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South African AIDS Conference: Special Issue

By Theo Smart

The [5th South African AIDS Conference](#), held from 7-10 June, 2011 in Durban, showcased the recent remarkable achievements of the country's HIV/AIDS response.

Consequently, the conference was less concerned with groundbreaking clinical research, and more with the work of improving the care and health of the country's millions living with and at risk of HIV.

Evidence was presented supporting the move towards nurse-initiated management of ART (NIMART), and other task-shifting measures to train lay staff and community supporters. Meanwhile, a number of sessions focused on service innovations or shared operational expertise to improve the reach and quality of services for the prevention of parent-to-child HIV transmission, HIV testing and counselling and early infant diagnosis, the provision of ART for children, adolescents and adults living with HIV, as well as services to reduce the burden of TB in people with HIV. Some of these topics will be covered in future editions of HATIP. (You can sign up to receive HATIP by email at www.aidsmap.com/bulletins) This edition focusses on prevention of parent-to-child HIV transmission, and on treatment for children and adolescents.

South Africa takes its place as a global AIDS leader

The big story of the conference was how the country has emerged from years of being an AIDS policy backwater to become a global champion in the fight against HIV/AIDS. On the international policy front, the country has become a sophisticated voice, quite literally representing the interests of millions of people living with HIV, one that had been largely missing from the discourse on global public health priorities.

Some of the sophistication may have been acquired through interaction with human rights champions such as South African Chief Justice Sandile Ngcobo, who gave a rousing plenary address describing how South Africa's constitution and legal system were used to push the government into action on HIV. This unique history has helped to shape South Africa's HIV policies, and place a greater emphasis on human rights and equity than in many other resource-limited settings, though there are clearly still gaps in delivery and service uptake due to stigma, discrimination and inequality that must be dealt with.

Nevertheless, the country's progressive policies and the growing successes of its HIV programme are the result, after years of discord, of a newfound collaboration between the community, the medical and research establishment and the government, which is now willing to listen.

The country's leadership now appears to view these resources as strengths, and the HIV response itself as 'an opportunity to invest in the quality of life of our communities.' In fact, the government plans to leverage the HIV/AIDS and TB response, and expertise acquired in dealing with those diseases, to turn around the country's public health system.

Conference sessions were dedicated to engaging the HIV establishment in re-engineering primary health care and providing a

forum for people from the communities to talk about how health services could be designed to better meet their needs.

The conference chair Professor Francois Venter predicted that if the country kept to this winning formula of 'having all the right people in the same room' it would succeed where academics and public health specialists have failed in designing and delivering effective community health services. In addition, with the West increasingly abandoning its commitments, Dr Venter said South Africa would have to increasingly come to the aid of the rest of the continent.

A very different kettle of fish

"You may have noticed," Prof. Venter said at the start of the meeting's opening plenary, "that among all of the very important dignitaries that we have here, we don't have the Deputy President."

At first this sounded like an all too familiar story — South Africa's dignitaries have failed to show up at the South African AIDS Conference before. But this time, it wasn't to snub the conference organisers or to avoid being humiliated by HIV/AIDS protesters.

"South Africa's Deputy President, Kgalema Motlanthe," Prof. Venter went on to explain, "has been called away at the last minute, due to an appeal for him to be in New York with the Minister of Health, Dr Aaron Motsoaledi, at the United Nations General Assembly Special Session (UNGASS) high level meeting on AIDS."

The UNGASS meeting brings together many of the world leaders and experts to take stock of the progress and challenges fighting HIV/AIDS and to shape the future AIDS response. When it was last held in 2006 the world finally seemed to be moving towards responding effectively to HIV/AIDS.

The policy environment today is markedly different. With the ongoing international financial crisis, and debates about aid funding and global health priorities, the world has been retreating from honouring its previous commitments to support universal access to HIV prevention, testing, care and treatment. In addition, governments and multilateral organisations have failed to learn that an effective HIV/AIDS response cannot be achieved without protecting the human rights and meaningfully engaging populations most at risk, and the communities of people living with HIV. Rather, in many settings, HIV stigma and repressive laws are worsening.

It should be painfully apparent that whenever world leaders get together to set global policy for HIV/AIDS, South Africa, with over 5.5 million people living with HIV, the world's largest infected population, ought to have a vested interest. This was a lesson previous leaders had been slow to learn, but it was clear that the Deputy President understood what was at stake.

"The Deputy President was urgently needed," Prof. Venter said, because neither of the two countries "which had been appointed to represent Africa's interests at the assembly," had "stellar human rights records or particularly good HIV programmes," he went on. "I think it's very important for all of us that he is there; he needs to go and advocate on behalf of the country.... And we are delighted that South Africa finally internationally is providing moral leadership that we have been expecting for so long."

This was a remarkable thing to hear at a South African AIDS Conference from a leading clinician and thought leader from the HIV/AIDS community. As Prof. Venter would say at the close of the conference, "this is a very different kettle of fish."

The ghosts of South African AIDS Conferences past

South African AIDS Conferences have always been highly politicised affairs. For readers who may be new to the field or perhaps have just blotted it out of their memory, during the Durban International AIDS Conference in 2000, which served as the model for biannual national (regional) conferences, former President Thabo Mbeki shocked the world by questioning the role of HIV as the primary cause of the AIDS epidemic during the opening plenary.

He went on to announce that he was forming a cabinet of experts (at least half of whom were known pseudoscientists and AIDS denialists) to 'investigate' alternative explanations for why southern Africa was so sorely affected.

In response, over 5000 leading scientists signed the Durban Declaration, which refuted AIDS denialism and called on the government to pursue science and evidence-based policies to combat the HIV epidemic.

But in addition to bringing scientists to South Africa to confront denial, the conference chair Professor Jerry Coovadia, now Emeritus Professor of Paediatrics and Child Health at the University of KwaZulu-Natal (UKZN), had another reason for bringing the conference to Durban — to draw the world's attention to the very epicentre of the pandemic, as well as the lovely people, and the promising young nation, that it threatened.

But the setting of the Durban AIDS Conference threw into sharp focus the glaring inequities in HIV care and treatment available in rich countries versus what was available in the more resource-constrained countries with the greatest burden of HIV disease — which was nothing. This was most poignantly represented when a young boy with AIDS, Nkosi Johnson, who died one year later stood on the same stage as his President, and asked for equal access to antiretroviral therapy. The conference helped revitalise AIDS activism, and would serve as a catalyst for the effort to make treatment available in the poorest nations. "We have a monumental task ahead of us," Prof. Coovadia predicted at the time.

In South Africa however, the conference was followed by years of antagonism and mistrust between Mbeki's government (whose Health Minister was infamous for promoting garlic and beetroot to treat AIDS), and the country's HIV community — made up of people living with HIV, treatment activists, CBO/NGOs, doctors, nurses, caregivers and researchers. This rift between the government and the HIV community, and the resentment of 'outside interference', provided a constant source of drama during the first three South African AIDS Conferences.

"These conferences for me, and for many people, have marked various terrible milestones in our fight with government," said Prof. Venter.

Despite denialism and neglect at the top of government, the country's HIV research and medical establishment grew in size and expertise.

HIV treatment, human rights and legal activists (the [Treatment Action Campaign](#) and the AIDS Law Project — now called "Section 27"), fought valiantly, and successfully, for lower drug prices and to force the government into action, paving the way for the country's evolving HIV/AIDS response.

There were also dedicated people in the Department of Health who contributed to the effort, whenever their hands were free.

Finally, this response was assisted in no small measure by the Global Fund and other bilateral and multilateral donors, — in

particular, the PEPFAR programme. (This was partly because of a quality PEPFAR has often been criticised for — it had few qualms about bypassing an inefficient national government.)

The last South African AIDS Conference, held in 2009, marked the start of a dramatic reversal in the direction of the nation's HIV policies. Months earlier Mbeki had been forced to resign (for reasons unrelated to his AIDS policies), and the caretaker interim government (headed by the Deputy President Motlanthe) had made a clear break from the HIV and treatment denialism associated with the previous administration. The government finally seemed to be on board, but no one could be certain at that point whether the spirit of collaboration would last after the next election.

When newly elected President Jacob Zuma announced his new cabinet, he appointed a former student of Prof. Coovadia, Dr Aaron Motsoaledi, to run the Department of Health — and he has exceeded expectations.

"I want to salute our minister of health. He is an amazing man, he's got energy that tires us all sometimes," joked Prof. Venter.

Minister Motsoaledi possesses great wit, tenacity and showmanship that win support for his programme — perhaps even enough to make burn-out healthcare professionals care again. That doesn't mean there aren't still major gaps in service delivery or blind spots in policy, or that every public health directive the health department issues is adequate or likely to succeed — and activists still have a clear function as government watchdog. Nevertheless, with the minister at the helm, the government's commitment to deal with HIV/AIDS has clearly strengthened, and its strategies are now more likely to be informed by the considerable expertise of South Africa's HIV researchers, clinicians and communities of people living with HIV.

"For the first time, I think we're in a situation where we're trying to work out these problems together, where we have a government that certainly wants to do the right thing and is open to the fact that it respects us enough to listen to what we have to say," Prof. Venter said. "The kind of conglomeration of people you've got working together now is everyone — from the generic manufacturers to the activists to the hardworking department of health people who had to suffer through ten years of mismanagement and are now back with a bang. All of those people came together and have given us a programme that we can now start with — it's not perfect, but at least it's starting to look like a work in progress."

"And we've got some successes to be proud of — they are recent successes," he added.

South Africa's accomplishments

Professor Venter and the Deputy President highlighted some of South Africa's accomplishments:

1) **Just under 12 million South Africans got tested in the last year for HIV** — almost a quarter of the South African population in less than a year.

2) **The cost of antiretroviral therapy for the country has been cut in half in the last six months.**

Prof. Venter credited this to the Department of Treasury and some hard bargaining by the Department of Health. "Bringing down the cost of antiretrovirals just in the last six months by more than half is no small achievement. It has meant that treating HIV is getting to the stage where it's one of the cheapest chronic diseases to treat, in the South African system," he said.

3) **South Africa's own public expenditure on HIV and AIDS has increased by 40% per annum.** "In the current financial year we have allocated US\$1 billion to HIV and AIDS programmes," the Deputy President said in an address to the UN.

4) **The number of South African facilities providing ART is now about 1668.**

5) **1.4 million South Africans are now on ART, 400,000 of whom started treatment in the last year.** "That's 1.4 million people who are alive and well on antiretrovirals who would be either dead or sick. Four hundred thousand people who would be dead in a year or two. Their families would be burying them," said Prof. Venter. "There are not many things in medicine that save this number of people. And we have to thank a Department of Health, a donor, an NGO, an activist nation who have got together and have collectively made this happen."

As would later be reported at the conference, this number includes around 100,000 children initiated on ART, which appears to be associated with a drop or at least a stabilisation in the national under-five child mortality.

"I really do think that is something to be proud of as a country. Coming from a situation where we weren't doing particularly well or benchmarking ourselves against countries like Botswana and Namibia, we are starting to step up and show the leadership that is required. It's going to require a lot more. We need to almost double that number by the end of 2012. It's going to require a lot of effort on the part of all of us to actually get there," said Prof. Venter.

6) **Reduction in mortality:** ART appears to have had a clear impact on survival. Several years back, before such rapid scale-up of ART was considered possible, modelling by the Actuarial Society of SA had predicted that, in 2010, there would be 388,000 deaths due to the HIV epidemic, up from 257,000 at last count in 2005. However, the number of AIDS-related deaths has clearly dropping over the last couple years. Last year, it is estimated to have dropped to around 194,000, about 60,000 less than in 2005 and half the number projected. This sharp decline is attributable to the ART programme, according to Professor Yunus Moosa, of the University of KwaZulu Natal.

7) **TB is finally receiving more attention:** "TB has been the orphan of the health world for decades. It hasn't been given the resources it deserves but for the first time, it's being regarded as the emergency that it actually is. For the first time, we're seeing new drugs, new diagnostics. We need to now start making sure that our healthcare system is one that can tackle TB," said Prof. Venter.

Two separate symposia focused on advances in TB diagnostics, in particular the roll-out of Gene Xpert for more rapid TB diagnosis, while another symposium focused on the government's efforts to scale up TB infection control in health facilities. Other presentations would describe the decentralisation of multidrug-resistant TB care in KZN, and the development of tools, training and support to improve the implementation of basic TB infection control measures by clinic staff.

8) **Strengthened prevention:** "We are making continuous efforts to strengthen our prevention strategies," said the Deputy President in his taped address, noting that more than 50,000 men have undergone medical male circumcision nationally, along with an increase in the numbers of both male and female condoms being distributed nationally.

Another highlight of the meeting was the performance of the programme to prevent parent-to-child HIV transmission (PPTCT), which has reduced the rate of transmission to 3.5% at around 6

weeks of age — a profound improvement compared to reports a few years ago.

Public policy and the law must remove barriers to access, such as stigma and discrimination

"We've made significant progress in HIV and AIDS science. That is why the tone of this conference rightly is different from the many that have gone before," South African Chief Justice Sandile Ngcobo said in a moving opening lecture at the conference. "These are massive gains and they are worth celebrating."

But he added that not everything that ought to be done is being done, and the benefits of recent legal rulings do not reach everyone who needs them.

"Why is that so? The answer I would like to suggest to you is that the problem perhaps is no longer the virus, the problem is us," he said. He added that the advances in scientific knowledge over the past decades must be matched by parallel advances in public health policy and law, in order for the advances in the laboratory to translate into better outcomes for affected communities.

South Africa has a particularly progressive constitution and activists used the courts to force the government to provide essential services such as PPTCT. Likewise, the courts have played a critical role in dismantling statutory discrimination against those with HIV and AIDS. For instance, in a ruling against employment discrimination, the Chief Justice said the courts reasoned that:

"People who are living with HIV have been subjected to systemic disadvantage and discrimination. They have been stigmatised and marginalised. Society's response has forced them not to reveal their HIV status for fear of prejudice. This in turn has deprived them of help they would otherwise have received. People who are living with HIV are one of the most vulnerable groups in our society. Notwithstanding the availability of medical evidence as to how this disease is transmitted, the prejudices and stigma against HIV-positive people still persist," he said.

The court ultimately declared that people who are living with HIV must all enjoy special protection in the law: "In view of the prevailing prejudice against HIV-positive people, any discrimination against them must be targeted as the fresh instance of stigmatisation. And this is an assault on their dignity," the justices wrote.

"The impact of discrimination of HIV-positive people is devastating. It is even more so when it occurs within the context of employment. It denies them the right to earn a living. And for this reason the court said they enjoy special protection in our law," said the Chief Justice.

He noted that criminalisation of people living with HIV still presents significant challenges to the AIDS response.

"Even within the African Union where a compassionate and rational approach to HIV and AIDS is so critical, there are countries whose immigration laws either ban the entry of all HIV-positive persons into their country, or include restrictions on their eligibility to stay or work in their country. Discriminatory policies and laws are often motivated — at least in the field — by public health concerns. Laws that discriminate on the basis of HIV status are premised on a misunderstanding of where we are in the science of HIV prevention, transmission and treatment. In that sense they reflect a risk assessment that is likely not grounded in current science. Science has long moved away from the days when it was feared that HIV could be transmitted by sneezing or shaking hands, but sadly the laws in many countries have not," he said.

Ultimately, this limits the effectiveness of the AIDS response.

"The fight against HIV and AIDS is a multi-front war that must be waged in the arenas of public policy and the law, and in addition in the laboratories. We will not win the fight against HIV and AIDS, so long as people suffering from the virus are inhibited from testing and seeking treatment for fear of the stigma and prejudice they would face if they discover they are HIV-positive. And we will not win the fight against HIV and AIDS until the poor and the most vulnerable have access to antiretroviral drugs they so desperately need," he said in conclusion. "Science has made tremendous advances in the fight against HIV and AIDS but only public policy and law are capable of making interventions necessary for HIV-positive persons to live free of stigma and prejudice and to have access to lifesaving drugs that allow them to live normal lives."

While the courts may have needed to force the South African government into action, its judgements have informed activism and the development of public policy in the country — which grounds the HIV/AIDS response more solidly upon a human rights foundation than other countries in the region. The regional AIDS response would benefit if South Africa were to provide more leadership in protecting the human rights of the most vulnerable groups and of people living with HIV outside its borders.

Extending the lessons and leadership shown on HIV/AIDS

One of the best ways to fight stigma and discrimination against people living with HIV and most-at-risk populations is to engage them in the response. More effective health services can only be designed with the input of the community.

In his taped address to the conference, Deputy President Motlanthe demonstrated his firm grasp of what is needed to move the HIV/AIDS response closer to its goals, and perhaps fix the South African health system as well.

"Collective ownership of the strategic interventions adopted must therefore speak to our ability to attain the highest impact and address those most at risk. Issues of resource allocation and mobilisation, leadership, accountability and improved service delivery by way of enhanced implementation of healthcare services are some of the key deliverables that we need to address," he said.

One of the more recent goals of the South African health system, which was discussed in at least one session of the conference, was the re-engineering of primary health care so that it effectively meets the needs of communities. This is an indication of the ambition and growing self-confidence of South Africa's Department of Health.

"It is probably one of the most profound changes that has been proposed by a healthcare system in the last 20 years," said Prof. Venter. "This is something we all are going to have to engage with and which is a very exciting community-led development which I'm hoping is going to mean that it's going to make healthcare much more available to the public."

But he also thinks the re-engineering of primary health care is one area where South Africa may be able to succeed precisely because of its experience with HIV/AIDS.

Prof. Venter also commented on the 'AIDS backlash': the complaints from some academics and public health specialists who claim that HIV/AIDS has received too much attention and weakened health systems, and that funding should instead be directed to other global health priorities.

Most of these complaints are unfounded, but Venter said the HIV world should take ownership of some of the criticisms, such as the need to increase efficiency — which is one of the reasons why task shifting needs to be scaled up. Additionally, HIV has received

attention that other diseases *also* deserve. But this should be seen as an opportunity to apply the AIDS industry's experience to these other health needs and the health system in general.

"Part of the challenge for us in the HIV world is to go and repair the rest of the healthcare system. We've made some real strides forward in terms of understanding health care for chronic illnesses. Diabetes, hypertension, asthma are crying out for the same sort of initiative," he said. "If there's a preventable disease out there I would hope that all of us will be out there to try and fight as hard for our other patients with other diseases that are not HIV as we do for HIV. And I think that that's what this primary health care re-engineering is about — it is an opportunity to take those lessons out."

"Sometimes when public health people, come to me and say: 'You know we've tried. Why couldn't we do this thirty years ago?' Well the reason is, you didn't get everyone in the room who needed to be in the room! You can't sit and make a policy at the top level in a room and then expect it to be implemented at primary healthcare level. You have to get everyone in the room and you need lots and lots of players. That is why the South African AIDS response has improved — we've got everybody in the room together. And I think that public health needs to take a lesson from us," said Prof. Venter.

While the backlash against AIDS funding is less prevalent within South Africa, it has contributed to weakening global commitment to the HIV response and must be confronted. A very real consequence of the AIDS backlash might require another kind of leadership from South Africa.

"I think in every country, except South Africa and Botswana, whose entire antiretroviral programme is funded from their tax payers, the fact that the donors are starting to say: 'Enough already!', is something that should make us all very, very scared. Because it's all very well to handle this in South Africa but I think we recognise the obligation we have to the rest of Africa, to try and help them dig themselves out of the sand pot we were in at the beginning," he said.

South Africa's lobbying at the UN

This was the sort of situation the Deputy President was trying to prevent with his trip to New York. At the close of the conference, Prof. Venter gave a glowing report of how the Deputy President had acquitted himself at the meeting in New York.

"The first thing he did, which is a direct firing across the bows, on everyone who thinks that we should inhibit and use our culture to oppress women, to oppress gay men, to oppress sex workers — he went out and he asserted that this is what's in our constitution," said Prof. Venter. In addition, the proceedings from the conference informed the Deputy President's testimony to the UN. "It's something we do need to report, that it came straight out of this conference, straight through his lips and straight into the UN."

The Deputy President also told the UN meeting that South Africa is currently considering how it might introduce treatment for all at a CD4 count of 350, and plans a social mobilisation strategy to get people to access treatment before they get very ill. South Africa's mass testing and counselling campaign will continue, and efforts to re-engineer primary health care will be stepped up.

He emphasised: "Global solidarity is critical and as we continue to explore alternative ways of resourcing this major crisis, we must work in partnership with communities, development partners and civil society. An AIDS-free world is an attainable goal: let us remain committed to this vision."

How much of an impact South Africa will have on the international global health policy front has yet to be seen. But

having corrected the course of its AIDS policy, the country recognises the threat that the AIDS backlash represents, realises that it has to represent its own interests and is becoming increasingly confident of what it has to offer.

The Community Exchange Encounters rapporteur of the conference expressed the new sense of possibility and promise, saying: "We must create a forum for civil society to set strategic and common goals that will allow South Africa to be the activist nation of the African continent".

Perhaps the rising young power will negotiate a better deal for the region. If not, perhaps South Africa can join together with some of the other emerging BRICS economies to fund and implement health policies that are not so dependent on the fickle whims and trade policies of the wealthiest nations and multilateral organisations.

South Africa is moving towards an AIDS-free generation, and improving survival in children living with HIV

By Theo Smart

Reductions in vertical HIV transmission to infants and improvement in paediatric survival attributable to the scale of and quality improvement of prevention of parent-to-child transmission (PPTCT) and antiretroviral therapy (ART) services for children were some of the biggest success stories reported at the South African AIDS Conference in Durban this June. Many HIV-positive children are living into adolescence, however there are also worrying signs that treatment options currently available in the country may not be adequate to keep all of them in good health into adulthood.

Leading off the good news were reports that South Africa is dramatically reducing perinatal HIV transmission among HIV-exposed infants. HIV prevalence is down to 3.5% at the first immunisation visit (4-8 weeks post-partum), according to the first national surveillance study of PPTCT (still often called prevention of mother-to-child transmission (PMTCT), conducted in the last half of 2010.¹ These findings were met with nothing short of jubilation — one report suggested that over 67,000 infants had been saved from HIV infection.

However, Dr Ameena Goga of South Africa's Medical Research Council, who presented the survey findings, cautioned that the percentage of children who ultimately become infected will be higher, particularly since a significant proportion of the children are not being fed safely (with either exclusive breastfeeding or exclusive formula feeding) by their caregivers (see *What about late postnatal HIV transmission?* below).

Nevertheless, poster presentations provided preliminary indications that much, though not all of the prevention benefit, is being sustained over time in some sites with well-supported programmes. While the better outcomes are partly a result of improved PPTCT guidelines (see below) the poster presentations also provided a wealth of information about a number of specific innovations that have been implemented at some sites, and that

could be scaled up more widely to improve service delivery of some of the key PPTCT interventions.

Background on prevention of vertical transmission in South Africa

Since the first projects to prevent vertical HIV transmission to infants were launched in South Africa in 2001 — after a hard-fought legal battle with the government — there have been several isolated reports on the impact of the intervention in the field. For most of the last decade single-dose nevirapine (sdNVP) at labour was the key intervention offered to pregnant women who had tested HIV-positive.

For instance, Dr Goga noted that the earliest report, a record review at Helen Joseph/Rahima Moosa Hospital from 2001-2002, reported an 8.7% HIV transmission rate in exposed infants at six weeks post partum. Similarly an assessment of the programme in Khayelitsha in the latter months of 2003, which used AZT prophylaxis from week 34 of pregnancy, reported that a similar percentage (8.8%) of exposed infants were HIV-infected when tested at week 6-10 post-partum.

Subsequently, the Good Start Study, conducted from October 2002 to November 2004 at three sites (Paarl (Western Cape), Umlazi (KwaZulu-Natal), and Umzimkulu, (Eastern Cape)), reported highly variable programme performance.² Perinatal HIV transmission ranged from 8.6% in Paarl up to 13.7% in Umzimkulu — but the study also found that much of the benefit of sdNVP was lost over time due to ongoing exposure to HIV in breastmilk, especially in Umzimkulu, where HIV-free survival at 36 weeks was only 65%. Poorer outcomes were partly due to feeding practices, as well as factors such as maternal viral load, prematurity, socioeconomic score, access to antenatal care and the quality of counselling received.

Distressing as these findings were, a subsequent study that measured both programme reach and effectiveness found very high rates of infection, 20.2%, among HIV-exposed infants attending their first immunisation at seven clinics in KZN (between Aug 2004 to July 2005).³ There was no improvement in a subsequent study at three primary health clinics in KZN between November 2007 and February 2008, with 21.9% of HIV-exposed infants testing positive.⁴

In some parts of the country at least, the programme was clearly failing to adequately protect HIV-exposed infants.

Consequently, reducing vertical transmission became one of the highest priorities in the South African National HIV/AIDS Strategic Plan (2007-2011). The goal has been to reduce HIV transmission to 5% in HIV-exposed infants by 2011. To accomplish this, performance would have to be improved along each step of what has been called the PMTCT cascade — meaning the separate interventions involved in the programme including coverage, HIV testing uptake, results delivery, intervention delivery, follow-up and support, etc.

In addition, two major updates have been made to the national regimen for prevention of vertical transmission (PVT), adding further steps to the cascade. First, in 2008, all HIV-positive pregnant women with CD4 counts below 200 were to be put on ART (for both their own health and to reduce transmission), while those with CD4 counts above 200 were to be placed on AZT from 28 weeks of pregnancy and given sd-NVP at labour. The infant was also to be given sd-NVP at birth followed by AZT to day 7 and then given an HIV DNA PCR test, 4-6 weeks after delivery (not just to monitor programme performance but because identifying HIV-infected infants and putting them on ART quickly dramatically improves

survival). This new regimen would require much better linkage and/or integration between the PVT programme, the ART programme in order to provide CD4 cell testing and ART, as well as maternal child health services.

Then in April 2010, South Africa updated its guidelines to offer ART to all pregnant women with CD4 cell counts below 350, and put the rest on AZT from week 14 after gestation, dropping sd-NVP for the mother as there was a potential for the development of resistance that could limit her future treatment options. Instead, the infant was to be placed on nevirapine for at least 6 weeks or for the duration of breastfeeding. Again early infant diagnosis was to be performed at the first immunisation visit.

Although there was no structured surveillance to evaluate the operational effectiveness of the programme, data from the National Health Laboratory Service submitted from infants under two months of age was 8.2% in 2008, dropping to 5.8% in 2009. However, these data could be biased because mothers who were most adherent to the programme would be most likely to bring in their children for HIV testing. A more rigorous study was needed to monitor the programme's effectiveness.

The South African PMTCT Evaluation (SAPMTCTE)

The South African PMTCT Evaluation is a cross-sectional survey designed to periodically assess HIV transmission in infants at their first immunisation visit. In addition, the survey was designed to assess coverage of the key interventions and services for prevention of vertical transmission, and look for any associations between the vertical transmission and ART regimen, maternal background characteristics, healthcare services and maternal and infant health status.

The study included infants aged 4 to 8 weeks making their first immunisation visit (excluding older or younger infants, or infants requiring emergency care) at randomly selected primary and community healthcare clinics (n=580) in each of the nine provinces (note, a limitation of this study is that it did not include hospitals). The study aimed to enrol 12,200 caregiver-infant pairs selected using consecutive or random sampling methods – depending on size of facility. Caregivers agreeing to participate in the study were interviewed, and their infant's dried blood spot (DBS) was sent in for HIV testing.

If the mother identified herself as being HIV-positive, her infant's specimen was sent directly for HIV DNA PCR testing. If she did not, her infant's specimen was first screened with an HIV ELISA test to identify HIV-exposed infants, and PCR was performed on all antibody-positive specimens. (HIV antibody testing will detect all HIV-exposed children because infants inherit maternal antibodies, which may remain in circulation for up to 18 months after birth. HIV DNA PCR can distinguish between infection with HIV and maternal antibodies by detecting HIV DNA.)

Between June and December 2010, 92% of caregivers of eligible infants agreed to participate in the survey, and interviews and DBS results were available for 9915 matched caregiver-infant pairs. This fell somewhat short of the target sample size that the researchers had calculated as necessary to obtain valid national and provincial level transmission. To adjust for the shortfall, the analysis was weighted based upon the sample size achieved in relation to the live births in the province over the study period – though the researchers noted that this assumed that the available sample was representative of the whole province, something less than certain in

the Eastern and Northern Cape, which reached less than 60% of desired sample size.

Results

The study found that infants in South Africa are at a very high risk of HIV exposure, but the PPTCT programme in most provinces has become more effective than in the earlier reports. According to the weighted analysis, 31.4% (95% confidence interval (CI) 30.1-32.6%) of all infants born in South Africa are HIV-exposed, ranging between 15.6% (95% CI 13.0-18.3%) in the Northern Cape (though this province was significantly undersampled), and 20.6% (95% CI 16.8-24.9%) in the Western Cape to a high of 43.9% (95% CI 39.7-48.0%) in KwaZulu-Natal.

HIV infection at 4-8 weeks was diagnosed in 3.5% (95% CI 2.9-4.4%) of the HIV-exposed infants nationally, but programme performance varied substantially by province. If the specimen in the Northern Cape was indeed representative, their programme has a low transmission rate of 1.9% (95% CI 0.1-4.5%), while Gauteng also does well with 2.3% (95% CI 1.3-3.3%) – however the Free State and Mpumalanga did substantially worse with 5.7% (95% CI 3.5-7.9%) and 6.2% (95% CI 4.5-7.9%) of the exposed infants testing positive, respectively.

Despite its very high maternal HIV prevalence KwaZulu-Natal has cause to be proud with only 2.8% (95% CI 1.7-4.0%) of its many HIV-exposed infants testing positive, somewhat better than the national average – and worlds away from the 20-21% transmission rate described in earlier reports.

Overall, the study found the weighted national HIV prevalence at 4-8 weeks was 1% (95% CI 0.8-1.2%).

During the survey interviews, the caregivers were asked about whether they had been offered or received the key interventions along the PMTCT cascade – such as HIV testing, the return of their results, if HIV positive whether they received a CD4 cell test, were put on ART, etc.). These data showed variabilities in service coverage and allowed the researchers to analyse the performance and uptake of the various individual interventions in each provincial programme.

Notably, ELISA testing revealed that 4.1% of infants whose mothers reported being HIV-negative were actually exposed to HIV – possibly because the woman had become infected in the time since her antenatal test. This underscores the need to provide repeat testing services in pregnancy and to offer couples testing to encourage the woman's partner to get tested.

What about late postnatal HIV transmission?

In other studies up to 40% of vertical transmission has been reported to occur in the late perinatal period as a result of exposure to HIV in breastmilk. Transmission primarily occurs when mixed feeding is practised (as opposed to exclusive breastfeeding which poses much less risk). Unfortunately, 18% of the caregivers of HIV-exposed infants reported practising mixed feeding of their HIV-exposed infant in the last eight days before their interview. Again, this varied substantially by region, with the lowest rates in the Western Cape but very high rates in Mpumalanga and Limpopo.

To the extent that they are implemented, South Africa's current guidelines for the prevention of vertical transmission should reduce the risk during the late postnatal phase when compared to previous years. Nevertheless, more infants can be expected to become positive and the rate of final HIV transmission will be higher than that reported at 6 weeks.

"This emphasises the importance of tracking MTCT rates until 18 months to measure the effectiveness of the complete PMTCT programme," said Dr Goga. So in 2011 and 2012, the SAPMTCTE will follow up the infants to measure HIV transmission rates between six weeks and 18 months. The survey will also be repeated each year to track vertical transmission rates over three years, and will ultimately be integrated into the Department of Health's routine M&E systems.

"The quality of the PMTCT programme varied across province," said Dr Goga. Consequently, these results will be shared with each province to show them where there are gaps in their service delivery – such as a failure to provide CD4 cell testing and deliver the results in a timely fashion, failure to get those women who qualify onto ART, or failure to provide adequate counselling or support for safer feeding options. The results will also be used to set new targets for each province

"The SAPMTCTE data shows that virtual elimination of paediatric HIV could be possible by 2015, with intensified effort. However, we need to address the postnatal component and variabilities in PMTCT service coverage," Dr Goga concluded.

Suggestions of further reductions in HIV transmission at 6 weeks AND 18 months at Kheth'Impilo supported sites

On the day before Dr Goga announced the survey results, a poster presentation from Kheth'Impilo, an NGO that supports health services and community-based adherence interventions at primary healthcare clinics and district hospitals in KZN, Mpumalanga and the Eastern Cape, reported similar findings at supported sites over a period beginning in October 2009 through the end of March 2011, suggesting continued improvement in a number of PPTCT indicators, including reductions in HIV transmission at six weeks and 18 months.⁵

Kheth'Impilo provides a number of support services to these facilities, including infrastructure support, patient flow adjustment, register development and supply, as well as critical staff including doctors, nurses, pharmacists, social workers and more recently PMTCT quality mentors (QMs), who rotate between several sites in a sub-district. The PMTCT quality mentors coach antenatal clinic staff using quality improvement approaches to identify service delivery gaps, help them identify and try out potential solutions, and assess the outcomes before scaling up implementation (plan, do, study, act). KI also employs a community services cluster – a team of patient advocates and community educators who support adherence to ART and the PPTCT protocol, make certain that patients aren't lost to follow-up and achieve successful referrals between services. They also encourage testing of partners and household members – including infant testing at six weeks and 18 months.

The poster described programme data aggregated from DHIS reports by quarter, drawn from the monthly reports supplied by each participating clinic. The data were cross-sectional, and are not individual level cohort data, so the denominators used are sometimes estimates. However, the clinics use the data to inform ongoing quality improvement, and the poster stressed that each site's personnel review and analyse the data closely to make sure they are an accurate reflection of outcomes, and identify and correct gaps in each monthly report before submitting it. Muddying the picture, however, is the fact that the number of sites being supported increased from 14 to 58 over the study period.

That being said, some trends worth noting emerge. There is a slight progressive increase in the women who are already aware of their status when first visiting the antenatal clinic – which the

poster authors suggest is possibly a result of the government's HIV counselling and testing campaign. The sites succeed in getting almost all of the women not already known to be HIV-positive to test at booking.

Moreover, an increasing proportion of women agree to be tested again around week 32 of gestation – from 15.7% in the first quarter to 27.9% in the most recent quarter. This measure is important because it seeks to detect HIV infections that occur during pregnancy.

Coverage of ARVs for PPTCT to women not on ART is almost universal. The percentage of women on ART for their own health has recently increased, largely, the authors say, due to the increased number of women qualifying for ART after the 2010 ART guidelines. Unfortunately, the poster did not report on the percentage of positive women getting their CD4 cell counts before delivery or the percentage of women qualifying for ART who received it – or how long before labour they received it.

About two-thirds of the women agreed to have their infants tested for HIV by PCR at six weeks – and there has been a marked reduction in early transmission since the first quarter of 2009, when 9.7% of the HIV-exposed infants tested positive, to the most recent quarter when 2.4% tested positive.

At 18 months follow-up, the poster reports a "massive undertesting" of infants. Nevertheless, the data here also suggested a substantial decline in HIV prevalence, with 10.7% of 18-month-old infants testing antibody positive in the first quarter, and 3.8% testing positive in the quarter ending in March 2011. While these figures are not a reliable measure of infection in the cohort, given the missing data, the trend over time is encouraging.

The authors note that the difficulty in obtaining timely CD4 and PCR results is a challenge to improving outcomes – and that point-of-care tests are needed that can be performed by a staff member on site who can also counsel patients. The authors state that another challenge for the PPTCT programme is the lack of adequate data management tools to monitor the key indicators and interventions of the programme. Meanwhile staff burnout and the difficulty of providing infant follow-up out to 18 months are perennial problems.

Strategies for improving PPTCT: examples of successful programme improvement

In addition to the quality improvement, mentorship and community-based interventions described above, several other posters provided valuable insights and strategies to improve PPTCT programme performance and outcomes in infants.

Proper data recording itself appeared to be associated with better programme performance in a study in a sub-district in the Northwest Province that evaluated recorded indicators that were associated with proper delivery of infant prophylaxis – which was only successfully provided to 78% of HIV-exposed infants in the sub-district. Significant predictors of successful infant prophylaxis delivery included making certain there was an ANC card in the delivery file and that the mother's HIV status was properly reported in the Maternity register.⁶ In addition, documentation that a CD4 cell count had been taken and that PPTCT ARVs were provided to the mother were also significant predictors of whether the infant would be appropriately treated. The authors noted that "each step of the PPTCT cascade properly completed seemed to build momentum towards successful provision of the intervention to the infant."

The need for better documentation – in particular, patient-held cards clearly documenting maternal and infant HIV status, was also

noted in a feasibility study for SAPMTCTE that looked at whether early infant diagnosis services could be provided by primary health clinics, integrated into routine immunisation and child healthcare services, and what sort of linkages existed between early infant diagnosis (EID) and ongoing treatment, care and support services.⁷

In answer to the latter question, significant problems were identified making successful linkages between the immunisation, PPTCT and maternal child health services. The authors concluded this was because of the lack of a consistent system clearly explaining her and her infant's situation to healthcare workers at the referral site. The recently released new *Road to Health* card, which records immunisation and growth to the age of five years had not been taken up widely at the time of the study, but could address some of these issues.

Referral systems for children testing HIV-positive to ART and community-based support services also need to be made more effective. Only 57% of clinics reported having a mechanism to ensure these children made it to ART services, and the ART services also had poor mechanisms for follow-up.

While most of the clinics had trained personnel, in particular professional nurses, who could draw blood for early infant diagnosis, clinic managers identified a clear need for task shifting to trained nurse assistants and lay counsellors. Maintaining adequate stock of dried blood spot kits was an issue for some provinces. The study also noted a need to develop communication strategies to update managers and healthcare providers when programme policies or guidelines are updated. Notably, a study of participants and healthcare workers in a PPTCT programme in Soweto reached essentially the same conclusion after finding that many of the women, and even a number of their PPTCT nurses, think they have a good understanding of the guidelines, but actually have poor or inaccurate knowledge in sometimes critical areas.⁸ The authors recommended improving community awareness of PPTCT and mentorship of staff.

One changing policy includes the recent changes in South African regulations to allow nurses to prescribe antiretrovirals. Another oral study presented at the conference described how, despite training, nurses at primary healthcare clinics were reluctant to prescribe — and this was delaying access to ART in pregnant women qualifying for treatment. A separate article in this HATIP on task shifting will describe how quality improvement measures helped nurses in one rural sub-district overcome their reluctance and begin putting pregnant women on ART.

The need to increase community awareness and demand for PPTCT services was also identified in a report describing the experience in sub-districts of the Eastern Cape supported by the international NGO PATH to reduce vertical transmission.⁹ In addition to improving the quality and access of HIV testing and counselling services during antenatal care, better patient education and support including improved counselling on family planning services and on safer infant feeding practices was also a clear objective. Enhanced community engagement and leadership in the programme was pursued as a strategy to reduce stigma and increase support for HIV-positive pregnant women. Consequently, regular radio talk shows were organised to discuss topics such as pregnancy planning for HIV-positive couples, care of HIV-positive pregnant women and safer infant feeding practices.

At the same time, PATH sought to strengthen the health system (with better data reporting, supply logistics, referral linkages, lab test performance and turn-around and developing training curricula etc). Training and support were also enhanced. PPTCT training was scaled up to all previously untrained staff members and updates

provided to trained staff on guideline revisions. This was accompanied by increased monitoring and supervision, as well as clinical mentoring.

PATH employed a quality improvement process at the supported sites. Once the clinic staff had been trained on the guidelines, a meeting was held where service delivery gaps were identified by comparing actual performance to the programme targets. Staff were asked open ended questions to identify the root causes of the gap and potential solutions. These were applied, the results were monitored and analysed on a monthly basis, and implementation went forward depending upon the results.

PATH also got a local cell phone service provider to supply clinics with free SMS bundles, which were used to remind mothers to bring their infant in for early infant diagnosis at six weeks.

The PATH poster provided a brief snapshot of some of the programme results. Antenatal testing rates in the four supported districts is above 100% (due to repeat testing). The HIV-positive test rate in HIV-exposed infants ranges from 3.1% to 4.7%, but on average appears to have steadily declined from close to 8% in September 2008 to less than 4% for the period concluding September 2010.

While not as rigorous or extensive as the SAPMTCTE survey, the results again appear to be consistent.

Pegging the increasing effectiveness of the PPTCT programme in South Africa to any single intervention may not be possible or sound at this point. Indeed, it is probably premature to attribute it to raising the threshold for pregnant women to start ART to 350 CD4 cells. Although this should ultimately lead to even lower transmission rates, it is not clear that this policy was in place long enough to have led to a profound change in the actual percentage of women getting on ART in time to make a difference — while they are still pregnant. Uptake of ART is still delayed by challenges providing access to CD4 cell tests at many primary healthcare sites, delays in getting the results, and the reluctance of nurses at some primary healthcare clinics to prescribe treatment.

So how did they do it? Perhaps more credit should be given to the many healthcare providers involved in South Africa's PPTCT programme, who have come up with and implemented these various interventions, which alone may only improve performance incrementally, but together amount to a significant number of infections averted, and a triumph for South Africa.

"I think it's sending out quite a positive message because I think there has been a lot of disappointment and morale has been quite low in terms of the effectiveness of programmes," Dr Goga said in an interview with Australian Broadcasting Company. "And I think here we have an example of success."

20,000+ Partnership contributes to dramatic reduction in PPTCT in KwaZulu Natal

There were a couple of oral presentations to suggest that it was the efforts of health workers to improve the quality of the PPTCT service they were providing, that may have been largely responsible for the reductions in vertical transmission being seen in the country.

"Quality improvement approaches have helped to close the service delivery gaps for PMTCT interventions and seem to be contributing to the reduced number of HIV infections in children in KZN," said Dr Wendy Dhlomo-Mphatswe, of the 20,000+ Partnership.¹⁰

The claim appears to be supported by evidence showing concurrent improvement in a number of indicators of performance at different steps of the PPTCT cascade.

HIV accounts for 50-60% of hospital deaths in children and 30-40% of all childhood deaths in KwaZulu Natal, with poor health system performance negatively affecting perinatal transmission rates. As already noted, previous studies suggest the rates of HIV diagnosis at first immunisation was above 21%.

The KZN Department of Health and the University of KwaZulu Natal developed the 20,000+ partnership. The Institute of Healthcare Improvement (IHI) which specialises in health systems intervention, and using data for quality improvement, contributed experienced staff to the project team.

The partnership aims to decrease the vertical transmission of HIV to infants a target of below 5%; this is the target set by the South African National Strategic Plan 2007-2011, and to improve overall child survival in KZN through health systems support interventions using Quality Improvement methods. The partnership is working across the three districts of Ethekwini, Umgungundlovu and Ugu, which each have an antenatal prevalence above 40%. 20,000 is the number of HIV infections in infants that can be prevented each year in KZN if every pregnant HIV-infected woman receives care according to the National PMTCT guidelines.

The partnership was tasked to work with the existing staff to improve the health system performance in the PPTCT programme, and to use routine health information (DHIS). The project involves 15 hospitals, over 200 clinics serving a population of around 5 million people, and runs from April 2008 until April 2013. In addition to the reducing PPTCT, the partnership's objective was to develop health systems improvement capacity at provincial, district and facility level that could sustain effective PMTCT programmes, but that could be applied to any other health domain and service delivery.

The partnership staff worked with improvement teams and leadership at every level. These included the district information office data team that fed data back and forth with the clinic and hospitals team, and each of these teams was in turn supervised by the district task team. The district task team reported back to the district leadership which reported to the provincial leadership.

The quality improvement process

"Quality Improvement" in healthcare is a simple method to identify gaps in the healthcare system, and a systematic way to close those gaps and safely improving the process of care," said Dr Dhlomo-Mphatswe. She said the project sought to "apply local wisdom; focus on the data (stop the blame game); work 'smarter' not just 'harder', and that partnership and teamwork is the only way forward."

The process begins with discussing the problem with the team, performing a system analysis of the activity or process to be affected. The team then exchange ideas about possible solutions, and choose a good one to move forward. Then the team follows the cycle of 'plan, do, study, act.' A plan is drawn up of what will be tried, how will it be done and by whom. Then the team 'do' the intervention, and 'study' the results closely. If the idea results in improvement, then the 'act' upon it. Then implementation goes forward to see whether the intervention continues to succeed and is sustainable.

In the case of PPTCT, they first needed to map out the processes of PMTCT care and track progress with data. For PPTCT, these are many, starting with the first ANC visit, then HIV counselling and testing, HIV positive women are then supposed to have get a CD4 cell test, the results of which determine whether she is referred to ART, or provided with AZT, while the infant is given nevirapine

prophylaxis, and six weeks after childbirth (around immunization), the caregiver and child pair should return for early infant diagnosis.

There should be data to track each part of this process resulting from data recording and reporting from each site. Then the data are processed and sent back in a form that allows the clinic team to see how they are doing, which in turn makes them realise the value of their data (and perhaps improve their data recording practices). Initially however, there were problems with the data, so the partnership then first had to focus on data improvement initiatives. Once that issue was taken care of, the teams could compare their performance with targets.

Dr Dhlomo-Mphatswe displayed graphs showing improvement in a number of indicators. For instance, the goal is to get all the women who come into the antenatal clinic tested for HIV at their first visit but when the project began there was a significant gap. Over time, that gap has been dramatically reduced. Likewise, there were significant increases in the number of women referred for ART, as all the districts can online, a subsequent increase during the ART campaign, and a further increase when ART started being initiated at the primary health centre.

The initiation of life-long ART for eligible women is following the same trend upwards — with an increase as the new art guidelines were released, though not, at first, when ART first started being initiated at the primary health centre. It turned out that despite training and now being qualified to prescribe, nurses still lacked confidence to do so. A separate presentation discussed in more detail in next week's HATIP described quality improvement of nurse-initiation management of ART in the Ugu district.¹¹ From June –September 2010, the percentage of clinics initiating eligible pregnant women on ART increased from 32% to 100% by December 2010. The absolute numbers also increased dramatically. Overall, though, the districts being supported by the 20,000+ Partnership are still about 25% shy of their targets for starting eligible pregnant on ART.

Early infant diagnosis remained mostly stable during the first year of the project, however, there are clear improvements when two of the districts began to focus on PCR from just under 40% to about 70%, and another jump when the infant testing guideline changed, to reach about 80% of exposed infants.

At roughly the same time as improvements of these indicators, the 6-week HIV transmission rate in Ugu district was declining, from 12% in 2008, to 8% in 2009, to the target of 5% in the first quarter of 2010 (and with about 90% of the HIV-exposed infants being tested for HIV).

Implications of a quality improvement approach on the health system

While the PPTCT regimens also improved significantly over this period, it would have had little impact if the poor performance of the health service persisted. For instance, changing the CD4 cell criteria on which to initiate ART or allowing the nurses to initiate ART doesn't matter if women are being referred for ART — which was the situation previously, or if nurses don't prescribe. Rather these quality improvement measures were synergistic and likely essential for outcomes to improve to the great extent they did.

"The quality improvement approach is a multi-faceted and multi-disciplinary approach that effectively improves the working and coordination of the health system through engaging the leaders, and the workforce to be part of the solution," said Dr Dhlomo-Mphatswe. "Data is used to guide improvement — and the end-product is better use of existing resources.... And in addition to reducing the number of HIV infections in children in KZN, the same

approaches can be applied to other areas of MCH care and help strengthen health systems.”

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Mothers2mothers: mothers helping mothers to save babies

by Lesley Odendal

An innovative method used in sub-Saharan Africa to support HIV-infected mothers to prevent the vertical transmission of HIV was presented at the 29th International Confederation of Midwives Congress held in Durban, South Africa, from June 20-23 2011.

Being supported by HIV-infected women who had been through the prevention-of-mother-to-child (PMTCT) programme themselves was found to yield better PMTCT uptake and psychological outcomes than when HIV-infected women had not been supported through the programme.

[mothers2mothers \(m2m\)](#) is a community-based organisation made up of mothers living with HIV who have personally received PMTCT care. These women, known as mentor mothers, provide education and support for pregnant women and new mothers living with HIV. By working side-by-side with doctors and nurses in public health care facilities, mentor mothers assume responsibility for ensuring that patients understand, accept, and adhere to interventions that are prescribed in the PMTCT programme.

A 2007 study which evaluated the results of the programme in KwaZulu-Natal yielded good results. Women who had been exposed to the m2m programme, reported significantly higher rates of having undergone CD4 testing during their last pregnancy (79 percent vs. 57 percent in non-participants; $p < 0.01$) and knowing their CD4

count after testing (88 percent vs. 72 percent; $p < 0.01$) than non-participants.

95 percent of all mothers in the m2m programme received nevirapine during labour (the standard of care in the PMTCT programme at the time) and 88% of infants received nevirapine. 89% of all women who had been involved in the programme were found to practice exclusive feeding methods of the infant to prevent vertical transmission of HIV. 70 percent of the women were also found to be using contraception after the birth of their baby.

Among postpartum women, women who had been through the m2m programme were significantly more likely to have disclosed their HIV status to someone than non-participants (97 percent vs. 85 percent; $p < 0.01$), and to have done so prior to delivery.

The programme evaluation by the Population Council used a pre-post, quasi-experimental study design to assess program effectiveness. There were three evaluation sites in the Pietermaritzburg area of KwaZulu-Natal where women from urban and peri-urban settings were recruited from. The eligibility criteria for the study included being between the ages of 18 and 49 years, knowing one's HIV status, and either 6–9 months pregnant or 12 weeks or less postpartum.

Two cross-sectional surveys were conducted. The first survey, conducted in 2005, collected baseline data before m2m was introduced. 183 HIV-positive pregnant women and 178 HIV-positive postpartum women were interviewed using a structured questionnaire.

The second survey was conducted in 2006, one year after m2m was introduced. 345 HIV-positive pregnant women and 350 HIV-positive postpartum women were interviewed using the same questionnaire but with additional questions about program exposure and interaction.

The study also demonstrated psychosocial benefits of the m2m programme. Pregnant women from the m2m programme were significantly more likely to report feeling they could do things to help themselves, cope with taking care of the baby, and live positively in comparison to non-participants.

Postpartum participants reported feeling less alone in the world, overwhelmed by problems, and hopeless about the future compared to women who had not been exposed to the m2m programme.

There are 348 public health facility sites in South Africa where 890 m2m staff are working. The programme has also spread to eight other countries in sub-Saharan Africa where mentor mothers are working in 366 sites, including in Kenya, Lesotho, Malawi, Rwanda, Swaziland, Tanzania, Uganda and Zambia.

m2m is based on the concept that “peer support is an optimal model for effective education and social empowerment, and that mothers themselves are the best vehicle to provide support to other mothers.” Mentor mothers provide one-on-one counselling for pregnant women, and also facilitates support groups in the health facilities. Mentor mothers also make daily visits to the labour and delivery wards to speak with expecting mothers who may be inpatients or newly delivered mothers who are awaiting discharge.

Another benefit of the programme is that by becoming a mentor mother, employment and professional development is given to local women living with HIV.

Each mentor mother participates in two weeks of training that covers basic medical knowledge about HIV infection and antiretroviral therapy, behaviours that help prevent mother-to-child transmission, safer feeding options for infants, counselling methods that can help women to disclose their status, strategies for

negotiating safer sexual practices, and nutritional guidelines for women living with HIV.

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Treatment in children and adolescents

By Theo Smart

Optimising nevirapine dosing in breastfed HIV-exposed infants

With South Africa's current PPTCT guidelines, breastfeeding infants have a much better chance of staying HIV-negative too. Giving nevirapine to infants for the duration of breastfeeding has proven efficacy, as demonstrated by the [Breastfeeding, Antiretrovirals and Nutrition \(BAN\) study](#), which reported a transmission rate of only 1.8%, and is both WHO and South African policy. However, the nevirapine dosing recommendations in "the WHO and South African guidelines might not be appropriate for preterm and low birthweight infants," said Dr Renée De Wall of the University of Cape Town, who presented data from a pharmacokinetic study of nevirapine in these small infants.¹

Currently, WHO guidelines recommend nevirapine dosage should increase according to age and weight – based on data from PPTCT efficacy studies, which were mostly conducted in full-term infants who weighed 3 kg, on average. For low birthweight neonates, WHO recommended doses of 2 mg/kg plus therapeutic drug monitoring (TDM) of nevirapine plasma trough concentrations.

"Those guidelines raised several concerns with clinicians as to their implementation in preterm and low birth-weight infants because of the limited safety, efficacy and pharmacokinetic data," said Dr De Wall. One issue is that prematurity is associated with immature drug metabolism which might increase toxicity from some drugs. Furthermore, nevirapine undergoes auto-induction of its metabolism, which is why in adults, the dose is increased after two weeks. However, WHO guidelines do not recommend an increase in the dose after two weeks, which might cause sub-therapeutic concentrations. Meanwhile, South Africa's guidelines, which recommend starting with 10 mg, might be associated with toxicity in preterm and low birthweight babies.

Western Cape nevirapine dosing recommendations

Age	Birth weight <1800 g*	Birth weight 1800–1999 g
≤14 days	2 mg/kg	5 mg
>14 days	4 mg/kg	10 mg
6 weeks to 6 months		20 mg
	*after discharge: as per 1800–1999 g	

Alternative recommendations accounting for low birth weight and 14 day dose adjustments were developed by a group of paediatricians and pharmacokineticists and made policy in the

Western Cape Province in February this year, though some facilities began using these doses earlier.

Therapeutic drug level monitoring (TDM) is also recommended on days 7, 14, 28 and 42, with a target nevirapine concentration in the range of 0.1–10 mg/L.

But clearly TDM is not something that can be done everywhere. So Dr De Wall and colleagues analysed samples that have been submitted in the Western Cape to see whether nevirapine trough concentrations were in the target range for preterm and LBW infants dosed according to Western Cape guidelines, and to see whether there was an association between nevirapine concentration and age post-delivery or weight. Unfortunately, most of the samples couldn't be used in the analysis, mostly because of poor documentation of weight, dose, and timing of the blood draw.

However, 65 samples from 56 infants could be included in the study from infants with a median gestation of 32 weeks at birth (range 28–36) and with weights mostly in the 1000–1799 g (though 18% weighed less than 1000 grams).

"We found no sub-therapeutic nevirapine concentrations, and no toxicity was reported by requesting clinicians," said Dr De Wall. In addition, they found that nevirapine trough concentrations were significantly lower after 14 days of age, so the recommended dosage adjustment is appropriate.

"Current Western Cape guidelines for dosing result in adequate nevirapine concentrations, but the WHO guidelines might result in sub-therapeutic concentrations," said Dr De Wall. However, that doesn't necessarily mean that the doses recommended by WHO are less effective, but this study does suggest that further studies may be needed to be certain that nevirapine 2mg/kg is adequate in preterm and low weight infants.

A dramatic increase in the initiation of ART in children with HIV in South Africa

"From 2005–2010, the South African Government, with assistance from PEPFAR, implemented a substantial scale-up of ART for children," said Elysia Larson of the US Centers for Disease Control (CDC) who is also a fellow with the Association of Schools of Public Health.² In fact, this is something of an understatement – since 2005 the number of children under 15 newly initiated on ART each year has increased 16-fold from 1,851 in 2005 to over 31,000 in 2010 – and this seems to be making a dent in South Africa's high under-5 mortality rates.

But there is still room for improvement.

"The HIV/AIDS epidemic has been hard on children in South Africa," said Larson. Between the mid-1990s and the mid-2000s, under-five mortality in South Africa had increased dramatically (almost doubling) – making a mockery of Millennium Development Goal 4, reducing child mortality by two-thirds between 1995 and 2015. "According to the South Africa Every Death Counts Writing Group, most of those deaths are caused by conditions that are either preventable or treatable, at least 35% are attributable to AIDS," said Larson. "About 3% of children aged 0–18 years old are HIV-infected, and just over one-third of those children are under the age of five."

The number would actually be much higher, were it not that most children with HIV who go untreated die quickly – 67.3% within the first five years according to UNAIDS estimates. A rather depressing poster presentation at the conference backed these estimates up with local data on the sad outcomes of many infants who became infected over the course of the Vertical Transmission (VT) Study, conducted from 2001 to 2004.³ This was before ART was made

widely available to HIV-positive children in South Africa — even though treatments were available elsewhere, and despite the pleas of the late Nkosi Johnson to his government to provide life-saving treatment at the opening plenary of the 2000 World AIDS Conference in Durban.

In the VT cohort, at the end of two years, only 102 out of 259 of the HIV-infected infants were still alive and on study at the end of two years, though 12 had ‘moved’ and a handful were lost-to-follow-up (and one can probably assume dead). There were 126 confirmed deaths overall, with a median age of 6.1 months at death. The authors noted a difference in the risk of mortality between children who were infected perinatally (only 28.9% of whom were still in follow-up at the end of the study — 76 confirmed dead out of 128 infants — compared to those who were infected postnatally (59.5% who still remained in study at the end of two years). However, the postnatally-infected children appeared to have a higher risk of serious morbidity, which the authors said underscored the need to maintain close follow-up of HIV-exposed who are uninfected earlier in life.

Since that time, putting HIV-infected infants on ART has been shown to dramatically reduce mortality — [by at least 75% if started in early infancy](#). Those findings have given a major impetus to scaling up early infant diagnosis at the first immunisation visit — and making effective linkages into care and treatment services for those children testing positive.

South Africa’s Department of Health eventually produced ART guidelines for children in 2004 and the PEPFAR collaboration began about the same time. At the start of 2005, there were 7,000 children on ART in the country but Stats SA estimated that about 183,000 children would be in need of ART by 2010. In the National Strategic Plan 2007-2011, the goal was to try to put over 150,000 on treatment by March 2011.

PEPFAR’s support for the paediatric ART programme has grown substantially, accounting for 20% of children receiving ART in 2005 and over 75% of those receiving treatment by September 2010. This amounts to quite a large number of children — beginning with about 2,412 children in September 2005 to 79,416 children in September 2010, a 32-fold increase.

“Our most recent data from January-March of 2011 shows that there are 89,421 children under fifteen currently on treatment in PEPFAR-assisted facilities,” said Larson. But this figure is still only half of those estimated to need treatment.

PEPFAR’s support is channelled through non-governmental organisations providing infrastructure, equipment, staff, mentorship and training primarily for the public sector programme — and does not usually involve buying the medications.

PEPFAR impact projections

One thing PEPFAR is known for, however, is an emphasis on data collection, monitoring and evaluation — and Larson reported on a retrospective analysis of routinely collected PEPFAR monitoring data from October 2005 through September 2010.

The analysis was restricted to outcomes in the children under five starting ART, and looked at trends in number of children receiving services, and the proportion of children remaining on treatment, to estimate the number of years of life gained by treatment for children under five. It included 26,207 children under five on PEPFAR-assisted ART programmes at the end of the analysis period.

For the analysis, 10% were removed from the total number as they could be expected to either stop treatment, transfer, or be lost

to follow-up. The 10% figure was based on an analysis of periodic cross-sectional data of children in the programme from April 2008 to September 2009 which found that 90% of children remained alive and on treatment after 1.5 years. That analysis had also found 0-4 year olds were 1.4 times as likely to transfer out of the programme or die as 5-14 year olds (95% CI: 1.3-1.5) and males were 1.3 times as likely to stop treatment as females (95% CI: 1.2-1.5).

“Then, using UNAIDS estimates for mortality of children under five who are receiving treatment versus those not on treatment, we calculated the number of years these children were expected to live on ART versus the number that would be expected to live if they were not on ART,” said Larson. Again, UNAIDS estimates are that 67.3% of children would die without ART, while they project that on ART approximately 15% of HIV-infected children will die the first year, followed by about 7% each subsequent year.

Of the 23,582 children under five expected to be retained in care, about 15,875 children would have died without ART compared to 9,877 deaths on ART.

“That means that providing therapy to these children will avert about 6000 deaths in the first five years on treatment,” she said. The analysis also found that after thirty years, the 26,207 children on ART will have lived a total of 255,123 years compared to 136,920 years if they were not given ART — a gain of 118,203 years of life. “Increasing access to ART for children under five has almost doubled the number of years these children will live,” said Larson. “And as more children are provided with treatment, more under-five deaths will be averted.”

This decrease in mortality has already begun to affect under-five mortality in the country, with a levelling off in the number of deaths after 2006, and what appears to be a decrease from 2007 to 2008, according to data from Statistics South Africa.

“This leads us to believe that the paediatric ART scale-up has been a tremendous public health accomplishment, however there is still a great unmet need for treatment,” she said, adding that she hoped that nurse-initiated and managed ART (NIMART) should help increase the number of children starting on treatment.

Remarkably consistent findings at Kheth’Impilo-supported sites

These nurses must be trained and mentored to fast-track HIV-infected infants onto ART, according to another poster presentation from the team at Kheth’Impilo, which reported findings remarkably consistent with Larson’s study.⁴ In addition, “closer integration of maternal, child health and HIV/ART clinics with efficient systems to perform early infant PCR testing and rapid retrieval of results are critical,” the poster’s authors concluded.

The Kheth’Impilo poster described a study looking at temporal trends in baseline characteristics and programmatic outcomes in children starting ART at thirty sites (18 primary care, twelve hospitals) that the NGO supports in four provinces (Western Cape, Eastern Cape, Mpumalanga, and KZN). As already noted KI provides infrastructure support, capacity development, clinical mentoring, community-based adherence support and electronic data collection systems at these sites.

The study included all children under 16 years of age enrolled on ART between January 2004 to September 2009 followed until March 2010, or until Kheth’Impilo finished supporting the site. This amounted to 3007 children. Consistent with the PEPFAR study, the number of children enrolling monthly increased from 1.9 per month when the study started to 106 in 2009. Amongst the 146 children lost to follow-up, 68 (46.5%) had a valid civil identification number, of whom 23 (33.8%) were registered as deceased in the national

registry by November 2010. The corrected mortality was 6.1% (CI: 5.10-7.3%) after 24 months on ART and retention in care was 89.6% (CI: 81-91%) with no differences between annual enrolment cohorts – which suggests that despite the rapidly increased numbers going onto treatment each year, South African paediatric ART programmes are quite effective. After four years of ART, 84.1% (CI: 80.9%–86.7%) of children remained in care.

As Ms Larson noted in her talk, the proportion of children continuing on treatment is high (89.7% after 1.5 years in the PEPFAR study) compared to adults and UNAIDS estimates.

“Nevertheless, because the primary reasons for attrition were loss-to-follow-up and transferred care, it suggests a patient tracking system, such as a national system utilising a unique patient identifier, could greatly facilitate the care of patients and the monitoring of patient outcomes, though it must protect human rights and patient confidentiality,” she said.

It may be more important to implement such a system in order to make certain that young children are appropriately screened for HIV at both their immunisation visits and at 18 months of age (at which point, ELISA tests can be used since weaned children should no longer express their mother’s antibodies). Such a system could also be used to make certain that the mother gets her child’s test results and that effective referrals are made to the ART clinic and to community-based support for the mother and her child.

Can these responses be sustained?

If there is a dark cloud on the horizon, it is that these children will require effective antiretroviral therapy for life – and careful monitoring and support to make sure that it remains effective.

While the prospect of sustaining lifetime antiretroviral treatment is daunting enough in adults who may have access to only first-line and second-line treatment, the prospect is even more challenging in children, who may experience failure of first-line treatment due to very high viral load, adherence problems or sub-optimal drug concentrations.

For young children, the options for second-line treatment are limited due to the lack of suitable formulations for children, and third-line treatment is even more difficult – and expensive – to piece together. Drug resistance that develops after the failure of first-line treatment critically restricts later options and further complicates the assembly of an effective second or third-line combination.

So issues of adherence, drug resistance, virological monitoring and drug access are particularly acute in this group of patients.

But monitoring for treatment failure, whether in adults or children in resource limited settings, is difficult because “current immunological definitions of immunological failure are poor at detecting viral rebound,” said Dr Mary-Ann Davies, who presented data on the use of different immunological criteria to monitor children receiving ART in the South African [International Epidemiologic Databases to Evaluate AIDS](#) (IeDEA) paediatric sites.⁵

The study included 2513 children below the age of sixteen, whose viral load had been completely suppressed during the first year on treatment.

These children were then monitored with CD4 cell count and viral load measurements every six months to determine sensitivity, specificity, positive and negative predictive values (PPV) and (NPV) of WHO and US definitions of immunological failure for identifying virological rebound in a child on ART for at least 18 months.

After following the children out until 3.5 years of ART, the WHO definition was found to have a very low sensitivity although PPV was

better (42%); the sensitivity was higher for the US definition (though still low), and the PPV was very low (20%).

To make these definitions work better, Dr Davies said that one could get another CD4 count to confirm failure, which would increase PPV, but decrease sensitivity. Furthermore, she noted that this simply isn’t done in practice in South Africa when viral load is available. So the researchers also looked to see whether the sensitivity and positive predictive value could be improved by combining the most sensitive immunological criteria with a single HIV-RNA measurement to define failure (a targeted viral load strategy). This approach increased the PPV for both the WHO and US criteria considerably, but the diagnostic accuracy was still sub-optimal.

Methods for determining immunological failure

WHO 2010	USA
CD4% <10 (2 – 4 yrs)	Sustained decline of CD4% by 5 percentage points (any age)
CD4 absolute <200 (2 – 4 yrs)	
CD4 absolute <100 (≥ 5 yrs)	Return of CD4 count to ≤ baseline value (≥5 yrs at baseline)

Essentially, immunological failure and virological failure seem even less likely to correspond in children than adults. It is important to point out however, as Dr Davies noted, that her study was merely an algorithm applied retrospectively to the data set, which had no clinical data on the participants. So it wasn’t possible to exclude the possibility that low CD4 cell counts may have been due to a clinical cause such as tuberculosis. Nevertheless, the researchers concluded that better access is needed to viral load monitoring in order to accurately diagnose treatment failure in children – otherwise, virological failure may simply go unnoticed.

Unfortunately, this would present some of the same challenges as it does in adults, where studies have shown that routine viral loads do not appear to improve patient management and are not cost-effective – at least not during the first few years when treatment works well in most people.

In the Kheth’Impilo study, the proportion of children achieving virological suppression after six months was fairly high, at 83% (95% CI: 80-85.1) and 79.7% (95% CI 76.6-82.6%) after twelve months on ART. The study did note however, that children aged over two years when they went onto treatment had significantly better virological suppression 81.8% (95% CI: 80.2-83.3%) compared to 72% (95% CI 67.4-77.7%, $p<0.0005$) in children aged under two years of age at any time-point on treatment. However, other cohorts in similar settings, perhaps where children and their caregivers receive less support, have described higher rates of virological failure. For instance, one recent report described 38% of children on ART for more than a year experienced virological failure, and the authors’ remarked that the “correlation between virologic failure and immunologic decline was nearly absent.”⁶

Treatment failure could reflect the inadequacy of antiretroviral formulations for infants and small children – and/or the difficulty young mothers may have making sure that their infants get the doses they need (see more on adherence below). But it also means that a significant proportion of the children will need to switch to second-line therapy at a fairly young age. Over time the number of children failing first and then second-line treatment can only be expected to increase.

But the available treatment options for switching are even more limited in children than adults in most resource-limited settings. Consequently, there are questions about how best to manage treatment failure. One approach could be to keep them on virologically failing treatment regimens as long as their CD4 cell count and/or clinical response is good. The danger, of course, is that over time on a failing regimen, they will develop drug-resistant virus that will be less likely to respond to subsequent ART regimens as they become available. Children who became infected in utero or despite PPTCT may already be at a disadvantage due to exposure to antiretrovirals that could have led to resistance.

Drug resistance increasing in children

Indeed, drug resistance is emerging in children on ART in South Africa.

One study described a large number of resistance mutations found in thirteen children at Kalafong Hospital in Pretoria, who were started on a protease inhibitor-based regimen when they were younger than 36 months of age (mean age 22.4 months), some of whom had already been switched to a second line NNRTI regimen.⁷ The mean duration of treatment at testing was 45.9 months. "All these children were deemed to be at high risk as they suffered co-morbid conditions and had documented poor adherence," according to the poster's authors. Three of the children had WHO Stage 3 disease, and ten had WHO stage 4 disease; while 62% of their caregivers reported poor adherence, and 54% had a history of missed clinic appointments. Only one had ever achieved an undetectable viral load.

Resistance testing found that all of these children had virus resistant to nucleoside analogues (the 3TC-related M184V mutation being the most common), five had major protease inhibitor resistance mutations, and nine had resistance to mutations to non-nucleoside analogue reverse transcriptase inhibitors (NNRTI, i.e. efavirenz or nevirapine) — only one of these had been exposed to nevirapine as PPTCT.

A second poster presentation found drug resistance was more common in paediatric than adult patients experiencing virological failure on their second line protease inhibitor-based regimen at Tshwane Academic Hospital (Pretoria).⁸ All patients had been started on d4T/3TC with either nevirapine or efavirenz, and they were all switched to either AZT/ddI/ or a variation (AZT/abacavir) with ritonavir-boosted lopinavir (*Kaletra* / *Aluvia*).

About half of the failing adult patients showed no evidence of resistance at all, suggesting that they simply were not taking their treatment, but the virus from 91% of the children (30 out of 33) of the paediatric patients failing treatment had resistance mutations. In these children, virus in seven out of 33 (21%) had major PI mutations, five had more than three PI mutations, and 27.3% still showed evidence of the K103 mutation conferring resistance to NNRTIs (note, the mutation would probably have been detected in more children if they were still taking nevirapine or efavirenz). Finally, 75.8% of the children had virus that was resistant to 3TC, and 18.2% had multiple thymidine analogue mutations (TAMs) that significantly decrease the chances of responding to subsequent nucleoside analogues.

Notably, some of these children had only moderate levels of viral load which — in the presence of less than universal resistance to the PIs — suggested that they may have been taking their treatment, but that adherence was suboptimal.

Nevertheless, the authors concluded that children exhibited increased levels of resistance to all three drug classes, perhaps because of higher levels of viral replication that typically occur in

children or perhaps because some of them had previous exposure to unboosted PI therapy (ritonavir monotherapy).

Dr Theresa Rossouw of the University of Pretoria, who was the lead author of the latter poster, also gave an oral presentation describing findings from the Southern African Treatment and Resistance Network (SATuRN), which is monitoring emerging patterns of drug resistance in the region.⁹ She described higher rates of resistance among 49 children in SATuRN (though it is not clear to what extent these patients overlap) with PI resistance being documented in almost one third of the patients and three or more PI resistance mutations in 20.4%. NNRTI Resistance was seen in 21/49 (42.86%). Resistance to the nucleoside analogues was detected in 41/49 (83.67%), with eleven out of 49 (22.45%) with TAMs, and eight out of 49 (16.28%) with three or more TAMs. She noted several other South African cohorts have also documented high levels of resistance among children failing treatment.^{10, 11, 12, 13}

Resistance, and limited treatment options will make it more difficult for these children to live with HIV into adolescence, when other challenges to treatment success seem to emerge.

High rates of virological failure in adolescents living with HIV compared to young adults

There are significantly poorer rates of virological suppression and higher rates of virological failure in adolescents compared to young adults, according to an observational cohort study in Gugulethu reported at the South African AIDS Conference, even though rates of mortality and loss-to-follow-up were similar in the two populations. "Further investigation is needed to determine what factors are associated with virological failure in adolescents," according to Dr. Mweete Nglazi of the Desmond Tutu HIV Foundation, though the underlying cause seems to be poorer adherence.

"Adolescence is a unique bio-psychosocial and behavioural stage of life, with characteristics — that may be exacerbated by HIV infection — that often result in poor adherence to medical programmes and chronic medication," said Dr. Nglazi.¹⁴ While studies in other settings have reported poor adherence and outcomes in adolescents living with HIV, she noted that there had been few studies in the region and far fewer that directly compared adolescents with adults.

So she and her colleagues looked at data from an ART cohort database derived from patient records to compare adherence, virological responses, loss to follow-up and mortality among adolescents and young adults receiving ART at the Hannan Crusaid clinic in Gugulethu, a Cape Town township. The study included 69 adolescents who started ART between nine and 19 years of age, and 818 young adults who started when they were between 20-28 years old. All of the patients received ART from between September 2002 to June 2009, with the follow-up data censored as of June 2010.

At baseline, a significantly lower percentage of the adolescents were female (66.2% vs. 86.6%) which would be expected since there would be an almost an equal number of boys among the adolescents infected as infants — while in later life sexual transmission puts more young women at risk. Median CD4 cell counts (133 and 116 respectively) and viral load (~4.8 log/mL) were similar for both groups. However, the adolescents were significantly more likely to be taking a regimen containing efavirenz (81.5 vs 49.2%) than nevirapine. Data on virological responses on the first year of treatment were available for a slightly smaller treatment-naïve cohort (46 adolescents and 716 adults) as some clients had transferred in from other facilities

Mortality and loss to follow-up were actually more common in the young adults than the adolescents, though these differences were not statistically significant.

Notably, a poster presentation reported similar findings of generally lower rates of mortality and loss to follow-up among adolescents (10-19 years old) than young adults (19.1-24 year old) or adults (24.1-28 years old) starting ART in a decentralised HIV/TB programme in rural Zimbabwe.¹⁵ This cohort included 1855 patients, 748 of whom were adolescents. Of the adolescents, 52.3% were female so this group was even more likely to have been infected as infants). The adolescent were also slightly less likely to have WHO stage 3 or 4 disease at baseline (62.2%, vs 71.4% and 78.3% in adolescents, young adults and adults respectively). Participants were initiated on ART between 2005 and 2010 (but mostly between the years of 2007 and 2009).

The young adults were the most likely to be lost to follow-up in this cohort, probably, the authors surmised, because they were more likely to move to seek out economic opportunities. Meanwhile adolescents were most likely to be retained in care. More importantly, the mortality rate was 2.6 (95% CI 1.9-3.6), 5.2 (95% CI 3.6-7.6 and 6.5 (95% CI 5.3-81) per 100 person years in adolescents, young adults and adults respectively. However, the study did not include data on virological responses.

Virological data were available for the Gugulethu adolescents, and frankly the results were somewhat puzzling. Initially, virological suppression was similar in both populations, with 97.3% of the adolescents and 89.6% of the young adults achieving viral loads below 400 copies/ml at week 16. However, something happened between week 16 and week 32, at which point only 37.5% of the adolescents had undetectable viral loads versus 75.1% of the young adults, which was a highly significant difference ($p < 0.001$). By week 48 only 27.3% of the adolescents versus 63.1% were virally suppressed ($p < 0.001$).

Mortality and loss to follow-up by age range in Gugulethu

Age group	Mortality			LTFU		
	Rates (per 100 PYS)	AHR*	p-value	Rates (per 100 PYS)	AHR*	p-value
9-19 yrs (ref)	1.2 (0.3-4.8)	1.00	–	7.2 (4.1-12.6)	1.00	–
20-28 yrs	3.1 (2.4-3.9)	1.79 (0.43-7.44)	0.423	10.2 (9.0-11.7)	1.35(0.74 – 2.44)	0.325

The likelihood that some of the adolescents had been exposed to nevirapine for PPTCT is extremely low, given that they were all over the age of nine and PPTCT wasn't available in South Africa when they were born. Likewise, it is unlikely that there would be a profound difference between regimens containing efavirenz versus nevirapine, unless side-effects were an issue.

The most likely factor would seem to be poorer adherence. Ironically, the Zimbabwean study concluded that its model of decentralised care had successfully managed the adolescents with less frequent clinic visits and adherence interventions than the norm in other programmes. In this model, ART was initiated by a mobile team, with intensive follow-up provided by nurses for three months, then three-monthly clinic visits with a clinician and counsellor out to 18 months, after which time the patient would be

provided with a three-month supply of medicine and a clinic visit would only be triggered by signs of clinical or immunological failure and poor adherence. But that study didn't monitor viral load responses – and it may be a mistake to assume that better survival rates among this cohort, who have already survived living with HIV for most if not all of their lives, indicates a better treatment response.

Or possibly, there are different barriers to adherence in periurban Gugulethu than rural Zimbabwe. Perhaps the family structures supporting adolescents with HIV are different in these settings. However, it is notable that in another presentation from Zimbabwe, that looked at ways to better monitor adherence on ART in slightly younger children (median around 8 years of age), “the children reported lower adherence levels than their caregivers,” according to Dr Linnetie Mugore of Rhodes University.¹⁶

Regardless, almost all of these studies stressed that specific adherence strategies targeting children and adolescents need to be developed. The authors of the Kheth'Impilo study wrote that “scale-up of community adherence support for young children initiating ART is... imperative.” Indeed, caregivers need specialised training to dose young children appropriately.

And there may be a gap between childhood and young adulthood where children are too old to be given doses, and yet, not old enough to take on the responsibility of taking chronic medications for the rest of their lives. Many adolescents may rebel against the notion, while for others, there are issues related to peer pressure and self worth.

The social pressures in the lives of children living with HIV were examined in more depth at the following International Conference on HIV and Social Science and Humanities that took place after the AIDS conference in Durban and will be discussed in a future HATIP.

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