AIDS: Modeling a Global Crisis (and Australia)

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Summary

We introduce the state of the epidemic in six countries: Australia, South Africa, Honduras, Mexico, Ukraine, and India. We describe some previous models and develop a model that uses historical population, HIV data, and historical and projected birth-rate data from each country. The model isolates the population aged 15 to 49 for study. We use the model to predict the infection dynamics during the next half-century in the following situations:

- The disease is left unchecked to infiltrate the population.
- Anti-retroviral treatment (ART) is provided for those diagnosed.
- A vaccine is introduced in the year 2005.
- ART efficacy is affected by resistant disease strains.

We present simulation results and interpret what factors led to the observed trends.

Introduction

HIV infection is primarily spread through sexual exposure. At the global scale, in areas of highest HIV presence, heterosexual contact seems to be the primary mode of transmission, accounting for 70% of the overall sexual transmission cases [Gayle 2000].

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We build a mathematical model to approximate the expected rate of infections from 2005 to 2050 for a number of countries chosen from around the world. Next, we consider the effect of antiretroviral (ARV) drug therapies (ART) vs. a preventive vaccine on the spread of HIV, using current and projected economic resources. We then consider the possibility of an ART-resistant virus strain emerging and consider the effects on our previous conclusions. Finally, we determine the important characteristics of our models and conclusions to formulate a white paper to the UN giving our recommendations for allocation of resources.

We project the rate of HIV infection in Australia, Honduras, India, Mexico, South Africa, and Ukraine in the absence of treatment. ART for both mutating and non-mutating strains of HIV increases life expectancy and total population over time, as expected. While our model predicts that ART does little to prevent further spread of the disease, there is a strong humanitarian and economic argument for global ART.

Vaccination is the best solution, because ART does little to stop the spread of the infection. We include the effects of a vaccine in our model for the spread of AIDS in our target countries.

HIV Epidemic Model

Disease Epidemic Models

The SIR Model

One of the simplest models of infectious disease is the static SIR model, a nonlinear model that considers three classes of persons in a population: Susceptible, Infected, and Recovered.

$$\begin{aligned}\frac{dS}{dt} &= -\alpha SI,\\ \frac{dI}{dt} &= \alpha SI - \beta I,\\ \frac{dR}{dt} &= \beta I,\end{aligned}$$

where α is the rate of infective incidence (the probability of infection occurring upon contact times the number of contacts that occur in some time interval) and β is the rate of recovery of an infected individual.

Applied to HIV, this model assumes:

- a fixed population size. This model does not account for birth rates, death rates, the possibility that infected individuals may die more frequently, etc.
- a perfectly homogeneous population, with no individuals treating their infection or modifying their behavior in response to illness.

However, this model is inappropriate for HIV:

- Current HIV patients have no chance of recovery, since there is presently no cure for the HIV virus.
- The model assumes no incubation period and a constant infection load, both false for HIV [Hyman et al. 2003].

A Multistage Model

The staged-progression (SI) model is similar to SIR but takes into account some of these concerns. It accounts for temporal changes in the infectiousness of an individual by a staged Markov process of n infected stages, progressing from initial infection by HIV to development of AIDS [Hyman et al. 2003].

$$\begin{aligned}
\frac{dS}{dt} &= \mu(S^0 - S) - \lambda S, \\
\frac{dI_1}{dt} &= \lambda S - (\mu + \gamma_1) I_1, \\
\frac{dI_i}{dt} &= \gamma_{i-1} I_{i-1} - (\mu + \gamma_i) I_i, \qquad i = 1, ..., n, \\
\frac{dA}{dt} &= \gamma_n I_n - \delta A, \\
\lambda(t) &= \sum_{i=1}^{n} \lambda_i(t), \qquad \lambda_i(t) = \beta_i \frac{I_i(t)}{N(t)},
\end{aligned}$$

where

S is the number of susceptible individuals,

I_i is the number of infected individuals in stage i,

A is the number of infected individuals no longer transmitting the disease,

S^0 is the constant steady-state population maintained by the inflow and outflow when no virus is present in the population,

$\lambda(t)$ is the infection rate per susceptible individual,

r is the partner acquisition rate,

β_i is the probability of transmission per partner from infected individuals in stage i of the infection, and

γ_i is the rate at which individuals move from stage i of infection to stage $i + 1$.

All individuals enter group $i = 1$ upon infection.

Although this model incorporates a birth rate, it is constant. Most importantly, the model does not account for the effect that treatment may have on infectiousness of the treated group, though we may imagine the multiple infection rates β_i being modified to account for both treated and untreated groups, as we will do later.

Characteristics of the Desired Model

Dynamic algorithms have been implemented that explore sexual activity and the effects of social networks on the spread of HIV as well as the effect of changes in sexual behavior as a result of ART [Bauch 2002; Boily et al. 2004].

There is dispute over the net effect of ART. ART generally reduces the infectiousness of an individual [UNAIDS 2005b]. This reduction is normally thought to combine with the social impacts of an HIV diagnosis, that an individual should limit his/her sexual contacts, to greatly reduce the infectivity of a diagnosed HIV patient. However, further research suggests there are competing effects. Law et al. [2001] show that increases in sexual behavior and life expectancy could negate the beneficial impact of decreased infectiousness on total AIDS incidence. Furthermore, treated patients may increase the frequency of sexual activity due to the decreased severity of their symptoms—or maybe the opposite. For example, Ivory Coast individuals reported low sexual activity following HIV diagnosis and this was not increased by the offer of ART [Moatti et al. 2003]. We find this real-world result convincing.

We use concepts from all of these models (as well as the undiscussed differential infectivity (DI) model) to create a model using nonlinear differential equations similar to the SIR model but differing from it in the following ways:

- The time-scale of the epidemic necessitates that time-dependent birth and death rates be included in a realistic model.
- Behavior plays a critical role in the transmission of the disease. Individuals who are unaware of their infection are (debatably) more likely to transmit the disease than individuals aware of their infection.
- Age plays a role in the disease dynamics. The susceptible and infected people that can affect the disease dynamics are overwhelmingly between the ages of 15 and 49 [UNAIDS 2005b].

The model below incorporates all of these considerations:

$$\begin{aligned}
\frac{dS}{dt} &= b(t-t_0)S(t-t_0) - \mu S - \lambda S I_s^u - \lambda S I_r^u,\\
\frac{dI_s^u}{dt} &= \lambda S I_s^u - (\mu + v_s^u) I_s^u - \gamma_s I_s^u,\\
\frac{dI_s^T}{dt} &= \gamma_s I_s^u - (\mu + v_s^T) I_s^T - \alpha I_s^T,\\
\frac{dI_r^u}{dt} &= -\gamma_R I_r^u - (\mu + v_r^u) I_r^u + \lambda S I_r^u,\\
\frac{dI_r^T}{dt} &= \alpha I_s^T - (\mu + v_r^T) I_r^T + \gamma_r I_r^u.
\end{aligned}$$

The model extends the SIR model with concepts from the SI model and others. We use five categories of people aged 15 to 49:

Table 1.
Parameters and their symbols.

S	Population susceptible to infection
$b(t-t_0)$	Birth rate t_0 years ago of the susceptible population: e.g., $t_0 = 15$ to model 15 year-olds entering the sexually active pool
μ	Death rate of susceptible population
v_s^u	Increase in the death rate for the untreated population with the ARV-*sensitive* strain
v_r^u	Increase in the death rate for the untreated population with the ARV-*resistant* strain
v_s^T	Increase in the death rate for the population undergoing treatment with the ARV-*sensitive* strain
v_r^T	Increase in the death rate for the population undergoing treatment with the ARV-*resistant* strain
I_s^u	Population infected with the ARV-*sensitive* strain and untreated
I_r^u	Population infected with the ARV-*resistant* strain and untreated
I_s^T	Population infected with the ARV-*sensitive* strain seeking treatment
I_r^T	Population infected with the ARV-*resistant* strain seeking treatment
γ_s	Rate at which those with the ARV-*sensitive* strain seek testing and treatment
γ_r	Rate at which those with the ARV-*resistant* strain seek testing and treatment
λ	Transmission rate of either strain to the susceptible population
α	Rate at which treatment induces ARV-sensitive $\rightarrow$ ARV-resistant mutation

- susceptible,
- infected with a sensitive strain and not undergoing treatment,
- infected with a sensitive strain and with treatment,
- infected with a resistant strain and without treatment, and
- infected with a resistant strain and with treatment.

Not only do individuals in treatment have a different death rate from individuals not in treatment, but they also behave differently: There is no transmission from this group.

Assumptions

- Although the absolute assumption that treated individuals no longer transmit is markedly false [Baggaley et al. 2005], it seems that the change in sexual behavior in infected individuals who know they are infected has had a significant impact on the recent spread of the disease [UNAIDS 2005b] and hence the assumption represents a best-case scenario for combination ART-treatment and counseling.

- The projected birth rates given in literature for the next century, assuming medium fertility, are valid. Our model normalizes the healthy birth rates to the ratio of healthy individuals in society.
- We approximate that the infected populations will not contribute to the birth rates, because infected offspring will not have a significant chance to play a role [UNAIDS 2005b]. This simplifying approximation ignores the fact that without treatment, pregnant mothers only have a 35% chance of passing the disease to their children.
- Both strains of the virus, the ARV-sensitive and ARV-resistant, have equal transmission rates.
- No significant mass migrations, natural disasters, or other demographic-altering events occur.

Features of the Model

Some interesting effects that this model can address include:

- By setting $\gamma_S = \alpha = 0$ and $I_r^u(0) = I_r^T(0) = 0$, the model becomes equivalent to the unchecked dynamics of an SIR model with birth and death rates. We use this approach in analyzing Task #1.
- By setting $\alpha = 0$ and $I_r^u(0) = I_r^T(0) = 0$, treatment effects can be modeled that include extension of life due to treatment. Based on the magnitude of I_s^T during each year and data on the cost of treatment per individual per year, the model could then describe how much funding would be required to provide treatment to that ratio of the population. We use this approach in analyzing Task #2.
- The model adapts to treatment-resistant strains. The same economic analysis is then possible by using the magnitude of $I_s^T + I_r^T$ against the rest of the population. We use this approach in analyzing Task #3.

Critical Countries

Our choices of critical countries were influenced by the UNAIDS December 2005 update on the AIDS epidemic [UNAIDS 2005b]. Some criteria that we considered were:

- the percentage of the country's total population infected,
- the total number of AIDS cases,
- the current resources available to the government,

- the rate of growth of AIDS cases, and
- the effect of the specific country on the global AIDS epidemic.

We selected as critical countries in their respective continents South Africa, Ukraine, India, Honduras, Mexico, and Australia.

Projected Unchecked Infections

We determine the expected rate of change in the number of infections for our critical countries from 2005 to 2050 with no treatment or vaccine.

Model

We do not consider resistant strains nor any kind of treatment. Thus, in the general model, we set $\gamma_S = \alpha = 0$ and $I_r^u(0) = I_r^T(0) = 0$. This allows a great simplification in the accessible states of the system as well as the independent variables.

The most important assumption is change in behavior when a person becomes aware of their infection. For simplicity, the model presumes best-case: An individual will not knowingly risk infecting another.

Procedure

To obtain country-specific parameters of death rates and infection rates, we first set the HIV transmission to zero, input the birth-rate data for 1950–2005, then set the death rate to accurately reflect the population data for the country between 1990 and 2005. The death-rate acceleration term is chosen so that $\mu + v$ reflects the $1/e$ lifetime of a population with AIDS. We then adjust the transmission parameter λ to match the AIDS cases in the same time period and choose γ to reflect the average time to exhibit symptoms. Then we integrate the differential equations to extrapolate the total population, the total diagnosed population, and the total healthy population. The total infected and diagnosed population is considered to be equivalent to AIDS fatalities, since death occurs within a few years of the onset of symptoms in the absence of ARV treatment.

Results

We show in **Figure 1** the projections for the critical countries with no treatment or vaccine.

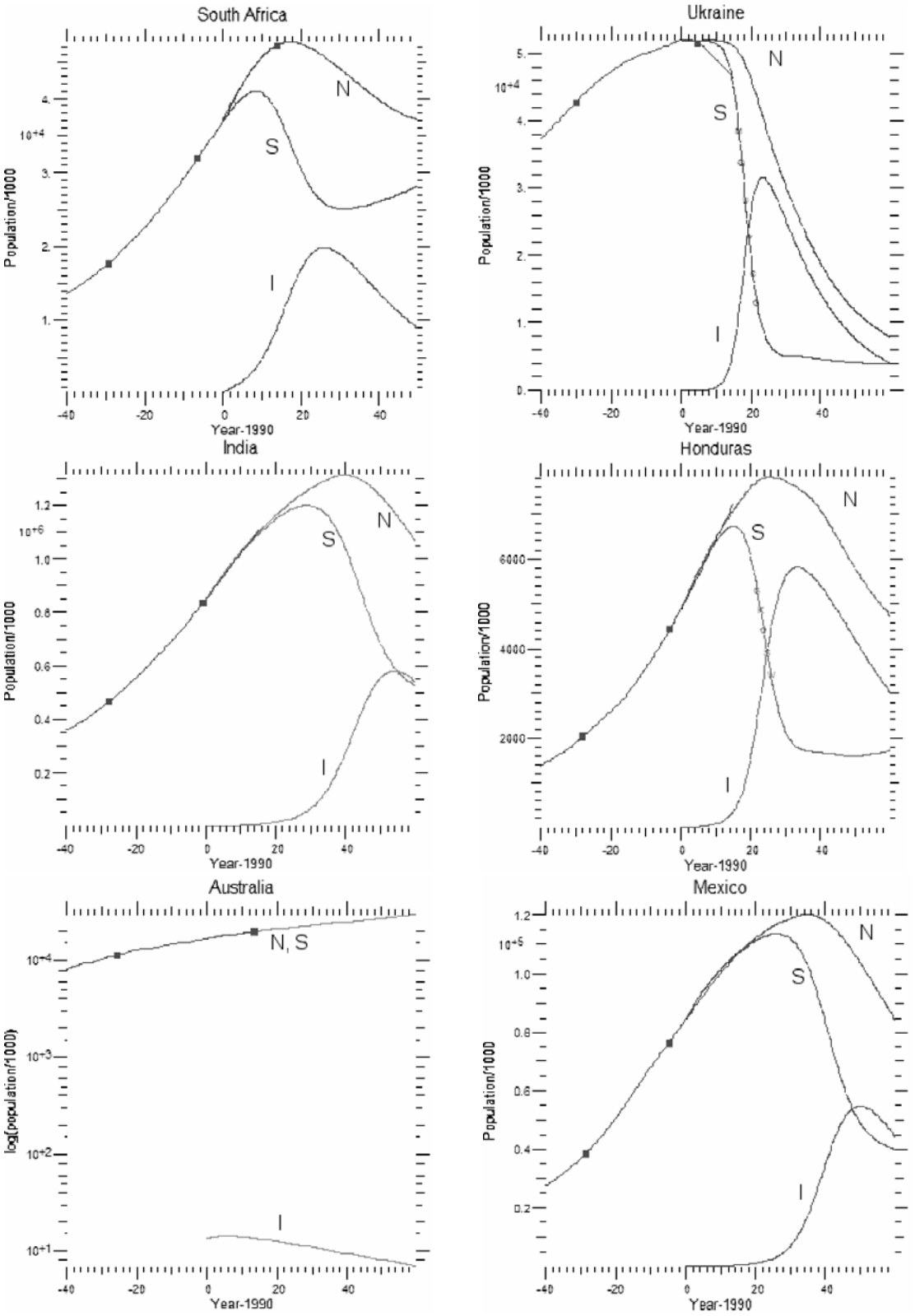

Figure 1. Model predictions for unchecked HIV infections. N: total population. S: susceptibles. I: infecteds.

South Africa

The model predicts catastrophic consequences for South Africa. Without treatment, the population would stop growing and even decline in the next few decades, with the number of HIV infections doubling or more before until infected individuals are nearly half the population.

Ukraine

Ukraine also experienced a dramatic increase in cases in the last century, but the the increase plays a lesser role in the model than the recent decline in population, which may have skewed the model parameters. Our model does not include migrations or other non-infection-related factors that affect population; therefore, the model likely exaggerates the problem in the Ukraine.

India

India's forecasted rate of growth is considerably affected after about 2015, and the population goes into decline around 2030. The inflection point of population growth is in the past decade, which is unsubstantiated by empirical data.

Honduras

Honduras too has a very large proportion of HIV infections, 1.8% in 2004. The increase from very few infections in 1990 to a great number in 2004 again affects the infection rate variable; if this rate of increase continues, the model shows catastrophic effects for the population as a whole.

Australia

The graph for Australia differs in being on a logarithmic scale. The number of infections is actually *declining*. The empirical data too shows a decline in infections over the past decade. Our model reflects the apparent inability of the virus to sustain itself with such low infection rates. That is, infected people are dying faster than they are infecting others. If this trend continues, the virus will simply not have the staying power to remain in the population.

Mexico

The data for Mexico reflect the rise and the decline in cases over the last decade, attributed to successful treatment and prevention programs [Ziga 1998], a force not represented in our simple model. The model shows a possibly unrealistically large growth in cases within the next decade; but the model is for infection rates without treatment or prevention measures.

Financial Resources and Foreign Aid

UNAIDS [2005a] has outlined the financial need and resources available in the fight against HIV, including a three-year projection of funds needed to accomplish the following tasks:

- Develop a concerted international effort focusing on all aspects of prevention and treatment.
- Provide 75% of the global group "in most urgent need" with ARV treatment by 2010 if current financial donor trends continue.
- Train medical staff in low-income countries.
- Create 2700 new health centers with funds available by 2010.

A total of $ 6.1 billion was available in 2004 [UNAIDS 2005a] and projections for 2005–2007 were $8.3 billion, $ 8.9 billion, and $ 10 billion.

If people in need are identified only one year before death and provided treatment for that year, 80% coverage could be provided by 2010 by $9.3 billion, assuming a constant geometric growth rate of cases of $1\frac{1}{3}$ from 2008 to 2010, as the study implies [UNAIDS 2005a].

Continued geometric growth quickly becomes unreasonable beyond 2010, the goal date for treating and controlling the majority of the epidemic.

Projections with ART and Vaccination

Model

To adapt our model to include ARV therapy and/or a preventive vaccine, we alter the "aware" category to include those who seek ART upon diagnosis. Thus, those who are infected and seeking abatement (though they may not receive it) have an overall increase in life expectancy that we model by reducing the death acceleration term, v^T. To include the effects of vaccination, we decrease the "birth" rate (the rate of entry) into the susceptible group to reflect the vaccination rate. For example, for a 75% vaccination rate, b would be reduced to 25% of its value in the absence of treatment.

Because our model assumes a best-case scenario—diagnosed individuals no longer transmit the infection—the addition of ARV treatment does not dramatically affect the population dynamics. Access to ARV treatment does, however, delay the decline of the total population. The coefficient λ describing the rate of infection remains the same; but due to the extended life-span of treated cases, infected individuals on average do not die as quickly—they live longer and hence constitute a greater percentage of the population.

Using reasonable values for v_j^i, the accelerated death terms, we obtain only mild influence on the unchecked trends from 1950 to 2050. Estimation of γ, the

rate at which people are diagnosed with HIV and seek treatment, is founded on the predicted aid that the country could receive.

On the one hand, if diagnosed infected individuals communicate the disease while living longer, the greater their population and the greater the growth of HIV. However, longer-living individuals would help offset the imminent danger to a hard-hit nation by adding to productivity and supporting the next generation of would-be orphans. Ethical mandates seem to require that ARV treatments be administered if at all possible.

Vaccination

An HIV vaccine would be one of the greatest medical accomplishments of the 21st century. With 100% vaccination, the existing AIDS population decays exponentially to zero. But 100% vaccination is not a plausible scenario for most countries.

For a 75% vaccination rate, the birth-rate term (rate at which people susceptible to HIV enter the general population), $b(t - t_0)$, would drop to 25%, assuming that the unvaccinated population is the least likely to have their children vaccinated. In this simplified scenario, in South Africa the total *susceptible* population would decrease starting in 2015, the year when our hypothetical vaccine is introduced (**Figure 2**).

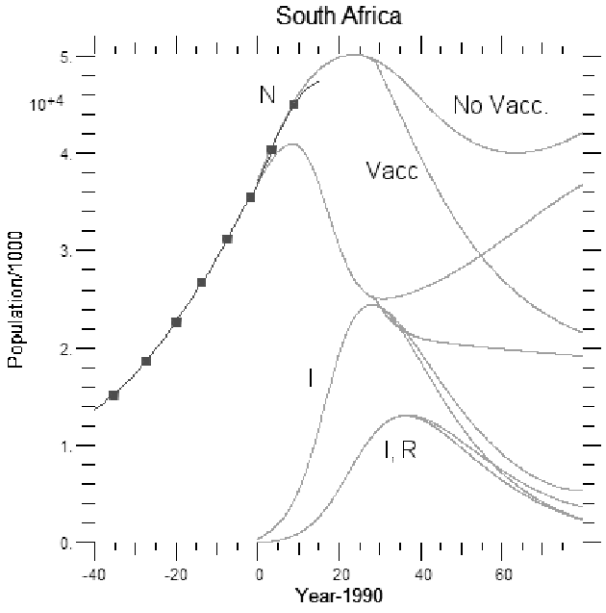

Figure 2. In the presence of ART and emergent ART resistance, the susceptible population in South Africa decreases at the introduction of an HIV vaccine in 2015, and the total number of AIDS cases immediately declines as well.

The vaccine causes a decrease in the total HIV-positive population and thus the total number of AIDS deaths. The HIV-negative vaccinated population is not considered in this model. The figure also incorporates the effects of ART

resistance of HIV, discussed in the following section.

The population dynamics show that the presence of a vaccine not only reduces the susceptible population but also causes a downward trend in the total number of AIDS cases as soon as those vaccinated would normally enter the susceptible population.

We assume that vaccination provides perfect immunity and does not cause infections, and that the vaccinated population secures vaccinations for its children so as to effectively isolate our model as a subset of the total population. Thus, only unvaccinated susceptible individuals contribute to the susceptible pool. This dramatic change to the dynamics only has an effect t_0 years after the vaccination is introduced.

Effect of ART

We show the effect of ART in **Figure 3**.

South Africa

If ART had been heavily supplied concurrently with the rise in cases in South Africa during the 1990s, the consequences would be visible even by 2006. The susceptible population is the same in ART and non-ART. The population of infected individuals in South Africa would have had extended lives with ARV treatment and resisted the downturn of total population.

Ukraine

Our model's prediction for the Ukraine population again shows that ART would have a large effect. If supplied during the last decade, the treatment would have slowed the population decline during the next half century. However, because our model unreasonably takes the Ukraine's recent population decline to be due to AIDS, the effect of the treatment almost certainly would be smaller than described.

India

ART supplied during and after the 1990s would not offset India's population trajectory until well into the twenty-first century, due to the low incidence of HIV relative to India's size and recent exponential growth. Nevertheless, the population would peak at a significantly higher value many years later with ART than without.

Honduras

Because Honduras experienced an especially large increase in HIV rate during the last decade, we fit the parameters of the model to a staggered trend.

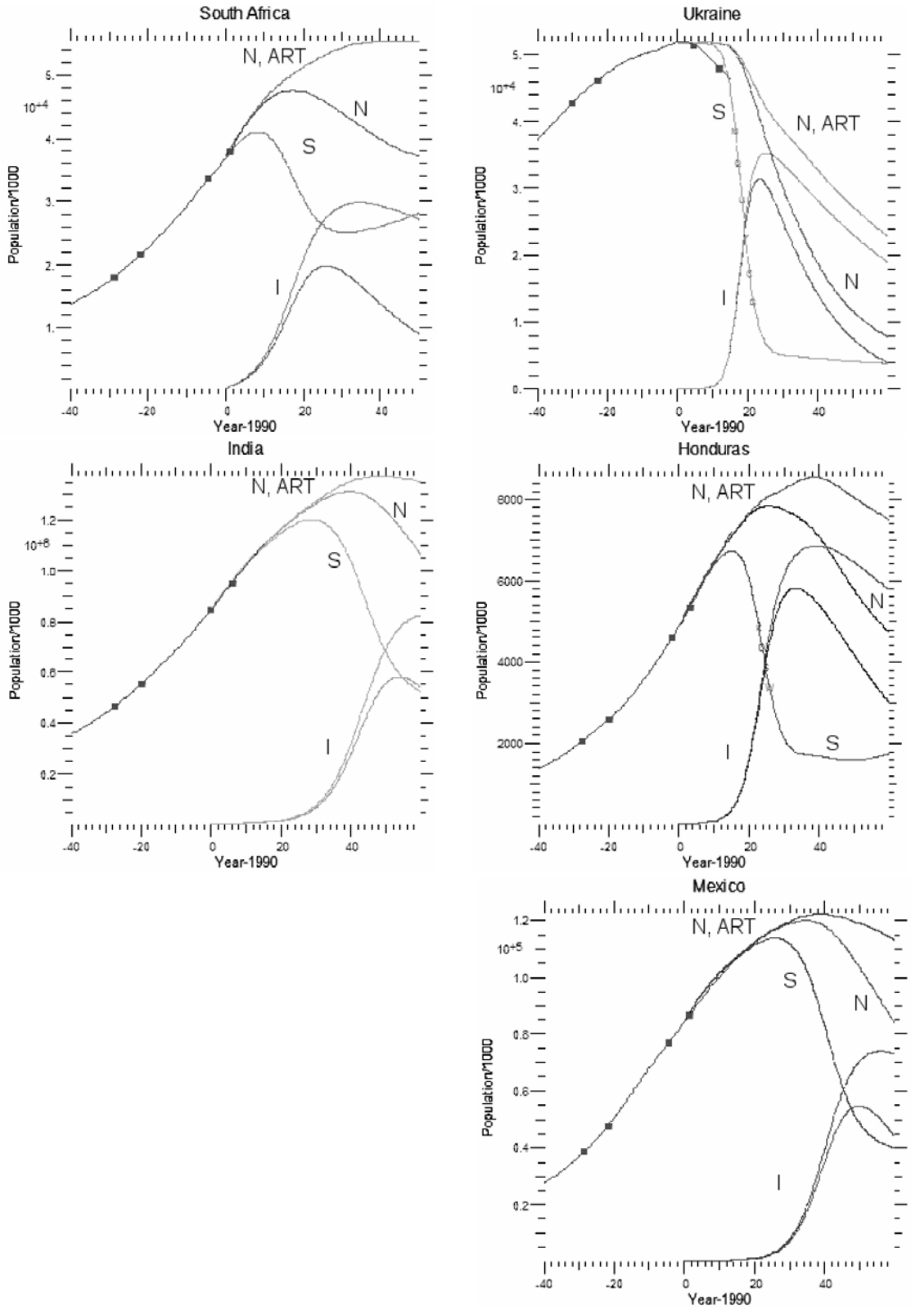

Figure 3. Model predictions with and without ART but with no development of ART-resistance. (N: total population. S: susceptibles. I: infected.)

ART treatment delays the population decline for only a few years but has a tremendous effect on total population by 2050.

Australia

Australia's HIV infection rate was already too small and not self-sustaining in the last model; we do not model it further here.

Mexico

ART in Mexico has a significant effect only when the infected group reaches a substantial proportion of the population. The low HIV rate in Mexico (and in Australia) leads to the prediction that treatment becomes nationally critical only after the year 2000. There is no change in the early population trajectory, due to very low incidence of AIDS.

The Economic Strain on Critical Countries

From the problem statement, the cost of administering treatment to an infected individual is \$1,100 per person per year of aid, although we found the cost to vary with country and country status [Cohen et al. 2005]. We argue, along the lines of the "Consensus Statement on Antiretroviral Treatment for AIDS in Poor Countries" [Adams et al. 2001] included with the problem statement, that donations from foreign countries can cover a good part of the current demand for treatment.

But even generous ART has only minor effects on the model, since ART is not a cure but only an extension of life that may have competing effects in HIV prevention.

Unless foreign donations, UN funding, and other public sector resources can afford to provide ARVs, it is unlikely that any but a small minority of patients would receive them.

Based on our models, in the worst-case scenario—where the only individuals treated are those who would live only 1–2 years more without treatment—public funds must cover 30% of HIV infections around the world (the percentage at this advanced stage) [UNAIDS 2005b]. Summing the HIV infections in each of our critical countries, by 2030 the UN could have been responsible for 90 million cases, costing \$90 billion—approximately the entire amount of funding available until then.

Providing a vaccine to the global population would cost \$12 billion to vaccinate the worlds' population, at \$0.75 cents per vaccination and a three-stage process.

Therapy-Resistant Strains

We include the possibility of development of ART-resistant strains of HIV. We use three countries, South Africa, India, and Mexico, as examples.

Model

The primary difference between the new model and the earlier model for ART is that the infected population variable I is split into two separate variables, I_r and I_s, to distinguish those seeking treatment from those unaware of their infection.

ARV resistant strain emergence and vaccination

We assume that initially there is no population infected with the resistant strain and that the emergence rate is proportional to treatment. Specifically, we set the death rate acceleration factor of those undergoing treatment with the resistant strain, v_r^T, to be equal to the death rate acceleration term for those with the treatment-sensitive strain but not seeking treatment, v_r^u. The effect is to blunt the effect of the ART and bring the population predictions towards the values that we obtained earlier in the absence of ART. **Figure 4** shows our model's predictions for total population and the resistant-strain emergence under ART for South Africa, India, and Mexico.

Conclusion

We feel that our model is appropriate for modeling the spread of HIV in otherwise stable countries and could be used to target AIDS funding better.

By modeling the spread of AIDS with a system of differential equations, we make relatively short-term assumptions about the course of the epidemic. We observe huge increases in global AIDS cases and population downturns for several of the critical countries that we modeled.

Vaccination appears to be the only pharmaceutical way to stop the spread of HIV. However, ART allows a country to maintain a larger population and thus should be undertaken to the maximum possible extent due to both humanitarian considerations and the effect of global population atrophy on the the world economy. Financial trends indicate increasing available funding for ART treatment globally. Should a vaccine ever become available, our financial analysis shows that it should be made available as quickly as possible.

Given the increasing availability of funds for the global fight against AIDS, all possible efforts should be made to distribute ARV medication to those populations most at need.

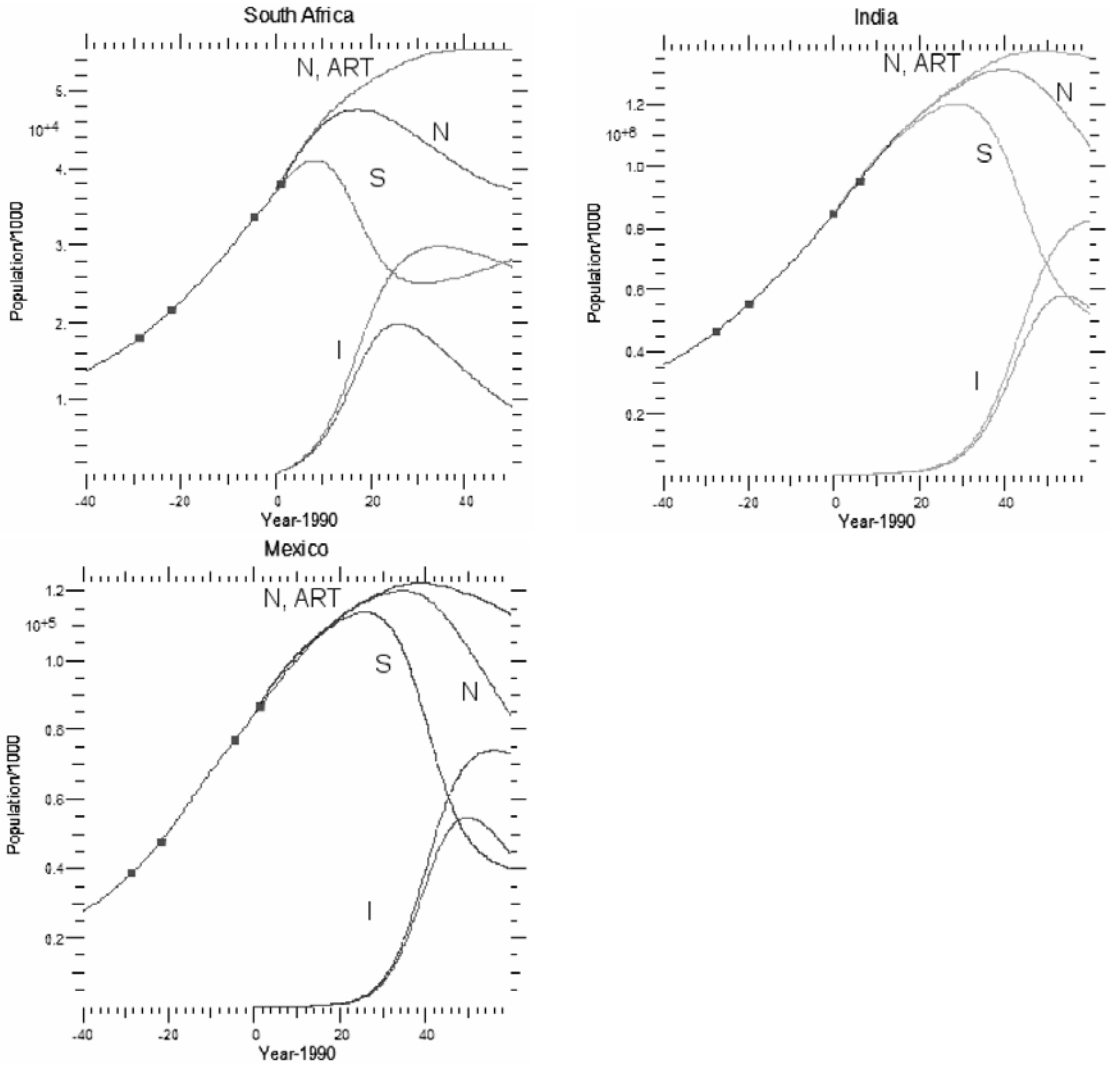

Figure 4. Model predictions with developed resistance under ART. The net beneficial effect of ART is decreased. (N: total population. S: susceptibles. I: infected.)

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