HIV transmission rates (htr and mtc).

2.3 Sexual behaviour

Age specific rates of entry in sexual life (first intercourse) were derived from the Zambia 2001 DHS survey (Zambia Central Statistical Office 2003). The cumulative distribution of the age at first intercourse was fitted for each sex by a Coale-McNeil model (Coale and McNeil 1972). This corresponded to a median age of 16.3 years for females and 15.7 years of males, and full exposure by age of 26 for women and by age 32 years for men. This parameter was important for our model since it defined age specific susceptibility, and had major implications for the age profile of seroprevalence rates.

The age and sex distributions of the number of partners were also derived from the Zambia 2001 DHS survey (Zambia Central Statistical Office 2003). Mean and standard deviation of the numbers of partners was fitted for each age and sex pair, from which normal distributions were deduced. On average, men had 1.25 partners per year (range 0-25), and women 0.87 partner per year (range 0-6), which includes those who had no partner over a 12 months period.

Similarly, age and sex distributions of the age of partners were derived from the same survey. Mean and standard deviation of partners' age were fitted for each age and sex pair, from which normal distributions were deduced. This was important since the age gap between partners tended to increase over time. The mean age gap between partners (male – female) was 4 years at age 15, 6 years at age 25, and 10 years at age 50. These matrices by single year of age and sex provided the distributions of number of partners and age of partners. The distribution of age of partners was used to calculate at each step (each year) the proportion of infected partners, for each age and sex separately. This level of details, rarely provided by other models, was considered important for accurate fitting of the Zambian situation, in particular for fitting HIV prevalence among women aged 15-24 years.

2.4 Risk of infection

The annual risk of infection $\lambda(a,s)$ depended on the number of partners (k) and the probability of having an HIV+ partner. This probability, noted $P(a,s)$ was the sum-product of the age distribution of partners of someone of age (a) and sex (s) ($Ap(a,s,a',s')$ is the probability for a person of sex (s) and age (a) to have a sexual partner in the opposite sex aged (a')) by the seroprevalence of the opposite sex; $Pv(a',s')$ is the prevalence of people of sex (s') and age (a'). The infection rate for (k) partners, noted $Ir(a,s,k)$, was provided by the probability computations knowing $P(a,s)$. The risk of infection $\lambda(a,s)$ is the sum-product of infection rates for (k) partners by the

distribution of the number of partners; Np(a,s,k) is the probability for people of sex s and age (a) to have (k) sexual partners by year.

As HIV transmission only occurs, for adults, through heterosexual contact, (s) and (s') always denote opposite sex.

$$P(a,s) = \sum_{a'} Ap(a,s,a',s') \times Pv(a',s')$$

$$Ir(a,s,k) = htr \times (1-(1-P(a,s))^k)$$

$$\lambda(a,s) = \sum_{k} Np(a,s,k) \times Ir(a,s,k)$$

2.5 Testing various hypotheses

The first test of the model (H0) was conducted by applying the baseline parameters and comparing the dynamics of the epidemic (seroprevalence by calendar year), and the age and sex pattern of seroprevalence in 2001 generated by the model with observed values in the DHS survey. In the second step, heterosexual transmission rate (htr) was adjusted to fit the peak prevalence for females (H1) and for males (H1') observed in 2001. In the third step, the number of partners was adjusted by adding an integer number to the baseline distributions of each sex in order to fit the peak prevalence for females (H2) and for males (H2'). In the fourth step, heterosexual transmission rate (htr) was again adjusted to fit the prevalence at typical ages, that is age 25 for females (H3) and age 35 for males (H3'). Likewise, in the fifth and last step, the number of partners was adjusted to fit the prevalence for females at age 25 (H4) and for males at age 35 (H4'). The different hypotheses are summarized in Table 2. Population dynamics simulated with the model, according to these assumptions, are described in Table 3. Furthermore, we tried to change the age difference between partners: results are not shown here since they had little impact on the transmission dynamics.

Table 2:   Hypotheses investigated and corresponding parameters (after optimization)

	Heterosexual transmission rate (htr)	Additional annual number of partners
H0: baseline (realistic parameters)	0.153	0
Same prevalence at peak (transmission rate)		
H1: for females	0.288	0
H1': for males	0.283	0
Same prevalence at peak (number of partners)		
H2: for females	0.153	+1
H2': for males	0.153	+1
Same prevalence at typical age (transmission rate)		
H3: for females (at age 25)	0.449	0
H3': for males (at age 35)	0.366	0
Same prevalence at typical age (number of partners)		
H4: for females (at age 25)	0.153	+3
H4': for males (at age 35)	0.153	+2

Table 3:   **Population dynamics according to various hypotheses investigated**

|	1980	1990	2000	2005
	Population size			
H0	5 636 807	7 407 136	9 806 428	11 311 792
H1	5 636 807	7 344 989	9 472 854	10 771 974
H2	5 636 807	7 344 038	9 478 284	10 787 243
H3	5 636 807	7 217 941	8 499 709	9 058 585
H4	5 636 807	7 138 936	8 233 748	8 748 307
	Susceptible population size			
H0	2 781 740	3 564 136	4 755 628	5 494 519
H1	2 781 740	3 410 716	4 294 678	4 849 395
H2	2 781 740	3 412 681	4 312 687	4 879 817
H3	2 781 740	3 029 903	2 902 249	2 886 834
H4	2 781 740	2 855 659	2 772 180	2 804 473
	Prevalence (general population)			
H0	0.010	0.009	0.005	0.004
H1	0.010	0.025	0.034	0.034
H2	0.010	0.025	0.032	0.032
H3	0.010	0.068	0.137	0.153
H4	0.010	0.087	0.142	0.154
	Female prevalence (15-49 years)			
H0	0.022	0.019	0.011	0.007
H1	0.022	0.055	0.075	0.074
H2	0.022	0.057	0.073	0.071
H3	0.022	0.154	0.304	0.331
H4	0.022	0.203	0.313	0.330
	Male prevalence (15-49 years)			
H0	0.021	0.013	0.005	0.002
H1	0.021	0.038	0.039	0.036
H2	0.021	0.036	0.035	0.032
H3	0.021	0.109	0.191	0.212
H4	0.021	0.133	0.198	0.213

3. Results

3.1 Using baseline values (H0)

Using baseline values (H0), considered realistic and as close as possible from what was known of heterosexual transmission of HIV and sexual behaviour, was assumed to fit the dynamics of the epidemic and the age patterns. Simulations with realistic parameters showed the opposite. With baseline parameters, the HIV seroprevalence among 15-49 years old produced by the model was stable for a few years, and tended to decrease overtime from 1980 to 2001 for both sexes, reaching 0.4% for males and 1.0% for females by year 2001, whereas in reality it increased steadily over time to reach the high values found in the DHS survey (Figure 1). In other words, realistic parameters led to a decline in the epidemic and not to an explosion as witnessed in the field. Similarly, the projected age and sex distribution showed a mild peak around age 50 (47 for females, 50 for males), whereas empirical values in 2001 showed a mode at age 31 for females and at age 36 for males (Table 4, Figure 2). In conclusion, realistic values of HIV transmission were unable to fit the observed values in any respect.

Table 4:   Main results according to various hypotheses investigated

	Prevalence 15-49		Age at peak (years)		Prevalence at peak		Prevalence at typical age (25/35)	
	Female	Male	Female	Male	Female	Male	Female	Male
Observed values								
Zambia, 2001	0.166	0.120	31	36	0.257	0.206	0.213	0.206
Model hypothesis								
H0	0.010	0.004	47	50	0.043	0.031	0.001	0.004
H1	0.075	0.039	44	48	0.257	0.220	0.017	0.063
H1'	0.070	0.036	44	48	0.242	0.206	0.016	0.057
H2	0.073	0.035	45	48	0.253	0.199	0.016	0.055
H3	0.311	0.195	43	48	0.868	0.846	0.212	0.488
H3'	0.176	0.100	43	48	0.560	0.520	0.068	0.206
H4	0.317	0.201	46	50	0.765	0.726	0.300	0.470
H4'	0.208	0.118	44	50	0.606	0.541	0.115	0.253

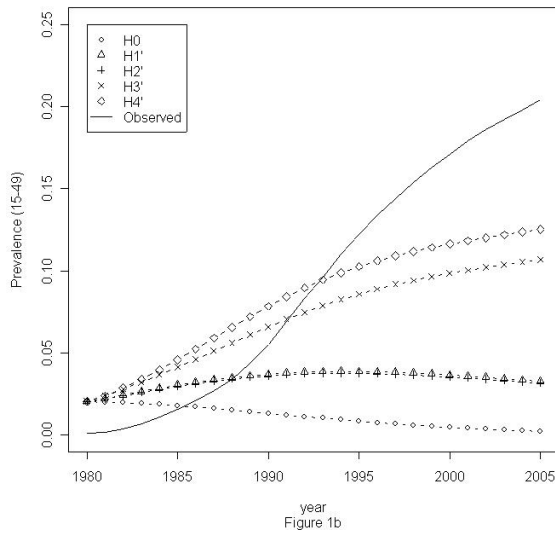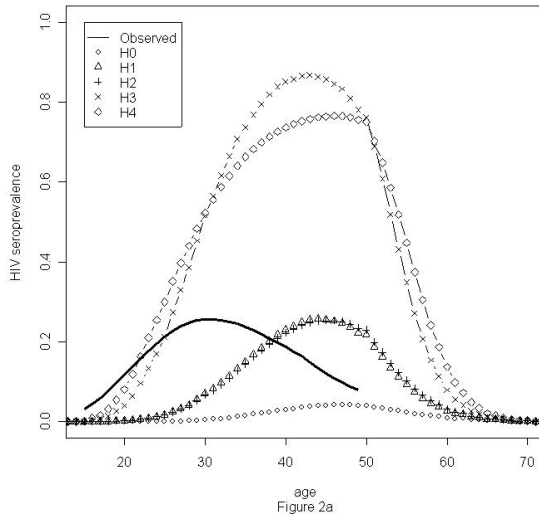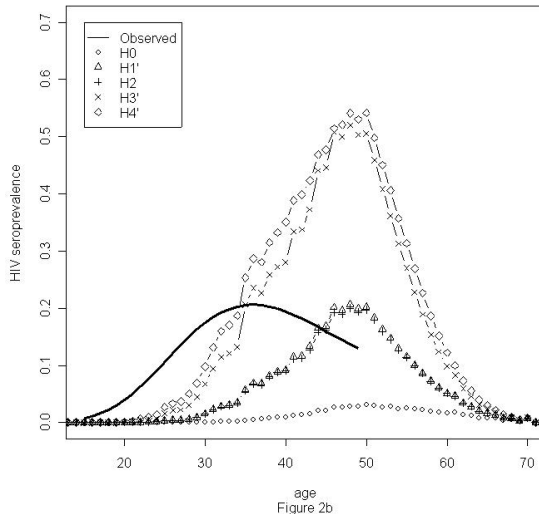**Figure 1:** **Dynamics of HIV epidemic, observed and simulated, Zambia**
(a) Female
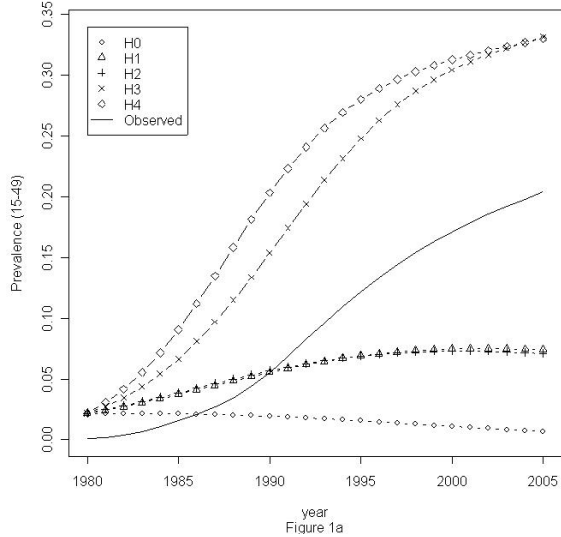
Figure 1a

(b) Male

Figure 1b

Figure 2: **Age patterns of HIV prevalence, observed and simulated, Zambia, 2001:**
(a) Female

(b) Male

3.2 Adjusting for peak prevalence (H1 and H2)

The two critical parameters for our model, the transmission rate and the number of partners, were let to vary in order to fit the peak prevalence observed in 2001. Under H1 (same prevalence at peak), heterosexual transmission should have been double of what was considered realistic (0.288 for females and 0.283 for males). In this case again, the epidemic should have stabilized by 1994 (males) or 2000 (females), unlike what was observed. Under this hypothesis the peak prevalence in year 2001 would have occurred at age 44 (females) or 48 (males), much higher ages than the peak prevalence observed (31 and 36 years respectively). In addition, the prevalence for the 15-49 age group would have been much lower than observed (0.075 for females and 0.036 for males). Letting vary the number of partners instead, in order to fit the same peak prevalence (H2) let to similar inconsistencies on the age at peak and the overall prevalence (Table 4, Figures 1 and 2).

3.3 Adjusting for prevalence at typical ages (H3 and H4)

Age 35 for men and age 25 for women are critical ages for HIV prevalence in Africa, usually close to modal ages. The same parameters were adjusted for fitting the observed prevalence at these ages: the htr values required for females (0.449) and for males (0.366) became unrealistic. In addition, peak prevalence did occur again at older ages (43 for females and 48 for males), and led to absurd values of prevalence at peak (0.868 for females and 0.520 for males). Likewise for changing the number of partners: the values needed for fitting the prevalence at typical age became unrealistic (+3 and +2 partners for females and males respectively), and led to much higher age at peak prevalence and to absurd values of prevalence at peak (Table 4, Figure 2).

Extreme values for both parameters (heterosexual transmission rate and annual number of partners) were also combined and unrealistic patterns of prevalence were found, with 100% of women aged 40-60 infected (data not shown).

Finally, changing the age difference between partners was done by shifting the distributions by some years, the same number for each sex and in opposite directions. This induced only a small effect on the dynamics of the epidemic, and only minor changes in age at peak prevalence (data not shown). For instance, adding seven more years of difference between partners induced a 3-year decline in age at peak for females, and a 5-year increase for males.

4. Discussion

The model investigated was unable to fit the dynamics of the HIV epidemic over time, and the age pattern of HIV prevalence found in year 2001 in the DHS survey. Three reasons could be evoked to explain the discrepancies: the model, the parameters, or the basic understanding of HIV transmission.

The model was straightforward, and took into account current understanding of heterosexual transmission, and its critical elements: entry into sexual life, number of partners and age of partners, all being taken by single year of age from survey data. However, a limitation of the model, which is the case for all compartmental models, is the pattern of changing partnership over time. The yearly step used in the model assumes *de facto* changing partner every year for those who have one partner, twice a year for those who have two partners etc. In reality, changing partnership is likely to be lower since a majority of persons with one partner will keep the same partner from year to year. However, this only reinforces our findings, since changing less often will tend to reduce prevalence estimates for the H0 hypothesis, and would lead to even higher values of heterosexual transmission needed for fitting the observed values.

The model also excluded complex interactions between variables. For instance, heterosexual transmission was considered constant, which assumes *de facto* that the annual number of intercourses is constant. One could however argue that persons who are more sexually mobile (more partners) have also more intercourse per year, and therefore have a higher risk. This is certainly the case for commercial sex workers, who were not considered separately in this model. However, in mature epidemics such as Zambia in 2001, commercial sex seems to play only a minor role, and most of the transmission seems to occur in the general population. Our model was designed for this purpose, and would certainly not be appropriate for other cases such as nascent epidemics where commercial sex is a key parameter (Buvé, Bishikwado-Nsarhaza and Mutangadura 2002, World Bank 1997). We also neglected higher transmission rates for short period of times after seroconversion, when viral loads are higher and transmission rates are likely to be higher too. This is in a way included in the average annual risk that we used. If this were to be included, then the annual risk for other periods should be diminished. This seems unlikely to change the overall pattern, though it might have an effect on the age pattern (if many transmissions occur right after seroconversion, the younger the partner, the younger will be the infected person). Further modelling will be necessary to fit this effect. In any case, this leaves open the question of partner's age pattern of infection: in the empirical data, young women were always more infected than their partners, which is only possible if young women have large numbers of partners, a fact not substantiated by sexual behaviour surveys.

The fixed parameters were taken from robust demographic and epidemiologic surveys. It is unlikely that real parameters were far from those that were used. Furthermore, it would require major changes in the fixed parameters to have an effect on the dynamics of the epidemics. Maybe, assuming a constant AIDS mortality is not as realistic as it could be and explicitly modelling the incubation period with a low mortality rate, followed by a later stage with a high mortality rate could have had an impact on the results of the model.

The two variable parameters (heterosexual transmission rate and number of partners) could be criticized, but they were let to vary to a great extent, including to unrealistic values. If transmission rates as high as 0.3 per person per year have been reported, and used in other models, they led to dynamics and age patterns which were inconsistent with empirical data. It is therefore unlikely that something was missed here because of the wide range of variations utilized.

Assuming that most data on sexual behaviour among young women are wrong and misleading remains in theory a possibility. Indeed, several authors have argued that sexual behaviour surveys have serious biases (Nnko et al. 2004, Cleland et al. 2004, Zaba et al. 2005, Leridon 1993). In this study generous assumptions were made on such biases, with adding up to 3 partners per year. Stronger biases are hard to conceive, unless one rejects all survey data. Even though one could always argue for large biases in sexual behaviour reporting for special groups, this is unlikely to apply to the whole population, as was investigated in this model. One should also remember that reports on number of partners and age of partners were quite consistent between male and female respondents, a further evidence that on the whole, data used in the model were robust.

Another possibility is the interaction between age and heterosexual transmission rates. There is casual evidence that very young women are more susceptible than older women (Carpenter et al. 1999). We plan to introduce this parameter in more sophisticated models. However, this leaves open the question why young women are more infected than their partners. If susceptibility is one side of the equation, exposure is definitely critical for infection.

Another possibility is that the age difference between partners is grossly underestimated. If women age 15-19 had in majority intercourse with the most infected men (age 30-34), then the dynamics of the epidemic would be changed. However, it is hard to conceive that all survey data on sexual partnership are wrong to that extent. All data available throughout Africa show similar features, and in addition places where the age gap of partners of teenage women is the largest are also places where the HIV prevalence is the lowest. This is the case for West African Sahelian countries where women marry very early and where polygamy is widespread, and not the case of Southern Africa. Furthermore, in the model the age gap between partners was let to be increased by 7 years without any major change in the age pattern of infection.

If the model is sound and the parameters realistic, only the basic mechanisms of HIV transmission can be questioned. Other authors have argued that if heterosexual transmission could not explain observed patterns in Africa, then other mechanisms are at play. Some argued that iatrogenic transmission (blood transfusion, unsafe injections, piercing, invasive medical practices, etc.) could explain high values of seroprevalence in Africa (Gisselquist and Potterat 2003, Gisselquist et al. 2002). However, this hypothesis has been seriously criticized by the World Health Organization and other authors (Schmid et al. 2004, Garenne, Micol and Fontanet 2004), for lack of evidence of widespread HIV transmission by unsafe medical practices, especially in the more advanced countries such as South Africa where the blood bank and injections are safe and where the HIV epidemic is raging, as well as for the strong correlation of increasing seroprevalence with entry into sexual life. If heterosexual transmission is the main route of HIV infection through sub-Saharan populations, one has to face the fact that we don't have a full understanding of the transmission mechanisms.

One has to recognize that something is missing in the HIV puzzle in Africa, and that one is not able to fit the current situation with current knowledge. Several points need to be clarified in order to have a satisfactory picture of the dynamics of HIV epidemics in sub-Saharan Africa.

5. Acknowledgements

References

Anderson R. M. and May R. M. (1991). "Infectious Diseases of Humans: Dynamics and Control". Oxford: Science Publications.

Anderson RM, May RM, Ng TW and Rowley JT. (1992). "Age-dependent choice of sexual partners and the transmission dynamics of HIV in Sub-Saharan Africa". *Philosophical Transactions of the Royal Society of London. Series B, Biological sciences* ;336,1277:135-55.

Buvé A, Caraël M, Hayes RJ, Auvert B, Ferry B, Robinson NJ, Anagonou S, Kanhonou L, Laourou M, Abega S, Akam E, Zekeng L, Chege J, Kahindo M, Rutenberg N, Kaona F, Musonda R, Sukwa T, Weiss HA and LagaM. (2001). "Multicentre study on factors determining differences in rate of spread of HIV in sub-Saharan Africa: methods and prevalence of HIV infection". *AIDS* ,15, Suppl 4:S5-14.

Buvé A, Caraël M, Hayes RJ, Auvert B, Ferry B, Robinson NJ, Anagonou S, Kanhonou L, Laourou M, Abega S, Akam E, Zekeng L, Chege J, Kahindo M, Rutenberg N, Kaona F, Musonda R, Sukwa T, Weiss HA and LagaM. (2001). "The multicentre study on factors determining the differential spread of HIV in four African cities: summary and conclusions". *AIDS* , 15, Suppl 4:S127-31.

Buvé A., Bishikwado-Nsarhaza B., Mutangadura G. (2002). "The spread and effect of HIV-1 infection in sub-Saharan Africa". *Lancet* , 359: 2011-7.

Carpenter LM, Kamali A, Ruberantwari A, Malamba SS, Whitworth JA. (1999). "Rates of HIV-1 transmission within marriage in rural Uganda in relation to the HIV sero-status of the partners". *AIDS* , 13, 9:1083-9.

Cleland J, Boerma JT, Caraël M, Weir SS. (2004). "Monitoring sexual behaviour in general populations: a synthesis of lessons of the past decades". *Sexually Transmitted Infections*, 80, Suppl II: iii1-ii7.

Coale AJ, McNeil DR. (1972). "The distribution by age of the frequency of first marriage in a female cohort". *Journal of the American Statistical Association*, 67, 340:743-9.

Dabis F, Ekpini ER. (2002). "HIV-1/AIDS and maternal and child health in Africa". *Lancet* , 359, 9323:2097-104.

Downs AM., De Vincenzi I. (1996). "Probability of heterosexual transmission of HIV: relationship to the number of unprotected sexual contacts. European Study Group in Heterosexual Transmission of HIV". *Journal of Acquired Immune Deficiency Syndromes and Human Retrovirology*, 11, 4: 388-95.

Garenne M, Micol R, Fontanet A. (2004). " Reply to 'Unsafe healthcare drives spread of African HIV'" [Letter]. *International Journal of STD & AIDS* , 15, 1:65-7.

Gisselquist D, Potterat JJ. (2003). "Heterosexual transmission of HIV in Africa: an empiric estimate". *International Journal of STD & AIDS* , 14:162-73.

Gisselquist D, Rothenberg R, Potterat J, Drucker E. (2002). "HIV infections in sub-Saharan Africa not explained by sexual or vertical transmission". *International Journal of STD & AIDS*, 13:657-66.

Glynn JR, Caraël M, Auvert B, Kahindo M, Chege J, Musonda R, Kaona F and Buvé A. (2001). "Why do young women have a much higher prevalence of HIV than young men? A study in Kisumu, Kenya and Ndola, Zambia". *AIDS*, 15, Suppl 4:S51-60.

Gregson S. (1994). "Will HIV become a major determinant of fertility in sub-Saharan Africa?" *Journal of Development Studies,* 30, 3:650-79.

Leridon H. (1993). "La fréquence des rapports sexuels – Données et analyses de cohérence". *Population*, 5:1381-1408.

Lewis JJC, Ronsmans C, Ezeh A, Gregson S. (2004). "The population impact of HIV on fertility in sub-Saharan Africa". *AIDS*, 18, Suppl 2:S35-43.

Mulder DW, Nunn AJ, Kamali A, Wagner HU, Kengeya-Kayondo JF. (1994). "Two-year HIV-1-associated mortality in a Ugandan rural population". *Lancet* 343:1021-3.

Newell ML, Brahmbhatt H, Ghys PD. (2004). "Child mortality and HIV infection in Africa: a review". *AIDS*, 18, Suppl 2:S27-34.

Newell ML, Coovadia H, Cortina-Borja M, Rollins N, Gaillard P, Dabis F. for the Gent International AIDS Society (IAS) working group on HIV infection in women and children. (2004). "Mortality of infected infants born to HIV-infected mothers in Africa: a pooled analysis". *Lancet*, 364: 1236-43.

Nnko S, Boerma JT, Urassa M, Mwaluko G, Zaba B. (2004). "Secretive females or swaggering males? An assessment of the quality of sexual partnership reporting in rural Tanzania". *Social Science & Medicine*, 59: 299-310.

Quinn TC, Wawer MJ, Sewankambo N, Serwadda D, Li C, Wabwire-Mangen F, Meehan MO, Lutalo T, Gray RH. (2000). "Viral load and heterosexual transmission of human immunodeficiency virus type 1". *New England Journal of Medecine*, 342, 13: 921-929.

Ryder RW, Batter VL, Nsuami M, Badi N, Mundele L, Matela B, Utshudi M, Heyward WL. (1991). "Fertility rates in 238 HIV-1 seropositive women in Zaire followed for 3 years post-partum". *AIDS*, 5:1521-7.

Schmid GP, Buvé A, Mugyenyi P, Garnett GP, Hayes RJ, Williams BG, Garcia Calleja J, De Cock KM, Whitworth JA, Kapiga SH, Ghys PD, Hankins C, Zaba B, Heimer R, Boerma JT. (2004). "Transmission of HIV-1 infection in sub-Saharan Africa and effect of elimination of unsafe injections". *Lancet*, 363:482-8.

Sewankambo NK, Carswell JW, Mugerwa RD, Lloyd G, Kataaha P, Downing RG, Lucas S. (1987) "HIV infection through normal heterosexual contact in Uganda". *AIDS*, 1,2:113-6.

Sewankambo NK, Wawer MJ, Gray RH, Serwadda D, Li C, Stallings RY, Musgrave SD, Konde-Lule J. (1994) "Demographic impact of HIV infection in a rural Rakai district, Uganda: results of a population-based cohort study". *AIDS*, 8,12:1707-13.

Todd J, Balira R, Grosskurth H, Mayaud P, Mosha F, ka-Gina G, Klokke A, Gabone R, Gavyole A, Mabey D, Hayes R. (1997). "HIV-associated adult mortality in a rural Tanzanian population". *AIDS*, 11:801-7.

UNAIDS (2005) - Epidemic update, December 2005. Available on web site: www.unaids.org

UNAIDS. (2006) "2006 Report on the global AIDS epidemic". Available on web site: www.unaids.org

World Bank. (1997). Confronting AIDS: Public Priorities in a Global Epidemic. New York: Oxford University Press.

Zaba B, Gregson S. (1998). "Measuring the impact of HIV on fertility in Africa". *AIDS*, 12, Suppl 1: S41-50.

Zaba B, Slaymaker E, Urassa M, Boerma JT. (2005). "The role of behavioural data in HIV surveillance". *AIDS*, 19, Suppl 2: S39-52.

Zaba B, Whiteside A, Boerma JT. (2004). "Demographic and socioeconomic impact of AIDS: taking stock of the empirical evidence". *AIDS*, 18, Suppl 2:S1-7.

Central Statistical Office[Zambia]. (2003).Census 2001. Central Board of Health, and ORC Macro. *Zambia Demographic and Health Survey 2001-2002.* Calverton, Maryland, USA: Central Statistical Office, Central Board of Health, and ORC.