HIV prevention: new pilots for beleaguered Swaziland

Swaziland, which has the world’s highest incidence of HIV, is embarking on pilot projects to offer treatment to people who are HIV-positive, irrespective of their CD4 count. Barbara Sibbald reports.

The good news is that the incidence of HIV in the Kingdom of Swaziland has stabilised over the past 5 years. The bad news is that it is still 31% among adults aged 18–49 years and, alarmingly, 43% among pregnant women. All told, an estimated 201,292 Swazis were HIV-positive in 2012, despite intensive efforts to mitigate the epidemic.

The government provides antiretroviral treatment (ART) and, in partnership with various organisations, is working to decentralise services, ramp up testing and treatment, and, due to a shortage of physicians and nurses, shift tasks to new cadres of health workers. Now the government and non-governmental organisations (NGOs) are testing a new approach: treat everyone who is HIV-positive, irrespective of viral load, CD4 count, or disease stage, with the aim of preventing the spread of HIV. Currently, in accordance with WHO’s 2010 protocol, only adults with a CD4 count below 350 receive ART, while those with a count above 350 receive prophylaxis azidothymidine (AZT) during pregnancy and for a week after birth, while the child gets nevirapine syrup daily for 18 months (throughout breastfeeding). In option B, women with a low CD4 count receive ART, while those with a count above 350 receive a prophylaxis of ART before and after birth, until 1 week after breastfeeding ends.

Three implementation studies are slated to launch this year. In February, Médecins Sans Frontières (MSF) will begin offering ART to all HIV-positive pregnant women in one health zone. In late winter, the International Center for AIDS Programs (ICAP) at Columbia University, NYC, USA, hopes to begin a comparison of two protocols for HIV-positive pregnant women. And as early as mid-2013, the Clinton Health Access Initiative (CHAI) plans to offer ART to all HIV-positive adults at ten sites.

Using treatment to prevent HIV transmission has been studied for years, but the turning point came with the August, 2011, publication by Myron Cohen and colleagues on the phase 3 clinical trial, HPTN 052 that showed a 96% reduction in risk of HIV transmission in serodiscordant couples.

Minister of Health and Social Welfare Benedict Xaba tells The Lancet “eliminating mother-to-child transmission of HIV by 2015 is the priority in order to ensure an HIV-free generation.”

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Swaziland currently uses option A of the two WHO-endorsed protocols for prevention of mother-to-child transmission (PMTCT). With option A, pregnant women with a CD4 count below 350 receive triple ART and the baby gets daily nevirapine syrup for 6 weeks; women with a count above 350 receive prophylaxis azidothymidine (AZT) during pregnancy and for a week after, plus a nevirapine injection at birth, while the child gets nevirapine daily for 18 months (throughout breastfeeding). In option B, women with a low CD4 count receive ART, while those with a count above 350 receive a prophylaxis of ART before and after birth, until 1 week after breastfeeding ends.

In some respects, Swaziland has had reasonable success with option A. Coverage is excellent: 97% of women attend at least one antenatal care appointment and 91% of those accept HIV testing. In 2011, 86% of HIV-positive pregnant women received either ART or AZT prophylaxis. At 6 weeks of age, 2.4% of infants tested are found to be positive.

“But after birth, things deteriorate”, says Kiran Jobanputra, MSF’s principal investigator in its Treatment for Prevention Research Programme. The total proportion of infants of HIV-positive mothers who tested positive in 2011 was 17%. There are problems with the data, says Jobanputra, but this is a “very worrying figure. It could suggest significant rates of transmission during breastfeeding”. This situation may be because babies are not getting their nevirapine syrup after mothers return to work.

There are also treatment difficulties before birth, says Velephi Okello, Swaziland’s national coordinator for antiretroviral drugs. Most health facilities lack CD4 testing, so HIV-positive women are given AZT and asked to come back for their CD4 results. But when they return, they won’t change their medication. “That means 55% are taking a suboptimal regime”, says Okello.

Within the past decade, Swaziland’s infant and maternal mortality ratios have increased by 26% and 160%, respectively, according to the UN. There are currently at least 69,000 HIV orphans in Swaziland. Okello says: “I’m happy [the HIV prevalence] is not rising, but it’s stabilising at a high level. With all the interventions, you would expect to see it going down.”

In April, 2012, WHO endorsed a third option for HIV-positive pregnant women in countries with
inadequate access to CD4 testing. With option B+, which was developed in 2010 in Malawi, women are put on ART as soon as they are diagnosed with HIV, irrespective of CD4 count, and they stay on treatment for life. In addition to preventing vertical transmission, B+ will likely benefit the women’s health and will help prevent sexual HIV transmission to uninfected partners. In September, Uganda began rolling out B+ in remote regions and other sub-Saharan African countries are considering it. B or B+ is already the norm in high-income countries.

“Putting someone on treatment as soon as they are positive is logical; it’s what we as doctors want”, says Jobanputra. “There’s no other infection where you wait until it has spread to treat it.”

B+ is a game changer, compared with option A. “You not only increase the number of people on ART”, says Jobanputra, “you also open up the idea that taking ART early is good and that’s a big barrier in Swaziland. People are reluctant to take it before they are sick. But starting early is healthier”, he maintains. “If you start early, you maintain a high CD4 for life. If you start late, you’re unlikely to get up to a high CD4 again.”

Pending MSF ethics review board approval, MSF’s 4-year implementation study is due to begin in February at Nhlangano, one of three health zones in the Shiselweni region. The study is expected to enrol 250 additional women per year; double the number of pregnant women now initiating ART. Each woman will be followed-up for 2 years.

WHO cautions that countries considering B+ should first do implementation studies to learn how best to put it into practice in their context. With this in mind, MSF’s research will assess the feasibility (uptake, adherence, and retention in care), effectiveness in terms of vertical transmission and treatment response of the mother, cost, and acceptability of B+. The latter is “one of the big questions”, says Jobanputra. MSF plans to interview health workers, patients, and relatives, particularly the partner, as well as observing clinical consultations. “Some won’t accept ART and we’ll find out why.”

If B+ is successful in Nhlangano and adopted by the National HIV Program, it will be rolled out nationwide. Pending approvals, MSF is also planning a second implementation study later in 2013 or early in 2014 to offer ART to all HIV-positive adults in the Nhlangano health zone, irrespective of CD4 count, viral load, and disease stage.

There is the fear that B+ could divert funds from testing and treating HIV-positive individuals, but MSF is planning to increase their testing and treatment efforts. Presently, 80% of those who need ART already have it; MSF is working with the Ministry of Health to increase that number to 90%. In the long term, treatment with prevention should save money since it reduces the incidence of HIV and opportunistic infections, says Jobanputra. A modelling study has shown that extending ART to everyone who is HIV-positive in South Africa would decrease infections by 45% and costs by US$10 billion over 40 years with break-even by 2023.

A second B+ implementation study, this one by ICAP at Columbia University, will compare the option A to B+ on a set of outcomes, primarily infant infection and mother and child retention on care. “We are testing the hypothesis that the outcomes will be better with B+ because it’s simplified and there are fewer opportunities for loss to follow-up in the cascade”, says ICAP’s Senior Director for Research and the principal investigator Elaine Abrams. “But the data supporting this hypothesis are sparse.”

ICAP’s study may begin by late winter, depending on approvals. It will last 3 years with 2500 to 3000 mother-baby pairs at ten facilities in the Manzini Region. “Scaling up clinical capacity to do B+ or B has the potential to greatly expand access to ART”, explains Abrams, who is also Chair of the WHO Maternal Child Health Guidelines. “This could be the turning point in the epidemic.”

The ICAP and MSF studies may well form the foundation of policy for offering B+ across Swaziland. “We will wait for results coming from these two pilot studies before a countrywide rollout takes place”, says Xaba.

CHAI is also involved in the treatment as prevention initiatives, but it hopes to focus on offering treatment to all adults who are HIV-positive in one geographical region. The 3-year implementation study is tentatively slated to begin in mid-2013. It will be led by Swaziland’s Ministry of Health and supported by other partners including CHAI and STOP AIDS NOW! as part of MaxART, a project to maximise ART for better health with the ultimate goal of zero new HIV infections. Specific study details are not yet available.

“The evidence behind treatment for prevention is really positive”, says CHAI Country Director Alison End. “It hasn’t yet been implemented on the ground in a government-managed health system and we don’t know if people will accept it. There are a lot of questions, but it is exciting.”

The three NGOs are collaborating with one another and the Ministry of Health. As End points out, a lot of their questions are similar to the MSF study, including understanding feasibility, accessibility, and acceptability, as well as scaleability; how much it really costs and whether it can be scaled up to the national level. The study outcomes may also be applicable to other sub-Saharan African countries, such as South Africa, Namibia, and Botswana, says Jobanputra. “You can’t generalise completely, but the context shows some similarities with other lower-middle income sub-Saharan countries.”

“We hope to become a model on the continent and globally”, says Minister of Health Xaba, “especially having been a country with a huge challenge of HIV”.

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