

## Summary

The HIV epidemic is a unique situation to model. The time period of interest spans decades, and only people of certain ages play a role. No one recovers from HIV, but treatments can extend lives tremendously. The virus evolves resistances to treatments, but the possibility of an HIV vaccine looms on the horizon. In the most affected countries, the total population could be reduced and dramatically alter the disease dynamics. Although the complexity of the situation extends beyond these points, we felt that a model incorporating these considerations could be rich in behavior.

In this paper, we introduce the state of the epidemic in six countries: Australia, South Africa, Honduras, Mexico, Ukraine, and India. We then describe some of the models used previously in literature. We develop a model that makes use of historical population and HIV data, and historical and projected birthrate 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:

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

We present simulation results and interpret what factors led to the observed trends. In a statement to the UN, we make observations about the characteristics of a successful fight against HIV and emphasize important results of the model.

# AIDS: Modeling a Global Crisis (and Australia)

## ICM Contest Question C

Team # 822

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### Contents

<b>1</b>	<b>Introduction</b>	<b>4</b>
<b>2</b>	<b>Derivation and discussion of phase 1 HIV epidemic model</b>	<b>5</b>
2.1	Introduction to Disease Epidemic Models . . . . .	5
2.1.1	The SIR Model . . . . .	5
2.1.2	A Multistage Model . . . . .	6
2.2	Characteristics of the Desired Model . . . . .	7
<b>3</b>	<b>Countries critical to the global AIDS pandemic</b>	<b>10</b>
3.1	Africa . . . . .	10
3.2	Europe . . . . .	11
3.3	Asia . . . . .	11
3.4	South America . . . . .	12
3.5	North America . . . . .	12
3.6	Australia . . . . .	12
<b>4</b>	<b>Projected unchecked HIV infections in critical countries</b>	<b>13</b>
4.1	Model . . . . .	13
4.2	Procedure . . . . .	14
4.3	South Africa . . . . .	15
4.4	Ukraine . . . . .	15
4.5	India . . . . .	15
4.6	Honduras . . . . .	17
4.7	Australia . . . . .	17
4.8	Mexico . . . . .	17

<b>5</b>	<b>Financial resources and foreign aid</b>	<b>17</b>
<b>6</b>	<b>Projected HIV infections under ARV therapy and vaccination</b>	<b>20</b>
6.1	Model . . . . .	20
6.1.1	Vaccination . . . . .	22
6.2	South Africa . . . . .	22
6.3	Ukraine . . . . .	24
6.4	India . . . . .	24
6.5	Honduras . . . . .	24
6.6	Australia . . . . .	24
6.7	Mexico . . . . .	24
<b>7</b>	<b>The economic strain of HIV on critical countries</b>	<b>27</b>
<b>8</b>	<b>Projected HIV infections taking into account therapy-resistant strains</b>	<b>28</b>
8.1	Model . . . . .	29
8.1.1	ARV resistant strain emergence and vaccination . . . . .	29
<b>9</b>	<b>Conclusion</b>	<b>32</b>
<b>10</b>	<b>Recommendations to the United Nations</b>	<b>32</b>
<b>A</b>	<b>Sample solver code</b>	<b>37</b>

## List of Figures

1	Unchecked HIV infections in South Africa. . . . .	16
2	Unchecked HIV infections in Ukraine. . . . .	16
3	Unchecked HIV infections in India. . . . .	18
4	Unchecked HIV infections in Honduras. . . . .	18
5	Unchecked HIV infections in Australia. . . . .	19
6	Unchecked HIV infections in Mexico. . . . .	19
7	The susceptible population decreases in the presence of an AIDS vaccine in South Africa. . . . .	23
8	South African populations in the presence and absence of ART. . . . .	23
9	Ukrainian populations in the presence and absence of ART. . . . .	25
10	Indian populations in the presence and absence of ART. . . . .	25
11	Honduran populations in the presence and absence of ART. . . . .	26
12	Mexican populations in the presence and absence of ART. . . . .	26
13	Developed HIV resistance under ART in South Africa. . . . .	30

14	Developed HIV resistance under ART in India. . . . .	30
15	Developed HIV resistance under ART in Mexico. . . . .	31
16	The susceptible population decreases in the presence of an AIDS vaccine in South Africa. . . . .	31

## 1 Introduction

In June 2001, the United Nations General Assembly held a special session on the Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome (HIV/AIDS) [10]. Beginning with a brief published report in *Morbidity and Mortality Weekly Report* of a rare pneumonia caused by *Pneumocystis carinii* as well as other unusual infections in 5 young homosexual men in Los Angeles, the disease has now killed over 25 million people, 3.1 million of those in just the last year [2, 11]. In the world, the estimated total number of people currently living with HIV is 40.3 million, with 5 million new cases in 2005 [2].

HIV infection is primarily spread through sexual exposure. There are many studies which focus on the acquisition of the HIV virus through homosexual contact and there is evidence which suggests an increase in the proportion of young gay men and ethnic minorities infected with the virus. However, at the global scale, in areas of highest HIV presence, heterosexual contact seems to be the primary mode of transmission, accounting for approximately 70% of the overall sexual transmission cases [12].

The growing rate of HIV infection in essentially every country [2] is a problem that must be addressed on a number of fronts. Mathematical models can be used to address questions regarding the potential impact and effectiveness of various approaches to this problem. In this paper, we address the HIV epidemic by building a mathematical model to approximate the expected rate of HIV/AIDS infections from 2005 to 2050 for a number of countries chosen from around the world (Task #1). Next, we consider the effect of antiretroviral (ARV) drug therapies (ART) versus a preventative HIV/AIDS vaccine on the spread of HIV using the current and projected economic resources of the UN as a constraint to be optimized (Task #2). We then consider the possibility of an ART-resistant strain of the HIV virus emerging and consider the effects this may have on our previous conclusions (Task #3). 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 available for HIV/AIDS among ARV provision and a preventative HIV vaccine (Task #4).

By applying our model, we obtained projections for the rate of HIV infection in Australia, Honduras, India, Mexico, South Africa, and Ukraine in the absence of treatment. For all the countries, the occurrence of HIV continued its upward trend, underlining the crucial need for intervention. We found ART for both mutating and non-mutating strains of HIV increases the life expectancy and total population over time as expected.

While our model predicted ART does little to prevent further spread of the disease, we agree that there is a strong humanitarian and economical argument for global ART, and that every possible international effort should be made to provide ARV medicine globally to AIDS victims.

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

## 2 Derivation and discussion of phase 1 HIV epidemic model

### 2.1 Introduction to Disease Epidemic Models

In this paper, we intend to create a model powerful enough to approximate a country's expected rate of change in the number of HIV / AIDS cases. This model must be extendable to consider development in anti-retrovirus treatments (ART) as well as provide information which can be used to evaluate cost-benefit relationships.

#### 2.1.1 The SIR Model

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

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

where  $\alpha$  is the rate of infective incidence - that is, the probability of infection occurring upon contact, times the number of contacts which occur in some time interval.  $\beta$  is the rate of recovery of an infected individual.

This model makes a number of assumptions which we recognize here and revisit later when creating a system more applicable to modeling the spread of HIV. First, the SIR 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. Secondly, this model assumes the population is perfectly homogenous and that no individuals are

treating their infection or modifying their behavior in response to their illness. Thirdly, current HIV patients do not have a chance for recovery as there is presently no cure for the HIV virus. Finally, SIR assumes no incubation period and a constant infection load, inappropriate assumptions for HIV infections. [14]

### 2.1.2 A Multistage Model

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

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

where  $S$  denotes the number of susceptible individuals,  $I_i$  denotes the number of infected individuals in each infected stage,  $A$  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, and  $\beta_i$  is the probability of transmission per partner from infected individuals in stage  $i$  of the infection. Note all individuals go into group 1 upon infection.  $\gamma_i$  is the rate at which individuals move from stage  $i$  of infection to stage  $i + 1$ . [14]

Again, this model makes a number of uncertain assumptions which we recognize here. First, although this model incorporates a birthrate, the birthrate is constant. Secondly, and most importantly, it does not account for the effect that treatment may have on the infectiousness of the treated group, though we may imagine that the multiple infection rates  $\beta_i$  being modified account for both treated and untreated groups, as we will see later.

## 2.2 Characteristics of the Desired Model

Many models exist which simulate the spread of an infectious disease through a dynamic population. These models may range from a series of linear differential equations to Bayesian networks, complex Markov chains, and stochastic algorithms [15]. Dynamic algorithms have been implemented which are aimed at exploring 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 [13, 21].

There is a general dispute over the net effect of ART in mathematical models which incorporate them into HIV infection predictions. ART treatment will generally reduce the infectiousness of an individual [2]. This 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* showed that increases in sexual behavior and life expectancy could negate the beneficial impact of decreased infectiousness on incidence [6]. Furthermore, the argument is made that treated patients may increase the frequency of sexual activity due to the severity of their symptoms decreasing. Still other research suggests exactly the opposite. For example, in Cote d'Ivoire individuals reported low sexual activity following an HIV diagnosis and this was not increased by the offer of ART [19].

We find the real world result of Moatti *et al* convincing and we address ART-treated individuals rather extremely as we will discuss in the following section.

In this section, we will use concepts from all of these models (as well as the undiscussed differential infectivity (DI) model) to construct a system which can be appropriately applied to the described tasks.

We chose to create the model using non-linear differential equations, similar to the SIR model, which provide a convenient, easy-to-interpret structure. We felt the HIV epidemic contained critical characteristics lacking in the SIR model. Most importantly, the SIR model is not meant to be applied to life-long diseases; no one with HIV recovers. The time-scale of the epidemic, necessitates that time-dependent birth and death rates be included in a realistic model. Second, 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 are individuals who are aware of their infection. A last critical characteristic of HIV is the role of age in the disease dynamics. The susceptible and infected people that can

affect the disease dynamics are overwhelmingly between the ages of 15 and 49 [2]. The model described below incorporates all of these considerations.

Definition of Parameters	
$S$	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.
$\mu$	Death rate of susceptible population.
$v_s^u$	Increase in the death rate for the untreated population infected 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.
$\gamma_s$	Rate with which those who have the ARV-sensitive strain seek testing and treatment.
$\gamma_r$	Rate with which those with the ARV-resistant strain seek testing and treatment
$\lambda$	Transmission rate of either strain to the susceptible population
$\alpha$	Rate at which treatment induces ARV-sensitive $\rightarrow$ ARV-resistant mutation

$$\frac{dS}{dt} = b(t - t_0)S(t - t_0) - \mu S - \lambda S I_s^u - \lambda S I_r^u \quad (1)$$

$$\frac{dI_s^u}{dt} = \lambda S I_s^u - (\mu + v_s^u) I_s^u - \gamma_s I_s^u \quad (2)$$

$$\frac{dI_s^T}{dt} = \gamma_s I_s^u - (\mu + v_s^T) I_s^T - \alpha I_s^T \quad (3)$$

$$\frac{dI_r^u}{dt} = -\gamma_r I_r^u - (\mu + v_r^u) I_r^u + \lambda S I_r^u \quad (4)$$

$$\frac{dI_r^T}{dt} = \alpha I_s^T - (\mu + v_r^T) I_r^T + \gamma_r I_r^u \quad (5)$$

The model uses the SIR model as its foundation, which it extends with concepts from the SI model and others. In all, this model is used to represent five categories of people aged 15 to 49 - 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 than individuals not in treatment, but they also behave differently; there is no transmission from this group.

We make the following assumptions:

- Although the absolute assumption that treated individuals no longer transmit is markedly false [15], 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 [2] and, therefore, 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 there is no birth rate in the infected groups at time  $t - t_o$  because infected offspring will not have a significant chance to spread the disease [2]. 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.

Some interesting effects which this model can address include the following.

- 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 which will include the 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 us

how much funding will be required to provide treatment to that ratio of the population. We will use this approach in analyzing Task #2.

- By carefully determining and calibrating all constants and initial conditions, the model adapts to allow for treatment resistant strains of HIV. 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 will use this approach in analyzing Task #3.

Taking into consideration both the restrictions as well as the abilities of this model, we feel it is strongly applicable to predicting overall trends in a variety of situations.

### 3 Countries critical to the global AIDS pandemic

The current HIV/AIDS crisis that the world now confronts is not limited to any subsection of society or the globe. AIDS is leaving its legacy on every corner of the world. On each continent, we highlight a country that portrays the critical nature of today's fight against AIDS. The countries we discuss in the following section exhibit characteristics that make them critical to the global fight against the pandemic.

There are many criteria that one could use to choose which country is the most critical for a given continent in terms of AIDS. Our choices were largely influenced by the UNAIDS December 2005 update on the AIDS epidemic [2]. Some criteria we considered were

- The percentage of the countries' total population infected.
- The total number of AIDS cases.
- The current resources available to the government.
- Rate of growth of AIDS cases.
- The effect of the specific country on the global AIDS epidemic.

#### 3.1 Africa

Over 65% of the 40.3 million cases of AIDS in the world are found in Sub-Saharan Africa [2]. Here, the complex behavior of the infection is clear. In the early 1990's, AIDS cases were concentrated in specific regions of the subcontinent. By the year 2000, some areas that were previously unaffected

experienced sharp rises in cases, sometimes overtaking the countries where the disease was present earlier. The extreme example is South Africa, which saw HIV in the general population grow from less than 1% in 1990 to an estimated 21.8% in 2003 [3], and with rates in pregnant women at 27.8% [5]. South Africa now has more cases than *any* other country, despite its relatively small population.

Additionally, the case of South Africa displays the complex dynamics that contribute to the sub-saharan AIDS epidemic. The geographic mobility of migrant workers, the lack of awareness of the disease and a shortage of funding for testing and treatment have all played a role in the spread of AIDS in these regions.

We chose South Africa as the most critical country for the most important country in Africa because of its large AIDS population, and infection rate.

### 3.2 Europe

In Eastern Europe, the AIDS epidemic is primarily driven by injected drug use, with Russia and the Ukraine as the hardest-hit countries. The estimated prevalence rate in 2003 in the Ukraine was 1.4% [4]. The pattern of the AIDS epidemic is that the disease gains a foothold through intravenous drug users and men before being spread to the general population. It thus appears that Eastern Europe is only in the early stages of infection and that intervention is extremely important to stop an increase in AIDS cases.

Western Europe is far better off both in terms of resources to prevent AIDS from spread, and for acquiring antiviral treatments. Access to these resources has in fact caused AIDS deaths per year in western Europe to decrease.

We chose the Ukraine as the most critical country in Europe because it exhibits both the highest AIDS occurrence rate and the greatest infected population other than Russia at an estimated 360,000 in 2003 [4]. Additionally, newly reported infections rose 25% in 2004 [8]. Since the infection appears in its early stages, an analysis of the effects of intervention is critical.

### 3.3 Asia

AIDS in Asia is currently spread primarily through sex workers and injection drugs although it has begun to spread to the general population in

several countries. In general, cultural factors and stigmatization greatly affect the governmental response. India, which has the second largest AIDS population in the world, has been slow to implement an ARV program. China, another potential choice of critical country, has recently become more proactive regarding an ARV program, with the goal of providing free drugs and counseling to poor and rural populations.

We chose India as the most critical population because of the large infected population, the lack of effective prevention measures that have helped reduce AIDS prevalence in many Asian countries such as, and the incipient nature of the epidemic in India.

### **3.4 South America**

The governmental response to AIDS in South America is as varied as the factors that contribute to its spread. For instance Brazil, with the greatest AIDS population, provides ARV treatment to almost all its citizens in advanced stages of illness [18]. However, other South American nations such as El Salvador, Guatemala, Honduras, Nicaragua, and Paraguay have not been as proactive in providing aid to their citizens [9].

In Honduras, AIDS has become the leading cause of death for women, and is found in 2% of the population. Due to the lagging government response, and highest per-capita incidence rate in South America, we chose Honduras to be the most critical country.

### **3.5 North America**

Canada, the United States, and Mexico all have relatively low rates of occurrence of AIDS compared to global rates of incidence. The greatest factor in determining which country is most critical rests solely on the governmental resources available to support prevention education and ARV treatments. Using this criterion, we chose Mexico as the country the most critical to North America.

### **3.6 Australia**

Australia's history of AIDS reaches back to the 1980's, but has remained relatively low. Nevertheless, high-risk behaviors have led to an increase in the number of recent cases [17].

## 4 Projected unchecked HIV infections in critical countries

We now determine the expected rate of change in the number of HIV infections for our critical countries from 2005 to 2050 if there were no treatment or vaccination plans to extend the life and protect people from the disease. To accomplish this, we easily modify our general model described above to make it applicable to the assumed constraints of this section.

### 4.1 Model

In this section, we do not wish to consider resistant strains or any kind of treatment of the infection. Thus, with respect to 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. In Table 6.1.1 we summarize the simplified set of variables now under consideration.

$S$	Population susceptible to infection.
$b(t - t_0)$	Birth rate $t_0$ years ago of the susceptible population.
$\mu$	Death rate of susceptible population
$v$	Death rate acceleration factor of infected population
$I^u$	Population infected with HIV and are unaware of their infection.
$I^a$	Population infected with HIV and are aware of their infection.
$\lambda$	Transmission rate of the HIV virus to the susceptible population.
$\beta$	Rate at which the unaware population becomes symptomatic and thus get tested to become aware.

We reiterate our simplified model below. These equations relate the above independent variables and form the basis of our predictions for the five critical countries we chose in Section 3.

$$\frac{dS}{dt} = b(t - t_0)S(t - t_0) - \mu S - \lambda SI^u \quad (6)$$

$$\frac{dI^u}{dt} = \lambda SI^u - \beta I^u - (\mu + v) I^u \quad (7)$$

$$\frac{dI^a}{dt} = \beta I^u - (\mu + v) I^a \quad (8)$$

Again, there are a number of assumptions that are made when adopting this model. The most important is our emphasis on the change in behavior when a person becomes aware of his infection. The model above presumes best-case scenario for simplicity: an individual will not knowingly infect another individual with HIV.

## 4.2 Procedure

In order to obtain reasonable, country-specific parameters of death rates and infection rates, we first set the HIV transmission to zero, input the birthrate data for 1950-2005, then set the death rate to accurately reflect the population data for the given country between 1990 and 2005. The death rate acceleration term was chosen so that  $\mu + v$  reflects the  $1/e$  lifetime of a population with AIDS. We then adjusted the transmission parameter,  $\lambda$ , to match the AIDS cases in the same time period.  $\beta$  was chosen to reflect the average time to exhibit symptoms. Then we integrated 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. To summarize,

- Input the country-specific birth-rate data
- Adjust the death rate to reflect population trends
- Adjust the infection rate to mirror the total number of Aids cases between 1990-2005 for the specific country
- Use the average lifetime of an HIV positive individual to approximate the death rate acceleration term

Thus, the values assigned to model parameters in each scenario are based, if possible, on empirical data detailing birth rates and total AIDS population of each country.

### 4.3 South Africa

South Africa's surge in AIDS cases during the last decade heavily influences the model dynamics. A canonical example of output from the implementation of our model is shown in Figure 1. Choosing the model parameters to fit the observed trends necessitates a very large rate of transmission. Coupled with the current high percentage of individuals with HIV in the country, the model predicts rather catastrophic consequences for South Africa. Without treatment, the population could stop growing and even decline in the next few decades, with the number of HIV infections doubling or more before until the ratio of infected individuals is nearly half the population.

### 4.4 Ukraine

Ukraine also experienced a dramatic increase in reported HIV cases in the last century, but the the increase played a lesser role in the model than the recent decline in population. In Figure 2, a striking result is observed. We surmise the recent decline of Ukraine's population in the past decade skewed the model parameters which resulted in massive deaths in Ukraine. We repeat that our model does not include descriptions of migrations or other non-infection-related events which affect the populous and, therefore, the model likely exaggerates the problem in the Ukraine.

### 4.5 India

India's large number of HIV cases is balanced by its enormous population. Shown in Figure 3 is the result of applying our model to India's state in the past decade and beyond. India's tremendous forecasted rate of growth is considerably affected after about a decade, and the population goes into decline at about 2030. We note the inflection point of population growth is in the past decade, which is unsubstantiated by empirical data. The incredible growth of the total number of HIV infections in India over the past decade is accountable for bringing the population estimates down so dramatically because it forced the rate of infection variable so high. Regardless, in the next two decades, the vast number of HIV infections in India, if left uncontrolled, could exponentiate and clearly have a significant effect on population numbers.

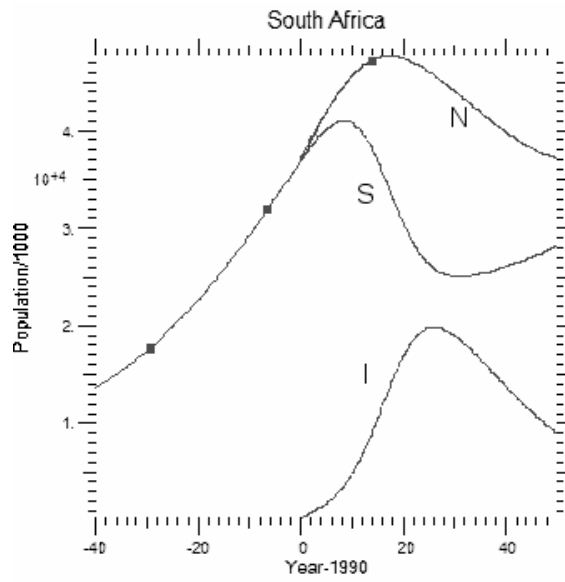


Figure 1: Unchecked HIV infections in South Africa.

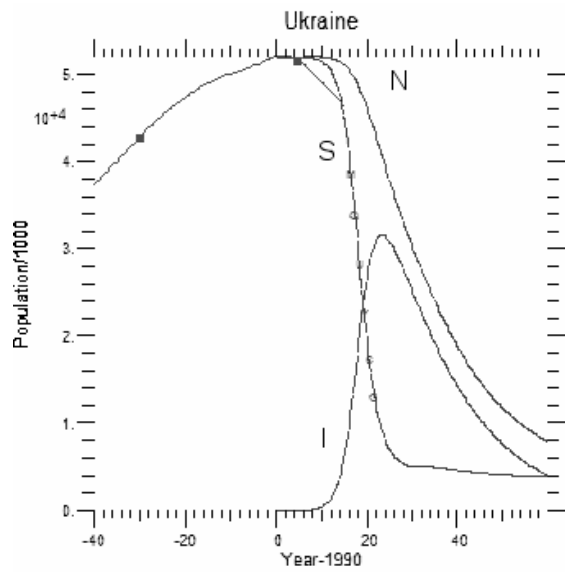


Figure 2: Unchecked HIV infections in Ukraine.

#### 4.6 Honduras

Honduras also has a very large number of HIV infections, 1.8% in 2004. The increase from very few infections in 1990 to a great number in 2004 again affected the infection rate variable and, if this rate of increase continues on an exponential scale, the model again shows catastrophic effects for the population as a whole.

#### 4.7 Australia

Australia is a unique case. In Figure 5, which we note is on a logarithmic scale for easy viewing, we see that the number of HIV infections is actually *declining*. We note the empirical data also shows a decline in the HIV infection numbers over the past decade. Our model is able to reflect the apparent inability of the HIV virus to sustain itself with such low infection rates. That is, the people infected with the HIV virus are dying faster than they are infecting others. Left unchecked, if this trend continues, we see the HIV virus will simply not have the staying power to remain in the population.

#### 4.8 Mexico

The data for the HIV situation in Mexico reflects the rise and the decline in new cases over the last decade. This is attributed to recent successful treatment and prevention programs being implemented in Mexico [20], a force that is not represented in our simple model. The model shows a possibly unrealistically large growth in HIV cases within the next decade. Essentially, this section is meant to model HIV infection rates without treatment or prevention measures while Mexico has implemented successful treatment and prevention plans over the last decade, making this section inapplicable to Mexico as it stands.

### 5 Financial resources and foreign aid

UNAIDS has completed numerous reports outlining the financial need and current financial resources available in the fight against the global HIV pandemic. UNAIDS provides a three year projection of US and foreign funds needed to accomplish the following tasks

- Develop a concerted international effort focusing on all aspects of prevention and treatment.

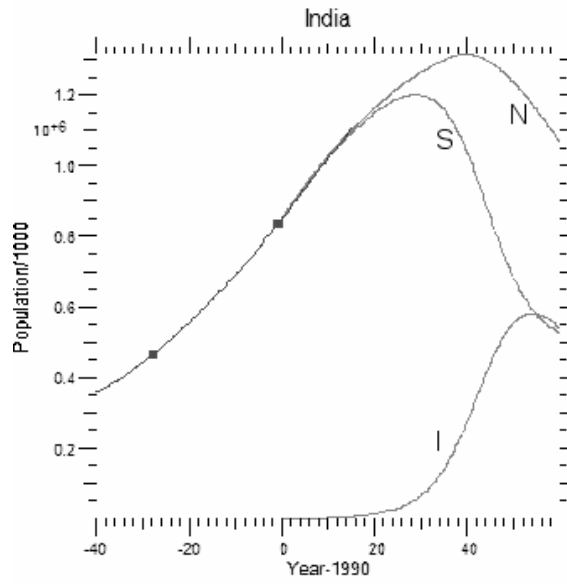


Figure 3: Unchecked HIV infections in India.

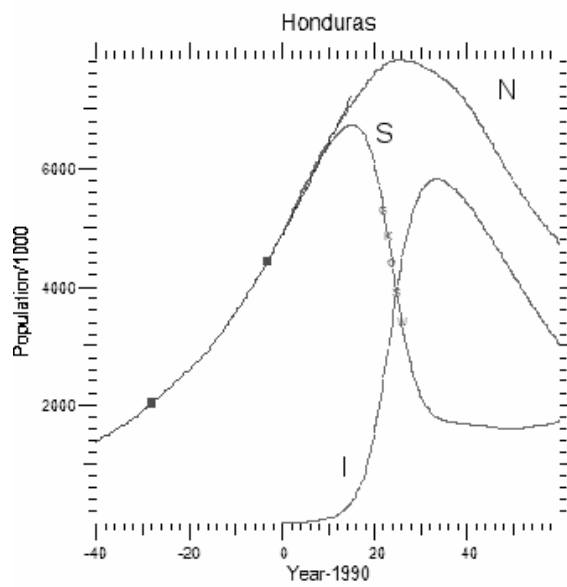


Figure 4: Unchecked HIV infections in Honduras.

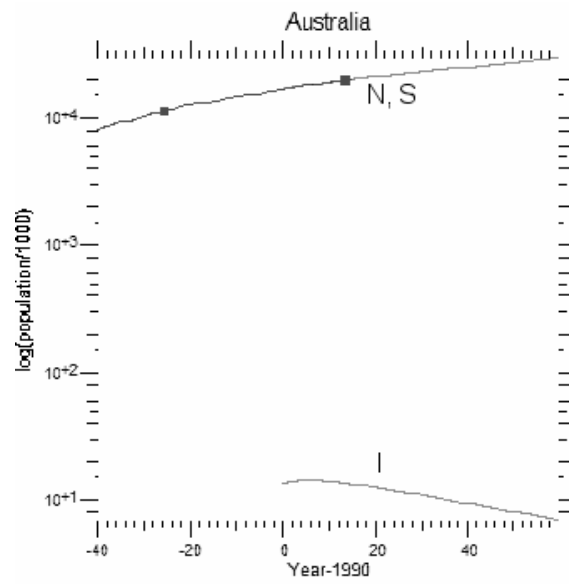


Figure 5: Unchecked HIV infections in Australia.

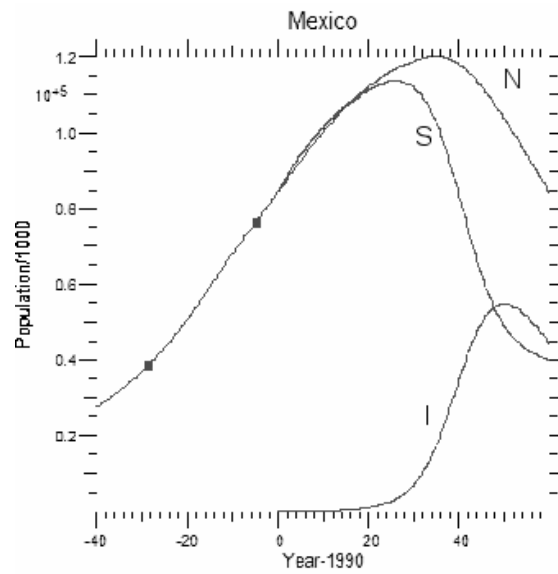


Figure 6: Unchecked HIV infections in Mexico.

- Provide 75% of the global group “in most urgent” 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.

For more information, see the UNAIDS complete list in the UN report of resource needs [1].

According to a recent estimate by UNAIDS, \$ 6.1 billion was available in 2004 for the global fight against AIDS [1]. They projected that there was \$ 8.3 billion available in 2005, and that there will be \$ 8.9 billion and \$ 10 billion available in 2006 and 2007, respectively.

By focusing only on the cost and economic demands of ART treatment alone, we find an unfortunate funding gap between resources needed and resources available. By UNAIDS current estimates, if people in need are identified only one year before death and provided treatment for that year, 80% coverage could be provided by 2010 assuming “universal access” by the allocation of approximately \$9.3 billion assuming a constant geometric growth rate of  $1\frac{1}{3}$  from 2008 to 2010, as the study implies[1].

The continued geometric growth quickly becomes unreasonable beyond the UNAIDS projected numbers in 2010, the goal date to be treating and controlling the majority of the epidemic. Alternatively, if the growth projected by UNAIDS continues linearly, there will be approximately \$63 billion available in 2050 to combat the epidemic with either ARV treatment or through vaccinations.

## **6 Projected HIV infections under ARV therapy and vaccination**

### **6.1 Model**

To adapt our model to include ARV therapy and/or a preventative HIV vaccine, we altered the model used in section 4. We altered the “aware” category of the previous model to include those who now seek ART treatment upon their diagnosis. Thus, those who are infected and seeking rebatement (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, given a

75% vaccination rate,  $b$  would be reduced to 25% of its value in the absence of treatment.

Definition of Parameters	
$S$	Population susceptible to infection
$b(t - t_0)$	Birth rate $t_0$ years ago of the susceptible population
$\mu$	Death rate of susceptible population
$v^u$	Death rate acceleration of unaware population
$v^T$	Death rate acceleration for treated population
$I^u$	Population unaware of their infection.
$I^T$	Population infected and seeking treatment
$\gamma$	Rate with which infected seek treatment
$\lambda$	Transmission rate to the susceptible population

$$\frac{dS}{dt} = b(t - t_0)S(t - t_0) - \mu S - \lambda SI^u \quad (9)$$

$$\frac{dI^u}{dt} = \lambda SI^u - (\mu + v^u)I^u - \gamma I^u \quad (10)$$

$$\frac{dI^T}{dt} = \gamma_s I^u - (\mu + v^T)I^T \quad (11)$$

The ARV treatment would only apply to a population that has been diagnosed and must be aware of its infection. Because our model assumes 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 term in the model describing the rate of infection,  $\lambda$ , remains the same but, due to the extended life-span of treated cases, infected individuals, on average, do not die as quickly. As a result, infected individuals live longer and will therefore 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. See figure 6.2, for example. Estimation of *gamma*, the rate at which people are diagnosed with HIV and seek treatment, is founded on the predicted aid that the country could receive, discussed elsewhere. Learning from this result is not easy. 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 will help offset the eminent dangers of a hard-hit nation by continuing to be productive members of society, adding to global productivity and supporting the next

generation of would-be orphans. Ethical mandates seem to require that ARV treatments be administered if at all possible.

### 6.1.1 Vaccination

Due to the low cost and efficacy of vaccination, an HIV vaccine would be the greatest medical accomplishment of the 21st century. With 100% vaccination, there would be no rate of entry into the “susceptible” category of our model, effectively reducing the birth rate of susceptible individuals and thus the existing AIDS population decays exponentially to zero. This is not a plausible scenario for most countries, however. Given 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 population who is unvaccinated is the least likely to have their children vaccinated. In this simplified scenario, we see that in figure 16 that the total *susceptible* population decreases starting 2005, the year our hypothetical vaccine is introduced into the model. This causes a decrease in the total HIV positive population and thus the total number of AIDS deaths in South Africa. The HIV negative vaccinated population is not considered in this model. In this figure, the effects of ART resistance of HIV are also considered, and will be discussed in the following section.

The population dynamics show that the presence of an HIV vaccine not only reduces the susceptible population, but causes a downward trend in the total number of AIDS cases the moment it is introduced. A vaccine is without a doubt the best choice for treatment, and its low cost would allow it to be administered to the general population in addition to ARV medication if current AIDS funding trends continue.

## 6.2 South Africa

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

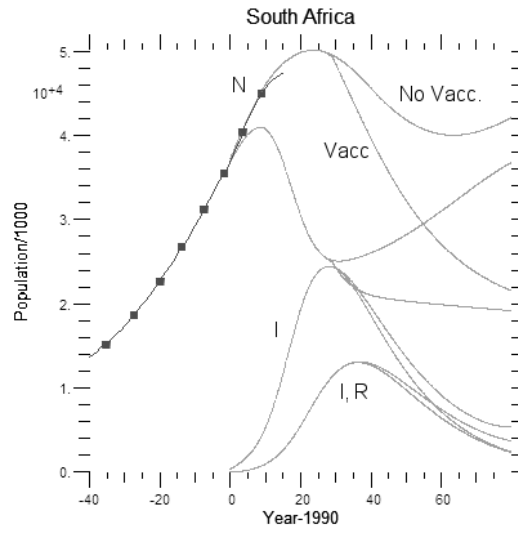


Figure 7: The susceptible population decreases in the presence of an AIDS vaccine in South Africa.

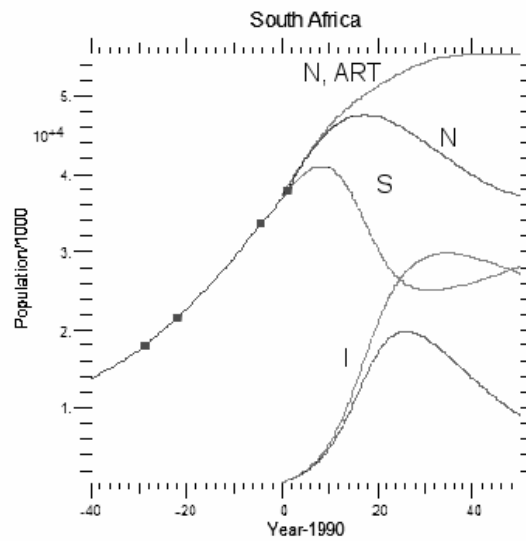


Figure 8: South African populations in the presence and absence of ART.

### **6.3 Ukraine**

Our model's catastrophic prediction for the Ukraine population again shows that ART would have a large effect. If supplied during the last decade, the treatment would slow 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.

### **6.4 India**

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

### **6.5 Honduras**

Because Honduras experienced an especially large increase in HIV rate during the last decade, the parameters of the model were fit to a staggering trend. ART treatment delays the population decline for only a few years, but has a tremendous effect on total population by 2050.

### **6.6 Australia**

Australia's HIV infection rate was too small and not self-sustaining in the last model. Furthermore, Australia has already implemented ARV treatment plans in the private sector. Thus, it does not contribute to our UN funding model and we need not evaluate it here.

### **6.7 Mexico**

As in the other cases, ART in Mexico has a significant effect only when the infected group reaches a significant proportion of the population. The low HIV rate in Mexico (and in Australia) leads to the prediction that treatment only becomes nationally critical after the year 2000.

There is no change in the early population trajectory, due to very low incidence of AIDS.

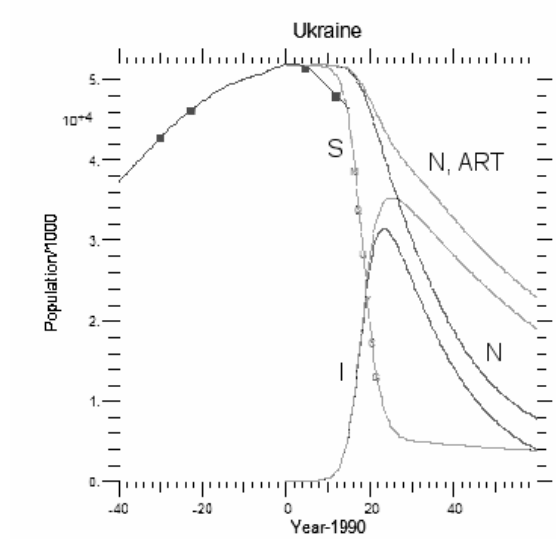


Figure 9: Ukrainian populations in the presence and absence of ART.

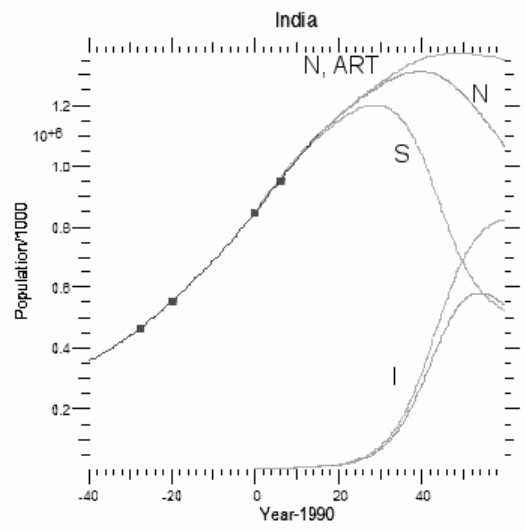


Figure 10: Indian populations in the presence and absence of ART.

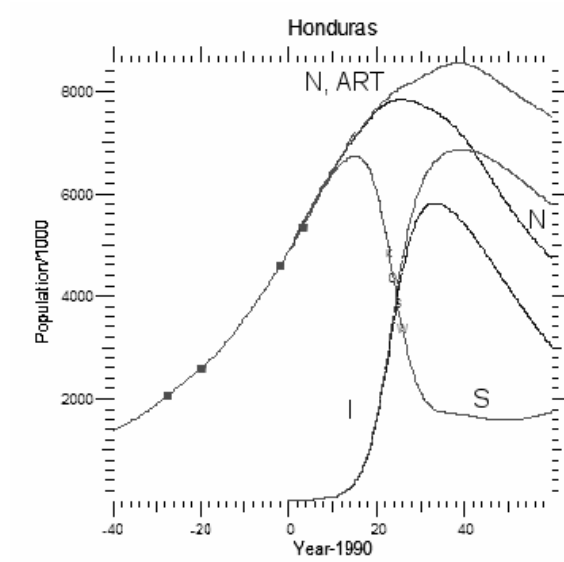


Figure 11: Honduran populations in the presence and absence of ART.

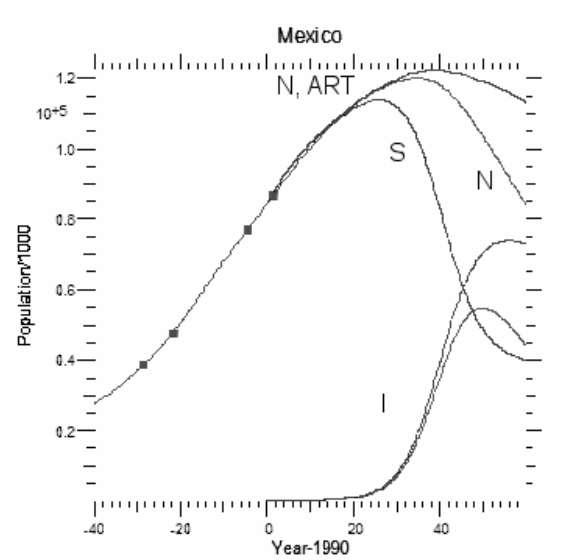


Figure 12: Mexican populations in the presence and absence of ART.

## 7 The economic strain of HIV on critical countries

From the provided information, we suppose the cost of administering treatment to an infected individual is \$1,100 per person per year of aid, although we found this number to change between country and country status in actual empirical data [22]. We argue, along the lines of the "Consensus Statement on Antiretroviral Treatment for AIDS in Poor Countries" included with the problem statement, that donations from foreign countries, if strongly solicited, can cover a good percentage of the current demand for treatment. Furthermore, if the crisis were to worsen, the arguments could be extrapolated accordingly into the near-future. This thinking is hopeful at best, but provides a basis for the coupled relationship of prevalence of the virus and HIV prevention/treatment funding.

It is concerning to note that in the above section, despite generous ARV treatment, the effects on the model are only minor. Again, we must note that ARV treatments are not meant as a cure, but only an extension of life which may have competing effects in HIV prevention. See Section ?? for a discussion of ART and its effects.

The primary approaches to present health care financing include taxation, social insurance systems, private insurance, user fees and community financing schemes and, in the special case of HIV, foreign aid and UN funding. Of these, cost recovery through user fees seems unrealistic because of the extremely high costs of treatment with respect to the per capita income of most low and middle-income countries. Experience with community financing schemes also tends to indicate that their revenue potential is not large, and mobilizing finance for medical treatment that does not realize individual benefits for everyone would be a significant challenge [22]. Private insurance companies, meanwhile, are in business to make money and as a consequence try to eliminate bad risks. Thus, unless foreign donations, UN funding, and other public sector resources can afford to provide ARVs, it is unlikely that their provision to anything but a small minority of patients could be possible and any additional funding will have to be financed through other means.

Country	GNP per capita	Funding Sources
Australia	US\$700	Private sector treatment
Honduras	US\$860	UNAIDS
India	US\$450	UNAIDS
Mexico	US\$5070	UNAIDS + Partial private sector funding
South Africa	US\$3020	UNAIDS + Partial private sector funding
Ukraine	US\$700	UNAIDS

The UN available funding estimates in Section 5 were total funds for public distribution to all countries in need. Based on our models, in the worst case scenario public funds will need to be allocated for 30% of the total HIV infections (those that would only live 1-2 years more without treatment [2]) around the world to provide those individuals with treatment. By summing the total number of HIV infections in each of our countries, we find the UN could be responsible for approximately 90 million cases, which, under our treatment cost could be priced at approximately US\$ 90 billion dollars, approximately the entire amount the UN could have accumulated at current rates by the year 2020-2030. We note that these are over-estimates. First, public treatment plans and preventive methods are already in effect and will continue to be in effect, so these models of HIV infection rates will likely not come to pass. Second, all cases will not be treated simultaneously and it is possible other financial sectors may be able to take some of the burden in the future.

Should a vaccine become available, providing it to the global population would be a top priority. With the extremely low cost of vaccination compared to ARV medication (approximately \$12 billion to vaccinate the worlds' population, given a cost of 75 cents per each vaccination and a three-stage vaccination process), very little trade-off exists between treating those who are sick and vaccinating those who could potentially become infected.

## 8 Projected HIV infections taking into account therapy-resistant strains

In this section we reformulate the models developed for predicting the HIV infection rates in the context of ART treatments and vaccination rates to include the possibility of development of ART-resistant strains of HIV. We use three countries, South Africa, India, and Mexico, as examples of the effect of an emergent ART-resistant strain on the population dynamics already established in the ART regime.

## 8.1 Model

The complete model described in section 2.2 was designed for the purpose of both modeling the effects of treatment and the emergence of a resistant strain.

$$\frac{dS}{dt} = b(t - t_0)S(t - t_0) - \mu S - \lambda S I_s^u - \lambda S I_r^u \quad (12)$$

$$\frac{dI_s^u}{dt} = \lambda S I_s^u - (\mu + v_s^u) I_s^u - \gamma_s I_s^u \quad (13)$$

$$\frac{dI_s^T}{dt} = \gamma_s I_s^u - (\mu + v_r^u) I_s^T - \alpha I_s^T \quad (14)$$

$$\frac{dI_r^u}{dt} = -\gamma_R I_r^u - (\mu + v_r^u) I_r^u + \lambda S I_r^u \quad (15)$$

$$\frac{dI_r^T}{dt} = \alpha I_s^T - (\mu + v_r^T) I_r^T + \gamma_r I_r^u \quad (16)$$

The primary difference between this model, and the model used in the previous section is that the infected population variable,  $I$ , is now split into two separate variables,  $I_r$  and  $I_s$  (we keep the distinction between those seeking treatment and those unaware of their infection to account for behavior changes on diagnosis).

### 8.1.1 ARV resistant strain emergence and vaccination

To implement our differential equations we assumed that there was no population infected with the resistant strain to begin with, and that the emergence rate was 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 we obtained earlier in the absence of ART. Figures 13, 14, and 15 show our model's predictions for both the total population and the resistant strain emergence under ART.

As was concluded in in section 6.7, the introduction of a vaccine would be an extraordinary development. Based upon figure 16, where the effects of ART immunity are also considered, we see that the vaccine produces the greatest effect in lowering the total number of cases, something ART cannot do.

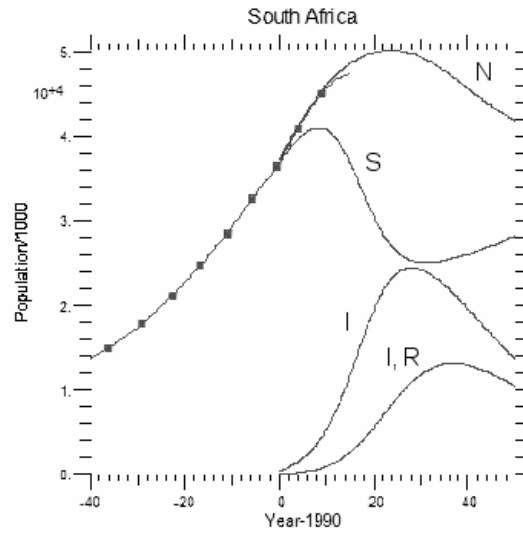


Figure 13: Developed HIV resistance under ART in South Africa.

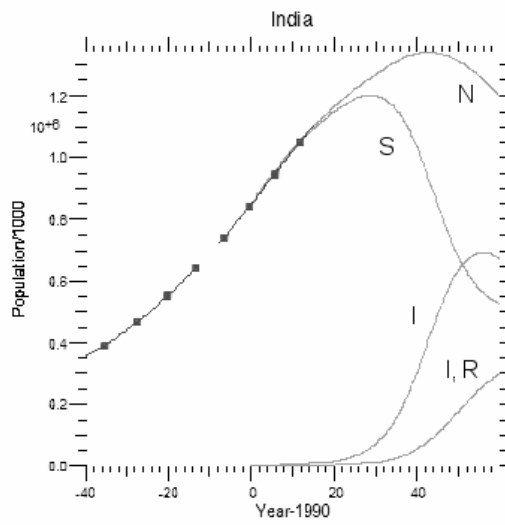


Figure 14: Developed HIV resistance under ART in India.

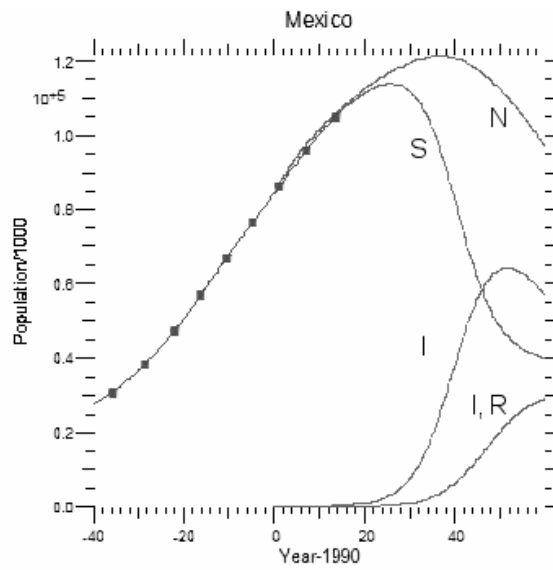


Figure 15: Developed HIV resistance under ART in Mexico.

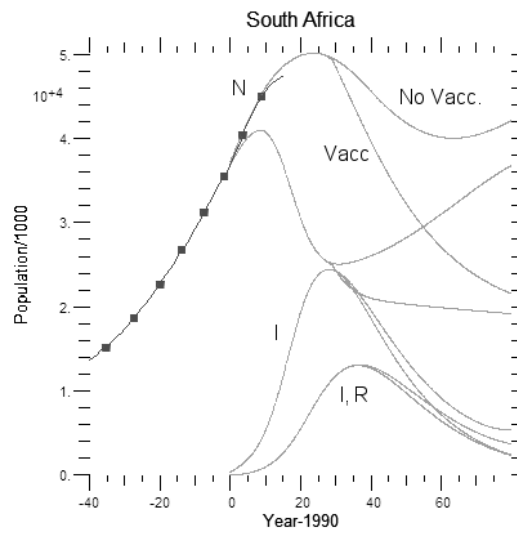


Figure 16: The susceptible population decreases in the presence of an AIDS vaccine in South Africa.

## 9 Conclusion

We feel our model is fairly appropriate for modeling the spread of HIV in otherwise stable countries, though there are many other factors that should be taken into account when applied to specific countries. This model could be used as a tool to UN to better target AIDS funding in an effort to minimize global fatalities and further spread of the disease.

By modeling the spread of AIDS with a system of differential equations, we were able to make relatively short term assumptions regarding the course of the epidemic. We observe huge increases in global AIDS cases and population downturns for several of the countries we modeled. These countries were chosen as critical based upon the findings of UNAIDS and the available data.

By observing the effects of ART and vaccination, we note that vaccination appears to be the only pharmaceutical way to stop the spread of HIV. However, our results do show that 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 affect of global population atrophy on the the world economy. The financial trends show that there should be increasing funding for ART treatment globally. Should a vaccine ever become available, our financial analysis clearly shows that it should be made available as quickly as possible. Additionally, the effects of a viral resistance to ART were considered in conjunction with vaccination.

We conclude that 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.

## 10 Recommendations to the United Nations

United Nations General Assembly  
Special Session on HIV/AIDS  
February 6, 2006

As the UNAIDS has reported, the HIV/AIDS epidemic is a dynamic, evolving, and quickly-growing crisis. For moral, economic, and world-stability reasons, action against the disease must be taken. Furthermore, recent studies show the critical time-dependence of the fight against AIDS.

The exponential growth of emerging diseases observed in simple models translates into a high cost of waiting to act. In essence, directing re-

sources toward stemming the disease now will save the world from paying costs many times greater in the future.

These funds must be directed toward appropriate objectives by well-informed coordinators. In particular, the complex dynamics of the disease propagation necessitate frequent feedback to the coordinators. Work should therefore be partnered with more intense research from organizations like UNAIDS. Accurate statistics coupled with model simulation can help create a more effective strategy.

Action must be integrated on the largest scale. In addition to providing support to the current victims of AIDS to prevent unbalanced age demographics, funding must be accelerated toward HIV vaccine research. Preventative measures have been shown to most greatly affect the long-term repercussions of AIDS, and may help avoid the build-up of treatment-resistant HIV strains.

Additionally, the importance of action on multiple fronts on the small-scale is paramount, as demonstrated by the successful HAART initiative. Relief programs need to provide not only equipment and funding, but also logistical aid and possibly support for an infrastructure to provide the treatments.

It is argued that the most critical nations in the fight against AIDS are those that cannot afford treatment to avert catastrophe. Therefore, securing international donation is as important as the strategy for action.

Donor involvement can be influenced by presenting a cost-analysis of not providing aid to potential donors. The loss of global productivity over the next few decades outweighs the cost of treatment for each individual; the costs are rising with the number of infections, and it is in the donors' best interest to act now; governments of some of the hardest-hit countries may not be able to recover, leading to dangerous instability in Africa, for instance; if unchecked, HIV's build-up in poor countries could cause an uncontrollable outbreak in potential donor countries. These incentives to provide aid are discussed extensively elsewhere, and it is every country's best interest to confront AIDS now.

Informing populations in rich countries of the emerging crisis could provide a firm foundation for the donation effort. The UN should allocate money for effective advertising of the emerging crisis in potential donor-nations, generating more funding. The ubiquity of AIDS organizations around the world offers a potential method to distribute the advertising effort. Indeed, these already-established organizations can be an invaluable connection to the donor-countries' general populations. The theme of a successful strategy with which to fight AIDS is an informed, integrated ap-

proach. To be effective on this issue, the UN needs to involve as much of the world as possible, collect frequent data about the epidemic, and progress on both treatment research and treatment delivery. The epidemic is not insurmountable, but is at a critical time in its development, and must be treated accordingly.

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## **A Sample solver code**

```

#incorporating the 'emerging trends' model #now using the ratio of
healthy births:infected will reduce healthy births

from scipy.optimize import * from scipy.integrate import odeint

def printToFile():
    f.write(str(parameters)+"\n[lambda1,mu,vus,gammaS,vts]"")
    f.write('\nS\t')
    for a in range(periodCount):
        for b in range(len(S[0])-1):
            f.write(str(S[a][b])+'\t')

    f.write('\nIus\t')
    for a in range(periodCount):
        for b in range(len(S[0])-1):
            f.write(str(Ius[a][b])+'\t')

    f.write('\nIts\t')
    for a in range(periodCount):
        for b in range(len(S[0])-1):
            f.write(str(Its[a][b])+'\t')

    f.write('\nIur\t')
    for a in range(periodCount):
        for b in range(len(S[0])-1):
            f.write(str(Iur[a][b])+'\t')

    f.write('\nItr\t')
    for a in range(periodCount):
        for b in range(len(S[0])-1):
            f.write(str(Itr[a][b])+'\t')
    f.write('\n\n')

def deriv(u,t):
    """
    Defines the SIA model of DE's

```

```

u: array of left side vars [S, I, A]
t: times for which ODE solutions will be returned
"""

#convert time -> index space
indexIntoThisPeriod = int(u[5]/timestep)

#where are we trying to look?; which period?
periodHistoryS = periodNum - int(.999*((enterIndex - indexIntoThisPeriod)/float(indicesPerPeriod)))
indexHistoryS = (indexIntoThisPeriod - enterIndex)%indicesPerPeriod

periodHistoryB = periodHistoryS # we look at the same time for b[.....] and S[]

if periodNum == 0:
    N = (u[0]+u[1]+u[2]+u[3])
    return array([
        bRateData[periodHistoryB+decadeIndexStart]*u[0] - mu*u[0] - lambda1*u[0]*u[1]
        - lambda1*u[0]*u[3], #S = 0
        lambda1*u[0]*u[1]-(mu+vus)*u[1]-gammaS*u[1],
        gammaS*u[1]-(mu+vts)*u[2]-lambda2*u[2],
        -gammaR*u[3]-(mu+vur)*u[3]+lambda1*u[0]*u[3],
        lambda2*u[2]-(mu+vtr)*u[4]+gammaR*u[3],
        1.0 ])
    #Ius = 1
    #Its = 2
    #Iur = 3
    #Itr = 4

if periodHistoryS < 0:
    periodHistoryS = 0; indexHistoryS = 0
    # if we have the birthrate data, use that. otherwise give earliest
    if -1*periodHistoryB > decadeIndexStart:
        periodHistoryB = -decadeIndexStart # look at first data we have
    else:
        if (periodHistoryS > periodNum-1):
            periodHistoryS = periodNum-1; indexHistoryS=len(S[0])-1
        if periodHistoryB > len(bRateData)-decadeIndexStart-1:
            periodHistoryB = len(bRateData) - decadeIndexStart - 1

N = (Ius[periodHistoryS][indexHistoryS]+Its[periodHistoryS][indexHistoryS]+Iur[periodHistoryS]

```

```

[indexHistoryS]+Itr[periodHistoryS][indexHistoryS]) # 1/N = 1/(S+Ius+Itr+...)
return array([
    bRateData[periodHistoryB+decadeIndexStart]*S[periodHistoryS][indexHistoryS]
        -mu*u[0]-lambda1*u[0]*u[1] - lambda2*u[0]*u[3],#S = 0
    lambda1*u[0]*u[1]-(mu+vus)*u[1]-gammaS*u[1], #Ius = 1
    gammaS*u[1]-(mu+vts)*u[2]-lambda2*u[2], #Its = 2
    -gammaR*u[3]-(mu+vur)*u[3]+lambda1*u[0]*u[3], #Iur = 3
    lambda2*u[2]-(mu+vtr)*u[4]+gammaR*u[3], #Itr = 4
    1.0])

""" INITIAL SYSTEM PARAMETERS """
window(1) # Activate window f = open('data.txt', 'w')
f.write('Data from the emerging trends model \n')

# index 6: 1980-85

timestep = 0.1 # Because we have to break up integral into "periods"
timePeriod = 1.0 # length of period in time periodCount = 80

#demographics parameters

decadeIndexStart = 40 #0 = 1950, 5 = 1955, 8 = 1958, 10 = 1960, 12 =
1962 #CHANGE

#South Africa popData = [13683.162, 13996.784, 14327.26,
14670.257, 15023.08, 15384.665, 15755.679, 16138.426,
16536.553, 16954.583, 17396.477, 17864.107, 18355.924,
18866.381, 19387.557, 19913.932, 20442.889, 20976.572,
21519.943, 22080.345, 22662.783, 23269.786, 23898.935,
24544.396, 25197.793, 25853.532, 26507.457, 27162.326,
27827.627, 28516.821, 29238.523, 30000.335, 30796.94, 31608.731,
32408.29, 33177.927, 33903.282, 34594.854, 35289.445,

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Iur0 = 0.
Itr0 = 0.

if vts == .005001:
    bRateData = bRateData2

initialCond = [S0, Ius0, Its0, Iur0, Itr0, 0.0] # 0 = strating cond for "time" in integration
parameters = [lambda1, mu, vus, gammaS, vts]

S = []; Ius = []; Its = []; Iur = []; Itr = []

m = mouse(-1,2,"\t\t Click to start. Right click to quit.")
if m[9] == 3:
    break

clr = (int((m[0]+1)*800%255),int((m[1]+1)*800%255),int((m[2]+m[3])*1*10000%237))

for periodNum in arange(0,periodCount):

    if vts == .05001:
        if periodNum == 10: #CHANGE ME when is prevention stepped up?
            gammaS = .2

    t=arange(periodNum*timePeriod,(1.5+periodNum)*timePeriod,timeStep) # need to eval well into next interval
    result=odeint(deriv,initialCond,t,rtol=10.**-1,atol=10.**-1)
    S = S + [result[:,0]]
    Ius = Ius + [result[:,1]]
    Its = Its + [result[:,2]]
    Iur = Iur + [result[:,3]]
    Itr = Itr + [result[:,4]]

#print timePeriod/timeStep+.1
#print len(S[periodNum])
# start with the last values from the prev time period
initialCond = [S [periodNum][(int)(timePeriod/timeStep+.1)],
               Ius[periodNum][(int)(timePeriod/timeStep+.1)],
               Its[periodNum][(int)(timePeriod/timeStep+.1)],
               Iur[periodNum][(int)(timePeriod/timeStep+.1)],
               Itr[periodNum][(int)(timePeriod/timeStep+.1)],

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Iur[periodNum][(int)(timePeriod/timestep+1)],
Itr[periodNum][(int)(timePeriod/timestep+1)],
0.0]

### Plot
t=range(periodNum*timePeriod,timePeriod*periodNum + 1,timestep)
pIg(S[periodNum][0:(int)(timePeriod/timestep+1)], t, color=clr)
#pIg(Ius[periodNum][0:(int)(timePeriod/timestep+1)], t, color=clr)
#pIg(Its[periodNum][0:(int)(timePeriod/timestep+1)], t, color=clr)
#pIg(Iur[periodNum][0:(int)(timePeriod/timestep+1)], t, color=clr)
pIg(Itr[periodNum][0:(int)(timePeriod/timestep+1)], t, color=clr)

totalInfect = add(Ius[periodNum][0:(int)(timePeriod/timestep+1)],Its[periodNum][0:(int)(timePeriod/timestep+1)])
totalInfe = add(totalInfect,Iur[periodNum][0:(int)(timePeriod/timestep+1)])
totalInfect = add(totalInfect,Itr[periodNum][0:(int)(timePeriod/timestep+1)])
percentInfect = divide(totalInfect,add(S[periodNum][0:(int)(timePeriod/timestep+1)],totalInfect))
N_toPlot=add(S[periodNum][0:(int)(timePeriod/timestep+1)],totalInfect)
pIg(N_toPlot, t, color=clr)
#pIg(percentInfect, t, color=clr)
pIg(totalInfect, t, color=clr)

pIg(popData,arange(-1.*decadeIndexStart,len(popData)-1.*decadeIndexStart,1), color = 'red', marker = 0)

xlabel('Year-1990')
ylabel('Population/1000')
title('South Africa')

print "Please insert system parameters list."
print "[lambda1,mu,vus,gammaS,vts]"
print "[" ,lambda1,mu,vus,gammaS,vts, "]"
print "Enter \"0\" to quit : "

printToFile()

parameters = (input())
if False==isinstance(parameters,list):
    break # quit

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[lambda1, mu, yus, gammaS, vts] = parameters
f.close()
```