According to the UNAIDS 2006 Report on the Global AIDS Epidemic, almost $8.9 billion has been allocated to finance the global response to AIDS. This funding falls short of the needed $14.9 billion for this year alone. Maximizing the limited funding is one of the many challenges that developing countries, which share the greatest burden of the 38.6 million people living with HIV/AIDS in the world, must face.

Health economics researchers, policy makers, and major international donors gathered together to examine these and other issues at the “HIV/AIDS Interventions in Developing Countries: Using Cost Benefit and Cost Effectiveness Analysis to Guide Policy and Action” conference, which was held from September 13-15 in Boston. Participants discussed and debated the intricate economic, social, and programmatic concerns that impact comprehensive HIV/AIDS care, particularly in the context of limited health systems and operational capacities. These concerns continue to gain worldwide attention because governments and donors require efficient fiscal accountability for program implementation and scale-up procedures. A way to measure economical expenditures is by using cost effectiveness analysis (CEA) and cost benefit analysis (CBA).

CEA and CBA are methods health economists use to identify where the most absorptive capacity exists in healthcare, community, public, and private settings. These methods also provide evidence based suggestions for what steps should be taken to efficiently scale-up capacity in particular regions. CEA uses models that can capture the processes and decisions associated with prevention and treatment, especially when clinical data is unavailable, and translates them into associated costs and consequences. These data can be used as planning and assessment tools which can provide national governments and financial partners with critical information on how to maximize health benefits through a mix of prevention and treatment program components.

The conference focused on key policy issues and programmatic constraints that were addressed in five topic areas: identifying cost savings and synergies of HIV prevention and treatment, using economic evaluation to guide policy and action, exploring the linkages between macroeconomic to microeconomic impacts, examining the impact of businesses on the AIDS crisis, and investigating the transportability of costing techniques to ensure the ability to generalize results.

Conference participants framed their research positions by citing findings and examples from costing and cost effectiveness studies conducted in India, Thailand, South Africa, Nigeria, Mexico, and Botswana. Recommendations on how economics can inform practical program implementation decisions and general policy questions on all levels were also raised.

The conference program included open discussion sessions in which issues that might impede progress and affect long-term planning processes were discussed. A panel of representatives from local and international governments and policy agencies fielded these concerns and offered opinions on useful strategies in working within these constraints. Representatives included Joy Phumaphi of the World Health Organization, Loeto Mazhani of the Botswana Ministry of Health, Robert Oelrichs of the World Bank, Dan Kress of the Bill & Melinda Gates Foundation, Joseph O'Neill of Immune Response Corporation, Peter Piot of the Joint United Nations Programme on HIV/AIDS, Jim Kim of the Harvard School of Public Health, Diane Thompson of the Elizabeth Glaser Pediatric AIDS Foundation, and Yves Souteyrand of the World Health Organization.

Joy Phumaphi, assistant director - general of the Family and Community Health division at the World Health Organization, offered suggestions to researchers on what tools they can provide to public policy makers. Phumaphi said, “The key areas where we need a lot of direction are linking different models of assessment and evaluation of programs in the critical areas that impact HIV/AIDS and development. So that the models we are currently developing for human resources, planning, analyzing strategic information, cost benefit models for assessing whether to invest in a program or scale it up and how to strengthen it – how you link all these together in order to enable a decision maker (continued on back page)
Richard Smith and Dr. Max Essex

On a warm April evening, HSPH Leadership Council member Irene Weigel and HAI International Advisory Council member Susan Carren, hosted an intimate discussion group. The conversation topic, The Continuing AIDS Crisis--Does the Answer Lie in Africa?, was led by HAI International Advisory Council member, Chairman, Editor-in-Chief, and Chief Executive Officer of Newsweek, Richard Smith and HAI’s Dr. Max Essex. The following is an excerpt of the dialogue that took place.

RS: Max to start with, as far as HIV/AIDS is concerned in the developed world, this is no longer the kind of automatic death sentence that it has been for so many years. And yet in the developing world the disease rages on. What is happening right in the developed world, and why is the problem still an enormous one in the developing world?

ME: I think a good breakthrough in the West was the recognition of three-drug combinations. These expensive drugs could readily save people and there was a lot of dedication to using them. Major efforts were made to educate people for getting tested and to find out whether or not their status was positive and help those people who needed drugs.

In the case for the developing world, those very expensive drugs still aren’t widely available, nor are the tests required to decide how best to treat these patients available. They are available in selective ways and in a few places, Botswana being one of the most advanced. But there is still a lack of education about how to use them in most countries for both the patient and clinician. The situation, though, is getting better because now many countries in Africa with good governmental systems have begun to address the epidemic.

RS: Is there something about the virus, the science of HIV/AIDS, that leads to the high-risk in Africa? What makes Africa ground zero?

ME: The viruses in Africa that cause HIV are wholly different from the viruses in the US and Europe. The main virus that is causing HIV in the US and Western Europe is called subtype B and although subtype B is present in Africa in very low numbers, it is one of the least virulent on the continent.

The virus in southern Africa, which is HIV 1-C, is undoubtedly more virulent than other forms of the virus because the transmissibility rates of the other viruses in East Africa or West Africa are not as high. The medical dictionary defines virulence as transmissibility and how quickly it kills. Although there is no evidence that the virus in southern Africa kills faster, there is evidence that it is transmitted more efficiently.

RS: Let’s talk about the mother-child transmission issue. To me, it is one of the bright spots in the work that is going on.

ME: There has been a lot of progress. Clearly by using just one relatively inexpensive drug, zidovudine, you can reduce transmissions from mother to infant by two-thirds, if the drug is administered four-to-six weeks before delivery. The mother-to-infant transmission rate can be further reduced if another class of drugs are used at the time of delivery, but the problem of drug resistance then arises. The same drugs that help pregnant HIV-positive mothers prevent transmission may be needed later to treat their own disease, and their prior use greatly increases the chance that they won’t be effective for treatment due to drug resistance.

In places like Botswana 35% of pregnant women are HIV-positive and 30-40% of infants born to those women become infected if drugs are not used to prevent transmission. That means one out of every six or eight children born in Botswana or Swaziland will be infected if nothing is done, so it is really important to treat them, but by the same note we have got to develop new systems to keep the mothers alive so the infants do not all become orphans.

RS: I well remember a [Newsweek] cover that we did about five or six years ago on AIDS in Africa, and the line on the cover was 10 million orphans. I feel that number is a low number now. Talk about the scale that we’re looking at here in the AIDS epidemic.

ME: That certainly is a low number now. There are about 40 million people living with HIV/AIDS and two-thirds of these people live in sub-Saharan Africa. There is a movement to treat a lot more people living with the virus. About a million people have now been treated with antiretroviral drugs in Africa. That’s a start and I think it will be 2 or 3 million in another year and 4 or 5 million and 6 million in a few years but we will need to cope with the inevitable newly emerging drug resistance problem. I
International Clinical Research Training

The Fogarty / Ellison Overseas Fellowship in Global Health and Clinical Research is in its fourth year, accepting applications from highly qualified graduate-level students in health fields across the U.S.

Each year, the Fellowship, supported by the Fogarty International Center and the Ellison Medical Foundation, along with the National Institute of Allergy and Infectious Diseases and the National Institute on Drug Abuse, provides 25 to 30 future health care professionals with the opportunity to develop clinical research skills in the unique setting of a developing nation. Fellows have the opportunity to train in National Institutes of Health-funded research institutions in Africa, Asia, and the Americas. Site countries include Bangladesh, Botswana, Brazil, China, Haiti, India, Kenya, Mali, Peru, South Africa, Russia, Tanzania, Thailand, Uganda, and Zambia. The Fellowship’s organizers hope that this one-year opportunity will strengthen students’ commitment to a future career in global health.

With a highly valued mentoring component, the Fellowship ensures that each participant is matched with both a researcher at the foreign site and a faculty member from the US institution, in this case HAI. Furthermore, each U.S. fellow is matched with a peer fellow from the foreign institution.

In Botswana, Fogarty/Ellison fellows work at the Princess Marina Hospital, mentored by members of the Botswana–Harvard School of Public Health AIDS Initiative Partnership for HIV Research and Education (BHP) and are matched with peers training in the Botswana health system.

For three years, fellows working with the BHP have been interacting directly with a population living with the HIV/AIDS epidemic and learning crucial research techniques firsthand in order to further clinical knowledge about the disease. This year’s fellow, Carl Davis, a Harvard College, Class of 2000 summa cum laude graduate and now a candidate for MD, PhD, from University of Pennsylvania School of Medicine, and David Nkwe his matching Botswana fellow, will both work on the acute HIV infection study. The deadline for submitting an application is December 8, 2006. More information can be found at http://aids.harvard.edu.

NEWS & EVENTS

Enhancing AIDS Care and Treatment
The Enhancing Care Initiative of the Western Region of Puerto Rico published an article in the June edition of the American Journal of Public Health. The team presented the results of their Needs Assessment which examined the HIV/AIDS services in the region.

Two main findings of the assessment were that depression symptoms were present in 98.1% of people living with HIV/AIDS, and that 7 of 15 municipalities in the region did not provide any specific services to this population. Furthermore, the most urgent needs identified by people living with HIV/AIDS were economic support, housing, mental and psychological services, medicines, medical treatment, and transportation. As a result, the Enhancing Care Initiative has planned two major interventions to address services coordination and mental health.

Breast Versus Formula Feeding: Overall Outcomes Similar
In the August 16th issue of the Journal of the American Medical Association, the Mashi Study revealed that infants who received zidovudine while breastfeeding from HIV-infected women had higher rates of HIV infection but lower rates of death and illness. However, formula feeding to prevent postnatal HIV transmission was associated with higher rates of mortality, with severe pneumonia and diarrhea, especially in HIV-infected children (although lower rates of HIV transmission to infants). Overall, very similar proportions of breastfed and formula-fed infants remained alive and HIV-negative.

Although additional research is needed to try and find effective ways of preventing HIV transmission through breastfeeding, these findings should cause HIV-infected mothers in developing countries to exercise extreme caution in using formula feeding.

Breastfeeding from HIV positive mothers still appears to provide important antibody protection for the infant against common bacteria and viruses. The World Health Organization will be considering these and other findings in a potential revision of their infant feeding guidelines for HIV-infected women. The current guidelines recommend that HIV-infected women for whom formula feeding is feasible, acceptable, and safe should exclusively formula feed their children to prevent transmission of HIV.

New HIV Vaccine Partnership
Founded in March 2005 by HSPH colleague Dr. Yichen Lu, the Haikou VTI Biology Institute’s mission is to advance the field of vaccinology through vaccine research and development, the production of vectors and cells for use in human gene therapy clinical trials, and the production of diagnostic kits. Institute scientists, based in the west coast of the Haikou City of Hainan Island in China, are working on new flu vaccines and new treatments for malaria. The Institute’s expertise in vaccine development coupled with existing HIV-1 subtype C vaccine development efforts at the Botswana–Harvard Partnership will further a joint HIV vaccine development program for southern Africa.

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to use all the information and apply it correctly to make a decision – I think this is the area where there is a gap. Also, we are talking about scaling up and moving to universal access, but the big question is the rate at which you can scale up given the resources that are available. And what levels of investment would be required to attain certain rates of scale up of programs. This is absolutely critical now. Otherwise the rate of scale up is determined by when the next election is going to be.”

Panel members suggested that research questions should be framed in locally appropriate context with methods that can be employed to ensure the transportability of results. Accessible language and common terminology for both researchers and policy makers should be used and sustained during the research investigation process. A clear explanation of how funding would be used is essential in emphasizing the cost effectiveness of an initiative.

Researchers and panel members strongly agreed that both parties should work together hand in hand throughout the research and program planning process. This would be one of the most effective ways to advance AIDS policy and action. The participants will expand upon the discussions and recommendations through the publication of a journal supplement, due next year.


To learn more about the program, please visit http://www.aids.harvard.edu.
think this is a serious problem that is going to be present in Africa for a long, long time unless we find a better solution than just drug treatment such as a successful vaccine or other biological means of prevention.

**RS:** You and your colleagues across the board have been working 15 years, why haven’t we seen one by now?

**ME:** HIV is a very special pathogen and one of the reasons why it develops drug resistance so quickly is the same reason that it is very difficult to make a vaccine. This virus mutates faster than any other virus. It has qualities that make it more difficult to cope with than other viruses, even Avian flu. This tremendous rate of genomic variation or virus evolution is what causes the problem for developing a vaccine.

The stage that vaccine research is at now is in modeling the three-dimensional structure of the unfolded surface of the virus at the time it attaches to two cell receptors with a hope that stabilizing the unfolded structure would allow you to induce immune responses to block attachment. This is the stage that develops solid infection. But this is a whole new generation of making vaccines, obviously anything we did with any of the other infectious diseases didn’t come close to that level of sophistication.

I really believe that we will have a vaccine in 10 or 20 years. Twenty years is a long time and we have to figure out what to do until then, but when we do I think we’ll also have built a solution, through the results of how to make vaccines, to a lot of different diseases, like herpes and some cancers. One can view HIV research as building and informing the general field of vaccinology.

**RS:** The HAI approach involves real collaboration with the Botswana government, not only in terms of informing them, but in training their researchers and bringing them into your program.

**ME:** Yes, we’ve been fortunate to have the support to train people from Botswana. We’ve also been fortunate to have bright, young physicians and scientists from the U.S. with training in infectious diseases who want to go to places like Botswana and spend a year or two participating in and running these trials. That has worked to everyone’s advantage.

In the spring of 2007, we’re going to start a program for Harvard undergraduates who will spend a semester in Botswana for academic credit. They’ll spend time in our lab here in Boston, then spend a semester on a research project in Botswana and also take a course or two in African history or languages at the university there.

**RS:** One of the things that really impressed me about HAI is that the research is tied to treatment on the ground. Obviously for all the sophistication that allows you to do the research and all of that there is an enormous human need in much less sophisticated places. Talk about how you help on the treatment side as well.

**ME:** Well, I should speak about Dr. Richard Marlink, who is a senior member of the BHP team. He developed a Botswana-based HIV/AIDS program to train physicians and nurses in AIDS treatment and care. More than 900 physicians and 4,000 nurses have completed various courses on how to use AIDS medications. These health practitioners can now write prescriptions for government supplied anti-retroviral AIDS drugs. And I think that sort of teaching makes a significant difference because it helps reach more people living with HIV/AIDS who need their medications.

**RS:** Botswana is the epicenter of the HIV/AIDS crisis on the continent and the home of your research center. What elements of the Botswana model are you trying to push out to the rest of Africa and to Asia, India, China, with their growing problem? What will you do to encourage that movement to other countries?

**ME:** We are making available to many countries all the educational material used to train physicians and nurses. That’s a start. We are doing similar trials in several other countries in other regions in Africa. We’re exchanging AIDS experts with other countries in Africa. For example, we have an exchange program where people from Tanzania can go to the Botswana lab to learn techniques and then return to their country with that new training.

Recently we were asked by the Southern African Development Community, an organization of 14 countries in southern Africa, to put on a week-long HIV/AIDS training course for parliamentarians, who ultimately decide on how to allocate resources for their national HIV/AIDS programs. This will be a tremendous opportunity to give the educational tools to leading government officials who can directly affect the health of their people.

**RS:** A lot of grant money is devoted to laboratory research, and less to training programs and the kind of research examining treatment programs that set HAI apart from everything else. What do you need to get more of the kind of work you’re doing done?

**ME:** It’s hard to find money to train AIDS experts from most countries in Africa. We managed to put together a program with people from Botswana, but we don’t have money specifically to train people from Zambia or Malawi, for example. And there are a lot of people in those countries who’ll need training if they are to make the kind of progress Botswana is making.

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The Initiative’s efforts depend upon your support. Contributions are tax deductible.

To make your contribution to HAI online, please visit the Harvard School of Public Health giving page at http://www.hsph.harvard.edu/give/.

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Michael Voligny
(617) 384-8980
e-mail: mvoligny@hsph.harvard.edu
**Micronutrient Therapy**

The Dikotlana Study aims to investigate the effect of micronutrient supplementation on the clinical progression of HIV to AIDS. Study participants are followed for 24 months and are randomized into four groups: combination of multivitamins with selenium, multivitamins alone, selenium alone, and placebo.

The team discovered some striking initial information about the trial. Researchers found that selenium supplementation has a strong potential to decrease genital HIV-1 shedding. Additional study in this area could lead to new ways to delay the progression of HIV to AIDS, thus improving quality of life and decreasing the financial burden of ARV treatment. This discovery was detailed in one of the four abstracts from this study accepted by the 2006 International AIDS Conference in Toronto for poster and oral presentations.

The program is managed by the Florida International University in cooperation with BHP and the Botswana Ministry of Health and is funded by the National Institute on Drug Abuse.

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**Potential Drug Resistance to HIV-1 Subtype C**

Scientists at the McGill AIDS Centre in Canada and the BHP have detected a potential complication with an AIDS drug considered for the prevention and treatment of HIV infections in southern Africa. Tenofovir is considered to have great potential for use in microbicides, as well as in the use of multiple drug regimens to treat AIDS patients. As a microbicide, tenofovir would be given to uninfected women to prevent the acquisition and establishment of HIV if the woman has sexual contact with an HIV-infected man.

In studies conducted in human blood cell cultures, drug resistance to tenofovir developed in just 12 weeks if the infecting virus was HIV-1 subtype C, the prevailing subtype of Botswana. If other viruses were infecting the cultures, such as HIV-1 subtype B, the virus commonly found in the US, resistance took a year or more to develop. The resistance with tenofovir is caused by a particular mutation, K65R, that develops faster in subtype C. However, this resistance mutation, when it develops, also gives resistance to several other drugs, such as didanosine (also known as DDI), lamivudine (3TC), and stavudine (D4T).

This study indicates the need to further monitor and research the development of drug resistance within HIV subtypes as well as prepare to adjust antiretroviral treatment regimens in developing countries. This is particularly important because different subtypes, such as HIV-1 subtype C, the virus of southern Africa, may have different patterns of drug resistance.

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**HIV Infection in Northern Tanzania**

Colleagues from HSPH, HAI, Kilimanjaro Christian Medical Centre, International Partnership for Microbicides and other institutions have been conducting epidemiological studies to determine the rate of expansion of the HIV epidemic in the general population and among high-risk groups, and examine the social and biological determinants of HIV infection. The studies will contribute valuable data which could be used in the development of effective HIV intervention programs and in the design of clinical trials to test promising interventions.

In a study on female bar and hotel workers in Moshi, a small bustling town located on the slopes of Mount Kilimanjaro, researchers found the rate of acquisition of HIV was very high in this population, and condom use remained low. Another finding from this research was that women who had sexual transmitted infections (STIs), had a higher risk of becoming HIV-infected than women who did not have a STI. The risk became even greater in women who had genital herpes, a common STI that causes frequent recurrent infections and genital ulcers, which appear to enhance HIV transmission. The researchers concluded that STIs and genital infections facilitated the HIV epidemic in this cohort of high-risk women.

The incidence of HIV could be reduced through the treatment of genital infections and increased consistent use of condoms.

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**Improving Access to ART in Nigeria**

When people living with HIV/AIDS (PLWHA) understand how their HIV drug treatments help manage their HIV, they are more likely to maintain their drug regimens. This is a major finding by researchers of AIDS Alliance in Nigeria, AIDS Prevention Initiative in Nigeria, and Harvard President’s Emergency Plan for AIDS Relief. This is also a significant step towards helping the growing number of 70,000 Nigerian PLWHA now receiving antiretroviral therapy.

Basic counseling training for PLWHA to help other PLWHA has become one of the most effective methods in reaching those within their community and also others who may seek treatment. Researchers further found that this form of patient education provides a greater sense of responsibility and commitment on the part of PLWHA to maintain their own health. These efforts ultimately support greater treatment adherence and fewer opportunities for drug resistance.

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