Declines in HIV prevalence can be associated with changing sexual behaviour in Uganda, Urban Kenya, Zimbabwe and Urban Haiti

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<< SUPPLEMENTARY MATERIAL >>

Full Description of the Mathematical Model

The model is defined by a set of partial differential equations with respect to time and age that are solved numerically with a four-stage Runge-Kutta algorithm (time-step = 0.02 years). The population is stratified by gender (k=1 for males, k=2 for females) and sexual activity (m=0 (lowest) to 4 (highest)). The model treats HIV infection status as either HIV negative (X), HIV acute infection (Y^1), latent infection (Y^2), pre-AIDS (Y^3) or full blown AIDS (Z). The model is run for 100 years to establish a stable population structure before the introduction of infection with 0.01% of males aged 25-29 years in the highest sexual activity group moving from X to Y^1.

The partial differential equations are:

$$\frac{\partial X_{k,m}}{\partial t}+\frac{\partial X_{k,m}}{\partial a}=-X_{k,m}\left(\mu_k(a).+\lambda_{k,m}(a,t)\right)$$

$$\frac{\partial Y^1_{k,m}}{\partial t}+\frac{\partial Y^1_{k,m}}{\partial a}=\lambda_{k,m}(a,t).X_{k,m}-Y^1_{k,m}\left(\mu_k(a)+\upsilon_1\right)$$

$$\frac{\partial Y^2_{k,m}}{\partial t}+\frac{\partial Y^2_{k,m}}{\partial a}=\upsilon_1(a).Y^1_{k,m}-Y^2_{k,m}\left(\mu_k(a)+\upsilon_2(a)\right)$$

$$\frac{\partial Y^3_{k,m}}{\partial t}+\frac{\partial Y^3_{k,m}}{\partial a}=\upsilon_2(a).Y^2_{k,m}-Y^3_{k,m}\left(\mu_k(a)+\upsilon_3\right)$$

$$\frac{\partial Z_{k,m}}{\partial t}+\frac{\partial Z_{k,m}}{\partial a}=\upsilon_3 Y^3_{k,m}-Z_{k,m}(\mu_k(a)+\alpha)$$

$\mu_k(a)$ is the gender and age-specific per-capita death rate; $\lambda_{k,m}(a,t)$ is the force of infection to individual of that gender, age and activity-group at time t; $\frac{1}{\upsilon_1}, \frac{1}{\upsilon_2(a)}$ and $\frac{1}{\upsilon_3}$ are the mean number of years spent with acute infection, latent infection and pre-AIDS, respectively; $\alpha(a)$ is the mortality rate for those with AIDS.

At each moment, the number of babies introduced into each gender and sexual activity-group in the population is:

$$X_{k,m}(0,t)=\varpi_k\gamma_m\int\varphi(a)\sum_m X_{2,m}(a,t)da+(1-\sigma)\int\varphi(a)\sum_m\left[f_1Y^1_{2,m}(a,t)+f_2Y^2_{2,m}(a,t)+f_3Y^3_{2,m}(a,t)\right]da$$

$$Y^1{}_{k,m}(0,t)=\varpi_k\gamma_m\sigma\int\varphi(a)\sum_m\left[f_1Y^1_{2,m}(a,t)+f_2Y^2_{2,m}(a,t)+f_3Y^3_{2,m}(a,t)\right]da$$

where $\varphi(a)$ is the age-specific fertility and f_1, f_2, f_3, and f_4 are the reduction in fertility associated with acute infection, latent infection, pre-AIDS and AIDS, respectively; σ is the probability of mother to

child transmission, ϖ_k is the fraction of babies born that gender and γ_m is the fraction of babies born into that sexual activity-group.

The risk of a susceptible individual becoming infected is a function of the yearly age group rather than a continuous function of age such that $\lambda_m(a-0.5 \leq a < a+0.5, t) = \lambda_{i,m}(t)$. We define the pattern of contact within the population through a matrix determining the age and activity group-specific rates of partnerships formation with the age and activity groups of the opposite gender. Here one's own age and activity category is denoted i and m, respectively, and those of members of the opposite gender are distinguished with a prime (i' and m').

$$\lambda_{i,m}(t) = \sum_{m'} \sum_{i'} \left(c_{i,m,i',m'}(t).P_{i',m'}(t).\psi_{i,i'} \right)$$

where $c_{i,m,i',m'}$ is the number of partnerships formed with individuals of the opposite gender by age and activity group, $P_{i',m'}$ is the risk of acquiring infection when forming partnerships with individuals of the opposite gender by age and sexual activity, and $\psi_{i,i'}$ is the chance that condoms are used consistently in partnerships formed between individuals of age i and i'. The definition of each of these terms follows.

$C_{k,i,m}$ is the total number of partnerships formed each year and they are shared amongst the age and activity groups of the opposite gender according to the matrix $c_{i,m,i',m'}$:

$$c_{i,m,i',m'} = C_{k,i,m} \left[(1-\varepsilon)\delta_{m,m'} + \varepsilon \left\{ \frac{N_{i',m'}C_{i',m'}}{\sum_{m'} N_{i',m'}C_{i',m'}} \right\} \right] \Delta_{i,i'}$$

where $N_{i,m}$ is the number of sexually-active individuals and $\delta_{m,m'}$ is the identity matrix. Thus the pattern of mixing with respect to activity ranges from assortative (like-with-like, $\varepsilon=0$) to random ($\varepsilon=1$) and the pattern of mixing with respect to age is determined by the distribution $\Delta_{i,i'}$ - the fraction of an *i*-aged individual's partnerships that are formed with individuals of age *i*'. Here we assume that $\Delta_{i,i'}$ depends only on the age difference between partners: (π = age of male – age of female) and is distributed as:

$$p(\pi) = \frac{\kappa\rho^{\kappa}(\pi'+r)^{\kappa-1}}{1+((\pi'+r)^{\kappa})^2} \quad \text{if } \gamma \geq 0$$

$$p(\pi) = 0 \qquad \text{otherwise}$$

Here κ, ρ and r are the shape parameters for log-logistic distribution. $\Delta_{i,i'}$ is scaled so that $\sum_{A^{1'}}^{A^{2'}} \Delta_{i,i'} = 1$ where A^1 and A^2 are the ages at which sexual activity begins and ends. This allows most partnerships to be formed between women and men a few years older but a few partnerships to involve women and men many more years their senior. Initially, $p(\pi)$ was parameterised by fitting to cross-sectional survey data collected in rural Zimbabwe (1) (see table S1) giving a mean age difference between partners of 7.4. Where available data from countries indicated a different mean partner age difference ρ was re-fitted.

The difference in rate of partnership formation between the sexual activity groups is defined as:

$$C_{k,i,m} = \frac{M_{k,i}}{\tau^{\sum m\gamma_m}} \tau^m$$

Here $M_{k,i}$ is the gender- and age-specific geometric mean of partnership formation rate and τ independently determines the common ratio partner change between the sexual-activity categories. Thus, for a mean partner change rate of 1.6, the number of sexual partners per year for each group (and percent of population in that group) would be: 0.79 (59%), 2.38 (25%), 7.13 (10%), 21.39 (5%) and 64.16 (1%).

At each moment, the pattern of partnership formation ($c_{i,m,i',m'}$) is constrained such that the total number of sexual partnerships formed by males of type *i,m* with females type *i',m'* must equal the total number of partnerships formed by females of type *i',m'* with males of type *i,m*. That is,:

$$N_{1,i,m} c_{i,m,i',m'} = N_{2,i',m'} c_{i',m',i,m}$$

Where $N_{k,i,m}$ is the number of sexually active individuals of that gender, age and activity-group. If this does not hold $c_{i,m,i',m'}$ and $c_{i',m',i,m}$ are adjusted:

$$D = \frac{N_{i,m} c_{i,m,i',m'}}{N_{i',m'} c_{i',m',i,m}}$$

$$c_{i,m,i',m'} \rightarrow \frac{c_{i,m,i',m'}}{\sqrt{D}}$$

$$c_{i',m',i,m} \rightarrow c_{i',m',i,m} \sqrt{D}$$

In this way the proportionate change in partner change rate and mixing pattern is made equal for males and females.

The other two components of $\lambda_{i,m}(t)$ are the chance of infection per partnership and the probability that condom are used correctly and consistently throughout those sexual partnerships.

The probability of getting infected through a sexual partnerships with individuals of the opposite gender aged i and in sexual activity group m, is $P_{i',m'}(t)$:

$$P_{i,m}(t) = \frac{\beta^1 Y^1_{i,m} + \beta^2 Y^2_{i,m} + \beta^3 Y^3_{i,m} + \beta^4 Z_{i,m}}{X_{i,m} + Y^1_{i,m} + Y^2_{i,m} + Y^3_{i,m} + Z_{i,m}}$$

where β^1, β^2, β^3 and β^4 are the probabilities of transmission of HIV during acute infection, latent infection, pre-AIDS and AIDS respectively.

The chance that condoms are used correctly and consistently in sexual partnerships between individuals aged i and i' is $\psi_{i,i'}$. We write $\psi_{i,i'} = \Theta\chi_{i,i'}$ so that the pattern of condom use reported in cross-sectional data collected in rural Zimbabwe (1) $\chi_{i,i'}$, is scaled by Θ to match the age-specific levels of condom use reported in each country's behavioural surveys.

If the relative sizes of each sexual activity group are to be kept constant (with respect to time and age) individuals may need to move between sexual activity groups to compensate for the greater AIDS mortality the higher sexual activity groups may suffer:

$$\Omega_i = \left(N_{k,i,\bullet}\gamma_m - \frac{N_{k,i,m}}{N_{k,i,\bullet}} \right)$$

Then iterating for m=4,3,2,1:

$$S_{k,i,m} \to S_{k,i,m} + \frac{S_{k,i,m-1}}{N_{k,i,m-1}}\Omega_i \qquad S_{k,i,m-1} \to S_{k,i,m-1} - \frac{S_{k,i,m-1}}{N_{k,i,m-1}}\Omega_i$$

$$Y^1{}_{k,i,m} \to Y^1{}_{k,i,m} + \frac{Y^1{}_{k,i,m-1}}{N_{k,i,m-1}}\Omega_i \qquad Y^1{}_{k,i,m-1} \to Y^1{}_{k,i,m-1} - \frac{Y^1{}_{k,i,m-1}}{N_{k,i,m-1}}\Omega_i$$

$$Y^2{}_{k,i,m} \to Y^2{}_{k,i,m} + \frac{Y^2{}_{k,i,m-1}}{N_{k,i,m-1}}\Omega_i \qquad Y^2{}_{k,i,m-1} \to Y^2{}_{k,i,m-1} - \frac{Y^2{}_{k,i,m-1}}{N_{k,i,m-1}}\Omega_i$$

$$Y^3{}_{k,i,m} \to Y^3{}_{k,i,m} + \frac{Y^3{}_{k,i,m-1}}{N_{k,i,m-1}}\Omega_i \qquad Y^3{}_{k,i,m-1} \to Y^3{}_{k,i,m-1} - \frac{Y^3{}_{k,i,m-1}}{N_{k,i,m-1}}\Omega_i$$

$$Z_{k,i,m} \to Z_{k,i,m} + \frac{Z_{k,i,m-1}}{N_{k,i,m-1}}\Omega_i \qquad Z_{k,i,m-1} \to Z_{k,i,m-1} - \frac{Z_{k,i,m-1}}{N_{k,i,m-1}}\Omega_i$$

Default model parameters are listed in table S1.

Country Behaviour Data

The data from each country used to specify model parameters (Table 1) is described below with the particular surveys and years from which data were available identified:

Haiti Mean number of different sexual partners per year, age at first sex for males and females and condom use (at last sexual intercourse) from IHE, Macro, DHS Survey (1994/5) {country paper ref}. **Kenya** Age at first sex from the Kenyan Demographic and Health Survey (KDHS) 1993, condom use (at last sex with any partner) from KDHS 1998 and difference in median age at marriage from KDHS 2003{country paper ref}. **Zimbabwe** Condom usage (with any partner in last four weeks) taken from the Zimbabwe Demographic and Health Survey 1994 {country paper ref}. **Cote d'Ivoire** Total number of different sexual partners in last year, condom usage (with any partner in last two months), age of spouse and females' age at first sex from the Cote d'Ivoire Demographic and Health Survey (CDHS) 1994 and males' age at first sex from CDHS 1998/9 {country paper ref}. **Malawi** Condom use (at last sex with non-marital/non-cohabitating partners) from Knowledge, Attitudes and Practices in Health Survey 1996, percent married by age from Malawi Demographic and Health Survey (MDHS) 1992 and age at first sex from MDHS, 2000{country paper ref}. **Rwanda** Median age at first sex from Enqête Démographique et de Santé (2000). **Uganda** Condom use (at last sex with any partner) from Ugandan Demographic and Health Survey (UDHS) (2000) and median age at first sex from UDHS (1995) {country paper ref}. **Ethiopia** Condom use (at last sex with any partner) and age at first sex from the Ethiopian Demographic and Health Survey (2000) {country paper ref}.

References

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3. Collaborative Group on AIDS Incubation and HIV Survival. Time from HIV-1 seroconversion to AIDS and death before widespread use of highly-active antiretroviral therapy: a collaborative re-analysis. Collaborative Group on AIDS Incubation and HIV Survival including the CASCADE EU Concerted Action. Concerted Action on SeroConversion to AIDS and Death in Europe. Lancet 2000;355(9210):1131-7.
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6. Ross A, Van der Paal L, Lubega R, Mayanja BN, Shafer LA, Whitworth J. HIV-1 disease progression and fertility: the incidence of recognized pregnancy and pregnancy outcome in Uganda. Aids 2004;18(5):799-804.

Legends

Table S1	**Default parameter values**. * indicates that this parameter was used to fit to the model to country-specific data. ** indicates that the effect of this parameter on trends in prevalence was investigated (Figure 1) and a value was chosen so as to maximise the drop in prevalence (Table S2).
Table S2	**Values of parameter used in the application of the model to specific countries.** These parameters are the most influential on the trends in prevalence and were used to maximise the drop in prevalence and fit the model to data as closely as possible. Due to paucity of available data, the larger number of parameters and the absence of uncertainty estimates for the recorded prevalence, statistical fitting could not be satisfactorily applied. [†]ANC stands ante-natal clinic. *see table S6 for full details of relationship between age and time spent in second stage of HIV infection. † Urban Kenya sites – Busia, Meru, Nakaru and Thika, ‡ Urban Kenya sites of Garissa, Kisii, Kitui and Nyeri.**Uganda sites were provided separately as N-Northern (St Marys Hospital, Lacor, Gulu), C-Central (St Francis Hospital, Nsambya, Kampala), Western (Mbarara Hospital,), E-Eastern (Jinja Hospital and Mbale Hospital).
Table S3	**Demographic data.** Per-capita mortality rate for males and females, and per-capita fertility rate for females (data from (2)). These data generate population growth of approximately 4% per year and a life expectancy at birth of 52.1 for males and 54.7 for females.
Table S4	**Mean time spent in secondary stage of infection.** Older individuals remain in the secondary stage of infection for less time giving an overall faster progression from infection to AIDS (values based on data from (3)).
Table S5	**Mean rate of partnership formation by gender and age**. Mean number of sexual partners in last twelve months, by age and gender (Cote d'Ivoire DHS 1994). *this value was not available from the survey – the value used for females was set equal to that for males.
Table S6	**Probability of correct and consistent condom use.** The fraction of sexual partnerships (by male and female age) in which a condom was used last time, as reported by either male or female (data from rural Zimbabwe (1)).

Parameter Value	Symbol (or formula)	Default Value	Justification or reference
Mortality rate	$\mu(a)$	Table S3	(2)
Fertility rate	$\varphi(a)$	Table S3	(2)
Mean time in primary infection stage	υ_{12}	3 months	(4)
Mean time in secondary infection stage	$\upsilon_{23}(a)$	Table S4**	(4)
Mean time in tertiary infection stage	$1/g$	6 months	(4)
Mean time in full blown AIDS before dying	$1/\alpha$	6 months	(4)
Transmission probability (primary stage, tertiary stage and full blown AIDS)	$10\,\beta$	n/a	(5)
Transmission probability (secondary stage)	β	(0.01 – 0.06)**	(5)
Probability of vertical transmission	σ	0.35	(4)
Fraction of contacts made randomly with respect to sexual activity class	E	(0.3-0.6)**	(4)
Age-difference between sexual partners (shape parameters for log-logistic distribution) r κ ρ	 r κ ρ	 0.15* 2 0.25	Behavioural survey in rural Zimbabwe (1)
Number of partnerships formed per year. Common ratio between sexual activity groups Age and gender-specific geometric mean	 τ $M_{k,i}$	 (3-4)** Table S5	DHS survey from Cote D'Ivoire (1994).
Probability of consistent condom use Age-specific pattern Scalar	 $\chi_{a,a'}$ Θ	 Table S6 *	Behavioural survey in rural Zimbabwe (1)
Age at first sex	A^1_k	16*	
Age at last sex	A^2_k	55*	
Proportion of population born into each activity group (ascending)	γ_m	0.59 0.25 0.10 0.05 0.01	

Odds Ratio of appearing in ANC sample			(6)
primary stage relative to HIV-	f_1	0.58	
secondary stage relative to HIV-	f_2	0.47	
tertiary stage relative to HIV-	f_3	0.43	
full blown AIDS relative to HIV-	f	0.14	

Table S1

	Haiti	Kenya (Busia….)†	Kenya (Garissa,…)‡	Zimbabwe	Uganda (N, C, W)**	Uganda (E)**	Ethiopia	Cote d'Ivoire	Malawi	Rwanda
Transmission probability per partnership for secondary stage of infection (β)	0.01	0.02	0.02	0.03	0.05	0.04	0.04	0.04	0.08	0.03
Mean years from infection to death (aged<30years)*	7.3	7.3	7.3	7.3	7.3	7.3	7.3	7.3	7.3	7.3
Common ratio in partner-change rate between sexual activity groups (τ)	3.3	2.7	3.3	2.7	2.2	2.7	2.7	2.1	3.0	4.0
Randomness of mixing between sexual activity groups (ε).	0.3	0.6	0.6	0.8	0.3	0.6	0.6	0.3	0.3	0.3
Probability of adults being in ANC† sample by sexual activity group (ascending)	1.0 1.0 1.0 1.0 1.0	0.1 0.2 0.5 1.0 1.0	0.5 0.5 0.5 1.0 1.0	0.1 0.2 0.5 1.0 1.0	0.1 0.2 0.5 1.0 1.0	1.0 1.0 1.0 1.0 1.0	1.0 1.0 1.0 1.0 1.0	1.0 1.0 1.0 1.0 1.0	1.0 1.0 1.0 1.0 1.0	1.0 1.0 1.0 1.0 1.0

Table S2

	Deaths per person-year ($\mu(a)$)		Births per female person-year ($\varphi(a)$)
Age-range	**Male**	**Female**	
<1	0.117	0.100	0
1-4	0.019	0.019	0
5-9	0.007	0.006	0
10-14	0.004	0.004	0
15-19	0.004	0.004	0.175
20-24	0.006	0.005	0.313
25-29	0.007	0.006	0.324
30-34	0.007	0.006	0.271
35-39	0.008	0.007	0.201
40-44	0.010	0.008	0.125
45-49	0.012	0.009	0.053
50-54	0.016	0.012	0
55-59	0.021	0.016	0
60-64	0.030	0.024	0
65-69	0.044	0.038	0
70-74	0.068	0.060	0
75-79	0.105	0.094	0
80+	0.189	0.174	0

Table S3

Age-range	Mean years spent in secondary stage of infection Y^2 ($v_{23}(a)^{-1}$)
0-9	0.75
10-24	6.0
25-29	4.8
30-34	4.0
35-39	3.4
40-44	3.0
45-49	2.7
50-59	2.4
60+	2.2

Table S4

	Mean number of partnerships formed per year ($M_{k,i}$)	
Age-range	**Males**	**Females**
15-19	1.6	1.2
20-24	1.6	1.2
25-29	1.6	1.1
30-39	1.7	1.5
40-49	1.6	1.1
50+	1	*1**

Table S5

	Probability condom used in partnerships ($\chi_{i,i'}$)	
	Female aged <25	**Female aged 25+**
Male aged <25	0.32	0.29
Male aged 25+	0.10	0.07

Table S6