



Swaziland, HIV and Option B+: What Can We Afford?

By 2007, sub-Saharan Africa had been hit harder by the HIV-AIDS epidemic than anywhere else in the world, suffering 15 million deaths since the 1980s. AIDS had dramatically reduced life expectancy and orphaned 15 million children in one of the world's poorest regions. Major funders, including the United States President's Emergency Plan for AIDS Relief (PEPFAR), and the Global Fund to Fight AIDS, Tuberculosis and Malaria among others, committed funding to stem the tide of the epidemic and help countries in the region develop the capacity to deal with the crisis. But high drug prices and limited access to healthcare presented huge challenges in treating the ill. Cultural factors, including stigmatization of people living with HIV, discrimination against women and high rates of concurrent sexual partners, also contributed to the ongoing spread of the disease.

The small, impoverished Southern African nation of Swaziland was particularly hard hit. In 1999, with the highest rate of HIV infection in the world, the country declared HIV-AIDS a national disaster. By 2003, one-third of the population and 56 percent of 25- to 29-year-olds were HIV-positive. In February 2004, the government created a 30-person Technical Working Group (TWG), chaired by Ministry of Health staff and including local and international NGOs and donors, to present and review HIV data and information, debate research protocols and treatment regimens, and advise the government on HIV-AIDS policy.

In October 2004, Dr. Velephi Okello was appointed Swaziland's national antiretroviral therapy (ART) coordinator and technical advisor to the Swazi National AIDS Programme (SNAP) at the Ministry of Health. Okello was a pragmatist, looking for ways to adapt international best practices to Swaziland's particular circumstances. Under her direction, the government assumed responsibility for paying for HIV treatment drugs (previously funded by international organizations), maintained drug stock levels in the face of budget and supplier issues, rolled out sophisticated treatment and tracking protocols in a decentralized health system run largely by nurses, worked to educate the population, and developed treatment regimens that aimed for the best while accepting hard political and socioeconomic realities.

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In 2006, ICAP at Columbia University, a center focused on global health and based at Columbia's Mailman School of Public Health, set up a program in Swaziland. ICAP partnered with SNAP to bring antiretroviral therapy services to the country's clinics, particularly those in rural areas. In April 2011, SNAP went the next step: it created a treatment-as-prevention framework to treat as many HIV-positive people as practical, including pregnant women, with ARTs in order to reduce the odds of transmission.

Just a year later, the WHO updated its guidelines for using antiretroviral drugs to prevent MTCT. The update introduced Option B+, which aimed to initiate lifelong treatment for all HIV-positive pregnant and breastfeeding women. As the Swazi TWG discussed the new option, the benefits were clear: it protected against MTCT in both current and subsequent pregnancies, avoided treatment starts and stops based on pregnancies, protected HIV-negative sex partners, and simplified the healthcare system's ART service delivery system.

But Swaziland's budget was already stretched thin. Could it afford the additional drugs needed to treat once-pregnant women for life? Could the decentralized healthcare system handle the change while retaining patients in treatment and maintaining quality of care? Should Swaziland roll out Option B+ all at once, as Tanzania had, or take a phased approach? Finally, was it ethical to prioritize pregnant women over other HIV-positive adults?

HIV in Sub-Saharan Africa

By 1984, the HIV-AIDS epidemic had begun to devastate sub-Saharan Africa. Uganda was particularly affected early in the epidemic, and in October 1986 the country began a public education campaign that included promoting monogamous sexual behavior.¹ By 1990, an estimated 5.5 million Africans were living with HIV and 650,000 suffered from AIDS.² The first antiretroviral drug, AZT, had been available since 1987, but it was beyond the means of all but the wealthiest few in Africa. By 1993, the number of individuals infected reached 9 million adults and the number of AIDS cases rose to 1.7 million. In 2000, 70 percent of all HIV-positive people lived in sub-Saharan Africa, although it held only 10 percent of the global population.³ Eighty percent, or some 1.1 million, of all HIV-positive children in the world lived in the region.⁴

¹ "Uganda: an AIDS control programme," *AIDS Action*, Issue 1, November 1987. See: <http://aidsaction.net/aa/aa01.html - page6>

² "Global estimates of AIDS cases and HIV infections: 1990," *AIDS 1990*. See: http://journals.lww.com/aidsonline/Citation/1990/01001/Global_estimates_of_AIDS_cases_and_HIV_infections_.45.aspx

³ Linda Morrison, "The Global Epidemiology of HIV/AIDS," *British Medical Bulletin*, 2001. See <http://bmb.oxfordjournals.org/content/58/1/7.full>

⁴ UNAIDS, "AIDS epidemic update: December 2000." See: http://data.unaids.org/publications/IRC-pub05/aidsepidemicreport2000_en.pdf

Throughout the 1990s, experts noted that infection rates for pregnant women in particular were shooting up; the women, in turn, were passing it to their newborns. From 1992-96, the prevalence of HIV in pregnant women aged 20-24 in Lesotho, for instance, rose from 3.9 to 26 percent.⁵ By 2001, 24.5 percent of pregnant South African women were HIV-positive.⁶ AZT administered during pregnancy, labor and delivery reduced transmission to the baby by 67 percent, but it was a tremendous challenge to get AZT to patients in Africa. Fortunately, single doses of the drug nevirapine were found to cut mother-to-child transmission (MTCT) by nearly half, and African governments and international organizations launched a campaign to provide the drug to pregnant women.

Despite the progress on reducing MTCT, the high cost of AZT helped keep the rate of HIV-AIDS in sub-Saharan Africa high. Africans—led by the South African activist organization Treatment Action Campaign in collaboration with others from the global community—pressed for lower antiretroviral drug prices. In 2001, UN Secretary-General Kofi Annan issued a global call to action aimed at increasing access to HIV-AIDS care and treatment in low-income countries. Still, funding remained a major challenge. In January 2002, the Global Fund to Fight AIDS, Tuberculosis and Malaria (Global Fund) was launched. It was a public-private organization that collected donations from governments and foundations (principally US and Western) for healthcare initiatives in developing countries. In July 2002, former US President Bill Clinton's newly formed Clinton HIV/AIDS Initiative began brokering deals with drug companies to cap antiretroviral drug prices.

Treating mothers-to-be

Meanwhile, motivated by the crisis in sub-Saharan Africa, a team of experts who had developed comprehensive programs for HIV at Harlem Hospital in New York City developed what it called the MTCT-Plus Initiative at Columbia University's Mailman School of Public Health. The team was led by Dr. Wafaa El-Sadr, university professor of epidemiology and medicine at Columbia. Its goal was to provide HIV care and treatment for families in poor countries, using prenatal care and prevention of mother-to-child transmission (PMTCT) as the entry point for HIV-positive people into HIV care programs. The idea was to link prevention and treatment programs, and combine HIV care and treatment with broader reproductive healthcare delivery.⁷ The initiative formally launched on July 10, 2002 with the announcement of 12 demonstration sites in Africa and

⁵ *An Audit of HIV/AIDS Policies in Botswana, Lesotho, Mozambique, South Africa, Swaziland and Zimbabwe*, Human Sciences Research Council, 2004. See

<http://apps.who.int/medicinedocs/documents/s17836en/s17836en.pdf>

⁶ "1 in 4 Pregnant Women in South Africa Has HIV," *The BMJ*, 2001. See

<http://www.bmj.com/content/322/7289/755.2.extract>

⁷ Myer et al., "Focus on women: linking HIV care and treatment with reproductive health services in the MTCT-Plus Initiative," *Reproductive Health Matters*, 2005.

Asia. At the time, few in sub-Saharan Africa had access to treatment, and for most HIV was a death sentence.

The team wanted to bring recent US successes in HIV treatment and preventing MTCT to developing countries. "It became clear that the pediatric epidemic in the US had changed pretty dramatically," says Dr. Elaine Abrams, the initiative's deputy director for programs, director of the Family Care Center at Harlem Hospital, and associate professor of pediatrics at Columbia. "We had figured out how to prevent babies from acquiring HIV infection. We were seeing fewer and fewer new children with HIV, and we were effectively treating those who had HIV," she says.⁸ The team planned to build on its experience in treating a poor population in the US, adds El-Sadr.⁹ She recalls:

We believed that it was quite relevant to meeting the epidemic in Africa... that if we used the same principles that we applied when we're working in a disenfranchised, highly impacted community in the US, that many of these same principles would be relevant to the work in Africa. There really are more similarities than differences between populations around the world in terms of their needs, in terms of their aspirations.

That meant treating patients holistically, including psychosocial needs, rather than just providing clinical care. "From day one, I felt that in Harlem we had to shape the response to the epidemic in a way that would be responsive to the needs of the families in the communities that we worked with," says El-Sadr.

PMTCT challenges. Mother-to-child transmission rates ranged from 15 to 45 percent. By 2003, antiretroviral treatments for pregnant women had been able to reduce transmission rates to below five percent for those fortunate enough to get the medication.¹⁰ Getting treatment to women who needed it, however, was a major challenge. Less than five percent of HIV-positive pregnant women in Africa accessed PMTCT services in 2003, and an average of 1,600 infants were born with HIV infection every day.¹¹ "The prices of ART were pretty staggering, so who would pay for it? Cost and availability of drugs was the major impediment," says Abrams.

The standard first attempt to prevent MTCT was to give the mother a single dose of the antiretroviral drug nevirapine when she went into labor, and a single dose to the infant within 72

⁸ Author's interview with Dr. Elaine Abrams In New York City on April 29, 2014. All further quotes from Abrams, unless otherwise attributed, are from this interview.

⁹ Author's interview with Dr. Wafaa El-Sadr In New York City on May 14, 2014. All further quotes from El-Sadr, unless otherwise attributed, are from this interview.

¹⁰ "Mother-to-child transmission of HIV," WHO website. See: <http://www.who.int/hiv/topics/mtct/en/>

¹¹ Philipa Musoke, Recent advances in prevention of mother to child (PMTCT) of HIV, African Health Sciences, 2004. See: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2688329/>

hours of delivery. The simplicity of giving single doses of a single drug made this approach appealing to poor countries. Moreover, WHO guidelines at the time called for giving mothers a more effective combination of ARTs—dubbed highly active antiretroviral therapy (HAART)—only if they qualified for treatment based on the criteria for all adults: Stage III or IV illness or CD4 counts below 200.¹² However, few people had access to such treatment.

As the crisis intensified, it became clear that preventing the spread of HIV had to involve a major effort to protect the next generation. Public health experts increasingly viewed prevention of mother-to-child transmission as an essential aspect of tackling HIV, especially in poorer settings. But healthcare systems in resource-constrained countries had minimal capacity to provide PMTCT services, even at the level of consistently providing HIV testing at prenatal care appointments. People living with HIV, including HIV-positive pregnant women, were stigmatized, which made it difficult for pregnant women to seek PMTCT services in their communities in the first place. Moreover, of HIV-positive women in treatment, pregnant and postpartum women were more likely to drop out of treatment than non-pregnant women, according to the WHO. Morning sickness, concern about the effect of drugs on the fetus, and the burden of caring for a newborn made it hard for the women to stay in treatment. Women also often lacked support from their male partners. In one study in Malawi, more HIV-positive pregnant women *wanted* to disclose their status to their spouses than actually did.¹³

ICAP's MTCT-Plus Initiative was the first multi-country HIV treatment program. From its inception, it enrolled nearly 14,000 women and children in sub-Saharan Africa and Thailand in ongoing HIV care and/or treatment. Prenatal care was often the first point of contact in the health system for an HIV-positive woman in sub-Saharan Africa. "Women were coming into the antenatal care clinic for an HIV test," says Abrams. "If they were positive, they got, usually, a single dose of medicine to protect the baby—not terribly well, but it protected the baby." MTCT-Plus offered not only the opportunity to prevent HIV transmission from the woman to her baby, but enabled her to access treatment if she was eligible. In addition, women in the program were invited to bring in family members for HIV testing, and those found to be infected were offered similarly comprehensive care and, if eligible, antiretroviral treatment.

Treatment. At the same time, given the magnitude of the crisis and the need for hundreds of thousands, if not millions, of people to access treatment, not everyone was sold on the idea of trying to treat so many people, pregnant or otherwise, in low-income countries. International

¹² CD4 cells, also known as T cells, were immune system cells that signaled the onset of infection so the body could defend against it. A healthy person had a CD4 count of 500-1,000 cells per cubic millimeter. AIDS compromised the immune system, driving down the cell count. WHO used a CD4 count of 200 or below to designate an HIV-positive person as having AIDS.

¹³ Tadesse et al., "Likely stakeholders in the prevention of mother to child transmission of HIV/AIDS in Blantyre, Malawi," *Africa and Health Sciences*, 2004. See: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2688327/>

health experts debated whether treatment or prevention should take priority in poorer countries. The principal issues were the still-high cost of antiretroviral drugs, concern about patient inability to adhere to treatment (and the resulting risk of drug resistance), and the lack of facilities and systems to deliver such services to so many people.

In 2003, the World Health Organization and the joint United Nations Programme on HIV and AIDS (UNAIDS), the UN's lead HIV-AIDS entity, came down firmly on the side of treatment. They launched the “3 by 5” initiative, a plan to provide antiretroviral treatment to 3 million people living with HIV-AIDS in low- and middle-income countries by the end of 2005.¹⁴ WHO positioned 3 by 5 as a step toward making universal access to HIV-AIDS treatment and prevention a human right.¹⁵ Access to antiretroviral drugs was especially restricted in sub-Saharan Africa, and barely one percent of the 4.1 million people who needed HIV treatment were receiving it.¹⁶

The WHO criteria for who should receive ARTs were based on clinical staging, in this case a combination of its own disease stage rankings and the state of a patient's immune system based on CD4 counts.¹⁷ WHO recommended that an HIV-positive adult or adolescent start antiretroviral therapy if s/he had stage IV HIV disease, irrespective of CD4 count; stage III HIV disease with CD4 counts of less than 350; or stage I or II HIV disease with CD4 cell counts of less than 200. It was an emergency response aimed at treating people with advanced HIV disease. In January 2003, the US also started a push toward treatment, announcing the President's Emergency Plan for AIDS Relief (PEPFAR), which promised \$15 billion over five years to support HIV programming in developing countries, principally in Africa.

¹⁴ WHO 3 by 5 Initiative website. See: <http://www.who.int/3by5/en/>

¹⁵ Ibid.

¹⁶ “WHO Issues Global Alert after Grim Report on HIV/AIDS,” *BMJ*, 2003. See: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC200831/>

¹⁷ Stage I: Asymptomatic

Stage II: Weight loss of less than 10 percent of body weight, minor mucocutaneous manifestations (seborrheic dermatitis, prurigo, fungal nail infections, recurrent oral ulcerations, angular cheilitis), herpes zoster within the last five years and/or recurrent upper respiratory tract infections. Normal activity.

Stage III: Weight loss of greater than 10 percent of body weight, unexplained chronic diarrhea for more than 1 month, unexplained prolonged fever for more than one month, oral candidiasis (thrush), oral hairy leucoplakia, pulmonary tuberculosis and/or severe bacterial infections. Bedridden less than half the time in the last month.

Stage IV: HIV wasting syndrome; pneumocystis carinii pneumonia; toxoplasmosis of the brain; cryptosporidiosis with diarrhea for more than one month; cryptococcosis extrapulmonary; cytomegalovirus disease of an organ other than liver, spleen or lymph node (e.g. retinitis); herpes simplex virus infection; progressive multifocal leucoencephalopathy; any disseminated endemic mycosis; candidiasis of esophagus, trachea and/or bronchi; atypical mycobacteriosis; non-typhoid Salmonella septicemia; extrapulmonary tuberculosis; lymphoma, Kaposi's sarcoma and/or HIV encephalopathy. Bedridden more than half the time in the last month.

HIV in Swaziland

In 2003, Swaziland was a small, poor southern African nation with a population of just over a million in an area not much larger than the US state of Connecticut. Swaziland was listed as a lower-middle income country, but it had a high level of inequality. Two thirds of the population lived below the poverty line, subsisting on less than a dollar a day, and women accounted for two thirds of the poor.¹⁸ For pregnant women, HIV prevalence was 39 percent.¹⁹ Life expectancy had plummeted to 43 years, with HIV-AIDS the leading cause of death by far.

Swaziland also had entrenched cultural practices that contributed to the spread of HIV-AIDS. For example, Swazis valued large families, and women were expected to have at least five children. Men largely controlled women's reproductive decisions. One long-established custom was for a man to marry his brother's widow. In fact, one study found that Swazis considered monogamy, family planning and birth control to be foreign practices.²⁰ King Mswati III, the country's monarch and ruler, was a case in point. He had more than a dozen wives. The king's father, Sobhuza II, had 70 wives and more than 200 children when he died in 1982 after a 60-year reign.²¹ Polygamy and promiscuity were not uncommon in sub-Saharan Africa generally, but the scale of the behavior in Swaziland posed a particular challenge.

As far back as 1987, the government had created the Swaziland National AIDS Programme (SNAP) to coordinate the health sector response to the epidemic. In 2001, it added the National Emergency Response Council on HIV/AIDS (NERCHA) to coordinate the national response across sectors, set the country's HIV-AIDS strategy, and channel money from the government and international community to implementing organizations such as SNAP.²² Beginning in June 2003, Global Fund began providing funds to Swaziland for the purchase of antiretroviral drugs, and in November the Elizabeth Glaser Pediatric AIDS Foundation created a partnership with the Ministry of Health to provide PMTCT services.²³ The same year, SNAP created the National ART Programme to deliver antiretroviral treatments and overall care.²⁴

¹⁸ About UNDP in Swaziland. See http://www.sz.undp.org/content/swaziland/en/home/operations/about_undp.html

¹⁹ WHO website. See: http://www.who.int/hac/crises/swz/Swaziland_Aug05.pdf

²⁰ "Swaziland: A culture that encourages HIV/AIDS," *IRIN*, April 15, 2009. See: <http://www.irinnews.org/report/83937/swaziland-a-culture-that-encourages-hiv-aids>

²¹ Dana Hughes, "Life of a Swazi King: Bare-Chested Brides and Rolls Royces," *ABC News*, January 28, 2009. See <http://abcnews.go.com/International/AroundTheWorld/story?id=6480460>

²² National Emergency Response Council on HIV and AIDS (NERCHA) website. See: <http://www.nercha.org.sz/>

²³ Elizabeth Glaser Pediatric AIDS Foundation Call to Action Project, *Semi-Annual PMTCT Program Report October 2003-March 2004*. See: http://aidstar-one.com/sites/default/files/promising_practices/g3p_docs/CTA-Semi-Annual-Program-Report-Oct-03-Mar-04.pdf

²⁴ Swaziland National HIV/AIDS Programme. See: http://www.gov.sz/images/stories/Health/swaziland_national_aids_programme.doc

Then, in February 2004, the government formed a Technical Working Group (TWG) to monitor programs, debate research protocols and treatment regimens, and advise the government on HIV-AIDS policy. The group consisted of some 30 specialists, chaired by Ministry of Health staff and including representatives of international organizations working on HIV-AIDS in Swaziland. The government realized the country had reached a critical mass of international and domestic expertise, and was in a position to chart its own way forward through the crisis.

Okello on board

In October 2004, the Ministry of Health hired Dr. Velephi Okello as national antiretroviral treatment coordinator. Okello likes to say that as a child, she played doctor during her first day at school—and was hooked. When she got home, she told her mother that she wanted to be physician. She earned her medical degree at Mbarara University of Science and Technology in Uganda in 2000. "I chose Uganda purposely," she says.

I could have gone to South Africa, but I wanted to learn medicine in a country that is not so affluent. I just wanted to understand how to help the really desperate, the low socioeconomic status people in this country, people in the rural areas.²⁵

She practiced medicine in Swaziland for several years, but couldn't shake the thought that she could do more to address her country's health problems. "When you start practicing medicine, you realize that [for all the] people I've seen today, how many other people are out there?" she says. "That made me start thinking, there must be a way to get out there and touch on a much broader population, which brought me to my interest in HIV."

When she took the helm at the National ART Programme, Okello was feeling her way as a public health official. The Programme's policy on treatment and prevention initially adhered closely to the 3 by 5 initiative, she says: "We didn't ask too many questions. We just followed the instructions." Soon, however, Okello and her staff began to adapt what they were learning to Swaziland's particular context. For example, they came to believe that it would make sense to treat HIV-AIDS patients in dedicated facilities adjacent to existing hospitals and clinics. Opponents argued that this approach would fail because of the stigma attached to AIDS. So the team started small—with one hospital. It worked. Patients came in great numbers, many showing up early to queue. With that early success, the Programme replicated the parallel structure at clinics across rural areas. "People [were] coming in, even in the clinics closer to their homes," says Okello.

²⁵ Author's interview with Dr. Velephi Okello in Mbabane, Swaziland on May 29, 2014. All further quotes from Okello, unless otherwise attributed, are from this interview.

Okello also observed that with most clinics located in larger population hubs, it was difficult to reach patients where they lived, especially in the countryside. So she decided to decentralize services. The Programme placed its HIV facilities in a hub-and-spoke configuration (dubbed mother-and-baby), so that physicians at a “mother” facility could monitor and periodically visit “baby” facilities. The “baby” facilities also sent lab tests to and ordered drugs through the “mothers.”

She also addressed management deficiencies in the national healthcare system that she believed impeded effective treatment for HIV-AIDS patients. As a start, she put in place a National ART Programme management structure parallel to the national system. The National ART Programme’s vertical hierarchy, which also oversaw treatment facilities, made it easier to train and retrain physicians and nurses. The vertical structure also allowed HIV-AIDS facilities to order and stock drugs for themselves rather than working through the existing pharmacy system. In addition, the National ART Programme created its own patient tracking system, critical because the government’s health information management system at the time was deeply flawed, says Okello.

Nurses. Finally, there was a chronic lack of physicians. As a result, clinics in rural and poor areas were often staffed by nurses. While the nurses could administer refills of antiretroviral treatments, they could not initiate a course of treatment. Swaziland wasn't the only country facing this problem. Gradually, the public health community in Swaziland and elsewhere decided to train nurses to initiate antiretroviral treatment in clinics in a program dubbed the Nurse Initiated and Managed ART (NIMART). In Swaziland, the program was dubbed Nurse-led ART Initiation In Swaziland (NARTIS).

ICAP arrives

As Okello did what she could domestically, she also learned to take advantage of what international organizations could offer. Sometimes, meeting international standards and best practices could seem a burden. For example, on January 1, 2006, the WHO's guidelines for treating HIV-positive pregnant women became more complicated. It recommended that those not yet at an advanced stage of the disease receive an antiretroviral prophylaxis with the drug azidothymidine (AZT) twice a day starting at 28 weeks of pregnancy; and a single dose of the antiretroviral nevirapine (NVP) and a combination of the antiretrovirals AZT and lamivudine (AZT/3TC) during delivery and for seven days after. The infant should receive NVP and AZT for one week. However, the sickest pregnant women—those with Stage IV HIV disease, Stage III disease with CD4 counts

below 350, or CD4 counts below 200 regardless of disease stage—should get three-drug antiretroviral therapy (HAART) for life.²⁶

ICAP. Fortunately, as the new WHO guidelines, dubbed Option A, took effect, a new international aid organization opened an office in Swaziland. Two years earlier, in July 2004, the MTCT-Plus team at Columbia University had created an umbrella center—ICAP at Columbia University—with a mission to build and strengthen HIV-AIDS treatment and prevention programs in low- and middle-income countries. ICAP included the MTCT-Plus Initiative and other large-scale HIV programs, all focused on responding to the HIV epidemic and transforming health systems. Like MTCT-Plus, ICAP focused on PMTCT (among other areas of HIV programming) and took a broad approach targeting families. El-Sadr was ICAP founder and director, and Abrams led its pediatric and PMTCT work. Says Abrams:

We really started with the idea of family-focused treatment. You can't just treat the baby, you can't just treat the mother, you have to treat everyone in the household who might need it. And that idea of family-focused care and treatment has been a core ICAP value since the very beginning.

ICAP opened an office in Swaziland in January 2006 with a staff of three. It supported Okello and the National ART Programme with research, logistics and training. ICAP Director El-Sadr recognized that the Ministry of Health needed more resources. "And by resources I mean not just money, but also the health workforce that's necessary, the logistics, the assessment systems," she says. ICAP, she hoped, could leverage local resources and support and strengthen the health system to deliver high-quality services.

For example, ICAP trained nurses. "Only doctors were prescribing ART, at least officially, and they had to make a plan to train nurses to do ART prescribing and monitoring," says Abrams. "You have to increase the number of people who are able to do that, increase the number of clinics where this can be done," adds El-Sadr. Over the next several years, ICAP worked hand-in-hand with SNAP to expand the country's capacity to treat HIV-AIDS. ICAP became Swaziland's primary international partner for delivering antiretroviral treatment, and the majority of Swazis receiving treatment did so at facilities supported by the organization. El-Sadr found ministry officials, especially Okello, open-minded, collaborative, progressive, and willing to take an evidence-based approach. "Despite the immense challenge that Swaziland faced, the HIV program leadership had a consistently positive, proactive approach to tackling HIV," says El-Sadr.

²⁶ WHO, *Antiretroviral Drugs for Treating Pregnant Women and Preventing HIV Infection in Infants*, 2006. See: http://www.who.int/hiv/pub/mtct/arv_guidelines_mtct.pdf?ua=1

Money headaches

Principal among the National ART Programme's many challenges was funding for drugs. Shortages, due sometimes to funding snafus within government, sometimes to logistical complications in dealing with international drug suppliers, occasionally affected treatment delivery. These episodes sometimes prompted political action—an unusual event in the small, tightly controlled monarchy.²⁷ In August and September 2008, for example, during the run-up to parliamentary elections, Swazi protesters took to the streets to complain about a lack of drugs. The compromise solutions were not ideal—sometimes clinics replaced a prescribed but unavailable medication with one that was on hand; sometimes they even rationed drugs, giving a two-week supply instead of the usual one-month. But Okello defended the measures as justified under the circumstances. As she told the media in 2008: “We have had a challenge of very low stock, but we didn't send anyone home [empty-handed].”²⁸

Okello became adept at securing discretionary funds to head off shortages. She kept tabs on the central medical stores and when a shortage appeared imminent, she informed the Ministry of Health's principal secretary. She also contacted the physician most directly threatened by the shortage and asked him or her to also contact the principal secretary and the Ministry's finance controller. “Our finance department is really Ministry of Finance staff who are seconded to Ministry of Health,” says Okello. She explains:

So these are people who know the Ministry of Finance system, and they know who to contact. So the principal secretary just needs to talk to the head of the finance department in Health, and then they can hook up something.

Donor demands. Free money could also be a problem. The National ART Programme had found common ground with ICAP and other international implementing organizations, but Okello sometimes felt that collaboration with international donors increased rather than relieved her workload. For example Global Fund, like all international donors, required strict accounting from its recipients. This proved challenging for the Swaziland government, especially at the clinic level. “Global Fund was ‘print, print, file, file, file’, but... the facilities were not used to filing. Oh my God, their files were mixed up,” says Okello. In 2010, in fact, Global Fund audited Swaziland and, while there was no evidence of corruption, found a lack of adequate accounting controls. As a result,

²⁷ “Swaziland: Treatment programme woes,” *IRIN*, September 18, 2008. See: <http://www.irinnews.org/report/80465/swaziland-treatment-programme-woes>

²⁸ Ibid.

Global Fund called for NERCHA to refund \$1.18 million.²⁹ The government struggled but eventually found the funds. .

Another donor, who funded antiretroviral drugs, micromanaged the grant.³⁰ The donor's staff dictated the type of medical record files the clinics should use and even where to place computers. "I found it very, very hectic. We found that much of our time was spent responding to the donors," recalls Okello. Worse, donors sometimes withheld money pending the resolution of logistical concerns. "Money for drugs is withheld because they want a report on A, B, C and D," says Okello. "And even when you do the report, then they're like 'no, we're not satisfied. Go back'."

Foot the bill. But Okello was working to lessen Swaziland's dependence on foreign donors. One way to do that was to assume responsibility for ART drug payments. International funding was always intended to be temporary. The goal was to bring the epidemic under control and at the same time develop Swaziland's capacity to handle the problem. "From the beginning, we have always been told by our donors that you must have a sustainability plan, or a plan for takeover," says Okello.

Our objective was to transition to a more sustainable method of procuring the drugs. The drugs are the central point in the treatment and care program.

From 2003, when Global Fund began funding antiretroviral drugs in Swaziland, the government had also contributed funds. Every year in his annual speech, the king declared that the country would provide antiretroviral drugs to everyone who needed them. The details of how the government would meet that commitment fell to budget negotiations between the Ministries of Health and Finance. Okello provided the authoritative figures on how many patients would need treatment and the types and quantities of drugs required. "We look at the breakdown of what regimens are being taken up more quickly, so we will estimate so much for this regimen, so much for that regimen, and so much for all the other regimens," says Okello. Each year the projected number of patients increased based on SNAP's goals and capabilities, which were influenced by WHO guidelines. "In every [budget] meeting, I will sit in and explain what has changed," she says.

The government's goal was to fund purchases entirely, in part to be free of the constraints of international donors. The Swazi contribution started small, but each year the Ministry of Health was generally able to increase the country's share, depending on what was required to meet the projected need. For example, Global Fund's commitment jumped from \$2.3 million (17.9 million emalangeni) in fiscal year 2009-10, to \$6.7 million (51.9 million emalangeni) in fiscal year 2010-11.

²⁹ The money had gone to purchase 38 vehicles for delivering supplies to clinics.

³⁰ Okello declined to identify the donor.

Thanks to Global Fund's large contribution in '10-11, the government's share declined from \$6.6 million (50.6 million emalangeni) in 2009-10 to \$4.8 million (36.9 million emalangeni) in 2010-11.³¹ But for the following year, 2011-12, the government's share rose to \$8.2 million (63.3 million emalangeni).

Collecting evidence

Slowly, SNAP was starting to turn the tide of the epidemic in Swaziland. In 2011, evidence arrived to support that claim. The previous year, the government planned a campaign of voluntary adult male circumcision.³² Male circumcision had been shown to reduce the risk of HIV infection, but only about 15 percent of Swazi adult males were circumcised. Increasing the rate of circumcision looked like a promising pathway for decreasing transmission rates, and USAID agreed to help the Swaziland government with a male circumcision campaign. The US Centers for Disease Control (CDC) decided to measure the impact of the campaign on the epidemic. CDC contacted ICAP, which agreed to conduct a national HIV incidence survey to establish a baseline.³³

From December 2010 to June 2011 ICAP, in collaboration with the Ministry of Health, surveyed 12,603 households—7,129 men and 11,040 women aged 18-49. The HIV Incidence Measurement Survey (SHIMS) measured both the prevalence of HIV, and the rate of new infections. USAID then began the circumcision campaign with a goal of circumcising 150,000 males within a year; eventually, they hoped 80 percent of males would be circumcised. Unfortunately, the campaign fell short of the goal with only 20 percent of men accepting circumcision, says Dr. Ruben Sahabo, ICAP country director in Swaziland.³⁴

Nonetheless, the survey itself proved valuable. Apparently, the epidemic had plateaued. The survey data demonstrated that 31 percent of Swazis aged 18-49 were HIV-positive, the same prevalence rate as five years earlier. Prevalence continued higher among women (39 percent) than men (24 percent).³⁵ Women 30-34 were infected at the highest rate (54 percent); while among men the 35-39 age group took the high score (48 percent)—higher than in the past. But HIV among

³¹ The overall budget for antiretroviral drugs, however, rose from \$9.3 million (71.3 million emalangeni) to \$12.2 million (93.9 million emalangeni) for 2010-11. The Clinton Health Access Initiative (CHAI) and the Joint United Nations Programme on HIV/AIDS (UNAIDS) contributed about \$700,000.

³² Ayanda Nqeketo, *Reflections of collaboration experiences in Swaziland*, January 7, 2012. See: <http://www.observer.org.sz/index.php?news=34056>

³³ Author's interview with Dr. Jessica Justman in New York City on May 7, 2014. All further quotes from Justman, unless otherwise attributed, are from that interview.

³⁴ Author's interview with Dr. Ruben Sahabo in Mbabane, Swaziland on May 30, 2014. All further quotes from Sahabo, unless otherwise attributed, are from that interview.

³⁵ George T. Bicego, et al., "Recent Patterns in Population-Based HIV Prevalence in Swaziland," *PLOS ONE*, 2013. See: <http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0077101>

women under 30 and men under 35 had declined. These age-specific shifts suggested that Swazis with HIV were living longer thanks to antiretroviral therapy, and that new infection rates were dropping.³⁶

Follow-up tests and interviews conducted through SHIMS provided the first national measure of new HIV infections. The HIV incidence (new infections) rate in Swaziland in 2011 was 2.4 percent: 3.1 percent for women and 1.7 percent for men. Peak incidence rates were 4.2 percent for women aged 20-24 and 35-39, and 3.1 percent for men aged 30-34. The results matched expectations, and suggested that the rate of new infections, while still high, appeared to be dropping.

Treat to prevent

Treatment, it seemed, had made the difference. Controlling an epidemic meant preventing new infections, and by 2011 a growing body of evidence showed that treating HIV-positive people with antiretroviral drugs also reduced new infections.³⁷ "The more people you can effectively treat, the fewer new infections you should be seeing in your population," says ICAP's Abrams. "What treatment does is it shuts down the virus in your blood, and the virus stops reproducing."

In April 2011, SNAP launched a treatment-as-prevention framework that made treatment Swaziland's primary approach to reining in the epidemic. "We found that people who were not on [antiretroviral therapy] had high viral loads, compared to those who are on ART," says Okello. "These high viral loads made us start thinking we need to have a goal to reduce new infections. So issues like early treatment came in, including treatment as prevention." She adds:

In the beginning, our problem was focusing on reducing morbidity and mortality. So now that that has been reduced—and the graphs are very positive showing that this is reduced—we are now moving into saying, can we reduce new infections using treatment, because of the high viral loads among the community.

The treatment-as-prevention framework focused on preventing mother-to-child transmission and prioritized treating pregnant women. The previous year, WHO had updated its guidelines for HIV-positive pregnant and breast-feeding women, resulting in a simplified approach. For the less seriously ill, instead of different regimens for pregnancy, delivery and breast-feeding, the WHO recommended triple antiretroviral therapy from the 14th week of pregnancy until one week after breast-feeding ended. This was convenient because it was easier to

³⁶ Ibid.

³⁷ "Treating HIV-positive People with Antiretrovirals Protects Partners from Infection," *National Institutes of Health (NIH) News*, May 12, 2011. See: <http://www.niaid.nih.gov/news/newsreleases/2011/pages/hptn052.aspx>

stock and administer one regimen than three. CD4 counts were the indicator of who was less seriously ill, and therefore who qualified for the simplified regimen. The 2010 guidelines were labeled Option B.

Option B+. Still, testing for CD4 levels, the cornerstone of determining eligibility for antiretroviral treatment, remained a challenge for developing countries, especially in rural areas. In July 2011, Malawi's Ministry of Health implemented a variant of Option B, dubbed Option B+, that did away with CD4 testing and simply gave all HIV-positive pregnant and breast-feeding women triple antiretroviral therapy for life.³⁸ By using a single approach, Malawi was able to increase the percentage of HIV-positive pregnant women who received treatment. Other countries, including Uganda and Tanzania, followed suit.

Others, including Swaziland, were intrigued. But there was a drawback. Unfortunately, while Option B+ increased the number of pregnant women in treatment, it also increased the volume of ARTs needed. Worse, just as Swaziland and several countries began to consider Option B+, a major international source of drug funding dried up. On November 23, 2011, Global Fund canceled all disbursements worldwide because it was unable to collect \$2.2 billion in pledged donations.³⁹ The end of Global Fund support forced Swaziland's transition almost completely to self-funding. Swaziland's budget for antiretroviral drugs that first year without Global Fund, 2012-13, was \$13.3 million (102.1 million emalangeni). SNAP survived the sudden loss of Global Fund, but it did so without the added financial burden of Option B+.

Despite the absence of Global Fund and the increased strain on individual country budgets for anti-retroviral drugs, just five months later, in April 2012, WHO formally recommended Option B+.⁴⁰ The benefits were compelling: more pregnant women likely to receive treatment, protection against mother-to-child transmission in subsequent pregnancies, protection for HIV-negative partners, and simplified ART service delivery. In addition to reducing transmission, it promised to save lives by improving mother and infant health, says Okello. Treating all HIV-positive pregnant women for life would mean "a reduction in maternal mortality [from] HIV related complications in

³⁸ "Impact of an Innovative Approach to Prevent Mother-to-Child Transmission of HIV-Malawi, July 2011–September 2012," *CEC Morbidity and Mortality Weekly Report*, March 1, 2013. See: <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6208a3.htm>

³⁹ Donald G. McNeil Jr., "Global Fund Will Pause New Grants and Seek New Manager," *New York Times*, November 23, 2011. See: http://www.nytimes.com/2011/11/24/health/global-aids-fund-cancels-fund-raising-and-seeks-new-manager.html?_r=0

⁴⁰ WHO, *Use of antiretroviral drugs for treating pregnant women and preventing HIV infection in infants*, April 2012. See: http://www.who.int/hiv/pub/mtct/iatt_optionBplus_toolkit/en/

pregnancy due to HIV positive mothers being healthier, [and] a reduction in infant mortality due to less opportunistic infections among children," she says.⁴¹

Is this right for Swaziland?

Spurred by Malawi's experience, Swaziland's Technical Working Group began discussing Option B+ in October 2012. The initial debate was whether HIV-positive new mothers who were not sick should continue or discontinue treatment after the end of breast-feeding. In other words, should Swaziland—which was still using Option A—switch to Option B or Option B+? "We kept throwing it back and forth: Which is better? What are the pros and cons?" says Okello. "Of course, there are some good things about starting [during pregnancy] and stopping [after breast-feeding]."

For example, a young, recently infected pregnant woman was more likely than not to have a fairly high CD4 count, so under the previous guidelines she likely would not have begun ART therapy for another 10 years or so. Delayed treatment saved the state money, and relieved the woman of years of side effects plus the burden of adhering to the treatment regime. Nevertheless, continued treatment seemed the better route to ensure adherence generally, says Okello. Moreover, the National ART Programme was concerned about sending mixed messages, she adds.

If you start telling our population that they can start and stop, then it will compromise adherence for everybody else, because they see that people are surviving. They start, and they stop for 10 years, and they're still fine.

Option B+ could bring into the healthcare system people—particularly those with CD4 counts above 350—who would otherwise have avoided any monitoring or treatment. "It was difficult to get them to even come in and be monitored," observes Okello.

We realized that we have to do something more to pull in those who are [not yet eligible for] ART to get into treatment, because they are not even keen on attending the pre-ART clinics where they get other services.

But Option B+ also raised ethical concerns. Was it right to introduce a treatment regimen that could result in a non-pregnant woman receiving treatment because she had been pregnant in the past while a never-pregnant sister or neighbor with the same or worse HIV status went without treatment? Should Swaziland prioritize pregnant women if drug shortages meant infected non-pregnant women and men were left behind? Option B+ could easily divert scarce resources from more sick people to the usually healthier HIV-positive pregnant women, says Okello. "Men in

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Author's e-mail communication with Okello on September 6, 2014.

Swaziland have shown poor health-seeking behaviour and ideally we should be focusing on them with services, but with B+ we [would] spend more resources on women," she says.⁴²

Hard realities. The discussions in the Technical Working Group quickly moved from whether Swaziland should move to Option B+ to whether it *could* make the move. It would mean buying more drugs, training more healthcare workers and managing more patients at a time when the budget was already strained. "We are asking ourselves, if we move to [Option B+], we are surely, surely, surely going to get more people on treatment," says Okello. "If we have been struggling... now, how much more do you want to overload the system?"

The primary question was the cost of drugs. All told, Global Fund had provided Swaziland with \$76.2 million since 2003.⁴³ Its 2011 cancellation created a shortfall of \$2.1 million (18 million emalangeni) that Swaziland had to make up to finish its fiscal year. Since 2012, Swaziland had paid for all of its antiretroviral drugs. At the time, 12,000-15,000 HIV-positive people (men and women) entered the ART program each year. Based on HIV rates among pregnant women and the pregnancy rate in Swaziland, the National ART Programme estimated that 11,000 HIV-positive pregnant women per year would be eligible for treatment under Option B+. But not all of them would present as new patients: about a third were already in treatment. Of those not already in treatment, some 33 percent already qualified in a different category—their CD4 counts were below 350. That left some 5,000 pregnant women a year who would newly qualify for treatment under Option B+, meaning Swaziland would need between 33-41 percent more antiretroviral drugs.

There were further complications, stemming from human behavior. Several factors might reduce the effectiveness of Option B+ in Swaziland, says Dr. Harriet Nuwagaba-Biribonwoha, ICAP research director in Swaziland and an epidemiology instructor at Columbia. For example, the low rate of male circumcision and the challenge of adherence could offset gains. If patients don't adhere to their ART regimens, what is going to happen when HIV becomes resistant to the first-line medicines? she asks. Resistance required patients to switch to second-line drug regimens. "We are worried about shifting people to second line, because second line is more expensive," says Okello. "Much more, like almost 10 times more expensive than the other, first-line regimen."

Long run. Yet if Swaziland could afford the upfront costs of expanding treatment under Option B+, it would reap financial benefits over the long term because the country would have fewer new infections and would save money on treatment. Similarly, the country would need fewer doctors and nurses if there were fewer patients. Option B+ was also the most effective at

⁴² Author's e-mail communication with Okello on September 6, 2014.

⁴³ Mark Daku, "Swaziland, HIV/AIDS and the Global Fund," *Africa Initiative*, August 21, 2012. See: <http://www.africaportal.org/articles/2012/08/21/swaziland-hiv-aids-and-global-fund>

reducing mother-to-child transmissions. “You have to do what you can to make sure that you have a generation that’s coming up that’s HIV free,” says Nuwagaba-Biribonwoha. She explains:

You have to struggle to keep [that generation] HIV free right into their adulthood. But at least you give them that start. I don’t think that you can afford to put so many more infected children into the [population] by not doing the best you can.⁴⁴

In the big picture, moving to Option B+ would give healthcare workers and policymakers welcome experience in implementing early treatment that they could eventually use for all HIV-positive people in Swaziland, says Okello. Treating every infected person was the ultimate goal of global public health community. Implementing Option B+ would lay the groundwork for making policy decisions for when test-and-treat becomes a universal strategy, she says. Adopting Option B+ could also increase the capacity of Swaziland’s healthcare system in general, says Nuwagaba-Biribonwoha. “Could you leverage whatever investments you’ve made in that particular disease in terms of systems, in terms of training, to manage other conditions that are pertinent?” she asks. For example, ICAP was already using its HIV experience to address other health conditions such as mental health, non-communicable diseases and palliative care.

But as tempting as the benefits of Option B+ were, the main question was, could Swaziland’s already overtaxed budget handle the 33-41 percent increase in the quantity of drugs needed to treat all HIV-positive pregnant women for life? “The reality is that we don’t have adequate drugs, but we do want to take up the new guidelines,” says Okello. “People are thinking, should we or should we not? Are [we] sure we can move to [Option B+]?” she says. Could the country’s decentralized healthcare system handle the change, particularly when retaining patients in treatment was already a major challenge? If Swaziland did make the move, should it roll out Option B+ aggressively or take a phased approach? Was it ethical to introduce a treatment strategy that prioritized pregnant women over other people?

⁴⁴ Author’s interview with Dr. Harriet Nuwagaba-Biribonwoha in Mbabane, Swaziland on May 29, 2014. All further quotes from Nuwagaba-Biribonwoha, unless otherwise attributed, are from this interview.