The Potential Epidemiological Impact of Prophylactic Vaccines: Results of the iwgAIDS Model

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Executive summary

A computational model encapsulated in the iwgAIDS software package is used to simulate prophylactic vaccine scenarios that vary vaccine efficacy (50%, 75%, 95%) and half-life of the vaccine (5-year duration, 10-year duration, 50-year duration). The vaccine scenarios focus on four target groups: adults in general, high-risk adults, teenagers, and paired females during their childbearing years. Comparisons also are made with behavior interventions to change condom use, to change concurrent partners, to change casual partner turnover rates, and to change STD rates. The potential impact of behavioral reversions (decreased condom use or increased partner turnover) is explored under the various vaccine scenarios. Separate analyses are provided for Kampala and Thailand.

(1) Vaccines of all efficacy levels have considerable impact on reducing cumulative HIV incidence in both contexts (Kampala and Thailand).
(2) Duration of effectiveness is not uniformly important in differentially reducing cumulative HIV cases, but it is sensitive to context and target (general adult population, high risk, teenagers, mothers).
(3) Targeting the general adult population is effective in both environments; targeting the others (high risk, teens, mothers) show context-specific sensitivities.
(4) The lowest efficacy vaccine outperforms all other interventions except an idealistic condom intervention.
(5) The impact of behavioral reversions on vaccine gains vis-à-vis cumulative HIV cases is sensitive to both context and target.
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Introduction

The struggle against HIV/AIDS hitherto has been limited to behavioral modification strategies for slowing the spread of the epidemic and therapeutic treatments to prolong the life of those infected. The discovery of the HIV virus as the causal agent in AIDS sparked hope that a prophylactic vaccine might soon follow, but realistic hopes for preventive vaccines only materialized in the early years of the 21st century. The initial prophylactic vaccines available for mass administration likely will be of lower efficacies than typically associated with historically successful vaccination programs. There may also be considerable uncertainty regarding the half-life of the vaccine’s protective coverage. Finally, the early vaccines may provide probabilistic reduction in susceptibility rather than total or near total elimination of susceptibility.

This paper explores the epidemiological impact of prophylactic vaccines if administered in mature epidemic environments such as Kampala, Uganda and Thailand. We use iwgAIDS, a computational model for HIV/AIDS transmission developed in the early 1990s and recently revised. The core questions explored in the paper compare four different vaccine strategies under different assumptions regarding efficacy and half-life of a prophylactic vaccine. Assuming delivery to approximately two-thirds of the relevant target group, the four strategies are vaccinating all adults, vaccinating teenagers, vaccinating only high risk groups, and vaccinating mothers at ante-natal clinics. We also compare the epidemiological impact of various vaccine strategies to older behavioral intervention strategies.

Computational Modeling

Computational modeling is a significant departure, both methodologically and epistemologically from pencil-and-paper forms of mathematical modeling. Problems that required several variables for proper specification were quickly simplified/reduced to a calculus of few variables, and the resulting toy universes were justified in terms strikingly similar to the science-as-cumulation epistemology. The implied belief was that little models would naturally concatenate with others, and that their synthesis would be a non-problematic outcome of normal science. This practice generates bodies of research that, while logically coherent for the most part, had very limited empirical fit (Seitz, 2000).

Mathematical modelers often respond to the complexities of computational modeling with two seemingly interrelated claims. First, the complexity of computational models reduces understanding. Second, complex models require more data than is typically available. There is a bit of disingenuousness here. Confining inquiries to available data is akin to the drunk searching for lost keys under a light pole some yards from the place where they were dropped to the ground. And ignoring processes relevant to a dynamic does not mean that simple is better, but that convenience leads to a caricature of universe of inquiry, with all the distortions inherent in reducing a complex non-linear world to a toy universe (Seitz, Hulin, Hanisch, 2000)
Computational modeling responds to the complexity charge with the methods of process decomposition. It responds to the lack of available data with the method of partial factorial sensitivity analysis. Research problems involving many dynamics can be concatenated in computer code in such a way that one or more can be turned on or off for a particular simulation run. This is process decomposition. The obvious virtue of this capacity is that a complex model can always be reduced to its simpler mathematical components by turning off enough processes to bring the computer analysis back to the level of pencil-and-paper output. The converse of course clearly distinguishes computational from mathematical models, because the computational technology allows the processes to be combined and their nonlinear interactions explored in a way that is inaccessible older technologies.

Partial factorial sensitivity analysis is more than postulating a possible range of parameter values and exploring the response surface for each of several parameter instances. The partial factorial sensitivity method (Plackett & Burman, 1946) recognizes the potential interaction of parameter values and processes as well as the uncertainty or available data. The tool itself is reasonable simple. For a given set of processes and the correlative parameters needed to instantiate those processes, the partial factorial sensitivity analysis takes the entire set of questionable parameters and allows the user to specify minimum and maximum value ranges for each parameter. An orthogonal draw matrix is then calculated with combinations of these parameters taken at their high or low values to generate a set of computer runs needed to explore the impact of various parameter changes on a designated response variable. Automated forms of the sensitivity analysis typically generate the run set ups and then execute the needed runs. Systematic analysis across these runs identifies those parameter changes to which the response surface is most sensitive and those parameter changes to which it is least sensitive.

The key to the science of computational modeling lies in the information-theoretic approach to explanation (Seitz, 2000). Using the metaphor of criminal justice, Seitz argues that a good defense attorney limits the information a guilty client provides, because the more the client says the greater the chance of self-incrimination. The more information provided, the greater the chance to find an inconsistency or contradiction with the facts. In the information-theoretic construction of scientific inquiry, the more complex a story is, the lower is its a-priori empirical probability. Changing one parameter value in a coupled, non-linear model does not have isolated consequences for just a single observation. If you do not have the correct story, changing one or another claim (or parameter) increases the chance that other factual mismatches appear. A properly formulated computational modeling strategy quickly reveals logical inconsistencies that lie hidden beneath verbal turf. The same strategy allows the researcher to simulate the dynamics of complex, information rich theories, and to compare patterns of virtual instantiations to their real world counterparts. Computational modeling is the appropriate vehicle for studying the dynamics of HIV pandemic transmission. Computational models allow the functional instantiation of real societies that change over time through endogenous and exogenous pressures.
The iwgAIDS model

The iwgAIDS computer program provides a vehicle for modeling all major vectors of HIV transmission: sexual (heterosexual, homosexual, bisexual), intravenous drug (stimulant and/or opiate), mother-to-child, and blood within the context of a fully articulated demographic model that includes modules for fertility, mortality, and migration. Transmission cofactors include other sexually transmitted diseases (ulcerative and/or inflammatories) and sexual practices (e.g., dry sex, anal sex, condom use). The model is age-structured and stratified by region (e.g. rural and urban), sex, marital status, sexual preference, and infection status. A continuous risk formulation incorporates age-specific parameters, by stratification, for type and concurrency of partnerships (long-term, short-term, single encounter) and contact rates (entropy distributions for high risk and low risk). Infectivity may vary over a long incubation period, and transition from HIV-infected status to AIDS is modeled using separate probabilistic transition grids for children and adults. Another probabilistic transition grid models the transition from AIDS to death. The user has control over all these parameters (e.g. the length of the transition grid, the structure of the probabilistic function over the long incubation period, etc.).

Prophylactic vaccine routines allow systematic modification of susceptibility and therapeutic routines modify infectivity. The vaccine modules allow separation of efficacy and decay by mode of infection. Similar distinctions may be entered for region, sex, and risk. The modeling reported here assumes a constant efficacy and decay across mode of infection and stratification.

Although the user may set the age of onset for sexual activity, these simulations assume that individuals begin entering the sexually active population at 15. For the adult vaccine series, the proportion vaccinated ramp up from 15 to 18.75 and then begin the ramp down process after 50. For the teen series, we begin the ramp up process at 12.75 and then ramp down starting at 18.75 years of age. The high-risk series focuses on specific strata (high risk single males, high risk single females, high risk paired males, and high risk paired females) in the simulation, although the distribution of risk in each environment has an associated age structure. For these simulations the antenatal mother series focuses on paired women during their childbearing years. Pairing rates in both environments are age-structured, so this is implicitly imported into the antenatal series as well.

The duration of a vaccine’s efficacy decays by a hazard function whose half-life is set alternately at 5 years, 10 years, or 50 years for the purposes of these simulations. Compared to a straight exponential decay, the half-life formulation results in slower extinction of coverage and hence this model will be less sensitive to changes in duration. While the straight exponential decay will demonstrate sensitivity to duration regardless of target series (all adults, teens, antenatal mothers, or high risk people), this formulation allows duration sensitivity to vary by target. The iwgAIDS model allows movement from one risk distribution to another with changes in age, pairing status, etc. The diffusion of high risk people into lower risk strata will in turn make this target less sensitive to
changes in duration of efficacy, because risk status is more a function of life cycle than a fixed attribute on an individual that remains constant over the individual’s life cycle.

**iwgAIDS equations**

The iwgAIDS computer program includes a fully elaborated demographic simulation program. Populations are aged by time step in a numerical solution of partial differential integral calculus equations. The demographic sub-model includes entry into the population through birth and migration and exit through death and migration. It is a multi-sector model, so population movements are simulated among sectors (internal migration) as well as population movements from sectors inside the simulation to those not formally represented (external migration). An example of internal migration is the movement from rural to urban areas in developing countries. An example of external migration might include refugees and another might be people wishing to change their current citizenship. The program also supports circular migration, or the temporary movement of people from one sector to another within the simulated environments. This type of movement might include college students away at college, labor away at the mines, etc.

Populations in each sector can have different fertility rates, different migration rates, and different mortality rates. Populations are arrayed by sex within each on a continuous age distribution. There are correlative continuous distributions for age-specific mortality and age-specific fertility, plus age-specific migration rates for each type indicated above. The general logic of demographic analysis is well presented elsewhere, so we will not elaborate further on the demographic equations here (Bogue, Arriaga, Anderton, 1993).

The iwgAIDS program also has an extensive epidemiological library for modeling all major processes for HIV/AIDS transmission. These include heterosexual, homosexual, and bisexual sexual transmission, IV drug transmission, perinatal transmission, and blood transfusions. The sexual routines distinguish frequency of contacts, the structure of partnerships (long-term partners, shorter-term partners, and one-night stands), the corresponding partner turnover rates), sexual preference, and sexual practice (e.g., dry sex, anal sex). IV drug use includes separate routines for opiates and stimulants. Perinatal transmission includes generic vertical transmission as well as routines for breast-feeding transmission. Cofactors in sexual transmission include other sexually transmitted diseases, which in turn are subdivided into ulceratives and inflammatories. The program generates independent prevalence rates for these STDs as a check on the risk-taking modules representing the combination of sexual dimensions above. IV drugs can act as cofactors on sexual activity as well as needle transmission dynamics. Other dynamics include interregional sexual contacts through transitory migration (e.g. truck drivers) and tuberculosis as a potential confounding influence on HIV dynamics. The transition from HIV to AIDS is modeled as a continuous distribution set by the user with probabilities of transition to AIDS associated with any point on the continuum. There are separate
continua for each sex and IV drug status. A second set of continua is used to model the transition from AIDS to death.

The program treats the sexual behavior of individuals not as a fixed trait assigned by the simulation but as life-cycle traits that can vary with the individual’s life cycle. Thus, sexual frequency varies with age but may also change with changes in partner status or movement from one region to another. Sexual risk is represented not as a set of bins into which proportions of the population are assigned but as two entropy distributions, one for low risk and one for high risk, with the means for each motivating the actual range of risk behaviors possible for low risk and high risk people. These means also vary with age, sex, and partnership status. The proportions of people at any age/sex/risk level may then vary over the course of the epidemic based on such factors as endogenous changes in pairing rates, migration, and AIDS-related mortality or exogenous changes introduced through user-specified interventions.

The program also supports a set of social dynamics, where shortages of such things as available spouses may alter the input parameters. For example, suppose abnormal death rates associated with AIDS results in a shortage of spouses vis-à-vis the expected marriage rates set at the outset of the simulation. The user can permit the program to compensate for these shortages from among a number of user options chosen to reflect the realities of the particular legal and social culture of the society under examination. Thus, pushing toward the left boundary the age of first marriage, or perhaps censuring the remarriage rates on the right boundary might fill the shortages. It is even possible to reduce desired number of contacts or change the sexual preference configurations. These endogenous social dynamics are turned on or off by the user, and the amount of change is determined by calculating the shortage between supply and demand and then changing the user-specified target parameters slowly by meeting the geometric mean of the different between supply and demand for each time step. This results in slow but persistent modifications of input parameters if the HIV/AIDS dynamics create pressures on the sexual dimensions underlying the society being simulated.

**Life cycle transitions**

How iwgAIDS generates disease reproducibility ($R_0$) has previously been described in Seitz (1994). We begin here with the illustration of generic risk level as a function of changing age, both for infected and uninfected populations. These aggregate measures of risk are concatenated from similar subdivisions within the infected and uninfected populations. These subdivisions or “status groups” include region, sex, marital status, current risk category, and IV drug use. The transformation of average risk across these status groups, per time step to reflect changes in aging and hence the life cycle effect, is computed as follows:

Let:

UIR uninfected risk
IR infected risk  
RTR(A) risk transition rate

d                   d  
--- UIR'(A) = --- UIR(A) + RTR(A)  
dA                  dA

d                   d  
--- IR'(A) = --- IR(A) + RTR(A)  
dA                  dA

A similar life cycle transition is used change the IV drug use characteristics as the population ages per time step. Separating the infected and uninfected population allows the propagation of any status biases (e.g. differences in sexual frequency) along with the aging of the infected and uninfected components of the population.

Let:

UI uninfected IV population  
UIT uninfected IV transition  
I infected IV population  
IT infected IV transition

d                   d  
--- UIIV '(A) = --- UIIV(A) + UITIV(A)  
dA                  dA

d                   d  
--- IIV'(A) = --- IIV(A) + ITIV(A)  
dA                  dA

Compute infections through sexual contacts

A primary vehicle for HIV transmission is through sexual contacts. The iwgAIDS program incorporates frequency of contact, partnership structure, partner turnover rates, and sexual preferences and practices in its sexual transmission modules. It also incorporates a host of cofactors that might affect sexual transmission.

1. Infections Through Marital Sexual Contacts

The model includes long-term partnerships for both heterosexual and homosexual pairings. Transmission is the product of infectivity times susceptibility, and there are appropriate formulations for the heterosexual and bisexual/homosexual components of
long-term pairing transmission. In particular, the model allows susceptibility and infectivity to vary with sexual preference.

Let:

- TRNS: transmission
- SUS: heterosexual susceptibility
- INF: heterosexual infectivity
- BHS: bi-hetero scalar
- HO: subscript for homosexuals
- HE: subscript for heterosexuals

For strictly heterosexual pairs:

\[ TRNS = SUS_{HE} * INF_{HE} \]

For strictly homosexual pairs:

\[ TRNS = SUS_{HO} * INF_{HO} \]

For bisexuals, the proportion currently in long-term heterosexual as opposed to homosexual pairings are set in a bi-hetero scalar (BHS) and transmissions is computed:

\[ TRNS = ((1 - BHS) * INF_{HO} * SUS_{HO}) + (BHS * INF_{HE} * SUS_{HE}) \]

Next, compute the sexual contacts within long-term partnerships by multiplying the age-specific paired heterosexual contact rates by sex and integrating over age (A) from age at first marriage (A<i>) to last age of marriage (A<n>). This is done separately for uninfected contacts (TU<hetC>M and TU<hetC>F) and infected contacts (TI<hetC>M and TI<hetC>F). For contact balancing purposes, we calculate a heterosexual harmonic scale (HHS).

We compute the age-specific heterosexual infectivity per contact as follows.

Let:

- HIPC: heterosexual infectivity per contact
- T<hetC>opp: total heterosexual contacts for the opposite sex
- I<hetC>opp: infected heterosexual contacts for the opposite sex
- DPCR(A): desired partner contact rate

\[ HIPC(A) = \frac{T_{hetC_{opp}}(A) * I_{hetC_{opp}}(A)}{DPCR(A) * T_{hetC_{opp}}(A)} \]

Next incorporate the partner age offsets.
Let:

- \( MPDA(A) \): mean partner desired age function
- \( OE(A) \): offset exponential function
- \( SP \): scaling product

\[
1 \quad r = \frac{\text{------------------------}}{MPDA(A) - A_{i+1}}
\]

\[
\text{OE}(A) = r \times e^{A_n}
\]

\[
\text{HIPC}''(A) = \int_{A_i} OE(A) \times SP \, dA
\]

2. **Infections Through Casual Sexual Contacts.**

Computing casual sex contacts is considerably more complex than paired contacts, because the computations involve additional dynamics such as inter-regional contacts or concurrent partners.

a. Initialize the co-circular migration scalars.

Co-circular migration is the temporary movement of people from one sector to another, such as migrant labor or students. Sexual contacts while absent from their primary environment create a diffusion of sexual mixing patterns across regions.

Let:

- \( CMS \): migration scale
- \( CMD \): the migration duration (proportion of year spent in another sector)
- \( CMR \): migration rate
- \( CMS' \): migration scale for target sector

\[
CMS(A) = 1 - CMD(A) \times CMR(A)
\]

\[
CMS'(A) = CMD(A) \times CMR(A)
\]

b. Now compute the total number of casual contacts
Let:

- NCG: number of contacts for a (status) group
- GP(A): group population
- CMS(A): circular migration scale for the region,
- GR(A): group risk

\[ \text{NCG}(A) = \text{GP}(A) \times \text{CMS}(A) \times \text{GR}(A) \]

IV drug use is separated into opiate use, stimulant use, or both. Each of these categories allows a separate multiplier on sexual contacts, and the number of contacts is modified accordingly.

- IVS: IV scaling type (infected or uninfected)
- TP: total population
- IVBS: IV behavior scalar

\[ \text{IVS} \quad \text{NCG}'(A) = \text{NCG}(A) \times (1 + \frac{\text{IVBS} - 1}{\text{TP}}). \]

Input to iwgAIDS allows the user to divide concurrent partners into long-term partnerships, shorter-term partnerships, and single encounters. To concatenate these, let:

- SEP: single encounter proportion
- CPI: number of concurrent partners for the given population group
- CP: number of concurrent partners
- CRI(A): concurrent risk infectivity
- A: age
- IN: infectivity

\[ \text{CP} = 1 + \text{SEP} \times (\text{CPI} - 1) \]

\[ \text{CRI}'(A) = \frac{\text{CP} \times (1 - e^{-A \times \text{IN}/\text{CP}})}{A \times \text{IN}} \]

Infectivity is separately calculated for homosexual, heterosexual, and bisexual concurrent partners:

- IN: infected
- S: susceptibility
- HS: bi-hetero scalar.

\[ \text{IN}(A) = \text{homoIN}(A) \times \text{homoS}(A) \]
IN(A) = heteroIN(A) * heteroS(A)

IN(A) = HS*heteroIN(A)*heteroS(A) + (1 - HS)*homoIN(A)*homoS(A)

Let:

GR group risk
GP group population

\[
GR(A) = \int_{-\infty}^{\infty} (MRD(A) * CRI(A) * GP(A))dA
\]

where an optional mean risk decay is defined as

\[
MRD(A) = e^{-A}
\]

And finally, update the number of contacts (NCG) for each status group by multiplying the old number of contacts by group risk (GR).

\[
NCG(A) = NCG(A) * GR(A)
\]

c. Incorporate casual partner preference.

Separate loops are computed for heterosexual, homosexual, and bisexual age preferences, and each for infected and uninfected subpopulations. After within region contacts are calculated, the between region contacts are calculated using the appropriate migration rates for the target region. The heterosexual form for within region contacts is as follows.

Let:

L desired age lag
MDPA mean desired partner age
RC regional contacts
A age

\[
MDPA(A) = \begin{cases} 
0 & \text{if } A < A_1 \text{ (the age at the first marriage)} \\
\max(L + A, A_1) & \text{if } A \geq A_1 
\end{cases}
\]

\[
A_1 - 1 + A
\]

---------------------

MDPA(A) - A_1 + 1
\[ RC'(A) = RC(A) \frac{e}{MDPA(A) - A_1 + 1} \]

DPCR: desired partner contact rate  
CN(A): number of heterosexual contacts

\[ DPCR(A) = \int_{A_1}^{A_2} RC(A) \quad \text{(for } A > A_1) \]

\[ CN(A) = CN(A) + DPCR(A). \]

d. Cross-Region Infections

Infections in one region attributed to sexual contacts with circular migrants from another region are calculated as follows.

NI(A): new infections  
UI(A): uninfected population  
CRM(A): circular migration scalar  
UIR(A): uninfected population risk

\[ NI(A) = UI(A) * CRM(A) * UIR(A) \]

A special form of cross-regional contact is transitory migration, such as pass through truck drivers, who bring special life style considerations to the cross-region infections rather than temporary changes in physical location.

Let:

HRTM(A): high risk total population for nth group  
A_1: age of the first marriage  
A_2: last age  
A: age  
TP: total population (of a region)  
CN(A): total number of contacts  
HRMC(A): mean number of high risk contacts

For high risk:

\[ CN(A) = HRMC(A) * HRTM(A) \]
HRMC = \int_{A_1}^{A_2} CN(A)dA

A similar loop is performed for low risk contacts and the total mean contacts per region are adjusted accordingly.

e. NI(A) is further updated if there are sex feedbacks from IV drug use or from the use of prophylactic vaccines. Additional updates are added for homosexual mixing subroutines. Yet another update is introduced for transitory migration. These modifications are not presented here.

f. Infections through IV drug transmission

The impact of cross-region infections is also incorporated into IV drug user HIV incidence rates.

Let:

\begin{align*}
\text{UI}_{IV} & \quad \text{uninfected IV population} \\
\text{I}_{IV} & \quad \text{infected IV population} \\
\text{INC}_{IV} & \quad \text{IV incidence} \\
\text{IVS} & \quad \text{IV scalar}
\end{align*}

\begin{align*}
\frac{d}{dA} \text{UI}_{IV} (A) = \frac{d}{dA} \text{UI}_{IV} (A) - \text{NI}(A) \\
\frac{d}{dA} \text{I}_{IV} (A) = \frac{d}{dA} \text{I}_{IV} (A) + \text{NI}(A) \\
\text{INC}_{IV} (A) = \text{INC}_{IV} (A) + \text{NI}(A)
\end{align*}

Other steps (not shown) include updates to the uninfected IV frequency, group size, uninfected group change probability, and uninfected bleach probability.

g. Additional updates (not shown) include changing infected risk, infection duration, and infection duration variance, and the transfer of partners to infected status.
3. Computing The Condom And STD Scales

The iwgAIDS program separates condom use by risk status and sexual preference. These parameters are incorporated as follows.

Let:

<table>
<thead>
<tr>
<th>Variable</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>HRTC</td>
<td>high risk total condom use</td>
</tr>
<tr>
<td>LRTC</td>
<td>low risk total condom use</td>
</tr>
<tr>
<td>HRMC</td>
<td>high risk mean condom use</td>
</tr>
<tr>
<td>CUP</td>
<td>condom use proportion</td>
</tr>
<tr>
<td>UIG</td>
<td>number of uninfected people</td>
</tr>
<tr>
<td>IG</td>
<td>number of infected people</td>
</tr>
<tr>
<td>HPR</td>
<td>proportion of high risk population</td>
</tr>
<tr>
<td>LRMC</td>
<td>low risk mean condom use</td>
</tr>
<tr>
<td>LPR</td>
<td>proportion of low risk population</td>
</tr>
</tbody>
</table>

\[
\begin{align*}
\text{HRTC} &= \text{HRMC} + \text{CUP} \times (\text{UIG} \times \text{HRP} + \text{IG} \times \text{HRP}) \\
\text{LRTC} &= \text{LRMC} + \text{CUP} \times (\text{UIG} \times \text{LRP} + \text{IG} \times \text{LRP}) \\
\end{align*}
\]

The bisexual/homosexual scalar (BHS) is incorporated in the following illustration.

\[
\text{HRTC} = \text{HRMC} + \text{CUP} \times (1 - \text{BHS}) \times (\text{UIG} \times \text{HRP} + \text{IG} \times \text{HRP})
\]

\[
\text{HRTC} = \text{HRMC} + \text{CUP} \times \text{BHS} \times (\text{UIG} \times \text{HRP} + \text{IG} \times \text{HRP})
\]

To incorporate the STD transmission dynamic multiplier for sexual contacts, the STD contact acquisition is computed for every region and each group and separately for ulcerative and inflammatory sexually transmitted diseases.

Let:

<table>
<thead>
<tr>
<th>Variable</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>HRA</td>
<td>acquisition per contact rate for high risk</td>
</tr>
<tr>
<td>HRI</td>
<td>high risk infectivity</td>
</tr>
<tr>
<td>HRS</td>
<td>high risk susceptibility</td>
</tr>
<tr>
<td>HCU</td>
<td>condom use for the high risk population</td>
</tr>
<tr>
<td>HCS</td>
<td>condom success for the high risk population</td>
</tr>
<tr>
<td>A</td>
<td>age</td>
</tr>
</tbody>
</table>

\[
\text{HRA(A)} = \text{HRI} \times \text{HRS} - \text{HRI} \times \text{HRS} \times \text{HCU(A)} \times \text{HCS(A)}
\]

Similar loops are performed for low risk and for each type of STD.
In the iwgAIDS program, STDs can be cofactors on HIV infectivity and/or HIV susceptibility. To incorporate STDs as an infectivity cofactor across regions and status groups, do the following.

Let:

- PRC: STD prevalence cofactor
- PRU: ulcerative prevalence
- PRI: inflammatory prevalence
- RRU: ulcerative recovery rate
- RRI: inflammatory recovery rate.

\[
\frac{\text{PRU}(A) + \text{PRI}(A)}{\text{RRU}(A) \times \text{RRI}(A)}
\]

- RR: risk ratio
- RMCP: mean number of contacts (by region, group, preference)
- CM: mean number of contacts for the given region.

\[
\frac{\text{RMCP}}{\text{CM}}
\]

- P1: ulcerative probability
- PRU: ulcerative prevalence
- PRC: prevalence cofactor
- P2: inflammatory probability
- PRI: inflammatory prevalence
- PT: probability of being infected with both kinds
- ICU: ulcerative infectivity
- ICI: inflammatory infectivity
- A: age

\[
\begin{align*}
\text{P1}(A) &= RR \times (\text{PRU}(A) - \text{PRC}(A)) \\
\text{P2}(A) &= RR \times (\text{PRI}(A) - \text{PRC}(A)) \\
\text{PT}(A) &= RR \times \text{PRC}(A) \\
\text{P1}'(A) &= \text{P1}(A) \times (\text{ICU}(A) - 1) \\
\text{P2}'(A) &= \text{P2}(A) \times (\text{ICI}(A) - 1) \\
\text{PT}'(A) &= \text{PT}(A) \times (\text{ICU}(A) \times \text{ICI}(A) - 1)
\end{align*}
\]
Condom protection is eventually incorporated into a larger infectivity scalar (IS(A)). The condom protection component (condom protection scalar, or CS(A)) is described here.

- **CDP**: condom protection parameter
- **HCF**: HIV condom failure rate
- **CS(A)**: the condom scalar
- **MCU**: mean condom use
- **A**: age

CDP = 1 - HCF

CS'(A) = MCU * (-CDP) + 1

Incorporating STD as a cofactor on HIV susceptibility parallels the logic for infectivity (not shown). The result is a susceptibility scalar (SS(A)) that includes the multiplier effects of inflammatory and ulcerative STDs.

**Prophylactic Vaccines**

Because the iwgAIDS computer program is a multi-sector model, we begin by computing the mean efficacy of the vaccine. Let:

- **PSR(i)**: prophylactic susceptibility reduction for the ith region
- **ME**: mean efficacy
- **N**: number of regions

\[
\sum_{i=0}^{n} PSR(i)
\]

\[
ME = \frac{\sum_{i=0}^{n} PSR(i)}{n}
\]

The iwgAIDS program allows vaccination rates to differ by risk group; so next we obtain the mean vaccination rate.

Let:

- **PVR**: mean prophylactic vaccination rate
- **HR**: high risk population proportion
- **PVRH**: prophylactic vaccination rate for the high risk population
- **PVRL**: prophylactic vaccination rate for the low risk population

PVR(A) = PVRH(A) * HR(A) + PVRL(A) * (1 - HR(A))
Similarly, obtain the mean expiration rate of the vaccine across high and low risk populations.

Let:

- \( \text{PER} \) mean prophylactic expiration rate
- \( \text{HR} \) high risk population proportion
- \( \text{PERH} \) prophylactic expiration rate for the high risk population
- \( \text{PERL} \) prophylactic expiration rate for the low risk population.

\[ \text{PER}(A) = \text{PERH}(A) \times \text{HR}(A) + \text{PERL}(A) \times (1 - \text{HR}(A)) \]

In the simulations presented here, the vaccine treatment does not require a booster regimen, so we focus only on calculations for the derivatives of non-booster vaccination proportion and efficacy levels.

Define a decay rate function \( \text{DR}(A) \) for prophylactic vaccination.

Let:

- \( \text{DR}(A) \) decay rate function
- \( \text{PER} \) prophylactic expiration rate
- \( S \) projection step size
- \( A \) age
  (set \( \text{PVP}(A) \) to zero at left and right endpoints)

\[
\begin{align*}
\text{DR}(A) &= \frac{1 - 2^{-S}}{4} \quad \text{if } \text{PER}(A) < 0.01 \\
\text{DR}(A) &= \frac{1 - 2^{-S}/\text{PER}(A)}{4} \quad \text{otherwise}
\end{align*}
\]

And then evaluate the derivatives for proportion and efficacy level:

Let:

- \( \text{PVP}(A) \) prophylactic vaccination proportion
- \( \text{PVL}(A) \) prophylactic vaccination efficacy level
- \( \text{PVR} \) prophylactic vaccination rate
- \( \frac{d}{dt}(\text{PVP}(t)) \) derivative of \( \text{PVP} \) with respect to time.
- \( \text{ME} \) mean efficacy of the vaccine
- \( \frac{d}{dt}(\text{PVL}(t)) \) \( \text{PVL} \) as a function of time.
\[
\frac{d}{dt} PVP(t) = PVR(A) \ast (1-PVP(A)) - PVP(A) \ast DR(A)
\]

\[
\frac{d}{dA} PVL(A) = ME \ast \left( \frac{d}{dA} (PVP(A)) + PVP(A) \right) - PVL(A) + \frac{d}{dA} PVL(t)
\]

The overall proportion vaccinated and overall efficacy level are integrated over age.

Let:

\[A_i\] age at first marriage
\[A_n\] last age
\[PVP\] prophylactic vaccination proportion
\[UI\] number of uninfected people
\[UIR\] uninfected risk
\[PVL\] prophylactic vaccination level
\[PP\] prophylactic proportion
\[PL\] prophylactic level
\[A\] age

\[PP = \int_{A_i}^{A_n} (PVP \ast UI(A) \ast UIR(A)) dA\]

\[PL = \int_{A_i}^{A_n} (PVL \ast UI(A) \ast UIR(A)) dA\]

**Demographic Parameters**

The demographic parameters used in the iwgAIDS program focus (1) on forces affecting age-specific population volumes in a given region at a given point in time and (2) dynamics that change these forces over time. The standard demographic forces include (1.a) births, (1.b) deaths, (1.c) aging, and (1.d) migration. The latter category can be further subdivided into (1.d.1) people flows between populations included in the simulation and all other populations, (1.d.2) people flows between regions or sectors within the population, (1.d.3) seasonal population movements from one sector to another, and (1.d.4) transitory or pass-through population movements between one sector to another. These are labeled, respectively, (1.d.1) external migration, (1.d.2) internal
migration, (1.d.3) circular migration, and (1.d.4) transitory migration. The iwgAIDS program is a multi-sector program, so if circular migration or transitory migration between sectors inside the simulation and other non-simulated sectors are crucial to understanding disease diffusion dynamics, then these relevant sectors should be added to the set of simulated sectors.

Each of these forces can change over time. Fertility rates sometimes change dramatically, as witnessed in Thailand. Increased access to preventive medical care can change mortality rates, as occurred in many African environments in the mid-twentieth century. Migrations rates are particularly volatile when viewed on a time scale of a decade or more. Changes in local economies can initiate or alter migrant labor patterns, can draw new residents from rural to urban areas, and can change immigration patterns. Civil unrest and ethnic strife can also create large refugee movements. Many of these dynamics are directly relevant to the spread of a behaviorally born disease, because they typically disrupt older cultural patterns and open opportunities for mixing that would otherwise not have occurred.

Most urban populations around the world were not capable of sustaining their populations without replacements from rural migrants, so it should not be surprising that strong rural-to-urban migrations rates are found in developing areas like Africa. There is, in turn, a strong age bias associated with this migration. Young adults, often males without families, are disproportionately represented, although there are some important exceptions to this pattern (e.g. Indonesia, where there is a disproportionate young male migration into periurban labor areas and a disproportionate young female migration into the urban core for education and office work). There is remarkably little research on specific migration patterns and it is often the case that unmeasured migration rates are assumed to be zero.

The iwgAIDS program has a trapezoidal estimation routine that permits the comparison of serial censuses. Typically, movement into and out of the population due to births and deaths are most likely observed at the left (age zero to five) and right boundaries (the decades following child-bearing years) of the age spectrum. When comparing serial censuses and an abnormal shortage occurs in the middle range of the age spectrum, it suggests loss due to wars, civil unrest, or migration, and gain due to migration. Losses due to war are in turn generally more age-concentrated than losses due to civil unrest and refugee movements. (Changes in death rates due to AIDS are simulated directly in the program.) The serial estimation procedure cannot identify the specific cause of the abnormal population volume in the middle of the age spectrum for one or another region, but it can identify these anomalies. Taking the social and political history of the area into account, it is then possible to estimate the residual population volume rates-of-change that can be attributed to external or internal migration.

We examine two environments here: an urban African environment patterned after Kampala, Uganda, and an Asian environment patterned after Thailand. The Kampala simulation begins in 1991 and the Thai simulation in 1999. The Kampala
simulation utilizes data from the 1991 Uganda census and triangulated on its previous censuses (1980 and 1969). The Thai simulations begin with the 1990 census data and projected forward to the population figures estimated for Thailand in 1999. The Thai data triangulates on two previous censuses (1990 and 1980). The actual data used in the iwgAIDS simulations is a continuous distribution over age, so the user can choose any definite integral on the age spectrum for closer analysis. The transitory migration parameter is discussed further in the next section on epidemiological parameters. The following table provides a coarse look at the remaining age-specific demographic parameters used in the simulation runs reported here.

<table>
<thead>
<tr>
<th>Table 1: Demographic Parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population (1,000s)</td>
</tr>
<tr>
<td>---------------------</td>
</tr>
<tr>
<td><strong>Kampala</strong> 1991</td>
</tr>
<tr>
<td>0-4 132</td>
</tr>
<tr>
<td>5-14 182</td>
</tr>
<tr>
<td>15-24 207</td>
</tr>
<tr>
<td>25-34 155</td>
</tr>
<tr>
<td>35-44 61</td>
</tr>
<tr>
<td>45-64 38</td>
</tr>
<tr>
<td>65+ 9</td>
</tr>
<tr>
<td><strong>Thailand</strong> 1999</td>
</tr>
<tr>
<td>0-4 5,395</td>
</tr>
<tr>
<td>5-14 11,724</td>
</tr>
<tr>
<td>15-24 11,236</td>
</tr>
<tr>
<td>25-34 10,142</td>
</tr>
<tr>
<td>35-44 10,487</td>
</tr>
<tr>
<td>45-64 9,749</td>
</tr>
<tr>
<td>65+ 2,123</td>
</tr>
</tbody>
</table>

**Epidemiological Parameters**

There are several sets of epidemiological parameters in the iwgAIDS program. These include parameters governing sexual transmission, perinatal transmission, transmission during IV drug use, and blood transfusion transmission. The blood transfusion parameters became less important during the 1990s and hence will not be discussed in detail here. Sexual transmission in iwgAIDS includes heterosexual, homosexual, and bisexual transmission. The sexual transmission modules focus on four dimensions: frequency or sexual contact rates, partnership structure (the mix of long-term pairings and polygamy or polyandry, medium term concurrent partners, and single encounters), partner turnover rates, and preferences and practices.

In the iwgAIDS program, frequency of sexual contact is age-structured and also varies by type of partnership (long-term or married vs. shorter-term relationships and
one-night stands), sex, region, and sexual preference. Partner turnover rate is defined as the probability that, on the next sexual encounter what is the probability that it will be with a different person. Serially monogamous people will have low partner turnover rates, while sex workers will have very high partner turnover rates. The reciprocal of divorce rates serves as the measure of partner turnover in long-term partnerships, and these can be opposite sex or same sex. Infectivity and susceptibility can vary by partnership preference (homosexual or heterosexual). The program also incorporates cofactors for such sexual practices as dry sex (drying of the vaginal mucosa), anal sex (whether heterosexual or homosexual couples), and the absence of circumcision in men. The presence of ulcerative or inflammatory sexually transmitted diseases may also affect HIV infectivity or susceptibility. The parameters used in the two simulation sites were estimated from a host of sources, including the HIV/AIDS Surveillance archives from the International Programs Office, U.S. Bureau of the Census and the DHS surveys.

The transitory migration parameter discussed in the previous section is applied in an epidemiological context. The parameter is translated into epidemiological terms through two scalars: how many of the sexual contacts in one region are with people in another sector, and is the source sector’s risk structure reflected in the contacts or are high risk people more likely to be involved in the cross-sector sexual contacts. For the Kampala simulations, one percent of the sexual contacts are with people in a different sector and high risk people are twice as likely involved compared to their rates in the source sector. About two and a half percent of contacts are interregional in the Thai simulations but the risk structure is kept the same as the source sector. There are no homosexual/bisexual processes used in the Kampala simulation. Homosexual and bisexual rates are age-structured, but overall about a quarter of one percent of Thai males are estimated in these simulations to be homosexual and less than 1% bisexual.

Table 2 presents some key age-structured sexual mixing parameters for each simulation environment. The iwgAIDS program distinguishes high risk and low risk sexual behaviors and these in turn by marital status and sexual preference. Members of each risk category do not have the same sexual contact rates. Rather, for each risk category, the iwgAIDS program establishes a contact continuum based on a single-parameter entropy distribution. Thus, within a high-risk segment of the population, the actual contacts are distributed on a continuum with the mean risk as the central tendency of a function designed to maximize the contact variation within the risk category. For low risk means, the distribution is skewed to the right and for high risk means the distribution is skewed to the left. It is possible under this formulation that those toward the upper reaches of the low risk continuum overlap those toward the lower reaches of the high-risk continuum. This blurring of contact distributions by risk status provides for a maximally heterogeneous distribution of risk in the target population. Concurrent partners are separated by risk status, marital status, sex, and region. The figures in Table 2 present the grand averages for this and other basic parameters used in the simulation.
### Table 2: Epidemiological Sex Parameters

<table>
<thead>
<tr>
<th></th>
<th>% Married</th>
<th># Monthly Sex Contacts</th>
<th>% Divorcing</th>
<th>% High Risk</th>
<th>Concurrent Partners</th>
<th>Casual Turnover Rate</th>
<th>% Condom Use</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Kampala</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-4</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>5-14</td>
<td>1</td>
<td>0.25</td>
<td>1.5</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>15-24</td>
<td>43</td>
<td>9.25</td>
<td>1.9</td>
<td>13</td>
<td>1.1</td>
<td>0.18</td>
<td>19</td>
</tr>
<tr>
<td>25-34</td>
<td>74</td>
<td>5.65</td>
<td>1.9</td>
<td>25</td>
<td>1.19</td>
<td>0.28</td>
<td>13</td>
</tr>
<tr>
<td>35-44</td>
<td>71</td>
<td>4.5</td>
<td>1.9</td>
<td>22</td>
<td>1.11</td>
<td>0.23</td>
<td>9</td>
</tr>
<tr>
<td>45-64</td>
<td>62</td>
<td>2.85</td>
<td>2</td>
<td>22</td>
<td>1.04</td>
<td>0.2</td>
<td>6</td>
</tr>
<tr>
<td>65+</td>
<td>36</td>
<td>1.15</td>
<td>2</td>
<td>12</td>
<td>1</td>
<td>0.12</td>
<td>1</td>
</tr>
</tbody>
</table>

|                |           |                        |             |             |                     |                      |             |
| **Thailand**   |           |                        |             |             |                     |                      |             |
| 0-4            | 0         | 0                      | 0           | 0           | 0                   | 0                    | 0           |
| 5-14           | 0         | 1.18                   | 1.4         | 0           | 1                   | 0                    | 6           |
| 15-24          | 25        | 14.2                   | 2           | 14          | 1.13                | 0.34                 | 29          |
| 25-34          | 73        | 7.25                   | 2.5         | 27          | 1.22                | 0.36                 | 27          |
| 35-44          | 85        | 3.41                   | 1.4         | 16          | 1.12                | 0.27                 | 22          |
| 45-64          | 79        | 1.55                   | 1           | 11          | 1.04                | 0.21                 | 21          |
| 65+            | 50        | 0.37                   | 1           | 2           | 1                   | 0.15                 | 27          |

The Thai environment also includes IV drug use. The estimated age-specific usage rates are provided in Table 3. Other parameters for these runs assume that about 15% of injections are sterilized (e.g. bleached), that the partner sharing groups are small (averaging just over 2), that the mean of the injection continuum is about 300 injections a year, that about 5% of injections involve contaminated needles (before sterilization), and that the susceptibility to a contaminated needle is .5. Stimulant injectors are assumed to increase their sexual activity by 50% relative to their respective status group (paired, single, heterosexual, homosexual, low risk or high risk, etc.).

### Table 3: Epidemiological IV Drug Parameters

<table>
<thead>
<tr>
<th>IV drug user rate</th>
<th>0-4</th>
<th>5-14</th>
<th>15-24</th>
<th>25-34</th>
<th>35-44</th>
<th>45-64</th>
<th>65+</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-4</td>
<td>0</td>
<td>0.0021</td>
<td>0.0183</td>
<td>0.01</td>
<td>0.0036</td>
<td>0.0002</td>
<td>0</td>
</tr>
<tr>
<td>5-14</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15-24</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>25-34</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>35-44</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>45-64</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>65+</td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>
Vaccine Intervention Parameters

There are two core aspects that require exploration when simulating possible vaccine interventions: (1) characteristics of the vaccine and (2) those targeted for vaccination. Vaccine characteristics include whether they provide full or partial protection at the individual level, the efficacy of the vaccine at the aggregate level, the duration of the protection, and whether boosters are required to maintain protection. Full (take) vs. partial (degree) protection is important because the former effectively removes people from the susceptible pool, while partial (degree) protection alters susceptibility and hence transmissibility. Take protections can also be thought of as the maximum benefit flowing from vaccines, while degree provide minimum threshold estimates. Because these explorations search for the minimum expected gain from a vaccine intervention, the simulations that follow report “degree” formulations. Boosters are also extremely important, because they raise the issue of recapture of initial vaccinates as well as slippage even under “take” formulations if subsequent boosters are not administered. These simulations do not explore the booster issue, but this is certainly an area that merits further study.

Using degree formulations, these simulations explore three levels of efficacy: 50%, 75%, and 95%. Each of these efficacy levels is in turn characterized by three durations of effective protection: 5 years, 10 years, and 50 years (life time). The iwgAIDS program implements the duration as the half-life of the vaccine’s protection. Thus, 50% of the protectiveness will be lost by year five for the five year duration, 50% will lose protectiveness by year ten for the ten year duration, and 50% will lost effectiveness by year fifty for the fifty year duration. The resulting hazard function has an exponential decay that centers around the median rather than the mean. Graphs 1-3 illustrate the comparisons between efficacy and aggregate effectiveness for a simulated Kampala vaccine program aimed at all adults.

The top three lines in Graph 1 show the implementation of a vaccine to all adults in the Kampala environment, with a hypothetical start date of 1992. Just under a third of eligibles are vaccinated each year for five years, and then a maintenance vaccine program is implemented which vaccinates enough eligibles to match the population rate of natural increase (3.3%). Although adult eligibles are drawn from across the age spectrum, the heaviest concentration of new vaccinates occurs at the left boundary of adulthood, or people aging from adolescence to adulthood. The 95% efficacy vaccine has an effectiveness level that closely parallels the percent vaccinated, while considerable drop off occurs with the 50% efficacy vaccine.
Graph 1: Percent of Adults in Kampala Vaccinated and Effectively Vaccinated with a Vaccine of Five Years Duration and Efficacy of 50%, 75% and 95%

Note: UA50_05A has 50% effectiveness, 5-year duration; UA75_05 has 75% efficacy, 5-year duration; UA95_05 has 95% effectiveness, 5-year duration. “Relative percent” refers to the percentage of all adults that are vaccinated. “Relative percent, effective vaccinated” refers to the percent of all adults effectively vaccinated.

The same procedure is used to instantiate the runs in Graph 2. The exit associated with a ten year half-life is now slower than the five year implementation schedule for the initial vaccine program, and hence the overall percentage vaccinated is higher in the year where the maintenance program starts and the aggregate asymptote is also a couple percentage points higher. The same general pattern seen in Graph 1 occurs for effectiveness, but the aggregate effectiveness levels are again couple percentage points higher.
Graph 2: Percent of Adults in Kampala Vaccinated and Effectively Vaccinated with a Vaccine of Ten Years Duration and Efficacy of 50%, 75% and 95%

Note: UA50_10A has 50% effectiveness, 10-year duration; UA75_10 has 75% efficacy, 10-year duration; UA95_10 has 95% effectiveness, 10-year duration. “Relative percent” refers to the percentage of all adults that are vaccinated. “Relative percent, effective vaccinated” refers to the percent of all adults effectively vaccinated.

The asymptote for the 50-year half-life shown in Graph 3 is several percentage points higher than that in either Graph 1 or Graph 2. In the Kampala environment, with relatively modest life expectancy and a pyramidal population structure with large proportions of the population aging from adolescence to adulthood, the upper boundary of the asymptote is lower than would occur under a similar vaccine scenario but administered in a country with high life expectancies and a more rectangular population pyramid.
Graph 3: Percent of Adults in Kampala Vaccinated and Effectively Vaccinated with a Vaccine of Lifetime Duration and Efficacy of 50%, 75% and 95%

Note: UA50_50A has 50% effectiveness, lifetime duration; UA75_50 has 75% efficacy, lifetime duration; UA95_50 has 95% effectiveness, lifetime duration. “Relative percent” refers to the percentage of all adults that are vaccinated. “Relative percent, effective vaccinated” refers to the percent of all adults effectively vaccinated.

This discussion of vaccine characteristics has implicitly raised the second issue, namely those targeted for intervention. These simulations explore four scenarios. The adult vaccine scenario has just been described. The simulations explore three others as well: administering the vaccine to high-risk people, vaccinating teenagers, and vaccinating mothers in the child-bearing years. The high-risk implementation delivers a vaccine to high-risk individuals primarily between the ages of 15 and 45. The implementation ramps up in the early teen years and then ramps down after age 45. The implementation aims at 80% of high-risk eligibles over a five-year period and then maintains that level. Since risk status is age structured, the maintenance essentially
vaccinates young adults as they enter the risk-taking environment. In a life cycle model, people can change their risk status as they change their life situations, such as getting married. Aiming the vaccine at high-risk individuals means that, depending on the length of effective duration; previously high-risk people may carry their vaccinated status into lower risk life stations. Thus, the overall proportion of the adult population affected by this vaccine strategy will vary with the expected half-life of the vaccine. For five-year half-life in the Kampala environment, this translates into slightly less than half the overall adult population vaccinated, although the effectiveness level is much lower. For the fifty-year half-life, the aggregate percentage of the population vaccinated has an asymptote around 60%. It is important to note that the aggregate asymptote level will vary with the overall proportion of high risk people in the environment being simulated and the rates of moving into and out of high risk status over the life cycle from adolescence to old age.

The teenager vaccination scenario follows an implementation similar to the high-risk scenario, except that the focus is on teenagers. The vaccine ramps up in the pre-teen years, aims at 80% coverage over a five year period for teenagers, and then ramps down in the waning teen years. In this scenario, the overall proportion of the population vaccinated will be very sensitive to the duration of the vaccine. The maintenance program following the initial five-year implementation focuses on eligibles, but these are disproportionately drawn from the left boundary (aging of pre-teens into teenagers). Under the five-year half-life, there is only modest decay during the teen years, because the teen ages only cover a seven-year period, but there would be significant decay in young adulthood.

Life cycle is different from cohorts, because a cohort effect (e.g. following 13 year olds as they age through the population) is more akin to generation effects, but life cycle effects are more variable for the individual than would be a successive comparison of individuals across generation cohorts. In short, the generation effect is more homogeneous than the life cycle effect for individuals. Some generational change may occur in any society, but this type of change is slow compared to life cycle changes and successive year cohorts will not demonstrate that much difference from its predecessor or successor. Compare those glacial differences to those associated with the movement from single status to married status.

The mother series is instantiated similarly to the adult scenario. Only paired females are targeted. Approximately one-third of eligibles are vaccinated in each of the first five years, and then a maintenance campaign is set to vaccinate eligibles to match the population rate of natural increase (3.3%). Like the adult scenario, this pushes many of the maintenance vaccinations toward the left boundary, where young women first get married. The asymptote behaviors for females under this scenario are similar to those for the adult population. In environments where the pairing rates are low, then the upper boundary of the asymptote would decline accordingly.

The simulations thus have two generic patterns: those for adults and those for paired mothers attempt to achieve 60-65% coverage in five years and the teen series and
The high risk series attempt to achieve coverage closer to 80%. In the teen case, with vaccinations ramping up in the early teen years and ramping down in the waning teen years, the end result is that some of the teens vaccinated in the early years of the five year program have aged out of the teenage life period by the time the five year program reaches its initial conclusion. Because risk in the iwgAIDS model is highly age structured (greater risky behavior is associated with younger ages) and is sensitive to life cycle (changes in risk status associated with marriage, for example), a similar phenomenon occurs in the risk series. At the end of a five-year program for open (real demographic) systems as opposed to toy universe systems, a fifth of more of the targeted population would have aged out of the target group. (Separate this effect from the decline in vaccine effectiveness over the same time period.) One fifth of 80% is approximately 16%, or 80% - 16% = 64%, which parallels the targeted amount in the other two simulation series where the entrants leave the eligible pool largely through the effects of death or migration rather than aging.

Graph 4 compares the overall proportion of adults vaccinated in each of the four Kampala scenarios. The graphs use 10-year duration and 50% efficacy runs. Note that duration has a significant impact on the cumulating proportion of those vaccinated. Re-eligibility for another vaccine does not occur until the half-life (measured by the duration) of the vaccine. Graph 5 compares these same runs for the Thai scenarios. The different asymptotes in these examples display important comparative characteristics when simulating real demographic environments.

The life expectancy is relatively low in Kampala, and this, coupled with a strongly pyramidal population structure with large portions of the population at the youngest ages, acts as an upper boundary on the vaccinated proportion in the adult population under these scenarios. The Thai case has considerably higher life expectancies and a more rectangular population pyramid; the upper boundary of the long-term maintenance program for adults is correspondingly much higher. Because risk is correlated with age and there are proportionately fewer older people in the Kampala environment, the proportion of the adult population under the high-risk scenario reaches a higher level than that found in the corresponding Thai scenario. There are similarly proportionately more teens in the Kampala than Thai environment and, coupled with the illustrate ten year half life of the vaccine, the proportion of the adult population (defined as 15 years and older) rises higher in the Kampala than in the Thai scenarios. The relatively similar levels for the mother series reflects two counterbalancing differences. Fewer paired women survive past their child-bearing years in Kampala and women of child-bearing age represent most of the adult female population. Although the proportion of child-bearing women of the adult female population is smaller in the Thai scenario, those of child-bearing age are more likely to survive into the post-child-bearing years and here the duration of the vaccination protection keeps more vaccinated in the overall adult population.
Graph 4: Percent of Adults in Kampala Vaccinated When Programs are Targeted to All Adults (A), High-risk populations (H), Teenagers (T) or Mothers (M)

Note: All projections use a vaccine of 50 percent efficacy and 10 year duration. UA50_10A targets all adults, UH50_10A targets high-risk populations, UT50_10 targets teenagers and UM50_10 targets mothers.
Graph 5: Percent of Adults in Thailand Vaccinated When Programs are Targeted to All Adults (A), High-risk populations (H), Teenagers (T) or Mothers (M)

Note: All projections use a vaccine of 50 percent efficacy and 10 year duration. TUA50_10A targets all adults, TH50_10A targets high-risk populations, TT50_10 targets teenagers and TM50_10 targets mothers.

Behavioral Reversions

One fear associated with vaccine strategies is that they may promote a false sense of security and lead to behavioral reversions such as reduced condom use or increased partner turnover than essentially cancels out the gains of a prophylactic vaccine. Two such scenarios are examined here. The first of these scenarios explores what would happen if condom use were to decline by 50%. This effect is implemented early in the vaccine delivery phase (the first year of the five year implementation). This was done for two reasons. The false sense of security relates as much to the promise as to the performance of the vaccine trial, and hence it is perhaps optimistic to expect the behavior reversion to occur as slowly as the vaccine implementation scenarios. Second, this gives an outer boundary for the potential impact of the behavioral reversion, and hence any overall gain from the vaccine, despite behavioral reversion, would be the minimum expected at the specified levels of vaccine efficacy, duration, and condom use.
The second scenario explores a reversion in casual partner turnover rates. The scenario explores what would happen if these rates were to double from their current social levels. Like the condom experiment, the casual partner turnover reversion takes place in the first year of the five-year vaccine implementation, and for the same reasons outlined for the condom reversion scenario.

**Alternate Intervention Parameters**

Vaccines are one of a set of possible public health interventions designed to ameliorate the impact of the HIV/AIDS pandemic. Older strategies include the promotion of condom use, behavioral changes such as the reduction in concurrent partners or reduction in partner turnover rates, aggressive control of other sexually transmitted diseases to reduce the cofactor impact on HIV transmission, and efforts to reduce mother-to-child transmission. Within each of these categories there are a host of alternate targets and strategies. Sample illustrations are drawn from each category in order to compare the effectiveness of these strategies with vaccines.

There are two ways of thinking about condom interventions. An idealistic form would be to encourage a particularly population subgroup to use condoms on all sexual encounters. This is roughly equivalent to the “take” formulation for vaccines that provide complete or near complete protection for the particular target group. A more realistic conception of condom interventions is akin to the vaccine degree approach, where the strategy is to get a certain proportion of sexual acts protected with condoms, permitting individuals to occasionally fail to use the condom even though that is their normal intention.

The condom simulations explore here focus on two targets under a “take” and “degree” scenario, respectively. The first “degree” scenario (c1) simulates condom use increase from the given social level in the environment under study up to 70% of single high-risk groups and 60% of paired high risk over a five-year period and then maintains those levels. The second “degree” scenario (c2) increases condom use among low risk people to 20% over a five-year period and then maintains those levels. The first “take” formulation (c1t) essentially removes 70% of single high-risk contacts and 60% of paired high risk contacts from the transmission pool. The second “take” formulation (c2t) essentially removed 20% of low risk contacts from the transmission pool.

The simulations explore two behavioral change scenarios unrelated to condom use. The first is to reduce concurrent partners (CC) to 85% of current levels. Concurrent partners might include polygamous relationships, a long-term partner and a lover, a long-term partner and a casual encounter, or a lover and a casual encounter. The second (CPT) is casual partner turnover, or the probability that on the next encounter a relationship outside a long-term pairing is with a different person. This scenario similarly reduces the target parameter to 85% of current levels. (Changes in divorce rates or paired partner turnover (PPT) are not considered here.)
There are several ways to think of STD interventions as well. The scenarios here explore two basic forms and two targets. The first form is to alter the duration of an individual’s infectious lesion. This typically occurs with early medical intervention and, in the case non-symptomatic STDs, aggressive screening. The second form essentially alters the infectivity of each STD. This might occur with poorly self-administered treatment regimens, incomplete medical treatment regimens, etc. Thus, the first scenario (STD1) aims at an 80% reduction in the duration of an infectious lesion in high-risk patients over a five year period and then maintained at that level. The second (STD2) aims at a 20% reduction over five years for low risk patients. The third scenario (STD1t) reduces infectivity for high risk cases by 80% over a five year period and then maintains that level. The fourth scenario (STD2t) reduces infectivity for low risk cases by 20% over a five year period and then maintains that level.

The final alternate simulation explored here is a reduction in perinatal transmission by 20%, or to 80% of current social levels. There are a host of alternatives that can be explored here, including vertical transmission before or during delivery and subsequent transmission through breastfeeding. The simulation here only explores a reduction in transmission around the time of birth. The mother-to-child (MTC) scenario reduces perinatal transmission to 80% of current levels over a five-year period.

**Results**

**Vaccine Efficacy**

Graphs 6-7 compare different vaccine efficacies for a 10-year duration vaccine in the Kampala and Thai simulation environments, and for the adult vaccination scenario. Both graphs show reductions in cumulative HIV incidence with increasing vaccine efficacy. There is a larger initial gain in the Thai environment with the 50% efficacy vaccine, because the overall prevalence at the start of the simulation is considerably less in the Thai than that in the Kampala environment. Graphs 8-9 repeat the same efficacy comparisons for the high-risk vaccine scenarios. Graphs 10-11 do this for the teen vaccine scenario, and Graphs 12-15 do the same for the mother scenario. The vaccine is administered to one sex in the mother scenario, and so it is necessary to examine the impact on the sexes separately.

The various Kampala series illustrate some interesting changes across scenarios. In the adult series, each efficacy level adds greater suppression to the cumulative HIV incidence curve (Graph 6). Not only does the high risk have less impact on cumulative HIV incidence, but also the efficacy levels illustrate less separation (Graph 8). In the teen series (Graph 10), the lowest efficacy level only modestly suppresses the cumulative HIV incidence. There is, conversely greater efficacy separation for females in the Kampala mother series (Graph 12), and there is even a respectable feed through to males in that series.
The Thai patterns illustrate considerable efficacy separation in the adult (Graph 7), high-risk (Graph 9), and teen series (Graph 11). The Thai mother series (Graph 13) show less relative efficacy separation than Kampala (Graph 12). The respectable feed through to males found in the Kampala series (Graph 14) is not only marginalized in the Thai case (Graph 15), but the lower efficacy vaccine ultimately leads to higher cumulative male HIV incidence.

These findings raise some interesting questions. Why do we see less efficacy separation in the Kampala high-risk than in the Thai high-risk scenarios? Why does the lower efficacy level in the teen series lose so much leverage in Kampala when compared to Thailand? And why does the mother series provide better leverage in the Kampala than in the Thai environment?

The differential efficacy separations for the high-risk scenarios reflect in part the different prevalence levels in the two environments. The Kampala epidemic has moved outside the high-risk environment into the lower risk environments, and delivering vaccines to the high risk environments alone is akin to boarding a train while it is pulling out of the station. The same issue helps explain the limited leverage of low efficacy vaccines in the Kampala teen series. Because the age-structured risk is quite high among adolescents, the passage through adolescence provides ample opportunity for infection, and modest levels of efficacy are limited in their ability to arrest transmission.

The mother series fares better in Kampala than in Thailand in part because of some core demographic differences between the two environments. In the Kampala environment, there is greater compression of various target groups. The lower life expectancy, high birth rates, and strongly pyramidal population structure puts extraordinary weight on transmission dynamics nearer the left boundary of the adult age spectrum (15 years of age and older). Relatively early age at first marriage adds to this social compression. Intervening with paired females in the Kampala environment focuses proportionately more effort on very young adults than is found under the same scenario in Thailand.

A final issue focuses on the potential for long-term greater cumulative HIV cases among Thai males under the low efficacy mother scenario. That there might be little or no feed through from women to men under the low efficacy scenario is not all that surprising, but the simulated finding that more men might be infected than without the vaccine strategy may seem a bit perplexing. A look at the age-structure of infected males shows that most of this gain occurs in the 30-something ages. These males in turn are paired to an uninfected spouse but have higher infection rates in the mother scenario than in no vaccine scenario. Further checks eliminate both IV drug and homosexual/bisexual transmission as a hidden variable. The increased transmission consequently is due to casual sexual encounters especially with high-risk single women. Further analysis shows an increase in infections among single high-risk women, and this in turn appears to have been driven by married infected men whose spouses were not infected. In the demographic dynamics, there were slightly more single women in the mother vaccine
scenario than in the standard scenario, resulting in a sufficiently expanded risk pool to generate a greater epidemic.

Graph 6: Cumulative HIV Incidence in Kampala with Vaccines Efficacies of 50%, 75%, and 95% Compared to No Vaccine

Note: U1 is the base case with no vaccine. UA50_10 is a vaccine of 50% efficacy and 10 years duration. UA75_10 is a vaccine of 75% efficacy and 10 years duration. UA95_10 is a vaccine of 95% efficacy and 10 years duration.
Graph 7: Cumulative HIV Incidence in Thailand with Vaccines Efficacies of 50%, 75% and 95% Compared to No Vaccine

Note: T1 is the base case with no vaccine. TA50_10 is a vaccine of 50% efficacy and 10 years duration. TA75_10 is a vaccine of 75% efficacy and 10 years duration. TA95_10 is a vaccine of 95% efficacy and 10 years duration.
Graph 8: Cumulative HIV Incidence in Kampala with Vaccines Efficacies of 50%, 75% and 95% Targeted at High-risk Populations Compared to No Vaccine

Note: U1 is the base case with no vaccine. UH50_10 is a vaccine of 50% efficacy and 10 years duration. UH75_10 is a vaccine of 75% efficacy and 10 years duration. UH95_10 is a vaccine of 95% efficacy and 10 years duration.
Graph 9: Cumulative HIV Incidence in Thailand with Vaccines Efficacies of 50%, 75% and 95% Targeted at High-risk Populations Compared to No Vaccine

Note: T1 is the base case with no vaccine. TH50_10 is a vaccine of 50% efficacy and 10 years duration. TH75_10 is a vaccine of 75% efficacy and 10 years duration. TH95_10 is a vaccine of 95% efficacy and 10 years duration.
Graph 10: Cumulative HIV Incidence in Kampala with Vaccines Efficacies of 50%, 75% and 95% Targeted at Teenagers Compared to No Vaccine

Note: U1 is the base case with no vaccine. UT50_10 is a vaccine of 50% efficacy and 10 years duration. UT75_10 is a vaccine of 75% efficacy and 10 years duration. UT95_10 is a vaccine of 95% efficacy and 10 years duration.
Graph 11: Cumulative HIV Incidence in Thailand with Vaccines Efficacies of 50%, 75% and 95% Targeted at Teenagers Compared to No Vaccine

Note: T1 is the base case with no vaccine. TT50_10 is a vaccine of 50% efficacy and 10 years duration. TT75_10 is a vaccine of 75% efficacy and 10 years duration. TT95_10 is a vaccine of 95% efficacy and 10 years duration.
Graph 12: Cumulative HIV Incidence Among Females in Kampala with Vaccines Efficacies of 50%, 75% and 95% Targeted at Mothers Compared to No Vaccine

Note: U1 is the base case with no vaccine. UM50_10 is a vaccine of 50% efficacy and 10 years duration. UM75_10 is a vaccine of 75% efficacy and 10 years duration. UM95_10 is a vaccine of 95% efficacy and 10 years duration.
Graph 13: Cumulative HIV Incidence Among Females in Thailand with Vaccines Efficacies of 50%, 75% and 95% Targeted at Females Compared to No Vaccine

\[ \times 10^5 \]

Note: T1 is the base case with no vaccine. TM50_10 is a vaccine of 50% efficacy and 10 years duration. TM75_10 is a vaccine of 75% efficacy and 10 years duration. TM95_10 is a vaccine of 95% efficacy and 10 years duration.
Graph 14: Cumulative HIV Incidence Among Males in Kampala with Vaccines Efficacies of 50%, 75% and 95% Targeted at Mothers Compared to No Vaccine

Note: U1 is the base case with no vaccine. UM50_10 is a vaccine of 50% efficacy and 10 years duration. UM75_10 is a vaccine of 75% efficacy and 10 years duration. UM95_10 is a vaccine of 95% efficacy and 10 years duration.
Graph 15: Cumulative HIV Incidence Among Males in Kampala with Vaccines Efficacies of 50%, 75% and 95% Targeted at Mothers Compared to No Vaccine

Note: T1 is the base case with no vaccine. TM50_10 is a vaccine of 50% efficacy and 10 years duration. TM75_10 is a vaccine of 75% efficacy and 10 years duration. TM95_10 is a vaccine of 95% efficacy and 10 years duration.
**Efficacy and Decay**

Graphs 16-17 take the two extreme efficacies (50% and 95%) in the adult scenarios and compare the impact of changing vaccine durations (5 year half life, 10 year, and 50 year) in each of the simulated environments, respectively. Duration provides little leverage in the adult scenarios, when compared to efficacy, in either environment. Graphs 18-19 show the same comparisons for the teen scenarios. Duration does leverage noticeable separation in the HIV cumulative incidence curves in the teen scenarios for Kampala, and for the 50-year half-life in the Thai environment.

In life cycle models that are designed to parallel status changes in individuals as they age, the higher transmission rates decline with age. The limited leverage that duration provides in the adult series reflects this dynamic, plus the fact that maintenance vaccines concentrate on left boundary entrants (young people moving into the adult category).

The teen series should be viewed as a censoring process on the adult dynamics. In the teen series, vaccines are limited to teenagers, and the primary focus of maintenance would be on children entering into the teen years, rather than adolescents entering into adulthood. Risk continues in both environments into young adulthood and is then mitigated by long-term pairing. A vaccine that has longer duration will essentially cover these early adulthood years as well, even those these people are not revaccinated or are not eligible for the vaccine program. The greater separation in the Kampala than in the Thai environment reflects the difference in overall prevalence between the two environments. The extra separation for the 50-year half-life in the Thai environment again focuses attention on the role of sex workers for middle age married men. While a 10-year duration would not provide protection for the 30-something population, the life-long vaccine would.
Graph 16: Cumulative HIV Incidence Among Adults in Kampala with Vaccines Efficacies of 50% and 95% and Durations of 5 Years, 10 Years and Lifetime

Note: UA50_05A is 50% efficacy and 5 years duration. UA50_10A is 50% efficacy and 10 years duration. UA50_50A is 50% efficacy and lifetime duration. UA95_05A is 95% efficacy and 5 years duration. UA95_10A is 95% efficacy and 10 years duration. UA95_50A is 95% efficacy and lifetime duration.
Graph 17: Cumulative HIV Incidence Among Adults in Thailand with Vaccines Efficacies of 50% and 95% and Durations of 5 Years, 10 Years and Lifetime

Note: TA50_05A is 50% efficacy and 5 years duration. TA50_10A is 50% efficacy and 10 years duration. TA50_50A is 50% efficacy and lifetime duration. TA95_05A is 95% efficacy and 5 years duration. TA95_10A is 95% efficacy and 10 years duration. TA95_50A is 95% efficacy and lifetime duration.
Graph 18: Cumulative HIV Incidence Among Teenagers in Kampala with Vaccines Efficacies of 50% and 95% and Durations of 5 Years, 10 Years and Lifetime

Note: UT50_05A is 50% efficacy and 5 years duration. UT50_10A is 50% efficacy and 10 years duration. UT50_50A is 50% efficacy and lifetime duration. UT95_05A is 95% efficacy and 5 years duration. UT95_10A is 95% efficacy and 10 years duration. UT95_50A is 95% efficacy and lifetime duration.
Graph 19: Cumulative HIV Incidence Among Teenagers in Thailand with Vaccines Efficacies of 50% and 95% and Durations of 5 Years, 10 Years and Lifetime

Note: TT50_05A is 50% efficacy and 5 years duration. TT50_10A is 50% efficacy and 10 years duration. TT50_50A is 50% efficacy and lifetime duration. TT95_05A is 95% efficacy and 5 years duration. TT95_10A is 95% efficacy and 10 years duration. TT95_50A is 95% efficacy and lifetime duration.

Behavioral Reversions

Graphs 20-21 report the impact of various behavioral reversions in the adult series when coupled with the standard vaccine scenario (50% efficacy with a 10 year half-life). The condom behavioral reversion is set a 50% of current rates and the casual partner turnover reversion is set at twice the current rate. Where condom use is initially low, as in Kampala, the reversion does not have a strong impact on cumulative HIV incidence (Graph 20). Where condom use is modestly higher, however, a reversion to lower levels
of condom use has a more discernible impact on cumulative HIV incidence (Graph 21). There are more serious consequences for casual partner turnover. In both environments examined, this reversion seriously erodes the gains made under the standard vaccine scenario. In the Thai case (Graph 21), the behavioral reversion nearly eliminates the leverage gained from the vaccine scenario.

Graphs 22-23 examine the impact of various behavioral reversions in the high-risk series coupled with high vaccine efficacy with a ten-year half-life. Casual partner turnover reversions resemble the adult series in the erosive effect on cumulative HIV incidence. In contrast to the adult series, however, condom reversion even under conditions of limited condom use (Graph 22) does erode the gains made by the high efficacy vaccine scenario. The same erosion does not appear in the Thai series (Graph 23).

This raises two related questions regarding condom reversion. Keep in mind that the condom change applies only to those groups receiving the vaccine and that there is considerably greater prevalence in the Kampala than in the Thai environment. Why does condom erosion appear in the adult Thai series but not in the high risk Thai series? Why does condom erosion appear in the high risk Kampala series but not in the adult Kampala series? There is a risk asymmetry between the sexes in Thailand that is substantially muted in Kampala. In the thirty-something phenomenon described earlier, there are a sizeable number of discordant pairs, with Thai males more often infected than their spouses. Condom erosion across adults puts these discordant spouses at risk. The vaccine dominates the high-risk transmission dynamic in this low prevalence environment. The paired partner asymmetry is far less marked in the Kampala environment, and the intervention opportunities focus more exclusively on (young) high risk because the infection status of spouses in this high prevalence environment are more likely concordant. Decreased condom use in concordant pairs is irrelevant to further spousal transmission, but decreased condom use among high-risk young, single adults is another opportunity lost in the battle against cumulative HIV incidence.
Graph 20: Cumulative HIV Incidence Among Adults in Kampala with and without Behavioral Reversal

Note: U1 is the base case with no vaccine. All other projections show the effects of a vaccine with 50% efficacy and 10 years duration. UA50_10A is no behavioral reversal. UCA50_10 is a reduction in condom use of 50% among those vaccinated. USA50_10 is a doubling of the partner turnover rate among those vaccinated.
Graph 21: Cumulative HIV Incidence Among Adults in Thailand with and without Behavioral Reversal

Note: T1 is the base case with no vaccine. All other projections show the effects of a vaccine with 50% efficacy and 10 years duration. TA50_10A is no behavioral reversal. TCA50_10 is a reduction in condom use of 50% among those vaccinated. TSA50_10 is a doubling of the partner turnover rate among those vaccinated.
Graph 22: Cumulative HIV Incidence Among Adults in Kampala with and without Behavioral Reversal when Vaccine is Targeted Toward High-risk Populations

Note: U1 is the base case with no vaccine. All other projections show the effects of a vaccine with 50% efficacy and 10 years duration. UH50_10A is no behavioral reversal. UHA50_10 is a reduction in condom use of 50% among those vaccinated. USH50_10 is a doubling of the partner turnover rate among those vaccinated.
Graph 23: Cumulative HIV Incidence Among Adults in Thailand with and without Behavioral Reversal when Vaccine is Targeted Toward High-risk Populations

*Note:* T1 is the base case with no vaccine. All other projections show the effects of a vaccine with 50% efficacy and 10 years duration. TH50_10A is no behavioral reversal. THA50_10 is a reduction in condom use of 50% among those vaccinated. TSH50_10 is a doubling of the partner turnover rate among those vaccinated.

**Alternate Interventions**

Graphs 24-25 examine alternate condom interventions in the Kampala and Thai environments, respectively. The two condom formulations that reduce the proportion of infectious exposures are the least effective in either environment. The condom formulations that essentially remove people from the sexual mixing pool through consistent coverage of all these people’s sex acts have far greater impact on cumulative HIV incidence. It should be noted, however, that the more successful formulations are also the more idealistic. There is a strong difference between the intention to use condoms more often and the commitment to use condoms all the time regardless of the
circumstances. It is under the latter scenario that the condom campaigns show their best impact on cumulative HIV incidence.

Graphs 26-27 look at behavior interventions and interventions in mother-to-child transmission. In the Kampala environment, with a high birth rate (Graph 26), the mother-to-child intervention has a noticeable impact on cumulative HIV incidence; in the Thai case (Graph 27), where the birth rate is much lower, the impact is quite marginal. Both reducing the number of concurrent partners and reducing the partner turnover rate have similar effects on the Kampala cumulative HIV incidence (Graph 26). Reducing partner turnover rates has greater leverage than reducing concurrent partners in the Thai environment (Graph 27). The distinction here is roughly equivalent to extra-marital affairs vs. one-night stands, with the latter representing considerably higher partner turnover. The thirty-something phenomenon described earlier involves these one-night stands.

Graphs 28-29 explore STD scenarios in the Kampala and Thai environment. There is little impact on cumulative HIV incidence that flows from STD interventions in the Thai environment, while each of the options explored has roughly similar impacts on reducing cumulative HIV incidence in Kampala. STDs act as multipliers on HIV transmission and their impact is statistically more easily seen in high prevalence than in lower prevalence environments. STD interventions early in an epidemic might help dampen the initial transmission chain among particularly high risk, but both these epidemics are mature and this window of opportunity has already passed.
Graph 24: Cumulative HIV Incidence Among Adults in Kampala with and without Condom Use

Note: U1 is the base case with no vaccine and no change in condom use. In UC1 condom use increases to 70% among single high-risk populations and to 60% among paired high-risk population. This includes both consistent and inconsistent use. In UC1T consistent condom use completely protects 70% of single high-risk people and 60% of paired high-risk people. In UC2 condom use increases to 20% among low risk populations. In UC2T consistent condom use completely protects 20% of low risk people.
Graph 25: Cumulative HIV Incidence Among Adults in Thailand with and without Condom Use

Note: T1 is the base case with no vaccine and no change in condom use. In TC1 condom use increases to 70% among single high-risk populations and to 60% among paired high-risk population. This includes both consistent and inconsistent use. In TC1T consistent condom use completely protects 70% of single high-risk people and 60% of paired high-risk people. In TC2 condom use increases to 20% among low risk populations. In TC2T consistent condom use completely protects 20% of low risk people.
Graph 26: Cumulative HIV Incidence Among Adults in Kampala with Behavior Change and PMTCT Programs

Note: U1 is the base case with no vaccine. In UCC the number of concurrent partners is reduced by 85%. In UCPT the rate of partner change is reduced by 85%. In UMTC the rate of perinatal transmission is reduced by 85%.
Graph 27: Cumulative HIV Incidence Among Adults in Thailand with Behavior Change and PMTCT Programs

Note: T1 is the base case with no vaccine. In TCC the number of concurrent partners is reduced by 85%. In TCPT the rate of partner change is reduced by 85%. In TMTC the rate of perinatal transmission is reduced by 85%. 

"Uninf, Cumulative HIV Incidence, T1.THF"
"Uninf, Cumulative HIV Incidence, TCC.THF"
"Uninf, Cumulative HIV Incidence, TCPT.THF"
"Uninf, Cumulative HIV Incidence, TMTC.THF"
Graph 28: Cumulative HIV Incidence Among Adults in Kampala with STI Treatment Programs

Note: U1 is the base case with no vaccine. In USDT1T the duration of STI infectiousness in high-risk populations is reduced by 80%. In USTD1T the infectivity of STIs in high-risk populations is reduced by 80%. In USTD2 the duration of infectiousness in low-risk populations is reduced by 20%. In USTD2T the infectivity of STIs in low-risk populations is reduced by 20%.
Graph 29: Cumulative HIV Incidence Among Adults in Thailand with STI Treatment Programs

Note: T1 is the base case with no vaccine. In TSTF1 the duration of STI infectiousness in high-risk populations is reduced by 80%. In TSTD2 the duration of infectiousness in low-risk populations is reduced by 20%.

Comparing Vaccines and Standard Interventions

Graphs 30-31 compare the four vaccine targets for low efficacy (50%) vaccines with a 10-year half-life. In both environments targeting the adult population has the greatest leverage on reducing cumulative HIV incidence. Targeting mothers in the Thai series has little impact (Graph 31) but it has greater impact in the Kampala environment (Graph 30). Targeting teens gives greater leverage than targeting mothers in the Thai environment (Graph 31), but the reverse occurs in Kampala (Graph 30). Vaccinating paired females in the Thai environment essentially only protects discordant females from infection by their spouse, but it does not protect single sex providers or married men seeking those services. In both environments the high-risk series performs second only to the overall adult target strategy.
Graphs 32-33 compare the adult vaccine strategy with low vaccine efficacy (50%) and a 10-year half-life. The STD interventions have little impact and were dropped from the Thai graph (Graph 33). The remaining comparisons have the same rank-order in both environments. The most effective intervention is the idealistic form of condom interventions designed essentially to remove a segment of the population from the infectious sexual mixing pool. The final intervention shown in both graphs is a reduction in casual partner turnover rate. In both environments this intervention also shows a respectable impact on reducing cumulative HIV incidence.

Graph 30: Cumulative HIV Incidence Among Adults in Kampala with Vaccines Targeted at All Adults, High-risk Populations, Mothers or Teenagers

Note: U1 is the base case with no vaccine. All projections use a vaccine with 50% efficacy and 10 years duration. UA50_10 is targeted at all adults. UH50_10A is targeted at high-risk populations. UM50_10A is targeted at mothers. UT50_10 is targeted at teenagers.
Graph 31: Cumulative HIV Incidence Among Adults in Thailand with Vaccines Targeted at All Adults, High-risk Populations, Mothers or Teenagers

Note: T1 is the base case with no vaccine. All projections use a vaccine with 50% efficacy and 10 years duration. TA50_10 is targeted at all adults. TH50_10 is targeted at high-risk populations. TM50_10A is targeted at mothers. TT50_10 is targeted at teenagers.
Graph 32: Cumulative HIV Incidence Among Adults in Kampala Comparing the Standard Vaccine with Condom Use, a Reduction in the Rate of Partner Change and STI Treatment

Note: U1 is the base case with no vaccine. All projections use a vaccine with 50% efficacy and 10 years duration. UA50_10 is targeted at all adults. UC2T shows the effects of consistent condom use of 20% among low risk populations. UCPT shows the effects of a 85% reduction in the rate of partner change. USTD2T shows the effects of a 20% reduction in STI infectivity among low-risk populations.
Graph 33: Cumulative HIV Incidence Among Adults in Thailand Comparing the Standard Vaccine with Condom Use, a Reduction in the Rate of Partner Change and STI Treatment

Note: T1 is the base case with no vaccine. All projections use a vaccine with 50% efficacy and 10 years duration. TA50_10 is targeted at all adults. TC2T shows the effects of consistent condom use of 20% among low risk populations. UCPT shows the effects of a 85% reduction in the rate of partner change.

Discussion

Computational modeling of HIV/AIDS provides several advantages over standard mathematical models. The computational model contained in the iwgAIDS program includes demographic as well as epidemiological processes that use a continuous age-structured model. Epidemiologically relevant parameters such as risk are allowed to vary with the life cycle of individuals. Computational models also allow multiple sectors (e.g. rural and urban) and population movement among these sectors. These population flows alter sexual mixing in both the source and target sector. These models do not require
equilibrium conditions, and indeed these models permit endogenous transformations of parameters under pressure, such as exploring the finite modes of transition for marriage rates when there is a shortage of one sex. The core tools of computational modeling include partial factorial sensitivity analyses that allow systematic search across many parameters to determine how sensitive a designated response surface may be to changes in these parameters. An equally important tool is process decomposition, where the a dynamic (e.g. IV drug use) in an environment can be turned on or off so that non-linear effects can be systematically decomposed.

Computational models are typically misconstrued as too complex or demanding too much data. If a problem is three or four dimensional, then a one or two-dimensional caricature that stays close to available data is hardly an appropriate fix. Caricatures or toy universes are in fact misleading, because they blind both the researcher and the consumer to non-linear complexities that may shed significant light on the problem under investigation, for which lower dimensional approximations are not simplifications but distortions. The complexity charge typically rests on assumptions of naive falsificationism (Popper, 1968). The appropriate framework for assessing complex models is the information theoretic approach; (Shannon & Weaver, 1949; Boudon, 1971; Seitz, 2000) Suppose we compare complex models to a structured item like a motorcycle helmet. Suppose in turn we compare simple models to a piece of cloth. If I take each of these items into a room, I will find many places where the cloth seems to fit. It can be draped over a chair, over a table, or across a radiator. The helmet on the other hand simply does not fit well on any of these surfaces. The cloth in this illustration has a high apriori probability of fitting where it is thrown. The helmet has a low probability. The cloth has considerably less information content than the helmet, because we can bet in advance that it will fit many places. The mark of a complex theory is that its apriori probability of fitting is very low; the test of complex theory is that is aposteriori fit is statistically unexpected.

Several years ago a claim was made that the iwgAIDS model did not fit the Thai environment. It is unclear what parameters or range of parameters was used in making that assertion, but a file prepared a decade ago for the Thai environment generated estimates of HIV infections within 45,000 cases of the current estimates. Incorporating known policy interventions with that old baseline file generated estimates within a few thousand of the currently estimated cases. The illustration raises two important considerations when examining a computational model designed to simulate real world epidemics. First, computational models of the behavioral universe do not have the same determinist precision as computational models of rocketry, because there is greater flux in the rules of the social universe than found in the rules of the physical universe. That said, however, the verisimilitude between computational models and the corresponding behavioral universe is well within an order of magnitude. Second, the social universe is always subject to interventions from which the physical universe is free. Policy makers typically do not alter the laws of gravity, but they can and do attempt to alter social and cultural processes.
The second point is important because the simulations examined here do not attempt to incorporate all on-going policy interventions in the two environments. Indeed, the vaccine scenarios were deliberately started at historical points in order to focus on the scenarios rather than on specific future case predictions. That exercise is possible, but it was not the intent of the analyses presented here. The analyses also present cumulative HIV incidence rather than HIV prevalence, because the latter is particularly sensitive to developments in therapeutic drugs that prolong the life of infected individuals. The analyses presented here assume that any changes in life expectancy for HIV-infected people will have no impact on additional HIV transmission due to their increased longevity. This assumption is a proper target of inquiry, but it is outside the scope of this paper.

The sizeable data inputs required by the iwgAIDS program can viewed as an obstacle or opportunity. The parameters needed are obstacles because the observational studies seldom speak “blf”, the file extender used for iwgAIDS baseline files. If demographic reports omit migration, for example, the data file preparation typically involves some trapezoidal estimations of these missing parameters to get a better first order fix on cross-sector population movements, even though they are difficult to observe directly. In the case of casual partner turnover rates, studies seldom ask “what is the chance that, on your next sexual encounter, it will be with a person different from your last encounter”. How many partners a person has had in the last six months is not an equivalent inquiry, yet the casual partner turnover rate is particularly important when factoring in the initial viral bursts immediately after infection (Seitz and Mueller, 1994). There is a many-to-one mapping between possible turnover rates and reported number of partners in a fixed period of time. In the iwgAIDS program, the prevalence of both ulcerative and inflammatory STDS is generated as a program output rather than a program input and hence these simulated levels can be checked against reported levels to see if we have gotten the sexual mixing picture “correct”.

The time and preparation required to build a baseline file is an obstacle, but it is also an opportunity to systematically examine the sometimes-contradictory information obtained in convenience samples and other non-generalizable data reports and triangulate on possible instantiations of an epidemiological environment at a given instant in time. Because computational models may contain hundreds of status groups (e.g., 19 year old single heterosexual males who inject opiates), there is a low apriori probability that picking and choosing parameter values will reproduce the infection details of these sub-populations unless the picture is reasonably coherent with the reality from which it is drawn. This is a common misunderstanding among non-modelers, who associate the number of parameters with degrees of freedom. If one only looks at aggregate totals, then it would be possible to mix and match parameters to produce the desired aggregate data but without much sub-group differentiation. To get the subgroup differentiation correct, given that these subgroups themselves have complex ties to other subgroups, moves attention back to the information theoretic perspective and the fact that changing any one
sub-population parameter has a low apriori probability of producing consistent results for other sub-groups affected by the target subgroup.

The simulations reported here examine only three efficacy levels and only three durations or half-life of protection. There are only four targeted groups examined as well. These combinations alone result in a considerable number of runs (3 x 3 x 4 = 36). The two behavioral reversions, coupled with the initial vaccine scenarios, produce 36 x 3 = 108 runs. Adding baseline and conventional interventions expands the number further. Add a second environment (e.g. Thailand) and the runs are doubled. Still, there are continua of efficacies and durations and other target groups that can be examined. The selections explored here are not meant to be exhaustive but illustrative of the interactive complexity of efficacy and target. Considerably more exploration is warranted here. There are almost certainly points of inflection in the various combinations of efficacy-duration-target where reductions in cumulative HIV incidence make faster or slower rates of change, and these in turn may likely vary with type of environment. Knowing where these points of inflection occur can provide invaluable background for policy makers.

The general finding reported here is nevertheless quite important. Vaccines, even those of low efficacy and moderate half-life, have a profound effect on reducing cumulative HIV incidence in quite different environments. These effects vary with targeting strategy, but the targets must be understood not as objects abstracted from their social context but as objects in social contexts. Viewed in this way it should be easy to understand that the relative effectiveness of targeting strategies may vary with demographic and epidemiological context, as illustrated with the teen, high risk, and mother series here. Equally important is the observation that the vaccine scenarios do well when compared to other, more traditional policy interventions. Only a particularly idealized form of condom intervention seems to outperform the modest efficacy vaccine strategy. Finally, behavior reversion is a potentially serious issue, but the extent of the setback must be assessed by target-in-context, such as increased casual partner turnover in the Thai adult environment.

References


*Demographic and health surveys*. http://www.measuredhs.com


