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Learning from Botswana

A report from Botswana's first national research conference on HIV/AIDS/STI/other related infectious diseases

This article was written by Theo Smart with additional contributions from Keith Alcorn.

Key points

- Botswana's antiretroviral treatment programme has been criticised as `falling short` and failing to achieve targets. A recent conference in Botswana reviewed the country's lessons for other nations planning treatment scale-up.
- Prevention and treatment are two sides of the same coin: containment of the epidemic. Any national treatment programme needs a good understanding of the complex relationship between risk behaviour, gender, stigma, willingness to test for HIV and uptake of treatment. Botswana has experienced difficulties in attracting people to learn their HIV status, despite the offer of free treatment. There is much still to learn about cultural obstacles to treatment uptake.
- HIV-1 subtype C appears to have characteristics that have contributed to the severity of the epidemic in Botswana. More needs to be learnt about it if prevention, vaccine and treatment efforts are to be successful in southern Africa.
- Botswana gives a high priority to research and partnerships with research institutions. Knowledge from Botswana research is likely to make an important contribution to developing effective programmes in other countries.
- Key challenges include balancing the needs of the sickest patients with the need to contain the burden of sickness by providing treatment to asymptomatic individuals too.
- Another serious challenge is lack of trained staff, not just in medical care but also in information technology, management, diagnostics and counselling. NGO/community capacity is weak too.
- Scaling up treatment appears to follow a sigmoid pattern, not a linear pattern, that is to say, progress looks slow at first but once it accelerates, it can do so rapidly.

Botswana reviews its progress

Recent articles in the press, notably in the *Boston Globe* and *Newsweek International*, have unfairly characterised Botswana's anti-HIV efforts and antiretroviral roll-out programme as "falling short" and "barely making a dent," despite the millions being invested in it.

However, the First National Research Conference on HIV/AIDS/STI/Other Related Infectious Diseases held earlier this month in Gaborone, Botswana, was one of the most dynamic meetings this reporter has ever attended. The conference demonstrated that the Government of Botswana and its international collaborators and development partners have put into place a model programme, the most sophisticated response to the HIV/AIDS epidemic on the African continent to date. As it is still ramping up, the programme is far from perfect, however, and has encountered unanticipated and complex problems from which other nations can learn.

But much of the meeting was dedicated to honestly assessing the gaps between the "needs" the programme is meant to meet and its actual performance, and then to the design and testing of interventions or policies to tackle those obstacles or gaps in provision. The leadership is so inspiring and the political will and drive behind the programme is so great that it is destined to continue refining itself until it succeeds at filling in those gaps.

Even so, they are not able to work magic. One of the key lessons of the meeting is that the vast infrastructure needed to treat HIV effectively cannot be built in a couple of years.

Why is Botswana so seriously affected?

One of the key issues facing country programmes considering the introduction of antiretroviral therapy is the potential size of the commitment. Unless there is some prospect of success in prevention activities, patient numbers will grow indefinitely. Participants at the conference devoted much discussion to the reasons why Botswana has been so severely affected, and what can be done to improve prevention efforts.

Ten or fifteen years ago in southern Africa, hardly anyone was worried about HIV. Although, the first cases of AIDS were diagnosed in 1982 in South Africa and in Botswana in 1985, the disease spread very slowly in the 1980s. In fact, most people in the region thought AIDS was a white man's disease, an effect of malnutrition, or even worse, a fiction. To a surprising extent, these perceptions still persist in many areas.

What is shocking is how swiftly and deeply HIV got its hooks into the population during the last ten years - in many areas 30-40% of the population has been infected, and the majority of people in some age brackets. Similar data were reported at this month's meeting by the Local Government Minister, T Shipinare, from the most recent Botswana HIV/AIDS Surveillance report.

275,000 adult (15-49 years) Botswana are now estimated to be living with HIV/AIDS (out of a total population of ~1.6 million). 37.4% of adult pregnant women are HIV-positive, tens of thousands of their children become infected and even more will become orphans.

Some areas are particularly hard hit. In the mining district Selebi/Phikwe, the prevalence runs as high as 52.2%, probably the highest level anywhere in the world. However, Botswana no longer has the world's highest seroprevalence - that dubious distinction likely belongs to either Lesotho or Swaziland.

According to the Surveillance report, "condom use in the last sexual act with a non-marital and non-cohabiting partner was over 60%." Cultural practices which encourage intergenerational and multiple partner sex also persist, according to the survey. "The proportion of people with multiple partners is still high at 32% for men and 17% for women."

A number of sessions were devoted to reports on the attempts to reduce transmission through standard interventions such as PMCT, screening and treatment for sexually transmitted infections and voluntary counselling and testing. Male circumcision and calls to ban or limit access to alcohol were also proposed as desirable interventions. There were also pleas to practice monogamy or abstinence rather than rely on the distribution of condoms, which some religious leaders present insisted was like "providing our youth with a license to fornicate."

In a plenary session on Africa's response to AIDS, United Nations Special Envoy for AIDS, Ambassador Stephen Lewis blamed such religious leaders for Africa's inadequate response to AIDS. "The religious leadership has been equally delinquent. The religious leadership say that they carry the moral flame, but it doesn't seem

to be burning very bright and in some instances has been totally extinguished, as with the Catholic church's stance on condom use."

But above all, Lewis stressed, "gender lies at the heart of the pandemic. You are not going to beat this epidemic until you tackle the massive gender inequality that exists on this continent. It's going to take generations, but you have to empower women today."

Several presentations highlighted the woman's unequal role in Botswana. They all added to evidence that has been highlighted for years, but evidence nevertheless worth restating: women often have little control over sex. If they refuse sex from their partner, he could interpret it as a sign of unfaithfulness, and the partner could then rape her. These patterns are not merely applied to marriages but in affairs, dating couples and intergenerational relationships as well.

The woman has no right to refuse sex, and therefore winds up being put repeatedly at risk, and yet, if she tests positive she is condemned as adulterous or a prostitute. Fear of the male partner's reaction if he found out that she was positive came up again and again in Botswana as a reason for women not to get tested, to not return for test results, to not disclose her results, to not go into PMTCT studies, and not to go onto treatment. If they did get treatment, they might be poorly adherent because they would try to conceal pill taking.

It is this fundamental feature of African society, argue some that is at the root of the slow uptake of treatment in Botswana. This feature is not unique to Botswana, and will need to be addressed in all nations where treatment access is planned. When we talk about stigma as an obstacle to treatment scale-up, we are talking about a phenomenon that is largely structured by gender.

Sub-type C HIV-1

Dr. A. B. Khan who is the head of the National AIDS Coordinating Agency (NACA) and was also the doctor who diagnosed the country's first AIDS case concurred that being both a woman and a doctor had sometimes placed her in dangerous situations. But there must be other factors besides male chauvinism that explain the severity of the epidemic, because that isn't unique to Botswana. And she said, "the rapid spread of the epidemic in the country has been phenomenal by any standard and the impact has been catastrophic."

As easy as it might be to demonise men or the effects of alcohol use the high HIV prevalence may not result entirely from culture or behaviour. President Mogae said: "We are giving serious thought to alcohol and substance abuse. In fact we have a liquor law in draft to maybe reduce the opening hours for liquor outlets and various other measures. But that doesn't explain why we are the most seriously affected country in the world."

And unlike other regional leaders, he doesn't blame the epidemic on poverty. "Poverty has always been an issue but not in Botswana. There is no correlation between income level and HIV/Aids. I'm saying to you that we are losing young professionals. The most affected population group is 15 to 49. Now the people between 15 and 18 and even 20 and up to 22 [are becoming infected], most of them are still in secondary and tertiary institutions at government expense."

"There's growing evidence for genotypic/phenotypic differences for HIV-1C of southern Africa to help explain differences in epidemics," Dr. Max Essex said during the opening plenary of the conference. Dr. Essex is Chair of the Harvard AIDS Institute, and the Botswana Harvard Partnership, just one of the several international collaborations that Botswana has set up. Harvard has built a

\$30,000,000 lab, partly to study these basic science questions. Dr. Essex also happens to have discovered HIV-1C.

"AIDS deaths are at a new high, reflecting HIV infections that happened 5-10 years ago and the lack of widespread use of HAART. But sub-Saharan Africa, especially southern Africa, has much higher rates than any other area. HIV-1C accounts for as many infections as the other major subtypes (A, B, D, A/G, A/E) combined."

Dr. Essex first detected HIV-1C, in 1989 but at the time there wasn't very much of it about. But since that time, it has spread so rapidly that it is by far the most common subtype. No one's really sure why this is the case, but Dr. Essex noted a number a unique features of HIV-1C.

First, the countries with HIV-1C have the highest HIV prevalence rates regardless of cultural differences. In general, non-subtype B viruses are more efficiently transmitted heterosexually than subtype-B.

Meanwhile, subtype-C seems to be more readily transmitted perinatally than subtypes A and D. There is also greater intrasubtype variation for C vs. B, but when subtype C recombines with other virus, subtype C's V3 loop (part of the viral envelope glycoprotein) and LTR (long terminal repeat, which plays a role in transcription) are always conserved, presumably because they give the virus some competitive advantage. Patients with subtype C tend to have higher viral loads than subtypes A or D, and this could have something to do with the LTR. Compared to subtype B, subtype C virus replication jumps dramatically when activated by TNF α , an inflammatory cytokine (chemical messenger between immune cells) produced at high levels in patients with coinfections.

Another curious difference between subtype C and other subtypes concerns how it attaches to a cell. Other strains of virus diversify in the body over time and develop the ability to bind to a certain cell surface protein called CXCR-4, in addition to a cell surface protein called CCR5. Subtype C doesn't do this. Instead, it just sticks to CCR5.

What's the significance of this? It's unclear. But the significance of having Dr. Max Essex presenting such information at the opening plenary was pretty clear.

This wasn't just going to be a touchy feely conference about home-based care. Botswana isn't satisfied with launching prevention programmes and voluntary testing. They don't merely want to provide free antiretrovirals (as if that is anything to sniff at when you are starting off with virtually no medical infrastructure). No, its clear

from the HIV prevalence rate that that may not be enough to defeat this virus. They want to go beyond that to become a country doing cutting edge research. A centre of excellence, because they've realised that HIV is a formidable enemy. And it isn't exactly the same HIV as is common in the West - they certainly can't take it for granted that the solution to their problem will be the same as in the rest of the world.

They are, as President Mogae has said more than once: "fighting for their very survival, not as individuals but as a nation." They may need to get to study that enemy very well to defeat it.

That was the very point of this meeting. This meeting wasn't simply about the ARV rollout. Botswana believes that it has to become more than a nation of "caregivers." In order to survive they must also become a nation of researchers.

Putting research into practice

In her opening welcome to conference, Dr. G K T. Chiepe explained that the research that had been conducted in the country to date was

too narrow, "making it extremely difficult to understand the broad dynamics of the HIV/AIDS epidemic in our country."

"The time has come for our researchers in Botswana and their collaborative partners within or outside Botswana to assist the existing policy and programmatic environment with more appropriate high quality data to inform decision-making."

It's true that the country has had some difficulty implementing their plans as quickly as they initially hoped, but there's a good chance that they will succeed because they are continually assessing their efforts in order to fix what isn't working. They are still two steps ahead of everyone else.

Dr. Khan and other advisers had kept President Mogae alerted to the growing severity of the crisis. Although Botswana is one of the wealthiest nations in Africa, it is still poor compared to developed countries with a per capita income of \$3000. They had a very limited public health system, no medical school, and few doctors with any experience of managing people with HIV. The facilities and technical expertise couldn't be built from scratch. There was no way Botswana could tackle the crisis on its own (and if this is true of Botswana, it will only be worse in poorer countries).

In 2000, Botswana could take advantage of its proximity to South Africa, the site of the Durban "Break the Silence" World AIDS Conference. While the leadership of South Africa continued to deliberate the cause of AIDS, Botswana didn't miss the opportunities to build alliances and form collaborative partnerships with some of the most experienced and well-funded teams in the world.

These include UNAIDS, the Botswana-Harvard Partnership, BOTUSA (a collaboration between Botswana and the US Centres for Disease Control, Bristol-Myer's Squibb Foundation and Baylor University Texas which focuses on paediatrics. Finally, Botswana joined with a new organisation: the African Comprehensive HIV/AIDS Partnership (ACHAP).

ACHAP is a public-private partnership between the Government of Botswana, Merck & Co., Inc. / The Merck Company Foundation and the Bill & Melinda Gates Foundation. The two foundations are contributing a total of US\$100 million over five years.

Much of this happened quietly enough. But in 2001, President Mogae announced that the government meant to launch a programme, called Masa, that would offer antiretroviral therapy free to any citizen with HIV who needed it. People began to take notice. Many experts and aid organisations had concluded that antiretroviral therapy was too complex to use in Africa. Could Botswana actually scale up and make it work? Botswana became the pilot study for the rollout of antiretroviral therapy. The successes and frustrations of Masa were described by its operations manager, Dr Ernest Darkoh, at the opening plenary.

The Masa antiretroviral therapy program in Botswana

In 2001, the challenge posed by offering free antiretroviral therapy was immense. The epidemic in Botswana was full blown and out of control. There were approximately 300,000 HIV positive people in the country. At least 35% of these were in the primary income earning stage of life. 110,000 would probably be eligible for therapy immediately, based on clinical criteria. But more than 90% of these didn't know their HIV status, and there were steep socio-cultural barriers to getting them tested.

The country did not have the capacity to offer treatment yet. There were few trained doctors, nurses, or lab personnel. There was

no infrastructure or equipment. They would need to create systems and policies for the programme.

They established a dedicated implementation team (based on a public/private model) and supporting structures. They decided to build four strategically located centres in Gaborone, Francistown, Maun and Serowe to serve patients who met the eligibility criteria (a CD4 count of 200 or less and/or the presence of an AIDS defining illness). They would establish a system to monitor early uptake and adjust eligibility criteria as necessary. They would build more capacity nationwide as rapidly as possible to address the full burden of disease. At the same time, they would try to strengthen ongoing prevention initiatives.

Progress

- The Gaborone site was first to open on January 22, 2001. By November 2003, it had tested 7899 eligible patients, 5517 of whom started therapy. 490 of the patients have died and 8% died while on treatment
- The clinic in Francistown opened next, on May 13, 2002. By November 2003, 2766 eligible patients had been tested, 2265 had been placed on therapy, 181 had died, 7% while on treatment. By November 2003, Serowe had tested 3639 eligible patients, 1147 were on treatment, and 157 (12%) died on treatment.
- The fourth clinic opened in Maun, by July 10, 2002. As of November 1014 eligible patients had been tested, 663 were on treatment, 116 (15% had died while on treatment. In 2003, they opened six more sites in Jwaneng, Orapa, Tutume, Molepolole, Mahalpye, and Kanye. As of November 2003, the combined Masa sites had tested a total of 16,400 eligible patients, 10,264 are on treatment and a total of 994 (9%) had passed away on treatment.

Masa has been criticised for the very large gap between the perceived need for treatment and its ability to deliver. Dr Darkoh pointed out however, that they could only scale up gradually and that the number of patients over the last several months has increased dramatically, in other words, as more centres have come online, the rate of uptake has improved significantly and should continue to increase dramatically.

Others have worried about the high rate of death on treatment, but Dr. Darkoh pointed out that these were very advanced patients with an average CD4 cell count of only 50-60 cells. However, the programme has shown that it can get good patient follow-up in Africa, with fewer than 10% lost to follow-up. Also, patient adherence, using a zero tolerance standard for missing or being late on a dose is high, at over 85%. Less than 7% had to switch medication due to toxicity. Complete viral load suppression was achieved in 85% of the patients.

The plan is to continue scaling up and expanding as long as necessary. Sites have been completed at two mining hospitals, and three more are planned at Botswana Defense Force facilities. The plan is to identify ten other potential sites for rollout by the end of fiscal year 2004, by using a decision matrix which weighs burden of disease against site readiness factors

But the key challenges going forward? The first and foremost is that most people in the country (including patients) still do not know their HIV status. Socio-cultural factors and stigma remain barriers. Also when each site opens, there is a large initial burden of very sick patients who use resources more intensively. This is partly because the epidemic is so far advanced in Botswana and there is a natural tendency to wait until getting sick before seeking health services.

Despite the substantial resources provided by ACHAP partners, fundamental human resource problems that cannot be solved by money alone continue to limit progress. Botswana continues to suffer from staff shortages and lack of training (ARV, IT, laboratory, counselling, project management). He also wishes there was greater NGO capacity, as they could help with adherence and drug security.

Initial treatment delivery was implemented at the hospital level, but with some people needing to travel over 200 miles to their nearest hospital, Botswana recognises that the next stage must be the devolution of care to the most local level possible, together with better integration of HIV care with primary care.

"Not all patients are going to be able to reach an ARV site," says Ernest Darkoh. "But we should still find ways to provide treatment. This could be done on a bicycle with a person going out handing antiretrovirals, if necessary."

Dr Darkoh says that they've learned several lessons from the experience.

- "Capacity or capability build-up follows a sigmoid rather than linear curve; it takes time in the beginning."
- Each new site experiences the same "teething problems" therefore spread the net as wide as possible after an initial "pilot."
- "The sickest come forward first: so we may need to "split" the queue to allow some healthier patients onto treatment before they become severely ill.
- VCT should be supplemented with routine testing to enable more rational demand management; we need to convince people that it would save their life AND livelihood. Much of the workload is follow-up of patients rather than initial assessment.
- Set up monitoring and evaluation systems early.

He also thinks that public private partnerships work well. "It can help accelerate implementation since each partner acts as a

"catalyst" for action. "Finally, management, political will, courage, information, accountability and capacity are more critical than money in the broader scheme."

Conclusion

Some argue that Botswana's experience is not a model for 3 x 5, that the country is too well resourced and has gone about things in too much of a top down manner to serve as a template for others. UN Ambassador Stephen Lewis believes that this argument misses the point of Botswana's experience.

"There is no other country where things are being addressed as thoroughly as here. No one has the same range of intervention or the documentation of it as Botswana. So many other countries can learn from this example. I emphasise the need to take the knowledge from Botswana and take it to the rest of the world. Botswana's experience has to be the centrepiece for 3 X 5."

Future issues of HATIP will continue to report on Botswana's experience, and will also take a more detailed look at South African plans for the implementation of ARV therapy. We will also provide more detailed analysis of recommendations from a WHO-sponsored expert meeting in November on scaling up ARV treatment.

We wish all our readers a healthy and happy New Year for 2004. The next edition of HATIP will be published on January 1st 2004.

about HATIP

A regular electronic newsletter for health care workers and community-based organisations on HIV treatment in resource-limited settings.

The newsletter is edited by Theo Smart (Cape Town) and Keith Alcorn, NAM's Senior Editor (London).

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