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2006 Interdisciplinary Contest in Modeling (ICM) Summary Sheet

(Attach a copy of this page to each copy of your solution paper.)

Type a summary of your results on this page. Do not include the name of your school, advisor, or team members on this page.

Aids Can Raid; We Can Decide

The purpose of this paper is to develop a mathematical model based on historical data that describes the current health problems associated with HIV/AIDS and create a set of computer based methods that predict the future behavior of this infectious disease. The program provides a basis for examining the effects of the AIDS virus on a given population and examines the spread of AIDS through specified populations each representative of the six continents. We also make further predictions, by changing specific parameters, the behavior of the AIDS virus in other possible situations such as: employment of antiretroviral therapy (ART), discovery of a vaccine and a more infectious strain of the virus. At last, we put forward some reasonable recommendations for the UN to tackle this tough problem.

Keywords: HIV/AIDS Population ART Vaccine Recommendation

Aids Can Raid; We Can Decide

Introduction

The purpose of this paper is to develop a model based on facts known about the spread of the Acquired Immune Deficiency Syndrome (AIDS) virus, and to predict its spread throughout the most critical populations that are statistically representative of the six continents. The spread of this disease is examined by creating a mathematical model, applying the model to numbers obtained from historical data, and then running the model through a computer program. The basic equation this program is based on is known as the SI (Susceptible Infected) model which is a mathematical formula that is commonly used to calculate the spread of infectious diseases.

Because there is no positive treatment for the cure of HIV/AIDS, additional in-depth research will be required in both developed and developing countries. For this purpose, we make realistic estimates of the expected level of financial resources and discuss the spread of HIV/AIDS under related possible scenarios. We also put forward some reasonable recommendations for the UN to tackle this tough problem.

Our Tasks

1. In the absence of any additional interventions, choose the countries to be most critical in terms of HIV/AIDS.
2. Under realistic assumptions, estimate the expected rate of change in the number of HIV/AIDS infections for selected countries.
3. Re-formulate our previous models, taking into consideration the development of ARV-resistant strains.
4. Recommendations for the UN.

The Demographic Impact of HIV/AIDS

Assumptions and Hypotheses

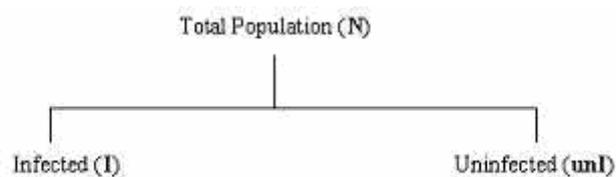
We set up an epidemiologically realistic model to estimate adult HIV prevalence, producing a national "best fit" curve of adult HIV prevalence using sentinel surveillance data pertaining to pregnant women. The application uses WHO/UNAIDS Epidemiological Reference Group assumptions about age-sex distribution and sex ratio of new infections, mother-to-child transmission rate, and disease progression.

- Assume no anti-retroviral therapy.
- Assume no HIV/AIDS vaccine.
- Allow for competing risk of death.
- Birth and death rates remain similar to what they are currently.
- There are no major population changes (due to war or a different disease).
- The virus does not adapt to changes in the populations.
- All members of specific age groups participate in similar activities.
- Immigration laws remain similar to what they are today.

The Model

Mathematical Bases

The Susceptible-Infected (SI) model, as shown below



$$\begin{cases} \frac{d(Ni)}{dt} = \lambda N(t)s(t)i(t) \\ s(t) + i(t) = 1 \end{cases} \quad i(0) = i_0$$

The basic SI model consists of four fundamental parameters; these are:

- contact rate(λ)
- susceptible population rate(s)
- infected population rate(i)
- and total population(N)

We arrive at
$$i(t) = \frac{1}{1 + \left(\frac{1}{i_0} - 1\right)e^{-\lambda t}}$$

Application to HIV/AIDS

To describe the spread of HIV/AIDS in a society, we write our equations as

$$\begin{cases} x'(t) = \alpha x(1 - x) - kxy/(x + y) \\ y'(t) = -ay + kxy/(x + y) \end{cases}$$

- $x(t)$: the number of the HIV negative people in society
- $y(t)$: the number of the HIV positive people in society

It is to be noted that in a random mating environment, the total number of mating partners to an x or to a y is $x + y$, so that an x may mate with a probability of $kxy/(x + y)$. Hence the above equations. We take one year to be the unit of time in this section. The three points of equilibrium are

$$P_1 = (0,0) \quad P_2 = (1,0) \quad P_3 = (x_1, y_1) \quad \text{Where } x_1 = (\alpha - k + a)/\alpha \quad \text{and } y_1 = (k - a)x_1/a$$

They correspond to (a) the society being eliminated, (b) the disease being eliminated and (c) the disease becoming endemic, respectively. It is of utmost importance for us to know which values of the parameters lead to these three equilibrium points and particularly, to the annihilation of the society.

Case	Values of a, k and α	Behavior of Solution
1	$\alpha \geq 1$	All solutions go to P_2 or P_3
2	$0 < \alpha < 1, a < k < a/(1 - \alpha)$	All solutions go to P_1 or P_3
2a	$B = 0, C > 0$	All solutions go to P_1 or P_3
2b	$B > 0, C > 0, B^2 > 4C$	All solutions go to P_1 or P_3
2c	$B > 0, C > 0, B^2 < 4C$	All solutions go to P_1 or P_3
2d	$B < 0$	All solutions go to P_1 or limit
3	$0 < \alpha < 1, k < a$	All solutions go to P_1 or P_2
4	$0 < \alpha < 1, k \geq a/(1 - \alpha)$	All solutions go to P_1
5	$0 < \alpha < 1, k = a$	All solutions go to P_1 or P_2
6	$a + \alpha < \min(1, k)$	All solutions go to P_1
7	$a + \alpha > \max(1, k)$	All solutions go to P_2 or P_3
8	$k < a + \alpha < 1$	All
9	$1 < a + \alpha < k$	All solutions go to P_1 or P_3

Various Possibilities

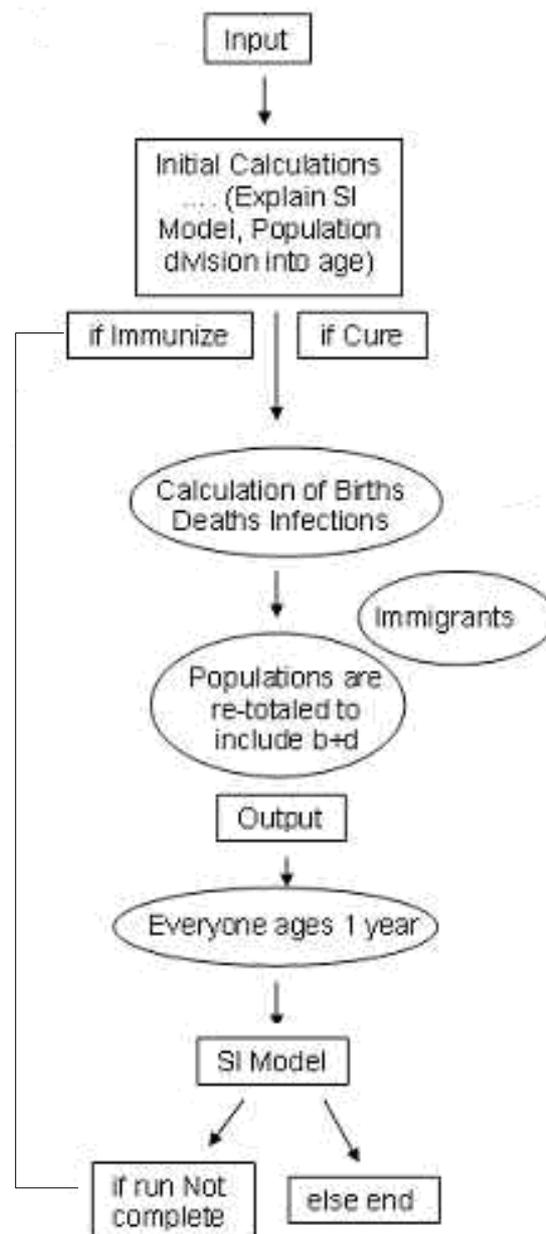
These variables are used to calculate the newly infected members of the population (IR) during each of the time steps. As the equation is run the susceptible population goes down and the infected population goes up. At first, the number of new infected increases each time; because a higher percentage of the population is infected more susceptible individuals come in contact with infected individuals. Eventually the susceptible population becomes small enough such that the new infected group within the population in each of the iterations cannot remain constant and begins to decline.

This rollover effect shown above is a trend that is repeated in most all epidemics. It is caused by the interaction of the susceptible and infected populations as the size of their populations increases and decreases throughout the spread of the disease. Although this trend can be found in epidemics in real world situations the curve is effected by many more variables, i.e. a population with immunity to the disease, certain population members who are less likely to contract the disease. This curve is most applicable to epidemics that spread rapidly through a population, kill many of the population's members, and finally leave mostly immune members of the population.

The HIV/AIDS epidemic is unique because it can take years before an infected individual shows symptoms of the virus. This means instead of modeling the epidemic for days it must be modeled over many years. Since it needs such an extended modeling time other variables must be taken into account. These variables include birth and death rates for all populations (different age groups, infected, uninfected) in the simulation. Another problem large time steps created in the creation of the program is that people, after being born have to grow old and eventually die. To solve this problem, different death rates were applied to each population group to reflect not only a population member's ability to die but also taking into account that individual's age. Also, there is approximately a 1% chance a person is born with immunity to HIV; therefore, in addition to adding age groups, a new population group called "unsusceptible" was added to the program.

In order to make the model more realistic during each time step, each person has a chance (determined using input variables) to have a child, die or become infected. Then each child born has a chance to be born susceptible, unsusceptible, or infected (if the parent is infected). When the program makes a decision it goes through this process: If a randomly generated number is less than the chance defined by the input variable then the event in question (birth, death, infection) takes place if the random number is greater than the chance the event in question does not take place.

Computer Applications



Flowchart of the Program

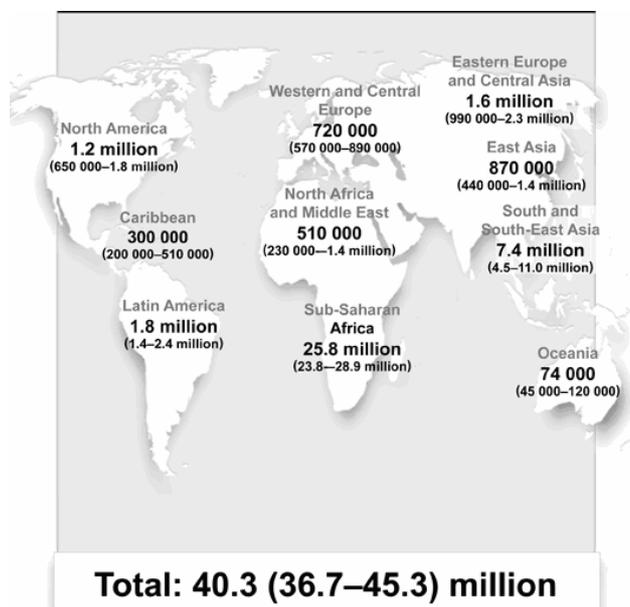
Many assumptions have to be made for the project. Most of them involve people's activities remaining consistent with how they are today. The following is a list of the assumptions that were made:

- Birth, death and immigration rates remain similar to what they are currently.
- There are no major population changes (due to war or a different disease).
- The virus does not adapt to changes in the populations.
- All members of specific age groups participate in similar activities.
- Immigration laws remain similar to what they are today.

Conclusions

At the global level, the number of people living with HIV continues to grow; over 20 million have died since the first cases of AIDS were identified in 1981. The epidemic varies in scale or impact within regions; some countries are more affected than others, and within countries there are usually wide variations in infection levels between different provinces, states or districts.

HIV estimates—whether they are based on household surveys or surveys of pregnant women—need to be assessed critically as the epidemic evolves. Achieving 100% certainty about the numbers of people living with HIV globally, for example, would require repeatedly testing every person in the world for HIV—which is logistically impossible.



Adults and Children Estimated to be Living with HIV in 2005
Source: UNAIDS/WHO AIDS Epidemic

Africa

An estimated 25 million people are living with HIV in sub-Saharan Africa. There appears to be stabilization in HIV prevalence rates, but this is mainly due to a rise in AIDS deaths and a continued increase in new infections. Prevalence is still rising in some countries such as Madagascar and Swaziland, and is declining nationwide in Uganda.

Sub-Saharan Africa is home to just over 10% of the world's population—and almost two-thirds of all people living with HIV.

There is no such thing as the "African" epidemic; there is tremendous diversity

across the continent in the levels and trends of HIV infection. In six countries, adult HIV prevalence is below 2%, while in six other countries it is over 20%. In southern Africa all seven countries have prevalence rates above 17% with Botswana and Swaziland having prevalence above 35%. In West Africa, HIV prevalence is much lower with no country having a prevalence above 10% and most having prevalence between one and five percent. Adult prevalence in countries in Central and East Africa falls somewhere between these two groups, ranging from 4% to 13%.

African women are at greater risk, becoming infected at an earlier age than men. Today there are on average 13 infected women for every 10 infected men in sub-Saharan Africa. The difference is even more pronounced among 15 to 24 year olds. A review compared the ratio of young women living with HIV to young men living with HIV; this ranges from 20 women for every 10 men in South Africa to 45 women for every 10 men in Kenya and Mali.

In North Africa and the Middle East, around 480 000 are living with HIV but systematic surveillance of the epidemic is not well developed, particularly among high-risk groups such as injecting drug users. Yet in much of the region HIV infection appears concentrated among this group. There is also concern that HIV may be spreading undetected among men who have sex with men, as male-male sex is widely condemned and illegal in many places.

Asia

The epidemic in Asia is expanding rapidly. This is most evident with sharp increases in HIV infections in China, Indonesia and Viet Nam. An estimated 7.4 million people are living with HIV in the region and 1.1 million people became newly infected last year alone—more than any year before. Home to 60% of the world's population, the fast-growing Asian epidemic has huge implications globally.

In Asia, the HIV epidemic remains largely concentrated among injecting drug users, men who have sex with men, sex workers, clients of sex workers and their immediate sexual partners. Effective prevention coverage in these groups is inadequate, partly because of stigma and discrimination. Asian countries such as Thailand and Cambodia, which have chosen to tackle openly high-risk behavior, such as sex work, have been more successful in fighting HIV, as shown by the reduction in infection rates among sex workers.

However there is no room for complacency. Although there is a reduction in the numbers of young Thai men visiting brothels, for example, there is also an increase in casual sex. Behavioral surveillance between 1996 and 2002 shows a clear rise in the proportion of secondary school students who are sexually active,

and at the same time consistently low levels of condom use.

If other Asian countries fail to target populations at higher risk, the epidemic will affect much greater numbers of people in the general population.

India has the largest number of people living with HIV outside South Africa—5.1 million. But knowledge about the virus and its transmission is still scant and incomplete, and there is concern that many men who have sex with men may be infecting women with whom they also have sex.

Europe

Europe continues to have expanding epidemics, fuelled by injecting drug use. About 1.3 million people are living with HIV, compared with about 160 000 in 1995. Strikingly, more than 80% of them are under the age of 30. Estonia, Latvia, the Russian Federation and Ukraine are the worst-affected countries, but HIV also continues to spread in Belarus and Moldova.

The main driving force behind the epidemic in this region is injecting drug use. But in some countries sexual transmission is becoming increasingly common, especially among injecting drug users and their partners.

Russia, with over three million injecting drug users, remains one of the worst-affected countries in the region. Women account for an increasing share of newly diagnosed cases of HIV—up from one-in-four in 2001 to just one-in-three one year later in 2003.

North America

An estimated 1.6 million people are living with HIV in these countries. Unlike the situation in other regions, the great majority of people living with HIV in North American countries who need antiretroviral therapy have access to it, so they are staying healthy and surviving longer than infected people elsewhere.

The report finds that infections are on the rise in the United States. In the US, an estimated 950 000 people are living with HIV – up from 900 000 in 2001. Half of all new infections in recent years have been among African Americans.

Australia

An estimated 74 000 people in Australia are living with HIV. Although less than 4000 people are believed to have died of AIDS in 2005, about 8200 are thought to have become newly infected with HIV. Among young people 15–24 years of age, an estimated 1.2% of women and 0.4% of men were living with HIV.

HIV infections have now been reported in every country and territory in Oceania, barring Niue and Tokelau. Although the epidemics are still in their early stages in most places, preventive efforts need to be stepped up.

More than 90% of the 11 200 HIV infections reported across the 21 Pacific Islands countries and territories by end-2004 were recorded in Papua New Guinea where an AIDS epidemic is now in full swing.

Australia, by contrast, has the oldest epidemic in the region. Having declined by about 25% from 1995–2000, the annual number of new HIV diagnoses in Australia has been edging upward again.

New Zealand's epidemic is small by comparison. However, new HIV cases have doubled in recent years. Sex between men accounted for about half the new diagnoses. Similar to Australia, more than 90% of people with heterosexually-acquired HIV diagnosed had been infected abroad.

HIV-infection levels are very low in the rest of Australia, with the total number of reported HIV cases exceeding 150 only in New Caledonia (246), Guam (173), French Polynesia (220) and Fiji (171). The data are based on limited HIV surveillance. Given the high levels of other sexually transmitted infections that have been recorded in some Pacific islands, none of these countries and territories can afford to be complacent.

South America

Around 1.6 million people are living with HIV in South America. The epidemic is concentrated among populations at high risk of HIV infection—injecting drug users and men who have sex with men.

Low national prevalence hides some serious local epidemics. For example, in Brazil (the region's most populous country), national prevalence is below 1%, but in certain cities 60% of injecting drug users are infected with HIV.

HIV is spread predominantly through sex – both heterosexual and among men who have sex with men. Three Caribbean countries have national HIV prevalence rates of at least 3%: the Bahamas, Haiti, and Trinidad and Tobago. Around 430 000 people in the region are living with HIV.

The Caribbean epidemic is mainly heterosexual, and in many places it is concentrated among sex workers. But it is also spreading in the general population. The worst-affected country is Haiti where national prevalence is around 5.6%, the highest outside Africa.

* denotes country selected

Country	2005	2010	2015	2020	2025
Australia *	15897.54	17579.12	19393.87	21365.46	23434.3
Botswana	309905.3	316367.9	322105.2	331567.5	341663.9
Brazil *	623703.3	698094.1	774063	851642.5	930805.6
Cambodia	263087.1	304954.9	351949.7	402391.5	454688
Canada	55219.65	60585.83	66278.28	72432.09	78971.22
Haiti	242591.8	273080.4	305661.9	339781.8	375252
India *	4315805	4864745	5446129	6049568	6661192
Russia *	134437.1	138191.3	141812	145155.1	148151
Swaziland	139558.1	142591	146188.5	151015.7	156290.7
Thailand	845597.4	923644.8	1003435	1084313	1164524
USA *	956753.8	1052990	1154531	1260833	1370944
Zimbabwe *	1648650	1773878	1907915	2040649	2172586

Country	2030	2035	2040	2045	2050
Australia *	24634.59	27698.57	29882.39	32151.95	34546.37
Botswana	355419.5	364738.5	378585.7	395145.3	415035.8
Brazil *	978324.1	1090498	1170039	1248690	1325652
Cambodia	477443.6	566037.6	626345.1	689324	753558.8
Canada	83011.27	92698.93	99807.44	107151.2	114873.9
Haiti	393794.4	450049.1	489401.1	529757.2	570582.7
India *	7001006	7878863	8502983	9130527	9748629
Russia *	155737.7	154145.5	157584.7	161122.2	164447.8
Swaziland	162964.5	169980.9	178902.6	189565.6	201979.5
Thailand	1223225	1319785	1392769	1462209	1528650
USA *	1440944	1603644	1725660	1851882	1983748
Zimbabwe *	2266481	2452355	2604363	2763812	2930091

HIV/AIDS Population Data ($\lambda = 0.01$)

Financing the Response to AIDS

Overview

U.S. billion	2006	2007	2008
Prevention	8.4	10.0	11.4
Treatment and Care	3.0	4.0	5.3
OVC	1.6	2.1	2.7
Program Costs	1.5	1.4	1.8
Human Resources	0.4	0.6	0.9
Total	14.9	18.1	22.1

Global Aids Resource Needs

Important progress has been made in raising additional funds to respond to the AIDS epidemic. By 2003, an estimated US\$ 5 billion was available, from donors, the UN system, international nongovernmental organizations, country governments and the “out-of-pocket” spending by people living with HIV and their families. Yet this amount is less than half of what is required by 2006.

National governments of developing countries are spending increasing amounts on AIDS programs—an estimated US\$ 2 billion in 2002, but this only accounts for 6-10% of AIDS expenditure. There are enormous global disparities in AIDS spending. Spending per person living with HIV in the United States exceeds that in the Latin America and Caribbean region by a factor of 35, and is 1000 times higher than in Africa.

As of early 2004, national governments, the Global Fund to Fight AIDS, Tuberculosis and Malaria, the United States President's Emergency Plan for AIDS Relief, and other bilateral donors and foundations had pledged just over US\$ 2 billion to scale up antiretroviral treatment access in 34 of the hardest-hit countries by the end of 2005. This leaves a shortfall of US\$ 3.5 billion. There are huge variations at country level. Some already have the funds to cover their proposed treatment targets while others have large funding gaps.

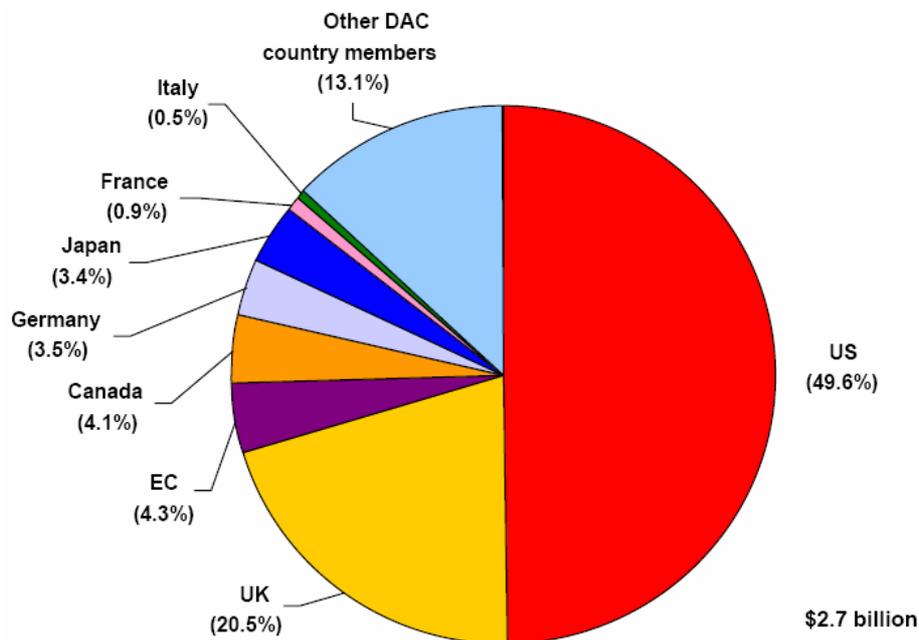
Even though financial resources are rising, in many heavily affected countries serious bottlenecks prevent effective spending of the money. These blockages include lack of human and institutional capacity, the persistent negative effects of stigma and discrimination, shortfalls in political commitment, slow transfer of funds from national to local and community levels, inadequate accounting and auditing mechanisms, and inconsistent funding processes of the global donor community.

Two-thirds of global funding for 2006 and subsequent years is expected to come from the international community. Most of this money will be spent to meet the needs of the poorest and worst-affected countries of Asia and sub-Saharan Africa; these countries will rely on external donors to meet up to 80% of their needs.

Problems for poor countries

Past objections to AIDS treatment in poor countries fall into several categories. First, poor countries lack the adequate medical infrastructure to provide AIDS treatment safely and effectively. Second, difficulties with adherence to complicated medication regimens would promote and spread drug resistance. Third, antiretroviral drugs are expensive, and the treatment cost is too high for the wealthy countries to finance without siphoning resources away from HIV prevention programs and other worthy development goals. Finally, commitment from political leaders in Africa and

other poor regions is not sufficient to underpin a major international effort towards providing AIDS treatment.



Current Global Aids Resource Data

ARV Drug Therapy

Although prevention is the mainstay of the response to AIDS, fewer than one in five people worldwide have access to HIV prevention services. Comprehensive prevention could avert 29 million of the 45 million new infections projected to occur this decade. Although antiretroviral treatment is bringing hope to millions, without sharply reducing the number of new HIV infections, expanded access to treatment becomes unsustainable. Providers of antiretroviral treatment will be swamped by demand.

Prevention programs are not reaching the people who need them, especially two highly vulnerable groups—women and young people. In order to prevent the high infection rates among women, the root causes of their vulnerability—their legal, social and economic disadvantages—must be addressed.

For young people, knowledge and information are the first line of defense; AIDS education is still far from universal. In sub-Saharan Africa, only 8% of out-of-school young people and slightly more of those in-schools have access to education on prevention. They also need access to confidential health information and condoms. Protecting the rights of young girls is also key to lowering HIV prevalence among young people.

The Model

The revised model, as shown below

$$\begin{cases} \frac{di}{dt} = (\lambda - ci)si - \mu i & i(0) = i_0 \\ \frac{ds}{dt} = -(\lambda - ci)si & s(0) = s_0 \end{cases}$$

It consists of five fundamental parameters; these are:

- contact rate(λ)
- susceptible population rate(s)
- infected population rate(i)
- control coefficient(c)
- death rate(μ)

Year	People on ART (millions)	Coverage ART 1 yr need	Coverage ART 2 yr need	Total Resource (U.S. millions)
2006	3.0	55%	41%	2 986
2007	4.8	67%	54%	4 029
2008	6.6	75%	63%	5 250
2009	8.3	79%	67%	--
2010	9.8	80%	68%	--

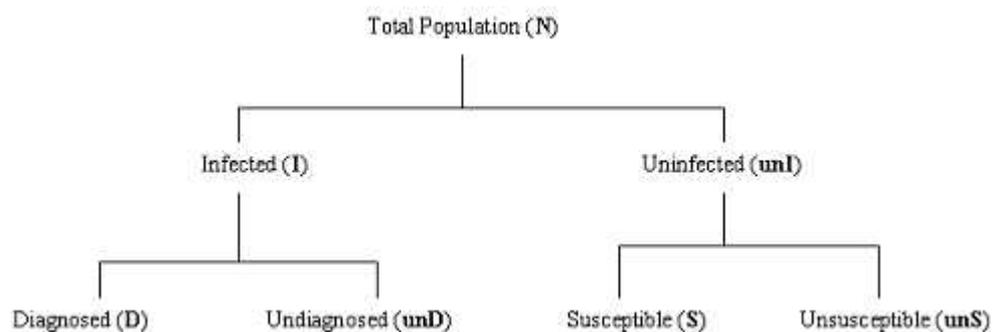
Antiretroviral Therapy (ART) Coverage

Vaccine Research and Development

Vaccine	HIV subtype
Adeno-associated virus expressing multiple genes	C
Adenovirus expressing multiple genes (replicating)	B
ALVAC expressing multiple genes	A
DNA and adenovirus (replicon) expressing multiple genes	B
DNA and adenovirus expressing novel gag-pol and novel env	B
DNA and MVA expressing multiple genes	B, A/G
MVA expressing multiple genes	A, D
DNA, Sindbis replicons expressing multiple genes	B, C
DNA expressing multiple HIV genes	B
DNA and fowlpox expressing multiple HIV genes	B, E
DNA-env and envelope protein	Multiple
Gp120 and regulatory proteins in novel adjuvants	B
MVA expressing multiple genes	B
MVA, NYVAC, DNA, Semliki Forest Virus expressing multiple genes	C
P55 VLP	B
Salmonella expressing multiple genes	A, A/G
Vaccinia-env and envelope proteins	Multiple

Vaccines in Preclinical Development

The Model



Let θ denote the relative susceptibility of a vaccinated uninfected compared to an unvaccinated uninfected person, and φ denote the relative infectiousness of a vaccinated infected compared to an unvaccinated infected person. Then the desired estimates are the protective efficacy on susceptibility and the efficacy in reducing infectiousness, respectively

$$VE_S = 1 - \theta \quad VE_I = 1 - \varphi$$

Our goal is to find the maximum likelihood estimates of θ and φ , and thus VE_S and VE_I .

For each individual, or individuals within partnerships, the required data are: vaccine status; infection status at the end of trial; and vaccine and infection status of partner, if the study subject has a partner.

Let:

- v denote vaccination status of primary study participants, 0 if unvaccinated, 1 if vaccinated;
- μ denote vaccination status of steady partners, 0 if unvaccinated, 1 if vaccinated;
- i, j denote infection status of primary participant and steady partners, respectively, where 0 denotes uninfected and 1 denotes infected by the end of the study;
- γ equal the probability of an unvaccinated trial participant becoming infected during the study period. For someone with a partner in the study, c represents the probability of being infected from sources outside the partnership;
- $\beta_{v\mu}^{ij}$ equal the per partnership transmission probability of partnerships with vaccination status (v, μ) , where either i or j equals 1.

Conclusions

Vaccines and microbicides are global public goods (goods that benefit others beyond those who use them directly); each prevented infection cuts off a

potential chain of infections resulting from the primary infection. Both private and public sector investment is needed for vaccines and microbicides. According to the International AIDS Vaccine Initiative, public sector investment in vaccine research looks set to expand but overall funding is not keeping up with the challenges.

Expanded access to vaccines and other treatment offers a critical opportunity to strengthen prevention efforts by encouraging many more people to learn their HIV status. The promise of treatment should encourage greater use of voluntary counseling and testing. The current reach of HIV testing is poor. The proportion of adults needing voluntary counseling and testing who received it ranged from almost none in South East Asia to 7% in sub-Saharan Africa, and 1.5% in Eastern Europe. Where services do exist, uptake is also often low because of fear of stigma and discrimination.

	Parameters of Interest	Classical Trial	Non-Randomized Partner Model	Randomized Partner Model
Mean	VE _s	0.198	0.198	0.199
	VE _i		0.501	0.484
Standard Deviation	VE _s	0.082	0.072	0.067
	VE		0.057	0.026
Mean Squared Error	VE _s	0.007	0.005	0.004
	VE _i		0.057	0.026
Power	VE _s	0.668	0.784	0.846
	VE _i		0.570	0.864

Testing Results

$$\gamma = 0.1 \quad \theta = 0.8 \quad \varphi = 0.5 \quad \beta = 0.5$$

Comprehensive Prevention

Key elements in comprehensive HIV prevention include:

- AIDS education and awareness
- Behavior change programs especially for young people and populations at higher risk of HIV exposure, as well as for people living with HIV
- Promoting male and female condoms as a protective option along with abstinence, fidelity and reducing the number of sexual partners
- Voluntary counseling and testing
- Preventing and treating sexually transmitted infections

- Primary prevention among pregnant women and prevention of mother-to-child transmission
- Harm reduction programs for injecting drug users
- Measures to protect blood supply safety
- Infection control in health-care settings
- Community education and changes in laws and policies to counter stigma and discrimination
- Vulnerability reduction through social legal and economic change

Possible Vaccine Outcomes

It is important to realize that scientists are still learning about how vaccines might work to prevent HIV infection. An HIV vaccine may be totally successful in preventing infection, known as "sterilizing immunity." Sterilizing immunity may be possible in 100% of the population, or perhaps only in certain groups. In another scenario, a preventive vaccine may not prevent primary infection, but decrease the possibility of HIV transmission from an infected individual to another person. Yet another possibility is that a vaccine may slow the process of infection, so that even if a person becomes HIV infected, the vaccine helps the vaccinated individual remain healthier longer. The following list provides details about the variety of ways that scientists believe a preventive HIV vaccine might work.

Sterilizing immunity

- complete protection from HIV infection
- no detectable HIV at any time
- no transmission of HIV to others

Transient infection

- infection occurs, but the immune system is able to detect and kill off infected cells
- disease process does not advance, because immune system is able to control the infection
- no detectable HIV at later times (6-12 months after infection)
- seroconversion (becoming HIV+) may or may not occur

Long-term controlled infection

- undetectable or very low viral load throughout life
- no immunodeficiency disease progression (HIV does not advance to AIDS)

Next Agenda

- Increase the resources committed to the AIDS pandemic from all sources to provide the required US\$ 12 billion annually by 2005.
- Identify and remove potential bottlenecks in funding flows. Radically improve and harmonize mechanisms for delivering funds through all levels – international, national, regional, community and local.
- Use resources in a “smarter” way. Build program capacity to demonstrate results by using funds efficiently and effectively, and monitoring performance and impact.
- Incorporate the concept of AIDS “exceptionality” into financing the AIDS response in countries in desperate need. Funds for AIDS must not draw away resources from other activities to the detriment of overall development. Action on AIDS should not further increase debt burdens. International financial institutions should think broadly and creatively about mechanisms to place more funds in the hands of countries now facing large debt-service payments.

Development of ARV-Resistant Disease Strains

We further develop a detailed density dependent model for propagation of HIV/AIDS. This model divides the society into three groups, those who are HIV negative, those who are HIV positive but have not developed AIDS, and those who have AIDS. The word “healthy” in this section means HIV negative. The various parameters are defined as follows

- $x(t)$: Number of healthy people in a society at any time t
- $y(t)$: Number of people who are HIV positive but do not have AIDS at any time t
- $z(t)$: Number of people with AIDS at any time t
- A_1x : Rate of birth of healthy babies near $x=0$
- A_1/A_2 : Maximum number of healthy people the country can support
- $A_3x(y+z)$: Rate at which healthy people become infected with HIV by contacting other people who are HIV positive (whether having AIDS or not)
- A_5y : Rate at which infected (i.e. HIV positive) people develop AIDS disease

- A6y: Rate at which infected people die before developing AIDS
- A7(y+z): Rate at which infected babies are born
- Kz: Rate at which sick people (having AIDS) die

The Model

$$\begin{cases} x'(t) = A1x - (A2 - A3)x^2 - A3xw \\ v'(t) = (A1 + A5 + A6 - A7)x - A2x^2 - (A5 + A6)v + A7w \\ w'(t) = (A1 + A6 - A7)x - A2x^2 + (k - A6)v - (k - A7)w \end{cases}$$

We write $u = y+z$ and treat x , u , and z as the independent variables. Now our equations are

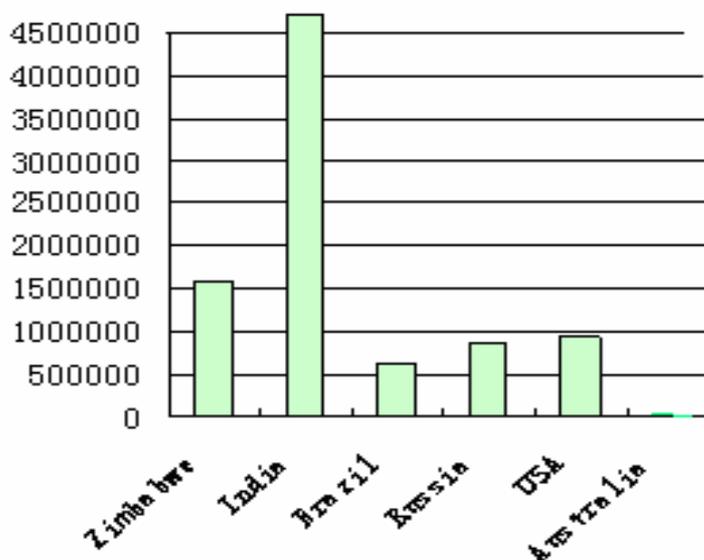
$$\begin{cases} x'(t) = A1x - A2x^2 - A3xu \\ u'(t) = A3xu - (A6 - A7)u + (A6 - k)z \\ z'(t) = A5u - (A5 + k)z \end{cases}$$

The equilibrium points of the above equations are
 P1(0,0,0) the society being annihilated
 P2(A1/A2,0,0) the disease being annihilated
 P3(x0,u0,z0) the disease becoming endemic respectively

Where $x0 = ((A6 - A7)k + A5(-A7 + k))/(A3(A5 + k))$
 $u0 = (A1 - A2x0)/A3$ $z0 = A5u0/(A5 + k)$

Regional	Country	Adult(15-49) HIV prevalence rate	Adults(15-49) living with HIV	Children(0-14) living with HIV	Women(15-49) living with HIV
Africa	Botswana	37.3%	330 000	20 000	190 000
	Zimbabwe	24.6%	1 600 000	200 000	930 000
	Swaziland	38.8%	200 000	20 000	110 000
Asia	Cambodia	2.6%	170 000	21 000	51 000
	India	0.8%	4700 000	300 000	1100 000
	Thailand	1.5%	560 000	10 000	200 000
South America	Brazil	0.7%	650 000	10 000	240 000
	Haiti	5.6%	260 000	20 000	150 000
Europe	Russia	0.9%	860 000	10 000	290 000
North America	USA	0.6%	940 000	10 000	240 000
	Canada	0.3%	55 000	10 000	13 000
Australia	Australia	0.3%	10 000	1 200	2 200

Countries Most Critical in Terms of HIV/AIDS



Countries Most Critical in Terms of HIV/AIDS

Treatment, Care and Support are Needed

U.S. million	2006	2007	2008
Palliative Care	308	302	295
Provider Initiated Testing	66	79	109
OI Treatment	686	703	707
OI Prophylaxis	287	403	510
ART, including Nutritional Support	1642	2482	3624
Laboratory Testing	54	79	104
Total	3043	4048	5349

Treatment and Care Components

Access to antiretroviral treatment and other HIV-related disease care remains low. It is high time that we try our best to tackle this problem.

Our next agenda should be:

- Strengthen human capacity in those countries whose scarcity of health workers is a barrier to antiretroviral programme success. In certain countries, the size of the health workforce must triple or quadruple if universal coverage of antiretroviral treatment is to be achieved. In countries most affected by AIDS, vacancy rates for doctors, nurses and other health staff are extremely high; in 2001, for example, Malawi had only filled half its public sector nursing posts. Incentives and working

conditions need to be improved to prevent migration to higher income countries.

- Expand voluntary counselling and testing to ensure widespread knowledge of HIV status, since it is the gateway to HIV treatment and prevention.
- Provide greater support for technology transfer and exports – from countries with antiretroviral manufacturing capacity to countries without it. All partners within the pharmaceutical industry must be part of the AIDS response to guarantee the huge increase in treatment access currently being planned.
- Ensure countries can take advantage of their rights to use trade agreement provisions to widen access to HIV medicines and technologies. This includes resisting stricter-than-necessary patient provisions in regional trade agreements that will otherwise undermine much of the flexibility provided in global trade agreements and declarations for developing countries.
- Reduce HIV-related stigma so that treatment can reach people in need.
- Place equity at the forefront of policies and programs to ensure fair access to treatment. If universal access is to become a reality, the barriers to treatment for women, children and other groups such as sex workers, injecting drug users and men who have sex with men, must be removed.

Strengths and Weaknesses of the Models

Strengths of the Models

Robustness: We derive our model from basic mathematical relationships and limit our use of assumptions. In every case where an assumption is required, we verify it with evidence and reasoning that illustrate why the assumption is cogent.

Grounded in theory and research: We construct our model based on both theory and research.

Ease of use: We create a computer program that allows anyone with a basic knowledge of computers to input the required data and get the expected result.

Adaptability: We validate the model for stability, sensitivity, and realism, and find that small changes in initial conditions do not cause drastic changes in the end result.

Weaknesses of the Models

Incompleteness of data required: We can not get the precise HIV/AIDS population data in our model and the exact materials concerning financial resources, some of the data we use have to be inferred, and corresponding errors may be incurred.

Limitation of consideration: There are parameters that we do not incorporate in our model, such as the incubation period and recovery rate, and they may influence the eventual result.

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