



Spotlight

Determining demand

Many organizations are teaming up to assess the global demand for a future AIDS vaccine

There is a tremendous need for vaccines that can effectively prevent diseases throughout the world. But for a variety of reasons, including inadequate healthcare systems, national immunization policies, or the inability to pay for the new vaccines, some governments may not readily adopt them for use in their countries. "We recognize that developing countries have to make hard choices," says John Wecker of the US-based non-profit organization Program for Appropriate Technology in Health (PATH), who is currently working with several countries to plan for introduction of rotavirus vaccines.

This often results in a long delay, historically around 10-20 years, between vaccine introduction in wealthy and developing countries. This isn't because there is less of a need; in fact in developing countries the disease burden is often higher. But the public health need for a vaccine is not the same as the demand, which is a more complex concept that takes into account all the variables that influence a government's decision to purchase and use a new drug or vaccine. These factors include the characteristics of the vaccine, its price, and the infrastructure or policy required to provide the product. Before any commercial product comes to market, manufacturers give considerable thought to how much of it will sell, attempting to strike a delicate balance

between making enough of the product and ending up with a surplus. This can be a tricky calculation for any item, but is particularly complex when the product is a potentially life-saving drug or vaccine.

Trying to predict the demand for a vaccine may seem to be like gazing into a crystal ball, but the pharmaceutical industry has vast experience in forecasting demand, and potential profits, based on formulas and modeling systems for wealthy countries. But the process in developing countries is much less clear. Many times companies overlook these markets because of a lack of data or because of the perception that they won't be profitable.

To fill this gap, public private partnerships (PPPs) and non-governmental organizations (NGOs) have recently stepped in to assess the demand for vaccines and therapeutics in developing countries as part of wider efforts to increase industry involvement in treating or preventing diseases that are prevalent there. These organizations are working to develop models that can accurately assess demand for both available products as well as those in earlier stages of development, like AIDS vaccines, with the goal of maximizing global access to these products in the future. "It's unfair to put the total burden of this on the manufacturer," says Wecker. "The global community needs to step up to make things happen in parallel."

To create these demand forecasts or assessments, PPPs and NGOs are seeking the advice of economists, industry experts, and consulting groups. IAVI, the Global Alliance for Vaccines and Immunization (GAVI), and PATH are

some of the groups currently conducting or developing plans to do assessments for different vaccines or therapeutics.

Getting it right

The accuracy of any demand prediction depends largely on whether a product already exists, is just being introduced, or is still in development. Determining demand for products that are currently available is more straightforward, since it can be based on concrete information. These are referred to as demand forecasts. But for products that are still in the research and development phase, researchers have to imagine probable scenarios in order to predict potential demand. This type of planning is less definite and is often referred to as a demand assessment.

"Frankly we don't think we can pinpoint scenarios for a product that will be launched years from now," says Wendy Woods of the Boston Consulting Group, which is working with IAVI to develop an AIDS vaccine demand assessment.

Current AIDS vaccine candidates fall into this category, since they are now mostly in the early stages of clinical trials, and many uncertainties still exist around the level of efficacy, number of doses, price, and delivery cost. These unknowns

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make the process of conducting demand assessments much more difficult.

While the starting point for any assessment is epidemiological information, or more specifically the prevalence and incidence figures for the disease in a country or region, there are also many other factors to consider for AIDS vaccines. The demand must take into account the target population—which could be a certain age group or vulnerable populations such as intravenous drug users (IDUs) or commercial sex workers—and the likelihood that each group will use the product based on the uncertainties around its efficacy and price.

Three global demand assessments have been conducted so far for preventive AIDS vaccines, each with differing assumptions about the properties of the vaccine and its uptake. The latest, which was conducted by the World Health Organization (WHO), the Joint United Nations Programme on HIV/AIDS (UNAIDS), and IAVI, was accomplished by staging workshops that brought together groups of stakeholders from various regions around the world. The stakeholders were asked, given a set of hypothetical vaccine characteristics, how widely they would adopt such a vaccine.

The final determination was that while the need was potentially 700 million doses, the demand would be significantly lower. They estimated that uptake of a vaccine would be only 20% for a low- to moderate-efficacy vaccine and 40% for a highly effective vaccine. “A vaccine with low- to medium-efficacy will be acceptable in countries with high incidence and prevalence, and will be used to target specific populations,” says Saladin Osmanov, coordinator of the joint WHO-UNAIDS HIV Vaccine Initiative.

In countries where the epidemic is concentrated mainly within at-risk groups, like men who have sex with men and IDUs, a vaccine would probably be deployed within these populations first. This means that many decisions regarding introduction will vary depending on the characteristics of the epidemic. “To ensure that the vaccine has most effect,” says Osmanov, “each country will have to develop its own vaccine strategy.”

A pliable model

IAVI is now taking a more in-depth look at demand assessments and, in

consultation with Boston Consulting Group, is developing a flexible and dynamic framework that can be continually updated. “As the state of AIDS vaccine research progresses, data input quality will improve and, correspondingly, our understanding of the determinants of demand will evolve,” says Gian Gandhi, manager of policy research and analysis at IAVI. “It is not a one-off answer or number that we want to generate but an ongoing process of scenario building and refinement.”

The new effort will place a greater emphasis on how stakeholder preferences change in relation to the factors that influence demand than did the WHO-UNAIDS-IAVI effort, which focused

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John Wecker

mainly on country needs. To better understand patterns of vaccine adoption across countries, IAVI will look at previous rollouts of vaccines such as for hepatitis B virus. The recently approved human papillomavirus (HPV) vaccine may also offer lessons on rolling out a vaccine targeted at adolescents and adults (see February 2006 *Spotlight* article, *Cervical cancer vaccines*).

Another way to estimate the potential adoption of an AIDS vaccine might be the levels of coverage that have been achieved by countries involved in the WHO's 3 x 5 initiative that has increased access to antiretrovirals. IAVI will also look at how well individual countries are able to deliver existing AIDS programs and whether any countries are conducting AIDS-related clinical trials, since adoption is often quickest in regions where trials have been conducted.

By identifying the factors that influence introduction in each country IAVI hopes to learn which of these can be influenced to facilitate more rapid adoption. “We are using our best guesses for what a future vaccine will look like to predict how the world might respond to its availability,” says Gandhi.

Possible outcomes

Creating a credible and realistic demand estimate can have many benefits. It may help companies determine the future market for their product and could even spur the manufacturers to enter new markets in developing countries that they may have previously ignored. “One of the things that pharmaceutical companies cite as a reason for their reluctance to serve the developing country markets is the risk associated with poor demand forecasts,” says Ruth Levine, director of programs and a senior fellow at the Center for Global Development, an organization that is in the process of organizing workshops on demand assessments.

Another benefit of studying demand is the actual process of bringing together all of the constituents that are involved in the development and eventual introduction of a new vaccine, including national health officials, outreach organizations that understand the challenges of delivery, donor organizations, and developers or producers that research, develop, and/or manufacture the products.

The process of assessing demand can get these stakeholders involved and interested early in the process and, if the assessments are done correctly, they can be important tools that allow country leaders and policymakers to evaluate required infrastructure investments, decide how to allocate funds for procurement, and look for ways to potentially offset the costs of treating a disease through preventive efforts. Donors can also use assessments to map out multi-year finance strategies and ensure that funds are used appropriately. And outreach organizations can begin educating the community so that individuals are willing to be vaccinated when the product is eventually introduced. All of these steps are critical to creating the platform for vaccine acceptance and use in developing countries.

Global News

United Nations convenes annual meeting on AIDS to adopt an updated political declaration

Just days before researchers and activists around the world marked the 25th year of battling the HIV epidemic, the United Nations General Assembly Special Session (UNGASS) on HIV/AIDS convened in New York City to revise the "declaration of commitment" on AIDS, which was created at the first meeting of this kind held five years ago. This high-level event, which took place from May 31 to June 2, was attended by more than 10 heads of state and leaders from more than 140 UN member states, as well as over 1000 representatives from activist groups and other civil society organizations.

Although few of the goals laid out in the 2001 declaration adopted by the General Assembly were achieved, the total expenditure on AIDS in developing countries, which reached \$8.3 billion last year, did fall within the target range set in the initial document. This money has in part provided treatment for the 1.3 million people now receiving anti-retrovirals (ARVs), up from just 240,000 in 2001, and helped to quadruple the number of people accessing voluntary HIV counseling and testing services.

But now the Joint United Nations Programme on HIV/AIDS (UNAIDS) estimates that \$20-23 billion will be needed each year until 2010 to control the spread of AIDS and provide ARV treatment, care, and prevention services. The record number of civil society groups involved in the meeting pushed for the assembly to endorse a new target of providing ARVs to 80% of HIV-infected individuals in need and to an equal number of HIV-infected pregnant women to prevent them from transmitting the virus to their infants. However, after extensive negotiations many of the organizations involved, including the International AIDS Society and the International Council of AIDS Service Organizations, were disappointed with the final declaration.

Many said that it failed to set concrete goals for the future by which progress could be measured. Prior to the meeting IAVI and its partners worked to

ensure that the UN leaders recognized how research into new prevention technologies, like vaccines and microbicides, could play an important role in combating the epidemic in the future. In the final declaration AIDS vaccines were acknowledged as crucial to global public health.

Just before UNGASS took place, UNAIDS also released the 2006 Report on the global AIDS epidemic (http://www.unaids.org/en/HIV_data/2006_GlobalReport/default.asp). This report cited a slowdown in the global epidemic for the first time, highlighted by a decline in HIV prevalence in Kenya, Zimbabwe, Burkina Faso, Haiti, and other countries in the Caribbean. But even as infection rates are dropping in some areas, the overall number of people dying from AIDS or AIDS-related illnesses continues to rise. Increasing HIV prevalence was reported in several countries, including China, Indonesia, Papua New Guinea, and Vietnam, and there is evidence of possible "HIV outbreaks" in Bangladesh and Pakistan, according to UNAIDS.

This report also declared India as the nation with the highest number of HIV-infected individuals at 5.7 million, surpassing South Africa, which still has the greatest prevalence owing to its much smaller population. While HIV prevalence is declining in four Indian states the epidemic in South Africa shows no evidence of decline.

Vaccine against human papillomavirus receives US approval

The first vaccine capable of preventing cervical cancer recently received approval and licensure by the US Food and Drug Administration (FDA) for use in females ages 9-26. Gardasil, the quadrivalent vaccine manufactured by Merck, also prevents the development of precancerous genital lesions and genital warts caused by four types of the human papillomavirus (HPV), which is one of the most common sexually-transmitted infections in the world (see February 2006 *Spotlight* article, *Cervical cancer vaccines*).

The efficacy of the vaccine, administered through 3 immunizations over a period of 6 months, was illustrated in 4 Phase III trials conducted in 21,000 women in several countries. The greatest need for the vaccines lies in developing

countries, where the majority of the 250,000 deaths from cervical cancer occur each year. On June 5, the Bill & Melinda Gates Foundation awarded the Seattle-based not-for-profit organization Program for Appropriate Technology in Health (PATH) a US\$27.8 million grant to conduct a five-year effort to ensure that this vaccine is made available to women and girls in developing countries. PATH is collaborating with Merck and GlaxoSmithKline, which also manufactures a cervical cancer vaccine that is expected to receive a license for use in the European Union, as well as officials in Peru, India, Uganda, and Vietnam to establish mechanisms for financing purchase of these vaccines and to ease introduction efforts.



Editor

Simon Noble, PhD

Science Writer

Kristen Jill Kresge

Production Manager

Nicole Sender

All articles written by Kristen Jill Kresge.

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VAX is a project managed by Kristen Jill Kresge.



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IAVI is a global not-for-profit organization working to speed the search for a vaccine to prevent HIV infection and AIDS. Founded in 1996 and operational in 23 countries, IAVI and its network of partners research and develop vaccine candidates. IAVI also advocates for a vaccine to be a global priority and works to assure that a future vaccine will be accessible to all who need it. For more information, go to www.iavi.org.

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How can home-based or mobile services for HIV counseling and testing improve community responses?

Voluntary counseling and testing (VCT) services are a key component of HIV prevention, treatment, and care programs. Individuals learn about behaviors that put them at risk of HIV infection and how they can reduce this risk through the counseling process, and this information can be a catalyst for people to alter their behaviors.

Individuals who undergo VCT also find out whether or not they are HIV infected (see November 2005 *Primer on Understanding HIV Testing*). VCT services, therefore, are often the primary entry point for infected individuals into treatment and care programs. These important outcomes make VCT programs a critical part of the community's response to HIV/AIDS.

There are various types of VCT services, including those given before enrollment in a vaccine trial or research study or sessions specifically tailored for couples (see April 2005 *Primer on Understanding Research Voluntary Counseling and Testing* and October 2005 *Primer on Understanding Couples Voluntary Counseling and Testing*). These almost always occur at community health clinics or clinical trial sites, but the stigma associated with HIV in many communities, as well as the distance people are required to travel to clinics in rural areas, can prevent people from seeking these services on their own. Since VCT is such a powerful tool in getting people information on HIV and access to treatment if needed, researchers have looked for ways to maximize the number of people utilizing these services. One of these approaches is taking VCT services directly to people in their homes or neighborhoods. Such home-based or mobile VCT services, while limited, have been successful in getting more people to be tested for HIV infection.

The process

The VCT services administered in people's homes are conducted similarly to those in clinics. Community health-care workers are trained to provide HIV

counseling and testing and must obtain consent from all individuals before administering VCT. The only difference is that these healthcare workers go door-to-door offering these services.

Some organizations, such as The AIDS Support Organization (TASO) in Mbale, Uganda, couple their home-based VCT services with at-home care programs. So when field officers deliver antiretrovirals (ARVs) directly to the homes of infected individuals they also offer VCT services to other family members in the household.

Others, like the AIDS Information Centre (AIC) in Uganda, have implemented a stand alone home-based VCT program in an effort to increase the number of people being tested for HIV. National surveys in the country reported that although 70% of people want to be tested for HIV infection, only about 10% have actually participated in VCT.

A pilot project, funded by the US Centers for Disease Control and Prevention (CDC) was started by AIC in 2004 in the districts of Tororo and Busia in Uganda in an attempt to reach as many people as possible in these districts and offer them home-based VCT services. Trained outreach teams visited each home and offered all family members information so they could decide if they wished to participate. Adults in the household were given the choice to receive these services individually, or as couples. Anyone who was found to be HIV infected during this process received referrals to treatment and care programs in their community.

Judging success

Many organizations have found that offering home-based VCT programs is an effective way to increase access to treatment and prevention services. The AIC program lasted for one year and during this time over 5000 individuals received VCT services in their homes, which was more than double the study's target. The outreach teams visited more than 2000 homes in these two districts of Uganda and in 65% of them at least one household member agreed to participate in VCT.

The results of this program were presented at the International AIDS Society

meeting on HIV Pathogenesis and Treatment, which took place last year in Rio de Janeiro, Brazil, and the CDC plans to use this program to create guidelines that will allow additional home-based VCT programs to be started in Uganda.

The AIC concluded that stigma seemed to be much less of an influence on a person's decision to undergo HIV testing when VCT services are administered in the home, instead of in clinics. Home-based VCT services could also be a promising strategy for reaching disempowered individuals, especially women.

Another option is providing just the test results and post-test counseling at home. In settings where rapid tests are unavailable, people sometimes do not return to the clinic to find out the results of their HIV test. In a study conducted by the Medical Research Council in Entebbe, Uganda, researchers found that offering test results in a person's home was an effective way to ensure that people received them.

Mobile units

Another method for bringing VCT services directly to communities is to utilize mobile VCT units. The Foundation Agency for Rural Development, a non-governmental organization in Nairobi, Kenya, uses bicycles to bring VCT to local communities. Four mobile sites are set up in different areas throughout the city and each week several individuals undergo VCT. Like home-based services, these mobile units can reach people who may be unable to travel to a clinic to receive VCT.

From community to country

The most ambitious home-based VCT program is currently taking place in Lesotho, where on World AIDS Day last year the president announced plans to take VCT services door-to-door in an effort to reach every household in the country by 2007. To meet this challenge the government trained 6500 healthcare workers to provide VCT services. Prior to this universal HIV testing initiative, it was estimated that only 1% of the population had accessed VCT.