In 1996, Botswana was at the epicenter of the AIDS epidemic ravaging southern Africa. That same year, Harvard teamed up with Botswana’s Ministry of Health to create the Botswana Harvard Partnership (BHP) to address the crisis. Twenty years later, we look back at the life-saving work done at the BHP and what the future may hold.
In January, the Botswana Harvard Partnership (BHP) celebrated its 20th anniversary. At the ceremony in Gaborone, Prof. Max Essex, Chair of both the BHP and the Harvard T.H. Chan School of Public Health AIDS Initiative, delivered these remarks:

Botswana and the Botswana Harvard Partnership have much to celebrate. Although AIDS in Africa was recognized as a major epidemic in east and central Africa in the early to mid 1980s, it was not yet a big deal in southern Africa. By the early to mid 1990s, however, UNAIDS and the World Health Organization prevalence estimates showed that southern Africa was much more impacted than all other regions of the world.

My colleagues and I at Harvard decided we should get involved to find out what was going on. We had experience in other parts of Africa and Asia, but those epidemics were modest in comparison to the situation in southern Africa. I had a discussion with Maurice Tempelsman, an old friend who had many friends in Africa and was the Chair of the Harvard AIDS Initiative’s International Advisory Council. He recommended Botswana.

Soon I was invited to a state dinner in Washington in honor of President Masire. After being introduced to President Masire, he, in turn, introduced me to Joe Makhema.

Ric Marlink and I made our first visit to Botswana in August 1996. We obtained blood samples from donors with HIV/AIDS. A few months later, we signed a five-year Memorandum of Understanding with the Ministry of Health, officially establishing the Botswana Harvard Partnership. The fifth renewal and expansion of that agreement will be signed tomorrow.

Cover photo: BHP Research Assistant Keotshepile Molokwane (left) prepares to test a study participant for HIV. Photo by Dominic Chavez
By the late 1990s, Botswana was ground zero for HIV/AIDS.

We analyzed the virus and showed that it was HIV-1C, quite different from other HIVs in east or west Africa, the U.S., Asia, or Europe. It was characterized by a very high rate of genetic variation.

BHP established a small lab in Gaborone. In 2001, a much larger lab opened, made possible through huge contributions from the Ministry of Health, with help from the Gates Foundation, Merck, Bristol-Myers Squibb, and of course the U.S. National Institutes of Health.

By the late 1990s, Botswana was ground zero for HIV/AIDS. According to UNAIDS, more than one in three pregnant women and about one in ten infants were infected. Otherwise, the country was doing well—a model of democracy, good economic development, high literacy and high childhood vaccination rates.

But one of the fastest growing sectors in the economy was the funeral industry. President Mogae, who followed President Masire in 1998, expressed great concern. For several years, he mentioned HIV/AIDS in every speech he made.

From the early days, the BHP had four major goals. In my opinion, one of these was a failure, while the other three have been tremendous successes.

The failure was our early attempt to make a preventive vaccine. Of course, that has also been a failure for AIDS researchers throughout the world. On the bright side, we have several projects underway on the use of vaccine-type antibodies for advances in treatment or prevention. Much of the research was useful scientific knowledge.

Our second major emphasis was the prevention of mother-to-child
transmission of HIV. An unbelievable success. With chemoprophylaxis—providing antiretroviral drugs to pregnant HIV-infected women—only a tiny fraction of infants now get infected. And this while allowing for safe breastfeeding so that infants don’t develop other problems, like diarrhea or respiratory infections that are associated with formula feeding. The protocols developed at BHP soon became guidelines for the world.

Our third major emphasis was antiretroviral treatment. We conducted clinical trials with different drug combinations. Again, a resounding success. Botswana is clearly the leader in Africa, with the highest fraction of HIV-infected people getting the best drugs. One of the top two or three countries in the world. This went beyond our wildest expectations, as treatment also became prevention, perhaps even minimizing the need for a protective vaccine.

The breakthrough for this was the HPTN 052 study, done at the BHP and other sites that collaborated to show that with drugs, adult heterosexual transmissions could be reduced by more than 95%. There is now a worldwide effort for implementation of “treatment as prevention,” which includes the Botswana Combination Prevention Project, a collaboration between the U.S. Centers for Disease Control (CDC) and BHP.

Our final area for emphasis has been teaching and training. Again, a major success. For the long-term future, this may be the most important of all. Over the last 20 years, Harvard and BHP have spent more than 25 million dollars in laboratory and clinical research training for people from Botswana, including about 100 people in the early days of the Masa program for national antiretroviral treatment. The BHP was also responsible for the short-term training of thousands of physicians and nurses through KITSO, the Master Trainer program, and other quality control programs under Drs. Marlink and Gaolathe. BHP now has local leaders that are internationally recognized, like Drs. Gaolathe, Moyo, Gaseitsiwe, and Makhema. For these and other reasons, the future looks bright.

HIV/AIDS is no longer a death sentence. Treatment will continue to get better, and costs will continue to go down. But we must keep up the research—find a complete cure, universal prevention, rapid control of TB, reduction of cardiovascular diseases and various cancer outcomes. The list is long and daunting. But just think of all we’ve done in the last 20 years.
CELEBRATING 20 YEARS OF RESEARCH, CAPACITY BUILDING AND SAVING LIVES!
The heart of BHP operations is the busy, three-story building on the grounds of Princess Marina, the main public hospital in Gaborone. The crowded research building houses the Botswana-Harvard HIV Reference Laboratory, the Data Management Center, and office space for BHP staff.

The ground floor of the building serves as the central lab for processing the high-volume of clinical specimens generated by Botswana’s national program to diagnose and treat those with HIV. Tests are automated and include HIV RNA PCR, viral load, CD4/CD8 counts by flow cytometry, serological ELISA assays, and routine chemistry and hematology.

In addition to offices, the top two floors house BHP research labs and a BL3 facility for virus isolation and culture. Over 1.5 million samples are stored in 60 freezers for possible use in future studies. In addition to its research role, the BHP also serves as a training facility for biomedical researchers and laboratory technicians.

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Dr. Simani Gaseitsiwe
BHP Laboratory Director

Botswana Combination Prevention Project team, Project Director, Dr. Tendani Gaolathe (far right)
The Botswana Harvard AIDS Institute Partnership (BHP) was established 20 years ago to help combat HIV/AIDS at the epicenter of the epidemic. At the time, about 37% of pregnant women in Botswana were infected with HIV. Dr. Joseph Makhema was a young physician working what seemed like unending hours at the public hospital in Gaborone, where effective treatment was not yet available. Today, Dr. Makhema is the CEO of the Institute he played an important role in establishing. Martha Henry, Executive Director of HAI, spoke with him about the BHP’s history and future.

Martha Henry: When an agreement was signed between Harvard University and Botswana’s Ministry of Health to create the Botswana Harvard AIDS Institute in 1996, how bad was the AIDS epidemic in Botswana?

Dr. Joseph Makhema: At that time, I was in the department of medicine at Princess Marina Hospital, which was overwhelmed by AIDS patients. All we could do was treat the opportunistic infections: pneumonias, meningitis, recurrent episodes of diarrheal illnesses. Some people were emaciated. The ward occupancy ran beyond capacity, with beds all over the place. Mortality was high.

In medicine, you are taught to save lives. When you feel unable to do so, it has an impact on morale. As the epidemic unfolded, there was an increasing sense of anxiety as to what the future held for the country. Within families, multiple funerals would occur on the same day with multiple relatives to bury. There was poor productivity within the workforce. The social fabric was stretched to the limit. I suppose that’s when you delve into your spirituality to help you through.

How did you become involved with the BHP?

I had a role being the president’s physician. I got to first meet Max [Essex] in Washington when he met with President Masire. Max had seen some of the data coming out of Botswana in terms of the high HIV prevalence and expressed his wish to set up a collaborative effort within Botswana.
As the epidemic unfolded, there was an increasing sense of anxiety as to what the future held for the country.

I briefed Ministry of Health officials when I returned. After initial contact, Max was keen on pushing things along. He wanted to start a study to determine the HIV subtype that was circulating in Botswana. Since I was working at Princess Marina, I facilitated the drawing of samples for that analysis.

Before we knew it, a memorandum of agreement was signed between the Ministry of Health and the Harvard AIDS Institute to establish the institution we now know as BHP. I formally joined BHP in 2003. I took over as Project Director in 2006.

What was the BHP’s role in helping to shape the Masa program?

Masa, the national antiretroviral program for HIV treatment in Botswana, was rolled out in 2002. (Masa means new dawn in Setswana, Botswana’s spoken language.)

The BHP worked hand in glove with Masa, whether it was for clinical skills to treat and monitor patients with HIV, laboratory testing, or pharmacy issues relating to antiretrovirals and their side effects.

Hermann Bussmann and Bill Wester helped set up the Infectious Disease Care Clinic (IDCC) and were the first physicians to run it. The Princess Marina IDCC was the first in Botswana and was established concurrently with the BHP’s clinical research infrastructure to conduct the Tshepo Study, a clinical trial that looked at different antiretroviral treatment options, their efficacy, and drug resistance among Botswana AIDS patients.

What is KITSO and why was it necessary?

KITSO is an acronym for Knowledge, Innovation and Training Shall Overcome HIV.

It was important to ensure that we had adequately trained health care personnel in the country. To do so, we set up a robust training program for HIV/AIDS nurses, physicians, laboratory technicians, and general staff. KITSO was established in 2001 and was initially funded by Merck and the Bill & Melinda Gates Foundation through the African Comprehensive HIV/AIDS Partnerships (ACHAP).

At BHP, we provided the first cohort of trainers who assisted in rolling out the program. They conducted core competency trainings required of all healthcare practitioners who would be involved in management of HIV patients, ensuring standardization of knowledge and application of protocols to manage patients in Botswana.

BHP staff members at the head of the Health Walk, part of the 20th celebration festivities.
As the needs for decentralization of HIV treatment services arose, it was also necessary for training to become decentralized. The Master Trainer Program was subsequently developed to complement KITSO and provide on-site training, support, and mentorship for clinics where HIV care was provided.

After ten years, thousands of healthcare workers had been trained and management of KITSO was transitioned to the Ministry of Health. Without the skills and training that KITSO provided, the Masa rollout would never have been possible.

**Will training remain an important part of the BHP’s mission?**

We are committed to building scientific capacity for research activities, not only in clinical trials, but also in basic laboratory science.

The BHP became a limited liability corporation (LLC) in 2007. **What are the advantages of being an LLC?**

It was important for the BHP to become a local entity. We now have access to funding meant exclusively for sub-Saharan African institutions. We have built administrative capacity and have the ability to apply independently and manage our own grants.

**A big percentage of the BHP’s operating costs is covered by grants from the U.S. National Institutes of Health (NIH) and the Centers for Disease Control (CDC). Will that change?**

We are exploring new avenues to support the future work of the BHP beyond competitive grants from the NIH and CDC. We are now able to approach other sponsors, including the European Union, through the European Development Capacity Training Programme, the Wellcome Trust, and the private sector.

We have developed a sustainability plan that centers on a new business model, which includes fee-for-service work based on competencies and skills we already have within the BHP. This revenue would be plowed back into the BHP to support the research agenda.

**The BHP’s official name is the Botswana Harvard AIDS Institute. Will you continue to focus primarily on HIV/AIDS research?**

The whole dynamic of how we view HIV has changed. It has become more of a chronic disease. With access to antiretroviral treatment for HIV, we are seeing a healthier population, which unfortunately has transitioned to some of the lifestyle non-communicable diseases such as high blood pressure, strokes, heart attacks, etc. The interface between infectious diseases and non-communicable diseases, including cancer, has become increasingly important. We must address this new challenge from a public health perspective.

We are also looking at the effects of exposure to antiretroviral drugs amongst HIV exposed-but-uninfected children, who may face other challenges, such as low birth weight or neurocognitive impairment.

There are other emerging public health challenges—infections like Ebola and the Zika virus, as well as a range of non-communicable diseases. These are threats, but they also offer opportunities for widening the scope of the BHP agenda. We are looking at transforming the BHP into more of a public health institute that will address the changing epidemiology of diseases that affect and

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*The KITSO Team marks over 8000 nurses, doctors and pharmacists trained in the fundamentals of HIV/AIDS care, circa 2008.*
are becoming prevalent in Botswana and across the region.

How do you set your research agenda?
We are in partnership with the Ministry of Health. Their agenda and priorities are of utmost importance. We also look at regional challenges. Our research and programs have mainly focused on advancing public health within Botswana and the region. Often those are also needs of the global community, so our research has a global impact.

What are the biggest challenges facing the BHP in the next decade?
One of the biggest challenges is how BHP will adapt over time to new patterns of disease. As we move towards becoming a public health institute, it will be important to have an epidemiology unit within BHP to study disease trends and interventions required to address the diseases.

There is also the question of retention of our key personnel. As we have developed and evolved over the years, we have trained a cohort of researchers that have left BHP for other institutions to work in different public health programs. How then can we retain our core personnel to ensure that over time they are available to provide the backbone of the work that we do? That will be a big challenge in the next decade. The solution is to continue to strengthen the BHP to become a center of research excellence that shall attract and offer the best environment and reward for scientific achievement.

What makes you want to come to work in the morning?
The fact that the work that we do has a positive impact in changing people’s lives. Knowing that the children that I drive past as they walk to school in the morning may not have been infected with HIV because of our work. Or that the healthy looking, HIV-infected but AIDS-free individual in our society can fulfill his or her full potential and contribute to the socio-economic development of their families and the country. That motivates me.

What accomplishment are you most proud of at the BHP?
Without a doubt, it is prevention of mother-to-child transmission of HIV. Transmission has fallen all the way from 40%, so we hardly have an infant now who is infected. Being able to say we have almost attained our goal of an HIV-free generation, which I could never ever have dreamt of previously.

That has to be one of the greatest accomplishments of this institution. We have been at the forefront and led the world in the programs and research for prevention of mother-to-child transmission.
The Celebration

Lives saved are always cause for celebration. The morning of January 26, 2017, in a hotel meeting room in Gaborone, Botswana, AIDS researchers, government officials, and others came together to celebrate 20 years of research, education, and training efforts by the Botswana Harvard AIDS Institute Partnership (BHP) to end the AIDS epidemic in southern Africa.

Former President of Botswana Sir Ketumile Masire received the Legacy Award for his founding role in the BHP. In 1996, then-President Masire invited Harvard professor Max Essex to Botswana to help address the country’s devastating HIV/AIDS epidemic. Essex outlined the successes and challenges the BHP has faced in two decades of work. BHP CEO Dr. Joseph Makhema reviewed research highlights and Deputy CEO Dr. Mompati Mmalane spoke about BHP’s strategy for the next five years. Others spoke about the importance of community-based research, implementation research, and capacity building.

The last time Dr. Soon-Young Yoon, a U.N. advisor and member of the Harvard AIDS Initiative (HAI) International Advisory Council, was in Botswana was in 2001, the year the BHP Lab opened. She returned for the 20th. “Imagine that in that period of time so many people have been trained and the project accomplished what it set out to do and more,” she reflected.

“I was eager to see the Partnership in action,” said Richard M. Smith, former Editor-in-Chief of Newsweek and HAI Council member, who also traveled to Gaborone for the 20th. “There’s nothing like the chance to walk through the research center, to see the inspiring young scientists and students of Botswana at work in the labs, to put flesh on the bones of a story.”

“The BHP is not just an HIV/AIDS focused public health effort,” said Smith. “It has a broader view of a society’s health challenges and is contributing not only on the HIV/AIDS front, but also on other emerging public health issues.”

After the official program, guests visited the BHP headquarters for a tour of the labs and offices. Members of study teams set up stalls in the courtyard to display information and answer questions about their work.

The next day, BHP leaders and staff traded dress clothes for casual attire and enjoyed a Field Day. The festivities included a morning Health Walk to the Gaborone stadium, foot races, dance performances, a tug-of-war, and a friendly game of soccer/football against the Ministry of Health squad.

It rained a bit, but in arid Botswana, rain is a sign of blessing and good luck. Pula!
We are celebrating 20 years of research, capacity building and saving lives. I want to underscore saving lives because it is saving lives in the truest of senses.

Hon. Dorcas Makgato
Minister of Health and Wellness

Foot races were part of the BHP staff field day.
HIV/AIDS is no longer a death sentence. Treatment will continue to get better and costs will continue to go down. But we must keep up the research—find a complete cure, universal prevention, rapid control of TB, reduction of cardiovascular diseases and various cancer outcomes. The list is long and daunting. But just think of all we’ve done in the last 20 years.

— Max Essex