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Editorial

HIV: The Math

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Roughly 1% of the world's adult population is infected with HIV, which currently results in 2.8 million deaths per year (3% of all deaths and almost three times as many as malaria).

What can mathematics offer in the struggle against this disease? Mathematics itself offers no protection and no cures. However, like claims early on that "everyone" can get AIDS, and revelations of false assurances of safety of the blood supply in the U.S. and France, mathematics can definitely help add to the scare effect. Many years ago, I rejected for publication in this *Journal* a paper by a student team that projected that most American adults would be infected by HIV—or dead from it—by now. Both the modeling and the conclusions were unsound. The dynamic of HIV, however, has since taught us again an old lesson, that fear is weaker than desire. (This *Journal* did publish a UMAP Module on HIV recently [Isihara 2005], dealing mainly with immunological aspects.)

What mathematics can do is project immediate past and current trends, to reveal what the future could be without basic change. In the case of HIV, the results are encouraging for some countries and discouraging for others. The teams in this year's Interdisciplinary Contest in Modeling were asked to focus their modeling on "critical" countries, with the teams determining for themselves the meaning of "critical" and selecting the countries. The Outstanding papers published here unsurprisingly focus on many of the same countries (ones with large HIV-positive populations or with a large proportion of their population HIV-positive) and project, in human and in economic terms, the results of different strategies of intervention.

Mathematics can certainly help quantify the varied consequences of differing policies, such as for preventing HIV. But many people mistrust the predictions of mathematics because they mistrust mathematics. And they mistrust

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mathematics because they never understood it nor learned to appreciate its relevance.

The thousands of interested students who take part in the ICM and MCM are one prong of COMAP's efforts to promote applications in mathematics instruction. However, it is those millions of students mistrustful of mathematics whom COMAP tries hardest to reach, with its high school mathematics textbooks [COMAP 2000; 2002; 2007; Crisler and Froelich 2006], its college-level textbook [Garfunkel et al. 2006], and other initiatives.

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About the Editor

Paul Campbell graduated summa cum laude from the University of Dayton and received an M.S. in algebra and a Ph.D. in mathematical logic from Cornell University. He has been at Beloit College since 1977, where he served as Director of Academic Computing from 1987 to 1990. He is Reviews Editor for *Mathematics Magazine* and has been editor of *The UMAP Journal* since 1984. He is a co-author of the COMAP-sponsored book of applications-oriented collegiate mathematics *For All Practical Purposes* (7th ed. W.H. Freeman 2006), already used by more than half a million students.

Modeling Forum

Results of the 2006 Interdisciplinary Contest in Modeling

Chris Arney, ICM Co-Director
Division Chief, Mathematical Sciences Division
Program Manager, Cooperative Systems
Army Research Office
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Research Triangle Park, NC 27709–2211
David.Arney1@arl.army.mil

Introduction

A total of 224 teams of undergraduates and high school students, from 122 departments in 80 institutions in 6 countries, spent a weekend in February working on an applied mathematics problem in the 8th Interdisciplinary Contest in Modeling (ICM).

This year's contest began on Thursday, Feb. 2, and ended on Monday, Feb. 6. During that time, the teams of up to three undergraduates or high school students researched, modeled, analyzed, solved, wrote, and submitted their solutions to an open-ended complex interdisciplinary modeling problem involving public-health policy decisions concerning the HIV/AIDS epidemic. After the weekend of challenging and productive work, the solution papers were sent to COMAP for judging. Four of the top papers, which were judged to be Outstanding by the panel of judges, appear in this issue of *The UMAP Journal*. Results and winning papers from the first seven contests were published in special issues in 1999 through 2005.

COMAP's Interdisciplinary Contest in Modeling along with its sibling contest, the Mathematical Contest in Modeling, are unique among mathematics competitions in that they are the only international contests in which students work in teams to find a solution. Centering its educational philosophy on

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mathematical modeling, COMAP supports the use of mathematical tools to explore real-world problems. The contests serve society by developing students as problem solvers in order to become better-informed—and better-prepared—citizens, consumers, workers, and leaders.

This year's public health problem was particularly challenging in its demand for teams to utilize many aspects of science and mathematics in their modeling and analysis. The problem required teams to understand the science of the HIV virus and understand and model the financial and policy issues associated with controlling the pandemic, in order to advise the United Nations on how to manage the resources available for addressing HIV / AIDS. The teams' job was to model several scenarios of interest and use their models to recommend the allocation of financial resources. In addition, to accomplish their tasks, teams had to consider trends in HIV / AIDS morbidity and mortality, together with historical demographic and health data on fertility, population, age distribution, life expectancy, and disease burden. The problem required analysis of issues of many kinds—economic, demographic, political, environmental, social, psychological, plus future technology, along with several challenging requirements needing scientific and mathematical analysis. The problem also included the ever-present requirements of the ICM to use thorough data analysis, creativity, approximation, precision, and effective communication.

The author of the problem was Heidi Williams, Ph.D. student in Economics at Harvard University, who served on the panel of final judges. The problem originated from her work with the Center for Global Development (a nonprofit think tank in Washington, DC) to contribute to public policy efforts aimed at speeding the development of (and increasing access to) vaccines for diseases that are concentrated in low-income countries. Commentary on the HIV / AIDS problem from Ms. Williams appears in this issue of *The UMAP Journal*.

All members of the competing teams are to be congratulated for their excellent work and dedication to scientific modeling and problem solving. This year's judges remarked that the quality of the modeling, analysis, and presentation was extremely high and the interdisciplinary modeling very robust. The award levels for this year's contest reflect the increase in quality.

The 2006 ICM was managed by COMAP via its information system connected to the World Wide Web, where teams registered, obtained contest materials, downloaded the problem, and also downloaded considerable amounts of provided data through COMAP'S ICM Website.

Next year, we will continue with the public health theme for the contest problem. Teams preparing for the 2007 contest should consider reviewing interdisciplinary topics in the area of public health modeling and analysis.

Teams should also be aware of the presentation style required for this kind of writing. This contest mirrors reality. A paper will have an impact only if it is read, and most readers make the decision whether or not to read a paper based on the summary and the first few paragraphs of the paper. Although triage judges do spend some time with each paper, they cannot read every paper completely. Therefore, we cannot overemphasize the importance of the

summary to the success of the paper. It should be clear, concise, and well-organized. Your summary should demonstrate your understanding of the problem by stating the key factors and the key trade-offs. Conclusions should be clearly stated along with the assumptions you made and the sensitivity of your conclusions to your assumptions. For the HIV/AIDS problem, two key assumptions were the extent to which ARV treatment changes the risk of contagion, and when a viable vaccine might be available.

Another factor is the length of the paper. Long papers are not necessarily good papers. Good writing is extremely important. If you cannot describe your models clearly and succinctly, then they probably are not good models. Complicated models are not necessarily good. In fact, a large part of the art of modeling is choosing the most important factors and using appropriate science and mathematics.

The final reminder, a very important one, is that any material that comes from other sources must be carefully and completely documented.

We look forward to both continued improvement in the quality of the contest reports and continued increase in interest and participation in the ICM. It has grown in participation every year of its existence.

Start-up funding for the ICM was provided by a grant from the National Science Foundation (through Project INTERMATH) and COMAP. Additional support is provided by the Institute for Operations Research and the Management Sciences (INFORMS) and IBM.

The HIV/AIDS Problem

As the HIV/AIDS pandemic enters its 25th year, both the number of infections and the number of deaths due to the disease continue to rise. Despite an enormous amount of effort, our global society remains uncertain on how to allocate resources to fight this epidemic most effectively.

You are a team of analysts advising the United Nations (UN) on how to manage the available resources for addressing HIV/AIDS. Your job is to model several scenarios of interest and to use your models to recommend the allocation of financial resources. The narrative below provides some background information and outlines specific tasks.

Task 1

Build a model to approximate the expected rate of change in the number of HIV/AIDS infections for the most critical country on each of the continents (Africa, Asia, Europe, North America, and South America) from 2006–2050, in the absence of any additional interventions. Fully explain your model and the assumptions that underlie your model. In addition, explain how you selected the countries to model.

Use as a list of countries for inclusion in your analysis the countries included in the attached spreadsheet, which include all member states of the World Health Organization (WHO) as of 2003.

Data: `list_WHO_member_states.xls`

Reliable data on HIV prevalence rates by country are generally difficult to obtain. The attached spreadsheet includes several worksheets of data which you may use in your analysis.

Data: `hiv_aids_data.xls`

1. `globalhiv-aidscases,1999`: These data come from UNAIDS (the Joint United Nations Programme on HIV / AIDS) and report the estimated number of HIV positive 0 to 49 year olds by country at the end of 1999.

2. `hiv-aidsinAfricaovertime`: These data come from the US government and give some piecemeal time series data on measured HIV prevalence rates among women of childbearing age, in urban areas, over time for some African countries.

3. `hiv-aidssubtypes`: These data come from UNAIDS and give the geographic distribution of HIV-1 subtypes by country.

Also attached for your use are some basic population and demographic data.

Data:

1. `fertility_data.xls`: These data come from the UN and give age-specific fertility rates by major area, region, and country, 1995–2050 (births per thousand women)

   (a) Estimates for 1995–2005

   (b) Projections (under the assumption of medium fertility levels) for 2005–2050

2. `population_data.xls`: These data come from the UN and give total population (both sexes combined) by major area, region, and country, annually for 1950–2050 (thousands).

   (a) Estimates for 1950–2005

   (b) Projections (under the assumption of medium fertility levels) for 2006–2050

3. `age_data.xls`: These data come from the UN and give population (for both sexes, and by gender) by five-year age groups, major area, region, and country, 1950–2050 (thousands)

   (a) Estimates, 1950–2005

   (b) Projections (under the assumption of medium fertility levels) for 2010–2050

4. `birth_rate_data.xls`: These data come from the UN and give crude birth rates by major area, region, and country, 1950–2050 (births per thousand population)

   (a) Estimates, 1950–2005

   (b) Projections (under the assumption of medium fertility levels) for 2005–2050

5. `life_expectancy_0_data.xls`: These data come from the UN and give life expectancy at birth (by sex and both sexes combined) by major area, region, and country, 1950–2050 (years)

   (a) Estimates, 1950–2005

   (b) Projections (under the assumption of medium fertility levels) for 2005–2050

There are a number of interventions that HIV/AIDS funding could be directed toward—including prevention interventions (voluntary counseling and testing, condom social marketing, school-based AIDS education, medicines to prevent mother-to-child transmission, etc.) and care interventions (treating other untreated sexually transmitted diseases, treating opportunistic infections, etc.). You should focus on only two potential interventions: provision of antiretroviral (ARV) drug therapies, and provision of a hypothetical HIV/AIDS preventive vaccine.

Task 2

First, estimate the level of financial resources from foreign aid donors that you realistically expect to be available to address HIV/AIDS, by year, from 2006–2050 for the countries you selected in Task 1.

Then use the model that you developed in Task 1 and the finance data to estimate the expected rate of change in the number of HIV/AIDS infections for your selected countries from 2006–2050 under realistic assumptions for the following three scenarios:

1. Antiretroviral (ARV) drug therapy

2. A preventive HIV/AIDS vaccine

3. Both ARV provision and a preventive HIV/AIDS vaccine

Assume in these scenarios that there is no risk of emergence of drug-resistant strains of HIV (you will examine this issue in Task 3).

Be sure to carefully describe the assumptions that underlie your model.

You can choose whether these scenarios should be implemented for all countries, or for certain subsets of countries based on income cut-offs, disease burden, etc. Available for use if you wish is a spreadsheet of country-level income data.

Data: `income_data.xls`: These data are from the World Bank (2002) and give per-capita gross national product (GNP) data as well as broad income classifications that you are free to use in your analysis if you wish.

ARV drug therapies can have tremendous benefits in terms of prolonging the lives of individuals infected with HIV/AIDS. ARVs are keeping a high proportion of HIV/AIDS-infected individuals in rich countries alive, and policy makers and international institutions are facing tremendous political pressure to increase access to ARVs for individuals in poor countries. Health budgets in low-income countries are very limited, and it seems unlikely that poor countries will be able to successfully expand these programs to the majority of their populations using their own resources. Appendix 1 presents country-specific data from UNAIDS on current access to ARVs for a number of countries.

The efficacy of ARVs depends in large part on adherence to the treatment regimen and to proper monitoring. The most favorable conditions for ARVs are structured programs with extensive counseling and physician care, as well as regular testing to monitor for disease progression and the onset of opportunistic infections. Non-adherence or inadequate treatment carries with it two very serious consequences. First, the treatment may not be effective for the individual undergoing treatment. Second, partial or inadequate treatments are thought to directly lead to the emergence of drug-resistant strains of HIV.

The price of the drugs initially used to treat patients has come down to several hundred dollars a year per patient, but delivering them and providing the necessary accompanying medical care and further treatment is the key administrative and financial challenge. It is estimated that purchasing and delivering antiretrovirals using the clinically-recommended approach (DOTS, or "directly observed short-course treatments"), which is intended to minimize the emergence of drug-resistant strains, would cost less than $1,100 per person per year [Adams, Gregor, et al., 2001, Consensus statement on antiretroviral treatment for AIDS in poor countries, `http://www.hsph.harvard.edu/bioethics/pdf/consensus_aids_therapy.pdf`].

For a preventive HIV vaccine, make assumptions that you feel are reasonable about the following (in addition to other factors that you may choose to include in your model):

1. The year in which an HIV/AIDS preventive vaccine might be available.
2. How quickly vaccination rates might reach the following steady-state levels of vaccination:
   (a) If you wish to immunize new cohorts (infants), assume that the steady-state level for new cohorts of the country-by-country immunization rates for the *third* dose of the diphtheria-pertussis-tetanus vaccine (DTP3), as reported by the WHO (2002):

Data: `vaccination_rate_data.xls`

(b) If you wish to immunize adults (any group over age 5), assume that the steady-state level for older cohorts is the *second* dose of the tetanus toxoid (TT2) rate, as reported by the WHO (2002):

Data: `vaccination_rate_data.xls`

3. The efficacy and duration of protection of the vaccine.

4. Whether there would be epidemiological externalities from vaccination.

5. Assume the vaccine is a three-dose vaccine, and can be added to the standard package of vaccines delivered under the WHO's Expanded Programme on Immunization (EPI) at an incremental additional cost of $0.75.

Task 3

Reformulate the three models developed in Task 2, taking into consideration the following assumptions about the development of ARV-resistant disease strains.

Current estimates suggest that patients falling below 90–95% adherence to ARV treatment are at a "substantial risk" of producing drug resistant strains. Use as an assumption for your analysis that a person receiving ARV treatment with adherence below 90% has a 5% chance of producing a strain of HIV/AIDS which is resistant to standard first-line drug treatments.

Second- and third-line ARV drug therapies are available; but assume for your analysis that these drugs are prohibitively expensive to implement in countries outside of Europe, Japan, and the United States.

Task 4

Write a white paper to the United Nations providing your team's recommendations on the following:

1. Your recommendations for allocation of resources available for HIV/AIDS among ARV provision and a preventive HIV vaccine.

2. Your argument for how to weigh the importance of HIV/AIDS as an international concern relative to other foreign policy priorities.

3. Your recommendations for how to coordinate donor involvement for HIV/-AIDS.

For (1): Assume that between now and 2010 the available financial resources could be allocated so as to speed the development of a preventive HIV vaccine—through directly financing vaccine research and development (R&D), or through other mechanisms. Any gains from such spending would move the date of development you assumed in Task 2 to some earlier date.

(Note: None of the data files, including the data in the appendices, are included in this article. They are available on the COMAP Website, at `http://www.comap.com/undergraduate/contests/mcm/contests/2006/problems/`.)

The Results

Solution papers were coded at COMAP headquarters so that names and affiliations of the authors were unknown to the judges. Each paper was then read preliminarily by at least two "triage" judges at the U.S. Military Academy at West Point, NY. At the triage stage, the summary, the model description, and overall organization are the primary elements in judging a paper. If the judges' scores diverged for a paper, the judges conferred; if they still did not agree on a score, additional triage judges evaluated the paper.

Final judging by a team of modelers, analysts, and subject-matter experts took place on February 24 and 25, again at West Point, NY. The judges classified the 224 submitted papers as follows:

	Outstanding	Meritorious	Honorable Mention	Successful Participation	Total
HIV / AIDS	4	48	114	58	224

The four papers that the judges designated as Outstanding appear in this special issue of *The UMAP Journal*, together with commentaries by the author and the final judges. We list those four Outstanding teams and the Meritorious teams (and advisors) below. The complete list of all participating schools, advisors, and results is provided in the **Appendix**.

Outstanding Teams

Institution and Advisor	**Team Members**
"The United Nations and the Quest for the Holy Grail (of AIDS)"	
Duke University	Aaron Wise
Durham, NC	Arnav Mehta
David Kraines	Qianwei Li
"Managing the HIV / AIDS Pandemic: 2006–2055"	
Duke University	Tyler Huffman
Durham, NC (INFORMS Prize winner)	Barry Wright III
David Kraines	Charles Staats III

"AIDS: Modeling a Global Crisis (and Australia)"
Harvey Mudd College
Claremont, CA
Lisette dePillis
Cris Cecka
Michael Martin
Tristan Sharp

"The Spreading HIV / AIDS Problem"
United States Military Academy
West Point, NY
Randal Hickman
Adam Seybert
David Ryan
Nicholas Ross

Meritorious Teams (48)

Beihang University, Beijing, China (Hongying Liu)
Beijing Jiao Tong University, China (3 teams) (Li Guiting) (Zhang Shangli) (Bingli Fan)
Beijing University of Chemical Technology (Cheng Yan)
Beijing University of Posts and Telecommunications, China (2 teams) (Yuan Jianhua) (He Zuguo)
Carroll College, Helena, MT (Holly Zullo)
Central University of Finance and Economics, Beijing, China (Li Donghong)
China University of Mining and Technology, Xuzhou, Jiangsu, China (Zhou Shengwu)
Chongquing University, China (2 teams) (Gong Qu) (Li Zhilang)
Dalian University, China (Tan Xinxin)
Dalian University of Technology, Institute of University Students' Innovation, Dalian, Liaoning, China (Fu Donghai)
Duke University, Durham, NC (William Allard)
East China University of Science & Technology, Shanghai, China (2 teams) (Ni Zhonxin) (Lu Xiwen)
Hangzhou Dianzi University, Hangzhou, Zhejiang, China (Shen Hao)
Harbin Engineering University, Harbin, Heilongjiang, China (2 teams) (Luo Yuesheng) (Fan Zhaobing)
Harbin Institute of Technology, Harbin, Heilongjiang, China (Jiao Guanghong)
Jinan University, Guangzhou, Guangdong, China (2 teams) (Hu Daiqiang) (Fan Suohai)
Maggie Walker Governor's School, Richmond, VA (2 teams) (John Barnes)
Nanjing University of Posts & Telecommunications, Nanjing, Jiangsu, China (2 teams) (Qiu Zhonghua) (He Ming)
National University of Defense Technology, Changsha, Hunan, China (2 teams) (Mao Ziyang) (Wu Mengda)
Nonlinear Science Center, Hefei, Anhui, China (Tao Zhou)
Peking University Health Science Center, Beijing, China (Zhang Xia)
Southeast University, Nanjing, Jiangsu, China (Dan He)
Shandong University, Jinan, Shangdong, China (Huang Shuxiang —2 teams)
Shandong University at Weihai, Weihai, Shandong, China (Cao Zhulou)
Sun Yat-Sen University, Guangzhou, Guangdong, China (Chen Zepeng)
Tsinghua University, Beijing, China (2 teams) (Lu Mei) (Xie Jinxing)
University of College Cork, Cork, Ireland (Ben McKay)
University of Colorado, Boulder, CO (Anne Dougherty)
University of Colorado at Colorado Springs, Colorado Springs, CO (Radu Cascaval)
Xidian University, Xi'an, Shaanxi, China (2 teams) (Qi Xiaogang) (Zhou Shuisheng)
Zhejiang University, China (3 teams) (Tan Zhiyi) (Fei Jiaer—2 teams)

Zhejiang University City College, Hangzhou, Zhejiang, China (Wang Gui)
Zhejiang University Ningbo Institute of Technology, Ningbo, Zhejiang, China (Wang Jufeng)

Awards and Contributions

Each participating ICM advisor and team member received a certificate signed by the Contest Directors and by the Head Judge. Additional awards were presented to the Duke University team advised by David Kraines from the Institute for Operations Research and the Management Sciences (INFORMS).

Judging

Contest Directors
Chris Arney, Mathematical Sciences Division, Army Research Office, Research Triangle Park, NC
Gary W. Krahn, Dept. of Mathematical Sciences, U.S. Military Academy, West Point, NY

Associate Directors
Richard Cassady, Dept. of Industrial Engineering, University of Arkansas, Fayetteville, AR
Joseph Myers, Dept. of Mathematical Sciences, U.S. Military Academy, West Point, NY

Judges
Kari Murad, Dept. of Natural Sciences, College of Saint Rose, Albany, NY
Edward Pohl, Dept. of Industrial Engineering, University of Arkansas, Fayetteville, AR
Luis Prieto-Portar, Dept. of Civil and Environmental Engineering, Florida International University, Miami, FL
Frank Wattenberg, Dept. of Mathematical Sciences, U.S. Military Academy, West Point, NY
Heidi Williams (Ph.D. student), Harvard University, Cambridge, MA

Triage Judges
Dept. of Mathematical Sciences, U.S. Military Academy, West Point, NY: Jong Chung, Amy Erickson, Keith Erickson, Andrew Glen, Alex Heidenberg, Michelle Isenhour, John Jackson, Sebastien Joly, Jerry Kobylski, Joseph Lindquist, Keith McClung, Barbara Melendez, Fernando Miguel, Joe Myers, Mike Phillips, Frederick Rickey, Heather Stevenson, Rodney Sturdivant, Frank Wattenberg, and Brian Winkel.

Acknowledgments

We thank:

- the Institute for Operations Research and the Management Sciences (INFORMS) for its support in judging and providing prizes for the winning team;
- IBM for their support for the contest;
- all the ICM judges and ICM Board members for their valuable and unflagging efforts;
- the staff of the U.S. Military Academy, West Point, NY, for hosting the triage and final judgings.

Cautions

To the reader of research journals:

Usually a published paper has been presented to an audience, shown to colleagues, rewritten, checked by referees, revised, and edited by a journal editor. Each of the student papers here is the result of undergraduates working on a problem over a weekend; allowing substantial revision by the authors could give a false impression of accomplishment. So these papers are essentially au naturel. Light editing has taken place: minor errors have been corrected, wording has been altered for clarity or economy, style has been adjusted to that of *The UMAP Journal*, and the papers have been edited for length. Please peruse these student efforts in that context.

To the potential ICM Advisor:

It might be overpowering to encounter such output from a weekend of work by a small team of undergraduates, but these solution papers are highly atypical. A team that prepares and participates will have an enriching learning experience, independent of what any other team does.

Editor's Note

As usual, the Outstanding papers were longer than we can accommodate in the *Journal*, so space considerations forced me to edit them for length. It was not possible to include all of the many tables and figures, nor the white papers.

In editing, I endeavored to preserve the substance and style of the paper, especially the approach to the modeling.

—Paul J. Campbell, Editor

Appendix: Successful Participants

KEY:
P = Successful Participation
H = Honorable Mention
M = Meritorious
O = Outstanding (published in this special issue)

INSTITUTION	CITY	ADVISOR	C
CALIFORNIA			
California State U. at Monterey Bay	Seaside	Hongde Hu	P
Harvey Mudd College	Claremont	Lisette de Pillis	O,H
		Darryl Yong	P
COLORADO			
University of Colorado	Boulder	Anne Dougherty	M
	Colorado Springs	Radu Cascaval	M
KENTUCKY			
Asbury College	Wilmore	Kenneth Rietz	H,P
MARYLAND			
Villa Julie College	Stevenson	Eileen McGraw	H
MASSACHUSETTS			
Franklin W. Olin College of Eng.	Needham	Burt Tilley	H
MONTANA			
Carroll College	Helena	Holly Zullo	M
		Kelly Cline	H,P
NEW YORK			
United States Military Academy	West Point	Randal Hickman	O
NORTH CAROLINA			
Duke University	Durham	David Kraines	O,O
		William Allard	M
OHIO			
Youngstown State University	Youngstown	George Yates	H,H
		Jay Kerns	H
VIRGINIA			
James Madison University	Harrisonburg	Hasan Hamdan	H
		David Walton	H
Longwood University	Farmville	M. Leigh Lunsford	P
Maggie L. Walker Governor's Schl	Richmond	John Barnes	M,M,H

INSTITUTION	CITY	ADVISOR	C
CHINA			
Anhui			
Anhui University	Hefei	Chen Huayou	P
(Stat)		Zhou Ligang	P
Hefei University of Technology	Hefei	Su Huaming	P
		Du Xueqiao	H
		Huang Youdu	H
Nonlinear Science Center (Phys)	Hefei	Tao Zhou	M
University of Science and Technology of China (Chm)	Hefei	Li Fu	H,P
(Foreign Language)		Zhang Manjun	H
(Eng)		Liu Yanjun	P
Beijing			
BeiHang Univ. (BHU) (Eng)	Beijing	Sun HaiYan	P
(Sci)		Liu Hongying	M
Beijing Institute of Technology	Beijing	Li Bingzhao	H
		Sun Huafei	H
		Li Yuan	H
Beijing Jiao Tong University	Beijing	Li Guiting	M,H
		Wang Xiaoxia	H
(CS)		Fan Bingli	M
		Shang Pengjian	P,P
(Eng)		Wang Bingtuan	P,P
		Yu Jiaxin	P
(Sci)		Feng Guochen	P,P
		Zhang Shangli	M
Beijing Language and Culture University (CS)	Beijing	Liu Guilong	H,H
(Finance)		Song Rou	P
Beijing University of Chemical Technology (Info)	Beijing	Yuan Wenyan	P
		Cheng Yan	M
(Sci)		Jiang Xinhua	H
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Editor's Note

For team advisors from China, I have endeavored to list family name first.

Abbreviations for Organizational Unit Types (in parentheses in the listings)

(none)	Mathematics	M; Pure M; Applied M; Computing M; M and Computer Science; M and Computational Science; M and Information Science; M and Statistics; M, Computer Science, and Statistics; M, Computer Science, and Physics; Mathematical Sciences; Applied Mathematical and Computational Sciences; Natural Science and M; M and Systems Science; Applied M and Physics
Bio	Biology	B; B Science and Biotechnology; Biomathematics; Life Sciences
Bus	Business	B; B Management; B and Management; B Administration
Chm	Chemistry	C; Applied C; C and Physics; C, Chemical Engineering, and Applied C
CS	Computer	C Science; C and Computing Science; C Science and Technology; C Science and (Software) Engineering; Software; Software Engineering; Artificial Intelligence; Automation; Computing Machinery; Science and Technology of Computers
Econ	Economics	E; E Mathematics; Financial Mathematics; E and Management; Financial Mathematics and Statistics; Management; Business Management; Management Science and Engineering
Eng	Engineering	Civil E; Electrical Eng; Electronic E; Electrical and Computer E; Electrical E and Information Science; Electrical E and Systems E; Communications E; Civil, Environmental, and Chemical E; Propulsion E; Machinery and E; Control Science and E; Mechanisms; Mechanical E; Electrical and Info E; Materials Science and E; Industrial and Manufacturing Systems E
Info	Information	I Science; I and Computation(al) Science; I and Calculation Science; I Science and Computation; I and Computer Science; I and Computing Science; I Engineering; I and Engineering; Computer and I Technology; Computer and I Engineering; I and Optoelectronic Science and Engineering
Phys	Physics	P; Applied P; Mathematical P; Modern P; P and Engineering P; P and Geology; Mechanics; Electronics
Sci	Science	S; Natural S; Applied S; Integrated S; School of S
Software	Software	
Stat	Statistics	S; S and Finance; Mathematical S; Probablity and S

The United Nations and the Quest for the Holy Grail (of AIDS)

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Summary

In response to the HIV/AIDS pandemic, worldwide interest in HIV treatments has grown, but uncertainty remains about how to fund treatments. Nations must choose between combinations of sexual education, antiretroviral treatments (ART), and vaccine research. We aim to quantify the effects of each of these treatments in order to determine how best to confront AIDS.

We propose an iterative deterministic model for measuring the progression of HIV through 2050. The crux of our model is use of expressions that predict infection and death rates. Our model accounts for the three main factors in transmission: unprotected intercourse, non-sterile drug needles, and births of children to HIV-positive mothers. Furthermore, we analyze country-specific parameters, such as prevalence of HIV among subpopulations (e.g., homosexuals) as well as condom usage and risky-sex rates, and model the influence of treatments. Additionally, we investigate the impact of multiple-drug resistance. Using data extrapolated from South African prenatal clinics, we recreate historical trends to demonstrate our model's capacity for accurate prediction.

Our goal is to assess which methods minimize the number of HIV cases in both the short run and the long run, and to use these results to guide policy decisions. Condom usage, ARV therapy, and a vaccine all affect the course of HIV development. Current aid efforts, including sexual education, which reduce risky sex and promote condom use, are very valuable.

We predict that current downward trends will continue and that the HIV outbreak is beginning to recede. If ART does not decrease the transmission rate, its widespread use may increase the scope of an outbreak; if it does decrease the

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transmission rate, it can be an important factor in containing HIV. We conclude that vaccines provide the greatest promise for long-term prevention.

We propose an economic model for distributing resources. Even with a vaccine, economic considerations promote ARV usage. We finally recommend universal sexual education, distribution of ARVs based on infection profiles, and adequate endowment for research toward a vaccine, the holy grail of HIV.

Introduction

We focus on countries selected for diversity of the origin of their outbreak and ability to be extrapolated to other outbreaks:

- South Africa has a large HIV/AIDS population but little drug use.
- India has an enormous population and a small but growing AIDS presence.
- Russia has a large HIV-positive injected-drug community.
- The United States has a fairly small HIV population (clustered among its homosexual population) limited by the high safe-sex rate.

Experimental

Overview

An important factor in the continuation of an epidemic is R_0, a measure of the reproductive rate of the disease: on average, each HIV carrier infects R_0 other people [Velasco-Hernandez 2002]. An epidemic spreads only if R_0 is greater than 1. A treatment is preventive if it decreases the reproduction rate.

We create an iterative deterministic model. In each iteration, the number of new HIV/AIDS cases is a function of the previous state of the system, along with the expected rate of disease transmission. Hence,

$$R_0 \propto \frac{d(\text{total AIDS population})}{d(\text{time})}.$$

Because R_0 is useful as a measure of the change in total population, we discuss results in terms of trends and total HIV-positive populations.

The model determines the change in HIV/AIDS victims based on both new cases of HIV as well as deaths of previous HIV victims due to AIDS.

The three primary vectors for transmission of HIV are unprotected sexual intercourse, use of "dirty" (reused) drug needles, and childbirth by HIV-positive mothers. We balance these factors against the death rate in order to determine the net number of new cases. We use a feedback-based model for death, where the number of AIDS deaths is based on the expected life span of a victim and the number of victims who contracted HIV at specific previous points in time.

Basic Model

The general system of the previous section can be written as:

$$\#\text{aids}(t) = \text{newInfections}(t) + \#\text{aids}(t-1) - \text{deaths}(t),$$

where $\#\text{aids}(t)$ is the total number of living HIV / AIDS victims in year t. Our initial point, t_0, is the year 2000. Values at indices $t < 0$ are from historical data.

New Infection Rate

The basic model assumes that HIV transmission occurs only during sex, that is, $\text{newInfections}(t) = \text{intercourseT}(t)$, the number of new HIV victims due to unprotected sexual intercourse. Later we model other methods of transmission.

We model HIV transmission due to sex as related to the number of instances of intercourse times a rate of transmission per sex act [Smith 2005]. The transmission rate male $\rightarrow$ female is twice as high as the rate female $\rightarrow$ male. We use ρ to represent the total risk of transmission through sexual contact; the number of instances of intercourse is proportional to ρ. We assume an average intercourse rate of 3 times per week, or about 160 times per year [Leynaert et al. 1998]. Taking into account heterosexual anal intercourse causes an increase of the risk factor ρ to 200 (or more).

Since we assume primarily heterosexual intercourse, we track separately the HIV / AIDS population of each sex. We use subscript M to denote a function (or variable) that includes only men, and F to denote a function including only women. Hence we represent the intercourseT rates as

$$\begin{aligned}\text{intercourseT}_{\text{M}}(t) = {} & (\text{percent unaffected men}) \times (\text{number of affected women}) \\ & \times (1 - (\text{condom use rate})) \times (\text{risk constants}).\end{aligned}$$

That is, for men:

$$\begin{aligned}\text{intercourseT}_{\text{M}}(t) = {} & (1 - \%\text{aids}_{\text{M}}) \times \#\text{aids}_{\text{F}}(t-1) \times (1 - \text{condomRate}) \\ & \times \left(\rho \times \text{riskSexCons}_{\text{M}}\right);\end{aligned}$$

and for women:

$$\begin{aligned}\text{intercourseT}_{\text{F}}(t) = {} & (1 - \%\text{aids}_{\text{F}}) \times \#\text{aids}_{\text{M}}(t-1) \times (1 - \text{condomRate}) \\ & \times \left(\rho \times \text{riskSexCons}_{\text{F}}\right).\end{aligned}$$

Assumptions

- Condom usage is static over time, a worst-case scenario, since it is unlikely that condom usage would decrease if sexual education programs follow the status quo or become increasingly well-funded and organized.

- Condoms are 100% effective. This assumption is very close to reality (>99% effective) and is a useful simplification.
- All sexual acts have the same (very low) chance of infection. This assumption allows us to treat monogamous and promiscuous sexual behaviors as equally likely to spread HIV.

Death Rate

Most carriers of HIV eventually die of AIDS; we assume that all do. On average, it takes 9 years for an HIV infection to become AIDS [Morgan 2002]. We assume that regular sexual activity stops when symptomatic AIDS occurs; hence, the number of years of activity after HIV infection is 9–10. We denote this parameter as averageDeath. We use a feedback loop for the death rate:

$$\text{deaths}(t) = \text{newInfections}(t - \text{averageDeath}).$$

Assumptions

- All HIV carriers die of AIDS. This major simplifying assumption prevents having to track population ages. Overall it causes a (slight) increase in the average life span of the HIV carrier, and hence is a worst-case estimate. This assumption is also tempered by our treatment of ART (see below).
- While ART increases life span, the average age at HIV contraction plus the new life span cannot exceed the life expectancy. This assumption minimizes the impact of the assumption that all carriers die of AIDS.
- Each carrier dies after being infected for exactly averageDeath years.

Additional Model Parameters

Transmission Due to Reproduction

A major social impact of HIV/AIDS is creation of an orphan population whose parents have both died of AIDS, a common phenomenon with large percentages of HIV-infected adults (such as in South Africa). The birth of infected babies, however, does not impact new cases, because they die before they participate in any form of transmission (intercourse, drug-needle use, and childbirth). For risk of transmission at childbirth, we use 35% in undeveloped countries and 1%–5% in developed countries [UNAIDS and WHO 2005]. Transmission due to childbirth is calculated as

$$\text{birthT}(t) = \text{birthRate} \times \#\text{aids}_{\text{F}}(t-1) \times \text{riskBirth}.$$

Assumptions

- All infected children die before contributing to the spread of HIV/AIDS.
- Women with AIDS are as likely as other women to have a child; because of the previous assumption, this assumption has low impact on the model.

Transmission Due to Drug Needles

Needle-sharing is an important factor in HIV transmission in many countries, including India and Russia. To incorporate drug needles, we re-express the infection rate as

$$\text{newInfections}(t) = \text{intercourseT}(t) + \text{needleT}(t).$$

We calculate the needle transmission rate based on a drug risk factor ρ_D, the average number of drug injections per drug user per year. We also assume that the dirty-needle rate is 35% [UNAIDS and WHO 2005]. We account for the sex difference in drug use (an 80/20 male/female split). We take the risk of infection from a single drug use (riskDrugCons) from Leynaert et al. [1998]. Hence, the drug transmission rate is

$$\begin{aligned}\text{needleT}(t) = {} & (\text{number of drug users HIV negative}) \times \\ & (\text{chance of sharing a drug needle with someone HIV positive}) \times \\ & (\text{risk factors and constants}),\end{aligned}$$

that is,

$$\text{needleT}(t) = \#\text{HIV}^{-}\text{DrugUsers}_{\text{M}} \times (0.35 \times \%\text{HIV}^{+}\text{Drug}) \times (\rho_D \times \text{riskDrugCons}).$$

Assumptions

- Constant dirty-needle rate.
- For each drug use, the chance of HIV transmission is the same.

Transmission Due to Homosexual Intercourse

In most countries, HIV/AIDS is not associated with the homosexual community; rather, the more common carriers are (heterosexual) sex workers. In the United States, however, a disproportionate portion of HIV victims are homosexual. In the model, we compute transmission due to homosexual intercourse very similarly to intercourseT(t). The major change is assuming that homosexuals have solely homosexual sex, with a different risk per sexual act constant (also from Leynaert et al. [1998]).

$$\begin{aligned}\text{intercourseT}_H(t) = {} & (\text{percent unaffected gay men}) \times \\ & (\text{number of affected gay men}) \times (1 - \text{condom use}) \times (\text{risk constants}),\end{aligned}$$

or

$$\text{intercourseT}_H(t) = (1 - \%\text{aids}_H) \times \big(\#\text{aids}_H(t-1)\big) \times (1 - \text{condomRate}) \times \big(\rho \times \text{riskSexCons}_H\big).$$

Antiretrovirals

The foremost effect of ARVs is not to prevent transmission but to extend life span. There is no scientific consensus on the effect of ART on transmission [Anderson 1992; Krieger 1991; Royce 1997]. Hence, we incorporate this effect as an input parameter, arvFactor; we let it vary between 0.25 and 1. Another input parameter is arvPortion, the percentage of HIV-positive individuals who receive ARV treatment. We implement ART by assuming that large-scale treatment begins around 2015, after deployment of infrastructure. We assume that ARV patients have a slightly decreased amount of risky sex, due to increased sexual education from repeated contact with health personnel.

We calculate the transmissions due to ART patients and other HIV victims separately:

$$\text{newInfections}(t) = \text{intercourseT}(t) \times (1 - \text{arvPortion}) + \text{intercourseT}(t) \times \text{arvPortion} \times \text{arvFactor}.$$

We assume 100% adherence (except when talking about resistant-strain development; see below).

Drug Resistance

A risk involved in antiretroviral therapy is the creation of treatment-resistant strains of HIV. This can occur when an ART patient follows the treatment regimen incompletely; selection pressures on the virus eases, allowing HIV to replicate once again in greater numbers resistant to the drugs.

We model drug resistance using the parameters in the problem statement. ARV-resistant infections are tracked separately, so that, while ARV-resistant carriers may continue to take ART, they do not benefit. The number of new ARV-resistant strains that develop as a direct result of missing ARV treatments is modeled as

$$\text{newInfections}_{\text{resistant}}(t) = (\%\text{ aids victims on ARV}) \times (1 - (\text{adherence rate})) \times (\text{chance to mutate}).$$

We assume that 85–95% of ART patients adhere to treatment [Rutenburg 2006].

The Holy Grail, or, The AIDS Vaccine

We model a vaccine by assuming that as immunizations increase, a growing portion of the population is unable to contract HIV. This is in direct contrast to

the way in which ARV affects HIV/AIDS rates. Originally we had

$$\text{intercourseT}_{\text{F}}(t) = (1 - \%\text{aids}_{\text{F}}) \times \#\text{aids}_{\text{M}}(t-1) \times (1 - \text{condomRate}) \times \big(\rho \times \text{riskSexCons}_{\text{F}}\big).$$

The factor $(1 - \%\text{aids}_{\text{F}})$ determines what portion of the population can catch HIV, which in the case of a vaccine becomes $\big((1 - \%\text{aids}_{\text{F}}) - \%\text{vaccinated}\big)$. We assume the same vaccination rate for both men and women, hence apply no subscript to that term.

To simulate %vaccinated, we fit a logistic curve. We assume that a vaccine will be available by 2015 and a well-regulated vaccine program will achieve steady-state vaccination by 2030. The curve starts at 0% and plateaus at a steady-state level equal to the second-dose tetanus-typhoid vaccination rate for that country (as given in 2002 WHO data for the problem statement). We use a logistic curve because the rate of increase

- will be low at first, since awareness will be low and infrastructure is needed;
- will increase as awareness builds and as infrastructure becomes established; and
- will decline as people become vaccinated and fewer remain unvaccinated.

Assumptions

- The vaccine is 100% effective.
- The vaccine distribution program is well-organized.

Country Choice and Country-Specific Parameters

To determine the countries most critical in terms of HIV/AIDS from 2006 to 2050, we used five indicators:

- trends in prevalence rates,
- demographics of infected population,
- level of HIV/AIDS education and awareness,
- routes of transmission,and
- integrity and availability of current and historical HIV/AIDS statistics,

Based on these indicators, we selected a country from each of the continents Africa, Asia, Europe, North America, and Australia, namely, South Africa, India, Russia, U.S.A., and Australia.

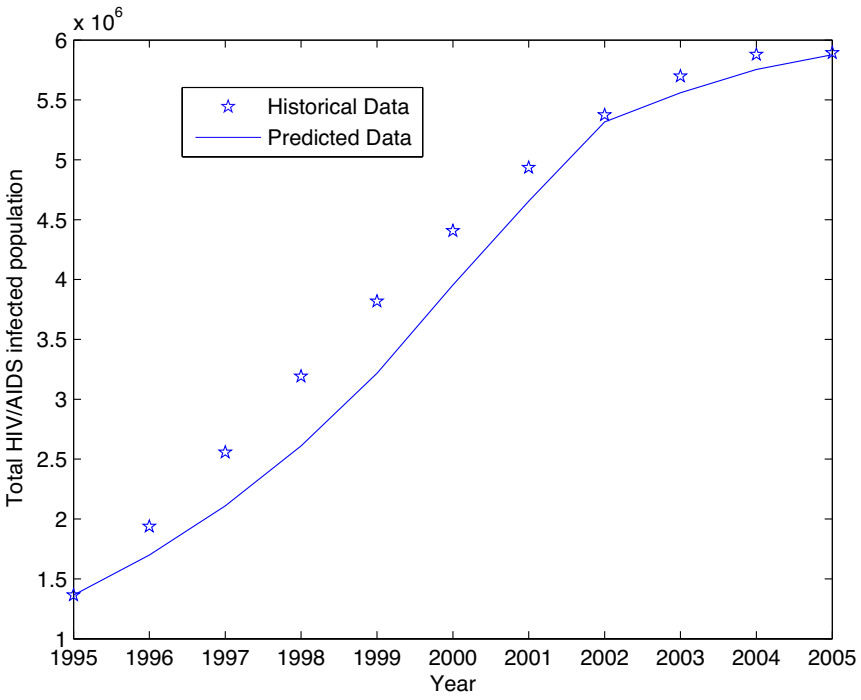

Figure 1. Comparison of model to South African historical data.

Results

Historical Fitting

We validate our model by examining historical HIV rates from prenatal clinics in South Africa between 1995 and 2005 (**Figure 1**). Our model fits the data well with three minor changes:

- a slight decrease in the life span of the average HIV patient (to 7 years from 9; this difference is probably due to lower sensitivity of HIV detection tests at earlier time points);
- an increase in the risky-sex rate constant (which is very unsurprising, since the data predate much sexual education effort); and
- increasing condom use rate over time.

Results by Country

The model predicts the following trends in the HIV / AIDS population:

- An increase in condom usage leads to a decrease in cases.
- An increase in the average life span of a patient leads to an increase in cases.
- A decrease in the transmission rate leads to a decrease in cases.

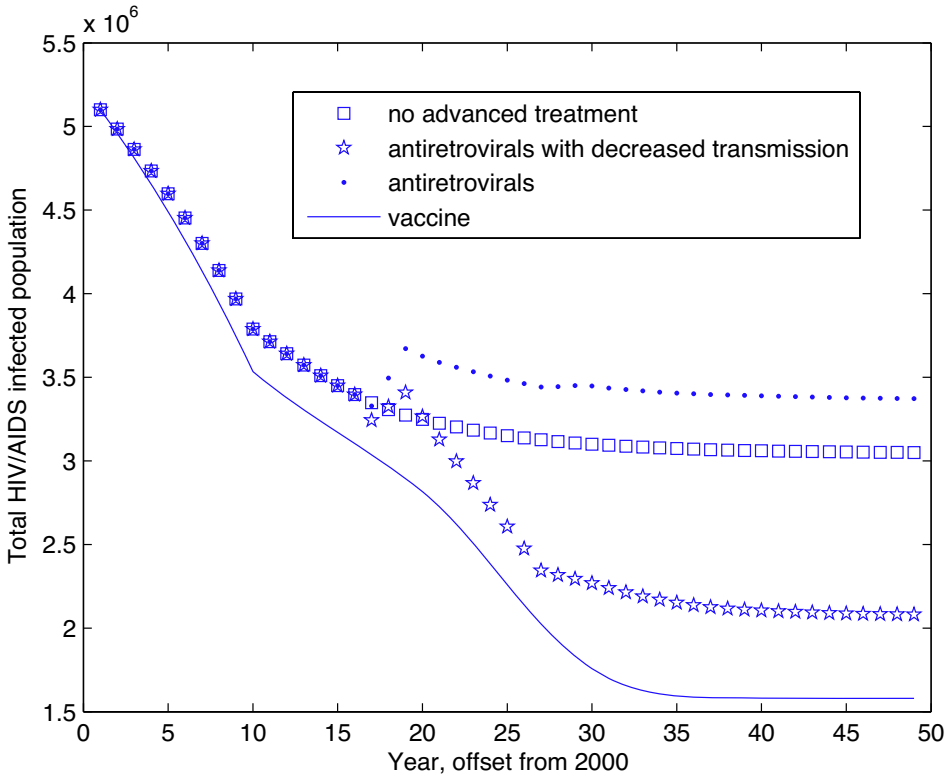

Figure 2. Prediction of HIV / AIDS epidemic in South Africa.

- Distribution of ARV drugs reduces the number of cases due to sexual acts only if ARVs cause a decrease in the per-act transmission rate.
- Steady distribution of a vaccine steadily decreases cases to a baseline level.

South Africa

The model (**Figure 2**) predicts a decrease in cases prior to 2015 for all scenarios. Introduction of ART shifts the steady-state level—to higher if no decrease in transmission, to drastically lower with decrease in transmission. The sudden increase in 2020 results from the assumption that ART instantaneously increases the life span of all infected individuals, thereby suddenly lowering the death rate. Thus, the deviation is an artifact of our assumptions.

Implementation of a well-regulated vaccine program starting in 2015 leads to a gradual decrease in cases over the next 20 years, with a significant portion of the disease eradication occurring between 2020 and 2025.

India

The model (**Figure 3**) indicates a steady increase in cases over the next 45 years. This differs from the observed trend in South Africa most notably because of significant drug usage in India.

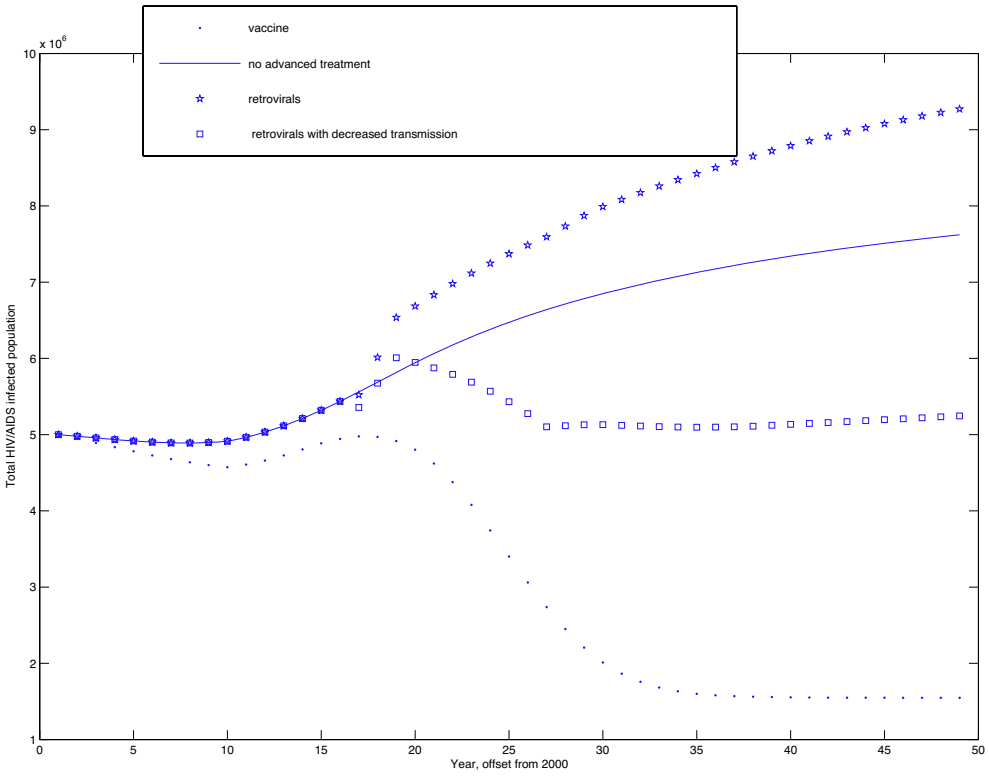

Figure 3. Prediction of HIV/AIDS epidemic in India.

The introduction of ART that increases only the life span increases cases every year; with accompanying decrease in transmission, cases decline. Again there is a small sudden jump around 2020, a consequence of our assumptions.

With a vaccination program, possibly supplemented with ARV drugs, the model predicts that cases will plateau soon after 2030, again with the most significant decrease 5 to 10 years after implementation of the vaccination program in 2020 to 2025.

United States

In the United States, HIV/AIDS is predominantly spread through homosexual interaction. The model predicts the number of cases to exceed 6 million by 2050 if no advanced treatment is available (**Figure 4**).

In the U.S., unlike the other countries that we examine, ARV drugs that do not affect transmission rate have no effect on cases. ARV drugs that decrease transmission curb new cases; the model predicts a stable number of slightly over 3 million cases after 2030.

A well-regulated vaccination program largely eradicates the virus by 2035.

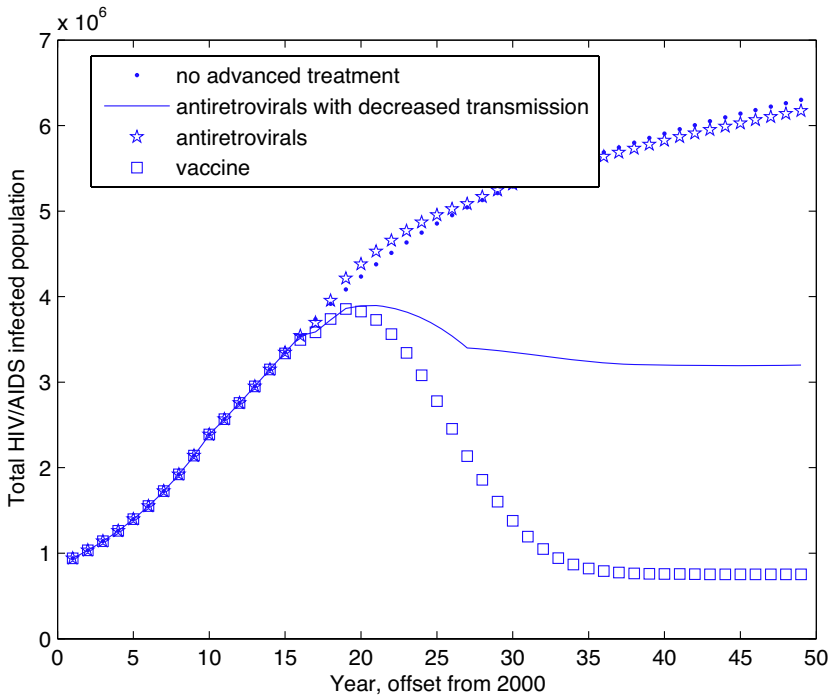

Figure 4. Prediction of HIV / AIDS epidemic in the United States.

Russia

The predominance of transmission through injected-drug use in Russia is much greater than in India and plays a larger role in spreading the virus.

For ART that decreases transmission, cases increase initially but level off much more quickly than for India or the U.S.

At the normal vaccination rate for a Russian adult, an HIV / AIDS vaccine causes the number of cases to decline from 2 million cases in 2020 (5 years after the implementation of the vaccine program) to 1 million cases by 2050. A vaccine program in Russia is not as effective as for India or the U.S. because of an unusually low adoption rate for vaccines (37%) in Russia. **Figure 5** shows a much faster eradication of the virus with a higher vaccination rate. Thus, Russia can significantly thwart cases by spending resources on increasing the general vaccination rate among adults.

Analysis

All of the models predict that vaccination is be the most effective method of HIV / AIDS eradication.

If ARV drugs do not influence the transmission rate, their introduction could be catastrophic. Increasing the life span of HIV / AIDS patients provides more time for each individual to spread the disease. Our model predicts more cases over the next 45 years for this scenario than for any other, for all countries.

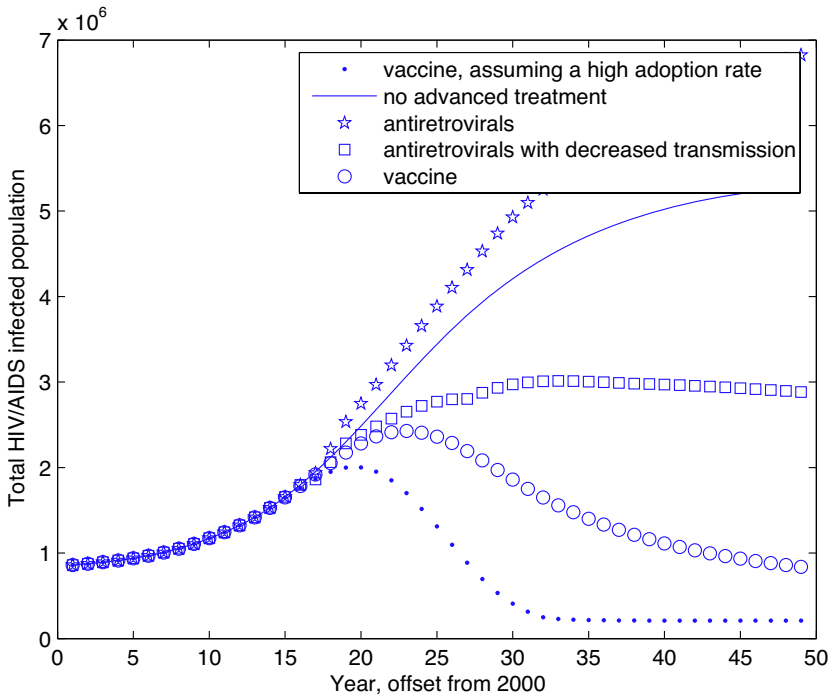

Figure 5. Prediction of HIV/AIDS epidemic in Russia.

The United States is an exception, where 63% of cases are among homosexuals [UNAIDS and WHO 2005]; an ARV program with no effect on transmission rate does not increase the number of cases. A possible reason is that though we assume that the use of ART implies that individuals are more informed and therefore less likely to perform risky sexual acts, there is not enough effect on people in the other countries modeled, while in the United States there is enough reduction in risky sexual acts to counterbalance the increase in life span.

ARV drugs that decrease transmission effectively curb the spread of HIV in every case, causing cases to remain fairly constant after 2030.

One of the least expected results is the decrease in cases in South Africa: The incidence of HIV/AIDS has peaked and is now on a downward turn. This however, is not completely unexpected, since HIV/AIDS has been present for the longest time in South Africa and general awareness about the disease has increased. Over time, an equilibrium point is reached; eventually the number of new cases equals the number of deaths due to AIDS, and the population of infected individuals remains fairly constant.

Analysis of Sensitivity and Individual Parameters

We tested condomRate (percentage of sexual acts performed with condoms) and arvPortion (percentage of HIV/AIDS population with access to ARV drugs). We also tested the effect of differences in transmission rate decreases due to ARV treatment and drug resistance.

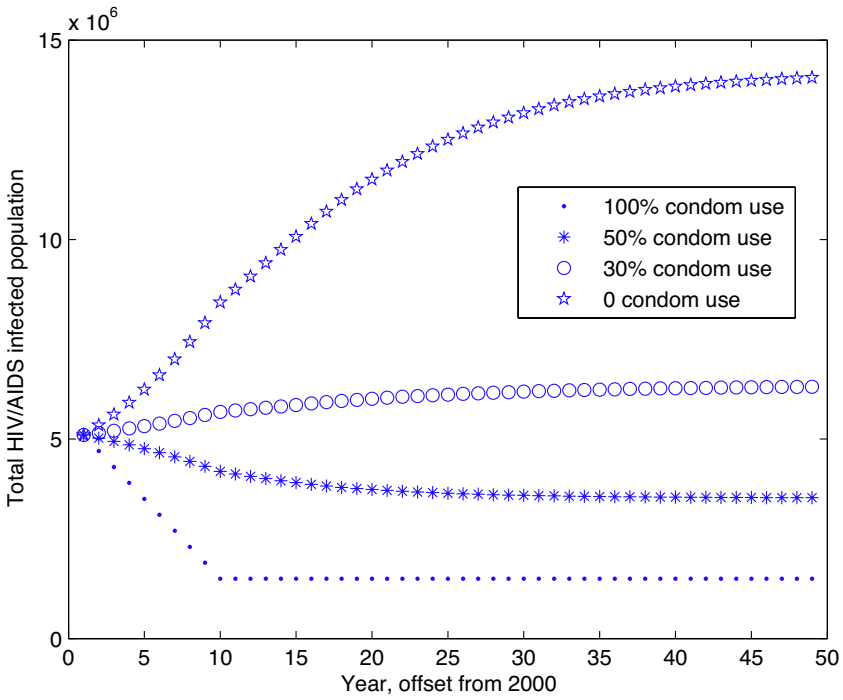

Figure 6. Effects of condom usage rate on model outcome

Figure 6 shows the effects of different values of condomRate on the number of cases in South Africa. The model is quite sensitive to the value. A rate of 50% results in gradual decrease in cases, and complete condom use results in disease eradication in 10 years (the time for pre-existing cases to die).

Figure 7 shows the effect of varying arvPortion. The assumption is that ART increases the life span of the patient but does not decrease the transmission rate; people infected now have a longer time to spread the disease. Fairly large changes in ART use lead to large changes in the number of cases, as expected.

Figure 8 assumes that ARV drugs reduce transmission rate by 25%.

Figure 9 shows the effects of ART adherence rates on the number of cases when ARV drugs lower the transmission rate. ART begins in 2020 and is swiftly followed by a decrease in the number of cases. When adherence is 100%, cases level off. As adherence decreases, multi-drug resistance is observed, resulting in a negation of the lower transmission rates of initial treatment with ARV drugs and a steady increase in cases in the following years. Moreover, the onset of multi-drug-resistant HIV/AIDS is earlier for lower adherence rates, which is intuitively correct. Our model is sensitive to the fairly large changes in adherence rates, which is what we would expect.

Economic Model for Administering ARVs

We discuss an economic model for administering ARVs abstractly in the absence of data, due to the difficulty of its collection.

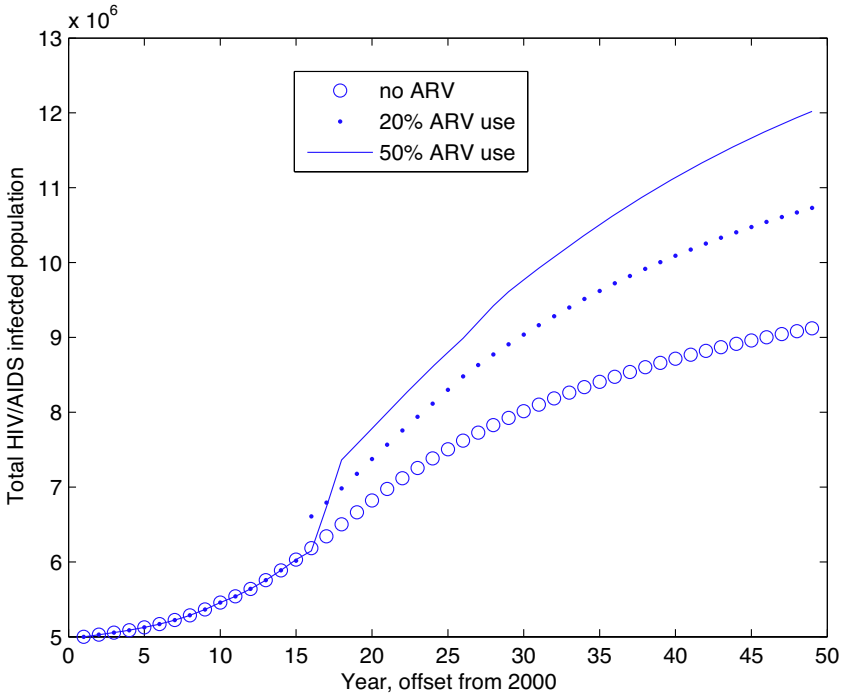

Figure 7. Effects of ARV therapy on model outcome, assuming no impact on transmission rate

Negative externalities can result from higher rates of infection as HIV / AIDS victims enjoy increased life expectancy and therefore have greater opportunity to spread the virus. Positive externalities can result from the cost savings that rich countries enjoy indirectly by reducing the infection rate in poor countries. For example, in Australia more than half of HIV infections attributed to heterosexual intercourse in 2000–2004 were in people from a high-prevalence country or whose partners were [UNAIDS and WHO 2005]. Hence, reducing infection rates in high-prevalence poor countries might reduce the rate of infection in rich countries.

[EDITOR'S NOTE: We omit the details of the authors' optimization analysis.]

Discussion and Conclusions

Strengths and Weaknesses

Strengths

- Ability to incorporate many data sources, such as condom usage rates, drug populations, and historical AIDS death rates.
- Scalable and easy to expand to account for new populational factors. Easy to adapt to new locations.
- High accuracy in fitting historical data.

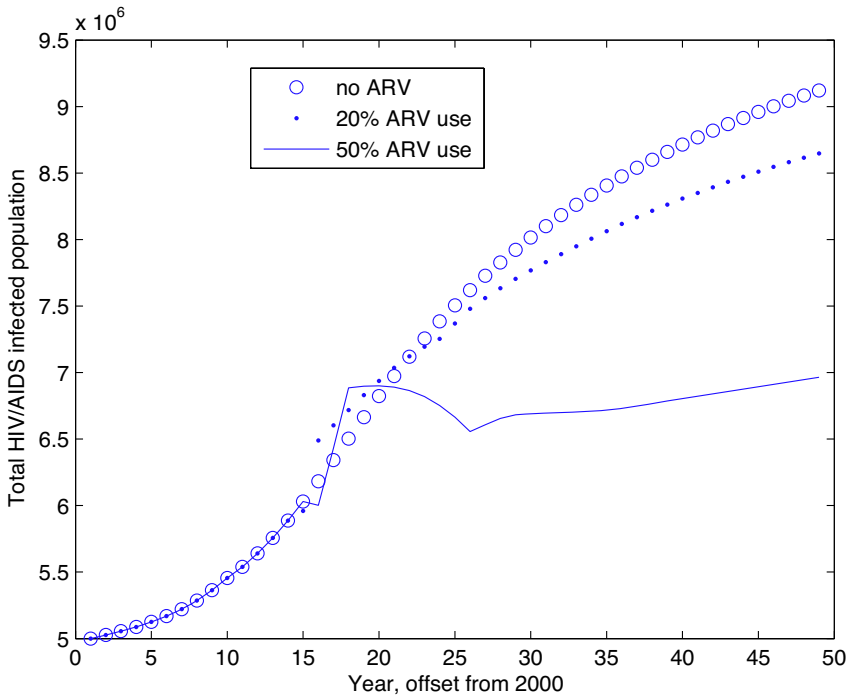

Figure 8. Effects of ARV therapy on model outcome, with ARV patients 25% less contagious.

- Comprehensive. Takes into consideration all the major factors concerned in HIV, including transmission factors, prevention techniques and economic considerations.

Weaknesses

- Large amount of prerequisite data required, some of which may be hard to acquire, such as historical HIV / AIDS death rates.
- Countries treated as isolated entities (does not account for migration).
- Fails to account for random differences between individuals, such as time to death after infection.

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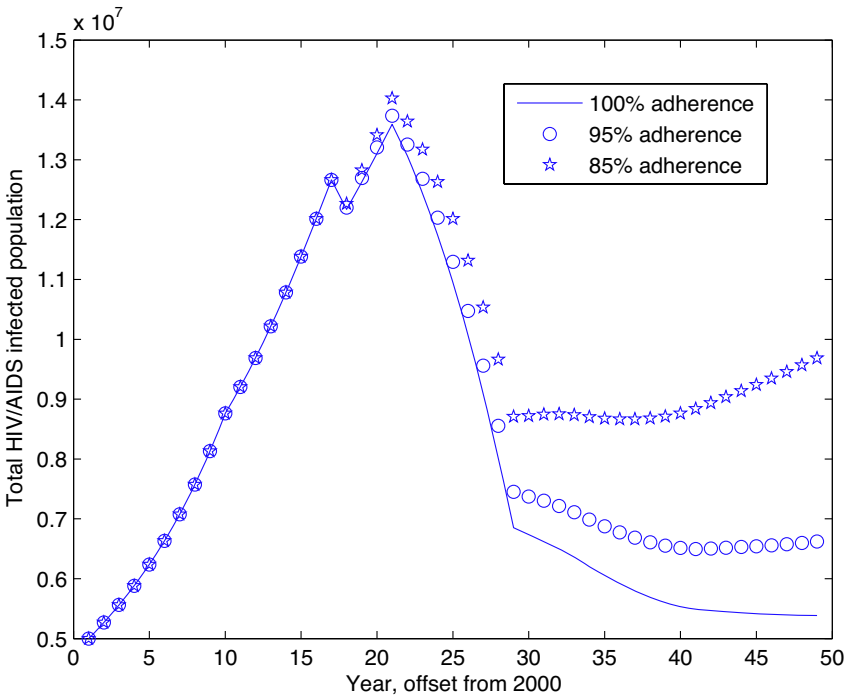

Figure 9. Effects of multiple drug resistance on transmission rate, assuming 100% ARV usage, and that ARV decreases transmission rate.

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Managing the HIV/AIDS Pandemic: 2006–2055

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Summary

We begin with a thorough consideration of which nations face the most critical situations with respect to HIV / AIDS. We model an adjusted life expectancy, using a short-term logistic differential equation model, and them mathematically define criticality. By continent, we conclude that the most critical nations are: Botswana, Thailand, Tonga, Ukraine, Bahamas, and Guyana.

We analyze the futures of these most critical nations with a versatile computer simulation that deals directly with people rather than homogenous populations, as a differential equations model would.

Treatment analysis includes estimation of the amount of foreign aid available through 2055 and predicts the effects of antiretroviral treatment (ART) and the possibilities of a preventive HIV / AIDS vaccine. We consider the ramifications of drug-resistant strains

We conclude with a series of recommendations for how best to allocate resources. We recommend intensive spending in the short term on research and development of a vaccine, followed by a global coverage of ART with heavy emphasis on maintaining adherence.

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Defining Criticality

Approach

What makes a country "critical"? The obvious answer is countries with the greatest number of cases, or the greatest proportion of cases; but this is not a complete analysis. A critical situation implies that progress can be made towards a solution. At this point, nothing beyond antiretroviral therapy can be done for an HIV/AIDS patient. Countries with high rates of treatment can do little more for their infected population, so such countries should not be deemed most critical. The term critical also implies that action is urgent, that HIV/AIDS will be very detrimental in the short term. We believe that the best way to measure the effect of HIV/AIDS on a population is to determine the *cumulative number of years of life lost* due to infection.

Assumptions and Terms

- ART patients have 100% adherence—a patient either receives ART treatment or not, there is no middle ground.
- No further intervention occurs within the next five years.
- ART percentages remain constant.
- No other major causes of death affect the population. Since we are predicting over a relatively short interval of time, it is unlikely that major events such as natural disasters, wars, or other pandemics will significantly affect the population.
- People-year: A unit equivalent to one person times one year. The number of people-years of a population equals the sum of all the lifetimes of people in the population.
- To measure the immediate effects of HIV/AIDS on a population receiving no further intervention, we define criticality over the next five years (2006–2010):
  - **Absolute Criticality**: The total number of people-years lost by a *population* over the next five years due to HIV/AIDS.
  - **Relative Criticality**: The average number of people-years lost by a *person* over the next five years, in other words, the change in life expectancy over the next five years.

Development

We derive a mathematical expression for criticality in terms of various parameters. Relative criticality ζ is given by

$$\zeta(\alpha, \beta, \gamma, \delta, \epsilon) = \alpha(\gamma + \delta) + \beta\epsilon,$$

where:

α is the average loss of life expectancy due to contracting HIV and without receiving ART,

β is the average loss of life expectancy due to contracting HIV and receiving ART,

γ is the number of current untreated cases divided by current population,

δ is the number of untreated cases contracted over the next five years divided by present population, and

ϵ is the number of treated cases contracted over the next five years divided by present population.

Absolute criticality is given by

$$\zeta_{\text{abs}} = \zeta P,$$

where P is the country's population.

It may seem counterintuitive that a country should be considered "less critical" if its life expectancy is innately lower, as our model would conclude. What this really means is that spending money on HIV/AIDS there may be less relevant than spending money on other causes of death.

Model A: Adjusting Life Expectancy

Approach

To determine the effects of HIV/AIDS on a population, we determine the life expectancy as if HIV/AIDS did not exist. We then adjust for the fact that life expectancy is a function of a person's year of birth.

Assumptions

- Life expectancy does not significantly change over five years, so we can assume that people of each five-year age group are the same age.
- Life expectancy data does not exist for birth years before 1950, so we assume that any person born earlier has the life expectancy of someone born in 1950.
- No immigration or emigration occurs.

Method

Using 2005 population data, we multiply the population for each age group by the life expectancy of the corresponding birth years. to arrive at the total number of person-years for the population. Dividing this by the population gives the *age-adjusted life expectancy* Γ_0.

We then determine a life expectancy value for infected people. Worldwide, we estimate that the average age for contracting HIV is 23. We assume that a person on ART has 100% adherence and never stops treatment. In developed nations, a person contracting HIV but untreated typically lives 12 years, hence on average to age $23 + 12 = 35$. Few people treated with ARV have died; however, the program began only 10 years ago. We estimate that ART patients in developed countries will live 20 years after contraction, hence on average to age $23 + 20 = 43$. To determine the average life expectancy for a person contracting HIV / AIDS, we use the formula

$$\Gamma_{\text{HIV}} = \frac{\Gamma_0}{70}\left[35(1-T) + 43T\right],$$

where T is the percentage of people currently receiving ARV treatment. The formula yields a weighted average of the life expectancies for untreated and treated patients, and we account for the difference in life expectancy due to causes other than HIV by multiplying by the age-adjusted life expectancy divided by 70, an assumed average for the life expectancy of a developed nation.

To derive an expression for the HIV-adjusted life expectancy, we take a more intuitive approach. We have data for the total number of people-years of a population, and given the number of HIV cases P_{HIV} and the average life expectancy for HIV patients, we know the total number of HIV people-years. If these people did not have HIV, the number of people-years that they contribute to the population would increase. Therefore, adding the number of people-years that the infected population loses due to premature death to the unadjusted number of people-years for a population yields the adjusted people-years, and consequently an HIV-adjusted life expectancy for that population. The formula for HIV-adjusted life expectancy Γ_A is

$$\Gamma_A = \frac{P(\Gamma_0 + P_{\text{HIV})}\Gamma_0 - \Gamma_{\text{HIV}}}{P}.$$

Expectations and Results

If our model is appropriate, a few things should certainly occur:

- The HIV-adjusted life expectancy should always be greater than the unadjusted life expectancy.
- The difference between the HIV-adjusted life expectancy and the unadjusted life expectancy should be proportional to the percentage of the population infected with HIV.

No country shows a decrease in life-expectancy after HIV-adjustment; and by taking the difference between the HIV-adjusted life expectancy and the unadjusted life expectancy and dividing by the percentage of the population infected with HIV, we find strong evidence for proportionality.

Model B: Logistic Growth

Approach

To implement our definition of criticality, we must predict the number of HIV / AIDS cases (both treated and untreated) over the next five years. A logistic growth model is easy to work with and incorporates a maximum sustainable population.

Assumptions

- Birth and death trends remain similar over the next five years.
- The incidence of HIV / AIDS is constant within each of 12 representative regions that we feel have minimal variation in HIV / AIDS growth rates: Africa, South East / Central Asia, North / East Asia, Oceania, Brazil, South America excluding Brazil, Canada, the United States, Mexico, Latin / Central America, the Caribbean, and Europe.

Development

The logistic growth model describes a population that grows in proportion to the current size of the population, in addition to factoring in a carrying capacity—in this case, a maximum sustainable AIDS population. The general form of the differential equation is

$$\frac{dP}{dt} = \frac{rP(K-P)}{K} = rP\left(1 - \frac{P}{K}\right),$$

where

P is the total HIV / AIDS population size,

r is the maximum population growth rate, and

K is the maximum sustainable HIV / AIDS population.

As the population gets closer and closer to the maximum sustainable population, its growth rate becomes a smaller proportion of the maximum growth rate r. The general solution to the differential equation is

$$P(t) = \frac{r}{ce^{-rt} + r/k},$$

where c is a constant determined by an initial condition. We must estimate k and r, using data for cases over the past 5 to 20 years. We rearrange the differential equation to the form

$$\frac{1}{P}\frac{dP}{dt} = a + bP,$$

with $a = r$ and $b = -r/k$. We then plot successive values of

$$\left(P(t_i),\ \frac{P'(t_i)}{P(t_i)}\right)$$

and fit a least-squares line to the data, yielding an estimated slope b and a y-intercept a. We estimate $P'(t_i)$ from the slope of the secant connecting the point before and the point after the chosen point.

Results

We use the above procedure to determine a function $P(t)$ for the size of the HIV/AIDS population at a given time up to 2005. For prediction, we extrapolated by evaluating the function at 2010.

Putting It All Together

Given the HIV-adjusted life expectancy, we can determine the values of α and β for each country;

$$\alpha = \Gamma_A - 35\left(\frac{\Gamma_0}{70}\right), \qquad \beta = \Gamma_A - 43\left(\frac{\Gamma_0}{70}\right).$$

Armed with a logistic model for the infected population of each region, we extrapolate to determine the number of cases that will arise over the next five years. We then make two further assumptions.

Additional Assumptions

- The proportion of cases treated by ARV will remain unchanged over the next five year.
- The proportion of HIV/AIDS cases of each country within its respective region, H_{relative}, will remain unchanged.

$$\delta = \frac{(1-T)[P_{2010} - P_{2005}]H_{\text{relative}}}{P_{2005}}, \qquad \epsilon = \frac{T[P_{2010} - P_{2005}]H_{\text{relative}}}{P_{2005}}.$$

Finally, the number of current cases is given by our data, so

$$\gamma = \frac{(1-T)H}{P}.$$

Results

We determine absolute and relative criticality values for the 108 countries for which all the required data were available. We then use relative criticality to select the most critical countries, by continent: Botswana, Thailand, Tonga, Ukraine, Bahamas, and Guyana. Fourteen of the 15 most critical nations worldwide are in Africa.

Using absolute criticality would give precedence to large nations, despite relatively mild HIV / AIDS situations.

Determining Growth Rates

Model C: Simulation of a Country with HIV/AIDS

Approach

We want a more detailed and elaborate model to forecast the long-term behavior of HIV / AIDS. We opted for a discrete computer simulation of the interactions of individuals. Such a model is much better able to cope with complicated demographic combinations, since the objects of the model are persons rather than homogeneous populations. A disadvantage is that directly simulating an entire country's population in this way is not feasible.

Assumptions

- An entire country can be modeled by simulating the course of the disease over a small representative community (population on the order of 1,000).
- Allowing the simulation to run for 10 years before introducing HIV allows for a base of existing relationships to form.
- With the exception of contraction before or during birth, all transfers of HIV occur from consensual events (drug- or sex-related) between two people.
- A person's probability of dying of natural causes is directly proportional to age.
- The effect of HIV is to multiply by some factor what would otherwise be a person's probability of dying of all other causes. This effect depends solely on whether or not a person has the virus; other factors, such as time since the virus was contracted, need not be considered.
- The sexual behavior of persons regarding number of partners, frequency of sex, etc., is essentially the same, regardless of sex and sexual orientation. The only exception is that only females can be sex workers and only males can be clients of sex workers.

- The populations of female homosexuals and bisexuals can be neglected.
- People's characteristics do not change as they grow older, except for changing stages from infant to child at age 2 and from child to adult at age 16.
- Only adults have sexual relationships or share intravenous drugs.
- A needle-sharing or sexual encounter with an infected person automatically results in transfer of the virus.

Development

Relationships

The basic tools that we use to model the spread of the disease are *relationships* and *events*. A relationship between two people can be initiated by either but to occur must be accepted by the other. An event occurs within a relationship and may result in the transfer of a virus, or multiple strains of a virus. Like a relationship, an event can be initiated by either person but must be accepted by the other. Different people have tendencies to engage in different sorts of relationships and events, and may thereby be classified into relevant demographic groups. The relationships types that we used included sexual relationships, mother-child relationships, and relationships for the social use of intravenous drugs.

Availability Pools

Formation of relationships is based on availability pools. Depending on their characteristics and on existing relationships, persons are placed into availability pools for particular sorts of relationships. A person seeking a relationship chooses an appropriate availability pool and queries it for a match. The availability pool chooses a potential match using an algorithm that attempts to preserve efficiency of data structures while providing some measure of randomness, and the chosen person is given the option of accepting or refusing the offered relationship. Either person may choose to end a relationship.

Events

A person who engages in relationships has a desired rate of events of that category. The chance of accepting an event or of requesting an event in a given cycle is based on whether or not the person has reached their satiation point for the given event.

[EDITOR'S NOTE: The authors offer further details on the mechanisms for drug-use, mother-child, and sexual relationships, as well as on abstinence, monogamy, casuality, and prostitution, which we must omit.]

Birth and Death Rates

For every adult woman who is not already pregnant, a sexual encounter with a man has a fixed probability of resulting in pregnancy. (Menopause is not taken into consideration.) Every pregnancy results in the live birth of a baby nine months after conception, unless the mother dies earlier. The probability of death by natural causes is assumed to be directly proportional to age. Additionally, children (especially infants) without mothers have a constant term added to their probability of dying. When HIV is present, the death rate as if it were not present is multiplied by a fixed constant; in a sense, the virus reduces a person's "death resistance."

Data and Parameter Values

The risk of a child contracting HIV during pregnancy and birth ranges from 15% to 30%, with the risk increased another 10% to 15% due to breastfeeding over the first two years of life [Orendi 1998]. We divide this range in half to determine the rate per year of breastfeeding contraction.

The demographic data come largely from the Central Intelligence Agency [2001].

We determine the percentage of the population using IV drugs by assuming that this value equals that of the surrounding region [United Nations Office on Drugs and Crime 2005]. To determine the acceptance, seeking, and breaking rates for drug relationships, we make reasonable assumptions based on reading about the typical social behavior of IV drug abusers. We use such an approach also in determining the maximum number of drug relationships and the rate of drug relationships per year [United Nations Office on Drugs and Crime 2005].

The HIV vulnerability parameter comes directly from the HIV-adjusted life expectancy model, and is simply an adjusted ratio of the HIV life expectancy and the unadjusted life expectancy.

We discern nearly all of the parameters for sexual relationships from Francoeur et al. [2004] and the Mackay [2000].

In connection with our assumption that a person's probability of dying is directly proportional to the person's age, we need to ascertain the constant of proportionality k based on the life expectancy. The statement about the death rate can be expressed as

$$\frac{-dP/dt}{P} = kt,$$

where P is the probability the probability of a person being alive at time t. (On another scale, P is the number of people born in the same year who remain alive after time t.) Solving, we find

$$P(t) = P_0 \exp\left(-\tfrac{1}{2}kt^2\right),$$

which—surprisingly (or not, if you are already familiar with this model for human aging, which we weren't)—turns out to be proportional to the right half of a Gaussian distribution.

To combine this equation with life expectancy, let r represent the death rate and consider that for a differential time quantity dt, the expression $-r\,dt$ represents a differential quantity of people who die at age t. Hence, the average age of death, or life expectancy, is

$$\frac{1}{P_0}\int_0^\infty rt\,dt = \int_0^\infty kt^2 \exp\left(-\tfrac{1}{2}kt^2\right)\,dt.$$

We calculate this integral numerically as a function of k. [EDITOR'S NOTE: In fact, the exact value is $\sqrt{\pi/2k}$.] Setting the result equal to the life expectancy calculated from other data for the country of interest lets us determine the relevant value for k.

Results and Discussion

After running the 50-year simulation a number of times, we noticed that there was almost always an initially explosion of HIV cases in the first few years, followed by much slower growth. This is likely the result of our assumption that every encounter results in the transmission of HIV; because of this, HIV spreads very quickly through relationships that were already in place at the beginning of the 50-year period.

Additionally, as time progressed, the HIV/AIDS population appeared to approach a steady state, or infected carrying capacity. Based on the structure of our model, the majority of the adult population ends up being infected with HIV, while only a small portion of children contract the virus; the steady-state value is merely a high percentage of the steady-state value for the adult population.

Model D: Treating the Pandemic

Approach

We determine the available funding to each of the critical countries and to the world as a whole for the years 2005–2055. Then we add additional parameters to the computer simulation model to determine the effects of increased antiretroviral therapy and preventive vaccination. Further simulation, devoting different proportions of the available funding to ARV and vaccinations, allows us to determine the best way to spend both national and worldwide HIV/AIDS funding.

Assumptions

- Economic trends remain relatively stable over time.
- Inflation in the cost of HIV treatment is comparable to that of the rest of the world economy.
- ART patients have 100% adherence.
- Vaccination, when developed, is 100% effective in preventing contraction of HIV.

Finding Aid

In 2004, $6.1 billion was provided in foreign aid for HIV/AIDS, worldwide. [Agence France-Presse 2004]. To account for the growth of the world economy and the increasing awareness with respect to HIV funding, we model the available funding A (in billions of dollars) exponentially, choosing the growth rate based on recent trends in funding:

$$A_{\text{world}}(t) = \$6.1 \times (1.05)^t.$$

We then analyze the funding available to each of the six critical countries. Of the funding for HIV/AIDS in developing/semideveloped nations, 85% comes from foreign aid and 15% from domestic spending [Martin 2003]. We assume that a government spends one-twentieth of one-percent (0.0005%) of its GDP on HIV/AIDS each year. Botswana, Tonga, Bahamas, and Guyana reasonably fit this 85/15 rule; however, Thailand and Ukraine are too developed for this assumption to apply, and we impose a 25/75 analog. From this, the equations for funding are as follows, where ρ is the growth rate of the GDP for each nation.

$$A_{\text{developing}}(t) = 0.0005\text{GDP}\left[\rho^t + (1.05)^t \frac{85}{15}\right],$$
$$A_{\text{developed}}(t) = 0.0005\text{GDP}\left[\rho^t + (1.05)^t \frac{25}{75}\right].$$

The predicted cost of supplying ART is $1,100 per person per year, and we assume that a person continues ARV treatment until death. We account for the potential inflation of costs, again using an exponential function, with growth rate of 2%. The maximum number of ARV patients that a nation can treat equals total funding divided by the current cost per person.

But what are the effects on the population of an increased number of patients treated with ARV? People strictly adhering to ARV treatment have extremely suppressed HIV virus figures [Porter 2003]. This means that is nearly impossible for a correctly treated ARV patient to transfer the virus to an uninfected person. Therefore, in our modification of the computer simulation, we prevent any person treated with ARV from transferring HIV to other people. This

change should lead to a significant decrease in the number of new HIV cases per year in comparison to the original model. In theory, if all HIV cases are treated with ARV, over time the virus should be removed from the population.

In determining when a preventive vaccine will be developed, we assume that research funding is from the worldwide aid pool and that changes in funding do not have a significant effect on when a vaccine will be found. Thus, the probability of finding a preventive vaccine should be a function of time. Multiple sources state that a vaccine will not be found within the next 10 years, so we define the probability of a vaccine being discovered by a given year as

$$S(t) = .03(t - 10), \qquad \text{for } 10 < t < 43.3,$$

where time t is measured in years after 2005. This probability function assumes that in 26.7 years, there will be a 50% chance of a vaccine being discovered.

Model E: Preventive Vaccine Distribution

Approach

To model the rate of vaccine introduction, we use a logistic growth model.

Assumptions and Terms

- The steady-state percentage of the population vaccinated will be equal to that of DTP_3 and Tetanus for infants and adults respectively, as reported by the WHO in 2002 in the datasheet accompanying the problem statement.
- The steady-state percentage value will remain constant over the next 50 years.

Development

We let V be the percentage vaccinated, λ the initial growth rate, and D the maximum percentage vaccinated. The logistic model leads to

$$V(t) = \frac{D}{C\exp(-\lambda t) + 1}.$$

We determine values for λ and C from initial conditions. We assume that in one year the vaccination rate would reach 10% of its maximum value and after 10 years would reach 95%. These conditions lead to

$$\lambda \approx 0.571, \qquad C \approx 15.9, \qquad V(t) = \frac{D}{15.9e^{-0.571t} + 1}.$$

Table 1 shows the values of D for the critical countries.

Table 1.
Maximum percentage vaccinated (D) for the critical countries.

Country	Child	Adult
Botswana	87	49
Thailand	97	90
Tonga	90	93
Ukraine	99	37
Bahamas	86	1
Guyana	91	1

Model F: Resistant Strains and Mutations

Approach

One of the most dangerous aspects of the HIV virus is its ability to mutate quickly. If a regimen of treatment does not destroy or incapacitate all of the viruses in a system, only the strong ones will remain to repopulate, over time forming a dangerous resistance that renders the drug useless.

The antiretroviral therapy associated with the HIV virus is difficult. Patients must take scores of pills, multiple times per day, for the rest of their lives; we cannot expected 100% adherence to the regimen.

Assumptions

- All people receiving ART intend to maintain 100% adherence. No patients are opposed to being treated for psychological, ethical or spiritual reasons.
- No patient is guaranteed to succeed in maintaining 100% adherence.
- A person with cumulative adherence below 90% has a 5% chance of developing a resistant strain.
- The opportunity for a resistant strain to develop occurs every time a treatment occurs in which cumulative adherence is below 90%.
- ART for a resistant strain will not be available before the year 2055. This allows us to make the simplification that only one resistant strain will exist.
- Resistant strains can be vaccinated against, but a new vaccine will have to be developed.
- The only property of a resistant strain that distinguishes it from the original HIV is the resistance to ART. The effects on the body and on life expectancy remain constant.
- The resistant strain, if it exists, takes precedence over the original strain, that is, a person will not carry both.

Development

We assume (with no data basis) that a person will adhere completely to a year of treatment 99% of the time.

By creating a new parameter within the main simulation, we can simulate the adherence behavior of every ARV patient within the model. A second parameter randomly decides whether a person with sufficiently low adherence (less than 90%) causes production of a resistant strain. We introduce a constraint on this behavior, not allowing resistant strains to occur within a person until after three years of treatment. This constraint minimizes the skewing effects that could occur if a person developed a resistant strain after missing the first treatment, which is biologically nonsensical, as the virus would have nothing to resist. The computer simulation runs as before, allowing for a resistant strain to occur. This strain would not be affected by ART or vaccination, and thus resistant-strain-infected people would behave like HIV-infected people who remain untreated.

Given that second- and third-line ARV drugs are so expensive, we assume that none of our critical countries will have access to them. We assess the probability of developing a vaccine against the resistant strain as

$$S_{\text{resistant}}(t) = .03t, \qquad 0 < t < 33.3,$$

where t is the number of years since finding the original vaccine to the non-resistant strain. We assume that the costs associated with the new vaccine are identical to those of the original vaccine.

Discussion of Models D-F

Assuming no economic disasters over the next 50 years, the world economy is well prepared to handle the HIV / AIDS situation and should be able to provide billions of dollars to the cause consistently. The question is not about availability of money but where to spend it.

ART is a powerful weapon; it almost certainly prevents transfer to uninfected people. There is, however, the danger of production of resistant strains of HIV. It is vital that the implementation of ARV programs be done with great emphasis on maintaining adherence to the program.

A preventive vaccine would provide quickly stall new cases and bring the disease down to a manageable level. We believe it probable that a vaccine will be discovered within 25 to 40 years. It is important to devote resources to its research and development.

We suggest that funds be allocated largely to ART in the next few years to bring raging epidemics in the critical nations under control, followed by a phasing in of an intense vaccine development program beginning in approximately 10 years.

Conclusion

The critical countries by continent—Botswana, Thailand, Tonga, Ukraine, Bahamas, and Guyana—are a springboard for a global control effort of the pandemic.

Foreign aid should be focused on the most critical nations, not necessarily by continent, but worldwide. Treatment should begin with sweeping programs of antiretroviral therapy focused on maintaining 100% adherence. Simultaneously, research should begin on developing a preventive vaccination, which could begin distribution immediately and reach stable levels within 10 years.

Strengths and Weaknesses

Weaknesses of the model included assumptions made for simplicity that likely do not hold. For instance, in most runs of our model on any country, cases exploded rapidly to include most of the adult population within three years—a feature that does not correspond to the past behavior of HIV. This feature is likely a result of our assumption that every single sexual encounter or sharing of a dirty needle with an infected person results in disease transmission.

However, a corresponding strength of our model is that it would be relatively easy to include a parameter for probability of transmission.

Our model is particularly appropriate for simulation of evolving strains of resistant viruses, a problem that naturally lends itself to such discrete modeling.

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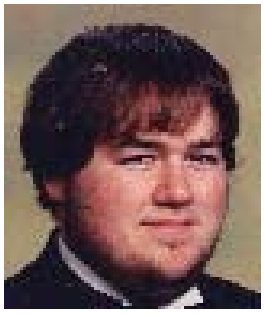

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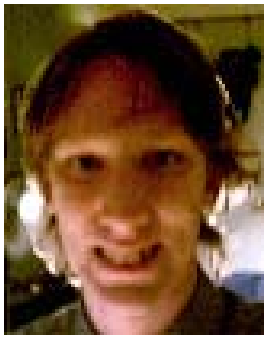

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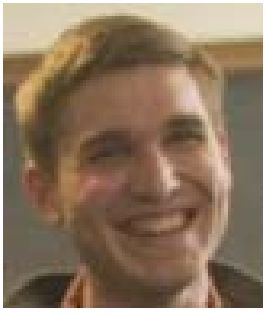

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AIDS: Modeling a Global Crisis (and Australia)

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Summary

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

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

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

Introduction

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

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

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

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

HIV Epidemic Model

Disease Epidemic Models

The SIR Model

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

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

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

Applied to HIV, this model assumes:

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

However, this model is inappropriate for HIV:

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

A Multistage Model

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

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

where

S is the number of susceptible individuals,

I_i is the number of infected individuals in stage i,

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

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

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

r is the partner acquisition rate,

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

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

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

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

Characteristics of the Desired Model

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

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

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

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

The model below incorporates all of these considerations:

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

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

Table 1.
Parameters and their symbols.

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

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

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

Assumptions

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

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

Features of the Model

Some interesting effects that this model can address include:

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

Critical Countries

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

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

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

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

Projected Unchecked Infections

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

Model

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

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

Procedure

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

Results

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

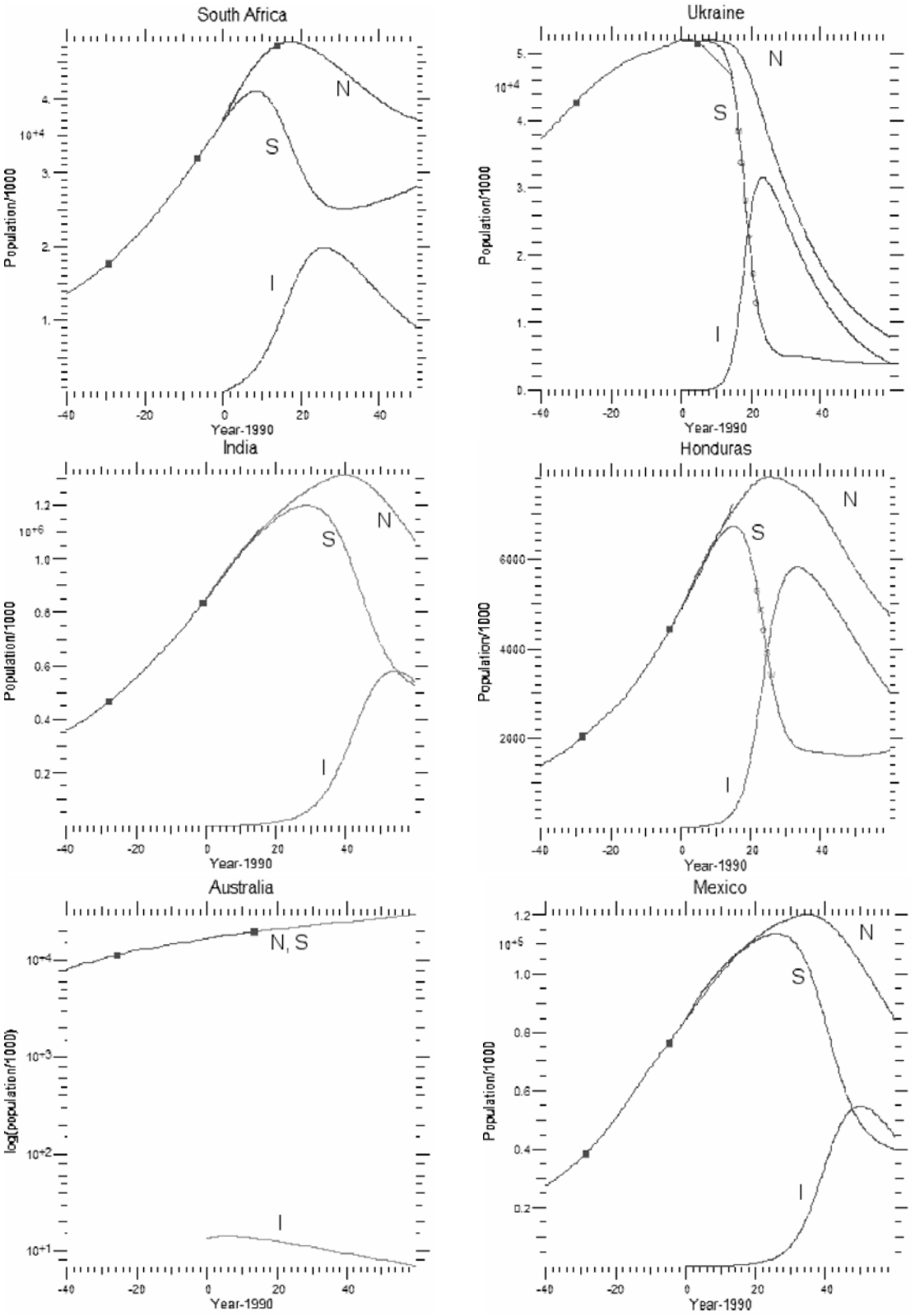

Figure 1. Model predictions for unchecked HIV infections. N: total population. S: susceptibles. I: infecteds.

South Africa

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

Ukraine

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

India

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

Honduras

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

Australia

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

Mexico

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

Financial Resources and Foreign Aid

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

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

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

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

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

Projections with ART and Vaccination

Model

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

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

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

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

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

Vaccination

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

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

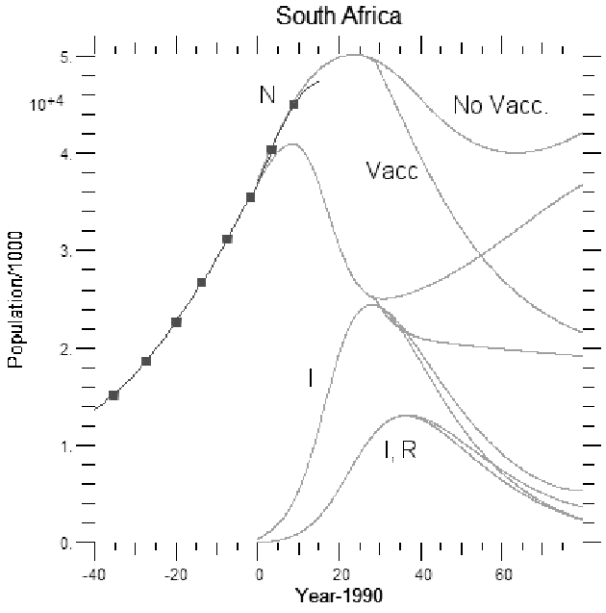

Figure 2. In the presence of ART and emergent ART resistance, the susceptible population in South Africa decreases at the introduction of an HIV vaccine in 2015, and the total number of AIDS cases immediately declines as well.

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

resistance of HIV, discussed in the following section.

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

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

Effect of ART

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

South Africa

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

Ukraine

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

India

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

Honduras

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

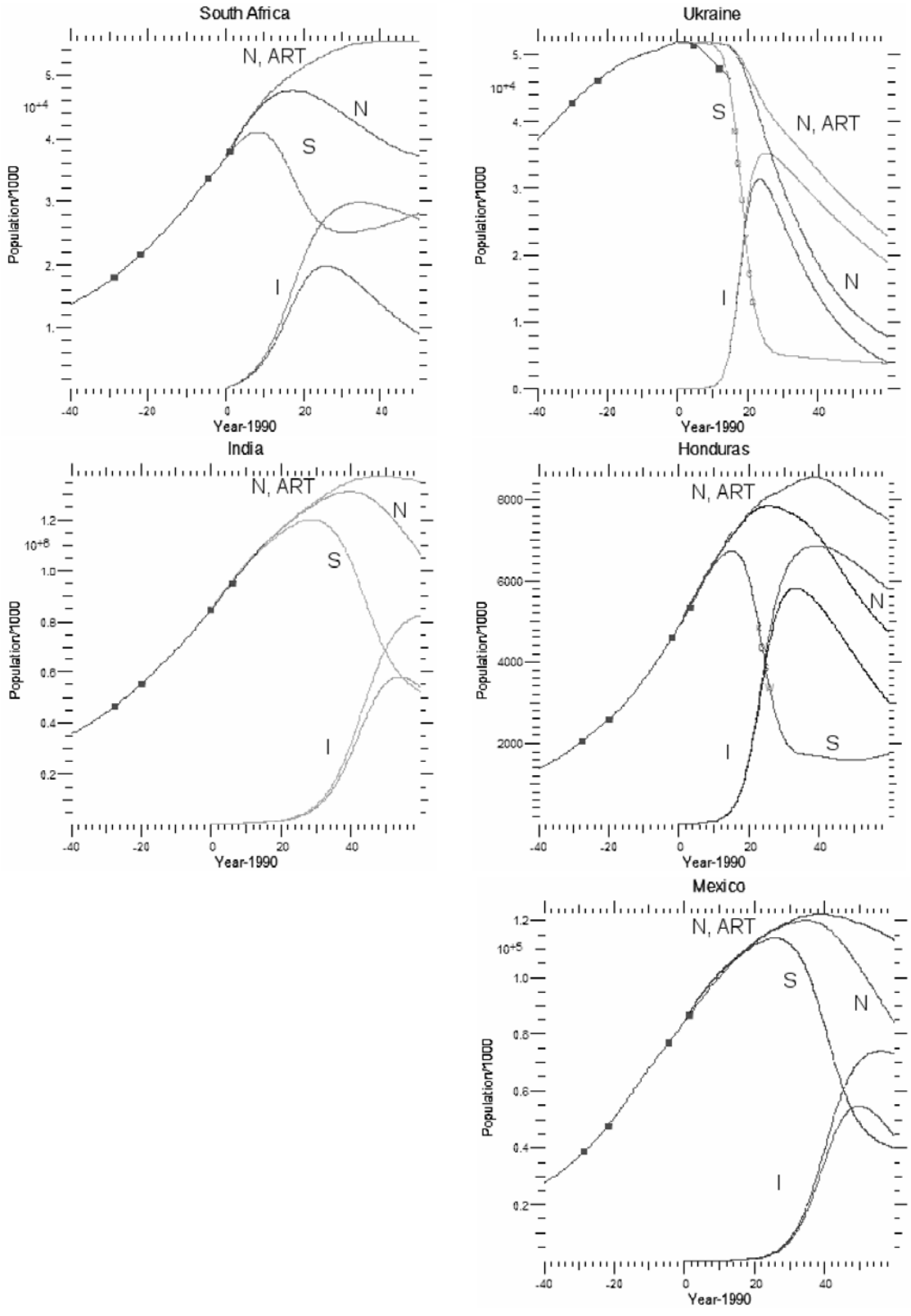

Figure 3. Model predictions with and without ART but with no development of ART-resistance. (N: total population. S: susceptibles. I: infected.)

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

Australia

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

Mexico

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

The Economic Strain on Critical Countries

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

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

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

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

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

Therapy-Resistant Strains

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

Model

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

ARV resistant strain emergence and vaccination

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

Conclusion

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

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

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

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

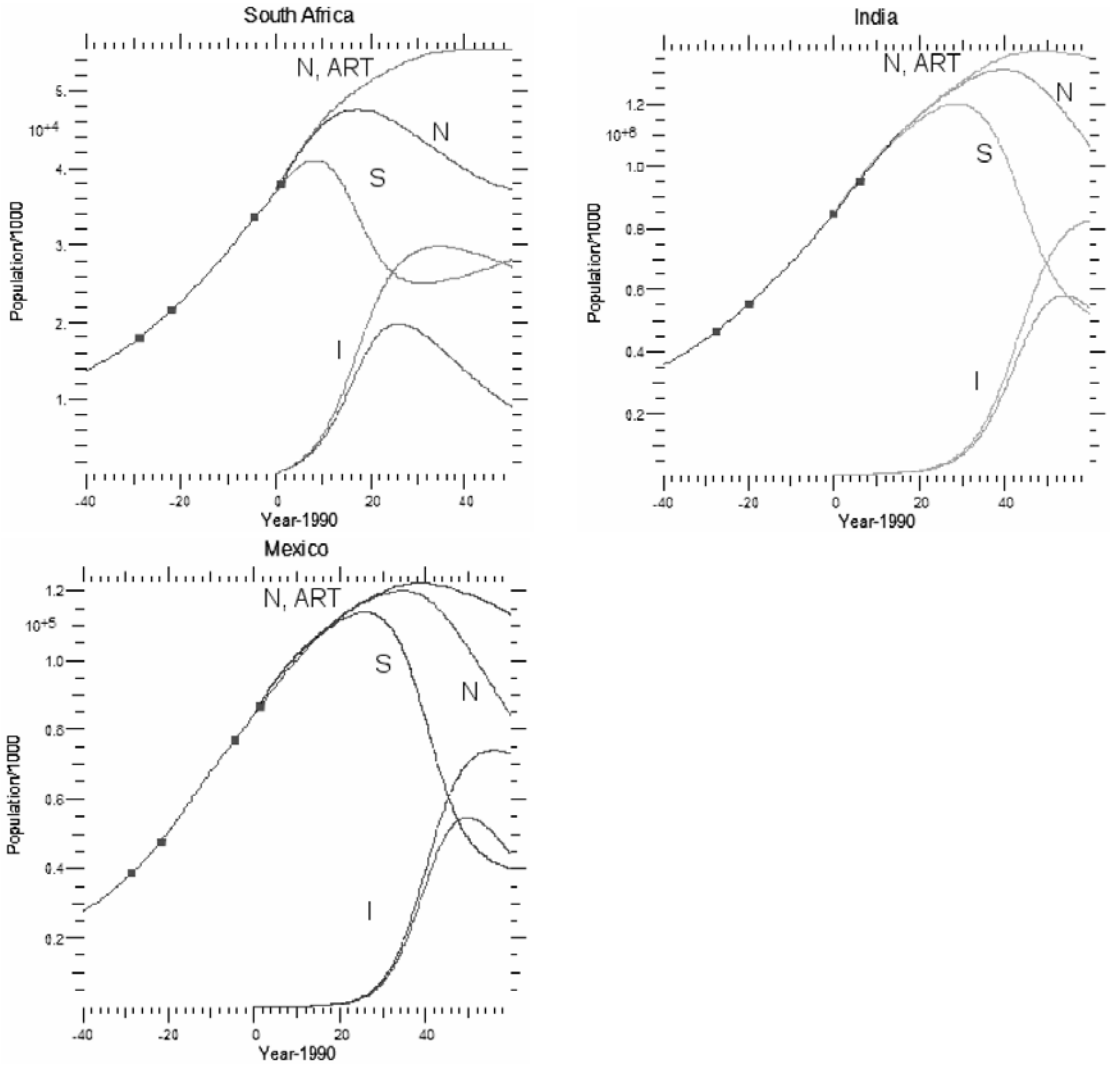

Figure 4. Model predictions with developed resistance under ART. The net beneficial effect of ART is decreased. (N: total population. S: susceptibles. I: infected.)

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Mike Martin graduated with high distinction from Harvey Mudd College in May 2006 with an honors degree in physics. His interests center on fundamental quantum theory and its applications to atomic, molecular, and optical physics. His undergraduate experimental work was conducted through the Sandia National Labs clinic project at Harvey Mudd, where he and teammates worked to characterize soot aerosols optically. In addition to studying physics, Mike spent a semester in Paris studying literature and art. He will begin graduate study in physics at the University of Colorado at Boulder in the fall of 2006.

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The Spreading HIV/AIDS Problem

Adam Seybert
David Ryan
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West Point, NY

Advisor: Randal Hickman

Summary

We propose four main focus areas in which the world can win its battle against AIDS:

- **Identifying** individuals who are HIV positive, through blood testing (in batches, to save money). People who are HIV-positive will recognize that they are infected and take measures to ensure that they do not spread the virus to other people. We plan to test everybody in sub-Saharan Africa by spending $1.5 billion/year for 3 years.
- **Educating** the public on how HIV can be prevented, in order to keep the incidence rate down. Showing people that AIDS is incurable, along with the ABCs of prevention, our hope is that they will inculcate the practices in order to stop the epidemic. These practices include remaining abstinent ("A"); being faithful ("B") to one uninfected partner if one chooses to be sexually active; and the use, availability, and effectiveness of condoms ("C") during intercourse.
- **Antiretroviral treatments** (ART) for women who are or become pregnant before our plan is implemented. These treatments help reduce the risk of an infected mother passing the virus to her child during pregnancy, birth, and nursing. This area will be the most difficult to support financially due to the cost of producing and distributing treatments. However, surplus funds will alleviate this problem after the testing phase is complete.
- A **vaccine**; one might be available by 2011. Though this date could be pushed forward with more funding, we suggest keeping vaccine research resources stable and focusing on the 100% guaranteed cure, the ABCs. The vaccine

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however, might not be completely effective and accidentally allow for drug-resistant HIV strains to evolve. By 2011, the testing phase will be complete, and hopefully governments would have established a basic national education program, thus freeing up additional assets, which can be put into manufacturing and dispensing the vaccine.

Problem Approach

- Task 1: To get the rate of change in HIV/AIDS for 2006 to 2050, we develop a model of the growth/decay of the population for each country. We use the prevalence rate, number of new cases, and the population each year (as the carrying capacity) to develop a logistic growth model for the virus, assuming that there is no intervention in the spread of HIV.
- Task 2: To account for the introduction of treatments, vaccinations, and a combination of the two, we develop state diagrams to show the possible paths of HIV. Using the diagrams and determining rates of change from one state to another, we formulate new plots of the total population and the spread of AIDS.
- Task 3: There is no way to predict the rate at which the virus would become drug-resistant. We would have to make too many assumptions such as the number of people being treated, the amount of treatment they were receiving, the effectiveness of that treatment, the frequency of each treatment, the adherence to the treatment regimen, and the probability of the virus to mutate. Hence, we offer a qualitative approach rather than a quantitative one. We look at what effect drug-resistant strains would have on our model, specifically the rates of change from one state to another.
- Task 4: In our white paper to the United Nations, we focus on allocating resources to treat the problem and not to the symptoms. The surest way to keep from getting HIV/AIDS is practicing abstinence, being faithful, and using condoms during intercourse. Therefore, HIV testing and education are our primary objectives in combating the epidemic.

Assumptions

- The population with HIV/AIDS is homogeneously distributed. This assumption is critical. I those infected with HIV and AIDS interact only with others with HIV and AIDS, then the infection will never spread to the uninfected populace; with homogeneity, the infection could spread to everyone.
- The number of people infected with HIV/AIDS includes those who have been diagnosed and those who have yet to be diagnosed. Without this

assumption, the number of people affected each year only from diagnosed patients would be too low.

- The probability of a person who has been vaccinated contracting HIV from someone who is undergoing ARV treatment is negligible.
- Each country to be modeled is a closed system. There is no immigration or emigration of infected individuals.

Task 1: The Rate of Change from 2006 to 2050

We chose the following countries: Haiti, Guyana, South Africa, Ukraine, India, and Australia, for reasons noted below.

The following is a state diagram that is the base for our models. We reserve the technical details of formulation of a system of differential equations to the **Appendix**.

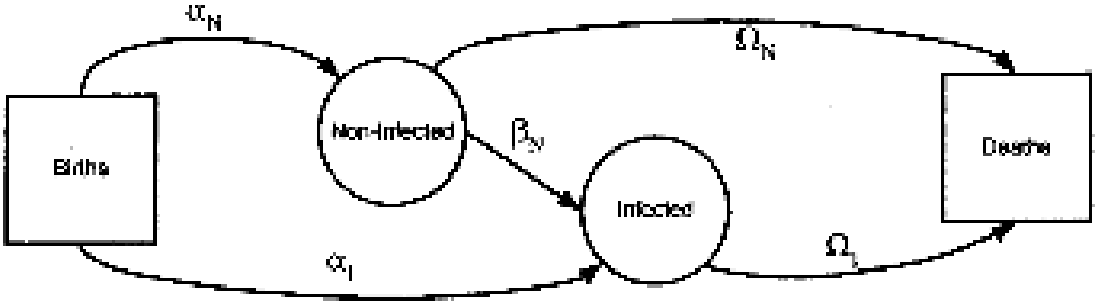

Figure 1. Simplistic HIV/AIDS state diagram.

People are born either infected with HIV or non-infected. A person who is not infected can become infected; but once a person becomes infected, there is no known way to rid oneself of the infection. Both states transition to deaths, but at different rates.

We chose to model Haiti from North America because of its relatively high prevalence rate of 2.6%—high compared to the 1.4% prevalence across the border in the Dominican Republic or the 0.15% and 0.29% prevalence in more developed countries such as Canada and the U.S. Haiti is also one of the poorest countries on the continent, with a GNP per capita of only $510 per year. With treatment cost at well over $1,000 per person per year [Adams et al. 2001], the average Haitian cannot afford HIV medication.

Guyana represents South America in our model. Guyana has a prevalence rate of 2.0%. While Brazil has 36 times as many cases of as Guyana, Guyana's small population makes the problem more widespread. In addition, Brazil has already taken steps to institute a solution to their AIDS problem, spending $444 million to provide 100% of the HIV infected with treatment [Andrews 2004]. Guyana, however, has a far lower GNP than Brazil and fewer resources to dedicate to HIV.

Although Africa is by far the hardest hit continent in the world in terms of HIV/AIDS, South Africa stands out even among African countries, leading the world with 4.2 million cases and a 9.33% prevalence. Additionally, 29.5% of pregnant women tested in South Africa test positive, meaning that the disease is being propagated to children [AVERT.org 2006].

In 1999, Ukraine reported 240,000 cases, with a total population that is decreasing rather than increasing.

India has begun to show disturbing signs that it may be the next hotbed of HIV/AIDS. It has the second-largest population, 1.1 billion, as well as the second-largest HIV-positive population, 3.7 million. This leads to a deceptively low prevalence rate——0.47%——but India is expected to surpass South Africa as the world's-leading HIV-positive population by 2010 [AVERT.org 2006].

From the continent of Australia, having not much choice, we selected Australia. All of the countries in the region have low rates of HIV infection; Australia has only 14,000 cases, the most in the region.

Assumptions

- For a simplified model, we assume that countries will not intervene to stem the spread of the virus through medical treatments.
- AIDS spreads through a population according to a logistic function.

This second assumption is realistic because many similar models, such as the spread of technology and the growth of a population, are based on logistic growth. Each infected person makes contacts with a fraction of the non-HIV population in a way that could transmit the virus, and only a fraction of those contacts actually transmit the virus. So the number of people whom an infected person infects in a year is the number of contacts per non-infected persons, times the infections per contact, times the non-infected population:

$$\left(\frac{\text{contacts}}{\text{non-HIV}}\right) \times \left(\frac{\text{transmissions}}{\text{contacts}}\right) \times (\text{non-HIV}). \qquad \textbf{(1)}$$

We call the product of the first two fractions the transmission rate β_N. So the total transmissions per year is $\beta_N NI$: the transmission rate times the non-infected population times the number of infected people I. Since the total population is growing logistically, HIV also spreads logistically.

Expression **(1)** assumes that the transmission rate is constant. However, since spreading HIV is much more common among certain human behaviors, such as sexual encounters and intravenous drug use, the transmission rate could be different for each infected person. Additionally, certain types of contacts have a higher fraction of transmissions per contact. For example, anal intercourse has a higher fraction of transmission per contact than vaginal intercourse; likewise, transmission of the virus from a male to a female is more likely than from a female to a male [World Bank Group 2006]. To simplify the model, we just consider an average fraction of transmissions per contact.

Logistic Models for Critical Countries

We now consider a graphical model of the spread of HIV in Haiti (**Figure 2**).

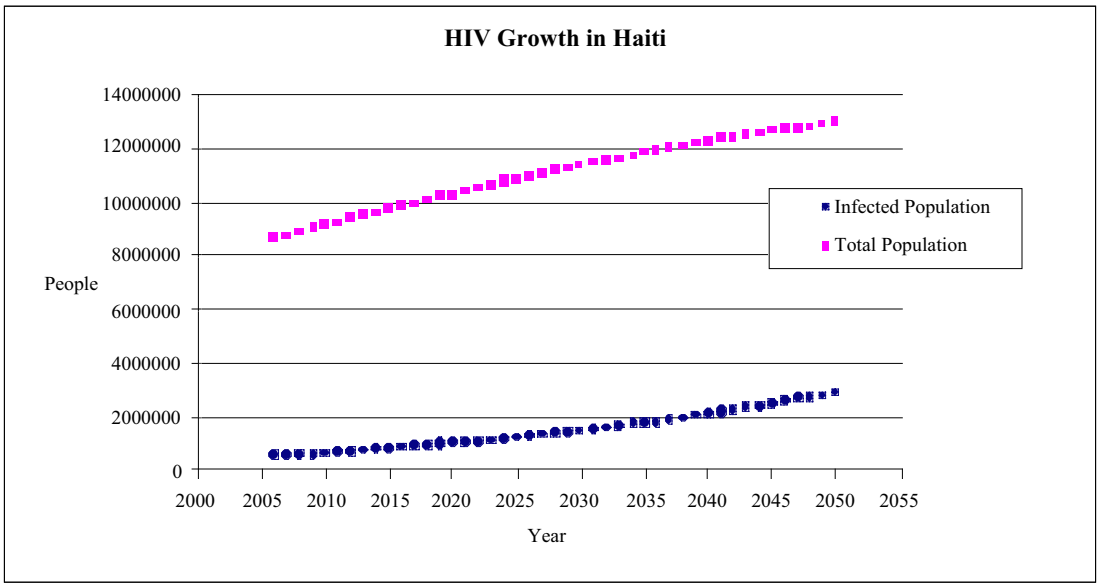

Figure 2. HIV and total population projections for Haiti.

To develop this graphical model, we follow our assumption that HIV follows simple logistic growth.

$$\frac{dI}{dt} = \alpha_I I - \frac{\alpha_I I^2}{K_I}, \tag{2}$$

where α_I is the initial growth rate of the infected population and K_I is its carrying capacity. We can find values for both of these by fitting a second-order polynomial to a graph of the infected population rate of change vs. the total population. To do so, we created a table of data for Haiti from 1985 to 2005: population, number of HIV infections, and prevalence rate [Central Intelligence Agency 2001; UNICEF 2005]. We graphed the change in the number of infections each year against the total number of infections that year. Based on the values obtained, we projected the infected population from 2006 to 2050.

Since the carrying capacity is based on the population, and the population increases, the graph doesn't appear to follow an exactly logistic model. However, it does show how quickly AIDS epidemic is spreading. Since HIV / AIDS has been around for only 25 years, predictions 50 years into the future, can only give an idea of the potential severity of the spread.

Following the same procedure, we created graphs for each of the other countries (**Figure 3**).

Guyana

The overall population is projected to decrease, which one would expect to lead to the AIDS level also decreasing. However, our models project the

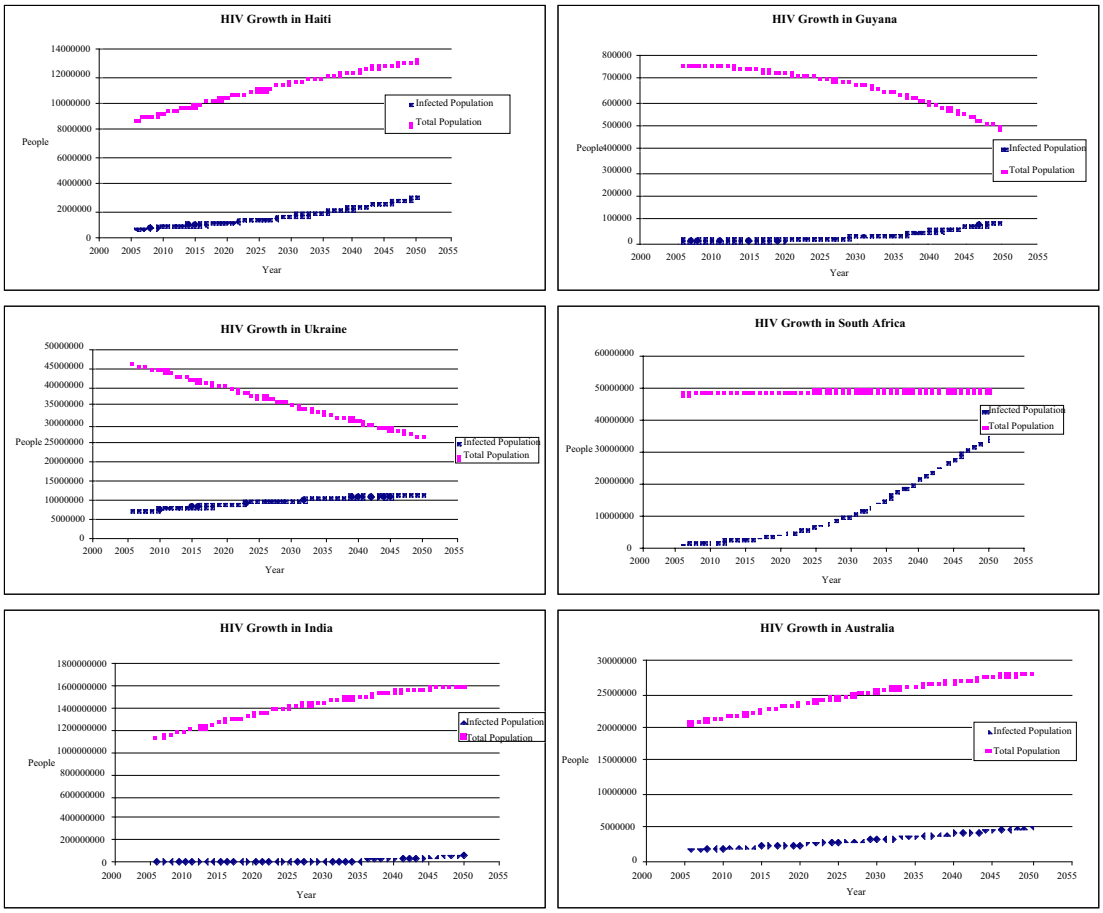

Figure 3. Total population and HIV population projections for the critical countries.

infected population growth rate and then calculate the number of cases based on this growth rate and the population. Therefore, as the infection growth rate increases and population decreases, the number of AIDS cases can either increase, decrease, or remain the same, depending entirely on the relationship between the growth rate and the rate of decrease of population.

Ukraine

presents a scenario similar to Guyana's. Were the population to remain stable, the number of infected people would rise much more quickly. This graphic model still presents an interesting issue: the infected population will eventually reach the total population in time.

South Africa

Based on the initial quick growth of HIV, the model predicts continued alarming increases in cases, barring intervention, to 69.3% of the population in 2050.

India

The large population creates a deceptively small prevalence rate. The graph makes it look as if the number of infected people is small and growing slowly, yet the numbers are large, increasing quickly, and perched to surpass South Africa by 2010.

Australia

HIV is seen to be growing steadily, yet more slowly than the population. This is a stark contrast to almost all of the other critical countries.

Task 2: Drug Therapy and Vaccination

Therapy refers to antiretroviral treatment(ART), which is currently prolonging the lives of many people living with HIV. ARV treatments lower the concentration of HIV in the bloodstream, allowing the body to fight the effects longer and making the disease more difficult to transmit to others. The decreasing transmission rate among infected individuals means that not as many people each year will contract HIV compared to the same scenario without ART. Introducing ARV treatment changes the state diagram to **Figure 4**.

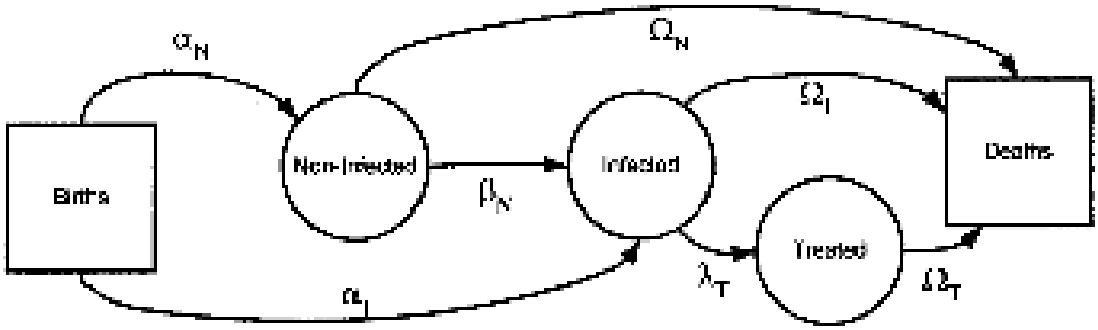

Figure 4. Treatment state diagram.

As treatments become available, infected people begin receiving them. Non-Infected people will not need treatment, which is why there is no transition from the Non-Infected state to the Treated state.

Although no vaccine exists yet, the state diagram in **Figure 5** depicts the changes in the model for a vaccine.

A vaccine would be administered only to the Non-Infected population or those being born. Since the vaccine is not an elixir of life, there will still be some death rate.

ARV treatments are available now, and should vaccines become available in the future, the two methods would be used together to attempt to eliminate AIDS. This creates still another model from which we can make predictions (**Figure 6**).

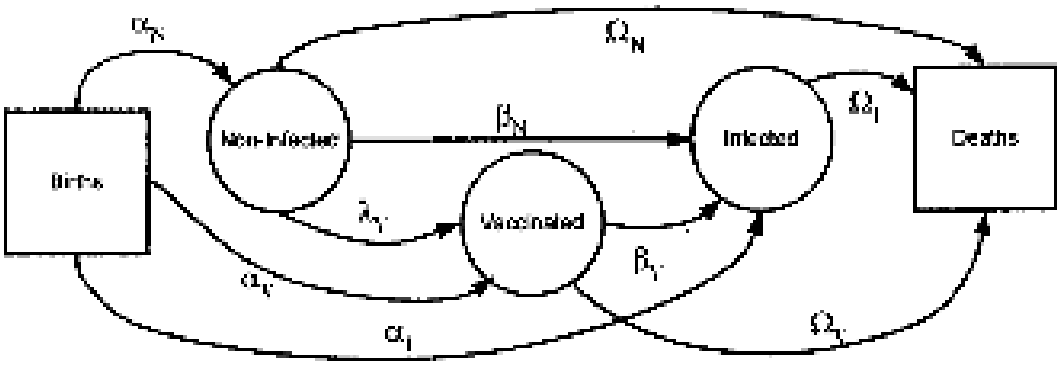

Figure 5. Vaccination state diagram.

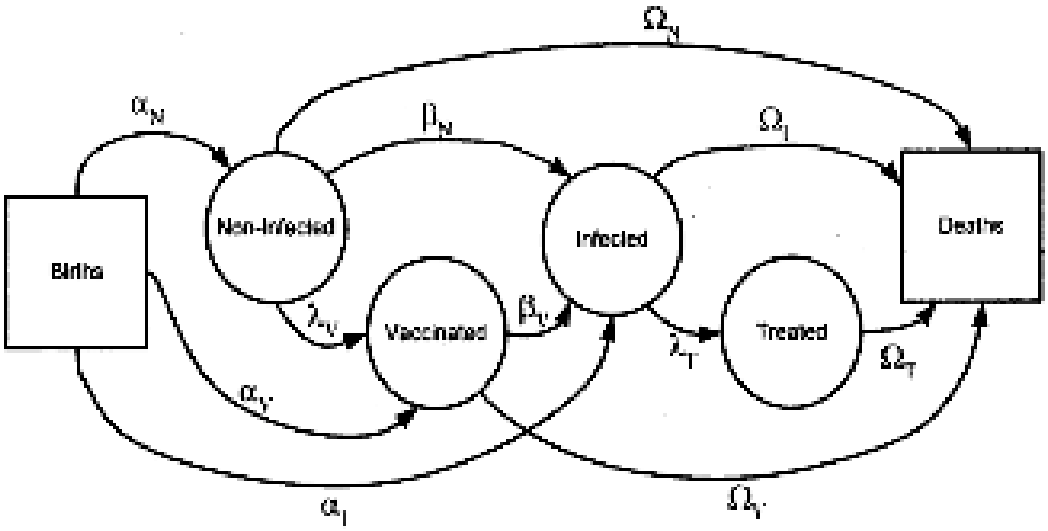

Figure 6. Vaccination and treatment state diagram.

Without strong data on ART and an actual vaccine, it is difficult to make a quantitative extrapolation of their effects. Qualitatively, however, the factors can be graphed and trends predicted. **Figure 7** shows a generic graph based on the differential equations developed at the end of the **Appendix**.

The graph suggests that ART and a vaccine will be fairly successful in battling AIDS but with some major drawbacks:

- ART is expensive and not widespread. It currently costs $800 per person per year to treat AIDS using the name-brand medications; this cost could drop as low as $300 with generic drugs [Andrews 2004].

- If price were the only obstacle, the problem would be clearer. However, ART also makes it much more likely that a patient will develop resistance to a drug, or that the virus will mutate. Both of these are extremely serious considerations that must be weighed against the effectiveness of the treatments themselves. We consider drug resistance in Task 3.

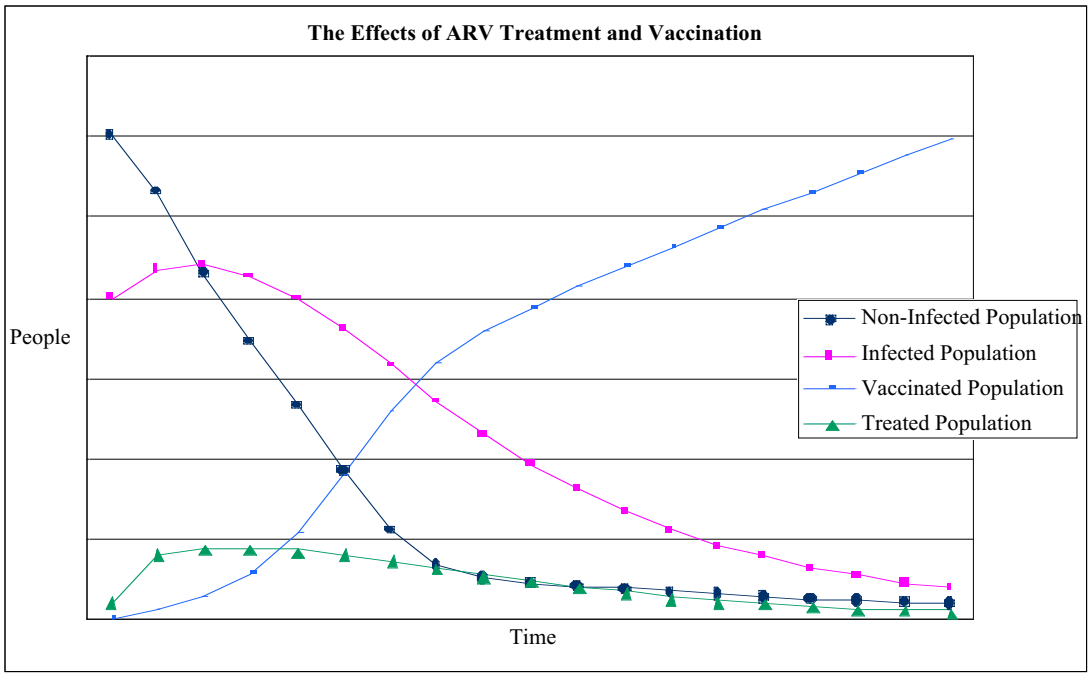

Figure 7. Effects of ARV treatment and vaccination.

- Cost and resistance also surface with a vaccine, as well as mutation that would render the vaccine useless. We discuss mutations in Task 3.

- Availability of financial resources has been a problem; a hopeful sign is that with the worldwide concern for AIDS growing quickly, the level of financial resources and relief is also on the rise.

Figure 8 shows a generic example of what can be expected to happen in South Africa with ART and prevention education. When compared with **Figure 2** (spread of AIDS left unchecked), the difference is immediately evident as well as inspiring.

Why, then, do people in the world still suffer from AIDS if it is so simple to make the line on the graph go down? Aside from the unavailability of a vaccine yet, the main factor is funding. South Africa, for instance, has a GNP per capita of only $3,020. While this is enough to purchase ART, an individual would have to make substantial sacrifices to do so. Additionally, wealth is concentrated in a small percentage of the population.

In deciding where to send aid and which areas represent the largest threat of infection expansion, GNP and a country's economic strength should be taken into consideration as major factors. Not all countries that are struggling against AIDS have even the mediocre GNP per capita of South Africa. Haiti, for example, is expecting a much sharper increase in the number of cases than Australia. Australia has a GNP per capita of $20,240, allowing individuals infected with HIV to afford ART. Haitians, with a per capita GNP of $510, cannot even afford a year worth of ART with an entire year's GNP. This is one major reason why

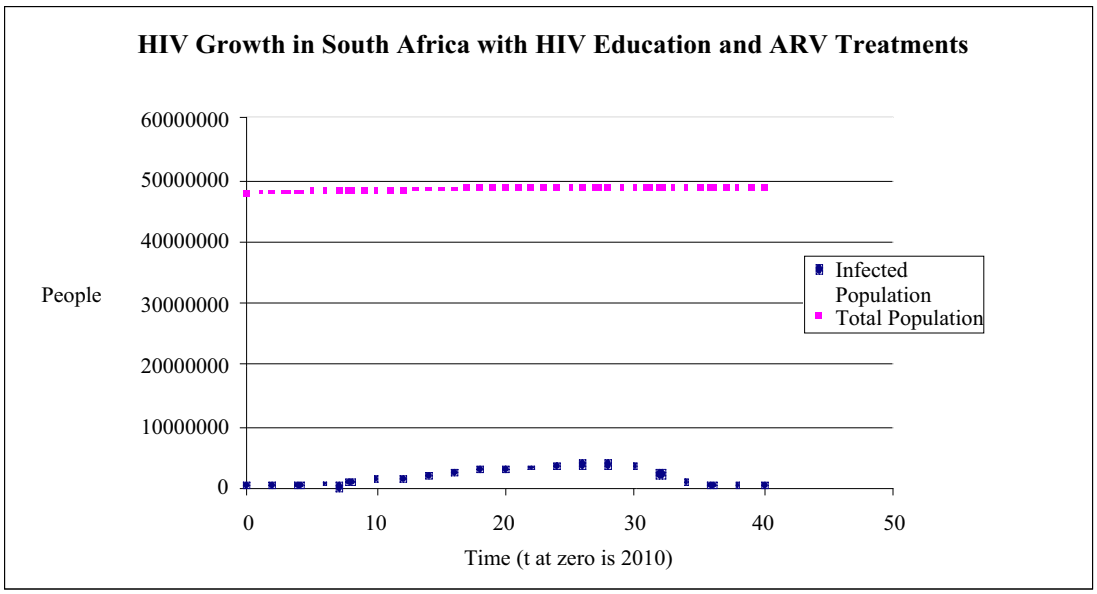

Figure 8. HIV growth with education and ARV treatments.

HIV prevalence is increasing so quickly in the Third World——the countries cannot stop it. This is why foreign aid is imperative and needs to be directed to the poorest countries.

Task 3: Drug-Resistant Strains

When treatments are weak or are not taken correctly, viruses can develop resistance to the treatments. Both β_T and β_V, the coefficients for transmission in the cases of treatment and of a virus would be changed by virus resistance. We can consider such a transmission rate as the reciprocal of the drug or vaccine's effectiveness. As resistance develops, effectiveness decreases; as effectiveness decreases, transmission (and the value of β) increases. In time, it is possible for this transmission rate to catch up with β_N, which would mean that vaccinating or treating people would make them more susceptible to the virus.

In addition to drug resistance, HIV could mutate as a result of treatment. Mutations could produce strains of the virus that are more active and destroy the body more quickly.

Conclusion: Recommendations

Sub-Saharan Africa is the decisive point for stopping the spread of AIDS. Of the expected $7 billion dollars to be spent on AIDS worldwide in 2006, we recommend that $4.5 billion be spent in sub-Saharan Africa on testing the population, educating the population about prevention, distributing preventive

measures, limited dispersal of treatment, and providing baby formula to nursing mothers infected with HIV. This would be a three-year program, spending the same proportion of money each year.

Following the three years of intensive effort in Africa, we would conduct an analysis of gains to determine success. If unsuccessful, the plan would be altered; if successful, focus would shift to India and Southeast Asia, though Africa would continue to receive money for education, prevention, treatment, and new mothers. In India, the distribution of resources would be similar to that in Africa, focusing initially on testing, education, prevention, limited treatment, and new mothers. This phase is expected to take longer in India than in sub-Saharan Africa, five years instead of three.

Southeast Asia and sub-Saharan Africa comprise the largest threat to world health due to AIDS. After they have been treated, our program will hopefully be able to enter a phase of vaccination, pending development. It is important to focus on testing, education, and prevention up to this point, using ARV treatments sparingly so as to avoid resistance and mutated strains. At this point, the plan will once again be assessed and adjusted to meet new threats.

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Appendix

We model the total population $P = N + V + I + T$ as composed of non-infected non-vaccinateds N, vaccinateds V, infected but untreateds I, and infected and treateds T, with corresponding subscripts for parameters. We let α

and Ω be rates of birth into and death out of each subpopulation; β_N, β_T, β_V be infection rates for non-infecteds, infected but treateds, and vaccinateds; and λ_V and λ_T be rates of vaccination of non-infecteds and treatment of infecteds. The resulting system of differential equations, corresponding to the state diagram of **Figure 6** and assumption that $\beta_V = 0$, is:

$$\begin{aligned}
\frac{dN}{dt} &= \alpha_P(N+V+I+T)\left(1-\frac{N+V+I+T}{K}\right) \\
&\qquad -(\alpha_I-\Omega_I)-(\alpha_V-\Omega_V)+\Omega_T-\beta_N NI-\beta_T NT-\lambda_V, \\
\frac{dV}{dt} &= \alpha_V+\lambda_V-\beta_V VI, \\
\frac{dI}{dt} &= \alpha_I+\beta_N NI+\beta_T NT-\lambda_T-\Omega_T, \\
\frac{dT}{dt} &= \lambda_T-\Omega_T.
\end{aligned}$$

Systems of equations for the state diagrams of the other figures are obtained by setting other appropriate parameter values to zero.

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Judges' Commentary: The Outstanding HIV/AIDS Papers

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Introduction

The final judging for the 2006 Interdisciplinary Contest in Modeling took place at the United States Military Academy on Saturday, February 25, 2006. The seven judges spent a full and enjoyable day reading and comparing a fine set of creative and enjoyable papers.

The Problem

This year's problem charged our teams with advising the United Nations on how best to allocate financial resources in the global fight against HIV/AIDS. Teams were provided a common set of historical and projected data in a variety of categories for various areas, regions, and countries around the world over time. This data included the global incidence of AIDS, the geographic distribution of HIV/AIDS subtypes, populations, fertility rates, age data, birth rates, and life expectancies. Teams were then charged with several related interdisciplinary tasks:

- Build a model to estimate the change in the number of HIV/AIDS cases in a variety of selected countries over time.

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- Estimate the level of financial resources realistically available from foreign donors. Estimate the expected rate of change in the number of HIV/AIDS cases in the selected countries under realistic assumptions if these resources were used to fund antiretroviral (ARV) drug therapy, if they were used to fund the development of a preventive HIV/AIDS vaccine, and if funding were split to fund both at a lower level of effort for each.
- Reformulate the above three models, but now taking into account the assumption that persons receiving ARV treatment (but at a less than 90% adherence rate) have a 5% chance of producing vaccine-drug-resistant strains.
- Write a white paper to the United Nations recommending how the projected available financial resources should be allocated between ARV treatments and a preventive vaccine, what level of emphasis to give HIV/AIDS relative to other foreign policy priorities, and recommendations for how to coordinate donor involvement for HIV/AIDS.

Analysis of Papers

The judges chose to organize their thoughts in the following areas as they studied student responses. We summarized what we saw and gave feedback on our perspectives along these same lines.

Executive Summary

Every team demonstrated that they knew that it was essential to provide a good executive summary, both in content and in clarity. Moderately successful efforts summarized what the requirements were and made statements like "In our analysis we project the decrease in HIV/AIDS cases if ARV treatments and/or preventive vaccines are developed." The more successful efforts recognized that this section should serve as a "bottom line up front" and actually summarized their most important conclusions here, making statements like "We find that the cost of ARV treatment is prohibitive in poorer countries and that wealthier countries have their own financial assets for the more costly ARV development, and therefore the UN effort should be exclusively toward development of a preventive vaccine that can then be distributed to all countries." *The most effective papers summarized the conclusions, not just the problem.*

Science

Many papers demonstrated knowledge of the science of HIV/AIDS with separate sections devoted to the biology of the disease, the mechanisms of transmission, the epidemiological spread, the efficacy of current ARV therapy and the potential value of a preventive vaccine. As an infectious disease, HIV/AIDS

is certainly one of the most problematic diseases in our current history due to its global spread, ease of transmission, its high mutation rate in terms of non-compliant ARV therapy, and its failure to induce preventive immunity in the many vaccine trials to date.

Add to this equation the widely differing global issues of governance, public health infrastructure, education, culture, and socioeconomics, and you have our current global state of infection with an estimated 40 million people living with HIV, according to the World Health Organization.

Although many papers addressed the basics of the HIV/AIDS epidemic, some papers certainly addressed this capacious issue better than others.

The least successful papers supported their science simply by dumping Internet data into this section of the paper, including more science than necessary to address the problem, not focusing on the correct areas of science for the problem, and/or failing to document their information—this type of paper was quickly eliminated from consideration for a high-level award.

The moderately successful papers clearly had the science section written by one member of the team and the subsequent modeling sections written by other teammates. Although each section was individually well-written, the sections were very self-contained and hardly connected with each other.

The most effective papers incorporated most if not all of the science background that was presented as a basis for their following models. For example, if the team talked about how ARV treatment prolonged the lifespan of the infected person but did nothing to prevent the transmission of the virus, then the model reiterated this fact when it assumed that the level of spending on ARV had no effect on the rate of spread of HIV/AIDS. The most effective papers presented the science that was essential to the model but very little science that was just gratuitous.

Modeling

The most effective papers made their assumptions explicit as they built or presented their model. They were explicit in tying assumptions to the science when appropriate. The two predominant types of models presented were differential (differential-equation based and/or difference-equation based) and stochastic (probabilistic, based on transition probabilities). Neither was favored over the other by the judges; we saw both mediocre and excellent examples of both types of models and made no value judgments based on the type of model used.

In both cases, the features that typified the mediocre models were:

- developing more model details than were required,
- refusing to make simplifying assumptions and instead attempting to capture details in the model that were too fine for the questions being asked,

- presenting reams of output without highlighting a few of the more pertinent numbers and explaining what they meant, and
- making no attempt to make an argument as to why the model output seems reasonable and why it is reasonable to proceed to use the model in analysis.

In some papers, the model selected seemed like an awkward fit for the scenario, such as an awkward selection of partitions in a differential equation model, giving the feeling that the model had been selected mostly because it was the one that had been "pre-positioned" before the competition or was first off the shelf rather than because it was the most appropriate model. As one judge reflected, some models appeared to be hammers looking for nails within the scenario.

The most effective models

- gave rationale for the hypotheses,
- made appropriate assumptions to make the model more tractable,
- showed just the output necessary for later analysis,
- explained what the output meant with a few specific cases, and
- made an argument why the model seemed to be working reasonably well and merited use in further analysis.

Teams demonstrated their ability to make appropriate model refinements in the third requirement, when the assumption of vaccine-drug-resistant strains was introduced; here, clarity in showing exactly what was being changed and in highlighting the change in output was most important.

In most contests, all of the models selected by teams tend to fall in a few fairly homogeneous groups, but occasionally a team adopts a truly novel technique of analysis. This year that occurred with a team that simulated the spread of HIV/AIDS with a cellular automata simulation. This team simulated the population with a representative group of 10,000 individuals with six characteristics (age, sex, level of connection in society, social status, health, and cliquishness). At each time step of the simulation, each cell is determined to change value (from not infected to infected) or not (remain uninfected or remain infected), depending on the values of the surrounding eight cells, according to a set of rules which are developed from the parameters of the problem. Statistics are gathered from many runs of the simulation and then applied to answer the questions at hand. Several of the judges found this to be an intriguing approach that would have required more set-up and tuning to get it running properly but that offers a unique level of customizability and analysis. While this report was not one of the Outstanding papers, it was definitely innovative and commendable interdisciplinary modeling.

Analysis/Reflection

The more effective papers took time to reflect on and discuss the ways in which their model appeared to be strong and the ways in which it appeared to be weak in addressing the problem. They also took time to demonstrate the sensitivity and robustness of their model, either by actually changing a few parameter values and demonstrating the change in output, or at least through a short discussion (such as "a 10% change in any coefficient in this system of linear ODEs is likely to only have a corresponding change in the output because the eigenvalues appearing in our solution are so far separated").

This problem asks a lot, and even a long weekend is not much time; even in the Outstanding papers, we found that the financial piece of the scenario received very thin treatment by way of analysis and reflection. That was disappointing for the judges, because it was intended to be a major part of the interdisciplinary modeling.

Implementation

Moderately successful papers often looked as if a member of the team wrote this section who had not been very involved in the modeling and analysis. Those recommendations for implementation relied more on insight and background research than they did on the results obtained from analyzing the model. Often the implementation recommendations made no distinctions between country, region, or class.

The most effective papers recommended "policy through analysis": The policies that they recommended were justified by the model analysis that they had just been completed. It was not always necessary to quote numbers, but these papers made reference to their analysis when they presented their recommendations. These papers also were the ones that often made recommendations on resources and policy based on country wealth or demographics. They were also explicit in the assumptions that led to their recommendations; e.g., whether they recommended that certain countries be given priority access to ARV therapy because they have the highest incidence of disease and the objective is to minimize suffering; or to give priority to vaccine therapy in different countries because the objective is to prevent HIV spread in other less-infected areas of the world.

Communication

All teams demonstrated that they understood that the clarity and style of writing were very important to an effective product. We were generally pleased with most papers; very few teams were not clear and effective in their prose, and therefore, many papers earned congratulatory comments by the judges.

The most effective papers ensured that all of the sections were connected to one another—not just by adding a few sentences, but by articulating the logical

connection between subsequent sections, in particular on Modeling, Analysis, and Recommendation, and those preceding. They also understood that well-selected graphics could be very effective in making a point, but that gratuitous graphics that were easy to make but which did not make an important point were distracting. Teams are reminded that proper documentation is always necessary to an effective paper. Judges saw some undocumented material for which they were sure they knew the source, and for which they felt it necessary to run checks.

As to length, short and succinct with adequate explanation is always preferred. Long, rambling papers were eliminated because of the frustration in reading too much detail or repetition.

Conclusion

The judges extend their thanks and congratulations to all of the teams. We truly enjoyed reading and studying your work and have come to have quite a bit of confidence in your abilities. We are interested and excited to see what problems you will attack as experienced interdisciplinary modelers when your studies are completed.

About the Authors

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Joe Myers has served for two decades in the Dept. of Mathematical Sciences at the United States Military Academy. He holds degrees in Applied Mathematics and other disciplines and is a licensed Professional Engineer. He currently serves as a Professor, having directed freshman calculus, sophomore multivariable calculus, the electives program, and the research program. He has been involved in several major initiatives to improve teaching and learning, including building interdisciplinary activities and programs under the NSF-sponsored Project Intermath; integrating technology and student laptop computers into the classroom; and weaving modeling, history, and writing threads into the mathematics curriculum. He enjoys modeling and problem solving, has posed and guided the research of dozens of math majors, and has been involved in several research projects with the Army Research Laboratory.

Author's Commentary: The Outstanding HIV/AIDS Papers

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Introduction

According to estimates by the World Bank, more than one billion individuals worldwide live on less than $1 per day. Internationally, countries have prioritized improving the lives of the world's poor through mechanisms such as the United Nations Millennium Development Goals—which seek, by 2015, to halve extreme poverty, halt the spread of HIV / AIDS, provide universal primary education, and achieve a number of other goals. Within the United States, President George W. Bush has supported "a new compact for global development" through institutions such as the recently-created Millennium Challenge Corporation.

Yet despite billions of dollars having been spent on attempts to improve the lives of the world's poor, we lack a consensus on how to allocate foreign aid most effectively. Such decisions inherently involve trade-offs: for any given level of financial resources, more funding devoted to building schools implies less funding devoted to programs aimed at reducing government corruption. In addition, foreign aid donors often must choose among diverse potential programs without any solid evidence on the relative effectiveness of such programs.

Such decisions are complex even within a more narrow focus. In funding health programs, for example, at the planning stage decisions must often be made based on unreliable data and assumptions that are difficult, if not impossible, to verify. For example, is the development of a malaria vaccine even scientifically feasible? What is the optimal pattern of introduction and use of second-line treatments for multi-drug resistant tuberculosis? Prospec-

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tively weighing the expected costs and benefits of alternative programs necessarily involves a complex set of assumptions, calculations, and estimations. Even once programs have been implemented, we often fail to conduct rigorous evaluations—thus resulting in missed opportunities to learn which programs are most effective.

The Contest Question

The main goal of this year's interdisciplinary modeling problem was to encourage teams to grapple with some of these issues within the relatively more narrow context of addressing HIV/AIDS. As the HIV/AIDS epidemic enters its 25th year, both the number of infections and the number of deaths due to the disease continue to rise. Despite enormous efforts on a number of fronts, we remain uncertain on how best to allocate resources to fight this epidemic.

In this year's problem, teams were asked to advise the United Nations on how to manage the resources available for addressing HIV/AIDS. Their job was to model several scenarios of interest and to then use their models to recommend the optimal allocation of financial resources.

We first asked teams to consider what trends could be expected in HIV/AIDS morbidity and mortality in the absence of any additional interventions. This is a complex problem that encouraged teams to analyze a variety of historical demographic and health data on fertility, population, age distribution, life expectancy, and disease burden.

In practice, HIV/AIDS funding could be focused on a wide range of interventions. Prevention-focused interventions include voluntary counseling and testing programs, school-based AIDS education, and distributing medicines to prevent mother-to-child transmission of the virus. Care interventions can include treating the virus as well as treating other opportunistic infections. For this work, we asked teams to focus on modeling only two potential interventions: provision of antiretroviral (ARV) drug treatments, and provision of a hypothetical HIV/AIDS preventive vaccine.

Evaluating the potential impacts of these two interventions required the teams to decide on realistic assumptions in order to generate estimates of the costs and benefits of each intervention. What year might a preventive HIV/AIDS vaccine become available? Should children or adults be targeted for vaccination, and what vaccine coverage rates could be expected for either group? What delivery costs should be assumed for the drug therapy and vaccine? Would there be epidemiological externalities from vaccination that should be taken into account? The teams were also asked to re-analyze their scenarios in light of the potential emergence of drug-resistant strains of HIV/AIDS.

A major focus of this year's problem was for teams to analyze these issues in the context of realistic political and economic constraints. For example, teams

were encouraged to base their models on the level of foreign aid resources that they realistically expected to be available. The teams were also asked to interpret the results of their models in light of such political and economic constraints—in part through drafting a white paper to the United Nations which provided their team's recommendations on the optimal allocation of resources as well as their recommendations for how best to coordinate donor involvement for HIV / AIDS.

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About the Author

Heidi Williams received her A.B. in mathematics from Dartmouth College, where her studies and research were focused on number theory and cryptography. She also received an M.Sc. in development economics from the University of Oxford, supported by a Rhodes scholarship. Heidi is currently a Ph.D. student in economics at Harvard University, where her research is focused in development, health, and public economics.

For the past several years, Heidi has worked with the Center for Global Development (a nonprofit think tank in Washington, DC) and in collaboration with Harvard economist Professor Michael Kremer and other academics to contribute to public policy efforts aimed at speeding the development of (and increasing access to) vaccines for diseases (such as malaria) that are concentrated in low-income countries. For more information, see `www.cgdev.org/vaccine` .