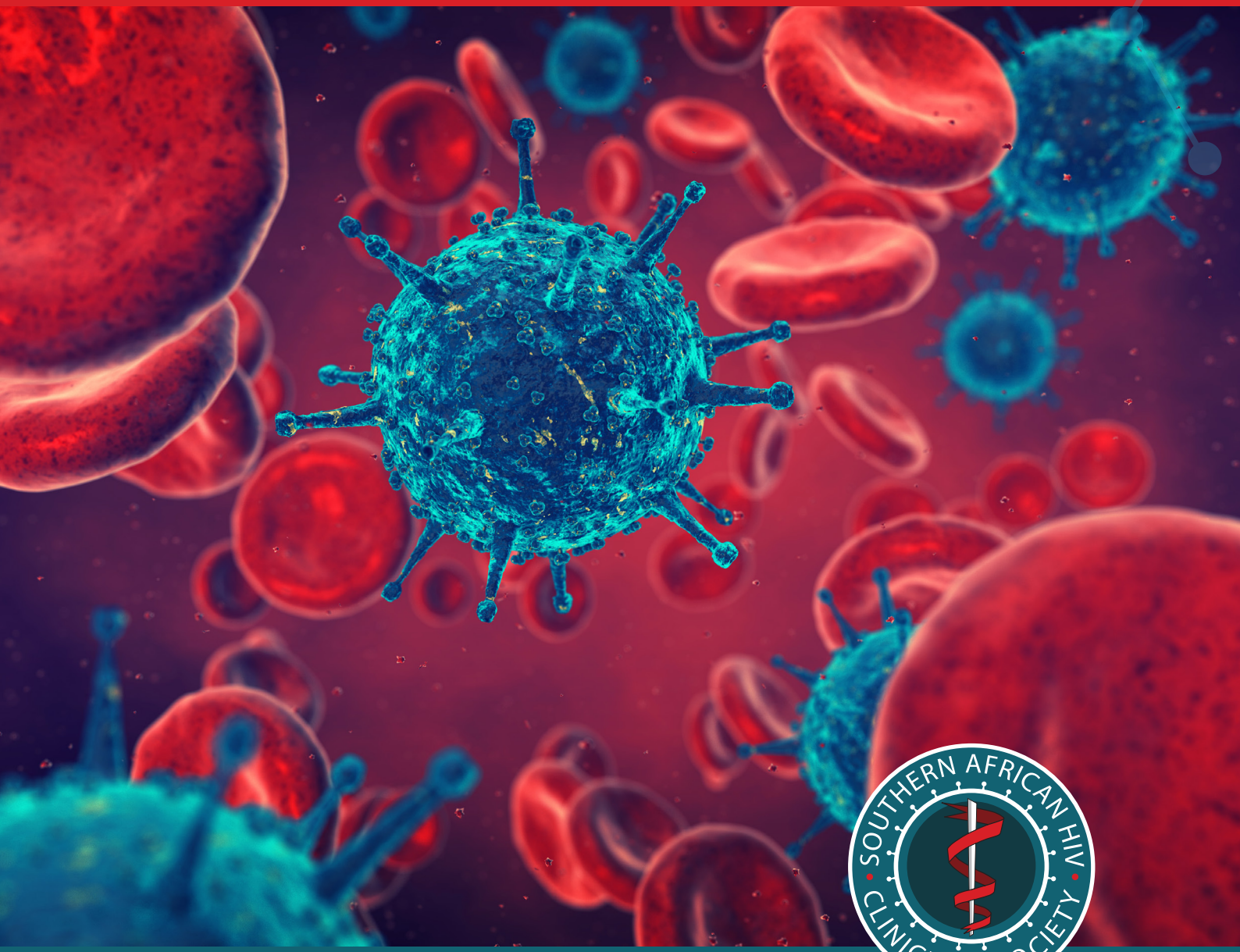
SOUTHERN AFRICAN JOURNAL OF

HIV MEDICINE

2021 SPECIAL ANNIVERSARY COLLECTION

21 Years of Science and Research towards the UNAIDS 2030 Targets



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- Dr David C. Spencer, Editor-in Chief

2021 SPECIAL ANNIVERSARY COLLECTION

Southern African Journal of HIV Medicine
ISSN: (Online) 2078-6751, (Print) 1608-9693

Southern African Journal of HIV Medicine August 2021

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How to cite this article:
Spencer DC. *Southern African Journal of HIV Medicine* August 2021. S Afr J HIV Med. 2021;22(1), a1309. https://doi.org/10.4102/sajhivmed.v22i1.1309

Special collection: UNAIDS targets for 2030

HIV/AIDS in Southern Africa. An end to new HIV infections by 2030? The views of our authors. Summaries of recent articles in the *Southern African Journal of HIV Medicine* (SAJHIVMED).

> Despite the passage of three decades, people living with HIV in South Africa are still at risk of serious morbidity and inappropriate mortality from HIV. In order to achieve the target of ending HIV by 2030, a more urgent public health response is required. This must include more innovative strategies to improve HIV awareness, new thought with regard to prevention, upgrading of ART services and a renewed dedication to the retention in care of all people living with HIV.[1]

> If significant improvements in differentiated service delivery, increases in human resources and HIV prevention can be realized, Botswana could become one of the first countries with a previously high-burdened generalized HIV epidemic to gain epidemic control, despite the demands of the COVID-19 [*coronavirus disease 2019*] pandemic.[2]

This year marks the 21st anniversary of the existence of the SAJHIVMED. The journal was first published in 2000. At the time, HIV denialism was rampant, many were confused and large numbers died unable or unwilling to accept or access antiretroviral treatment (ART). At the time, the Southern African HIV Clinicians' Society believed that a journal of HIV medicine was necessary to showcase the work of local researchers and to underpin the southern African HIV epidemic with credible science. Though times have changed, the mandate has not. There is much talk of an end to new HIV infections by 2030. My thanks to the guest authors who have submitted articles to the journal addressing this topic. Like Dorothy,[3] 'we're not in Kansas anymore!' We are not where we were. Antiretrovirals have changed the epidemic. Still no protective vaccine exists. And no cure has been found. If there is a rainbow at the end of our story, it is not yet in sight. We are in Africa. And the task ahead – an end to new HIV infections by 2030 – is still far off. In the following pages, I summarise several SAJHIVMED articles that address this story. If you have the opportunity, please read the parent articles. These can be accessed through the links provided at the end of each citation. COVID-19 has demonstrated the vulnerability of our world – particularly the low- and middle-income countries. Climate change is here. We have an uncertain future on this planet. Substantial fault lines have emerged in South African society in recent days. Here, too, the winds of change are blowing. As healthcare workers, it is time to do what we can to heal our world and the angry communities around us. We are the so-called experts. All of us seek an end to this HIV epidemic.

David C. Spencer
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SAJHIVMED

References

1. Laher AE, Venter WDF, Richards GA, Paruk F. Profile of presentation of HV-positive in-patients to an emergency department in Johannesburg, South Africa. S Afr J HIV Med. 2021;22(1):a1177. https://doi.org/10.4102/sajhivmed.v22i1.1177
2. Jefferis K, Avalos A, Phillips H, et al. Five years after treat-all implementation: Botswana's HIV response and future directions in the era of COVID-19. S Afr J HIV Med. 2021;22(1):a1275. https://doi.org/10.4102/sajhivmed.v22i1.1275
3. Frank Baum, L. The wonderful wizard of Oz. Chicago, IL: Geo. M. Hill Co. Publishers; 1900.

Summaries of scientific articles published in the 2021 edition of the SAJHIVMED

1. Parker E, Judge MA, Macete E, et al. HIV infection in eastern and southern Africa: Highest burden, largest challenge, greatest potential. S Afr J HIV Med. 2021;22(1):a1237. https://doi.org/10.4102/sajhivmed.v22i1.1237

Summary: The authors review the HIV epidemic in eastern and southern Africa (ESA) in the light of the failure of most countries in the region to meet the 2020 UNAIDS 90-90-90 targets and the call to meet the new UNAIDS targets by 2030 (See the full article for the UNAIDS 2020, 90-90-90 targets).

The UNAIDS 2025–2030 targets include the following: ≥ 95% of those living with HIV to know their HIV status, ≥ 95% of this group to have started and remain on antiretroviral therapy (ART) and ≥ 95% of those on treatment to have persistently undetectable viral loads by 2025–2030.

'Know your epidemic, know your response' (Wilson et al. 2008, Further reading). Our authors argue that a new commitment and new targets are needed for the current decade. A total of 20.7 million, or 54%, of the globe's 38 million people living with HIV live in ESA. Most (87%; range: 15% – 98%) are aware of their diagnosis, 83% (37% – 98%) are on ART, and 90% (68% – 97%) of these have suppressed viral loads. Interpret the numbers with caution: ranges and confidence intervals are wide, the background data is incomplete, and many clinics and individuals are likely to have been missed. The problems include the following:

- *Retention in care*. Africa's men are still too easily lost from care.
- *Infrastructure*. There are too few high-throughput labs and insufficient point-of-care tests and testing.
- *The neglected*. How well represented are our key populations and are these being adequately reached? Our men who have sex with men, those who inject drugs, female sex workers, the truck drivers, the migrants, mobile miners, the serodiscordant couples, pregnant women and their infants? Why are these so often missed?

The authors question whether these key groups are on the 2030 roadmap. To this, they add the 'acutely infected' – a high-risk transmission group. How well are these groups being recognised and targeted in ESA? The authors draw attention to multiple gaps – multiple opportunities – throughout ESA. This is an important article. It asks pertinent questions and gives some answers:

- Promote and expand local *prevention* research (and implementation).
- Improve *accessibility* to HIV education and testing.
- Ramp up in-country *point-of-care* clinical trials of affordable and available viral load and CD4 testing diagnostics.

Read the article. In particular, look at the figures, especially Figure 1b (See link: https://doi.org/10.4102/sajhivmed.v22i1.1237) South Africa's HIV numbers dwarf its regional neighbours'. 'Highest burden, largest challenge, greatest potential'. Do we want a world without new infections by 2030? Yes. Yes. Yes. However, as a region, we are languishing far behind target.

Further reading

- Wilson D, Halperin DT. 'Know your epidemic, know your response': A useful approach if we get it right. Lancet 2008;372(9637):423–426. https://doi.org/10.1016/S0140-6736(os)60883-1

2. Pillay Y, Johnson L. World AIDS Day 2020: Reflections on global and South African progress and continuing challenges. S Afr J HIV Med. 2021;22(1):a1205. https://doi.org/10.4102/sajhivmed.v22i1.1205

Summary: With regard to eliminating new HIV infections by 2030, where are we? Three 2020 reports are reviewed: UNAIDS (global), the HIV Policy Lab (global) and Thembisa version 4.3 (local, South African) (Further reading: UNAIDS 2020; HIV Policy Lab 2020; Johnson 2020). Table 1 in this article outlines South Africa's 2020 90-90-90 goal attainment by province, gender and age (follow the link above to see the article and the table in the SAJHIVMED). *Adult females do best* (94-74-92). This is followed by adult males (91-67-92) and lastly children (79-70-72). An important detail is recorded in the table's columns: only 54% of adult males living with HIV in the North West province have been diagnosed. Only 58% of children living with HIV in the province of Limpopo have been diagnosed and are on ART! In Gauteng, the economic hub of South Africa, only 66% of children living with HIV are on ART – and only 63% are virologically suppressed!:

> Five years into the implementation of [*South Africa*] Sustainable Development Goals SDG [*Sustainable Development Goals*], our children lag behind their adult counterparts. Urgent action is called for. (Nyasulu et al. 2021, see Further reading)

The article provides the reader with numbers. Between 2010 and 2019, South Africa's total HIV-infected population increased from 5.9 to 7.64 million. In the same period, the overall HIV incidence rate fell by 55%. New infections still occur: 201 000 in 2018/2019. However, the percentage of 'ever-tested' South Africans has risen, from 47.3% in 2010 to 76.3% currently. Has there been improvement? Yes. However, we need more … please.

Prevention? Politicians, health administrators and regulatory bodies, industry and healthcare workers *must* make it easier for *all* South Africans to access antiretrovirals and care. 'U=U: an undetectable viral load on ART = an untransmissible virus' (Further reading: Thigpen et al. 2012). In modern practice, ART is both treatment and prevention. However, condom use at 'last sex' among 15–24-year-old South Africans was 23% in 2012 and was still only 29% in 2019. Among pregnant Sowetan women, HIV prevalence rates have not changed in two decades:

28.9% in 2002, 33.1% in 2009 and 27.4% in 2015 (Further reading: Mnyani 2020). And in 2019, the national South African antenatal HIV prevalence rate was 30.7% (confidence interval [CI], 30.4% – 31.3%) (Further reading: Woldesenbet et al. 2019).

Can the prevention gap be closed? Pre-exposure prophylaxis (PrEP) represents an underutilised opportunity. Only 3% of South African female sex workers and 1% of men who have sex with men use PrEP regularly. Rates in the general population are similarly low; PrEP reliably protects the uninfected. The SAJHIVMED's 2020 PrEP guidelines speak to its efficacy, safety and affordability (Further reading: Bekker et al. 2020). Every clinician in Africa must become familiar with these guidelines and ensure that all are protected. The at-risk groups are known, but with a countrywide HIV prevalence of 19.7% among 15–49-year-old South Africans, virtually all are at risk. Long-acting antiretroviral (ARV) injectables represent a new day in HIV prevention. Data from the HPTN 083 and HPTN 084 cabotegravir studies confirm PrEP's utility (efficacy) in Africa and its value in the poorly adherent (Further reading: Clement et al. 2020; Landovitz et al. 2020; Delany-Moretlwe et al. 2021). Looking to 2030, long-acting PrEP must be a front-runner.

Has the COVID-19 pandemic taught us lessons that may help us achieve the UNAIDS 2030 goals?:

- *Leadership*. Competent, respected, visible and committed to an HIV-free society.
- *A defined strategy and a defined target population*. Be strategic and inclusive. Acknowledge that the individual is important. Provide differentiated care. Address stigma. Make HIV clinics accessible and welcoming. We need new thoughts on adherence: where should we be placing the long-acting ARVs?
- *Aim to reduce harm*. Antiretrovirals reduce harm; we need to involve key groups, providing ART for the infected and PrEP for the uninfected: *ART is for the entire community*. Retention in care for the infected. Push the 95-95-95 agenda.
- *In-your-face and regularly updated science-based HIV education*. Promote the 2030 targets. Keep all informed, with a regular slot on every television and radio channel. Keep the foot on the accelerator.
- *Involve the community*. We are all in this together. Close the gaps.

Further reading

- UNAIDS. Prevailing against pandemics by putting people at the centre [homepage on the Internet]. Geneva; 2020 [cited n.d.]. Available from: https://www.unaids.org/sites/default/files/media_asset/ prevailing-against-pandemics_en.pdf
- HIV Policy Lab. 2020 global HIV policy report: Policy barriers to HIV progress [homepage on the Internet]. 2020 [cited n.d.]. Available from: https://www.hivpolicylab.org/documents/reports/2020GlobalReport/2020%20HIV%20 Policy%20Lab%20 Executive%20Summary%20
- Johnson LF, Dorrington RE. Thembisa version 4.3: A model for evaluating the impact of HIV/AIDS in South Africa [homepage on the Internet]. 2020 [cited n.d.]. Available from: https://www.thembisa.org/
- Nyasulu JCY, Maposa I, Sikakhane BP, Pandya H. Access to HIV services and viral load suppression among children during the 90-90-90 strategy implementation in South Africa: A time-series analysis. S Afr J HIV Med. 2021;22(1):a1187. https://doi.org/10.4102/sajhivmedv22i1.1187
- Thigpen MC, Kebaabetswe PM, Paxton LA, et al. Antiretroviral preexposure prophylaxis for heterosexual HIV transmission in Botswana. N Engl J Med. 2012;367(5):423–434. https://doi.org/10.1056/NEJMoa1110711
- Mnyani C, Tait CL, Peters RPH, et al. Implementation of a PMTCT programme in a high HIV prevalence setting in Johannesburg, South Africa: 2002–2015. S Afr J HIV Med. 2020;21(1):a1024. https://doi.org/10.4102/sajhivmed.2020.v21i1.1024
- Woldesenbet SA, Kufa T, Lombard C, et al. The 2017 national antenatal sentinel HIV survey key findings, South Africa [homepage on the Internet]. [cited 2021 Sept 22] Available from: nicd.ac.za/wp-content/uploads/2019/07/Antenatalsurvey-report-24July19.pdf
- Bekker LG, Brown B, Joseph-Davey D, et al. Southern African guidelines on the safe, easy and effective use of pre-exposure prophylaxis: 2020. S Afr J HIV Med. 2020;21(1):a1152. https://doi.org/10.4102/sajhivmed.v21i1.1152
- Clement ME, Kofron R, Landovitz RJ. Long-acting injectable cabotegravir for the prevention of HIV infection. Curr Opin HIV AIDS. 2020;15(1):19–26. https://doi.org/10.1097/COH.0000000000000597
- Landovitz R, et al. HPTN 083 final results: pre-exposure prophylaxis containing long acting cabotegravir is safe and highly effective for cis-gender man and trans-gender women who have sex with men. International AIDS Conference (IAC); July 6–10, 2020 [cited 2021 Jan 29]. Available from: https://llwww.natap.org/2020/IAC/IAC_28.htm
- Delany-Moretlwe S, Hughes JP, et al. Long acting cabotegravir is safe and effective in preventing HIV infection in cisgender women: Interim results from HPTN 084, HIV R4P. HIV Research for Prevention conference - Virtual, January 27-28 and February 3-4, 2021. HY01.02.

3. Meya DB, Tugume L, Nabitaka V, et al. Establishing targets for advanced HIV disease – A call to action. S Afr J HIV Med. 2021;22(1):a1266. https://doi.org/10.4102/sajhivmed.v22i1.1266

Summary: The World Health Organization (WHO) defines advanced HIV disease (AHD) as HIV-associated disease in persons living with HIV and presenting to care with a CD4 cell count of < 200 cells/μL or with a WHO Stage 3 or 4 infection. The definition includes *all* children under the age of 5 years irrespective of their CD4 count (Further reading: WHO 2017). Advanced HIV disease

carries a high mortality and is more frequent in the hospitalised (Further reading: Carmona et al. 2018; Laher et al. 2021).A third of those who enter or who cycle in and out of HIV care have AHD. Many are ART experienced. *Can AHD be harnessed by 2030?* The 95% UNAIDS-2030 targets are a strategic opportunity (Meya et al. 2021 above):

> [*W*]e suggest that these specific targets … CD4 testing, CrAg [*cryptococcal antigen*] and *TB* testing, and treatment ... aligned to the WHO AHD package of care would be a step in the right direction.

The authors suggest a focus on:

- the newly HIV diagnosed
- those previously in care and (now) returning to care
- those failing antiretroviral treatment.

Identify persons with CD4+ counts of < 200 cells/µL, and prioritise checking the serum CrAG lateral flow assay and urine Xpert/tuberculosis (TB) lipoarabinomannan (LAM). Institute rapid ART initiation if patients are ART naïve or returning to or failing care. Always anticipate TB and TB-associated immune reconstitution – *never let it surprise you*. The writers urge the strengthening of measures to track and retain patients in care throughout sub-Saharan Africa.

Much in this article has been said before. However, this is a timely call to Africa's healthcare community to do something memorable: close the door on HIV by 2030. Is it doable? Read the article.

Further reading

- WHO. Guidelines for managing advanced HIV disease and rapid initiation of antiretroviral therapy. Geneva: World Health Organization; 2017.
- Carmona S, Bor J, Nattey C, et al. Persistnet high-burden of advanced HIV disease among patients seeking care in South Africa's National HIV Programme: Data from a nationwide laboratory cohort. Clin Infect Dis. 2018;66(Suppl_2):S111–S117. htpps://doi.org/10.1193/cid/ciy045
- Laher AE, Venter WDF, Richards GA, Paruk F. Profile of presentation of HIV-positive in-patients to an emergency department in Johannesburg, South Africa. S Afr J HIV Med. 2021;22(1):a1177. https://doi.org/10.4102/sajhivmed.v22i1.1177

4. Laher AE, Venter WDF, Richards GA, Paruk F. Profile of presentation of HIV-positive patients to an emergency department in Johannesburg, South Africa. S Afr J HIV Med. 2021;22(1):a1177. https://doi.org/10.4102/sajhivmed.v22i1.1177

Summary: This observational study examines the demographics, clinical presentation, diagnosis and outcome of 1224 persons living with HIV (PLWH) consecutively admitted to the emergency department of a large public hospital in Johannesburg between July 2017 and October 2018. Of these, 17.3% were ART naïve. Of the 75.2% who had started ART prior to this admission, 32.2% reported non-adherence.

This is a description of South Africans who sought medical help when sick – for some, too late. Although the group is young (median age, 36 years; interquartile ratio [IQR], 31–44 years), in-hospital mortality was high (n = 166; 13.6%). Immunity often severly weakened: the median CD4 count was 112 (IQR, 34–295) cells/µL, and almost half, n = 527 (47.5%), had a baseline CD4 of < 100 cells/µL. Active TB was diagnosed in 244 (20%), and 213 (86.3%) had extrapulmonary or disseminated TB infection.

The study has limitations: it is observational and its generalisability is limited. A priori, it has an emergency room bias that leans towards severity and poorer outcomes. Nevertheless, the authors draw a credible picture of the practice of everyday medicine in South Africa's public sector. Their article asks, '[*w*]hy the late presentation? Why the break with prior antiretroviral care?'

It is a timely story with which to address the call for an end to new HIV infections by 2030. The authors remind the reader that (Laher et al. 2021 above):

> [*T*]wo-thirds of the global population of people living with HIV (PLWH) are in sub-Saharan Africa (SSA). South Africa (SA) contributes approximately 7.5 million to the global number, more than twice that of any other country worldwide … the burden of HIV-related illness is still substantial, especially among the newly diagnosed, ART-naïve and those recently initiated onto treatment.

This article speaks to the practice of medicine in South Africa. It deserves to be read widely, as a reminder that HIV medicine is also about caring for the sick. I ask myself, what went wrong? Why are PLWH still dying in emergency room wards?

5. Archary M, Van Zyl R, Sipambo N, Sorour G. Optimised pediatric antiretroviral therapy to achieve the 95-95-95% goals. S Afr J HIV Med. 2021;22(1):a1278. https://doi.org/10.4102/sajhivmed.v22i1.1278

Summary: Eighty-four percent of new global HIV infections in children in 2019 were in Africa. The first half of this opinion piece reviews South Africa's experience in meeting the 2020 UNAIDS 90-90-90 targets in children.

South Africa's children are falling behind. The achieved overall targets in children were 79-47-34! While peripartum and pregnancy-related mother-to-child transmission in South Africa is now uncommon, breastfeeding-related transmission (4.3%) continues. And children infected in infancy still slip through the net to reappear, treatment naïve, in late childhood or adolescence. The second half of the article discusses advances in the management of children living with HIV in South Africa. Medication, adherence and 'responsible care' are nonetheless persistent points of worry, as are health systems. The authors cite the 7-year delay between registration of

an essential fixed-dose paediatric generic-combination antiretroviral by the Food and Drug Administration in the United States and registration in South Africa.

The good news in this report is in the new drug formulations for the very young: a dispersible, scored combination of abacavir/lamivudine (120/60 mg) for children weighing from 3 kg to 25 kg and a dispersible, scored 10 mg dolutegravir tablet to treat children from 4 weeks of age or weighing > 3 kg. These await approval by the South African Health Products Agency (SAHPRA). Future innovations? The long-acting injectables (8-weekly cabotegravir/rilpivirine) for children and adolescents aged 12–18 years. Will these be the answer to the current unimpressive viral suppression rates?

What about the larger context of children's health on our subcontinent? Consider that in the first year of the COVID-19 epidemic, 23 000 teenage (10–19 years) pregnancies occurred in South Africa's Gauteng province, of which 934 were in girls aged 10–14 years (Further reading: Bengu 2021). Gender-based violence takes many forms. This is one. The subtext of this article is exactly that society's children, particularly those living with HIV, deserve better. Children lag behind. The childhood gap in the diagnosis of HIV, treatment and viral suppression must be closed before 2030.

Further reading

- Bhengu L. Gauteng records more than 23 000 teen pregnancies in one year, some moms as young as 10. News24 , 2021 August 17.

6. Jefferis K, Avalos A, Phillips H, et al. Five years after treat-all implementation: Botswana's HIV response and future directions in the era of COVID-19. S Afr J HIV Med. 2021;22(1):a1275. https://doi.org/10.4102/sajhivmed.v22i1.1275

Summary: This review of Botswana's current and projected response to the HIV epidemic is clear-headed, thoughtful, data based and, in the main, optimistic. It details the country's roadmap from 2016 to the anticipated goal of no new or incident HIV infections by 2030. Unlike most of Africa, Botswana achieved the 90-90-90 UNAIDS targets before 2020! The country's population (2.4 million) is small and mostly urbanised: 375 900 (IQR, 353 500–400 150), or 15.7%, live with HIV.

Results from the current Botswana AIDS Incidence Survey are due in 2022. The expectation is that these will validate the country's positive trajectory towards the 2030 UNAIDS goals and perhaps achieve these before that date! Some issues remain. Women aged 15–24 years are at great risk of infection. Innovative, targeted ideas around prevention are needed. Many 'first-time' ART initiates (25%) do so with a CD4 count of < 200 cells/μL, that is, with advanced immune suppression. And many (76%) with CD4 counts of < 200 cells/μL are actually 'ART experienced', some poorly adherent and failing treatment and others with a dysfunctional immune response and a suppressed viral load. This represents a group needing more attention.

In their economic assessment, the authors anticipate a contraction of gross domestic product as a result of COVID-19. Botswana's government has had to increase spending. Budget deficits have been unavoidable. However, public spending is still expected to fill the gaps.

Looking to 2030, the authors define what is still needed:

- greater investment in sexual reproductive health interventions such as PrEP, particularly for young women
- national and international advocacy to reduce the exorbitant costs to Africa of laboratory reagents, commodities and supplies
- strengthening of differentiated care to those living with HIV and the streamlining of the care of those stable on minimal intervention (e.g. fewer laboratory tests)
- the upskilling (capacitation) of healthcare workers to identify and manage patients with AHD.

This article is a hopeful look at Botswana's future. It is recommended reading.

7. Lilian RR, Davies N, Gilbert L, et al. CD4 testing after initiation of antiretroviral therapy: Analysis of routine data from the South African HIV programme. S Afr J HIV Med. 2020;21(1):a1165. https://doi.org/10.4102/sajhivmed.v21i1.1165

Comment: I have included this article with our 2021 articles looking at achieving the UNAIDS 2030 guidelines because it speaks to the role of the CD4 cell count in long-term HIV care. This, too, has bearing on achieving the 2030 goals.

The authors follow the trajectory of the CD4+ cell count post-ART initiation in a large anonymised electronic South African patient database, the Three Interlinked Electronic Registers project, or TIER.Net. Records are from 2004–2021 and describe 1 178 190 persons in the South African public sector on ART in two urban (Gauteng) and two rural (Limpopo) settings. Overall, baseline CD4+ cell counts were low: 50% had CD4+ counts of < 200 cells/μL. By 2017, this percentage had improved to 37.2%. However, only 46.5% of CD4 counts captured on TIER.Net were repeated. Of these, 14.3% PLWH (n = 78 494) remained with CD4 counts of < 200 cells/μL. Indeed, 20% (n = 18 566) of those on ≥ 4 years of ART *and* with viral suppression, viz. a viral load (VL) of < 1000 copies/mL, were immune-non-responders or immune-discordant responders (Further reading: Yang et al. 2020; Laprise et al. 2013). The latter were likely to be on second-line ART (adjusted odds ratio [aOR], 1.79), older, viz. 35–45 years and particularly, > 45 years (aOR, 1.15 and 1.50, respectively), male (aOR, 2.28) and to have confirmed tuberculosis (aOR, 2.49). *Baseline* CD4 cell counts of > 350 cells/μL were protective of long-term immune deficiency (aOR: 0.35)!

So, when should CD4 tests be repeated in those on ART? 'Every 6 months post-baseline if the preceding CD4+ count was < 200 cells/μL'. However (Further reading: Nel et al. 2020):

> [*I*]f the CD4 count is > 200 cells/μL at baseline or it increases above this threshold on ART, then CD4 testing can be stopped, as therapeutic monitoring of ART is best accomplished with VL, not with CD4 count or clinical criteria. The efficacy of ART is measured not with repeated CD4 cell counts, but with regular VL monitoring.

Beyond the mechanics of treating those with a persistently low CD4+ count, Lilian et al.'s article is asking a bigger question: Does the immune system *ever* fully recover from HIV? What does this mean for the future? We are not at the end of the chapter on HIV. Nor do we fully understand what lies ahead.

This is an article that should be read and its message ruminated on.

Further reading

- Yang X, Su B, Zhang X, et al. Incomplete immune reconstitution in HIV/AIDS patients on antiretroviral therapy: Challenges of immune non-responders. J Leuko Biol. 2020;107(4):597–612. https://doi.org/10.1002/JLB.4MR1019-189R
- Laprise C, De Pokomandy A, Baril J-G, et al. Virologic failure following persistent low-level viremia in a cohort of HIV-positive patients: Results from 12 years of observation. Clin Infect Dis. 2013;57(10):1489–1496.
- Nel J, Dlamini S, Meintjes G, et al. South African HIV clinicians' society guidelines for antiretroviral therapy in adults: 2020 update. S Afr J HIV Med. 2020;21(1):a1115. https://doi.org/10.4102/sajhivmed.v21i1.1115

Importance of global communication to combat global pandemics: Lessons from the HIV Online Provider Education programme

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2021 SPECIAL ANNIVERSARY COLLECTION

Southern African Journal of HIV Medicine
ISSN: (Online) 2078-6751, (Print) 1608-9693

Importance of global communication to combat global pandemics: Lessons from the HIV Online Provider Education programme

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Dates:
Received: 22 June 2021
Accepted: 21 July 2021
Published: 31 Aug. 2021

How to cite this article:
Airewele EA, Sunpath H, Moosa M-YS, Gandhi RT. Importance of global communication to combat global pandemics: Lessons from the HIV Online Provider Education programme. S Afr J HIV Med. 2021;22(1), a1281. https://doi.org/10.4102/sajhivmed.v22i1.1281

In many ways, the coronavirus disease 2019 (COVID-19) pandemic mirrors the challenges, lessons and opportunities of the HIV pandemic. In this article, we argue that global pandemics such as COVID-19 and HIV require a global response. We highlight the HIV Online Provider Education (HOPE) programme as an example of the importance of global communication when combating a pandemic. From both the COVID-19 and HIV pandemics, we have learned that to optimise health worldwide, it is necessary to have effective and efficient means of swiftly sharing experiences, expertise, best practices and guidelines. To prepare for the next public health emergency, clinicians and researchers must put in place and promote effective programmes for global communication.

Keywords: HIV; AIDS; COVID-19; COVID; pandemic; communication; collaboration; global health; public health.

Twin pandemics: Coronavirus disease 2019 and HIV

When the novel coronavirus emerged in late 2019, much was unknown about its transmission, treatment and trajectory. In response to the rapidly growing case numbers and global spread, the World Health Organization declared the coronavirus disease 2019 (COVID-19) outbreak a public health emergency of international concern on 30 January 2020.[1] At the time, there was widespread uncertainty and fear about the mode of spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), leading to hysteria and responses such as washing down groceries and other measures that were ultimately discarded. Early on, there were no known treatments for COVID-19, and in many places around the world, medications that ultimately proved ineffective – like hydroxychloroquine – were frequently administered out of desperation.[2,3] In addition, it soon became clear that COVID-19 was disproportionately affecting key populations such as racial and ethnic minorities in the United States (US) and other countries and the poor all around the world. In many ways, these early responses to COVID-19 were eerily reminiscent of the world's first tentative responses to HIV/AIDS (Box 1).

Similar to the COVID-19 pandemic, when the first patient with AIDS was identified in the early 1980s, there was widespread fear of a new, unknown virus. Because of uncertainties about how HIV was spread, people were shunned and stigmatised. In addition, people with HIV then – and now – often belonged to the most vulnerable and marginalised communities. The parallels between HIV and COVID-19 treatments are also telling. As with COVID-19, early treatments for HIV were largely ineffective and often harmful. By 1987, the United States (US) Food and Drug Administration had approved the first antiretroviral medication, zidovudine, but it soon became evident that single-drug therapy had serious limitations. Since then, significant progress has been made in developing well-tolerated, highly effective combination antiretroviral treatments (ART), resulting in dramatic reductions in both morbidity and mortality.

Despite the similarities, there are also vast differences between COVID-19 and HIV. The former is primarily a respiratory viral infection transmitted by droplets and through the airborne route, with the majority of patients recovering spontaneously. The latter is a sexually transmitted and blood-borne viral disease that causes immunodeficiency and opportunistic conditions and is usually fatal if not treated. The former has had an unprecedented impact on the global economy, in part because of its rapid trajectory necessitating widespread lockdowns. Nevertheless, the parallels summarised above, and the global nature of both pandemics, highlight the critical need for global communication in our response.

BOX 1: Parallels between the HIV and coronavirus disease 2019 pandemics.

- Initial uncertainty about transmission leading to stigma and ineffective prevention measures
- Prior to definitive clinical trials, desperation leading to the use of unproven and potentially harmful therapies
- Disproportionate impact on key populations, like the poor and racial/ethnic minorities
- Highlights the intertwining of politics and public health: for HIV, initial neglect and a lack of funding; for COVID-19, contradictory evaluations of the severity of the pandemic and mixed messages regarding prevention measures
- Global response required to end the spread of the pandemic
- Importance of global communication and the exchange of experiences by clinicians to develop optimal management strategies

COVID-19, coronavirus disease 2019.

A prime example of global communication to advance health occurred during the roll-out of HIV treatment throughout the world. The largest number of people with HIV reside in sub-Saharan Africa, specifically South Africa. In the early days of ART, management of HIV was rapidly evolving, and it was critically important to keep clinicians abreast of the latest in the treatment of this disease. It was in this context that the HIV Online Provider Education (HOPE) programme was developed and now serves as an important example of how a global communication network can be utilised to advance health in disparate parts of the world.

Development of the HIV Online Provider Education programme

The HOPE programme was established in 2003, around the time of the launch of the President's Emergency Plan for AIDS Relief (PEPFAR). The HOPE programme was developed by three collaborators: Dr Rajesh Gandhi, Director of HIV Clinical Services and Education at Massachusetts General Hospital, Professor of Medicine at Harvard Medical School and, at the time, Director of the Harvard University Center for AIDS Research Clinical Core; Dr Henry Sunpath, then Chief of Medicine at McCord Hospital; and Dr Yunus Moosa, Chief of Infectious Diseases at the King Edward VIII Hospital, University of KwaZulu-Natal. From the beginning, HOPE and a face-to-face yearly conference called the Annual Workshop on Advanced Clinical Care – AIDS, or AWACC – were joint projects of the McCord Hospital, the University of KwaZulu-Natal, Massachusetts General Hospital and the Harvard University Center for AIDS Research. As a result of Drs Sunpath and Moosa's collaborative activities with the KwaZulu-Natal Department of Public Health, there were frequent discussions and dynamic exchanges of ideas between the conference organisers and public health officials. Most importantly, unlike some educational activities that have originated in the Global North and spread to the Global South, HOPE was in its essence a joint and highly collaborative project – a digital 'two-way street' – that fostered global communication around the treatment of people with HIV.

The early interactions between researchers and clinicians in South Africa and the US exemplify the collaborative nature of the HOPE programme and affiliated activities. In 2002, before the national ART roll-out strategy began in South Africa, McCord Hospital was one of the largest centres providing dedicated HIV care in South Africa, where AIDS denialism existed for many years. Early on, clinicians struggled with developing treatment guidelines to manage adverse events, treatment failure and coinfections within the constraints of a limited ART formulary and laboratory support. In 2003 clinicians and researchers from the US, including Prof. Gerald Friedland from Yale and Prof. Bruce Walker from Harvard Medical School, reached out to leaders at McCord Hospital, resulting in joint site visits by senior infectious disease specialists. Jointly and collaboratively, clinicians and researchers developed clinical algorithms to manage a broad array of diagnostic and therapeutic problems. The infectious diseases unit at the University of KwaZulu-Natal also participated in the joint working group with colleagues from the US and McCord and participated in case-based discussions as the ART programme grew to about 3500 patients. As word of the success of the work at McCord Hospital spread in the community, many clinicians from KwaZulu-Natal and throughout South Africa were keen to collaborate with us to develop ART programmes. In 2004, PEPFAR came on board to support the McCord Hospital programme, and the numbers of patients on ART expanded significantly. In addition, many surrounding clinics sent healthcare workers to our regular continuing medical education meetings. The Department of Health was also interested in working with us to develop treatment protocols and training programmes. With the leading roles of Prof. Gandhi and our team in Durban, we started the first AWACC in 2006. The meeting was widely acclaimed as a most relevant exchange of expertise in HIV care in resource-limited settings in Africa.

The HIV Online Provider Education programme

The HOPE programme focuses on topics relevant to the care of people with HIV in resource-limited settings. Through regular internet-based conferences, the HOPE programme serves as an opportunity for continuing education and the sharing of best practices in HIV medicine for clinicians worldwide. In addition to a programme focused on physicians, a parallel conference was designed specifically for nurses.[4]

During the early years of the HOPE programme, clinicians in the US had more experience treating patients with ART. Because of this, HOPE conferences were primarily case based and followed the 'mentoring the mentor' model to support South African, Zimbabwean, US, Haitian, Dominican and Indian clinicians. It was realised early on that clinicians learned best when clinical problems were constructed around a real-life clinical case, and this led to a case-based as opposed to a didactic approach to teaching.

Initially, because of the toxicities of the available antiretroviral medications, much of the focus was on managing the

complications arising from treatment. In particular, the unavoidable reliance on antiretroviral agents such as stavudine and didanosine led to a rise in complex metabolic complications such as lactic acidosis, pancreatitis, lipodystrophy and peripheral neuropathy.[5] Through the HOPE programme, clinicians gained familiarity with the adverse events commonly associated with ART and developed confidence in identifying and managing these conditions using locally available resources. Physicians in the US offered advice based on years of clinical experience with similar toxicities and often influenced discussions and policies in South Africa. The HOPE conferences and in-person conferences like AWACC also served as opportunities for clinicians to advocate for access to better-tolerated and less toxic medications, like tenofovir. Eliminating stavudine and didanosine from the ART formulary in South Africa took approximately 6 years, during which time physicians worked collaboratively to develop guidelines to manage toxicities.

In addition to toxicities, antiretroviral drug resistance emerged as a significant threat to the impact of these medications in reducing morbidity and mortality. A 2008 study from two clinics in Durban, South Africa, demonstrated that > 83% of patients with virological failure had a least one major resistance mutation, and, of particular concern, mutations resulting in resistance to at least two classes of drugs were present in more than half of those tested.[6] The HOPE conference served as a critical forum for clinicians to discuss and develop management strategies for patients with drug-resistant HIV. Again, these discussions influenced policies related to the management of virological failure.

Attending the HOPE conferences in real time served as an opportunity for the immediate exchange of knowledge while simultaneously facilitating networking with physicians around the world. Through the HOPE programme, physicians in the US and South Africa have been able to connect and engage in collaborative research. The potential to serve as a networking platform was an unexpected beneficial outcome of the real-time nature of the HOPE conferences. For those unable to join the conferences live, recordings, references and slide presentations have been made available at no cost on the HOPE website after each conference.

What has been the utilisation of and response to HOPE? When HOPE first started, 2000–3000 users logged in annually. In recent years, this number has increased at least threefold to around 9000 attendees per year. Since tracking began in 2012, almost 20 000 users have viewed the conferences, with almost 95 000 conference page views. About 60% of those accessing conferences are medical doctors, 20% are nurses, 10% are nurse practitioners and 10% are medical students. In terms of geographic distribution, visitors are most frequently from the US, South Africa, Dominican Republic, Canada and Argentina.

Surveys of HOPE conference attendees reveal that 95% of the participants report the content is relevant to their practice and that a similar proportion report that there is an appropriate mix of didactic and interactive material. In its early years, attendees asked for additional content relevant to nurses, which led to the development of a parallel HOPE nurses' conference. The cost of the programme has mainly been the time and effort of the organisers who arrange the speakers and discussants, as well as the project coordinator for the programme, whose time and effort has been supported by the Harvard University Center for AIDS Research as a component of its training mission. The HOPE conference itself is free of charge for all participants.

Over time, as South African clinicians gained experience in the care of patients with HIV, they themselves evolved into experts in their own right, and the HOPE programme shifted focus to summarising the latest in HIV research and innovation. These conferences now serve as an important platform to keep providers in the US, South Africa and other parts of the globe up to date with the latest advances in the field. Of late, the HOPE programme has pivoted to incorporating content geared towards confronting the latest global pandemic, COVID-19. One such recent conference described the impact of the B.1.351 (beta) variant of SARS-CoV-2, which was instrumental in alerting US clinicians to the challenges ahead.

Looking ahead

Through the HOPE programme, we can see how global communication positively impacts health education internationally. By expanding and developing other programmes like HOPE, clinicians can position themselves to mount an effective global response to health threats like HIV and COVID-19. Interactive online clinical discussions are one of many ways in which the global medical community can bridge the gap in medical education to promote better health outcomes for people everywhere. To reach the Joint United Nations Programme on HIV/AIDS targets for 2030, it is of the utmost importance that collaborative educational initiatives that started at the turn of this century expand and continue.

Acknowledgements

Competing interests

The authors declare that they have no financial or personal relationships that may have inappropriately influenced them in writing this article.

Authors' contributions

All authors contributed to the conception of the presented work. E.A.A. and R.T.G. wrote the original manuscript with support from M.-Y.S.M. and H.S. All authors contributed to the final manuscript and approved of the version to be published.

Ethical considerations

This article followed all ethical standards for research without direct contact with human or animal subjects.

Funding information

R.T.G. received grant funding from the Harvard University Center for AIDS Research (NIH P30 AI060354) and the AIDS Clinical Trials Group (NIH/NIAID 2 UMAI069412-09).

Data availability

Data sharing is not applicable to this article as no new data were created or analysed in this study.

Disclaimer

The views and opinions expressed in this article are those of the authors and do not necessarily reflect the official policy or position of any affiliated agency of the authors.

References

1. World Health Organization. Statement on the second meeting of the International Health Regulations (2005) Emergency Committee regarding the outbreak of novel coronavirus (2019-nCoV) [homepage on the Internet]. 2020 [cited 2020 Jan 30]; [updated 2020 Jan 30]. Available from: https://www.who.int/news/item/30-01-2020-statement-on-the-second-meeting-of-the-international-health-regulations-(2005)-emergency-committee-regarding-the-outbreak-of-novel-coronavirus-(2019-ncov)
2. Siedner MJ, Gandhi RT, Kim AY. Desperate times call for temperate measures: Practicing infectious diseases during a novel pandemic. J Infect Dis. 2020;222(7):1084–1085. https://doi.org/10.1093/infdis/jiaa209
3. Airewele E, Gandhi RT. Trials and therapeutics: Important lessons from the COVID-19 pandemic. Harvard Health Pol Rev [serial online]. 2021 [cited 2021 Apr 30]. Available from: http://www.hhpronline.org/articles/2021/4/30/trials-and-therapeutics-important-lessons-from-the-covid-19-pandemic
4. Kiviat AD, Geary MC, Sunpath H, et al. HIV Online Provider Education (HOPE): The Internet as a tool for training in HIV medicine. J Infect Dis. 2007;196(Suppl 3):S512–S515. https://doi.org/10.1086/521117
5. Murphy RA, Sunpath H, Kuritzkes DR, Venter F, Gandhi RT. Antiretroviral therapy-associated toxicities in the resource-poor world: The challenge of a limited formulary. J Infect Dis. 2007;196(Suppl 3):S449–S456. https://doi.org/10.1086/521112
6. Marconi VC, Sunpath H, Lu Z, et al. Prevalence of HIV-1 drug resistance after failure of a first highly active antiretroviral therapy regimen in KwaZulu-Natal, South Africa. Clin Infect Dis. 2008;46(10):1589–1597. https://doi.org/10.1086/587109

Optimised paediatric antiretroviral treatment to achieve the 95-95-95 goals

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2021 SPECIAL ANNIVERSARY COLLECTION

Southern African Journal of HIV Medicine
ISSN: (Online) 2078-6751, (Print) 1608-9693

Optimised paediatric antiretroviral treatment to achieve the 95-95-95 goals

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Dates:
Received: 21 June 2021
Accepted: 14 July 2021
Published: 01 Sept. 2021

How to cite this article:
Archary M, van Zyl R, Sipambo N, Sorour G. Optimised paediatric antiretroviral treatment to achieve the 95-95-95 goals. S Afr J HIV Med. 2021;22(1), a1278. https://doi.org/10.4102/sajhivmed.v22i1.1278

While the progress towards reaching the UNAIDS 95-95-95 targets in South African adults seems promising, the progress in the paediatric population is lagging far behind; only 79% percent of children living with HIV know their status. Of these, only 47% are on treatment, and a mere 34% of those are virally suppressed. Thus, virological suppression has been attained in only 13% of children living with HIV in South Africa. Multiple factors contribute to the high treatment failure rate, one of them being a lack of paediatric-friendly antiretroviral treatment (ART) formulations. For example, the Lopinavir/ritonavir syrup, which is the current mainstay of ART for young children, has an extremely unpleasant taste, contributing to the poor tolerability and lack of adherence by children using the formulation. Furthermore, the lack of appropriate formulations limits the optimisation of regimens, especially for young children and those who cannot swallow tablets. Switching from syrups to dispersible tablets will improve ease of administration and adherence and result in cost-saving. Despite the approval of simplified paediatric-friendly formulations internationally, including other sub-Saharan African countries, unnecessary delays are experienced in South Africa. Clinician groups and community organisations must speak up and demand that approvals be expedited to ensure the delivery of life-changing and life-saving formulations to our patients as a matter of urgency.

Keywords: paediatric; HIV/AIDS; ART; 95-95-95 goals; PMTCT.

According to the latest global Joint United Nations Programme on HIV and AIDS (UNAIDS) estimates, 1.8 million children live with HIV worldwide, with 150 000 new infections in children aged 0–14 years contributing to 9% of the overall new infections in 2019. Of these new infections, 84% occurred in sub-Saharan Africa, with around 95 000 HIV-related deaths in children reported in 2019.[1] While South Africa's prevention of mother-to-child transmission programme has been successful in decreasing the rate of vertical transmission of HIV to 3% (from 16% in 2010), paediatric HIV treatment programmes have not been as successful.[2]

In 2019, HIV-related deaths in South African children declined to 4100, and the number of children living with HIV remained more or less stable at 340 000.[1] As part of working towards ending the HIV pandemic by 2030, attaining and maintaining virological suppression is critical. The current South African statistics in the overall population in terms of the UNAIDS 95-95-95 targets (diagnosis of 95% of all people living with HIV, achieving 95% on antiretroviral treatment [ART] among those diagnosed and 95% virally suppressed among those being treated) are 92-75-92.[1] In the paediatric population, however, the progress towards meeting the treatment cascade goals is lagging far behind. Only 79% of children living with HIV know their status. Of these, only 47% are on treatment, and a mere 34% of those on treatment are virally suppressed.[1]

Treatment failure is multifactorial, but suboptimal adherence remains the most significant contributing factor. One of the reasons for non-adherence is the difficulty in obtaining treatment. The barriers to accessing treatment include physical challenges such as getting to clinics in remote areas, drug stock-outs and, recently, interrupted clinical services resulting from coronavirus disease 2019 (COVID-19) restrictions. Although the effect of lockdown had a more significant impact on HIV testing and the initiation of ART, the provision of ART was also affected.[3] Disruptions to HIV programmes during the COVID-19 pandemic will have the most significant impact on HIV-related deaths. Based on modelling studies, the interruption of ART for 6 months in 50% of patients on ART will result in over 296 000 estimated deaths in sub-Saharan Africa annually.[4]

In the paediatric population, adherence is dependent on the motivation and commitment of the parent or caregiver. A lack of appropriate paediatric ART formulations adds to the burden of giving treatment to a child regularly enough to maintain high levels of adherence and obtain viral suppression. The classic 'culprit' is lopinavir/ritonavir (LPV/r) syrup: toddlers often refuse to

take the treatment or vomit after the parent or caregiver administers the syrup because of the extremely unpleasant taste. In addition, the lack of fixed-dose combinations (FDC) for children results in complicated dosing regimens that negatively affect long-term adherence and retention in care.

Supporting the move to simplified paediatric-friendly formulations

The shift away from multiple syrup formulations for children unable to swallow tablets, previously the mainstay of the paediatric HIV treatment regimens in South Africa, has been delayed compared to other sub-Saharan African countries. This has been because of the painstakingly slow regulatory approval of generic FDC formulations designed for children. For example, the United States Food and Drug Administration (USFDA) approved the generic FDC of abacavir (ABC) and lamivudine (3TC) (120/60 mg) in 2014 (see Figure 1).[5] The South African product submission to the South African Health Products Regulatory Authority (SAHPRA), then called the Medicines Control Council, only followed in 2016. Approval, however, only occurred in 2021, 7 years later.

The impact of optimised paediatric formulations cannot be overemphasised. For example, an 11 kg infant on ABC and 3TC will require a 6 mL twice-daily dose of each syrup, or 24 mL per day, and a total monthly supply of 672 mL, compared to a child who is switched to an FDC of ABC/3TC (120/60 mg) dispersible tablet (DT). Switching to the FDC ABC/3TC requires two tablets daily, or a bottle of 56 pills per month.[7] These changes impact the patient and caregiver acceptability and adherence as well as the health system costs, including cost savings on syringes and a decrease in the required storage space.

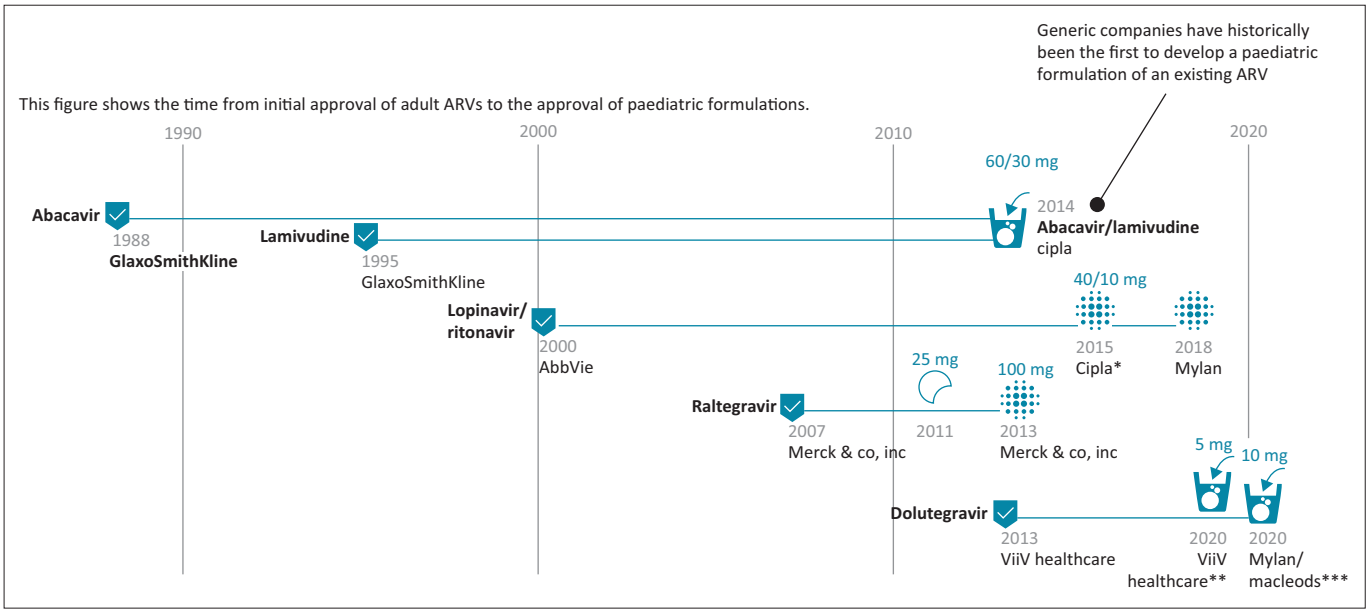
Abacavir/lamivudine fixed-dose combination formulations

The FDC of ABC/3TC (600/300 mg) was registered for use in South Africa from 2012 and was included in the paediatric and adolescent dosing guidelines soon afterwards, facilitating a once-daily nucleoside/nucleotide reverse transcriptase inhibitor (NRTI) backbone in children above 25 kg.[8] This film-coated tablet should be swallowed whole and not cut or crushed, preventing the use of the formulation in younger children.

The new dispersible scored ABC/3TC FDC (120/60 mg) allows for flexible dosing and administration. The formulation can be dissolved in liquid and administered, chewed or swallowed whole, allowing the use of the formulation from young infants to older children. The dose proportions align with the World Health Organization (WHO) dosage recommendations developed to facilitate once-daily dosing of the NRTI backbone in children over 4 weeks of age and weighing 3 kg. The scored DT allows dosing in increments of 60/30 mg, which, when cut in half, allows for dosing across a wide weight range from 3 kg to 25 kg. In addition, the child-friendly flavouring of the formulation adds to the appeal. In South Africa, two generic manufacturers have made this FDC available to patients in the public sector.[7]

Dolutegravir

The basis for introducing integrase inhibitors into the adult guidelines was the higher genetic barrier to resistance, improved side-effect profile and viral suppression rate associated with dolutegravir (DTG). While evidence for a potential association with neural-tube defects (NTDs) and increased weight gain has slowed down the introduction of DTG, especially in women of child-bearing potential, the opening into the paediatric population has been delayed by



Source: Access to Medicine Foundation. Ending the burden of HIV, malaria and TB in children: Children and the 'big three' epidemics: Despite significant advances in HIV, many children remain at risk, June 2020 [homepage on the Internet]. [cited 2021 June 17]. Available from: https://accesstomedicinefoundation.org/publications/ending-the-burden-of-hiv-malaria-and-tb-in-children.[6]
ARV, antiretroviral.

FIGURE 1: Timelines for paediatric antiretroviral approvals are shortening, but unnecessary delays remain.

the lack of appropriate formulations. The inclusion of adolescents early into studies such as IMPAACT P1093[9,10] has allowed their concurrent access, if weighing over 30 kg, to the 50 mg formulation as per the adult formulations in the national guidelines.[8]

The initial registration trial for DTG included 35 mg and 25 mg doses for children weighing 20 kg – 30 kg and 15 kg – 20 kg, respectively, requiring two additional formulations of a 25 mg and 10 mg tablet. Further pharmacokinetic evaluation conducted as a substudy of the Odyssey trial evaluated the use of the 50 mg tablet in children between 20 kg and 30 kg.[11] Acceptable pharmacokinetics and side-effect profile supported the USFDA registration of DTG 50 mg daily in children from 20 kg. In addition, the new dosage recommendation was added to the WHO and several national guidelines, including the South African national ART guidelines.[8]

To dose children weighing below 20 kg, a 5 mg dispersible tablet of DTG (DTG DT) was developed by the originator, ViiV. Pharmacokinetic evaluation as part of the P1093 and Odyssey trials again supported the registration of the new formulation by the USFDA and European Medicines Agency in 2020 starting at 4 weeks of age and 3 kg in weight.[12] In addition, as part of ViiV's commitment to providing early access to DTG in low- and middle-income countries (LMICs), a sharing of the technical specifications with generic manufacturers has allowed the development of a scored 10 mg DTG DT.[13] This has allowed DTG to be the first-line ART of choice across the age spectrum from 4 weeks of age in the new consolidated WHO guidelines. Registration of this new dispersible formulation by SAHPRA is eagerly awaited and will allow inclusion in the South African guidelines. The approval of DTG DT will facilitate the move away from using LPV/r syrup formulations and their associated problems.

At a recent conference presentation of the results of the Odyssey trial, there was no significant difference in weight gain in participants on a DTG versus non-DTG-containing regimen.[14] In addition, the frequency of metabolic adverse events was lower in the DTG arm. These findings are reassuring and further support the use of DTG-based regimens in children. Furthermore, with an increase in the available cohort data, the association of NTDs and the use of DTG in the first trimester has decreased. The additional data support the use of DTG in women of child-bearing potential and has implications for introducing DTG in adolescent girls.

Tuberculosis is a common coinfection in South Africa, especially in people living with HIV. Co-treatment with rifampicin (Rif)-containing tuberculosis treatment and DTG results in a significant decrease in the DTG plasma concentration. Data in the adult population have supported 50 mg twice daily while on Rif to counteract the increased hepatic metabolism. In addition, a substudy of the Odyssey trial provided supportive data for this strategy in adolescents receiving Rif and DTG 50 mg tablets.[15] There is a lack of data on the pharmacokinetics of Rif and DTG DT; however, based on the data from adults and adolescents, the USFDA in the registration of DTG DT recommended twice-daily dosing of DTG DT in children receiving Rif. Further studies are required to confirm this strategy; however, international guidelines are likely to support this approach while awaiting more supporting data.

As other global medicine regulatory authorities have extensively reviewed the formulation, advocates for the right of children to have access to the best available treatment options, clinician groups and community organisations need to be more vocal in demanding that the approval of this formulation be expedited in South Africa.

Future innovations for simplified paediatric-friendly formulations

Further simplification of both treatment and prophylactic regimens for children in the future is likely to positively impact the goal of eliminating mother-to-child transmission and achieving the 95-95-95 milestone.

The recent registration of long-acting injectable cabotegravir/rilpivirine (LA CAB/RPV) administered every 2 months in HIV-infected individuals over 18 years by the USFDA highlights the direction of future treatment simplification. Results from the Mocha trial will support the registration of LA CAB/RPV in adolescents between 12 and 18 years old. While the need for refrigeration during storage of LA CAB/RPV may limit the use in LMICs, it opens up new treatment options. This is because LA CAB/RPV is administered intramuscularly, where it forms a crystalline structure that slowly releases the active drug into the plasma. A planned study in protocol development (IMPAACT 2036) hopes to explore LA CAB/RPV in younger children 2–12 years of age and aims to start in 2022. As we move these formulations into younger patients, the injection volumes, injection site (gluteal vs lateral thigh), changes in weight between injections and changes in the absorption and metabolism will need further evaluation.

Other formulations and delivery mechanisms in development include long-acting oral and implantable formulations (e.g. islatravir and lenacapavir), long-acting broadly neutralising antibodies and microarray patches. Each of these formulations is likely to play a significant part in the future treatment and prevention options for children and adolescents.

The scope for simplifying paediatric ART regimens has vastly improved, with the potential for a once-a-day solid formulation regimen from 4 weeks of age. Robust advocacy from clinicians and the community is required to ensure that these life-changing formulations are made available to our patients as soon as possible.

Acknowledgements

The authors acknowledge Leora Sewnarain for formatting, language editing and proofreading the article.

Competing interests

The authors declare that they have no financial or personal relationships that may have inappropriately influenced them in writing this article.

Authors' contributions

M.A., R.v.Z., N.S. and G.S. read and approved the final manuscript.

Ethical considerations

This article followed all ethical standards for research without direct contact with human or animal subjects.

Funding information

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Data availability

Data sharing is not applicable to this article as no new data were created or analysed in this study.

Disclaimer

The views and opinions expressed in this article are those of the authors and do not necessarily reflect the official policy or position of any affiliated agency of the authors.

References

1. Joint United Nations Programme on HIV/AIDS (UNAIDS). UNAIDS Data 2020 [homepage on the Internet]. [cited 2021 June 17]. Available from: https://www.unaids.org/en/resources/documents/2020/unaids-data
2. Woldesenbet SA, Jackson DJ, Lombard CJ, et al. Structural level differences in the mother-to-child HIV transmission rate in South Africa: A multilevel assessment of individual-, health facility-, and provincial-level predictors of infant HIV transmission. J Acquir Immune Defic Syndr. 2017;74(5):523–530. https://doi.org/10.1097/QAI.0000000000001289
3. Dorward J, Khubone T, Gate K, et al. The impact of the COVID-19 lockdown on HIV care in 65 South African primary care clinics: An interrupted time series analysis. Lancet HIV. 2021;8(3):e158–e165. https://doi.org/10.1016/S2352-3018(20)30359-3
4. Jewell BL, Mudimu E, Stover J, et al. HIV modelling consortium: Potential effects of disruption to HIV programmes in sub-Saharan Africa caused by COVID-19: Results from multiple mathematical models. Lancet HIV. 2020;7(9):e629–e640. https://doi.org/10.1016/S2352-3018(20)30211-3
5. FDA Approved Drugs. ABACAVIR Sulfate and Lamivudine No. 202381 [homepage on the Internet]. [cited 2021 June 17]. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/pepfar/202381PI.pdf
6. Access to Medicine Foundation. Ending the burden of HIV, malaria and TB in children: Children and the 'big three' epidemics: Despite significant advances in HIV, many children remain at risk, June 2020 [homepage on the Internet]. [cited 2021 June 17]. Available from: https://accesstomedicinefoundation.org/publications/ending-the-burden-of-hiv-malaria-and-tb-in-children
7. Republic of South Africa Department of Health. Antiretroviral drug dosing chart for children 2021 [homepage on the Internet]. [cited 2021 June 21]. Available from: https://sahivsoc.org/Files/PaedDosingChart_2021.pdf
8. Republic of South Africa Department of Health. ART clinical guidelines for the management of HIV in adults, pregnancy, adolescents, children, infants and neonates [homepage on the Internet]. 2019 Oct [updated 2020 Mar; cited 2021 June 17]. Available from: https://www.knowledgehub.org.za/system/files/elibdownloads/2020-05/2019%20ART%20Guideline%2028042020%20pdf.pdf
9. Viani RM, Alvero C, Fenton T, et al. P1093 study team: Safety, pharmacokinetics and efficacy of dolutegravir in treatment-experienced HIV-1 infected adolescents: Forty-eight-week results from IMPAACT P1093. Pediatr Infect Dis J. 2015;34(11):1207–1213. https://doi.org/10.1097/INF.0000000000000848
10. Viani RM, Ruel T, Alvero C, et al. P1093 study team: Long-term safety and efficacy of dolutegravir in treatment-experienced adolescents with human immunodeficiency virus infection: Results of the IMPAACT P1093 study. J Pediatric Infect Dis Soc. 2020;9(2):159–165. https://doi.org/10.1093/jpids/piy139
11. Bollen PDJ, Moore CL, Mujuru HA, et al. ODYSSEY trial team: Simplified dolutegravir dosing for children with HIV weighing 20 kg or more: Pharmacokinetic and safety substudies of the multicentre, randomised ODYSSEY trial. Lancet HIV. 2020;7(8):e533–e544. https://doi.org/10.1016/S2352-3018(20)30189-2
12. International Maternal Pediatric Adolescent AIDS Clinical Trials Network (IMPAACT). P1093 abstracts [homepage on the Internet]. [cited 2021 June 17]. Available from: https://www.impaactnetwork.org/publications/abstracts?search_api_fulltext=P1093
13. Medicines Patent Pool. Dolutegravir – Paediatrics (DTG) [homepage on the Internet]. ViiV Healthcare, April 2014. [cited 2021 June 17]. Available from: https://medicinespatentpool.org/licence-post/dolutegravir-paediatrics-dtg/
14. Turkova A. Dolutegravir-based ART is superior to NNRTI/PI-based ART in children and adolescents [homepage on the Internet]. 28th conference on retroviruses and opportunistic infections (CROI). Abstract No. 174; June 3 – Nov 3, 2021 | Virtual [cited 2021 June 17]. Available from: https://www.croiconference.org/abstract/dolutegravir-based-art-is-superior-to-nnrti-pi-based-art-in-children-and-adolescents/
15. Waalewijn H, Mujuru HA, Amuge P, et al. Adequate dolutegravir exposure dosed BID with rifampicin in children 6 to <18 years [homepage on the Internet]. 27th conference on retroviruses and opportunistic infections (CROI). Abstract No. 847; Mar 8–11, 2020. Boston, MA. [cited 2021 June 17]. Available from: https://www.croiconference.org/abstract/adequate-dolutegravir-exposure-dosed-bid-with-rifampicin-in-children-6-to/

Ten years of nurse-initiated antiretroviral treatment in South Africa: A narrative review of enablers and barriers

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2021 SPECIAL ANNIVERSARY COLLECTION

Southern African Journal of HIV Medicine
ISSN: (Online) 2078-6751, (Print) 1608-9693

Ten years of nurse-initiated antiretroviral treatment in South Africa: A narrative review of enablers and barriers

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Dates:
Received: 13 Nov. 2020
Accepted: 24 Dec. 2020
Published: 11 Mar. 2021

How to cite this article:
Crowley T, Mokoka E, Geyer N. Ten years of nurse-initiated antiretroviral treatment in South Africa: A narrative review of enablers and barriers. S Afr J HIV Med. 2021;22(1), a1196. https://doi.org/10.4102/sajhivmed.v22i1.1196

Background: The roll out of nurse-initiated and managed antiretroviral treatment (NIMART) was implemented in 2010 by the National Department of Health (NDoH) in South Africa in response to the large numbers of persons living with HIV who needed treatment. To enable access to treatment requires shifting the task from doctors to nurses, which had its own challenges, barriers and enablers.

Objectives: The aim of this narrative is to review content on the implementation of NIMART in South Africa over the period 2010–2020, with a focus on enablers and barriers to the implementation.

Method: A comprehensive search of databases, namely, PubMed, Google Scholar and Cumulative Index to Nursing and Allied Health Literature (CINAHL), yielded qualitative, quantitative and mixed-method studies that addressed various topics on NIMART. Inclusion and exclusion criteria were set and 38 publications met the inclusion criteria for the review.

Results: Training, mentorship, tailored tuberculosis (TB) and HIV guidelines, integration of services and monitoring and support have enabled the implementation of NIMART. This resulted in increased knowledge and confidence of nurses to initiate patients on antiretroviral treatment (ART) and decreased time to initiation and loads on referral facilities. Barriers such as non-standardised training, inadequate mentoring, human resource constraints, health system challenges, lack of support and empowerment, and challenges with legislation, policy and guidelines still hinder NIMART implementation.

Conclusion: Identifying barriers and enablers will assist policymakers in implementing a structured programme for NIMART in South Africa and improve access, as well as the training and mentoring of professional nurses, which will enhance their competence and confidence.

Keywords: nurse-initiated; NIMART; South Africa; antiretroviral treatment; enablers; barriers.

Introduction and background

The implementation of nurse-initiated and managed antiretroviral treatment (NIMART) was a direct response to the high rate of persons living with HIV and requiring treatment. Initially, antiretroviral treatment (ART) was provided in hospitals and initiation was performed by doctors. With more patients requiring treatment, as HIV infections soared and doctors' capacity exceeded, a task shifting model was implemented, with nurses in the public sector having to initiate ART to scale up HIV treatment and increase access for more South Africans living with HIV.[1] Poor socio-economic conditions and distances that patients had to travel to access care brought the need to decentralise HIV management services to primary healthcare (PHC) facilities. This, in turn, increased pressure to have more nurses trained to initiate ART and manage stable patients following national guidelines.[2]

The evidence that task-shifting may improve health outcomes, quality of care and patient satisfaction,[3,4] together with the additional benefits of decentralisation of treatment[5] and the growing numbers of persons living with HIV in South Africa, necessitated the wide-scale implementation of NIMART training. The World Health Organization recommendations and guidelines for task-shifting[6] advocate that task-shifting should be implemented alongside efforts to increase the skilled workforce, health systems reorganisation and an enabling regulatory framework. Continued quality of care can only be maintained with standardised competency-based training, supportive mentoring and effective referral systems.[6] Whilst there has been evidence that NIMART-trained nurses can initiate and manage patients successfully, researchers cautioned that we may not know

enough about key patient-, provider- and organisational-level enablers and barriers of wide-scale implementation.[7]

It has been 10 years since the initial NIMART implementation in South Africa in 2010. Human immunodeficiency virus treatment and management guidelines have been revised several times since the ART implementation, and HIV care has been integrated into various other services such as general PHC,[8] tuberculosis (TB) management[9] and antenatal care.[10] Nurse-initiated and managed ART has also expanded to include the management of children and patients with virological failure.[11]

With such wide-scale implementation and the evolving role of nurses in the context of NIMART and HIV management, it is inevitable that there may be challenges. Recent reviews that have summarised the enablers and barriers of the implementation of NIMART in the context of South Africa could not be found in the literature. It therefore became critical to search the literature in order to identify enablers and barriers and to make recommendations that will improve NIMART implementation.

Aim

The aim of the article is to review published literature on NIMART in South Africa, with particular focus on the enablers and barriers to implementation.

Method

In order to provide a comprehensive synthesis of the evidence and a broad perspective on NIMART, articles on the topic, its history and development were searched and presented in a narrative format.[12] A narrative overview or review is a non-systematic narrative synthesis of previously published literature.[12]

Search strategy and study selection

PubMed, CINAHL and Google Scholar databases were searched for relevant South African articles published between January 2010 and June 2020. Different search strategies were applied, using the MESH term combinations. In PubMed and CINAHL, we used Boolean operations such as (['nurse-initiated'] AND NIMART) AND 'South Africa') and in Google Scholar we used a string (NIMART South Africa). We identified additional records by reviewing master's or PhD e-theses, conference abstracts and published studies known to the authors. Relevant grey literature, such as Department of Health documents, was also included.

One of the authors and a research assistant screened the abstracts for relevancy. Articles were included if they met the following criteria: published in English, between January 2010 and June 2020 and reported studies conducted in South Africa. Records were excluded if the results did not relate directly to NIMART or if the study was not conducted in South Africa.

Data extraction and evidence appraisal

Data on the study aim, methods, sample and key enablers and barriers were extracted in tabular format. The quality of evidence was appraised using the John's Hopkins Evidence Level and Quality Guide.[13]

Ethical consideration

This article followed all ethical standards for research without direct contact with human or animal subjects.

Results

A total of 479 records were identified: 7 from PubMed and CINAHL, 475 from Google Scholar and 15 through the authors of this article. After removing duplicates and excluding studies not relevant to the topic, 38 publications were included in our narrative literature review. The review includes qualitative, quantitative and mixed-methods studies and literature reviews that reported on evidence related to the NIMART implementation in South Africa.

Almost all the studies were classified as level III, B (non-experimental studies of good quality).[13] Most of the quantitative and qualitative studies were descriptive in nature. However, the studies had sufficient sample sizes and provided reasonably consistent results and recommendations.

The studies' findings are presented narratively under the headings 'enablers' and 'barriers' to NIMART implementation. A summary of the included studies is provided in Annexure 1. A summary of the enablers and barriers is depicted in Table 1.

Enablers to nurse-initiated and managed antiretroviral treatment implementation

The Streamlining Tasks and Roles to Expand Treatment and Care for HIV (STRETCH) trial, conducted before the official implementation of NIMART in 2010, reported on key enablers in the South African setting.[14] Key components of effective implementation included tailored guidelines, training and support to build the clinical confidence of nurses and health services reorganisation.[14] Since then, several other studies have highlighted similar enablers. We identified key enablers of NIMART implementation as being: (1) training and mentorship; (2) HIV and TB management guidelines; (3) integration of services; and (4) monitoring and support.

Training and mentorship

In order to enable NIMART implementation, nurses need additional training. Nurses undergoing NIMART training have to complete HIV training covering various topics, clinical guideline training (Practical Approach to Lung Health and HIV/AIDS in SA [PALSA PLUS] and Integrated Management of Childhood Illnesses [IMCI]), and complete a portfolio of evidence (POE) containing a range of

TABLE 1: Summary of enablers and barriers to the implementation of nurse-initiated and managed antiretroviral treatment in South Africa.

Enablers and barriers	Key themes
Enablers	
Training and mentorship	• Adequate training and mentorship results in increased knowledge, confidence and empowerment of nurses • Training results in increased ART initiations and decreased load on referral facilities • Patients are satisfied and retention in care is improved
HIV and TB management guidelines	• User-friendly, easy to follow guidelines may contribute to improvements in HIV and TB care • Continuous training on guidelines promote the appropriate use thereof
Integration of services	• Integration of NIMART in primary, antenatal and TB care results in increased ART initiations and reduced time to initiation
Monitoring and support	• Feedback about performance and teamwork amongst nurses promotes NIMART implementation
Barriers	
Non-standardised training and inadequate mentoring	• Training programmes that are not standardised and the lack of continuous mentoring and professional development, leads to knowledge and confidence gaps amongst NIMART-trained nurses
Human resource constraints	• Integration of NIMART with other services results in increased workloads, administrative duties and the performance of non-nursing tasks • There is a lack of further delegation of tasks to lower cadres and the implementation of alternative models of care
Health system challenges	• More services are provided whilst there are still a lack of infrastructure, resources, referral systems, data management and quality improvement systems
Lack of support and empowerment	• Ineffectual managerial and doctor support as well as negative attitudes from colleagues and patients results in disempowerment
Challenges with legislation, policy and guidelines	• There is no legislative framework or formal scope of practice for NIMART-trained nurses • Guidelines are not always updated and adhered to
Patient-related factors	• Poverty, stigma, lack of transport and non-adherence to treatment compromise NIMART outcomes

ART, antiretroviral treatment; HIV, human immunodeficiency virus; TB, tuberculosis; NIMART, nurse-initiated and managed antiretroviral treatment.

competencies. Nurse-initiated and managed antiretroviral treatment nurses are required to initiate and follow up a minimum number of patients in various age groups, including adults and children.[15] Only after the successful completion of the POE, nurses receive a certificate of competence to initiate NIMART. In some settings, nurses' competence are formally tested through objective structured clinical examinations (OSCE).[15]

With the introduction of the Department of Health's Clinical Mentoring Manual for Integrated Services,[16] mentorship was formally introduced to enhance clinical expertise. The model advocates a Clinical Proficiency Pathway starting with didactic training accompanied by clinical practice, assessment and continuous mentoring to ensure clinical expertise. Doctors or nurses can become clinical mentors, provided that they undergo mentoring training.[17]

Many non-governmental organisations (NGOs) and other private organisations rose to the task of assisting the National Department of Health (NDoH) with training and mentoring. These courses included, for example, the Clinical Competency in Antiretroviral and Tuberculosis (CCART) course developed by the University of Stellenbosch in collaboration with John's Hopkins University and the United States Agency for International Development (USAID),[18] a course presented by the Foundation of Professional Development (FPD)[19] and a course developed by the University of KwaZulu-Natal.[2] Across the courses, various challenges were reported such as difficulty to complete assignments, dispensing certificates and POEs for ART initiations.[18] Success stories included improvement in pre-and post-course knowledge and confidence and increased rates of POE completion because of a team of roving mentors.[2,18,19]

Adequate training results in improved knowledge of HIV management, greater confidence and clinical competence, particularly if accompanied by mentoring.[14,20,21,22] A study conducted in an urban and rural district in the Western Cape found that the majority of NIMART-trained nurses had adequate HIV management knowledge and were very confident to manage adult patients.[22]

The survey was specific to adult HIV management as nurses are only involved to a limited extent in the management of children in the Western Cape.

Nurse-initiated and managed antiretroviral treatment training leads to feelings of empowerment because of expanded roles.[20] Appropriate training and support can lead to increased quality of patient care, confidence and professional development.[17] Nurses may experience work satisfaction because of the difference they are making in patients' lives.[23] In the North West province, the ability to work independently boosted nurses' self-esteem and self-worth.[24] In Venda, some nurses reported that they felt proud that they were contributing to the NIMART programme.[25]

In Johannesburg, the training of nurses in NIMART increased access to ART as shown by an increase in the number of monthly initiations. It also resulted in reduced workloads at referral facilities.[26] A qualitative study in Johannesburg reported that referrals to tertiary hospitals were significantly reduced after the introduction of NIMART. Nurses observed an improvement in the quality of life of their patients and the retention of patients in care, which they felt reflected the success of NIMART.[27] Similarly, in KwaZulu-Natal, a cross-sectional study revealed that in 98% of the primary care clinics in one district, nurses initiated patients on ART. The majority of nurses also indicated that children were initiated in their clinics, with only some still being initiated by a doctor.[28] Accelerating NIMART in paediatric patients, coupled with mentoring and support were considered enablers in the provision of ART in infants and children living with HIV in the Eastern Cape.[29] Clinical exposure

further contributes to knowledge and confidence as was found in a study conducted in the Western Cape where a higher caseload of HIV patients was associated with higher knowledge and confidence.[22] In the North West province, effective placement, specifically at Community Health Centres, contributed to POE completion.[24]

The mentoring of nurses had a positive effect on patient care by improving the clinical skills of professional nurses and by raising the standard of HIV care in the Eastern Cape.[30] In Khayelitsha, Cape Town, a mentoring programme led to improvements in the quality of care nurses provided and their knowledge and confidence.[17] Nurses initiated 77% of ART-eligible patients after completing a mentorship programme and improvements in their ART management were observed.[17] If the majority of persons living with HIV are managed by nurses, doctors can attend to the more complicated cases, which, in turn, may result in better overall patient outcomes. Another study in the Western Cape found that a 2-week mentoring period was associated with greater HIV confidence compared with other periods. A period of 2 weeks of 'dedicated mentoring-time' with a mentor may be sufficient to complete competencies.[22]

Jobson et al.[31] conducted a qualitative study, evaluating the role of mentoring in the support of the scale-up of ART across three provinces of South Africa. The study explored the role of targeted mentoring using a needs-based approach to support NIMART, pharmacy management and data management.[31] The study adopted a two-stage approach, which they classified as proactive and reactive mentoring. For NIMART-trained nurses, the proactive approach entailed having nurse mentors accompanying them during patient consultations, which provided support in transferring skills learnt during training to actual implementation when providing care. Participants stated that they had gained knowledge after training and mentoring, which empowered them to up-scale services through NIMART. The reactive role required the mentor (nurse) to be a problem solver and a source of support, as required at various stages during HIV care and management. This type of support is important for NIMART-trained nurses who were starting to initiate and manage patients on ART. Mentorship strengthened skills and knowledge transfer, allowed mentees to develop their own skills and provided a source for psychosocial support as mentees became confident and felt empowered to take on new responsibilities in providing HIV care.[31]

HIV and TB management guidelines

The introduction of tailored guidelines such as the Practical Approach to Care Kit (PACK) was critical to assist nurses to implement NIMART.[14] A mixed-methods study conducted in the Limpopo province found that nurses practiced rational prescription and followed ART guidelines, with lower patient mortality (below 1%) and loss-to-follow-up rates compared with that of surrounding hospitals. In addition, 91.1% of NIMART-managed patients had undetectable viral loads after 1 year on treatment. Patients also reported high levels of satisfaction.[32] A study conducted in the North West province found that nurses preferred guidelines to be user-friendly, easy to follow and keep on their person and available in all consulting rooms.[33] Nurses also wanted to be supported and supervised until they are familiar with applying the guidelines in practice. They preferred continuous training and education about guidelines. Organisational and structural changes such as manageable workloads and improved communication were thought to enable adherence to ART and TB treatment guidelines.[33]

Integration of services

Initially, NIMART was implemented as a vertical programme. Now it is increasingly being integrated into a range of primary care services.[8] The integration of HIV care into PHC services is reported as a structural facilitative factor for the implementation of NIMART.[27]

The integration of HIV care into antenatal care and the introduction of option B+ meant that all pregnant women living with HIV needed to be initiated on ART. A retrospective record analysis conducted in the Gauteng province comparing time to initiation of ART amongst antenatal clients before and after NIMART implementation showed no significant reduction in the time to initiation on ART.[10] However, the study was conducted in the early stages of NIMART training and not all midwives may have been trained; therefore, they could only initiate clients on certain days.

Contrary to this, a study conducted in KwaZulu-Natal, soon after NIMART implementation in 2011, found that 97% of women were initiated on ART in antenatal care settings, illustrating a shift in care from ART clinics to nurse-managed antenatal clinics. This also resulted in reduced time to ART initiation from 38 to 4 days.[34] One study evaluated the effectiveness of the NIMART programme in the Waterberg district of the Limpopo province and found the number of patients initiated in the hospital dropped as did the number lost-to-follow-up, after the introduction of NIMART in primary care.[35]

Monitoring and support

A study conducted in the Western Cape found that regular feedback about clinic and personal performance was associated with higher HIV management knowledge,[22] with a study in Limpopo highlighting that support from visiting doctors and management were viewed as very helpful, even if management could not resolve all their problems.[23] Support amongst nurses is a further enabler to the implementation of NIMART.[25] Supportive teamwork (ongoing support from facility managers and colleagues), motivation and support from mentors were found to be key contributors to POE completion in the North West province.[24]

Barriers to nurse-initiated and managed antiretroviral treatment implementation

The implementation of NIMART may have been too hasty, not providing enough time for crucial capacity-building interventions such as mentoring and systems reorganisation.[20] Barriers identified in this review include: (1) non-standardised training and inadequate mentoring, (2) human resources constraints, (3) health system challenges, (4) lack of support and empowerment, (5) challenges with legislation, policy and guidelines and (6) patient-related factors.

Non-standardised training and inadequate mentoring

Inadequate or non-standardised *training* and the lack of continuous *clinical mentoring* and supervision by clinic managers were mentioned in most studies as barriers to the implementation of NIMART.[19,20,23,24,25,27,28,35,36,37]

As mentioned before, NIMART training was, and is being conducted by various NGOs, the NDoH and private training providers. One of the challenges is that *training is not standardised*, ranging from a few days to a few weeks or even months, which makes it difficult to evaluate its effectiveness or quality. Each provider determined their own programme's content, duration, instruction methods and assessment strategies. This limits the ability to set guidelines for structured training and mentoring. In some cases, nurses initiated patients even before attending or successfully completing NIMART training.[19] The process of submitting POE's and doing an additional course in dispensing was found to be dysfunctional as many nurses could not complete it.[15,18,38] In the North West, prerequisites such as PACK training and IMCI were barriers to the completion of POEs.[24] In rural North West province, challenges relating to NIMART training included the lack of a standardised curriculum, lack of involvement of quality assurance bodies, nursing colleges and universities and inadequate continuous professional development (CPD).[39] Another barrier identified in the North West province was disorganisation at the level of the Regional Training Centre (not receiving POE's directly after the training) and at the level of the trainee (lack of planning).[24] This partly defeated the aims of NIMART, which was meant to be an intervention intended to improve healthcare access and equity, ideally without compromising the quality of care and a key strategy for expanding access to HIV treatment at PHC level.

There is a lack of evidence in South Africa regarding the effectiveness of different NIMART training programmes and the impact on patient outcomes.[2] One should also question the sufficiency of a once-off NIMART training and further explore the role of continuing education and CPD. A study conducted in the Western Cape found that NIMART nurses with recent training on guidelines (less than 3 years) had better knowledge compared with nurses who reported to be trained more than 3 years ago.[22] In general, NIMART-trained nurses identified the need for continuing education.[2,19,20,21,35,39]

Whilst NIMART training enabled access, a *lack of mentoring* following training was a barrier in terms of the gap between the number of nurses who received training and those who could initiate treatment. Despite the large-scale training to upskill nurses, not all nurses initiated ART after receiving training. A study conducted in rural North West province found that although NIMART increased access to care, there was no steady increase in the initiation of adults, children and pregnant women on ART. Initiation was especially low amongst children. This was despite the fact that 75% of nurses in 99% of healthcare facilities were NIMART trained.[40] Facilities were also performing below the targets for retention in care and viral load completion and suppression rates, indicating poor quality of care and non-compliance to guidelines. Another study conducted amongst NIMART-trained nurses across 7 provinces found that of the 126 nurses sampled, only 79 initiated treatment and only 9 initiated treatment in children.[19]

Factors contributing to low initiation rates include inadequate training, lack of confidence and lack of mentoring and supervision. A study conducted in the Western Cape amongst 77 NIMART nurses working across 29 healthcare facilities on factors influencing the knowledge and confidence of professional nurses prescribing HIV treatment concluded that training, mentorship and clinical practice experience were associated with confidence and knowledge.[22] A qualitative study conducted in Johannesburg found that a lack of mentoring was likely to have contributed to a lack of nurses' confidence to initiate ART. They recommended a nurse-mentor model where experienced nurses can supervise and support colleagues; as well as access to telephonic support.[20] Nurse-initiated and managed antiretroviral treatment-trained nurses in Venda reported that because of the limited 1-week didactic training, they ended up learning most of the competencies at work, highlighting the need for mentoring support.[25] The need for supportive mentoring was underscored by the fact that only 63% of the nurses who completed a training course in KwaZulu-Natal felt confident enough to initiate ART following the training.[2] With the escalating number of persons living with HIV requiring treatment, it became crucial to nationally upskill the nurses who were not initiating as a result of a lack of mentorship and standardised training.

Whilst some of the NGOs had a mentorship programme as part of their training, this was not a norm across all trainings. The NDoH subsequently developed a national Clinical Mentorship Programme, which was aimed at providing practical on-site support to NIMART-trained nurses and ensure a competent and confident workforce. A manual was developed, with didactic content and practical tools that could be used to design, implement and evaluate a clinical mentorship programme at facility level and following clinical guidelines on HIV care. Of importance was that the manual could also be used by pharmacists, medical officers and other members of the multidisciplinary team providing HIV care services.[16] However, even with this Clinical Mentorship

Programme in place, challenges with regard to mentoring exist. One of these challenges include that during proactive mentoring, it often happened that the mentors ended up delivering the actual service themselves and were sometimes not available when needed because of being responsible for several facilities.[31] There is also no standardised time or method for clinical mentorship and it varies from a minimum of 40 h in the Western Cape[17] to targeted mentoring in other settings.[15,31]

Several studies identified key *knowledge and confidence gaps* amongst NIMART-trained nurses, further indicating a need for improved training and mentoring. A lack of confidence to manage children was identified in a study in the North West province.[39] Naude[21] similarly found low levels of competency in certain areas of HIV management, particularly for ART initiation and follow-up in children, in the North West province. In Venda and Limpopo, nurses reported that they faced problems in performing certain tasks such as obtaining blood from children.[25,41]

Mashudu[35] also found that few children were initiated on ART in Limpopo. Low initiation rates amongst children should be investigated further. It may be that the policy in many provinces, such as the Western Cape, is that children must be managed by doctors or that paediatric NIMART training and mentoring is not sufficient. In a study to explore the experiences of healthcare professionals regarding the provision of ART for children in PHC settings in Nelson Mandela Bay Health District in the Eastern Cape, the need for training, mentoring and debriefing was expressed as one of the challenges related to providing decentralised ART to children. Nurses were apprehensive to work with children and noticed incongruence in the interpretation of ART side effects in children.[29]

An analysis of nurses' queries to the National HIV and TB Health Worker Hotline showed that 66% of the queries received were from NIMART-trained nurses and most were related to ART initiation and adverse drug reactions. The most common knowledge gap identified was on the interpretation of blood results before initiation of ART,[42] which was also confirmed by Rasalanavho.[25] In the study conducted in the Western Cape, low confidence was reported in prescribing for concurrent illnesses and in identifying the signs and symptoms of immune reconstitution inflammatory syndrome. Nurses had less than optimal knowledge of virological failure and drug–drug interactions.[22] In KwaZulu-Natal, most NIMART nurses knew the correct ART regimens, ART eligibility criteria and when blood for CD4 count and viral load should be taken, although worrying gaps were identified.[28]

Human resources constraints

Human resources constraints, increased workloads and administrative duties such as paperwork, were cited in many studies as negatively influencing the implementation of NIMART,[14,19,20,21,23,25,27,32,35,39] with doctors reportedly not fully supporting the NIMART programme.[25]

Excessive workloads also interfere with the completion of mentorship programmes.[24]

In one study, 55% of nurses reported seeing more than 30 patients a day and 30% saw more than 40 patients a day.[21] As a result of integration of HIV management in primary care, NIMART-trained nurses also have other tasks to perform.[22,25] Nurses reported the inability to delegate tasks to lower cadres and also reported having to do non-nursing tasks such as collection of drugs from depots[27] or using their own transport to collect drugs.[25]

Despite human resource challenges, NIMART nurses display resilience. In the Western Cape, even though 44.4% of nurses felt that their workload was unacceptable, and 48.1% were dissatisfied with their work environment, salary and work hours; 88.3% were nonetheless still motivated to work.[22] The challenge of high workloads was mitigated by nurses in Venda through problem-solving and innovative strategies such as allocating different times for collecting tablets and reviews as well as group counselling.[25]

The growing number of patients on ART necessitates looking at decentralising ART care further and utilising chronic care models for stable patients on ART to decongest clinics.[20] Several studies mentioned the utilisation of lower cadres of healthcare workers such as lay workers to trace patients,[27] the education of the community, increased community management of HIV and addressing poverty and stigma, as crucial to the continued success of the HIV programme in South Africa.[23,43]

Health systems challenges

Although integration of services can be an enabling factor, it is not without challenges. High HIV–TB co-infection rates and high antenatal HIV prevalence rates in South Africa necessitate integration of HIV into TB and antenatal care. This means that primary care nurses and midwives have to expand their competencies to include NIMART. These changes also have an effect on the scope of practice and the training of nurses. It may also impact the quality of care that can be provided to other patient populations in primary care and women's healthcare settings. A study conducted in the Free State to evaluate patients' perceptions of the effect of the integration of NIMART into primary care on quality of care showed that there was no decrease in patient satisfaction with staff. This was despite increases in patient numbers. However, satisfaction scores were lower for child health and chronic care patients (except TB), suggesting that there may be a knock-on effect on other services.[44]

A study in the Limpopo province on the views of registered nurses of the prevention of mother-to-child transmission (PMTCT) programme revealed considerable challenges to integrate NIMART into antenatal and postnatal care.[43] These challenges related particularly to having to spend more time with patients when initiating ART during the antenatal period; the additional workload was not accompanied by additional support.

Integration of services should be accompanied by the provision of adequate resources and reorganisation of services.[14] However, several studies reported inadequate *infrastructure and resources* such as consultation rooms, inadequate workspace compromising patient privacy and confidentiality, as well as the lack of resources such as stationery, drugs, equipment needed for blood collection, telephones, electronic drug ordering systems, information systems and slow turnaround times of blood investigations.[15,19,21,23,25,27,32,33,35,41,43] Poor data management, including lack of compliance with standard operating procedures, incomplete records and inadequate audits hampered performance.[23] Nurses also experience poor referral feedback systems.[27] There is a necessity for quality improvement teams to ensure quality of care.[20]

Lack of support and empowerment

Health system issues and lack of *managerial support* was identified in several studies.[20,23,25,33] In Venda, nurses reported a lack of support from doctors and refusal to see complicated cases requiring expert management.[25]

Naude,[21] through a mixed-methods study, explored empowerment amongst NIMART-trained nurses. Quantitative findings revealed that nurses were only moderately structurally empowered.

With regard to psychological empowerment, professional nurses felt that they only minimally influenced their work environment. Management and organisational processes were identified as being central to the empowerment of NIMART nurses.[21] In the Eastern Cape, barriers to paediatric NIMART implementation included ineffective management, disharmony and non-conducive work environments.[29]

A negative attitude towards the management of HIV and TB patients was identified by Mboweni and Makhado.[38] Negative attitudes and discrimination from non-NIMART-trained nurses and refusal to manage HIV positive patients was also reported in a study conducted in Venda.

Nurses reported that patients questioned their ethical values to keep information confidential and had negative attitudes towards the NIMART programme.[25] A study conducted in the Limpopo province found that nurses also had fears of infecting themselves with HIV,[41] indicating that there may be a lack of workplace-based support.

Challenges with legislation, policy and guidelines

The lack of enabling *legislation* and *regulations*,[45,46] the lack of clear guidelines and standard operating procedures,[37] unclear roles or scope of practice – nurses sometimes perform the roles of medical practitioners and pharmacists,[21] and salary or remuneration challenges were also reported.[32] Provincial governments and the NDoH were mandated to maintain records of all nurses authorised to prescribe ART and to communicate this to the South African Nursing Council. Anecdotal reports suggest that this has not happened. There is no formal scope of practice for NIMART-trained nurses and they do not receive additional remuneration for expanded roles.

Some studies reported the lack of updated guidelines, particularly in rural areas.[28] A study in KwaZulu-Natal and North West provinces revealed that nurses may not be following HIV and TB guidelines. Barriers to adhering to guidelines included a lack of agreement with the guidelines or guidelines not being clear or understandable; insufficient knowledge as a result of not being updated or involved in guideline development; frequent guideline changes; poor motivation; and lack of supportive supervision.[9] Continuous revision of guidelines requires frequent updated training, but training programmes are not always communicated timeously to ensure that staff can attend.[43]

Patient-related factors

Many studies also highlighted patient-related factors hindering the implementation of NIMART such as poverty, stigma, lack of transport and non-adherence to treatment.[25,27] However, the discussion of patient factors is beyond the scope of this review and could perhaps be a focus for future studies.

Discussion

It has been 10 years since the implementation of NIMART in South Africa. Evidence from observational studies indicates that there are several enablers and barriers to implementation. Based on the evidence presented here, we discuss implications for practice, education and research.

Implications for practice

The narrative review identified two frameworks developed from rigorous research that could be implemented in practice to strengthen NIMART training and implementation and empower NIMART-trained nurses.[21,37] The conceptual framework for strengthening NIMART training and implementation developed by Mboweni and Makhado[39] outlines structural attributes that advocates for adequate resources, infrastructure, supportive legislation and policy, effective training strategies and a supportive healthcare system culture.[37] This is supported by the framework of Naude[21] who outlined the following elements of structural empowerment: training and mentoring (knowledge, technical skills and professional growth); resources (human, equipment and supply chain); support (clinical supervision, guidance from managers and feedback); communication (information, protocols and guidelines) and power (formal in the form of role clarification and decision making and informal in the form of team acceptance and remuneration).[21] Many of these infrastructural and resource inadequacies may be addressed by investing in and improving the leadership and management of PHC services.

Implications for education

Mboweni and Makhado's framework identified that effective NIMART education and implementation requires (1) an integrated curriculum and effective training strategies for in- and pre-service education and (2) a healthcare system culture that includes support through mentoring or coaching, discipline, communication and referral systems.[37]

Although NIMART training is still being provided by NGO's and various private organisations, there is now a greater effort to incorporate comprehensive HIV training, including NIMART, in undergraduate pre-service programmes.[2,46,47,48] Evidence suggests that pre-service nurses still have inadequate HIV management knowledge.[47] Some researchers advocate for specialisation programmes for the management of chronic conditions, including HIV and TB.[21] One study recommended future research regarding the role of the postgraduate diploma in Primary Care Nursing in the implementation of NIMART as nurses felt that those who had the qualification were better equipped to manage patients on ART.[27] However, in the same study, as reported in other studies,[2,19] the majority of NIMART nurses did not have a qualification in Primary Care (Health Assessment, Diagnosis, Treatment and Care). More research is needed to explore if a Primary Care qualification is important for NIMART implementation[2] or whether NIMART competencies should be integrated in the undergraduate programme or the postgraduate diploma in Primary Care Nursing. Nonetheless, there is a need to standardise 'in-service' types of NIMART training across provinces, aligning them to the competencies outlined in the Clinical Mentorship Manual for Integrated Services,[16] as well as ensuring formal competency assessment.

Implications for research

Further research is needed on the standardisation and effectiveness of NIMART training and mentoring programmes and the long-term impact on patient outcomes towards attaining national and international targets for HIV care and management. Evidence-based guidelines for the integration of NIMART into primary care services and continuous monitoring and support are urgently needed.

Strengths and limitations

The search strategy was not comprehensive and some relevant studies may have been excluded.

However, the authors are confident that we have provided an exhaustive description of barriers and facilitators to NIMART implementation in South Africa.

Conclusion

Although training, mentorship, guidelines, integration of services and monitoring and support have enabled the implementation of NIMART, several barriers such as non-standardised training, inadequate mentoring, human resource constraints, health system challenges, lack of support and empowerment, and challenges with legislation, policy and guidelines still hinder its effectiveness.

Various key role players such as the NDoH, the South African Nursing Council, training providers and researchers need to work together to standardise training and provide evidence-based guidelines for mentoring, integration of services and continuous monitoring and support.

Acknowledgements

The authors would like to acknowledge Eveline Kabongo for conducting the initial literature search.

Competing interests

The authors declare that they have no financial or personal relationships that may have inappropriately influenced them in writing this review article.

Authors' contributions

T.C., E.M. and N.G. reviewed the literature and provided feedback on the manuscript.

Funding information

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Data availability

Data sharing is not applicable to this article as no new data were created or analysed in this study.

Disclaimer

The views and opinions expressed in this article are those of the authors and do not necessarily reflect the official policy or position of any affiliated agency of the authors.

References

1. Simelela NP, Venter WDF. A brief history of South Africa's response to AIDS. S Afr Med J. 2014;104(3):249–251. https://doi.org/10.7196/SAMJ.7700
2. Mngqibisa R, Muzigaba M, Ncama BP, Pillay S, Nadesan-Reddy N. Upskilling nursing students and nurse practitioners to initiate and manage patients on ART: An outcome evaluation of the UKZN NIMART course. African J Heal Prof Educ. 2017;9(3):153. https://doi.org/10.7196/AJHPE.2017.v9i3.879
3. Kredo T, Bateganya M, Pienaar ED, Adeniyi FB. Task shifting from doctors to non-doctors for initiation and maintenance of HIV/AIDS treatment. Cochrane Database Syst Rev. 2014;(7):CD007331. https://doi.org/10.1002/14651858.CD007331.pub2
4. Emdin CA, Chong NJ, Millson PE. Non-physician clinician provided HIV treatment results in equivalent outcomes as physician-provided care: A meta-analysis. J Int AIDS Soc. 2013;16:18445. https://doi.org/10.7448/IAS.16.1.18445
5. Kredo T, Ford N, Adeniyi FB, Garner P. Decentralising HIV treatment delivery in middle-and low-income countries. Cochrane Database Syst Rev. 2013;(7):CD009987. https://doi.org/10.1002/14651858.CD009987
6. World Health Organization. Task shifting: Global recommendations and guidelines [homepage on the Internet]. Vol. 53. UNAIDS; 2008 [cited 2020 Oct 07]. Available from: https://www.who.int/workforcealliance/knowledge/resources/taskshifting_guidelines/en/
7. Colvin CJ, Fairall L, Lewin S, et al. Expanding access to ART in South Africa: The role of nurse-initiated treatment. SAMJ. 2010;100(4):210–212. https://doi.org/10.7196/SAMJ.4124
8. Mathibe MD, Hendricks SJH, Bergh AM. Clinician perceptions and patient experiences of antiretroviral treatment integration in primary health care clinics, Tshwane, South Africa. Curationis. 2015;38(1):1–11. https://doi.org/10.4102/curationis.v38i1.1489

9. Makhado L, Davhana-Maselesele M, Farley JE. Barriers to tuberculosis and human immunodeficiency virus treatment guidelines adherence among nurses initiating and managing anti-retroviral therapy in KwaZulu-Natal and North West provinces. Curationis. 2018;41(1):1–8. https://doi.org/10.4102/curationis.v41i1.1808
10. Mnyani CN, Marinda E, Struthers H, Gulley M, Machepa R, McIntyre J. Timing of antenatal care and ART initiation in HIV-infected pregnant women before and after introduction of NIMART. S Afr J HIV Med. 2014;15(2):55–56. https://doi.org/10.7196/SAJHIVMED.1009
11. Republic of South Africa. National Department of Health. ART clinical guidelines for the management of HIV in adults, pregnancy, adolescents, children, infants and neonates [homepage on the Internet]. 2019 [cited 2020 Oct 07]. Available from: https://www.knowledgehub.org.za/elibrary/2019-art-clinical-guidelines-management-hiv-adults-pregnancy-adolescents-children-infants
12. Green BN, Johnson CD, Adams A. Writing narrative literature reviews for peer-reviewed journals: Secrets of the trade. J Chiropr Med. 2006;5(3):101–117. https://doi.org/10.1016/S0899-3467(07)60142-6
13. Johns Hopkins. Johns Hopkins nursing evidence-based practice appendix C: Evidence level and quality guide evidence levels: 1–3 [homepage on the Internet]. [cited 2020 Oct 07]. Available from: https://www.hopkinsmedicine.org/evidence-based-practice/_docs/appendix_c_evidence_level_quality_guide.pdf
14. Georgeu D, Colvin CJ, Lewin S, et al. Implementing nurse-initiated and managed antiretroviral treatment (NIMART) in South Africa: A qualitative process evaluation of the STRETCH trial. Implement Sci. 2012;7(1):1–13. https://doi.org/10.1186/1748-5908-7-66
15. Jones M, Cameron D. Evaluating 5 years' NIMART mentoring in South Africa's HIV treatment programme: Successes, challenges and future needs. South African Med J. 2017;107(10):839–842. https://doi.org/10.7196/SAMJ.2017.v107i10.12392
16. South African Department of Health. Clinical mentorship manual for integrated services [homepage on the Internet]. 2011 [2020 Oct 07]. Available from: https://sahivsoc.org/Files/clinical%20mentorship%202011.pdf
17. Green A, De Azevedo V, Patten G, Davies MA, Ibeto M, Cox V. Clinical mentorship of nurse initiated antiretroviral therapy in Khayelitsha, South Africa: A quality of care assessment. PLoS One. 2014;9(6):e98389. https://doi.org/10.1371/journal.pone.0098389
18. Crowley T. The effect of a HIV/TB competency-based short course on professional nurses' knowledge and confidence in managing patients with HIV and TB. In: Annual Nursing Education Conference (ANEC), South Africa. 2013. [conference proceedings not published]
19. Cameron D, Gerber A, Mbatha M, Mutyabule J, Swart H, West N. Nurse initiation and maintenance of patients on antiretroviral therapy: Are nurses in primary care clinics initiating ART after attending NIMART training. SAMJ. 2012;102(2):98–100. https://doi.org/10.7196/SAMJ.5195
20. Davies NECG, Homfray M, Venables EC. Nurse and manager perceptions of nurse initiated and managed antiretroviral therapy (NIMART) implementation in South Africa: A qualitative study. BMJ Open. 2013;3(11):e003840. https://doi.org/10.1136/bmjopen-2013-003840
21. Naude SM. Framework to empower professional nurses for nurse initiated management of anti-retroviral therapy North West province. Sefako Makgatho Health Sciences University; 2017 [cited 2020 Apr 8]. Available from: https://repository.smu.ac.za/xmlui/bitstream/handle/20.500.12308/463/S%20Naude%20thesis%20final%20February%202018%20.pdf?sequence=1&isAllowed=y
22. Solomons DJ, Van der Merwe AS, Esterhuizen TM, Crowley T. Factors influencing the confidence and knowledge of nurses prescribing antiretroviral treatment in a rural and urban district in the Western Cape province. South Afr J HIV Med. 2019;20(1):1–7. https://doi.org/10.4102/sajhivmed.v20i1.923
23. Mabelane T, Marincowitz GJO, Ogunbanjo GA, Govender I. Factors affecting the implementation of nurse-initiated antiretroviral treatment in primary health care clinics of Limpopo Province, South Africa. S Afr Fam Pract. 2016;58(1):9–12. https://doi.org/10.1080/20786190.2015.1114704
24. Motlokoa MN. Factors influencing submission of portfolios of evidence amongst nurses trained in nurse initiation and management of antiretroviral therapy in North West. University of the Witwatersrand; 2016 [cited 2020 Apr 8]. Available from: http://wiredspace.wits.ac.za/bitstream/handle/10539/22461/Final%20Research%20Report%20-(2016-10-21)edited.pdf?isAllowed=y&sequence=1
25. Rasalanavho RN. Nurses implementing the nurse-initiated- and-managed antiretroviral treatment programme in Vhembe district, South Africa. University of Venda; 2015 [cited 2020 Apr 7]. Available from: https://www.semanticscholar.org/paper/Challenges-confronting-professional-nurses-the-and-Rasalanavho/c0fa7dea657ec59795bede7ab214f25159161803
26. Nyasulu JCY, Muchiri E, Mazwi S, Ratshefola M. NIMART rollout to primary healthcare facilities increases access to antiretrovirals in Johannesburg: An interrupted time series analysis. SAMJ. 2013;103(4):232–236. https://doi.org/10.7196/SAMJ.6380
27. Mophosho Z. The implementation of nurse initiated and managed antiretroviral therapy in the City of Johannesburg clinics: Perceived facilitators and barriers. University of Witwatersrand; 2015 [cited 2020 Apr 7]. Available from: http://wiredspace.wits.ac.za/handle/10539/18539
28. Xaba P. An implementation evaluation study of a nurse initiated and managed antiretroviral therapy (NIMART) program in primary health care clinics in the Ugu district of kKwazulu-Natal. University of KwaZulu-Natal; 2016 [cited 2020 Apr 7]. Available from: https://researchspace.ukzn.ac.za/bitstream/handle/10413/15808/Xaba_Pearl_2016.pdf?sequence=1&isAllowed=y
29. Williams M, Van Rooyen DRM, Ricks EJ. Provision of antiretroviral therapy for children in Nelson Mandela Bay: Health care professionals' challenges. African J Prim Heal Care Fam Med. 2018;10(1):1–11. https://doi.org/10.4102/phcfm. v10i1.1490
30. Jones M, Stander M, Van Zyl M, Cameron D. Recall of lost-to-follow-up pre-antiretroviral therapy patients in the Eastern Cape: Effect of mentoring on patient care. SAMJ. 2012;102(9):768–769. https://doi.org/10.7196/SAMJ.5957
31. Jobson G, Mabitsi M, Railton J, et al. Targeted mentoring for human immunodeficiency virus programme support in South Africa. South Afr J HIV Med. 2019;20(1):1–6. https://doi.org/10.4102/sajhivmed.v20i1.873
32. Visser CA, Wolvaardt JE, Cameron D, Marincowitz GJO. Clinical mentoring to improve quality of care provided at three NIM-ART facilities: A mixed methods study. African J Prim Heal Care Fam Med. 2018;10(1):1–7. https://doi.org/10.4102/ phcfm.v10i1.1579
33. Makhado L, Davhana-Maselesele M, Lebese R, Maputle S. Factors facilitating trained NIMART nurses ' adherence to treatment guidelines: A vital matter in the management of TB/HIV treatment in South Africa. BMC Nursing. 2020;19:77. https://doi.org/10.1186/s12912-020-00470-6
34. Nozulu N, Gaede BM. Antiretroviral initiation of pregnant women and antenatal care booking practices in eThekwini District, KwaZulu-Natal, South Africa. Afr J Prm Health Care Fam Med. 2018;10(1):a1606. https://doi.org/10.4102/phcfm.v10i1.160
35. Mashudu M. An evaluation of the effectiveness of the nurse-initiated-and-managed antiretroviral treatment (NIMART) programme, Waterberg District, Limpopo Province. University of Venda; 2015.
36. Mangi NG, Goon D Ter, Yako EM. Self-efficacy and clinical performance of nurses initiated and management of antiretroviral therapy: Narrative review. Open Publ Health J. 2019;12:86–93. https://doi.org/10.2174/1874944501912010086
37. Mboweni SH, Makhado L. Conceptual framework for strengthening nurse-initiated management of antiretroviral therapy training and implementation in North West Province. Healh SA Gesondheid. 2020;25:1–10. https://doi.org/10.4102/hsag.v25i0.1285
38. Stellenbosch University. ART2Scale final technical report update 25 Nov. 2010.
39. Mboweni SH, Makhado L. Challenges influencing nurse-initiated management of antiretroviral therapy training and implementation in Ngaka Modiri Molema district, North West province. Heal SA Gesondheid. 2020;25:1–11. https://doi.org/10.4102/hsag.v25i0.1174
40. Mboweni SH, Makhado L. Impact of NIMART training on HIV management in Ngaka Modiri Molema District, North West province. Int J Africa Nurs Sci. 2019;11(January):100170. https://doi.org/10.1016/j.ijans.2019.100170
41. Sekatane PT. A protocol for professional nurses regarding the management of nurse initiated management of antiretroviral therapy (NIMART) in the Ehlanzeni district, Mpumalanga province, South Africa. University of Limpopo; 2014 [cited 2020 Apr 7]. Available from: http://ulspace.ul.ac.za/handle/10386/1377
42. Swart AM, Chisholm BS, Cohen K, Workman LJ, Cameron J, Blockman M. Analysis of queries from nurses to the South African National HIV & TB health care worker hotline. South Afr J HIV Med. 2013;14(4):179–182. https://doi.org/10.7196/SAJHIVMED.948
43. Hanrahan BA, Williams A. Prevention of mother-to-child transmission of HIV guidelines: Nurses' views at four primary healthcare facilities in the Limpopo Province. S Afr J HIV Med. 2017;18(1):1–6. https://doi.org/10.4102/sajhivmed.v18i1.690
44. Rawat A, Uebel K, Moore D. Patient responses on quality of care and satisfaction with staff after integrated HIV care in South African primary health care clinics. J Assoc Nurses AIDS Care. 2018;29(5):698–711. https://doi.org/10.1016/j.jana.2018.04.014
45. Ford P. Nurse initiated and managed anti-retroviral treatment: An ethical and legal analysis in South Africa. MSc Med (Bioethics Health Law). Johannesberg; 2013 [cited 2020 Apr 7]. Available from: http://wiredspace.wits.ac.za/bitstream/handle/10539/14413/Research_Report_NIMART__Final_Submission_with_Amendments-20-07-13.pdf?sequence=1
46. Zuber A, McCarthy CF, Verani AR, Msidi E, Johnson C. A survey of Nurse-Initiated and -Managed Antiretroviral Therapy (NIMART) in practice, education, policy, and regulation in East, Central, and Southern Africa. J Assoc Nurses AIDS Care. 2014;25(6):520–531. https://doi.org/10.1016/j.jana.2014.02.003
47. Lekhuleni ME, Kgole JC, Mbombi MO. Knowledge of student nurses in nurse initiated and management of antiretroviral therapy at the University of Limpopo, South Africa: TB, HIV/AIDS and other diseases. African J Phys Heal Educ Recreat Danc. 2015;21(October):53–61.
48. Modeste RM, Adejumo O. Strengthening the preparation of student nurses to participate in the provision of nurse initiated and monitored Antiretroviral (NIMART) in South Africa [homepage on the Internet]. 2016 [cited 2020 Oct 07]. Available from: https://hdl.handle.net/10755/603007
49. Colvin CJ, Fairall L, Lewin S, et al. Expanding access to ART in South Africa: The role of nurse-initiated treatment. SAMJ. 2010;100(4):210–211.

Annexure 1 start on the next page→

ANNEXURE 1: Summary of included studies.

Authors/year	Study aim	Methods	Sample	Key enablers and barriers	Level and quality of evidence
Cameron et al.[19]	To determine the percentage of nurses initiating new HIV positive patients on therapy within 2 months of attending the NIMART course and to identify possible barriers to nurse initiation.	Quantitative: Telephonic interviews, structured questionnaire	A total of 126 out of 1736 PHC nurses in 7 provinces	Enablers: training – 79 out of 126 initiating ART Barriers: Low initiation in children (9 out of 126), staff shortages/ workload, allocation of other tasks	Level III B
Colvin et al.[49]	To describe the expanding access to ART in South Africa and the role of nurse-initiated treatment	Opinion article pre-NIMART rollout summarising evidence from STRETCH trial	Literature	Enablers: Realignment of health system, systems strengthening	Level IV B
Crowley[18] *(Conference proceedings)*	To determine the effect of a HIV/TB competency-based short course on professional nurses' knowledge and confidence in managing patients with HIV and TB	Quantitative: pre- and post-test	A total of 65 students completed the pre-test and 56 completed the post-test	Enablers: Training and mentoring improving knowledge and confidence	Level III B
Davies et al.[20]	To explore nurse and facility and programme manager perceptions of NIMART implementation in Gauteng, South Africa	Qualitative: Interviews and focus groups	A total of 12 nurses and 18 managers involved in NIMART	Enablers: Nurse empowerment because of expanded roles Barriers: Human resources, training, clinical mentoring, health systems issues	Level III B
Ford[45] *(Master's research report)*	To review and analyse the existing legal framework and provisions for NIMART in South Africa and to identify ethical issues and implications of NIMART within the current legal framework	A comparative analysis of literature	Literature	Enablers: NIMART framework founded by Constitution and enabled by health policy Barrier: Aspect of enabling legislation related to nurse training and accreditation required	Level IV B
Georgeu et al.[14]	To develop a contextualised understanding of factors affecting the implementation of the NIMART programme (STRETCH trial)	Qualitative: Focus groups[16] and interviews[25]	Nurses, patients, managers, coordinators, managers and site physicians	Enablers: Acceptability, confidence to deliver ART, support, training Barriers: Changes in working and referral relationships, capacity and workload constraints, logistical and infrastructure challenges	Level III B
Green et al.[17]	To assess quality of care of clinical mentorship of NIMART in Khayelitsha, South Africa	Quantitative: A before-after cross-sectional study	Routine clinical data from 229 patient folders and 21 self-assessment questionnaires	Enablers: Mentoring, increased clinical confidence, professional development	Level III B
Hanrahan & Williams[43]	To determine what the registered nurses' perspectives are on the PMTCT programme as implemented at four PHC facilities in the Limpopo province	Qualitative: Semi-structured interviews	A total of 21 nurses	Enablers: Education of staff, updates on the PMTCT programme guidelines and policies, effective communication with patients Barriers: Increased workloads, staff shortages, poor planning of training, equipment and medication shortages	Level III B
Jobson et al.[31]	To understand the implementation process of targeted mentoring for clinical practice, data management and pharmacy management, at public healthcare facilities in South Africa	Qualitative: Structured interviews	A total of 74 healthcare workers from 3 South African provinces	Enablers: Mentoring improving self-efficacy, knowledge and skills transfer, psychosocial support Barriers: Mentors responsible for several facilities, unavailable when help needed, over-dependence on mentors, lack of communication and planning, taking over clinical work	Level III B
Jones & Cameron[15]	To describe and analyse the achievements and evolution of clinical mentoring for NIMART-trained professional nurses by roving mentor teams in PHC facilities in the health districts of Tshwane (Gauteng province), Nkangala (Mpumalanga province) and Capricorn and Vhembe (Limpopo province) over a period of 5 years	Primarily qualitative: Semi-structured interviews. Data obtained from routine monitoring and evaluation reports, and from the DoH District Health Information System	A total of 92 professional nurses who had completed classroom training in NIMART, 20 facility managers, 4 subdistrict programme managers, 45 roving mentors and 12 Foundation of Professional Development (FPD) operational managers	Enablers: Targeted mentoring Barriers: Low completion rates of training, large number of nurses requiring mentoring, lack of mentors/mentoring, lack of ongoing mentoring	Level III B
Jones et al.[30]	To evaluate the effect of a NIMART mentor	Quantitative: Record review	Existing pre-ART patient files (n = 286)	Enablers: Mentoring plays an important role in professional nurse training and support	Level III C
Lekhuleni et al.[47]	To determine the knowledge of student nurses in NIMART	Quantitative: Questionnaire	A total of 106 third and fourth level student nurses University of Limpopo	Barriers: Undergraduate training – students have insufficient knowledge on ensuring sufficient ART stock, TB screening on HIV positive patients and privacy during NIMART	Level III B
Mabelane et al.[23]	To identify the factors affecting the implementation of nurse-initiated ARV treatment in PHC clinics referring patients to Dr C.N. Phatudi Hospital, Limpopo province	Qualitative: Focus groups and interviews	A total of 15 registered nurses	Enablers: Support from management, visiting doctor, work satisfaction Barriers: General lack of resources including healthcare workers, drugs, stationery, telephones, poor training, inadequate workspace	Level III B

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ANNEXURE 1 (Continues...): Summary of included studies.

Authors/year	Study aim	Methods	Sample	Key enablers and barriers	Level and quality of evidence
Makhado et al.[33]	To determine factors facilitating trained NIMART nurses' adherence to treatment guidelines: A vital matter in the management of TB/HIV treatment in South Africa	Qualitative: Focus groups	A total of 24 NIMART nurses	Enablers: Improved accessibility, usability (user-friendly) and availability of treatment guidelines, motivation, support and supervision, improved knowledge and awareness, organisational-structural changes	Level III B
Makhado et al.[9]	To explore and describe barriers to treatment guidelines adherence amongst nurses initiating and managing anti-retroviral therapy and anti-TB treatment in KwaZulu-Natal and North West provinces	Qualitative: Focus groups	A total of 24 NIMART nurses	Barriers: Lack of agreement with guidelines, poor motivation to implement, poor clinical support and supervision, insufficient knowledge or lack of awareness, organisational factors – time pressures, heavy workload, poor access to guidelines	Level III B
Mangi et al.[36]	To review and analyse literature on self-efficacy and clinical performance amongst professional nurses regarding quality of care in implementation of NIMART programme	Literature review	Literature	Barriers: Lack of mentoring, support and exposure to clinical practice had negative effect on nurses' self-efficacy	Level III B
Mashudu[35]	To evaluate the effectiveness of the NIMART programme, Waterberg District, Limpopo province	Quantitative: Descriptive cross-sectional	All PHC clinics and NIMART nurses	Barriers: Workload, administrative duties, insufficient consultation rooms, human resources challenges, managerial support, mentoring, health system issues	Level III B
Mathibe et al.[8]	To explore clinicians' perceptions and patients' experiences of integration of antiretroviral treatment in PHC clinics	Mixed methods: Questionnaires and focus groups	A total of 4 PHC facilities; 35 clinicians; 4 focus groups with HIV positive patients	Enablers: Integration of care promotes access to care, prevention of stigma, staff development and support Barriers: Workload, poor staff attitudes, poor communication	Level III B
Mboweni et al.[40]	To determine and evaluate the impact of NIMART training on HIV programme in order to make recommendations leading to effective training and implementation	Quantitative: Records analysis. (Ngaka Modiri Molema District, North West province)	The statistics of ART indicators were collected from the DHIS from January 2012 to December 2016	Enablers: NIMART training increase access Barriers: Poor quality of HIV management, non-compliance to guidelines and monitoring of treatment effectiveness	Level III B
Mboweni & Makhado[37]	To develop a conceptual framework to strengthen NIMART training and implementation in the North West province to improve patients and HIV programme outcomes	Mixed methods: Explanatory, sequential	ART statistics from the DHIS & Tier.net of 10 PHC facilities and 5 focus group discussions amongst 28 NIMART nurses and 3 HIV programme managers	Barriers: Low ART initiation, poor monitoring on ART, human resource ratio's, no framework to guide training and mentoring	Level III B
Mboweni & Makhado[39]	To explore and describe the challenges influencing NIMART training and implementation amongst professional nurses and programme managers. (Molema district, North West province)	Qualitative: Focus groups and individual interviews	A total of 28 NIMART nurses and managers directly involved in the programme	Barriers: Inadequacy of NIMART training, lack of a standardised curriculum, healthcare system challenges	Level III B
Mngqibisa et al.[2]	To evaluate the effectiveness of the NIMART course in increasing the knowledge of trainees in select clinical competencies	Quantitative: A single-group pre- and post-quasi-experimental design	A total of 369 trainees who had benefitted from the course during the implementation period	Enablers: Training improves knowledge in HIV and its management Barriers: Need for on-the-job mentoring and support to maximise clinical outcomes	Level III B
Mnyani et al.[10]	To assess timing of antenatal care and ART initiation in HIV-infected pregnant women before and after introduction of NIMART	Quantitative: Records analysis	Records of 1436 ART-eligible pregnant women	Enablers: NIMART training decreases time to ART initiation	Level III B
Modeste & Adejumo[48] *(Conference proceedings)*	Exploration of the integration of NIMART training in the pre-service nursing curriculum at one university in South Africa	Qualitative: Focus groups and individual interviews	A total of 52 nurse educations in 7 provinces in South Africa	Enablers: Training – educators have different views some preferring NIMART to be part of the postgraduate programme whilst others feel it should be done at pre-service level, current legal framework is enabling Barriers: Limited knowledge related to pharmacology, ART, side-effects, interpretation of blood results amongst practicing nurses, gaining experience to provide NIMART upon graduation may be problematic	Level III B
Motlokoa[24] *(Master's thesis)*	To identify barriers and facilitating factors affecting the submission of POEs by NIMART-trained nurses in the North West province	Qualitative: Focus groups	A total of 30 NIMART Nurses in three focus groups	Enablers: Support, teamwork, effective placement and motivation Barriers: Disorganisation, NIMART prerequisites, lack of human resources	Level III B

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ANNEXURE 1 (Continues...): Summary of included studies.

Authors/year	Study aim	Methods	Sample	Key enablers and barriers	Level and quality of evidence
Mophosho[27] *(Master's thesis)*	To explore and describe perceptions of operational managers, facility managers and professional nurses on the facilitators and barriers to the implementation of NIMART in the City of Joburg (CoJ) clinics	Qualitative: Interviews	A total of 26 participants comprising operational managers, facility managers and professional nurses	Enablers: Adequate training – opportunities for continuing education, mentoring, NIMART guidelines, integration of NIMART into PHC services Barriers: Shortages of health workforce, ART stock outs, poor referral feedback, food insecurity mobility of patients	Level III B
Naude[21] *(PhD thesis)*	To develop a framework to empower professional nurses for NIMART therapy in PHC facilities in the North West province	Mixed methods: Questionnaires and interviews	A total of 182 professional nurses completed questionnaires and 20 interviews	Enablers: Knowledge and skills, mentoring and support, guidelines, positive psychological experiences, feedback from managers and evaluation of performance, conducive working environment, power to perform tasks Barriers: Incompetence, training and clinical opportunities based on favouritism, negative psychological experiences, workload, lack of structural and psychological empowerment, clear role delineation needed, availability of drugs, equipment and consulting rooms	Level III B
Nozulu[34]	To evaluate ART initiation of pregnant women attending antenatal care in eThekwini district Community Health Centres (CHCs) between the Financial Years (FY) 10/11 (when NIMART was newly introduced) and FY13/14 (when NIMART was in full implementation)	Quantitative: Observational descriptive retrospective chart review	Records of pregnant women living with HIV that initiated ART	Enablers: A shift in point of care for ART initiation of pregnant women from ART clinics to nurse-managed antenatal clinic, reduced time to initiation	Level III B
Nyasulu et al.[26]	To determine if NIMART rollout to PHC facilities increases access to antiretrovirals in Johannesburg: An interrupted time series analysis	Quantitative: Interrupted time series analysis	A total of 20 535 ART-naïve patients from Region F of the CoJ who were initiated on ART from October 2009 to March 2012	Enablers: NIMART increase ART uptake and reduce workload on referral facilities, capacity building, training and mentoring	Level III B
Rasalanavho[25] *(Master's thesis)*	To explore and describe the challenges confronting professional nurses implementing the NIMART programme in PHC facilities under Thulamela B Municipality, Vhembe District	Qualitative: Interviews	A total of 15 professional nurses	Enablers: Health systems reorganisation, for example, appointment systems, club systems, peer support between nurses Barriers: Shortage of infrastructure, medication, lack of support from management and non-NIMART-trained nurses, training (lack of skills to work with children), doctors not fully supporting the NIMART programme	Level III B
Rawat et al.[44]	To explore patient responses on quality of care and satisfaction with staff after integrated HIV care in South African PHC clinics	Quantitative: Surveys	A total of 910 patients and caregivers at two time points after integration in four clinics in Free State, South Africa	Enablers: Integration of HIV care in PHC – patient satisfaction and quality of care Barriers: Possible knock on effect on other services (child health lacking, scores higher for TB attendees compared with chronic disease care attendees)	Level III B
Sekatane[41] *(Master's thesis)*	To develop protocol for professional nurses regarding NIMART management that is based on data and specific challenges that are faced in the Ehlanzeni district by professional nurses	Quantitative: Cross-sectional questionnaire	A total of 135 professional nurses who are NIMART trained	Barriers: Lack of professional nurses, fear of infecting themselves whilst treating patients, shortage of ART, lack of doctor support, patients not coming for treatment, not able to trace defaulters	Level III B
Solomons et al.[22]	To investigate factors influencing the knowledge and confidence of professional nurses in managing patients living with HIV in PHC settings in a rural and urban district in the Western Cape	Quantitative: A cross-sectional survey	A total of 77 NIMART-trained nurses from 29 healthcare facilities	Enablers: Training on guidelines, knowledge and confidence, support and regular feedback about personal performance, adequate 2 weeks of mentoring, caseload – frequently managing persons living with HIV in practice	Level III B
Swart et al.[42]	To describe the queries received from nurses by the hotline between 01 March and 31 May 2012 and identify problem areas and knowledge gaps where nurses may require further training	Quantitative: Retrospective record review	A total of 1479 HIV- and TB-related queries from healthcare workers	Barriers: Not all nurses NIMART trained, knowledge gaps of nurses – interpretation of laboratory results before initiating ART	Level III B
Visser et al.[32]	To evaluate the quality of care provided, the barriers to the effective rollout of antiretroviral services and the role of a clinical mentor	Mixed methods: Data were collected using patient satisfaction surveys, review of clinical records, facility audits, focus group interviews, field notes and a reflection diary	A total of 537 clinical records A total of 354 patient satisfaction surveys focus groups participants (n = 15)	Enablers: Ongoing mentoring and support, following guidelines, rational prescription, patient satisfaction Barriers: Salary challenges, excessive workload, lack of trained nurses, infrastructural barriers, drug shortages	Level III B

Annexure 1 continues on the next page→

ANNEXURE 1 (Continues...): Summary of included studies.

Authors/year	Study aim	Methods	Sample	Key enablers and barriers	Level and quality of evidence
Williams et al.[29]	To explore the experiences of healthcare professionals regarding the provision of ART for children at PHC clinics	Qualitative: In-depth interviews	A total of 19 interviews with healthcare professionals	Barriers: Lack of resources, need for training and mentoring and debriefing, disharmony in the work environment, ineffective management, non-conducive work environment, incongruence in the interpretation of side-effects of ART in children, apprehension to work with children, lack of patient attendance and adherence	Level III B
Xaba[28] *(Master's thesis)*	To conduct an implementation evaluation study of the NIMART programme in PHC clinics in the Ugu district of KwaZulu-Natal	Quantitative: Cross-sectional questionnaires	A total of 52 professional nurses	Enablers: Nurses initiating patients in practice (lower for children); nurses' knowledge on ART regimens, eligibility and monitoring good on average, some knowledge gaps identified, availability of latest guidelines	Level III B
Zuber et al.[46]	To describe the extent of NIMART in practice, education, policy and regulation in East, Central and Southern Africa	Quantitative: Survey	Senior nursing leadership teams from 15 African countries	Barriers: NIMART authorised in policy but not reinforced by regulation nor incorporated into pre-service education	Level III B

Key for levels of evidence:[13]
Level I: Experimental, RCT, systematic review or RCTs
Level II: Quasi-experimental study, systematic review of quasi-experimental/combined with RCTs
Level III: Non-experimental, qualitative studies, systematic reviews of non-experimental studies
Level IV: Opinions, clinical practice guidelines, consensus panels
A: High quality
B: Good quality
C: Poor quality, major flaw

HIV, human immunodeficiency virus; NIMART, nurse-initiated and managed antiretroviral treatment; PHC, primary healthcare; ART, antiretroviral treatment; STRETCH, Streamlining Tasks and Roles to Expand Treatment and Care for HIV.

Five years after Treat All implementation: Botswana's HIV response and future directions in the era of COVID-19

- Keith Jefferis, Ava Avalos, Heston Phillips, Mpho Mmelesi, Dinah Ramaabya, Bornapate Nkomo, Charles Muthoga, Joseph N. Jarvis, Siphiwe Ratladi, Robert Selato, John Stover.

2021 SPECIAL ANNIVERSARY COLLECTION

Southern African Journal of HIV Medicine
ISSN: (Online) 2078-6751, (Print) 1608-9693

Five years after Treat All implementation: Botswana's HIV response and future directions in the era of COVID-19

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Background: As the relentless coronavirus disease-2019 (COVID-19) pandemic continues to spread across Africa, Botswana could face challenges maintaining the pathway towards control of its HIV epidemic.

Objective: Utilising the Spectrum GOALS module (GOALS-2021), the 5-year outcomes from the implementation of the Treat All strategy were analysed and compared with the original 2016 Investment Case (2016-IC) projections. Future impact of adopting the new Joint United Nations Programme on HIV/AIDS (UNAIDS) Global AIDS Strategy (2021–2026) targets and macroeconomic analysis estimating how the financial constraints from the COVID-19 pandemic could impact the available resources for Botswana's National HIV Response through 2030 were also considered.

Method: Programmatic costs, population demographics, prevention and treatment outputs were determined. Previous 2016-IC data were uploaded for comparison, and inputs for the GOALS, AIM, DemProj, Resource Needs and Family Planning modules were derived from published reports, strategic plans, programmatic data and expert opinion. The economic projections were recalibrated with consideration of the impact of the COVID-19 pandemic.

Results: Decreases in HIV infections, incidence and mortality rates were achieved. Increases in laboratory costs were offset by estimated decreases in the population of people living with HIV (PLWH). Moving forward, young women and others at high risk must be targeted in HIV prevention efforts, as Botswana transitions from a generalised to a more concentrated epidemic.

Conclusion: The Treat All strategy contributed positively to decreases in new HIV infections, mortality and costs. If significant improvements in differentiated service delivery, increases in human resources and HIV prevention can be realised, Botswana could become one of the first countries with a previously high-burdened generalised HIV epidemic to gain epidemic control, despite the demands of the COVID-19 pandemic.

Keywords: Botswana; Spectrum; GOALS; economic modelling; COVID-19; treat all.

Introduction

Botswana has made substantial gains against the HIV epidemic and is one of the few countries in Africa to have reached the Joint United Nations Programme on HIV/AIDS (UNAIDS) 90-90-90 targets.[1] It was also one of the first African countries to successfully implement a Treat All strategy, which included antiretroviral (ART) treatment optimisation using the integrase inhibitor dolutegravir, following extensive programmatic and economic modelling contained within the 2016 Investment Case (2016-IC).[2] This strategic investment was aimed at reinvigorating the country's National HIV Response and safeguarding the gains already made against the HIV epidemic. For more than 20 years, the Government of Botswana had financed the largest portion of its National HIV Response, contributing more than 65% of its total HIV expenditures.[2] Together with generous donor and development partner funding as well as a progressive government-led multisectoral approach, the country was able to decrease infections, save lives and approach epidemiologic control of HIV.

Dates: Received: 17 June 2021|Accepted: 18 Aug. 2021|Published: 15 Oct. 2021

How to cite this article: Jefferis K, Avalos A, Phillips H, et al. Five years after Treat All implementation: Botswana's HIV response and future directions in the era of COVID-19. S Afr J HIV Med. 2021;22(1), a1275. https://doi.org/10.4102/sajhivmed.v22i1.1275

As the global coronavirus disease-2019 (COVID-19) pandemic, however, continues to negatively impact the country's medical infrastructure and its global economic standing, Botswana may face serious challenges to maintain its current level of healthcare capacity and control of its HIV epidemic. It, therefore, remains critical to clearly delineate and prioritise the areas of HIV prevention, treatment and care that will have the greatest impact to ensure economic and programmatic sustainability over the next decade. To this end, in cooperation with the Ministry of Health and Wellness and National AIDS and Health Promotion Agency, a technical working group composed of programmatic, economic, clinical and modelling experts used the GOALS module of Spectrum (GOALS-2021) to analyse the 5-year outcomes since the implementation of the Treat All strategy in 2016. The outcomes are then compared with the original 2016-IC projections. The work also considers the future programmatic and economic impact of adopting the new UNAIDS Global AIDS Strategy targets through 2030 to end HIV as a public health threat. Additional macroeconomic analysis estimates how the financial constraints resulting from the COVID-19 pandemic might impact the available resources required to maintain the country's National HIV Response. Whilst it was projected that the adoption of the Treat All Strategy and the use of dolutegravir would reduce new HIV infections, HIV mortality and overall costs, this was the first analysis since 2016 that aimed to quantify and test these estimations.

Methods

Modelling analysis

Spectrum is a modelling system used by HIV experts and policymakers as an analytical tool to support the decision-making processes. The model is designed to use the available country-level data within specific modules to produce outputs that are relevant to programme policy and planning, and the software is continuously updated. Using Spectrum version 6.06 (2021),[3] programmatic costs, as well as demographic, prevention and treatment-related outputs, were determined.

The original 2016-IC data were also uploaded into Version 6.06 for comparison. Prevention data and revised inputs were then used to produce the GOALS-2021 module through 2030. Inputs for the Resource Needs and Family Planning modules of Spectrum were derived from published reports, strategic plans, programmatic data and expert opinion (See Appendix 1: Inputs and targets by 2030 for the 2016-IC, AIM-2020, GOALS-2021 and the UNAIDS Global AIDS Strategy and Appendix 3: Data sources for Spectrum).

Additional Spectrum modules used for this analysis included DEMPROJ for demographic characteristics of the population by age and sex, including assumptions on fertility, mortality and migration; AIM to estimate the consequences of the HIV epidemic, such as the number of people living with HIV (PLWH), new HIV infections, and AIDS deaths; FAMPLAN to determine the family planning requirements to reach national goals; GOALS to estimate the costs and impact of the HIV interventions; and Resource Needs to estimate resources needed for the implementation of the HIV programme, including the cost of care and treatment, prevention, and policy and programmes.

Economic analysis

The 2016-IC whilst published in 2016 was prepared in 2015 and was based mainly on economic and fiscal data up to 2014, with projections of the period up to 2030. In 2021, the 6-year period from 2015 to 2020 was evaluated based on actual data. Economic projections were recalibrated with consideration of the possible impact of the COVID-19 pandemic, as well as the updated GOALS-2021 cost projections. Currency conversions were made at $1.00 to 11.2 Botswana Pula (BWP), consistent with the conversions used in the 2016-IC. The following assumptions were also made:

- Donor funding is reduced by 5% a year in real USD terms from the 2016 level (BWP 550 million; $51 million), resulting in the contribution being reduced by 50% in real terms to $25m (in 2016 prices) by 2030.
- Private funding (through direct corporate spending and medical aid schemes) will remain constant at 10% of total national treatment costs through to 2030.
- Public spending is sufficient to fill the gap between the donor and private funding and total treatment and programme costs.
- The COVID-19 pandemic is well controlled without catastrophic economic or human resource demands.

Modelling results

Total HIV population

Comparisons of the GOALS-2021 outputs for the total HIV population were made using the UNAIDS Global AIDS Strategy outputs. By adopting the new UNAIDS strategy, Botswana could see a decline in the HIV population of approximately 41 500 over the period 2021–2030 because of reductions in HIV infections. However, without implementation, it is unlikely that there would be substantial decreases overall in the HIV population through 2030.

GOALS-2021 estimated the total HIV population for Botswana at 375 900 (353 520 – 400 150) in 2020. It is important to note, however, that from routine adjustments of the Spectrum model and the addition of actual programmatic data over the last 5 years (2015–2020), the estimates of the overall HIV population are lower by 44 404 cases from the original 2016-IC model estimates.

New HIV infections

The estimates of annual new HIV infections that were projected in the 2016-IC are closely aligned with the GOALS-2021 projections, with a predicted decrease in annual newly acquired HIV infections from 9067 in 2016 to approximately 4406 by 2030. By implementation of the UNAIDS Global AIDS Strategy, there would be predictably further reduction to 2772 new infections by 2030.

There are two important points to note: firstly, although the 2021 National Spectrum AIM Model projects 8568 annual new HIV infections by 2021, which is significantly higher than the GOALS-2021 estimates at 4640, the AIM Module does not consider how all prevention and behavioural interventions impact these projections.[4] Secondly, the Botswana AIDS Incidence Survey (BAIS) is a household epidemiological survey that should be completed every 4 years so that all the Spectrum projections can be aligned with the results of the actual country incidence survey. The last BAIS survey was carried out in Botswana in 2012. Until the updated results are made available, there remains some degree of uncertainty with all Botswana HIV modelling projections. It is expected that the results of BAIS-V, currently underway, will be available in early 2022, at which time incidence projections can be validated.

The larger decreases in HIV infections demonstrated using the new targets of the UNAIDS Global AIDS Strategy suggests that even further decreases in new HIV infections could be realised by expanding prevention interventions, such as broadly increasing access to pre-exposure prophylaxis (PrEP) across all high-risk populations including men who have sex with men (MSM), female sex workers (FSWs) and those who participate in transactional sexual encounters.

HIV incidence

As concluded in the 2016-IC, young women remain at the highest risk of HIV acquisition (Figure 1). At the current prevention levels, young women will continue to have greater than four times the incidence of young men by 2030 and more than double the incidence of adults overall. This indicates that unless even more resources are invested into programmes targeting young women, their HIV infection rates will continue at the current levels without improvement, and they will continue to suffer the burden of HIV disproportionately.

Although the incidence rates of HIV have fallen steadily since 2016 when the Treat All Strategy was first launched, the continued higher levels of HIV infections reported amongst young women demonstrate that there is a transition of HIV epidemic in Botswana from being a generalised epidemic to one that requires a more targeted and differentiated approach towards high-risk populations. This is particularly true for young women who continue to experience higher levels of unemployment, further exacerbating vulnerability to transactional sexual encounters and other high-risk sexual behaviours.[5]

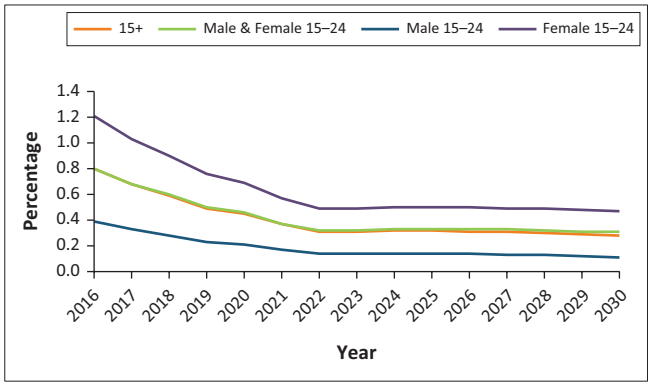


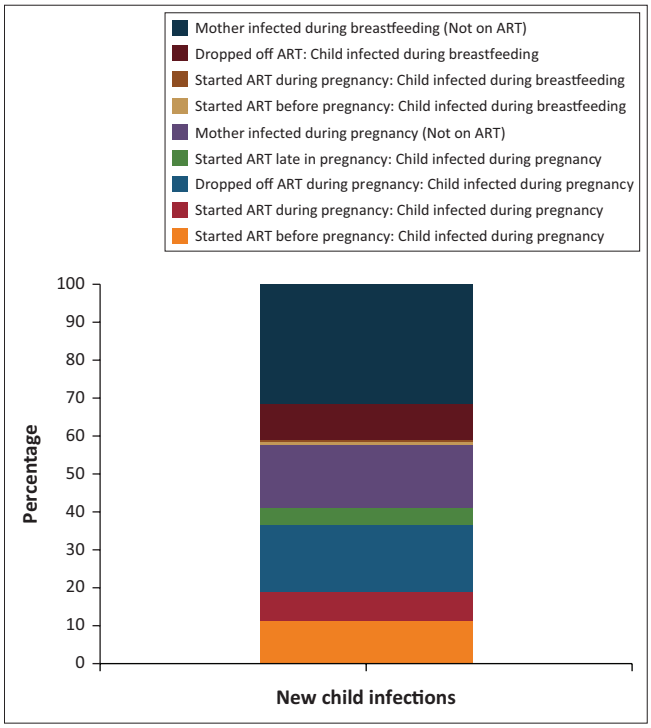
FIGURE 1: Incidence amongst young people aged 15–24 and adults aged 15+.

Figure 2 highlights the need for also targeting high-risk women of child-bearing age to prevent mother-to-child transmission of HIV, with the overall transmission rate in Botswana for 2020 being less than 2%, one of the lowest estimated globally.[4] There were 229 infections estimated in 2020, 9.6% because of mothers who dropped off antiretroviral treatment (ART) during pregnancy and 42.4% of all childhood infections occurring during the breastfeeding period.[6] The results from GOALS-2021 reveal that Sexual Reproductive Health (SRH) interventions such as the expansion of the contraceptive method mix and training in its delivery, as well as providing PrEP during pregnancy and breastfeeding to high-risk women, are now critical to reverse these trends and decrease the incidence of HIV during pregnancy.

Although the Spectrum model does not estimate the prevalence of gender-based violence (GBV), its rise in Botswana is well documented with estimates as high as double the global average.[7] Increases in GBV during the lockdown as a result of the COVID-19 pandemic, and the lack of contraception and shelter for abused women and children continue to put women at greater risk of HIV infection.[8,9]

HIV Mortality

For the past decade, HIV continues to be the number 1 cause of death in Botswana.[10] Figure 3 demonstrates that gains



Note: For further details, see Appendix 4: Numbers and Percentage of MTCT Statistics GOALS-2021.

FIGURE 2: Source of new child infections.

against HIV mortality could be made by expanding prevention interventions, as well as improving the management of advanced HIV cases and comorbidities. Both the UNAIDS Global AIDS Strategy and the 2016-IC models incorporate higher HIV prevention targets than what is currently being implemented in Botswana. Reinvigorating Botswana's HIV prevention programmes will not only prevent HIV infections but also save hundreds more lives.

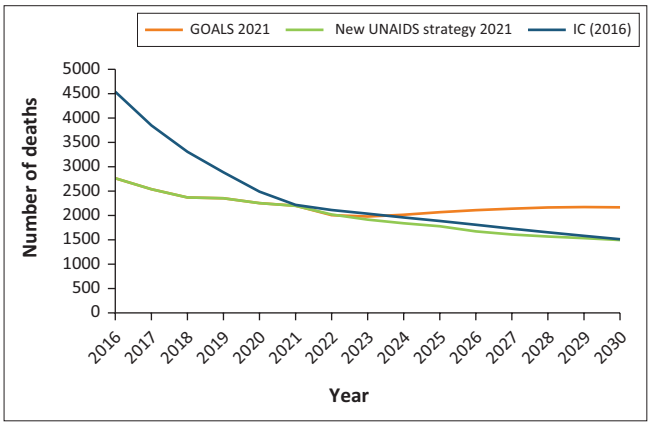
Further decreases in rates of HIV mortality would be achieved through continued efforts to expand HIV testing availability, including home testing and linkage to care. Expanding the clinical capacity of healthcare workers to manage advanced HIV disease and comorbidities must also be prioritised. Studies conducted in 2020 reported that out of 14 423 newly initiated patients on ART in urban Botswana, 25% presented for ART initiation with CD4 counts < 200 cells/mL.[11] As the average age of patients on ART continues to rise, managing serious comorbidities and non-communicable diseases will also increase the risks of clinical complications and drug-drug interaction from polypharmacy.

A brief report published in the *Journal of Clinical Infectious Disease* in 2020 shared results from a cryptococcal antigen study conducted in 2018–2019, which revealed that 76% of patients identified with CD4 counts < 200 cells/mL were already ART experienced, highlighting the importance of tracking patients who default or are lost to follow-up and improving adherence and psychosocial interventions.[12]

Deaths from cancers also continue to rise within the HIV population in Botswana. According to the National Cancer Registry in 2015, 61.6% of all cancer patients were infected with HIV.[13] In 2020, tuberculosis became the fifth highest cause of mortality in 2009 and the seventh highest cause of mortality by 2019.[10] According to the WHO, HIV represented 53.8% of all tuberculosis cases in 2018.[14] Whilst the incidence of tuberculosis is reducing, it remains a serious risk for PLWH.

Epidemic transition

Until the results of BAIS V-2021 are complete, it will remain uncertain whether Botswana is trending towards or has already achieved epidemiologic transition, defined as when a country is on a trajectory to control the epidemic. Remarkably, all the three models predict that epidemic transition may occur as early as the end of 2022 (Figure 4). Although promising, this should not cause complacency within the National HIV response but rather highlight the urgent need for continuing to initiate more effective prevention interventions to decrease infections and deaths overall, and better safeguard the HIV population in the era of COVID-19, and global political and economic uncertainty.



UNAIDS, Joint United Nations Programme on HIV/AIDS.

FIGURE 3: Annual AIDS deaths: 2016–2030.

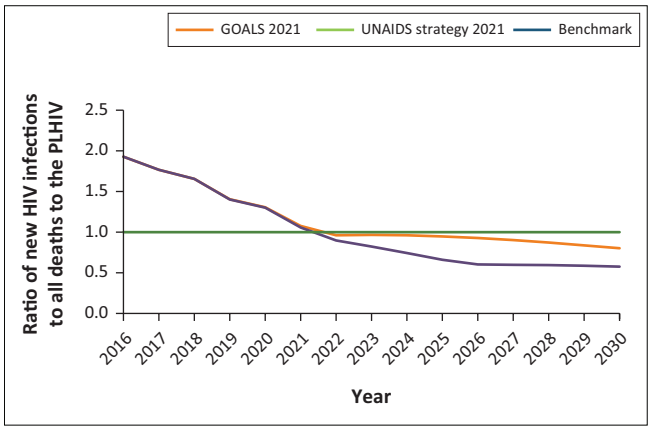
Economic analysis

GDP

Economic growth has been slightly higher than expected since the completion of the 2016-IC, with total GDP growth of 19.2% between 2015 and 2019, compared with the 17.3% projected in 2015. However, the most dramatic impact has been observed in 2020 as a result of COVID-19, leading to a GDP contraction of almost 9%, compared with the expected growth of around 4%. As a result, real GDP in 2020 was 11% lower than anticipated at the time of preparation of the 2016-IC. Much of this loss will be permanent, and although there will be some recovery of GDP lost in 2020, it is projected that real GDP in 2030 will now be 6% smaller than what was projected when the 2016-IC was prepared.

Government budget

The government budget also followed a different course to that anticipated in the 2016-IC (Figure 5). It was assumed then that there would be consistent efforts to contain spending and reduce budget deficits given the anticipated decline in revenues. In fact, spending has been higher than anticipated and budget deficits larger, compounded by the impact of COVID-19. In the medium term, the smaller size of the economy will have implications for the availability of funds to meet the needs of public spending across the board. The long-term need to contain spending in line with the anticipated decline in revenues remains. By 2030, total government spending is projected to be 11% lower than what was estimated in the 2016-IC.



Note: Also see Appendix 2: Selected Outputs and Results for the 2016-IC, GOALS-2021, the National AIM-2020 and UNAIDS Global AIDS Strategy.

UNAIDS, Joint United Nations Programme on HIV/AIDS.

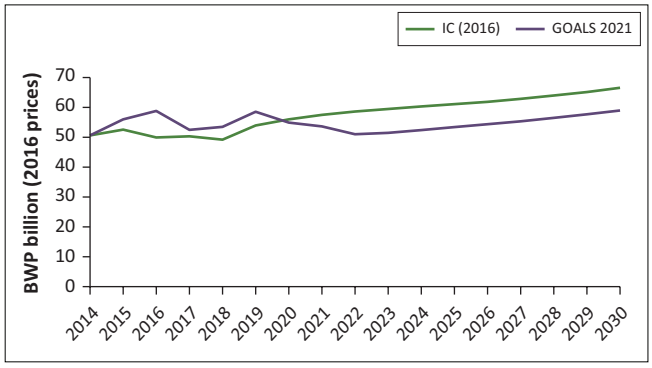
FIGURE 4: Incidence mortality ratio.

Fiscal resources for HIV-AIDS spending

Fortunately, the lower projected costs for HIV spending under the GOALS-2021 scenario appears to be manageable even within the reduced overall envelope for public spending. The requirements for public spending on HIV depend on projections of donor funding and private healthcare spending. Even with the assumptions outlined in the methodology of decreased donor funding by 50% in real terms and maintaining the private funding at 10% of total national treatment costs by 2030, public spending is sufficient to fill the gap between the donor and private funding and total treatment and programme costs.

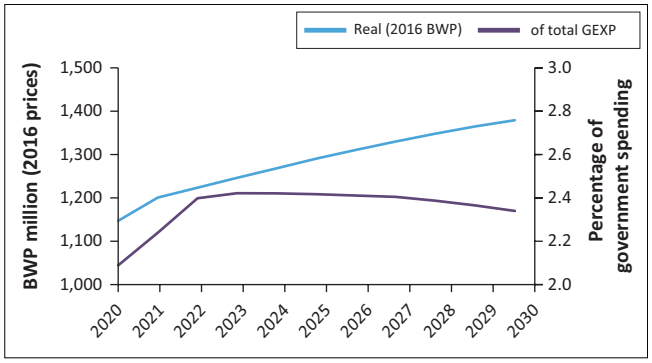
The outcome is that public spending on HIV will need to increase modestly from P1.15 billion (in constant 2016 BWP prices) in 2020 to P1.38bn in 2030. As a proportion of total public spending, the requirement will increase from an estimated 2.1% in 2020 to 2.4% in 2023 before declining slightly to 2.3% by 2030. This is lower than the estimated P1.66bn (2.8% of total spending) that would have been required to fully fund HIV spending needs in 2016 (Figure 6). If, however, public spending on HIV does not increase as indicated and is maintained at the same proportion of overall public spending as in 2020, then a financing gap of up to P235m (2016 prices) is projected, which would have to be filled by donor funding if total HIV spending is to be maintained.

It is important to note that costs of first-line ART regimens fell substantially since the implementation of the Treat All strategy in 2016.[15] The estimated future costs for ART regimens contained within the IC-2016 were set before the global generic costs for dolutegravir had been established.[16] Anticipating a significant cost reduction, the price of ART was set at 50% less beginning in 2020. In fact, the cost of generic co-formulated tenofovir-3TC-dolutegravir (TLD) fell to levels that were 66% less than the original 2016-IC projections.[15]



BWP, Botswana Pula.

FIGURE 5: Real government spending (total).



GEXP, total government expenditure; BWP, Botswana Pula.

FIGURE 6: Public spending on HIV.

Costs of laboratory commodities and reagents that were used in the 2016-IC, however, significantly increased.[17] This may be the result of a more comprehensive costing that was completed in 2021.[18] Whilst it is highly unlikely that global prices for ART will decline any further, advocacy for reductions in laboratory reagents and commodities should be taken up on the national and global level with the same ferocity as was seen for the reduction in ART treatment costs and current demands for global COVID-19 vaccine equity. This advocacy is now taking place by necessity as low- and middle-income countries demand international patent waivers for COVID-19 vaccine technologies and other essential medications, including access to affordable contraception.

Discussion

Botswana's progressive National HIV Response has continued to optimise the delivery of ART treatment and care, as evidenced with the adoption of the Treat All strategy and the first use of dolutegravir in 2016. Five years later, more than 97% of patients on ART have achieved and maintained viral suppression,[19] and the incidence of HIV is expected to have dropped to less than 1%.[4] With low overall HIV positive testing yields and estimated ART coverage of 95% projected in GOALS-2021 by 2030, it appears that there is a transition of HIV epidemic in the country from a generalised epidemic to one that is concentrated within specific geographical locations and amongst the most vulnerable and high-risk populations.[20] The results of the BAIS V-2021, expected in early 2022, will confirm whether these modelling predictions hold. Nonetheless, it is likely that results will fall somewhere between the National Model (AIM-2020) and GOALS-2021 Model estimates (see Appendix 2: Selected Outputs and Results by 2030 for the 2016-IC, AIM-2020, GOALS-2021 and UNAIDS Global AIDS Strategy). These projections are encouraging, as all models show significant reductions in key HIV response indicators.

Economic estimates predict that if the Government of Botswana can overcome the substantial economic hardships and human resource constraints caused by the COVID-19 pandemic, it should be able to continue to finance the greatest share of the financial requirements of its National HIV Response through 2030 – even at the current level of treatment costs and before optimisation of laboratory expenses – if the current level of public spending follows the national economic expectations. However, in order to ensure further reductions in HIV infections and cost savings, Botswana must focus its efforts on more targeted interventions for maximal impact. Priority areas should include at a minimum the following:

- Greater investment in SRH programming for young women of child-bearing age. This includes improved implementation of the availability of contraception, PrEP for high-risk pregnant and breastfeeding women, larger investment in economic opportunities for young women, and substantial investment in the reduction of maternal mortality and GBV that has continued to rise as a result of the COVID-19 pandemic.
- With low levels of HIV transmission and high coverage of ART, targeted HIV prevention interventions should continue to be rapidly and broadly expanded for those at highest risk for HIV infection. Expanded community interventions should also be prioritised for districts with the highest incidence rates and for geographically hard-to-reach populations, as well as those who may avoid public healthcare facilities, such as MSM, FSW, and those who engage in transactional sexual encounters. Additionally, detailed costing and efficiency gains studies of targeted ART-based prevention programmes should be carried out.
- Action and advocacy at the national and international level for cost reductions in laboratory reagents, commodities and supplies should be made a strategic priority. Laboratory expenses are now more than three times the cost of ART in Botswana.[18] Therefore, further laboratory costing and cost-efficiency studies are required as a matter of urgency. Additional laboratory saving would also be realised if the Botswana National ART Treatment Guidelines were revised to decrease laboratory requirements for long-standing virally suppressed and treatment adherent PLWH, who might need less frequent monitoring.
- Investment in the establishment of differentiated care for people living with advanced HIV disease and streamlined service delivery for stable patients would substantially decrease opportunity costs for patients and provide much needed relief at all levels for health workers involved in HIV care and treatment. Financial investment in medical service delivery innovation within primary care for PLWH would likely show solid financial and human resource returns for the government and patients alike.
- Further investment in capacitating healthcare workers to competently manage advanced HIV care patients should also be prioritised. This is particularly important as the complications and comorbidities that will arise from acute and long-term COVID-19 infection emerge. Additional investments in COVID-19 and HIV co-infection surveillance and clinical research will also prove essential as the medical and economic aftermath of the pandemic becomes known.

Conclusion

The implementation of the Botswana Treat All strategy in 2016 reinvigorated the country's HIV response and contributed positively to decreases in HIV infections, mortality and costs, based upon modelling results and economic analysis completed 5 years after the strategy was launched. Costing estimates made in the IC-2016 also proved to be accurate, despite significant increases in laboratory expenses, which were offset by the lowered estimates of the overall HIV population.

With continued widespread access to HIV testing, ART treatment and care, Botswana is likely to achieve the UNAIDS 95-95-95 before the year 2025, if targeted HIV prevention interventions can be sustained and successfully implemented across all high-risk populations. If the final incidence results of the BAIS V-2021 Survey prove to be aligned with the GOALS-2021 Spectrum estimates and if significant improvements in differentiated service delivery can be realised, Botswana could become one of the first countries with a previously high-burden, generalised HIV epidemic to transition to epidemic control. Importantly, as a result of the country's progressive financial investment and the continued optimisation of ART treatment, along with the dramatic decline in the costs of ART, the HIV epidemic in Botswana is no longer the major driver of health costs overall.

Moving forward, by ring fencing approximately 2.4% of GDP, in addition to continued donor and private funding, the Government of Botswana should be able to financially maintain its current HIV response. However, if the health demands of the country's COVID-19 pandemic are not controlled successfully and the country's economic recovery falls short, this could, instead, negatively impact the success of the country's HIV epidemic control. Therefore, the economic impact of COVID-19 must continue to be closely monitored, and the commitment towards ending Botswana's HIV epidemic must be further strengthened.

Acknowledgements

Special thanks go to Ms Mia Lebanna for administrative assistance, Sikhulili Moyo, PhD, and Kago Kagiso for critical review, and Dr Chelsea Morronni for contributing SRH expertise.

Competing interests

A.A. has received research support from Mylan and participated in the Advisory Boards for ViiV, Johnson & Johnson and Mylan. All other authors have declared that no competing interest exists.

Authors' contributions

The following authors contributed to the report conceptualisation, methodology, formal analysis and writing of the article: A.A., H.P., K.J. and M.M. The following authors contributed their programmatic expertise with data curation, resources, validation and critical review: D.R., B.N., S.R., R.S., J.N.J. and C.M. The following authors contributed their lab costing expertise: J.N.J. and C.M. The following author completed macroeconomic analysis: K.J. The following authors wrote, reviewed and edited the first and final drafts: K.J., A.A. and H.P. Project administration was led by A.A.

Ethical considerations

The manuscript consists of excerpts of the public health document and did involve research or human subjects. The report was approved by the Ministry of Health and Wellness and the National AIDS Health Promotion Agency of Botswana. Ethical clearance number: HPDME 13/18/1.

Funding information

The research work received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Data availability

All data used are within the public domain. Spectrum National file is available on the UNAIDS website (http://aidsinfo.unaids.org/).

Disclaimer

The views and opinions expressed in this article are those of the authors and do not necessarily reflect the official policy or position of any affiliated agency of the authors.

References

1. UNAIDS. 2020 Global AIDS update – Seizing the moment – Tackling entrenched inequalities to end epidemics [homepage on the Internet]. 6 July 2020. Available from: UNAIDS.org/sites/default/files/media_asset/2020_global-aids-report_en.pfd
2. Botswana Ministry of Health and Wellness. The 2016 Botswana investment case. Gaborone: UNAIDS; 2016.
3. Spectrum Version 6.06 (2021) [homepage on the Internet]. Available from: https://www.avenvirhealth.org/software-spectrum php. (https://www.avenirhealth.org/services-modeling.php
4. UNAIDS. 2021 HIV county estimates, Botswana [homepage on the Internet]. Available from: http//aidsinfo.unaids.org/
5. Statistics Botswana. Quarterly multi-topic survey: Labour force module report, Quarter 4 2020, Table YE2b [homepage on the Internet]. Available from: statsbots.org.bw/sites/default/files/MULTI-TOPIC%20SURVEY%20QUOTA%204%20 2020%LABOUR% 20 FORCE%MODULE%REPORT.pdf
6. UNAIDS. GAM: UNAIDS, 2021, Global AIDS Monitoring Report [homepage on the Internet]. Available from: unaids.org/sites/default/files/media_assets/global-aids-monitoring_en.pdf
7. UNFPA. Gender-based violence. What We Do. UNFPA Botswana Website [homepage on the Internet]. 2020. Available from: botswana.unfpa.org/en/topics/gender-based-violence-1
8. Botswana Universal Periodic Review (UPR). Civil Society Mid-Term Review Stakeholder Report [homepage on the Internet]. Third UPR Cycle; 2020. Available from: bw.undp.org/content/Botswana/en/home/library/democratic_governance/Botswana//universal-periodic-review—upr----civil-society-mid-te.html
9. UN. As the pandemic rages, women and girls face intensified risk. COVID-19 Response Newsletter [homepage on the Internet]. 2020. Available from: Unfpa.org/news/pandemic-rages-women-and-girls-face-intensified-risks
10. Institute of Health Metrics and Evaluation, University of Washington. Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: A systematic analysis for the Global Burden of Disease Study. Lancet [serial online]. 2019. Available from: Thelancet.com/journals/lancet/article/PIIS140-67-36(20)30925-9/fulltext
11. TB Leeme, M Mine, K Lechile, et al. Utility of CD4 measurement in the era of universal antiretroviral therapy: An analysis of routine laboratory data in Botswana. HIV Med. 2021;22(1):1–10. https://doi.org/10.1111/hiv.12951
12. Tenforde MW, Milton T, Rulaganyang K, et al. Outcomes of Relfex Cryptococcal antigen (CrAg) screening in human immunodeficiency virus (HIV) – Positive patients with CD4 counts of 100–200 cells/mL in Botswana. Brief Report. Clin Infect Dis. 2021;72(9):1635–1638. https://doi.org/10.1093/cid/ciaa899
13. Botswana. Princess Marina Hospital Chemotherapy Register, 2020–2021. Gaborone: Princess Marina Hospital; 2021.
14. World Health Organization. 2019 Global Tuberculosis Report. Geneva: WHO; 2019.
15. Botswana Ministry of Health and Wellness. Drug costing and forecasting technical working group in collaboration with Central Medical Stores. Gaborone: MoH; 2020.
16. Botswana Ministry of Health and Wellness. Drug Costing and Forecasting Technical Working Group. Direct communications with ViiV healthcare on their intention to release the dolutegravir patent protections for generic production of dolutegravir for Lower-to-middle-income-countries. Gaborone: MoH; 2015.
17. Menon V., Lang E., Silva R., Mosime W. Estimated resource needs for key health interventions offered under Botswana's Essential Health Service Package 2013–2018 [homepage on the Internet]. Washington, DC: Futures Group, Health Policy Project; 2015. Available from: avenirhealth.org/download/OHTCounty Applications/PDF/Estimated%20Resource%20Needs%20four%20Key%20 Health%Intervention%20Offered%20under %20bots….pdf
18. Muthoga C, Jarvis JNL. Meningitis prevention and treatment in Botswana. Gaborone: Wellcome Trust; 2021.
19. Botswana Ministry of Health and Wellness. The National HIV Data Warehouse. The National ART Data Repository. Gaborone: MoH; 2021.
20. USAID & MOHW. Botswana 2017 biological and behavioral surveillance survey of HIV/STIs among select key populations. Gaborone: USAID; 2017.

Appendices starts on the next page→

Appendix 1

TABLE 1-A1: Inputs and targets by 2030 for the 2016-IC, GOALS 2021 and UNAIDS global AIDS strategy.

MODELS	2016 (%)	2020	2025	2030
ART coverage (Adults 15+ years)				
IC2016	75	85	92	95
GOALS 2021	75	87	93	95
UNAIDS	75	87	95	95
PrEP coverage (MSM & FSW)				
IC2016	MSM & FSW: 0	MSM & FSW: 1.0	MSM & FSW: 20	MSM & FSW: 20
GOALS 2021	MSM & FSW: 0	MSM & FSW: 2.0	MSM & FSW: 6	MSM & FSW: 10
UNAIDS	MSM & FSW: 0	MSM: 6% FSW: 9	MSM: 28 FSW: 45	MSM: 50 FSW: 80
SRH family planning needs met				
IC2016	64	69	74	80
GOALS 2021	63.5	6767	70	75
UNAIDS	63.5	-	80	90
Condon coverage				
IC2016 (General Population)	67	77	84	90
GOALS 2021	67	72	83	90
UNAIDS	67	72	83	90
SMC				
IC2016	48	60	70	80
GOALS 2021	35	46	60	77
UNAIDS	35	46	68	90
HIV testing (Adults)				
IC2016	75	80	85	90
GOALS 2021	75	82	87	90
UNAIDS	75	82	87	90
Community mobilisation				
IC2016	25	35	43	50
GOALS 2021	28	3535	58	80
UNAIDS	28	-	58	80

MSM, men who have sex with men; FSW, female sex workers; UNAIDS, Joint United Nations Programme on HIV/AIDS; PrEP, pre-exposure prophylaxis; SRH, sexual reproductive health; SMC, safe male circumcisio.

Appendix 2

TABLE 1-A2: Selected Outputs and Results for the 2016-IC, GOALS 2021, and UNAIDS Global AIDS Strategy for 2016, 2020, 2025, 2030.

Models	2016	2020	2025	2030
Total PLWH population				
IC2016	415 140	422 200	420 500	413 430
GOALS 2021	366 200	377 800	379 230	375 030
UNAIDS	-	-	376 980	369 950
Total new HIV infections				
IC2016	9642	4738	4140	3720
GOALS 2021	9070	5540	3800	3120
UNAIDS	-	-	2878	2770
Incidence (adults 15+ years)				
IC2016	0.75	0.35	0.28	0.24
GOALS 2021	0.80	0.45	0.27	0.20
UNAIDS	-	-	0.21	0.18
Total deaths to the HIV population				
IC2016	6711	5050	5200	5812
GOALS 2021	4700	4240	4440	4945
UNAIDS	-	-	4350	4810
Total AIDS deaths				
IC2016	4541	2589	1886	1510
GOALS 2021	2760	2250	1855	1610
UNAIDS	-	-	1780	1500

UNAIDS, Joint United Nations Programme on HIV/AIDS.

Appendix 3: Data Sources For Spectrum V. 6.06 (2021)

DemProj:

- United Nation Statistics Division. 2020, World Population Prospects: The 2020 Revision. United Nations, New York, USA.

AIM File:

- MOHW, 2020. HAART Patient Update Summary, December 2020, DHAPC
- MOHW, 2020. Programme statistics: Breastfeeding, DHAPC, MOH.
- MOHW, 2020. Programme statistics: PMTCT coverage 2010–2020, DHAPC
- MOHW, 2020. Programme statistics on Knowledge of Status & Viral load suppression
- NACA BAIS, (II-2004, III-2008, IV-2013)
- NACA (2011) ANC Sentinel Surveillance Study

GOALS and Resource Needs:

- MOHW, 2020. Drug Costing and Forecasting Technical Working Group.
- MOHW, 2019. Mapping size estimation and behavioral and biological surveillance survey (BBSS) of HIV/STU among select high-risk sub-populations in Botswana. Technical Report, Botswana.
- Futures Group, 2013 One Health Tool. Futures Group.
- Charles Muthoga and Joseph N. Jarvis. Botswana Laboratory Costing. 2021

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Appendix 4

TABLE 1-A4: Numbers and percentage of MTCT Statistics GOALS-2021.

Category	Number	%
Started ART before pregnancy: child infected during pregnancy	26	11.4
Started ART during pregnancy: child infected during pregnancy	17	7.4
Dropped off ART during pregnancy: child infected during pregnancy	41	17.9
Started ART late in pregnancy: child infected during pregnancy	10	4.4
Mother infected during pregnancy (Not on ART)	38	16.6
Started ART before pregnancy: child infected during breastfeeding	2	0.9
Started ART during pregnancy: child infected during breastfeeding	1	0.4
Dropped off ART: child infected during breastfeeding	22	9.6
Mother infected during breastfeeding (Not on ART)	72	31.4
Total	**229**	-

MTCT, mother to child transmission.

Geographical variation in HIV testing in South Africa: Evidence from the 2017 national household HIV survey

- Sean Jooste, Musawenkosi Mabaso, Myra Taylor, Alicia North, Yolande Shean, Leickness C. Simbayi, Tarylee Reddy, Leonard Mwandingi, Tenielle Schmidt, Portia Nevhungoni, Samuel Manda, Khangelani Zuma.

2021 SPECIAL ANNIVERSARY COLLECTION

Southern African Journal of HIV Medicine
ISSN: (Online) 2078-6751, (Print) 1608-9693

Geographical variation in HIV testing in South Africa: Evidence from the 2017 national household HIV survey

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Background: Identification of the geographical areas with low uptake of HIV testing could assist in spatial targeting of interventions to improve the uptake of HIV testing.

Objectives: The objective of this research study was to map the uptake of HIV testing at the district level in South Africa.

Method: The secondary analysis used data from the Human Sciences Research Council's 2017 National HIV Prevalence, Incidence, Behaviour and Communication Survey, where data were collected using a multistage stratified random cluster sampling approach. Descriptive spatial methods were used to assess disparities in the proportion of those ever tested for HIV at the district level in South Africa.

Results: The districts with the highest overall coverage of people ever having tested for HIV (> 85%) include West Rand in Gauteng, Lejweleputswa and Thabo Mofutsanyane in Free State, and Ngaka Modiri Molema in North-West. These provinces also had the least variation in HIV testing coverage between their districts. Districts in KwaZulu-Natal had the widest variation in coverage of HIV testing. The districts with the lowest uptake of HIV testing were uMkhanyakude (54.7%) and Ugu (61.4%) in KwaZulu-Natal and Vhembe (61.0%) in Limpopo. Most districts had a higher uptake of HIV testing amongst female than male participants.

Conclusion: The uptake of HIV testing across various districts in South Africa seems to be unequal. Intervention programmes must improve the overall uptake of HIV testing, especially in uMkhanyakude and Ugu in KwaZulu-Natal and Vhembe in Limpopo. Interventions must also focus on enhancing uptake of HIV testing amongst male participants in most districts. Strategies that would improve the uptake of HIV testing include HIV self-testing and community HIV testing, specifically home-based testing.

Keywords: HIV; HIV testing; thematic mapping; districts; South African.

Introduction

Eastern and Southern Africa is home to 53% of the 36.9 million people living with HIV globally,[1] with an estimated 75% of people living with HIV who actually knew their HIV status by the end of 2017.[1]

Furthermore, there was a 42% reduction of AIDS-related illnesses, as a result of the increase in HIV testing and treatment coverage between 2010 and 2017.[1]

South Africa has one of the largest HIV testing services (HTS), which is a crucial component of national HIV response.[2] HIV testing services are vital in directing HIV-positive people to the treatment continuum, starting with antiretroviral therapy and, therefore, is critical in the fight against HIV.[2] The Joint United Nations Programme on HIV (UNAIDS) launched the 90-90-90 targets stipulating that by 2020, 90% of people living with HIV should know their status, 90% of those who know their HIV-positive status should receive antiretroviral therapy and 90% of those on treatment have a suppressed viral load to end the epidemic by 2030. The UNAIDS has

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Dates: Received: 28 May 2021|Accepted: 21 July 2021|Published: 31 Aug. 2021
How to cite this article: Jooste S, Mabaso M, Taylor M, et al. Geographical variation in HIV testing in South Africa: Evidence from the 2017 national household HIV survey. S Afr J HIV Med. 2021;22(1), a1273. https://doi.org/10.4102/sajhivmed.v22i1.1273

revised 2030 targets of 95-95-95, which are set out to be achieved by 2030.[3]

South Africa has made progress towards the UNAIDS 90-90-90 targets, especially regarding HIV testing and viral load suppression.[4] Over the past decade, the country had made excellent progress in involving more people to test and become aware of their HIV status, after the launch of two national HIV testing initiatives: firstly, the national HIV testing and counselling (HTC) campaign that took place in 2010, and secondly, the HTC revitalisation strategy in 2013.[5] As a result of these campaigns and other similar campaigns, more than 10 million people in South Africa test for HIV every year.[5] In scaling up efforts around HTS interventions, civil society organisations continue to work with government departments in South Africa. The South African National AIDS Council continues to provide a platform for engagement between the civil society and government to work together on the HIV response.[6]

Although South Africa has made steady progress towards reaching the UNAIDS targets, many people affected with HIV are still unaware of their HIV status.[7] Despite the availability of HTS, research studies have revealed that only a fraction of South Africans who are at risk get tested for HIV.[8] Evidence shows that access to HTS may be limited geographically because of the inadequacy and heterogeneous distribution of available services.[9,10] Achieving high coverage of HIV testing is critical for linking HIV-positive people to care across the country. Therefore, equitable geographical distribution of HTS is vital for achieving optimal coverage for HIV testing.[10] This highlights the importance of conducting and collecting population-based HIV testing covereage data at the sub-national level needed for decision making.

In South Africa, gathering spatial data on HIV and mapping its distribution have been carried out in selected micro-geographical areas, limiting the generalisability of the findings to the country.[11] The main source of estimating the number of people who tested for HIV in the country comes from the District Health Information System and from modelling.[12] Both sources have limitations and rely on healthcare facility and programme data from districts to produce estimates.[13,14] The current study used large-scale nationally representative population-based household survey data to describe the spatial coverage in the uptake of HIV testing amongst youth and adults 15 years and older. The aim of this research study was to identify the spatial gap in the uptake of testing in people who had ever tested for HIV at the district level in South Africa.

Methods

Study design and sampling

The data used in the secondary analysis were obtained from the National HIV Prevalence, Incidence, Behaviour and Communication Survey conducted in 2017.[15] The survey used a multistage stratified, cluster randomised, cross-sectional design. The survey chose a systematic probability sample of 15 households randomly from 1000 small area layers (SALs), selected from 84 907 SALs released by Statistics South Africa in 2015.[16] The sampling of SALs was stratified by province and locality type (urban formal, urban informal, rural formal and rural informal localities). An additional 457 SALs were sampled in 13 high-priority districts, which included iLembe, uMzinyathi, uThukela and King Cetshwayo in KwaZulu-Natal province; Ehlanzeni and Gert Sibande in Mpumalanga province; O.R. Tambo in the Eastern Cape province; Sekhukhune in Limpopo province; Bojanala Platinum in North-West province; and Ekurhuleni, Sedibeng, Tshwane and West Rand in Gauteng province. This study focused on the population aged 15 years and older who reported ever testing for HIV.

Measures

The primary outcome measure 'ever testing for HIV' was obtained from individuals who responded to the original survey question 'have you ever been tested for HIV?' The response was dichotomised into a binary outcome (yes = 1 and no = 0).

Ethical considerations

The survey protocol was approved by the Human Sciences Research Council's (HSRC) Research Ethics Committee (REC: 4/18/11/15), and the Associate Director for Science, Center for Global Health, Centres for Disease Control and Prevention (CDC). Ethical clearance was also obtained from the University of KwaZulu-Natal's Biomedical Research Ethics Committee (BE 646/18). Verbal or written informed consent was sought before undertaking both the behavioural data and blood specimen collection.

Statistical analysis

Statistical analysis was carried out in STATA 15.0 (Stata Corporation, College Station, TX, United States [US]) software.

Descriptive statistics were used to summarise the sample characteristics. Multilevel mixed-effects logistic regression models were used to estimate the excess probability of prior testing for HIV after adjusting for the effect of age and sex. District-level random effects predicted from the model, including age and sex were used to estimate the excess probability of prior testing. Results are shown with 95% confidence intervals (CI), and p-values < 0.05 were reported for all statistically significant associations. The proportion of the population, aged 15 years and older, that have ever been tested for HIV were geo-located using the South African district-level boundaries. The maps were generated in QGIS, version 3.14.10. An adjusted weight, benchmarked to the general population by age and sex at the national level, was computed to facilitate this analysis.

Results

Socio-demographic characteristics of the study sample

Table 1 shows the mean age and sex distribution amongst the respondents in all 52 districts. uMkhanyakude, King

Cetshwayo (both in KwaZulu-Natal) and Gert Sibande in Mpumalanga had the youngest mean age of under 35 years. Amathole in the Eastern Cape, Fezile Dabi in Free State and Namakwa in the Northern Cape had the oldest mean age of 43 years. Harry Gwala, uThukela, uMzinyathi (all in KwaZulu-Natal) and Buffalo City in the Eastern Cape had the highest proportion of female participants (over 59%). Fezile Dabi in Free State, West Coast in Western Cape, Nkangala in Mpumalanga and uMgungundlovu in KwaZulu-Natal had the highest proportion of male participants (over 54%).

TABLE 1: Mean age and sex distribution of youth and adult 15 years and older by district, South Africa 2017.

Province	District name	*n*	Mean age (years)	Male (%)	Female (%)
Eastern Cape	Alfred Nzo	278	40.2	42.0	58.0
Eastern Cape	Amathole	337	44.6	46.4	53.6
Eastern Cape	Buffalo City	329	41.7	40.9	59.1
Eastern Cape	Chris Hani	243	42.0	47.9	52.1
Eastern Cape	Joe Gqabi	188	41.1	53.1	46.9
Eastern Cape	Nelson Mandela Bay	1213	41.9	48.6	51.4
Eastern Cape	O.R. Tambo	1369	39.9	45.3	54.7
Eastern Cape	Sarah Baartman	712	39.8	49.0	51.0
Free State	Fezile Dabi	263	44.2	55.8	44.2
Free State	Lejweleputswa	365	39.0	49.0	51.0
Free State	Mangaung	1068	39.7	48.9	51.1
Free State	Thabo Mofutsanyane	776	39.2	48.7	51.3
Free State	Xhariep	243	39.2	52.6	47.4
Gauteng	City of Johannesburg	1754	40.0	49.4	50.6
Gauteng	City of Tshwane	1718	38.9	50.3	49.7
Gauteng	Ekurhuleni	2011	38.0	51.6	48.4
Gauteng	Sedibeng	2894	39.1	50.9	49.1
Gauteng	West Rand	1192	38.2	52.5	47.5
KwaZulu-Natal	Amajuba	287	41.4	41.5	58.5
KwaZulu-Natal	eThekwini	3583	41.7	47.3	52.7
KwaZulu-Natal	Harry Gwala	427	37.7	38.6	61.4
KwaZulu-Natal	iLembe	3605	36.0	44.2	55.8
KwaZulu-Natal	King Cetshwayo	4003	34.3	43.9	56.1
KwaZulu-Natal	Ugu	958	40.0	48.1	51.9
KwaZulu-Natal	uMgungundlovu	601	41.2	54.6	45.4
KwaZulu-Natal	uMkhanyakude	651	33.5	41.0	59.0
KwaZulu-Natal	uMzinyathi	3227	37.5	40.6	59.4
KwaZulu-Natal	uThukela	3770	36.4	40.1	59.9
KwaZulu-Natal	Zululand	480	37.5	46.0	54.0
Limpopo	Capricorn	659	40.0	42.2	57.8
Limpopo	Greater Sekhukhune	1292	39.2	42.9	57.1
Limpopo	Mopani	604	41.2	46.3	53.7
Limpopo	Vhembe	705	37.8	47.7	52.3
Limpopo	Waterberg	480	40.7	53.1	46.9
Mpumalanga	Ehlanzeni	2731	35.3	47.5	52.5
Mpumalanga	Gert Sibande	3585	34.4	52.2	47.8
Mpumalanga	Nkangala	1247	36.7	54.9	45.1
North West	Bojanala	2322	37.3	48.5	51.5
North West	Dr Kenneth Kaunda	761	37.2	51.9	48.1
North West	Dr Ruth Segomotsi Mompati	372	39.6	43.4	56.6
North West	Ngaka Modiri Molema	447	39.1	48.0	52.0
Northern Cape	Frances Baard	749	38.7	50.6	49.4
Northern Cape	John Taolo Gaetsewe	262	36.7	50.3	49.7
Northern Cape	Namakwa	200	43.3	50.5	49.5
Northern Cape	Pixley ka Seme	1005	37.2	49.2	50.8
Northern Cape	Z F Mgcawu	830	37.2	50.7	49.3
Western Cape	Cape Winelands	750	40.9	45.7	54.3
Western Cape	Central Karoo	108	42.3	44.0	56.0
Western Cape	City of Cape Town	2362	38.5	49.9	50.1
Western Cape	Eden	374	39.5	51.7	48.3
Western Cape	Overberg	305	40.9	46.8	53.2
Western Cape	West Coast	468	36.4	55.8	44.2

District-level coverage of ever being tested for HIV

Figure 1 illustrates the geographical distribution of people who have ever been tested for HIV in the 52 districts of South Africa (Table 1-A1). The overall HIV testing uptake range was between 54.7% and 86.1%. Free State and North-West had more districts with an HIV testing coverage of over 80%, while no district in the Eastern Cape or Limpopo had an overall coverage higher than 80%.

Overall, uMkhanyakude (54.7%), Vhembe (61.0%) and Ugu (61.4%) districts had the lowest coverage for HIV testing. Ngaka Modiri Molema district (86.1%) reported the highest coverage for testing, followed by Lejweleputswa (85.2%) and Thabo Mofutsanyane (84.8%) district.

In the Eastern Cape, Joe Gqabi district had the highest overall coverage (78.5%), while Sarah Baartman district had the lowest (66.2%) coverage for HIV testing.

In the Free State, Lejweleputswa district had the highest testing uptake, followed by Thabo Mofutsanyane district, while Xhariep district (73.0%) had the lowest. In Gauteng, West Rand district had the highest coverage (83.3%), and the City of Johannesburg had the lowest coverage for testing (78.2%).

In KwaZulu-Natal, Amajuba district (83.1%) had the highest coverage, followed by Ugu district (61.4%), while uMkhanyakude district (54.7%) had the lowest coverage in the country. KwaZulu-Natal was the only province with a significant difference in testing coverage between its districts ($P < 0.001$).

In Limpopo, Waterberg district had the highest overall coverage (75.9%), while Vhembe district (61.1%) had the lowest coverage for testing. In Mpumalanga, Nkangala district had the highest overall coverage (80.4%), while Gert Sibande district (74.3%) had the lowest coverage for HIV testing. In North West, Ngaka Modiri Molema district (88.6%) had the highest coverage, while Dr Kenneth Kaunda district (76.9%) had the lowest coverage for testing. In the Northern Cape, Namakwa district (67.2%) had the lowest coverage, while Frances Baard district (81.4%) had the highest coverage.

In the Western Cape, Central Karoo district was the only district with over 80% coverage. In comparison, the West Coast and Cape Winelands district had the lowest coverage (< 70%), while the remaining districts' coverage ranged from 70% to 79%.

District-level coverage of ever being tested for HIV by sex

Figure 2 illustrates the geographical coverage of those who have ever been tested for HIV (Table 2-A1). The results are

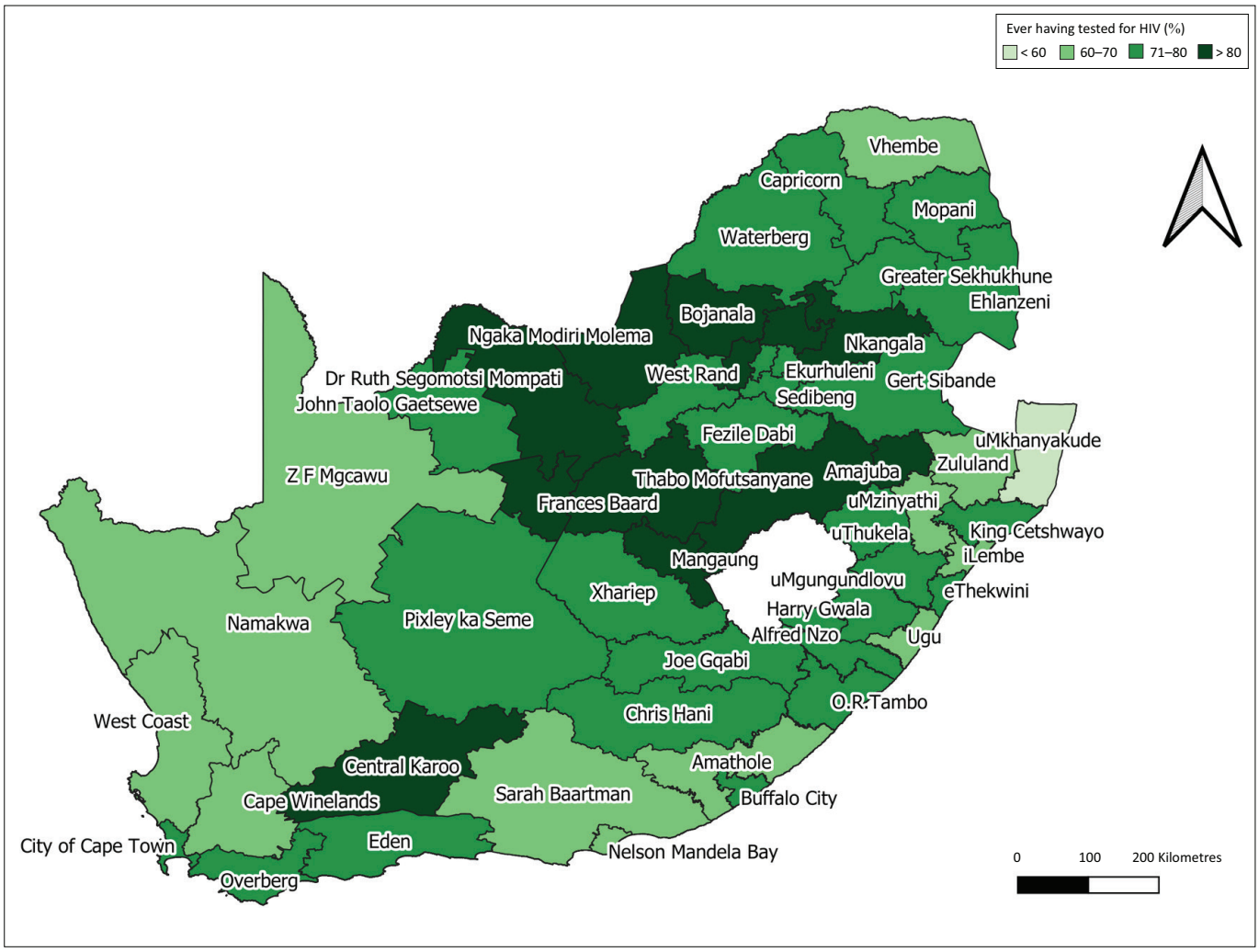


FIGURE 1: Geographical uptake of those aged 15 years and older who have ever been tested for HIV in the 52 districts of South Africa.

revealed for (1) male and (2) female participants, aged 15 years and older, across the 52 districts in South Africa. Overall, the maps show that female participants had coverage of over 80% in more districts than male participants. Female participants had a higher HIV testing rate of 20% more than male participants in Vhembe district (73.7% vs 46.6%), Eden (81.3% vs 61.1%), Alfred Nzo (85.5% vs 58.9%) and O.R. Tambo districts (79.6% vs 59.2%).

The proportion of female participants who had ever been tested for HIV ranged from 59.0% to 88.6%. uMkhanyakude district had the lowest proportion of female participants who had ever been tested for HIV (59.0%), followed by Ugu district (63.3%). Districts with the highest coverage of female participants who had ever been tested for HIV included Ngaka Modiri Molema (88.6%), Frances Baard (88.4%) and Lejweleputswa (88.4%). The coverage range of male participants who have ever been tested for HIV was 46.6% – 89.9%. Vhembe and uMkhanyakude were the only districts with < 50% coverage, that is, at 46.6% and 48.5%, respectively. Amajuba had the highest coverage (89.9%) of male participants who have ever been tested for HIV.

Adjusted coverage of ever being tested for HIV

Figure 3 illustrates the geographical coverage of the excess probability of ever having tested for HIV in the 52 districts of South Africa after adjusting for age and sex (Table 3-A1). Both age and sex were significantly associated with previous testing (Table 4-A1). Specifically, female participants had a significantly higher odds of testing (OR: 1.59; 95% CI: 1.51–1.66) and a 1-year higher age associated with a 0.4% increase in the odds of testing. After adjusting for age and sex, the excess probability of ever having tested for HIV was different amongst the districts, illustrating that true heterogeneity (explained by variables other than sex and age) between the districts is present. The districts in Free State still had the highest probability for testing. Nkangala district had the second-highest probability for HIV testing. uMkhanyakude, Ugu, uMzinyathi, O.R. Tambo, Amathole, Chris Hani, Buffalo City, Vhembe and Greater Sekhukhune had the lowest probability for HIV testing.

Discussion

HIV testing is a crucial component of the national HIV response in South Africa.[17] This study presents the first geographic analysis of youth and adults (≥ 15 years) who

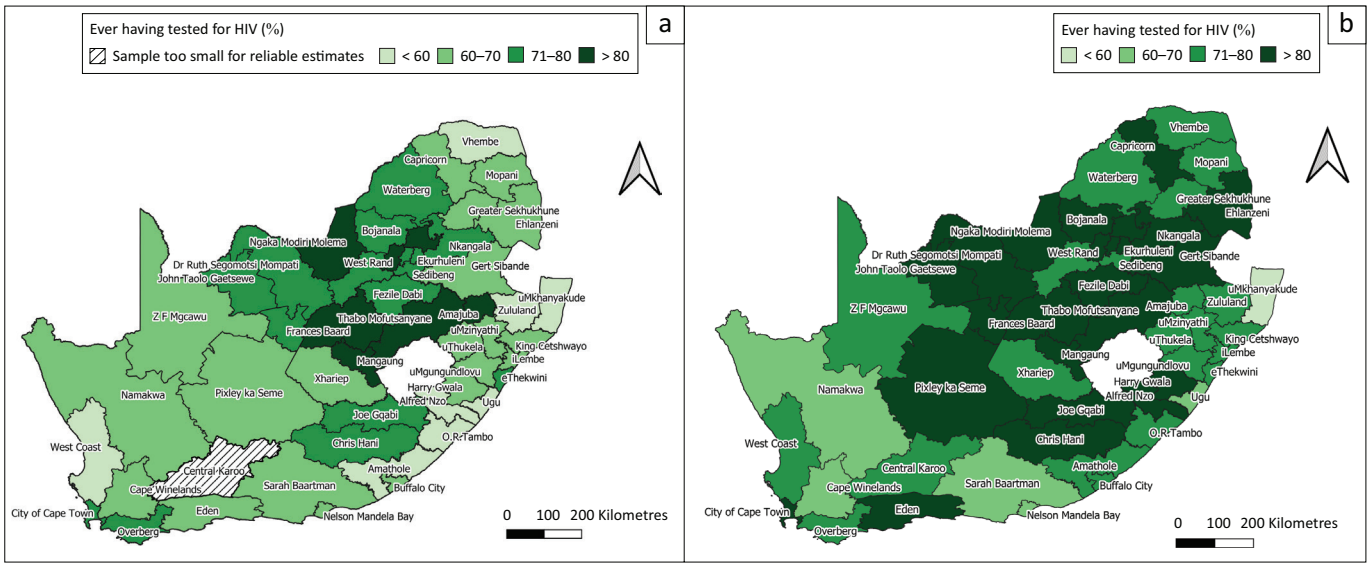
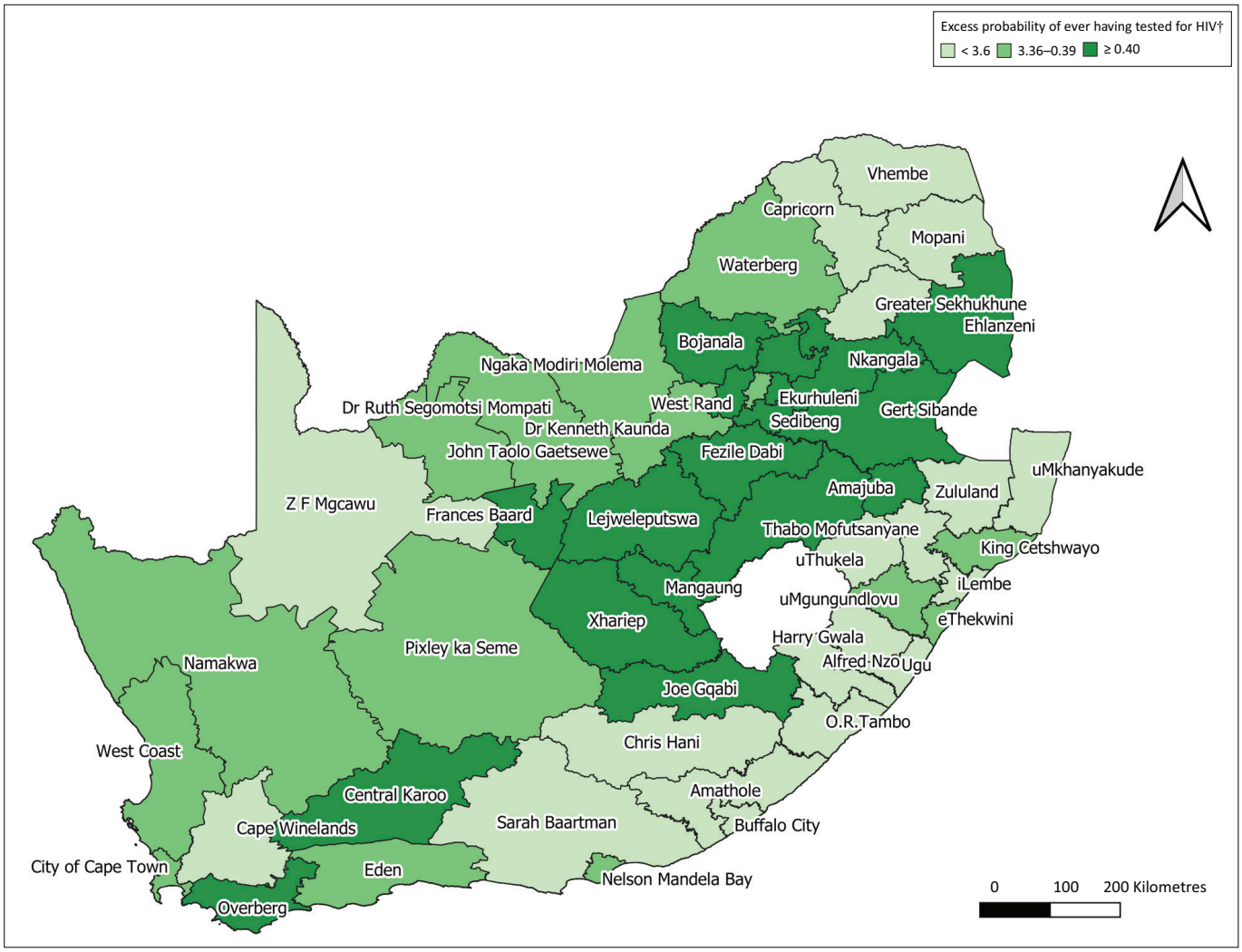


FIGURE 2: Geographical coverage: proportion of people who have ever been tested for HIV amongst (a) male and (b) female participants aged 15 years and older in the 52 districts in South Africa.



†, Estimated from a multilevel model with district-level random effect.
FIGURE 3: Geographical coverage of excess probability of ever having tested for HIV after adjusting for age and sex in the 52 districts in South Africa.

have ever been tested for HIV in South Africa using simple GIS mapping and data obtained from a cross-sectional nationally representative population-based survey.

The mapping results revealed that the uptake of HIV testing varied across the various districts in South Africa. The age and sex distribution across the districts were different.

Studies have revealed that age and sex are crucial factors in HIV testing.[18,19] The estimates from a multilevel model with district-level random effects showed that excess probability of ever having tested for HIV was different among the districts after adjusting for age and sex. Variations in the quality of healthcare services, health promotion activities, easier access to healthcare facilities and socio-economic status could have an impact on the uptake of HIV testing in districts.

The overall proportion of people who had ever tested for HIV at the district level in South Africa ranged from 54.7% to 86.1%. uMkhanyakude and Ugu districts in KwaZulu-Natal and Vhembe district in Limpopo had the lowest overall testing coverage of < 62%. Ngaka Modiri Molema district in North West, and Lejwelepuswa and Thabo Mofutsanyane districts both in Free State reported the highest coverage for HIV testing. None of the districts in the Eastern Cape or Limpopo had an overall coverage of higher than 80%. These districts are characterised as being predominately rural. Other studies have also found that people living in rural informal or tribal areas were significantly less likely to test for HIV when compared with those from urban areas.[20,21] The finding that uptake of HIV testing was less likely amongst those in rural areas could be linked to limited resources and structural barriers to healthcare in terms of geographical and financial accessibility.[22,23] Additional barriers included fear, discrimination and stigmatising attitudes, as well as lack of education and awareness.[24]

Another factor playing a major role in the higher coverage districts included the epidemic control plans implemented by the President's Emergency Plan for AIDS Relief (PEPFAR), which aims to achieve maximum impact and reach in areas with the highest burden of disease (COP19). This is informed by population-based surveillance. The PEPFAR country operational plan (COP) for 2017, in 27 districts with an estimated number of people living with HIV of 5.6 million, which account for 79% of number of people living with HIV in South Africa (COP19), identified 1969 sites for intensified support as part of the country's district-level implementation plan (DIP).[25] According to the National Strategic Plan for 2012–2016,[26] the objectives included maximising opportunities for testing and screening to ensure that everyone in South Africa got tested for HIV and was screened for TB. The overall investment for HTS programmes in 2016–2017 was $126 663 865.00, with the South African Government funding being 45% and PEPFAR funding 55% (COP-19).

Most districts had a higher coverage of ever having tested for HIV amongst female than male participants. uMkhanyakude and Ugu had the lowest coverage for female participants. Vhembe and uMkhanyakude had the lowest HIV testing coverage for male participants. Despite the countrywide scale-up, the observed geographic disparities in HIV testing are relevant from an epidemic control perspective, especially if the people who do not get tested are at higher risk of HIV infection.[6] Therefore, achieving high coverage of HIV testing amongst men is critical in the fight against HIV in the country. However, data elsewhere suggest that boys and men are lagging.[27,28] Men were found to have lower levels of participation in HIV testing.[29] Some of these reasons include fear of damaging reputations, losing their masculine pride, fearing both community rejection and a loss of emotional control because of the psychological burden of knowing one was HIV positive.[29] HIV testing programmes, therefore, need to carefully review who is being reached by their services and implement interventions specifically tailored to engage people who might be missed.

There are various settings in which HTS can be provided to the public and expanded further, for instance in healthcare facilities, such as hospitals, clinics and mobile clinics, and at community sites, be these stand-alone or even home-based services, where testing services are provided within the community.[2] There is also an option for HIV self-testing (HIVST), which is carried out by an individual who wants to know his or her HIV status and is carried out privately by the individual alone.[5] HIV self-testing provides an opportunity for testing to be carried out discreetly and at one's convenience, which could increase the uptake of HIV testing amongst those unable or unwilling to access other healthcare services.[2] Concerns raised regarding HIVST include lack of HIV counselling,[30] instructions are difficult to follow[31] and there should be more of a focus on linkage to care.[32]

This research study has a few limitations. 'Ever testing' for HIV is self-reported, and therefore, prone to biases related to social desirability, recall and under-reporting. Nevertheless, the results of the nationally representative population-based survey can be generalised to adults aged 15 years and above who tested for HIV in South Africa. There may be a high degree of within-district heterogeneity. In future, work will include examining the sub-district level estimates applying the robust methodology of small area estimation, which involves using auxiliary predictors to improve the precision of imprecise district-level estimates.

Conclusion

This study demonstrated the utility of visually displaying spatial inequities in HIV testing using nationally representative data by presenting simple maps for targeted priority setting. The findings suggest that provinces and districts with low testing coverage, especially amongst male participants, should prioritise tailored interventions to improve uptake of HIV testing. The strategies for HTS should include scaling up of HIVST and community HIV testing, specifically home-based testing to improve the uptake of HIV testing in those districts that are lagging behind in order to ensure equity in the geographical coverage of HIV testing.

Acknowledgements

The authors thank study participants who allowed the survey fieldworkers into their households and provided the article information. They also thank the project team, especially the fieldwork teams who collected the survey data used in the analysis.

Competing interests

The authors declare that they have no financial or personal relationships that may have inappropriately influenced them in writing this article.

Authors' contributions

S.J. drafted the manuscript. S.J. and T.R. performed statistical analysis. L.M. and P.N. designed the maps. S.J., M.M., A.N., Y.S., M.T. and L.S. participated in the implementation of the survey that provided the data for the analysis. All authors contributed to the review of the draft manuscript and approved the final manuscript.

Funding information

This research work was supported by the President's Emergency Plan for AIDS Relief (PEPFAR) through the Centres for Disease Control and Prevention under the terms of Cooperative Agreement Number (NU2GGH001629), as well as the South African Department of Science and Technology, South African National AIDS Council (SANAC), Global Fund to Fight AIDS, Tuberculosis and Malaria, Right to Care, United Nations Children's Fund (UNICEF), Centre for Communication Impact, Soul City, and LoveLife.

Data availability

Data used in this analysis are available from HSRC's public data repository (data set). SABSSM 2017 Combined. Version 1.0. Pretoria South Africa: Human Sciences Research Council [producer] 2017, Human Sciences Research Council [distributor] 2020. https://doi.org/doi:10.14749/1585345902.

Disclaimer

The findings and conclusions of this research study are those of the authors and do not necessarily represent the official position of any affiliated agency of the authors or the funding agencies.

References

1. UNAIDS. Miles to go. Global AIDS update. Geneva: Joint United Nations Programme on HIV/AIDS; 2018.
2. NDOH. National HIV testing services: Policy 2016. Pretoria: National Department of Health; 2016.
3. UNAIDS. Understanding fast-track: Accelerating action to end the AIDS epidemic by 2030. Geneva: Joint United Nations Programme on HIV/AIDS; 2015.
4. Marinda E, Simbayi L, Zuma K, et al. Towards achieving the 90–90–90 HIV targets: Results from the South African 2017 national HIV survey. BMC Public Health. 2020;20(1):1375. https://doi.org/10.1186/s12889-020-09457-z
5. NDOH. Health sector HIV prevention strategy. Pretoria: National Department of Health; 2017.
6. SANAC. Let our actions count: South Africa's national strategic plan for HIV, TB and STIs 2017–2022. Pretoria: South African National AIDS Council; 2017.
7. Havlir DV, Balzer LB, Charlebois ED, et al. HIV testing and treatment with the use of a community health approach in rural Africa. N Engl J Med. 2019;381(3):219–229. https://doi.org/10.1056/NEJMoa1809866
8. Kalichman SC, Simbayi LC. HIV testing attitudes, AIDS stigma, and voluntary HIV counselling and testing in a black township in Cape Town, South Africa. Sex Transm Infect. 2003;79(6):442–447. https://doi.org/10.1136/sti.79.6.442
9. Chamla DD, Olu O, Wanyana J, et al. Geographical information system and access to HIV testing, treatment and prevention of mother-to-child transmission in conflict affected Northern Uganda. Confl Health. 2007;1:12. https://doi.org/10.1186/1752-1505-1-12
10. Chen W, Zhou F, Hall BJ, et al. Is there a relationship between geographic distance and uptake of HIV testing services? A representative population-based study of Chinese adults in Guangzhou, China. PLoS One. 2017;12(7):e0180801. https://doi.org/10.1371/journal.pone.0180801
11. Cuadros DF, Li J, Branscum AJ, et al. Mapping the spatial variability of HIV infection in sub-Saharan Africa: Effective information for localized HIV prevention and control. Sci Rep. 2017;7(1):9093. https://doi.org/10.1038/s41598-017-09464-y
12. SANAC. Republic of South Africa. 2018 global AIDS monitoring report. Analysis of current status and progress towards targets. Pretoria: South African National AIDS Council; 2018.
13. Garrib A, Stoops N, McKenzie A, et al. An evaluation of the District Health Information System in rural South Africa. S Afr Med J. 2008;98:549–552.
14. Van Schalkwyk C, Dorrington RE, Seatlhodi T, Velasquez C, Feizzadeh A, Johnson LF. Modelling of HIV prevention and treatment progress in five South African metropolitan districts. Sci Rep. 2021;11(1):5652. https://doi.org/10.1038/s41598-021-85154-0
15. Simbayi LC, Zuma K, Zungu N, et al. South African national HIV prevalence, incidence, behaviour and communication survey, 2017. Cape Town: HSRC Press; 2019.
16. StatsSA. Mid-year population estimates 2017. Pretoria: Statistics South Africa; 2017.
17. Johnson LF, Van Rensburg C, Govathson C, Meyer-Rath G. Optimal HIV testing strategies for South Africa: A model-based evaluation of population-level impact and cost-effectiveness. Sci Rep. 2019;9(1):12621. https://doi.org/10.1038/s41598-019-49109-w
18. Maughan-Brown B, Venkataramani AS. Accuracy and determinants of perceived HIV risk among young women in South Africa. BMC Public Health. 2017;18(1):42. https://doi.org/10.1186/s12889-017-4593-0
19. Mhlongo S, Dietrich J, Otwombe KN, Robertson G, Coates TJ, Gray G. Factors associated with not testing for HIV and consistent condom use among men in Soweto, South Africa. PLoS One. 2013;8(5):e62637. https://doi.org/10.1371/journal.pone.0062637
20. Makusha T, Mabaso M, Richter L, Desmond C, Jooste S, Simbayi L. Trends in HIV testing and associated factors among men in South Africa: Evidence from 2005, 2008 and 2012 national population-based household surveys. Public Health. 2017;143:1–7. https://doi.org/10.1016/j.puhe.2016.10.017
21. Magadi MA. Understanding the urban–rural disparity in HIV and poverty nexus: The case of Kenya. J Public Health. 2017;39(3):e63–e72. https://doi.org/10.1093/pubmed/fdw065
22. Madiba S, Mokgatle M. Parents support implementation of HIV testing and counseling at school: Cross-sectional study with parents of adolescent attending high school in Gauteng and North West Provinces, South Africa. AIDS Res Treat. 2016;2016:4842814. https://doi.org/10.1155/2016/4842814
23. Shamu S, Slabbert J, Guloba G, et al. Linkage to care of HIV positive clients in a community based HIV counselling and testing programme: A success story of non-governmental organisations in a South African district. PLoS One. 2019;14(1):e0210826. https://doi.org/10.1371/journal.pone.0210826
24. Ncitakalo N, Mabaso M, Joska J, Simbayi L. Factors associated with external HIV-related stigma and psychological distress among people living with HIV in South Africa. SSM – Popul Health. 2021;14:100809. https://doi.org/10.1016/j.ssmph.2021.100809
25. PEPFAR. South Africa country operational plan 2017 [homepage on the Internet]. [cited 2021 May 27] Available from: https://za.usembassy.gov/wp-content/uploads/sites/19/2017/03/SA-PEPFAR-COP-2017-Strategic-Directions-Summary-final-draft-16-March-2017-Public-Version.pdf
26. SANAC. National strategic plan on HIV, STIs and TB 2012–2016. Pretoria: South African National AIDS Council; 2011.
27. Madut DB, Manavalan P, Mtalo A, et al. Increasing the uptake of HIV testing among men in Tanzania: A novel intervention for bar patrons. AIDS Behav. 2021;25:2014–2022. https://doi.org/10.1007/s10461-020-03131-6
28. Ziraba AK, Madise NJ, Kimani JK, et al. Determinants for HIV testing and counselling in Nairobi urban informal settlements. BMC Public Health. 2011;11:663. https://doi.org/10.1186/1471-2458-11-663
29. Orr N, Hajiyiannis H, Myers L, et al. Development of a national campaign addressing South African men's fears about HIV counseling and testing and antiretroviral treatment. J Acquir Immune Defic Syndr. 2017;74(S69–S73). https://doi.org/10.1097/QAI.0000000000001204
30. Spyrelis A, Abdulla S, Frade S, et al. Are women more likely to self-test? A short report from an acceptability study of the HIV self-testing kit in South Africa. AIDS Care. 2017;29(3):339–343. https://doi.org/10.1080/09540121.2016.1234687
31. Peck RB, Lim JM, Van Rooyen H, et al. What should the ideal HIV self-test look like? A usability study of test prototypes in unsupervised HIV self-testing in Kenya, Malawi, and South Africa. AIDS Behav. 2014;18 Suppl 4:S422–S432. https://doi.org/10.1007/s10461-014-0818-8
32. Hamilton A, Thompson N, Choko AT, et al. HIV self-testing uptake and intervention strategies among men in sub-Saharan Africa: A systematic review. Front Public Health. 2021;9(60):594298. https://doi.org/10.3389/fpubh.2021.594298

Appendices starts on the next page →

Appendix 1 : Summary statistics and model output used in the secondary data analysis

TABLE 1-A1: Uptake of those aged 15 years and older who have ever been tested for HIV in the 52 districts of South Africa.

District name	*n*	%	95% CI
uMkhanyakude	393	54.7	45.9–63.2
Vhembe	447	61.0	56.5–65.3
Ugu	606	61.4	54.6–67.7
Sarah Baartman	450	66.2	60.7–71.4
Amathole	207	66.3	59.5–72.5
Nelson Mandela Bay	767	66.3	62.0–70.4
West Coast	306	66.6	56.5–75.4
Cape Winelands	463	67.1	60.8–72.8
Namakwa	130	67.2	51.0–80.2
Z F Mgcawu	541	67.7	61.6–73.3
iLembe	2213	68.0	62.4–73.1
uMzinyathi	1952	68.0	64.5–71.3
Zululand	303	68.8	60.4–76.2
O.R. Tambo	848	70.4	65.8–74.6
uMgungundlovu	395	70.4	59.4–79.5
uThukela	2291	70.9	67.3–74.2
Eden	239	71.1	61.2–79.3
Mopani	383	71.2	64.9–76.8
Greater Sekhukhune	791	71.8	67.4–75.7
Buffalo City	202	71.9	63.8–78.7
Xhariep	155	73.0	58.9–83.6
King Cetshwayo	2449	73.4	65.9–79.7
Alfred Nzo	173	73.5	62.8–81.9
Gert Sibande	2308	74.3	70.9–77.5
Capricorn	400	74.4	68.0–79.9
Pixley ka Seme	637	74.9	69.1–79.9
City of Cape Town	1494	75.3	72.4–78.0
eThekwini	2258	75.8	70.2–80.6
Waterberg	313	75.9	66.5–83.3
Ehlanzeni	1720	76.6	73.2–79.6
Harry Gwala	258	76.6	67.9–83.5
Dr Kenneth Kaunda	495	76.9	66.4–84.8
John Taolo Gaetsewe	169	77.4	64.5–86.6
Overberg	187	77.4	64.4–86.7
Chris Hani	152	78.2	67.4–86.1
City of Johannesburg	1123	78.2	74.8–81.3
Fezile Dabi	178	78.5	68.5–86.0
Joe Gqabi	121	78.5	75.5–81.3
Sedibeng	1838	78.8	71.3–84.8
Ekurhuleni	1289	79.0	74.9–82.7
Dr Ruth Segomotsi Mompati	231	80.3	68.1–88.6
Nkangala	813	80.4	77.0–83.4
City of Tshwane	1096	81.2	78.1–83.9
Bojanala	1458	81.3	78.6–83.7
Frances Baard	490	81.4	75.5–86.1
Central Karoo	66	81.7	70.8–89.2
Amajuba	175	83.1	72.2–90.3
Mangaung	680	83.1	78.6–86.8
West Rand	780	83.3	78.2–87.3
Thabo Mofutsanyane	491	84.8	81.3–87.8
Lejweleputswa	234	85.2	81.7–88.2
Ngaka Modiri Molema	284	86.1	79.4–90.9
Total	**38 442**	**75.1**	**74.1–76.0**

CI, confidence interval.

TABLE 2-A1: Uptake of male and female participants aged 15 years and older who have ever been tested for HIV in the 52 districts of South Africa.

District name	Male participants			Female participants		
	n	%	95% CI	*n*	%	95% CI
Alfred Nzo	68	58.9	43.8–72.5	105	85.4	78.7–90.2
Amajuba	63	89.9	75.5–96.3	112	78.2	66.8–86.5
Amathole	77	57.6	45.9–68.5	130	73.6	64.2–81.2
Bojanala	594	78.6	74.4–82.4	864	83.8	80.8–86.3
Buffalo City	75	64.8	55.1–73.4	127	77.3	68.0–84.5
Cape Winelands	176	68.4	61.7–74.4	287	66.0	56.6–74.3
Capricorn	141	64.6	54.0–74.0	259	81.4	77.1–85.1
Central Karoo	24	87.7	83.1–91.2	42	76.8	58.8–88.4
Chris Hani	61	75.7	57.6–87.7	91	80.4	67.1–89.2
City of Cape Town	626	70.1	66.1–73.8	868	80.5	76.9–83.7
City of Johannesburg	492	71.9	65.5–77.5	631	84.4	80.2–87.8
City of Tshwane	474	80.9	75.4–85.5	622	81.4	77.5–84.8
Dr Kenneth Kaunda	229	77.1	68.1–84.2	266	76.6	61.2–87.1
Dr Ruth Segomotsi Mompati	90	71.2	48.3–86.8	141	87.0	77.5–92.8
Eden	104	61.1	48.6–72.3	135	81.3	64.8–91.1
Ehlanzeni	709	69.4	65.0–73.5	1011	83.0	79.6–85.9
Ekurhuleni	567	74.4	68.6–79.5	722	84.0	80.3–87.1
eThekwini	933	72.8	67.7–77.3	1325	78.4	70.7–84.6
Fezile Dabi	93	73.9	61.2–83.6	85	84.3	71.5–92.0
Frances Baard	231	74.7	67.9–80.5	259	88.4	81.5–93.0
Gert Sibande	1031	69.0	64.5–73.2	1277	80.2	75.9–83.9
Greater Sekhukhune	290	62.0	55.2–68.3	501	79.1	74.0–83.3
Harry Gwala	89	69.9	60.0–78.2	169	80.9	69.0–89.0
iLembe	821	64.2	56.6–71.2	1392	71.0	66.5–75.0
Joe Gqabi	54	76.5	69.2–82.5	67	80.7	69.8–88.3
John Taolo Gaetsewe	76	73.0	56.1–85.2	93	82.0	70.3–89.7
King Cetshwayo	895	68.3	60.5–75.1	1554	77.4	69.0–84.1
Lejweleputswa	103	81.9	73.7–87.9	131	88.4	84.6–91.4
Mangaung	292	83.1	75.2–88.9	388	83.1	77.7–87.4
Mopani	162	67.2	58.9–74.5	221	74.8	67.0–81.2
Namakwa	60	68.3	45.7–84.7	70	66.1	51.7–78.0
Nelson Mandela Bay	321	62.9	56.1–69.3	446	69.5	64.4–74.2
Ngaka Modiri Molema	121	83.4	74.1–89.8	163	88.6	82.8–92.6
Nkangala	379	76.7	70.9–81.7	434	84.9	81.0–88.0
O.R. Tambo	327	59.2	53.1–65.1	521	79.6	74.9–83.7
Overberg	69	79.8	63.2–90.2	118	75.4	64.3–83.9
Pixley ka Seme	269	69.2	61.2–76.2	368	80.2	73.0–85.9
Sarah Baartman	188	63.7	57.7–69.4	262	68.6	60.0–76.0
Sedibeng	782	78.9	69.3–86.2	1056	78.7	71.2–84.7
Thabo Mofutsanyane	206	83.1	77.5–87.6	285	86.4	82.7–89.4
Ugu	254	59.3	50.4–67.7	352	63.3	54.6–71.1
uMgungundlovu	189	66.5	47.6–81.2	206	75.4	59.3–86.5
uMkhanyakude	135	48.5	37.8–59.3	258	59.0	46.6–70.3
uMzinyathi	677	62.8	57.1–68.1	1275	71.6	67.4–75.5
uThukela	812	61.8	56.2–67.1	1479	76.9	73.7–79.8
Vhembe	189	46.6	39.3–53.9	258	73.7	68.6–78.3
Waterberg	146	72.2	59.5–82.2	167	79.9	70.1–87.2
West Coast	144	58.7	46.2–70.2	162	75.8	64.0–84.6
West Rand	368	81.6	74.7–86.9	412	85.1	78.0–90.2
Xhariep	67	66.8	60.4–72.6	88	79.9	33.7–96.9
Z F Mgcawu	252	60.0	51.5–67.9	289	75.4	69.2–80.7
Zululand	126	59.9	47.8–71.0	177	76.4	70.5–81.4
Total	**15 721**	**70.7**	**69.4–72.0**	**22 721**	**79.2**	**78.1–80.1**

CI, confidence interval.

TABLE 3-A1: Excess probability of ever having tested for HIV after adjusting for age and sex in the 52 districts of South Africa.

District name	Excess probability
O.R. Tambo	0.26
Amathole	0.27
Chris Hani	0.30
Buffalo City	0.30
Sarah Baartman	0.33
Alfred Nzo	0.34
Nelson Mandela Bay	0.36
Joe Gqabi	0.41
Mangaung	0.44
Fezile Dabi	0.47
Lejweleputswa	0.48
Thabo Mofutsanyane	0.49
Xhariep	0.54
City of Johannesburg	0.36
City of Tshwane	0.41
Ekurhuleni	0.42
Sedibeng	0.43
West Rand	0.46
uMkhanyakude	0.23
uMzinyathi	0.31
Ugu	0.31
iLembe	0.32
uThukela	0.32
Zululand	0.33
Harry Gwala	0.34
uMgungundlovu	0.38
King Cetshwayo	0.38
eThekwini	0.39
Amajuba	0.50
Vhembe	0.26
Greater Sekhukhune	0.30
Capricorn	0.33
Mopani	0.34
Waterberg	0.37
Ehlanzeni	0.40
Gert Sibande	0.44
Nkangala	0.50
Dr Ruth Segomotsi Mompati	0.37
Dr Kenneth Kaunda	0.39
Ngaka Modiri Molema	0.39
Bojanala	0.42
ZF Mgcawu	0.33
John Taolo Gaetsewe	0.37
Namakwa	0.37
Pixley ka Seme	0.38
Frances Baard	0.47
Cape Winelands	0.35
City of Cape Town	0.38
West Coast	0.38
Eden	0.39
Overberg	0.40
Central Karoo	0.42

TABLE 4-A1: Multilevel mixed-effects logistic regression model.

Variable	OR	95% CI	*p*
Sex	1.6	1.5–1.7	< 0.001
Age	1.0	1.0–1.1	< 0.001

CI, confidence interval; OR, odds ratio.

Looking back at paediatric HIV treatment in South Africa. My, how we have grown!

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2021 SPECIAL ANNIVERSARY COLLECTION

Southern African Journal of HIV Medicine
ISSN: (Online) 2078-6751, (Print) 1608-9693

Looking back at paediatric HIV treatment in South Africa. My, how we have grown!

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Dates:
Received: 28 June 2021
Accepted: 01 Aug. 2021
Published: 16 Sept. 2021

How to cite this article:
Levin LJ, Horak JL, Nuttall J. Looking back at paediatric HIV treatment in South Africa. My, how we have grown! S Afr J HIV Med. 2021;22(1), a1283. https://doi.org/10.4102/sajhivmed.v22i1.1283

Antiretroviral treatment has undergone major changes in the last 20 years, from monotherapy, to dual therapy and finally to triple therapy. Lately, more focus has been placed on better, more well-tolerated combinations and formulations. As in most other disciplines in medicine, the development of paediatric HIV dosages and formulations always tends to lag behind adult research. Twenty years ago, it could take several years before data were available to enable the use of life-saving antiretrovirals in children. Paediatricians, being ever resourceful, were not prepared to let their paediatric patients suffer despite the lack of data or formulations and so made a plan. This article describes some of the trials and tribulations that we went through trying to make sure that our paediatric HIV patients not only survived but thrived. Clinicians treating paediatric patients today have it so much easier because of what our colleagues and their patients went through in those early days.

Keywords: HIV; paediatric HIV; paediatric antiretroviral treatment; South Africa; history.

It is hard to convey the sense of helplessness felt by those of us who worked in the pre-antiretroviral treatment (ART) era when faced with a sick HIV-infected child and mother. We had little to offer except the treatment of opportunistic infections and co-trimoxazole prophylaxis. We have come a long way since then.

In the mid-1990s, when HIV treatment had evolved only as far as dual nucleoside reverse transcriptase inhibitors (NRTIs), an article appeared in the *New England Journal of Medicine* suggesting that didanosine (ddI) monotherapy was as good as the combination of zidovudine (AZT) and ddI and better than AZT alone.[1] At the time, viral load monitoring was unavailable, and the less useful marker of HIV disease progression and/or death was used in clinical trials. Because ddI monotherapy was quite affordable (R80.00 a month for a baby), a few patients in the state sector were able to afford ddI monotherapy, and this did provide a brief respite from the ravages of the disease.

In 1998, two developments spurred the cause of paediatric HIV treatment in South Africa. The first was the launch of stavudine (d4T) in South Africa. We now know that this is a very toxic drug, but in those days, it was heralded as a new, very potent NRTI. However, no matter how low the required paediatric dosage, d4T remained expensive and often unaffordable, at approximately R1000.00 a month. To help our patients, one of us would purchase a month's supply of the adult 40 mg capsules costing R1000.00 and have a chemist split the contents of the capsule into two and put each half back into another capsule. That way, the 20 mg capsules were made available at half price. Stavudine powder for reconstitution with water to form a suspension of 1 mg/mL and dosed at 1 mg/kg per dose twice a day was subsequently released but required refrigeration and the administration of relatively large volumes of liquid medication to young children. To get around these problems, many clinicians treating children unable to swallow capsules or in whom a lower dose was required used a technique of opening d4T capsules, dispersing the powder contents in water and administering an appropriate weight-based dose. Some years later, pharmacological and pharmacokinetic evaluations using high-performance liquid chromatography confirmed the accuracy of the off-label opened-capsule dosing method for stavudine and showed that plasma drug exposure after stavudine administration as a solution in this way was bioequivalent to intact capsule administration.[2,3]

However, ARVs were still very expensive, and few individuals could afford them. They were not available in the state sector, and medical aids were generally not paying for them, either. In 1998, Aid for AIDS (AfA) was launched to assist medical insurance schemes to manage HIV in the private sector. It was revolutionary, but there was a limit – adult patients could only receive dual therapy and not triple therapy. One of the researchers (L.J.L.) approached AfA (Dr Leon

Regensburg) and asked if it would be possible for paediatric patients to receive triple therapy, because they could get three drugs for the same price as two drugs in adults. AfA did, as a result, allow paediatric patients triple therapy; this is why some paediatric patients in the private sector received triple therapy as early as 1998. Although many were on d4T/ddI/ritonavir (RTV) – not a great regimen in anybody's book – many survived and are alive and well today. While paediatric ARV experience was evolving in the private sector, nothing was available in the state sector. Hydroxyurea, a cheap drug used in oncology and believed to be synergistic with ddI, was tried. Because of its low cost, patients, including children, were treated with the combination.[4,5] However, its toxicity – lactic acidosis, often with fatal consequences – was quickly recognised, and this therapy ended.

From 2000, things changed for the better. The AIDS 2000 conference was a watershed moment, as was the launch of the *Southern African Journal of HIV Medicine*. In the early 2000s, very limited access to paediatric ART in the public sector was mostly via international humanitarian non-governmental organisations such as Médecins sans frontiers (Doctors Without Borders) and donor-supported hospital-based programmes.[6,7] On 01 April 2004, the national ARV roll-out began.[8] This was wonderful, but paediatric formulations were far from optimal. Children were given d4T/lamivudine (3TC) combined with lopinavir/r (LPV/r) if they were under 3 years of age or efavirenz if they were over 3 years. Besides the problem of the terrible taste and poor tolerability of LPV/r, it was not used in children under 6 months in the absence of data on its use in this age group. So, any child under 6 months was given full-dose RTV, as were any patients on concurrent rifampicin-containing antituberculosis treatment. Besides the bad taste of RTV, this protease inhibitor (PI) presents HIV with a low genetic barrier to resistance, resulting in many children developing PI resistance.[9] Several years later, the NRTI backbone was changed to abacavir and 3TC, a safer combination and one that allowed for once-daily dosing – a big help in terms of adherence.

One of the obstacles to achieving widespread coverage of paediatric ART has been the simplification of the prescribing process for non-paediatricians, including doctors and nurses who are more familiar with prescribing ART for adults but who are also involved in treating children, particularly at the primary care level. Calculating individualised doses of separate and mostly liquid oral ARV formulations for an infant or young child at each clinic visit using the current weight or body surface area is complicated and time-consuming. The development and updating of an integrated weight-based ARV dosing chart for children based on World Health Organization guidelines and adapted for the ARV formulations available in South Africa has contributed to building confidence amongst prescribing clinicians and pharmacists and helped facilitate children's access to ART.

However, issues of ARV tolerability and access to formulations appropriate for children remain. The LPV/r formulation is very unpleasant to taste, and whilst young babies tend to tolerate it when their taste buds are still undeveloped, as they grow older, they often spit or vomit it out. Only in 2020 did the LPV/r pellets become available both in the state and private sectors. However, in the state sector, it may only be prescribed for patients over 6 months of age who are not tolerating the LPV/r solution.[10] In the 2019 national guidelines, tenofovir/3TC/dolutegravir fixed-dose-combination tablets can be used from 10 years of age and 35 kg upwards,[11] making a well-tolerated single-tablet regimen available for the first time to these adolescents. Another issue that is still a problem is adolescent disclosure, because very few healthcare workers feel comfortable disclosing to their adolescent patients, and parents are obviously petrified to do so because of feelings of guilt and worries that the children may be angry with them. This and other adolescent issues are resulting in very low rates of adolescent viral suppression.[12]

In South Africa, HIV viral resistance testing first became available in the early 2000s. At the time, a prevailing practice was to keep children with high viral loads on the same ART regimen as long as the CD4 count was acceptable. This was a pragmatic approach because of the limited treatment options available and the restricted access to resistance testing but is likely to have contributed to the accumulation of progressive resistance mutations in some children, thereby limiting future treatment options. A national third-line ART expert committee was established in 2013, focusing on patients with virological failure on a PI-based ART regimen. New-generation PIs and the integrase strand transfer inhibitor (INSTI) class of ARV drugs became accessible, though on a limited basis. This has provided real hope for treatment-experienced adults and children and their clinicians in achieving better long-term treatment outcomes.

Alongside the changes in paediatric ART, the reduction in mother-to-child transmission (MTCT) resulting from maternal ART has been dramatic. Between 2009 and 2015, new paediatric infections decreased by 84% as a result of our national prevention of MTCT guidelines evolving rapidly,[13] culminating in January 2015 in the provision of lifelong triple ART for all pregnant and breastfeeding women. Whilst fewer children are acquiring HIV through vertical transmission, we are finding these children particularly challenging to deal with. Pregnant women who know their HIV status and are able to take ART rarely transmit HIV to their babies. Of course, some mothers acquire HIV for the first time during their pregnancy or whilst breastfeeding and have unfortunately already transmitted the infection to their baby before they are aware of their status. However, the majority of infected babies in the era of ART are born to mothers who for complex social reasons have defaulted on their ART or take it inconsistently. Poverty, stigma, and drug and alcohol abuse are all contributory factors. Unfortunately, many of these mothers in turn find it difficult to give ARVs to their children and to access treatment for them. Many of the children who acquire HIV now are born into families with the least ability to deal with it. The hopelessness we felt in the pre-ART era is now replaced by the heartbreak and frustration of having life-saving treatment that is not taken.

In summary, paediatric ART in South Africa has come a long way: monotherapy, dual therapy, toxic regimens with d4T, ddI, and RTV. However, a universally available, well-tolerated, single formulation available from birth to adolescence still eludes us. Whilst advocating for new, simpler and better-tolerated paediatric regimens, an underlying constraint remains – that of improving the support of vulnerable patients, especially pregnant and breastfeeding mothers, so that they are able to take ART consistently and ensure the protection of the next generation of South Africans.

Acknowledgements

Competing interests

L.J.L. has received honoraria from Abbvie, Cipla Medpro and Johnson and Johnson for serving on advisory boards and delivering lectures.

Authors' contributions

L.J.L. wrote the first draft. J.L.H. and J.N. added to the article and reviewed and edited it.

Ethical considerations

This article followed all ethical standards for research without direct contact with human or animal subjects.

Funding information

The article processing fee was sponsored by the Southern African HIV Clinicians Society.

Data availability

Data sharing is not applicable to this article as no new data were created or analysed in this study.

Disclaimer

The views and opinions expressed in this article are those of the authors and do not necessarily reflect the official policy or position of any affiliated agency of the authors.

References

1. Englund JA, Baker CJ, Raskino C, et al. Zidovudine, didanosine, or both as the initial treatment for symptomatic HIV-infected children. N Engl J Med. 1997;336:1704–1712. https://doi.org/10.1056/NEJM199706123362403
2. Innes S, Smuts M, Cotton M, Seifart H, Rosenkranz B. Comparative study of different brands of stavudine capsules for the off-label 'opened capsule' dosing method recommended for HIV-infected infants and children in resource-limited settings. SAJCH. 2009 Jul;3(2):44–47.
3. Innes S, Norman J, Smith P, et al. Bioequivalence of dispersed stavudine: Opened versus closed capsule dosing. Antivir Ther. 2011;16(7):1131–1134. https://doi.org/10.3851/IMP1876
4. Zachary KC, Davis B. Hydroxyurea for HIV infection. AIDS Clin Care. 1998 Apr;10(4):25–26, 32.
5. Sanne I, Smego RA. Systematic review of combination antiretroviral therapy with didanosine plus hydroxyurea: A partial solution to Africa's HIV/AIDS problem? Int J Infect Dis. 2001;5:43–48.
6. Reddi A, Leeper S, Grobler A, et al. Preliminary outcomes of a paediatric highly active antiretroviral therapy cohort from KwaZulu-Natal, South Africa. BMC Pediatr. 2007;7:13. https://doi.org/10.1186/1471-2431-7-13
7. Eley B, Nuttall J, Davies M-A, et al. Initial experience of a public sector antiretroviral treatment programme for HIV-infected children and their infected parents. S Afr Med J. 2004;94(8):643–646.
8. Simelela NP, Venter WDF. A brief history of South Africa's response to AIDS. S Afr Med J. 2014;104(3 Suppl 1):249–251.
9. Van Zyl GU, Van der Merwe L, Claassen M, et al. Protease inhibitor resistance in South African children with virologic failure. Pediatr Infect Dis J. 2009 Dec;28(12):1125–1127.
10. National Department of Health Circular. Notice: Availability of Lopinavir/ritonavir oral pellets to children on antiretroviral treatment, version 2021 [homepage on the Internet]. Reference 2021/22/02/EDP/02. [cited 2021 Jun 22]. Available from: https://drive.google.com/file/d/1uFlscKm0IwGEeUhxjkecCL9HfPzNEsjj/view?usp=sharing
11. South African National Department of Health. National Consolidated Guidelines for the Management of HIV in adults, adolescents, children and infants and prevention of mother-to-child transmission [homepage on the Internet]. 2020 [cited 2021 Jun 22]. Available from: https://www.knowledgehub.org.za/system/files/elibdownloads/2020-07/National%20Consolidated%20Guidelines%2030062020%20signed%20PRINT%20v7.pdf
12. Nglazi M, Kranzer K, Holele P, et al. Treatment outcomes in HIV-infected adolescents attending a community-based antiretroviral therapy clinic in South Africa. BMC Infect Dis. 2012;12:21. https://doi.org/10.1186/1471-2334-12-21
13. Joint United Nations Programme on HIV/AIDS (UNAIDS). On the fast-track to an AIDS-free generation. The incredible journey of the global plan towards the elimination of new HIV infections among children by 2015 and keeping their mothers alive. Geneva: Joint United Nations Programme on HIV/AIDS; 2016.

Establishing targets for advanced HIV disease: A call to action

- David B. Meya, Lillian Tugume, Vennie Nabitaka, Proscovia Namuwenge, Sam Phiri, Rita Oladele, Bilkisu Jibrin, Mojisola Mobolaji-Bello, Cecilia Kanyama, Werner Maokola, Sayoki Mfinanga, Cordelia Katureebe, Ikechukwu Amamilo, Brian Ngwatu, Joseph N. Jarvis, Thomas S. Harrison, Amir Shroufi, Radha Rajasingham, David Boulware, Nelesh P. Govender, Angela Loyse.

2021 SPECIAL ANNIVERSARY COLLECTION

Southern African Journal of HIV Medicine
ISSN: (Online) 2078-6751, (Print) 1608-9693

Establishing targets for advanced HIV disease: A call to action

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The World Health Organization (WHO) has published a guideline for the management of individuals with advanced HIV disease (AHD) to reduce HIV-related deaths. The guideline consists of a package of recommendations including interventions to prevent, diagnose and treat common opportunistic infections, including tuberculosis (TB), cryptococcosis and severe bacterial infections, along with rapid initiation of antiretroviral treatment and enhanced adherence support. Currently no clear targets exist for these key interventions. Emerging programmatic data from Uganda, Tanzania and Nigeria suggest that an estimated 80% of eligible people continue to miss the recommended cryptococcal or TB testing, highlighting the remaining challenges to the effective implementation of WHO-recommended AHD packages of care in real-world resource-limited settings. The absence of mortality indicators for the leading causes of HIV-related deaths, because of the lack of mechanisms to ascertain cause of death, has had a negative impact on establishing interventions to reduce mortality. We suggest that setting 95-95-95 targets for CD4 testing, cryptococcal antigen and TB testing, and treatment that are aligned to the WHO AHD package of care would be a step in the right direction to achieving the greater goal of the WHO End TB strategy and the proposed new strategy to end cryptococcal meningitis deaths. However, these targets will only be achieved if there is healthcare worker training, expanded access to bedside point-of-care diagnostics for hospitalised patients and those in outpatient care who meet the criteria for AHD, and health systems strengthening to minimise delays in initiating the WHO-recommended therapies for TB and cryptococcal disease.

Keywords: advanced HIV disease; cryptococcal antigen; tuberculosis; TB-LAM; targets.

Introduction

In 2017, the World Health Organization (WHO) published a guideline for the management of individuals with advanced HIV disease (AHD) (defined as having a CD4 count of < 200 cells/μL or HIV stage 3 or 4 disease in adults and adolescents or children younger than 5 years), as part of the strategy to reduce HIV-related deaths.[1] This guideline outlines a package of care for persons with AHD and includes interventions to prevent, diagnose and treat common opportunistic infections (OIs), including tuberculosis (TB), cryptococcosis and severe bacterial infections, along with rapid initiation of antiretroviral treatment (ART) and enhanced adherence support.

Although the United States (US) Centers for Disease Control and the US President's Emergency Plan for AIDS Relief facilitate implementation of the WHO guideline on the AHD package of care in many sub-Saharan African countries, especially in settings with a high number of persons with

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Dates: Received: 14 May 2021|Accepted: 27 June 2021|Published: 10 Aug. 2021

How to cite this article: Meya DB, Tugume L, Nabitaka V, et al. Establishing targets for advanced HIV disease: A call to action. S Afr J HIV Med. 2021;22(1), a1266. https://doi.org/10.4102/sajhivmed.v22i1.1266

AHD, no clear targets exist for these key interventions to reduce OIs and mortality in persons with AHD. Such targets should include the proportion of persons accessing CD4 testing, persons with a CD4 count of < 200 cells/μL who are screened for TB and cryptococcal disease, and co-infected persons subsequently started on therapy (Table 1). These targets are akin to the broader 95-95-95 targets of the Joint United Nations Programme on HIV/AIDS (UNAIDS): to achieve by 2030 95% of persons tested for HIV, 95% of those HIV-positive started on ART and 95% of those on ART attaining virological suppression.

Despite the reduction in HIV-related deaths by 39% since 2010, nearly 700 000 HIV-related deaths occurred in 2019,[2] with HIV-related illness remaining the leading cause of death in sub-Saharan Africa. Notwithstanding the rapid roll-out of ART globally, data from South Africa show that about a third of individuals entering or cycling in and out of HIV care have advanced disease, with minimal change over the last decade.[3] Similarly, in Uganda and Botswana approximately 20% – 25% of persons entered care with advanced HIV in 2020.[4,5] Considering that most AHD is diagnosed among ART-experienced persons,[6] ART non-adherence with treatment failure will remain a significant contributor to incident OIs despite expanded ART initiation.[7]

Based on the WHO guidance, each person diagnosed with HIV should have a CD4 test performed.[1] Of those with a CD4 count of < 200 cells/μL, cryptococcal antigen (CrAg) and TB testing should be offered using a CrAg lateral flow assay (LFA) and Xpert/TB lipoarabinomannan (LAM) assay.[1] Those with evidence of disease (i.e. positive tests) should be started on appropriate treatment; for example, TB preventive therapy should be started for those with latent TB infection. In many countries, some steps in this cascade are not always executed. Multiple reasons can exist for this failure to implement, including basic stock-outs of CD4 reagents, diagnostic test kits and the medicines required for OI treatment.[8] There is a significant deleterious impact on AHD outcomes when only some of these resources and not all are available. In some cases, the implementation of these interventions is not prioritised by healthcare workers, who may have limited training on AHD management[9] and consider these screening tests as less imperative compared to initiating ART. In addition, weak health systems may result in greater attrition of persons entering HIV care even after a CD4 test, in the absence of tracking mechanisms to complete this cascade of care when they fail to return.

TABLE 1: The basic indicators for advanced HIV disease care.

Indicator	Reason for monitoring and evaluation
Number of persons with a new HIV diagnosis; number of persons with an HIV diagnosis returning to care; number of persons on ART without HIV viral suppression	These categories of persons are at high risk of subclinical OIs and require a CD4 test (< 200 cells/mL) and/or clinical evaluation to determine whether they may have a Stage 3 or 4 illness – to identify them as having advanced HIV disease.
Number of persons in the above categories receiving cryptococcal antigen testing	To determine persons who require treatment and further evaluation for cryptococcal meningitis.
Number of persons in the above categories receiving urine TB-LAM testing	To determine persons who require treatment and further evaluation for disseminated TB.
Number of persons with evidence of cryptococcal or TB infection(s) who receive appropriate treatment	To determine linkage to treatment for TB and cryptococcal disease.

ART, antiretroviral treatment; TB-LAM, tuberculosis lipoarabinomannan; OIs, opportunistic infections.

Many national programmes lack mortality indicators for the leading causes of HIV-related deaths, which is partly a result of poor data around ascertaining a cause of death. Data from the last quarter of 2020 from the AIDS Control Programme of the Ministry of Health in Uganda[10] showed that only 36% of newly diagnosed HIV-infected patients received a CD4 test. Of these, 25% met the definition of AHD with a CD4 count of < 200 cells/μL. Subsequently, of those with AHD, 61% received CrAg testing (8% CrAg test positive), and 89% of CrAg-positive persons were then started on pre-emptive fluconazole. For TB screening, only 56% of those with a CD4 count of < 200 cells/μL received urine LAM testing (19% positive for urine LAM), and 92% of these received TB treatment. Overall, this extrapolates to an estimated 80% having missed the recommended cryptococcal or TB screening. Similarly, among persons with virological failure, 6% received CD4 testing, with 25% having a CD4 count of < 200 cells/μL. Among those with CD4 testing, 73% received CrAg testing (12% CrAg test positive; 82% treated), and 74% received urine TB-LAM testing (20% urine LAM test positive; 80% treated).[11] A gap in knowledge remains for the OI prevalence among those persons returning to care after attrition. There are challenges in obtaining data on longer-term disease outcomes among persons who screened for these OIs during the cascade of AHD management. However, cryptococcal survival outcomes remain 30% – 40% better when CrAg-positive persons are pre-emptively treated while asymptomatic, rather than treating symptomatic meningitis.[12]

Data from a retrospective cohort in Mwanza, Tanzania, of 700 participants showed that 261 (35%) had WHO stage 3 and 4 HIV disease, and 258 (35%) had baseline CD4 counts of < 200 cells/μL.[13] These programmatic data in Tanzania show a similar trend to data reported from Uganda. Among persons who initiated ART in 2018, 21% had WHO clinical stage 3 or 4, and 31% had a CD4 count of < 200 cells/μL.[14] In this cohort, the mortality rates decreased with increasing CD4 count at enrolment. Persons with a CD4 count of < 200 cells/μL had a high mortality rate of 61.69 per 1000 person/year, compared to the mortality rate of 18.01 per 1000 person/year for those enrolled with CD4 counts of ≥ 350 cells/μL (mortality rate ratio: 3.43). The data also showed a higher mortality rate of 117.03 per 1000 person/year for those enrolled with WHO clinical stage 4, compared to the mortality rate of 53.25 per 1000 person/year for patients enrolled with WHO clinical stage 3 (mortality rate ratio 2.20). The Nigerian national 2020 data for people living with HIV and on active TB on treatment is 83.5%,[15] while there are currently no data from the Nigeria repository on CrAg and urine TB-LAM testing. However, preliminary data from a pilot AHD implementation project at a large ART centre (Lagos University Teaching Hospital, Lagos, Nigeria) revealed that

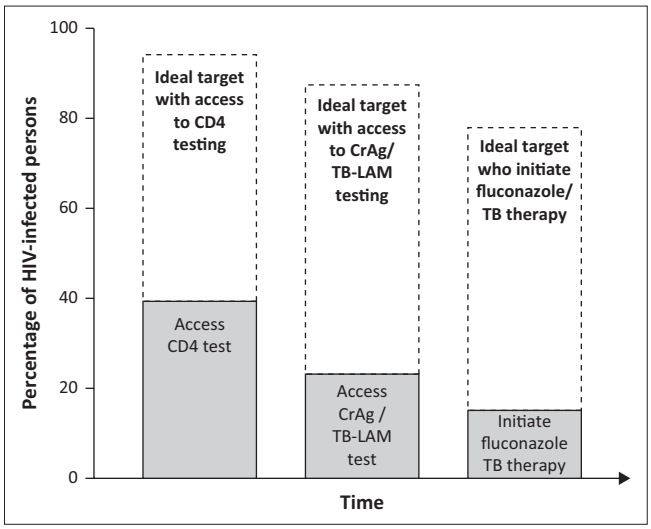
from August 2020 to January 2021, 47.9% (69/144) of newly enrolled people living with HIV had a CD4 count of < 200 cells/μL, with all receiving reflex CrAg screening and 65 (94.2%) receiving TB lateral flow LAM testing.

Sub-Saharan Africa bears the brunt of HIV-associated OIs, with an estimated 162 500 cases of cryptococcal meningitis in 2014 (73% of the global burden) and 135 900 deaths (75% of the estimated global burden).[16] In 2019, of the 1.4 million TB-related deaths that occurred, 208 000 were among people living with HIV.[17] The WHO End TB strategy is designed with the aim of achieving a 90% decrease in TB deaths by 2030.[18] As a step towards achieving this goal, it is critical that persons with AHD be identified, screened and treated for TB in a timely manner. Therefore, we suggest that setting targets for CD4 testing, CrAg and TB testing, and treatment, that are aligned to the WHO AHD package of care would be a step in the right direction to achieving the greater goal of the WHO End TB strategy and the proposed new strategy to end cryptococcal meningitis deaths.[19]

Efforts should be aimed at ensuring that all individuals recently diagnosed with HIV, those returning to care or those who are not virologically suppressed have access to CD4 testing. Prompt identification of persons at high risk in the setting of AHD remains important for minimising poor outcomes. The roll-out of the WHO-approved point-of-care VISITECT CD4 Advanced HIV Disease LFA by Omega Diagnostics (Alva, United Kingdom) provides an instrument-free, semi-quantitative result for CD4 (greater than or less than 200 cells/μL), which should be rapidly expanded; however, feasibility studies for point-of-care use in routine care settings are needed to inform placement and scale-up. Unitaid and the Clinton Health Access Initiative have launched an early market access vehicle to provide access to this test at no cost in over 130 countries to determine operational feasibility in routine care settings.[20,21]

We further recommend that national HIV programmes set 95-95-95 targets for 95% of persons with a new HIV diagnosis, those returning to care or non-suppressed populations to receive CD4 testing, 95% of those with a CD4 count of < 200 cells/μL to be screened with CrAg and TB LAM, and 95% testing CrAg or LAM positive to be treated for those by 2030 (Figure 1). These targets would apply to both outpatient and inpatient settings and spur the design and implementation of real-world interventions to reduce the morbidity and mortality complicating AHD. In addition, these targets will drive countries to establish mechanisms for tracking these targets as well as AHD-related mortality within their national reporting systems. We believe that these targets are achievable, given the progress towards the even more challenging UNAIDS 95-95-95 targets set for 2030.

In a CrAg screening model for Uganda, Rajasingham and colleagues suggested that CrAg screening and treatment (assuming a national CrAg prevalence of 1.4%) would save 7320 lives at a cost of $459.00 per life saved.[22] In contrast, the cost of treating a person with AHD who develops



AHD, advanced HIV disease; TB-LAM, tuberculosis lipoarabinomannan; CrAg, cryptococcal antigen.

FIGURE 1: Schematic detailing comparison between ideal AHD targets and current AHD indicator performance.

cryptococcal meningitis using the current WHO-recommended regimen of amphotericin B and flucytosine for 1 week is $1861.00,[23] making CrAg screening and fluconazole pre-emptive therapy a more cost-effective approach. Menzies and colleagues similarly showed that expanding TB diagnostics and care access produced substantial health gains to achieve the goals set out in the End TB strategy, based on an analysis of nine cost-effectiveness models in China, India and South Africa.[24] We posit that these gains and cost savings can only be maximised if the AHD package is fully implemented with everyone who should receive CD4, CrAg and TB-LAM testing, with the appropriate therapy for those diagnosed with disease. For instance, cost savings for CrAg screening would be maximised by screening individuals with a CD4 count of < 200 cells/μL with an expected prevalence of 6% – 7%[16] as opposed to 1.4% in the general HIV population. This can be enhanced if point-of-care CD4 testing is implemented adequately as the next step following HIV testing. In order to achieve this, it is imperative that procurement and supply systems for the resources required, are coordinated efficiently while anchored within strong health systems and regular healthcare worker training. Furthermore, implementation research is still required to improve clinical outcomes among patients with AHD, for example by evaluating the effectiveness and feasibility of performing lumbar punctures in those with a positive CrAg test result.

The $20 million investment by Unitaid through 2022 to avert preventable deaths among persons with AHD in eight African low- and middle-income countries and India is certainly a step in the right direction.[25] Participating countries should utilise the catalytic procurement of commodities to generate local evidence and leverage the programmatic support during the project period to ensure that AHD interventions are sustainable. Furthermore, these interventions need to be expanded to other countries in sub-Saharan Africa and beyond 2022 through increased and coordinated demand for commodities through

entities like institutional donors, along with expanded regular training and health systems strengthening.

Expanded access to bedside point-of-care diagnostics for hospitalised patients to minimise delays in initiating standard-of-care therapies (for TB and cryptococcal disease) would improve survival. However, waiting for persons with AHD to be hospitalised exposes weaknesses in the health system when ambulatory HIV care neglects essential interventions to prevent AHD complications. By prioritising training, mentorship and health systems strengthening such that outpatient clinicians have excellent clinical skills and are empowered with point-of-care diagnostics (e.g. CD4, CrAg, TB-LAM) and adequate resources for optimal treatment, the proposed targets could be met, resulting in potentially fewer hospitalisations and AHD-related mortality. While OIs will continue to occur screening and pre-emptively treating OIs at an early stage in an outpatient setting is far less expensive than hospital care and results in better outcomes.

We believe that establishing and implementing country-specific interventions to ensure that 95% of persons with a new HIV diagnosis or those without HIV viral suppression receive CD4 testing, 95% of persons with a CD4 count of < 200 cells/μL receive CrAg and TB-LAM testing, and 95% of those with positive CrAg and LAM tests initiate prompt treatment would go a long way in reducing HIV-related mortality. Creating targets and ensuring accurate documentation of the metrics including AHD-related mortality would help national programmes focus efforts on addressing interventions to meet targets for optimal AHD care to minimise HIV-related deaths.

Acknowledgements

Competing interests

The authors declare that they have no financial or personal relationships that may have inappropriately influenced them in writing this article.

Authors' contributions

D.B.M. conceived the idea for this study. D.B.M., L.T and V.N. wrote the manuscript, with support from R.R., D.B., S.P., C. Kanyama, I.A., B.N., J.N.J., T.S.H., A.S. and A.L. P.N., R.O, B.J., M.M.-B., S.M., W.M., N.P.G. and C. Katureebe provided critical data for the manuscript. All authors provided critical feedback and helped shape the manuscript.

Ethical considerations

This article followed all ethical standards for research without direct contact with human or animal subjects.

Funding information

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors. Authors D.B.M., R.R., D.R.B. and N.P.G. are supported by the National Institute of Allergy and Infectious Diseases (K23AI138851, R01AI118511 and U01AI125003).

Data availability

The data that are reported in this manuscript are available from the Ministries of Health in Uganda, Nigeria and Tanzania.

Disclaimer

The views and opinions expressed in this article are those of the authors and do not necessarily reflect the official policy or position of any affiliated agency of the author.

References

1. World Health Organization. Guidelines for managing advanced HIV disease and rapid initiation of antiretroviral therapy. WHO guidelines approved by the guidelines review committee. Geneva: WHO; 2017.
2. UNAIDS. Global HIV & AIDS statistics – 2020 fact sheet. Geneva: UNAIDS; 2020.
3. Carmona S, Bor J, Nattey C, et al. Persistent high burden of advanced HIV disease among patients seeking care in South Africa's National HIV Program: Data from a nationwide laboratory cohort. Clin Infect Dis. 2018;66(Suppl_2):S111–S117. https://doi.org/10.1093/cid/ciy045
4. Ministry of Health. Consolidated guidelines for the prevention and treatment of HIV/AIDS in Uganda. Kampala: Uganda Ministry of Health, 2020; p. 84–86.
5. Leeme TB, Mine M, Lechiile K, et al. Utility of CD4 count measurement in the era of universal antiretroviral therapy: An analysis of routine laboratory data in Botswana. HIV Med. 2021;22(1):1–10. https://doi.org/10.1111/hiv.12951
6. Osler M, Hilderbrand K, Goemaere E, et al. The continuing burden of advanced HIV disease over 10 years of increasing antiretroviral therapy coverage in South Africa. Clin Infect Dis. 2018;66(Suppl_2):S118–S125. https://doi.org/10.1093/cid/cix1140
7. Ellis J, Bangdiwala AS, Cresswell FV, et al. The changing epidemiology of HIV-associated adult meningitis, Uganda 2015–2017. Open Forum Infect Dis. 2019;6(10):ofz419. https://doi.org/10.1093/ofid/ofz419
8. Lofgren SM, Nalintya E, Meya DB, Boulware DR, Rajasingham R. A qualitative evaluation of an implementation study for cryptococcal antigen screening and treatment in Uganda. Medicine (Baltimore). 2018;97(31):e11722. https://doi.org/10.1097/MD.0000000000011722
9. Vallabhaneni S, Longley N, Smith M, et al. Implementation and operational research: Evaluation of a public-sector, provider-initiated cryptococcal antigen screening and treatment Program, Western Cape, South Africa. J Acquir Immune Defic Syndr. 2016;72(2):e37–e42. https://doi.org/10.1097/QAI.0000000000000976
10. Uganda Ministry of Health. September – December 2020 – Advanced HIV disease quarterly report. Kampala: Uganda Ministry of Health; 2020.
11. AIDS Control Program. Programatic data on advanced HIV disease cascade. Kampala: Ministry of Health Uganda; 2020.
12. Rhein J, Huppler Hullsiek K, Tugume L, et al. Adjunctive sertraline for HIV-associated cryptococcal meningitis: A randomised, placebo-controlled, double-blind phase 3 trial. Lancet Infect Dis. 2019;19(8):843–851.
13. Gunda DW, Nkandala I, Kilonzo SB, Kilangi BB, Mpondo BC. Prevalence and risk factors of mortality among adult HIV patients initiating ART in rural setting of HIV care and treatment services in North Western Tanzania: A retrospective cohort study. J Sex Transm Dis. 2017;2017:7075601. https://doi.org/10.1155/2017/7075601
14. National AIDS Control Program. HIV care and treatment Report 2019. Dar-es Salaam: Ministry of Health, Community Development, Gender, Elderly and Children; 2020.
15. Ministry of Health. Advanced HIV report, Nigeria. Lagos: Nigeria Ministry of Health; 2020.
16. Rajasingham R, Smith RM, Park BJ, et al. Global burden of disease of HIV-associated cryptococcal meningitis: An updated analysis. Lancet Infect Dis. 2017;17(8):873–881. https://doi.org/10.1016/S1473-3099(17)30243-8
17. Fukunaga R, Glaziou P, Harris JB, Date A, Floyd K, Kasaeva T. Epidemiology of tuberculosis and progress toward meeting global targets - worldwide, 2019. MMWR Morb Mortal Wkly Rep. 2021;70(12):427–430. https://doi.org/10.15585/mmwr.mm7012a4
18. Chakaya J, Khan M, Ntoumi F, et al. Global tuberculosis report 2020 – Reflections on the global TB burden, treatment and prevention efforts. Int J Infect Dis. 2021:S1201–9712. https://doi.org/10.1016/j.ijid.2021.02.107
19. Stott KE, Loyse A, Jarvis JN, et al. Cryptococcal meningoencephalitis: Time for action. Lancet Infect Dis. 2021. https://doi.org/10.1016/S1473-3099(20)30771-4
20. Clinton Health Access. Clinton health access initiative. Unitaid and CHAI announce agreement with Omega Diagnostics to increase access to new, instrument-free CD4 test for people living with HIV in over 130 low- and middle-income countries [homepage on the Internet]. [cited 2021 Apr 2021]. Available from: https://wwwclintonhealthaccessorg/unitaid-and-chai-announce-agreement-with-omega-diagnostics-to-increase-access-to-new-portable-cd4-testing-device-for-people-living-with-hiv-in-over-130-low-and-middle-income-countries.
21. Clinton Health Access Initiative. Early market access vehicle for VISITECT® CD4 advanced disease test [homepage on the Internet]. [cited 2021 Apr 21]. Available from: https://wwwclintonhealthaccessorg/early-market-access-vehicle-for-visitect-cd4-advanced-disease-test/

22. Rajasingham R, Meya DB, Greene GS, et al. Evaluation of a national cryptococcal antigen screening program for HIV-infected patients in Uganda: A cost-effectiveness modeling analysis. PLoS One. 2019;14(1):e0210105. https://doi.org/10.1371/journal.pone.0210105

23. Chen T, Mwenge L, Lakhi S, et al. Healthcare costs and life-years gained from treatments within the advancing cryptococcal meningitis treatment for Africa (ACTA) trial on cryptococcal meningitis: A comparison of antifungal induction strategies in sub-Saharan Africa. Clin Infect Dis. 2019;69(4):588–595. https://doi.org/10.1093/cid/ciy971

24. Menzies NA, Gomez GB, Bozzani F, et al. Cost-effectiveness and resource implications of aggressive action on tuberculosis in China, India, and South Africa: A combined analysis of nine models. Lancet Glob Health. 2016;4(11):e816–e826.

25. Unitaid invests to cut HIV-related deaths [homepage on the Internet]. n.d. [cited 2021 Mar 22]. Available from: https://unitaid.org/unitaid-invests-to-cut-hiv-related-deaths/#en

26. Medecins Sans Frontieres. Advanced HIV disease toolkit [homepage on the Internet]. 2020. Available from: https://samumsforg/sites/default/files/2019-07/OPD%20AHD%20indicators_version%202pdf2020

Celebrating 21 years and introducing the 21st anniversary issue

- Yunus Moosa, Lauren Jankelowitz.

Southern African Journal of HIV Medicine
ISSN: (Online) 2078-6751, (Print) 1608-9693

Celebrating 21 years and introducing the 21st anniversary issue

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How to cite this article:
Moosa Y, Jankelowitz L. Editorial: Celebrating 21-year anniversary and introducing the 21st anniversary issue. S Afr J HIV Med. 2021;22(1), a1317. https://doi.org/10.4102/sajhivmed.v22i1.1317

The *Southern African Journal of HIV Medicine* (SAJHIVMED) is focused on HIV, in particular disease prevention and treatment, and includes topics relevant to clinical and public health practices. The primary purpose of the SAJHIVMED is to disseminate original research; however, the journal also includes editorials, case reports and series, clinical reviews, evidence based clinical practice guidelines, national guidelines, and other correspondence relevant to the field of HIV.

It has been 21 years since the inaugural publication of the SAJHIVMED in June 2000. Up until 2016, the journal was published quarterly. Since then, articles have been published online as they become available, with all the articles compiled into a single printed copy at the end of the year. Supplements have been published intermittently to address special themes or mark events, such as the Southern African HIV Clinicians Society's (SAHCS') biennial conference. Since 2020 and the onset of the COVID-19 pandemic, annual editions have been published as online e-books only.

During the past 21 years, over 660 articles, 50 guidelines and 45 case reports have been published in the journal, covering diverse areas ranging from basic science to clinical practice within the field of HIV, as well as areas closely related to the field. Authors and contributors range from local to the Southern African region, to global experts, providing the journal with a vast breadth of varied inputs.

The SAJHIVMED, which already boasted Scientific Electronic Library Online South Africa (SciELO SA); SCOPUS; Clarivate Analytics Web of Science Core Collection, Science Citation Index Expanded (SCIE/ISI [Institute for Scientific Information]); African Index Medicus; African Journals Online; Directory of Open Access Journals; Ebscohost; Embase; Gale, Cengage Learning; Google Scholar; and ProQuest indexing, and was added to the Norwegian Register for Scientific Journals, Series and Publishers, Level 1, in 2017, was awarded PubMed Central accreditation status in 2018.

By being an open access journal, all content is freely available at no cost to the reader or institution. In accordance with international best practice and in alignment with the Budapest Open Access Initiative (BOAI; https://www.budapestopenaccessinitiative.org/), users are allowed to read, download, copy, distribute, print, search or link to the full texts of the articles, or use them for any other lawful purpose, without asking prior permission from the publisher or the author.

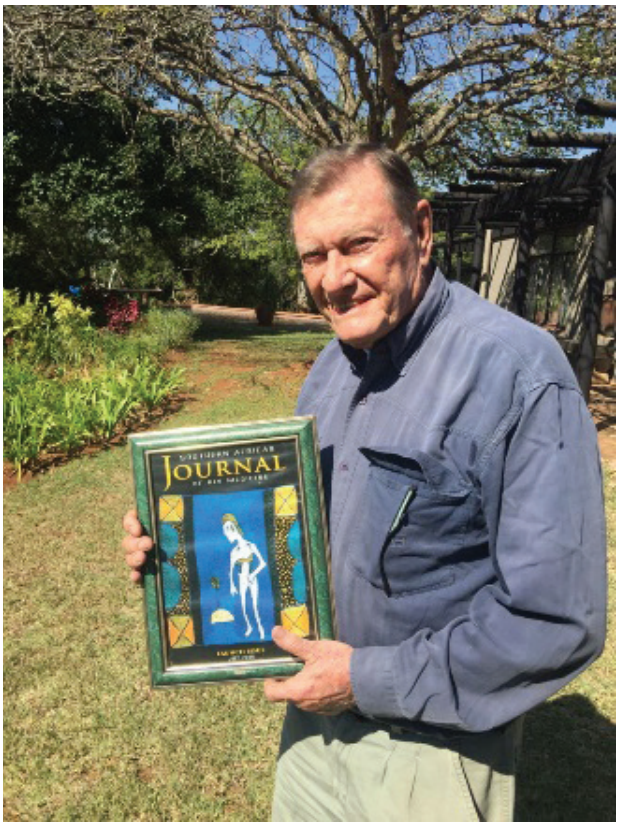
Following confirmation of all relevant documentation, such as ethics clearance, the manuscript is then reviewed initially by the Editor-in-Chief with a view to establishing appropriateness of scope for the journal. Following this the blinded manuscript is assigned to at least 2 independent external reviewers. Reviewer feedback is then sent to the authors and a process of finalisation begins between the author/s and the Editors.

At the time of the launch of the journal in 2000, Prof. Des Martin (MBBCH, MMed, FCPath, DTM&H, DPH), the first President of the SAHCS and the first Editor-in-Chief of the SAJHIVMED wrote:

> This first issue of the Southern African Journal of HIV Medicine coincides with the International AIDS conference in Durban, SA, and it is hoped that it will find a place in the reading of medical, scientific and allied professionals dealing with HIV disease in our region. It is also hoped that it will receive broader recognition amongst the international community, which is urged to engage actively in the discourse surrounding the epidemic in our region.[1]

He went on to say:

> The Journal will provide a home for original scientific articles, review articles and continuing medical education and will also provide a forum for debate and discussion on the topical issues of the day.[1]



Source: Photo taken by Renata Tressel and used with permission from Prof. Martin.

FIGURE 1: Prof. Des Martin, Founding Editor of the Southern African Journal of HIV Medicine, May 2021, with his framed copy of the first edition.

Prof. Des Martin (Figure 1), now retired to Mpumalanga, was involved in the field of HIV medicine at various levels for over 35 years. Martin held a number of prestigious positions, including Past President of SAHCS from 1998 to 2008; Editor-in-Chief of the SAJHIVMED; Deputy Director of the National Institute for Virology; Convenor of Examiners for the Colleges of Medicine of South Africa; Chair of the Basic Sciences Track at the 13th International Aids Conference, Durban, SA, in 2000; visiting Professor Johns Hopkins Hospital Baltimore (1998); and Professor in the Department of Clinical Virology, Faculty of Health Sciences, University of Pretoria.

In May 2021, Prof. Martin (personal communication) commented that:

> 'The Southern African Journal of HIV Medicine was born in July 2000, as it was launched at the IAS Durban 2000 International AIDS conference. These were particularly vexed times in the local HIV/AIDS arena because of the intense activity of the "AIDS dissidents" who had found favour with a number of prominent persons in South Africa and beyond. The "Durban Declaration" was formulated by a number of the foremost HIV scientists of the day, including many from the Society, which effectively countered the misinformation spread by the dissidents. The Journal has now "come of age" and continues to provide education, teaching, dissemination of the results of the latest local research and much more to the HIV-community of our region, and indeed, of Africa. Congratulations to all who contribute to the publication of the Journal.'

There have been a further five Editors-in-Chief, all of whom have contributed immensely to the growth and credibility of the SAJHIVMED. Dr Shaun Conway, who co-created the Journal, spent a brief time as its first Managing Editor whilst serving as the Director of SAHCS. He was also the founder of Right-to-Care, co-founder of Re-Action! and founded numerous digital innovation start-ups. He worked as an advisor to the World Health Organization (WHO), and as the HIV and Health Systems Advisor to the UK Department for International Development. Building on his extensive experience in HIV, Global Health and International Development, Dr Conway has been building ixo (https://ixo.world), an ambitious project to create a blockchain-based Internet of Impact, which he describes as a 'global digital immune system for humanity'. Dr Conway, expressing surprise at how quickly the years have flown by, sent his heartfelt congratulations to SAHCS and the SAJHIVMED for it's milestone of 21 years.

Dr Conway's tenure was followed by Prof. Linda-Gail Bekker (MBChB, DTMH, DCH, FCP[SA], PhD), who is Deputy Director of the Desmond Tutu Health Centre at the Institute of Infectious Disease and Molecular Medicine at the University of Cape Town (UCT) and Chief Operating Officer of the Desmond Tutu Health Foundation. Bekker is a physician-scientist and infectious disease specialist focusing on programmatic and action research around antiretroviral rollout, tuberculosis (TB) integration, and HIV prevention in key populations. She is Principal Investigator of the UCT Clinical Trials Unit funded by the US National Institutes of Health, and is actively involved in the work of its associated clinical research sites and networks. She has chaired protocols for the HIV Vaccine Trials Network and HIV Prevention Trials Network and has been the investigator of record in a number of network-related protocols. Prof. Bekker has served on numerous national, international and federal scientific and working committees, and is the current Chair of the SAHCS pre-exposure prophylaxis (PrEP) and post-exposure prophylaxis (PEP) guidelines. Bekker leads the Desmond Tutu Centre of Adolescent Health and Wellbeing at UCT, which aims to develop evidence-based best practices around adolescent treatment and prevention of HIV, TB and sexually transmitted infections (STIs), including the integration of these services within a robust, adolescent-friendly sexual and reproductive service platform. She was president of the International AIDS Society from 2016 to 2018.

Prof. Bekker, as SAJHIVMED Editor-in-Chief, wrote at the start of 2005 that:

> Since inception of the journal in July 2000 an impressive list of guidelines has been compiled and peer reviewed by local experts. This year will also see the journal launched online, increasing accessibility of previous guidelines and journal articles.[2]

Prof. Bekker was the editor until late 2011 and has remained involved with the direction of the Journal by sitting on the editorial board of the SAJHIVMED since then. Prof. Bekker reminisced earlier this year that (personal communication, 2021):

> 'The wonderful – and persuasive – Des Martin asked me to take this important role on when I was a relatively green-about-the ears HIV doctor and researcher. I was both thrilled and honoured and I loved the experience. My small role in the development of this important publication and its future wellbeing is something I am really proud to be counted a part of. I recall being particularly obsessed about getting the PubMed accreditation and understanding how that system worked. I'm delighted it has grown in both circulation and significance under the great curatorship of the recent editors.'

Prof. Landon Myer (MBBCH, PhD), who followed Prof. Bekker in the role of editor, is director and head of the School of Public Health and Family Medicine at the UCT. He had undergone training in social anthropology, clinical medicine and epidemiology. His research study focuses on women's, maternal and child health in the context of HIV, which includes behavioural, clinical and health systems research. He has led multiple clinical and health systems studies investigating the health of HIV-infected women receiving antiretroviral therapy (ART) during pregnancy and postpartum, as well as the health and development of HIV-exposed and -infected children and adolescents. Within the School, he is professor and head of the Division of Epidemiology & Biostatistics, teaches epidemiological methods and is an academic convenor of the master's in the public health programme. In Prof. Myer's first editorial in 2011, he wrote that he was:

> [*L*]ooking forward to continuing the journal's emphasis on presenting research and clinical experiences from across the region, and keeping readers updated around local and international developments … by seeking to expand several sections, including: feedback reports from local and international conferences; editorial reviews intended to share viewpoints and promote discussion on important topics; and programmatic reports that share local experiences in implementing HIV treatment and prevention services on the ground.[3]

At the start of 2014, Prof. Myer whilst introducing a special anniversary edition, to mark 10 years of ART in the public sector, commented that:

> In considering the HIV epidemic and its impact, many of our anniversaries are sad ones … Clinicians or scientists may mark the anniversary of the first documented AIDS case in a country, or the discovery of the virus itself, but these aren't generally moments for celebration per se. So, it's not often that we have cause to smile about an anniversary related to the epidemic. However, 1 April 2014 marks one happy anniversary worth remembering – a decade of antiretroviral therapy (ART) in the public sector. Like many anniversaries, the exact details can depend on where you were, and sometimes dates themselves can be fuzzy. Antiretrovirals were available from the 1990s in the private sector, and a trickle was accessible through trials and small donor-funded initiatives in urban centres from the early 2000s. Some provinces moved more quickly towards making ART available ahead of the National Department of Health, often with the assistance of partners in local and international non-governmental organisations. After the announcement of a national rollout of ART in public sector facilities, some hospitals received supplies of antiretrovirals within weeks. Elsewhere, especially in clinics in rural settings, health services took years to have local providers dispensing ART. Today the number of facilities dispensing ART is expanding still, but most communities across the country have reasonable access, and ART coverage continues to increase.[4]

Prof. Myer, reminiscing about his time as editor and the SAJHIVMED, said in 2021 (personal communication, Sept 9):

> 'Another happy anniversary, worth pausing a moment to celebrate. The position of the SAHCS, and with it the journal, has shifted in the health landscape in South Africa – paralleling the shifting position of HIV – from addressing a single, specialised and focused health topic, to a cross-cutting, mainstream institution of sorts that is concerned with the health landscape of the country. It's an incredible recognition of the central place of HIV in our health system and services – there is no concern that is more integral to our primary healthcare system than HIV and its associated conditions. It's a credit in great part to the work of SAHCS. Congratulations to SAHCS and SAJHIVMED for continuing to provide important clinical updates, news and research, and being a leading voice of reason over the past 2 decades.'

Dr Michelle Moorhouse (MBBCh, DA, FRSPH) is a senior Global Medical Director at ViiV Healthcare. Prior to this, she worked at Ezintsha as Head of Treatment Strategies (2014–2019), where she was the co-Principal Investigator on the large Advance Study as well as working on other HIV treatment optimisation studies, policies and guidelines. Moorhouse was awarded an Honorary Clinical Fellowship at the Royal Free Hospital in London in 2003. Returning to South Africa in 2007, she re-established her general and HIV practice and set up a research centre focusing on HIV clinical trials, whilst consulting at an HIV clinic for an Eastern Cape based non-profit organisation (NPO). She served as a SAHCS board member between 2012 and 2018 and became a member of the Editorial Board of HIV Nursing Matters, shortly before becoming editor of the SAJHIVMED between 2015 and 2018. Her career has been focussed on making a difference in the lives of people affected by HIV (Moorhouse M, 2021, personal communication, Sept 9):

> 'We always think of 21 as a "coming of age" or achieving maturity. I think the SAJHIVMED is an exception to this, in that right from the start it was clearly a powerful publication that has delivered high quality research, informative guidelines and great educational reads from which I personally have learned so much. A testament to the high calibre of the journal is the fact that it is listed on PubMed, which is a great achievement and one of which to be exceedingly proud. It was my great pleasure and privilege to be at the helm for a short while and I wish the journal continued growth over the next 21 years.'

Finally, in his first editorial mid-2019, Dr Dave Spencer (MBChB, MMed, DTM&H), current Editor-in-chief, summarised several key articles, so as to encourage journal readership, and stated that:

> The articles address contemporary and regional issues in HIV medicine. The topics speak to all aspects of the epidemic: epidemiology, public health, prevention, clinical medicine, tuberculosis and opportunistic diseases, management guidelines, opinion pieces, editorials, and case reports. For the teachers,

> trainers, healthcare managers and administrators among us, there is a wealth of local information in these papers. Please acknowledge our talented researchers by reading what they write.[5]

Dr Spencer is a specialist physician who started treating HIV patients formally whilst completing a 2-year Infectious Diseases Fellowship at Case Western Reserve University in the United States, 1988–1990. In 1991, he took over as head of the HIV Clinic of the Johannesburg General Hospital. He was in private practice in Johannesburg from 1997 until 2011. Also trained in oncology and infectious diseases, Spencer was thereafter the Head of Infectious Diseases and ran the Themba Lethu HIV Clinic at Helen Joseph Hospital. Dr Spencer is renowned as a lecturer and teacher in the field of medicine that he loves. He is a sought-after speaker at continuing medical education (CME) meetings and other academic events. His book *The Clinical Practice of HIV Medicine* (2005) is a primer on HIV care for doctors and a summation of his experience as a practitioner in this field and is to be found on the desks of many practitioners. He has always been committed to imparting his knowledge through lectures, guidelines and one-on-one teaching in his clinic; he has taught HIV medicine throughout Africa, and many practitioners have benefitted from these sessions. Owing to his background and beliefs, he has been able to instil the need for assessing the patient more broadly than just paying attention to the physical components of the disease. Dr Spencer has published extensively in the field of HIV and was a local lead investigator for several early studies of ART. Finally, he was a founding executive member of SAHCS. Recently retired, Dr Spencer currently serves as the Editor-in-Chief of the SAJHIVMED, and is a key content developer, expert reviewer, teacher and guidelines contributor at SAHCS.

Dr. Spencer, who continues to identify key articles and summarise these in 'newsletters' to SAHCS' members (2021, personal communication, September), often remarks:

> 'The pages of the SAJHIVMED showcase many of the best of Africa's researchers and clinicians. Original articles, opinion pieces, guidelines and reviews that emerge from the global epicentre of the HIV pandemic. What better place to understand the impact of an incurable disease on society and its people? What better place to do good and to influence the continent's future?'

Southern African HIV Clinicians Society is proud to publish this anniversary special edition.

We express our sincerest gratitude to all the editors and peer reviewers who have contributed, and continue to contribute, to the growth of the journal. A special thanks to our authors whose impact on the SAJHIVMED continues to be felt. Thanks are also due to our publishers, AOSIS, who have walked the last few years of the SAJHIVMED journey together with SAHCS.

Prof Yunus Moosa
Southern African HIV Clinicians Society
President

Dr Lauren Jankelowitz
Southern African HIV Clinicians Society
Chief Executive Officer

References

1. Martin D. Editorial. 2000. S Afr J HIV Med. 2000;1(1), a489. https://doi.org/10.4102/sajhivmed.v1i1.489
2. Bekker L-G. Looking back, looking forward. S Afr J HIV Med. 2005;6(1), a589. https://doi.org/10.4102/sajhivmed.v6i1.589
3. Myer L. From the Editor. S Afr J HIV Med. 2011;12(3), a175. https://doi.org/10.4102/sajhivmed.v12i3.175
4. Myer L. Message from the Editor. S Afr J HIV Med. 2014;15(1), a28. https://doi.org/10.4102/sajhivmed.v15i1.28
5. Spencer DC. Editorial. S Afr J HIV Med. 2019;20(1), a1037. https://doi.org/10.4102/sajhivmed.v20i1.1037

HIV infection in Eastern and Southern Africa: Highest burden, largest challenges, greatest potential

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2021 SPECIAL ANNIVERSARY COLLECTION

Southern African Journal of HIV Medicine
ISSN: (Online) 2078-6751, (Print) 1608-9693

HIV infection in Eastern and Southern Africa: Highest burden, largest challenges, greatest potential

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Background: The burden of HIV is especially concerning for Eastern and Southern Africa (ESA), as despite expansion of test-and-treat programmes, this region continues to experience significant challenges resulting from high rates of morbidity, mortality and new infections. Hard-won lessons from programmes on the ground in ESA should be shared.

Objectives: This report summarises relevant evidence and regional experts' recommendations regarding challenges specific to ESA.

Method: This commentary includes an in-depth review of relevant literature, progress against global goals and consensus opinion from experts.

Results: Recommendations include priorities for essential research (surveillance data collection, key and vulnerable population education and testing, in-country testing trials and evidence-based support services to improve retention in care) as well as research that can accelerate progress towards the prevention of new infections and achieving ambitious global goals in ESA.

Conclusion: The elimination of HIV in ESA will require continued investment, commitment to evidence-based programmes and persistence. Local research is critical to ensuring that responses in ESA are targeted, efficient and evaluated.

Keywords: HIV epidemiology; public health; risk factors; vulnerable populations; prevention and control; early diagnosis.

Introduction

In the decades since HIV-1 first emerged, the response has been marked by strong global commitments, extensive education campaigns and the development of improved tests and life-saving antiretroviral treatments (ART) that are reaching more and more individuals.[1] With evidence-based prevention and treatment strategies available, nations have united to set goals, with the end of the HIV epidemic potentially attainable by 2030.[2]

One hallmark concept in the fight against HIV has been the 'know your epidemic, know your response' approach to deliver programmes in different settings.[3] More than 70% of persons living with HIV (PLWH) reside in sub-Saharan Africa (SSA), where resources for healthcare are disproportionately limited. Eastern and Southern Africa (ESA), in particular, continues to record the highest rates of HIV-1 prevalence and incidence worldwide.[4] In this region, knowing where and among whom the infection is spreading has been challenging, and key populations are only recently being highlighted.

A second hallmark of the fight against HIV has been the Joint United Nations Programme on HIV/AIDS (UNAIDS) 'Fast-Track' targets, whereby 90% of PLWH should know their status,

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Dates: Received: 02 Mar. 2021 | Accepted: 01 Apr. 2021 | Published: 28 May 2021
How to cite this article: Parker EL, Judge MA, Macete E, et al. HIV infection in Eastern and Southern Africa: Highest burden, largest challenges, greatest potential. S Afr J HIV Med. 2021;22(1), a1237. https://doi.org/10.4102/sajhivmed.v22i1.1237

90% of those diagnosed should receive ART and 90% of those on ART should achieve viral suppression by 2020 ('90-90-90').[5] Despite remarkable progress towards these targets in ESA, the sheer scale of the epidemic in this region leaves much to be done.[6] In the next decade, efforts must be redoubled for raised targets of 95-95-95 by 2030.[7] Programmes on the ground have identified region-specific challenges to be overcome and lessons that should be broadly shared with ESA and potentially with many communities globally.

An important barrier preventing progress in ESA is the timely detection and treatment of acute HIV infections. The earliest stage of HIV infection is characterised by high viral loads and a high potential for onward transmission, but it is typically missed using existing testing algorithms.[8] As ART coverage improves, the proportion of transmissions attributable to undiagnosed acute HIV infection increases.[9] Furthermore, new HIV infections disproportionately affect key populations.[10] Affordable testing solutions for acute HIV detection in high-prevalence, resource-limited settings are needed.[9]

As the 2020 deadline passed, trends indicated that the 90-90-90 targets were not reached across most of ESA.[2]

Renewed efforts looking ahead to the 2030 UNAIDS targets of 95-95-95 will be required. To this end, a group of regional experts was invited to collate their expertise, with a view to addressing the local challenges that prevent the achievement of global goals.

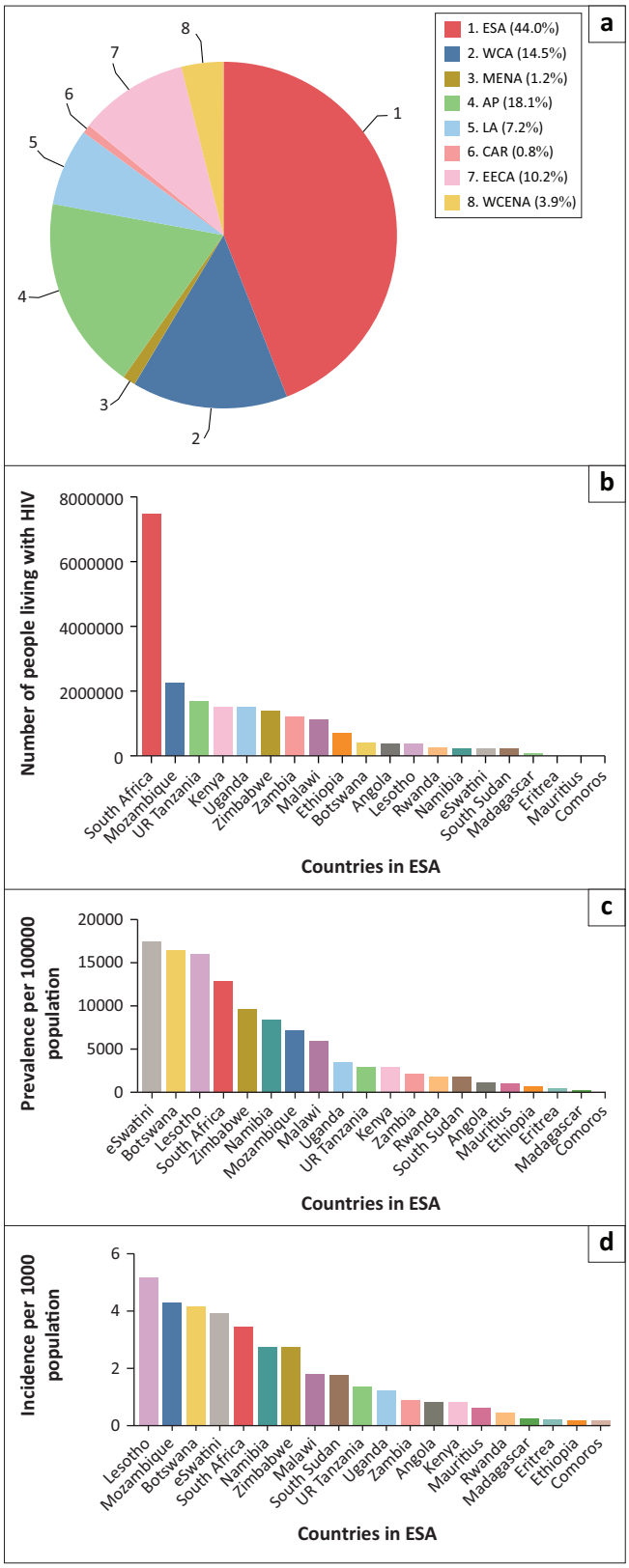
State of the global epidemic

According to UNAIDS, there were an estimated 38 million PLWH worldwide at the end of 2019, with 1.7 million new infections and 690 000 AIDS-related deaths that year (Figure 1).[10] A successful vaccine and functional cure for HIV are yet to be developed, and lifelong ART remains the cornerstone of management.

The 2020 UNAIDS report highlights a 'prevention crisis'.[10] Programmes aiming to prevent new HIV infections (such as education, barrier contraception, voluntary male medical circumcision and pre-exposure prophylaxis [PreP]) must be a priority alongside test-and-treat programmes and must appropriately target key populations and their partners, who comprise 62% of new HIV infections globally.[10]

HIV epidemiology in ESA

Regional HIV epidemics look markedly different across the world and require tailored responses. In ESA, there are 20.7 million adults and children living with HIV (54% of global HIV prevalence),[10] and in 2019 44% of all new infections occurred here.[10] Key populations make up an estimated 28% of new infections in ESA.[10] In some areas,



Source: All data were derived from The Joint United Nations Programme on HIV/AIDS (UNAIDS). UNAIDS Data 2020. Geneva: UNAIDS; 2020. Report No.: JC2997E; 2020 and United Nations, Department of Economic and Social Affairs, Population Division. New York, World population prospects 2019 [homepage on the Internet] [cited 2020 Aug 16]. Available from: https://population.un.org/wpp/

AP, Asia and the Pacific; CAR, Caribbean; EECA, Eastern Europe and Central Asia; ESA, Eastern and Southern Africa; LA, Latin America; MENA, Middle East and Northern Africa; WCA, Western and Central Africa; WCENA, Western and Central Europe and North America.

FIGURE 1: (a) Worldwide distribution of new HIV infections identified by UNAIDS in 2019. (b) Distribution of people living with HIV infection in ESA in 2019. (c) Prevalence of HIV infection per 100 000 population among countries in ESA. (d) Incidence of HIV infection per 1000 population among countries in ESA.

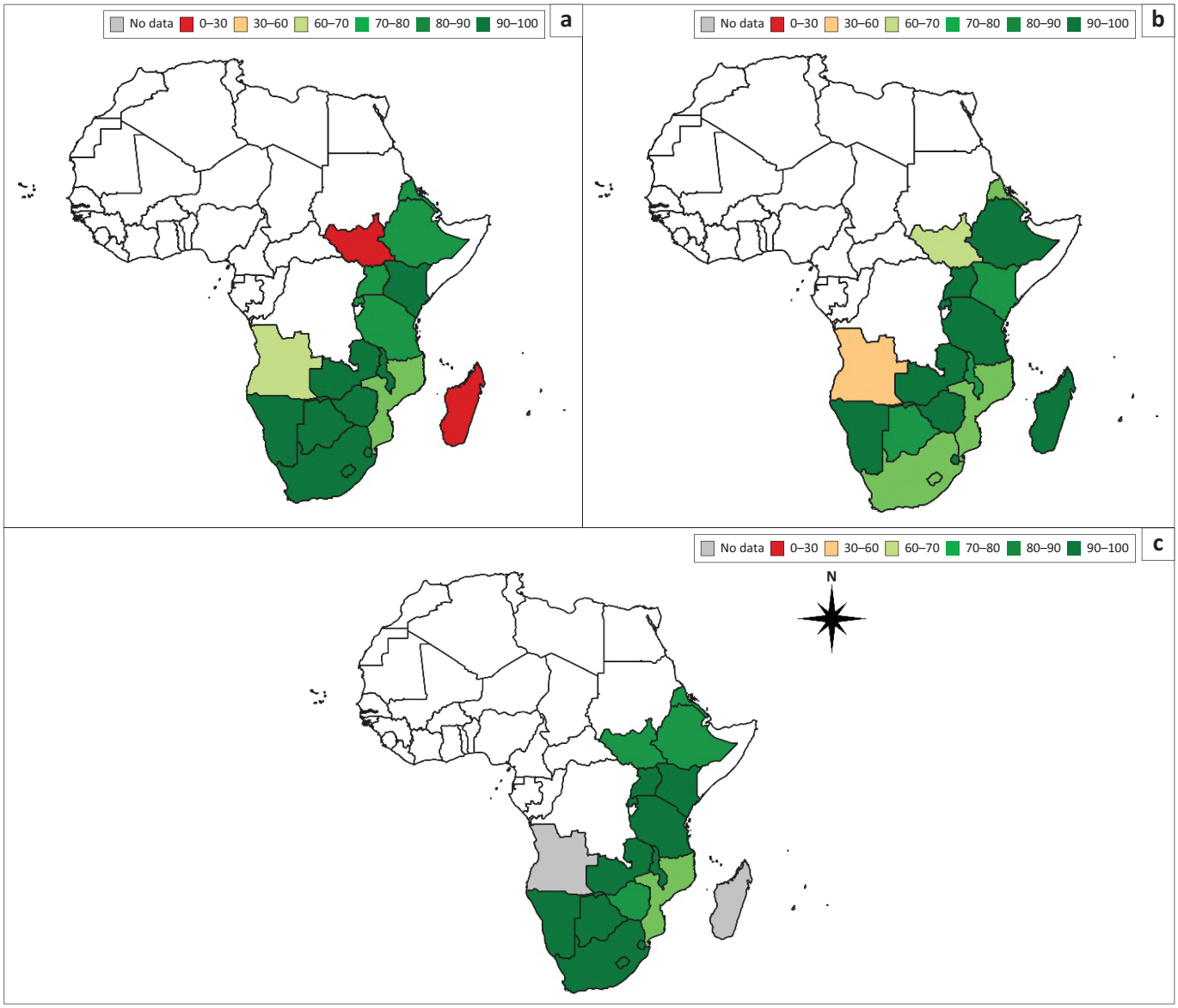


FIGURE 2: Data on the ESA 90-90-90 goals in all ages by country from the UNAIDS data 2020 report.[10] (a) First 90; (b) second 90; (c) third 90.

reasonable progress has been made towards the Fast-Track targets (e.g. eSwatini, Namibia and Zambia); in other areas, progress is more limited (e.g. Mauritius and South Sudan). An estimated 87% of PLWH in ESA are aware of their status (the 'first 90'; Figure 2); however, this figure ranges from 15% to 98% between countries.[10]

Of those diagnosed with HIV in ESA, approximately 83% have commenced ART (the 'second 90').[10] This figure ranges from 37% to 98% between countries,[10] highlighting deep inequities within and across countries. Of those on treatment, 90% have achieved viral suppression (the 'third 90'); this figure ranges from 68% to 97% between countries, with 2 of 21 countries unable to provide estimates. Combatting the epidemic in ESA is a multifaceted challenge, and progress must occur within a broader context of socio-economic development. Despite some successes, the 2020 milestones were not achieved in many countries across ESA, and the greatest challenges persist as the focus shifts to achieving the new 95-95-95 targets.

Challenges for achieving 95-95-95 in ESA

The first 95

In high HIV prevalence settings, obtaining accurate measures of the first 95 is challenging. In ESA, HIV care commonly takes place in rural settings, utilising paper-based records.[11] To estimate the first 95, the denominator is typically the number of people testing positive for HIV during randomised household or community-based serosurveys and/or at antenatal clinics; the numerator is those among them known to have previous positive results (either disclosed to surveyors or identified in medical records).[12]

Rates of non-disclosure can be high.[13] When people are retested in southern Mozambique, non-disclosure of previous results occurs in over one-third of people, but the rate is higher for tests performed in a community setting (38.9%) or initiated by the provider (29.4%) than in those presenting for voluntary testing (13%).[13] Similar findings have been

described in Tanzania and Malawi.[14,15] Cross-checking survey responses against medical records is impossible in many countries where HIV testing is performed anonymously.[11] The high percentage of HIV-positive people who do not disclose, and are thus repeatedly deemed recently infected, leads to an overestimation of new HIV cases and an underestimation of progress towards the first 95. In Mozambique, non-disclosure resulted in underestimation of the first 95 by around 8.5%.[13]

Improving testing coverage to achieve the first 95 is feasible but must be accompanied by interventions that support the whole care cascade. In the Treatment as Prevention (TasP) trial of universal test-and-treat in KwaZulu-Natal, South Africa, repeated rounds of home-based testing increased the proportion of people knowing their HIV status to 91.5%.[16] However, only 58.0% of these individuals commenced ART; many did not link to care.[16] This suggests that to reach 95-95-95, all three targets must be understood and addressed in parallel.[17]

The second 95

The second 95 is more readily measured, as countries (or their health facilities and non-governmental organisations) generally have stronger records on the number of people receiving ART. According to World Health Organization recommendations, early ART commencement has reduced HIV/AIDS-related mortality, with some models showing an estimated 75% fewer deaths per annum.[18] Test-and-treat strategies recommending commencement of ART within 14 days of a positive diagnosis (independent of the CD4+ T-cell count) are relatively recent in most of SSA,[19] and uptake has been commendable.[20] Broader implementation is limited not only by the political will but also by the resources required to upskill staff and provide a sustainable treatment supply. Given the scale of the epidemic in ESA, the rollout of any advances in treatment regimens to the front lines can present a formidable challenge. The system's fragility has been highlighted by COVID-19 over the past year, with reports of delays in the delivery of treatment stock from international suppliers, depleted national stockpiles and periods of lockdown limiting individuals' access to HIV medications.[21]

Based on country guidelines, in 2014–2015, of those eligible for ART in Manhiça, Mozambique, 83.7% started ART within 3 months.[22] In July 2016, Mozambique phased in the implementation of test-and-treat and undertook qualitative research into the patterns of ART initiation or refusal.[23,24] The acceptance of treatment depends on the availability and accessibility of services, as well as appropriate and considered explanations following diagnosis.[25]

Linkage to care is improved by the desire to live, family support and subjective illness.[23,24] Barriers to linkage to care include the fear of dissemination of one's HIV status, feeling subjectively healthy, migration, health system issues and fears of discrimination.[23,24,26]

The third 95

Achieving viral suppression requires retention in care, maintenance of ART and regular testing of the HIV viral load. Retention in care is improved by feeling better after ART initiation, confidence in the health system and support from family and providers.[27] Communication about continuing treatment despite feeling better also helps.[24] Barriers to retention include provider authoritarianism, which limits patient autonomy and engagement in their healthcare, and the adverse effects of ART.[27] Men across the region are a hard-to-reach group; they test less, and more abandon ART after initiation.[22] There are additional complexities related to paediatric care, such as the health literacy of parents and their confidence in managing HIV. For children, retention is highest when both mother and child register concurrently.[28] Innovative strategies to improve testing uptake and support early ART initiation and nutritional supplementation can improve retention.[29,30]

Before the introduction of the universal test-and-treat programme, there were concerns that commencing ART among people with high CD4+ T-cell counts would overburden the health system and that those feeling healthy would not adhere to treatment.[31] However, of the PLWH in KwaZulu-Natal with CD4+ T-cell counts of > 500 cells/μL, 78% accepted ART,[32] 86% were adherent[33] and 96% achieved viral suppression.[34] Furthermore, retention in care and viral suppression were similar among people who initiated ART with CD4+ T-cell counts of > 500 cells/μL compared to those with lower CD4+ T-cell counts.[35]

Measuring the third 95 requires country-wide laboratory systems capable of processing large volumes of viral load requests and returning results; thus, many ESA countries score poorly.[10] For example, in Mozambique, only 45% of PLWH achieve documented viral suppression[10]; however, viral load testing is available to few, particularly in rural settings.[36,37] Under-developed laboratory systems also delay diagnoses of virological failure, leading to increased transmission, illness progression and treatment resistance.[38] Point-of-care (POC) viral load testing improved viral suppression, retention in care and the communication of results to patients in KwaZulu-Natal,[39] and it proved feasible and cost-effective in Botswana and Zambia.[40,41] Further development of centralised, high-throughput laboratory-based testing alongside decentralised POC testing will be crucial to ensure adequate monitoring of viral suppression throughout ESA.

The impending challenge of acute HIV infections

Acute HIV infection is commonly defined as the period prior to seroconversion, between 3 and 12 weeks in duration.[42,43] Gene expression is vastly upregulated in the initial months, driving inflammation, immune responses and cell turnover.[44] This correlates with a substantial peak in viral load, meaning the risk of onward transmission

during acute HIV is 8–25 times higher than during chronic infection.[45,46,47] The estimated prevalence of acute HIV infection in ESA is 1% – 3%.[48,49,50,51] Undiagnosed acute HIV is particularly concerning for the following: pregnant and breastfeeding women who have poorer health outcomes as well as increased perinatal transmission risk[52,53,54,55]; people who received blood transfusions screened for HIV serology but not viral load[56,57]; and those who started PreP when already infected, as this may confer an increased risk of drug resistance mutations.[58]

The earliest time period that an acute HIV infection can be detected is 5–14 days by nucleic acid amplification.[59] This is not feasible in low-resource settings, so other options include viral load POC testing (Gene Xpert[60] and AlereQ[61]), p24 antigen testing (if developed into rapid tests),[62] non-viral immune response biomarkers (e.g. IP-10)[63] or a symptom/risk score.[8,64] Rapid testing and ART for all HIV-seropositive individuals remains the priority; however, a focus on this alone will miss seronegative HIV-infected individuals. As ART coverage increases, the proportion of HIV transmission attributable to acute HIV will increase. Affordable rapid tests for p24 or non-viral immune markers combined with a risk score may be the best way to identify acutely infected individuals in high-HIV-burden, low-resource settings.

Disproportionate impact of new HIV infections on key and vulnerable populations

Of the 1.7 million new HIV infections in 2019, 62% occurred in key populations and their sexual partners.[6] Key populations include men who have sex with men,[65] people who inject drugs,[66] female sex workers[67] and transgender people.[6] Vulnerable populations at increased HIV risk in ESA include prisoners,[6,68] long-haul truck drivers,[69] mobile mining workers,[70] migrants[71] and serodiscordant couples.[6] Also at disproportionately high risk of HIV infection are young women,[72] who are 2–3 times[73,74] more likely to be newly infected than their 15–24-year-old male counterparts.

Pregnant and breastfeeding women and their infants are an often-overlooked vulnerable population.[52] Infants of mothers who acquired HIV during pregnancy or postpartum are at increased risk of HIV transmission compared to infants of chronically HIV-infected mothers.[52]

Approximately 45% of new global infections in 2019 were in ESA.[6,10] No country in ESA has sufficient data to describe the size of their key populations,[10,75] although several have commenced population-specific mapping (Table 1).[76] Control of HIV in these populations will contribute to the deceleration of the HIV epidemic in the general population. National surveys of key populations biennially are recommended, as knowing the epidemic is the first key to design the response.

Recommendations for research priorities

- Promote and expand local prevention research, including programme and policy evaluations.
- Investigate and implement methods to improve the accessibility of HIV education and testing, including routine surveillance, particularly for key populations.

TABLE 1: Prevalence of HIV among certain key and vulnerable populations in ESA.

Country	HIV prevalence among				Reference
	MSM (%)	Sex workers (%)	PWID (%)	Prisoners (%)	
Angola	2.0 [2017]	8.0 [2017]	-	15.9 [2017]	10
Botswana	14.8 [2018]	42.2 [2018]	-	-	75
Comoros	0.0 [2018]	0.3 [2017]	1.8 [2017]	-	10
Eritrea	-	10.4 [2014]	-	1.4 [2019]	10, 75
eSwatini	12.6 [2015]	60.5 [2015]	-	34.9 [2015]	75
Ethiopia	-	24.3 [2014]	6 [2018]	4.2 [2016]	75, 77, 78
Kenya	18.2 [2011]	29.3 [2011]	18.3 [2011]	5.7 [2016]	78, 79
Lesotho	32.9 [2014]	71.9 [2014]	-	31.4 [2017]	10, 75
Madagascar	14.9 [2014]	5.5 [2016]	8.5 [2016]	0.3 [2018]	75
Malawi	6.8 [2019]	55.0 [2018]	-	19.0 [2019]	10
Mauritius	17.2 [2015]	15.0 [2015]	32.3 [2017]	17.3 [2017]	75
Mozambique	3.1–9.1 [2015]	17.8–31.2 [2016]	19.9–50.1 [2019]	24.0 [2019]	75, 80, 81, 82
Namibia	12.4 [2009]	40.7 [2016]	-	-	75, 83
Rwanda	4.0 [2016]	45.8 [2016]	-	-	75
Seychelles	13.2 [2013]	4.6 [2015]	23.0 [2019]	9.9 [2019]	10, 79
South Africa	18.1 [2018]	57.7 [2015]	21.8 [2018]	11.1 [2019]	75, 79
South Sudan	-	11.4 [2019]	-	5.3 [2016]	10, 84
Uganda	13.2 [2013]	31.3 [2017]	17.0 [2017]	4.0 [2019]	10, 79
UR Tanzania	8.4 [2018]	15.4 [2018]	15.5 [2013]	6.7 [2015]	10, 79
Zambia	-	48.8 [2017]	-	27.4 [2015]	10
Zimbabwe	21.1 [2019]	42.2 [2019]	-	28.0 [2015]	10

Note: Data on the HIV prevalence among transgender people are not presented in this table because of a lack of data on this key population in ESA; of the vulnerable populations, only prisoners and incarcerated people have sufficient data in ESA to be presented in this table.

MSM, men who have sex with men; PWID, people who inject drugs; [year], year of publication.

- Support in-country trials of viral load and CD4 T-cell count POC testing and the surrounding services required to improve ART adherence, clinical management and retention in care.

Conclusion

The road to HIV elimination in ESA requires continued strong and sustained national and international investment, commitment to evidence-based programmes and persistence. The region contains over half of the world's population of PLWH and continues to have major challenges to achieving 90-90-90, let alone the looming target of 95-95-95. The priority must remain diagnosing, treating and virally suppressing all existing HIV infections. However, in high-prevalence settings, the prevention of new infections and early diagnosis of acute infections remain important goals. Research must ensure that responses in the region are targeted, efficient and evaluated. In particular, ESA will benefit from strengthened surveillance and key and vulnerable population research, in-country development and validation of HIV tests, and supported rapid transition to new ART regimens to ensure sustainable progress towards important global goals.

Acknowledgements

The authors thank Eva Kiwango, the UNAIDS country director for Mozambique, for the contribution to this article.

Competing interests

The authors declare that they have no financial or personal relationships that may have inappropriately influenced them in writing this article.

Authors' contributions

E.P. and M.J. are co-first authors and have contributed equally to the article. E.P., M.A.J., E.M., T.N., D.N. and P.N.L.S. planned and organised the collaboration; all authors contributed region-specific knowledge and expertise. E.P., M.A.J., D.N. and P.N.L.S. wrote the manuscript, with review and revision by all authors.

Ethical considerations

This article followed all ethical standards for research without direct contact with human or animal subjects.

Funding information

This study was supported by the Manhiça Foundation, Mozambique, and a Research Impact Grant (RA/1/2799/40) from the University of Western Australia.

Data availability

Publicly available data sets were accessed from https://www.unaids.org/sites/default/files/media_asset/2020_aids-data-book_en.pdf (associated with Figures 1 and 2) and https://population.un.org/wpp/ (associated with Figure 1).

Disclaimer

The views and opinions expressed in this article are those of the authors and do not necessarily reflect the official policy or position of any affiliated agency of the authors.

References

1. Ford N, Ball A, Baggaley R, et al. The WHO public health approach to HIV treatment and care: Looking back and looking ahead. Lancet Infect Dis. 2018;18(3):e76–e86. https://doi.org/10.1016/S1473-3099(17)30482-6
2. The Joint United Nations Programme on HIV/AIDS (UNAIDS). Seizing the moment. Geneva: UNAIDS; 2020. Report No.: JC2991.
3. Wilson D, Halperin DT. "Know your epidemic, know your response": A useful approach, if we get it right. Lancet. 2008;372(9637):423–426. https://doi.org/10.1016/S0140-6736(08)60883-1
4. The Joint United Nations Programme on HIV/AIDS (UNAIDS). Global AIDS Update 2019 – Communities at the Centre. Geneva: UNAIDS; 2019. Report No: JC2956.
5. The Joint United Nations Programme on HIV/AIDS (UNAIDS). 90-90-90 An ambitious treatment target to help end the AIDS epidemic. Geneva: UNAIDS; 2014. Report No.: JC2684.
6. The Joint United Nations Programme on HIV/AIDS (UNAIDS). Miles to go: Closing gaps, breaking barriers, righting injustices. Geneva: UNAIDS; 2018. Report No.: JC2924.
7. The Joint United Nations Programme on HIV/AIDS (UNAIDS). Fast track – Ending the AIDS epidemic by 2030. Geneva: UNAIDS; 2014. Report No.: JC2686.
8. Sanders EJ, Wahome E, Powers KA, et al. Targeted screening of at-risk adults for acute HIV-1 infection in sub-Saharan Africa. AIDS. 2015;29(Suppl 3):S221–S230. https://doi.org/10.1097/QAD.0000000000000924
9. Rutstein SE, Ananworanich J, Fidler S, et al. Clinical and public health implications of acute and early HIV detection and treatment: A scoping review. J Int AIDS Soc. 2017;20(1):21579. https://doi.org/10.7448/IAS.20.1.21579
10. The Joint United Nations Programme on HIV/AIDS (UNAIDS). UNAIDS Data 2020. Geneva: UNAIDS; 2020. Report No.: JC2997E; 2020.
11. Bernardo EL, Fuente-Soro L, Lopez-Varela E, Naniche D. Anonymity in HIV testing: Implications for public health. Lancet. 2017;390(10112):2546.
12. UNAIDS Reference Group on Estimates, Modelling and Projections. Annex on methods. Geneva: UNAIDS; 2018.
13. Fuente-Soro L, Lopez-Varela E, Augusto O, et al. Monitoring progress towards the first UNAIDS target: Understanding the impact of people living with HIV who re-test during HIV-testing campaigns in rural Mozambique. J Int AIDS Soc. 2018;21(4):e25095. https://doi.org/10.1002/jia2.25095
14. Rentsch CT, Reniers G, Machemba R, et al. Non-disclosure of HIV testing history in population-based surveys: Implications for estimating a UNAIDS 90-90-90 target. Glob Health Action. 2018;11(1):1553470. https://doi.org/10.1080/16549716.2018.1553470
15. Choko AT, MacPherson P, Webb EL, et al. Uptake, accuracy, safety, and linkage into care over two years of promoting annual self-testing for HIV in Blantyre, Malawi: A community-based prospective study. PLoS Med. 2015;12(9):e1001873. https://doi.org/10.1371/journal.pmed.1001873
16. Iwuji CC, Orne-Gliemann J, Larmarange J, et al. Universal test and treat and the HIV epidemic in rural South Africa: A phase 4, open-label, community cluster randomised trial. Lancet HIV. 2018;5(3):e116–e125.
17. Fox MP. Are we shifting attrition downstream in the HIV cascade? Lancet HIV. 2016;3(12):e554–e555. https://doi.org/10.1016/S2352-3018(16)30149-7
18. Johnson LF, May MT, Dorrington RE, et al. Estimating the impact of antiretroviral treatment on adult mortality trends in South Africa: A mathematical modelling study. PLoS Med. 2017;14(12):e1002468. https://doi.org/10.1371/journal.pmed.1002468
19. Tymejczyk O, Brazier E, Yiannoutsos CT, et al. Changes in rapid HIV treatment initiation after national 'treat all' policy adoption in 6 sub-Saharan African countries: Regression discontinuity analysis. PLoS Med. 2019;16(6):e1002822. https://doi.org/10.1371/journal.pmed.1002822
20. Ford N, Vitoria M, Doherty M. Providing antiretroviral therapy to all who are HIV positive: The clinical, public health and programmatic benefits of Treat All. J Int AIDS Soc. 2018;21(2):e25078. https://doi.org/10.1002/jia2.25078
21. Jewell BL, Mudimu E, Stover J, et al. Potential effects of disruption to HIV programmes in sub-Saharan Africa caused by COVID-19: Results from multiple mathematical models. Lancet HIV. 2020;7(9):e629–e640. https://doi.org/10.1016/S2352-3018(20)30211-3
22. Lopez-Varela E, Fuente-Soro L, Augusto OJ, et al. Continuum of HIV care in rural Mozambique: The implications of HIV testing modality on linkage and retention. J Acquir Immune Defic Syndr. 2018;78(5):527–535. https://doi.org/10.1097/QAI.0000000000001720
23. Magaço A, Dovel K, Cataldo F, et al. 'Good health' as a barrier and facilitator to ART initiation: A qualitative study in the era of test-and-treat in Mozambique. Cult Health Sex. 2019;21(9):1059–1073. https://doi.org/10.1080/13691058.2018.1535091
24. Nhassengo P, Cataldo F, Magaco A, et al. Barriers and facilitators to the uptake of test and treat in Mozambique: A qualitative study on patient and provider perceptions. PLoS One. 2018;13(12):e0205919. https://doi.org/10.1371/journal.pone.0205919

25. Govindasamy D, Ford N, Kranzer K. Risk factors, barriers and facilitators for linkage to antiretroviral therapy care: A systematic review. AIDS. 2012;26(16):2059–2067. https://doi.org/10.1097/QAD.0b013e3283578b9b
26. Fuente-Soro L, Iniesta C, López-Varela E, et al. Tipping the balance towards long-term retention in the HIV care cascade: A mixed methods study in southern Mozambique. PLoS One. 2019;14(9):e0222028. https://doi.org/10.1371/journal.pone.0222028
27. Maixenchs M, Boene H, Anselmo R, et al. Post-ART symptoms were not the problem: A qualitative study on adherence to ART in HIV-infected patients in a Mozambican rural hospital. PLoS One. 2015;10(9):e0137336. https://doi.org/10.1371/journal.pone.0137336
28. Nhampossa T, Fernandez S, Augusto O, et al. Discordant retention of HIV-infected mothers and children: Evidence for a family-based approach from Southern Mozambique. Medicine (Baltimore). 2020;99(32):e21410.
29. Rosen S, Maskew M, Fox MP, et al. Initiating antiretroviral therapy for HIV at a patient's first clinic visit: The RapIT randomized controlled trial. PLoS Med. 2016;13(5):e1002015. https://doi.org/10.1371/journal.pmed.1002015
30. Saghayam S, Wanke C. The impact of nutritional status and nutrition supplementation on outcomes along the HIV treatment cascade in the resource-limited setting. Curr Opin HIV AIDS. 2015;10(6):472–476. https://doi.org/10.1097/COH.0000000000000202
31. Geffen N, Low M. When to start antiretroviral treatment? A history and analysis of a scientific controversy. S Afr J HIV Med. 2017;18(1):a734. https://doi.org/10.4102/sajhivmed.v18i1.734
32. Garrett N, Norman E, Leask K, et al. Acceptability of early antiretroviral therapy among South African women. AIDS Behav. 2018;22(3):1018–1024. https://doi.org/10.1007/s10461-017-1729-2
33. Iwuji C, McGrath N, Calmy A, et al. Universal test and treat is not associated with sub-optimal antiretroviral therapy adherence in rural South Africa: The ANRS 12249 TasP trial. J Int AIDS Soc. 2018;21(6):e25112. https://doi.org/10.1002/jia2.25112
34. Dorward J, Drain PK, Osman F, et al. Early antiretroviral therapy is associated with better viral suppression and less HIV drug resistance after implementation of universal treatment in South Africa. AIDS Res Hum Retroviruses. 2020;36(4):297–299. https://doi.org/10.1089/AID.2019.0206
35. Dorward J, Sookrajh Y, Gate K, et al. HIV treatment outcomes among people with initiation CD4 counts >500 cells/μL after implementation of Treat All in South African public clinics: a retrospective cohort study. Journal of the International AIDS Society. 2020;23(4):e25479.
36. Mozambique Ministry of Health (MISAU). 2017 annual report of activities related to HIV/AIDS. Maputo, Mozambique: MISAU; April 2018.
37. Swannet S, Decroo T, De Castro SMTL, et al. Journey towards universal viral load monitoring in Maputo, Mozambique: Many gaps, but encouraging signs. Int Health. 2017;9(4):206–214. https://doi.org/10.1093/inthealth/ihx021
38. Petersen ML, Tran L, Geng EH, et al. Delayed switch of antiretroviral therapy after virologic failure associated with elevated mortality among HIV-infected adults in Africa. AIDS. 2014;28(14):2097–2107. https://doi.org/10.1097/QAD.0000000000000349
39. Drain PK, Dorward J, Violette LR, et al. Point-of-care HIV viral load testing combined with task shifting to improve treatment outcomes (STREAM): Findings from an open-label, non-inferiority, randomised controlled trial. Lancet HIV. 2020;7(4):e229–e237. https://doi.org/10.1016/S2352-3018(19)30402-3
40. Moyo S, Mohammed T, Wirth KE, et al. Point-of-care Cepheid Xpert HIV-1 viral load test in rural African communities is feasible and reliable. J Clin Microbiol. 2016;54(12):3050–3055. https://doi.org/10.1128/JCM.01594-16
41. Girdwood SJ, Nichols BE, Moyo C, Crompton T, Chimhamhiwa D, Rosen S. Optimizing viral load testing access for the last mile: Geospatial cost model for point of care instrument placement. PLoS One. 2019;14(8):e0221586. https://doi.org/10.1371/journal.pone.0221586
42. Cohen MS, Gay CL, Busch MP, Hecht FM. The detection of acute HIV infection. J Infect Dis. 2010;202(Suppl 2):S270–S277. https://doi.org/10.1086/655651
43. Hecht FM, Wellman R, Busch MP, et al. Identifying the early post-HIV antibody seroconversion period. J Infect Dis. 2011;204(4):526–533. https://doi.org/10.1093/infdis/jir304
44. Parker E, Judge M, Pastor L, et al. Signature of the storm: RNA-seq analysis of the extensive host transcriptome dysregulation caused by acute HIV-1 infection in a Mozambican cohort. Abstracts of AIDS 2018; 2018 Jul 23–27; Amsterdam; Abstract WEPEA018. Geneva: International AIDS Society; 2018.
45. Pilcher CD, Tien HC, Eron JJ, Jr., et al. Brief but efficient: Acute HIV infection and the sexual transmission of HIV. J Infect Dis. 2004;189(10):1785–1792. https://doi.org/10.1086/386333
46. Wawer MJ, Gray RH, Sewankambo NK, et al. Rates of HIV-1 Transmission per Coital Act, by stage of HIV-1 infection, in Rakai, Uganda. J Infect Dis. 2005;191(9):1403–1409. https://doi.org/10.1086/429411
47. Powers KA, Ghani AC, Miller WC, et al. The role of acute and early HIV infection in the spread of HIV and implications for transmission prevention strategies in Lilongwe, Malawi: A modelling study. Lancet. 2011;378(9787):256–268. https://doi.org/10.1016/S0140-6736(11)60842-8
48. Pilcher CD, Price MA, Hoffman IF, et al. Frequent detection of acute primary HIV infection in men in Malawi. AIDS. 2004;18(3):517–524. https://doi.org/10.1097/00002030-200402200-00019
49. Fiscus SA, Pilcher CD, Miller WC, et al. Rapid, real-time detection of acute HIV infection in patients in Africa. J Infect Dis. 2007;195(3):416–424. https://doi.org/10.1086/510755
50. Serna-Bolea C, Munoz J, Almeida JM, et al. High prevalence of symptomatic acute HIV infection in an outpatient ward in southern Mozambique: Identification and follow-up. AIDS. 2010;24(4):603–608. https://doi.org/10.1097/QAD.0b013e328335cda3
51. Bebell LM, Pilcher CD, Dorsey G, et al. Acute HIV-1 infection is highly prevalent in Ugandan adults with suspected malaria. AIDS. 2010;24(12):1945–1952. https://doi.org/10.1097/QAD.0b013e32833bb732
52. Drake AL, Wagner A, Richardson B, John-Stewart G. Incident HIV during pregnancy and postpartum and risk of mother-to-child HIV transmission: A systematic review and meta-analysis. PLoS Med. 2014;11(2):e1001608. https://doi.org/10.1371/journal.pmed.1001608
53. De Schacht C, Hoffman HJ, Mabunda N, et al. High rates of HIV seroconversion in pregnant women and low reported levels of HIV testing among male partners in Southern Mozambique: Results from a mixed methods study. PLoS One. 2014;9(12):e115014. https://doi.org/10.1371/journal.pone.0115014
54. De Schacht C, Mabunda N, Ferreira OC, et al. High HIV incidence in the postpartum period sustains vertical transmission in settings with generalized epidemics: A cohort study in Southern Mozambique. J Int AIDS Soc. 2014;17(1):18808. https://doi.org/10.7448/IAS.17.1.18808
55. González R, Rupérez M, Sevene E, et al. Effects of HIV infection on maternal and neonatal health in southern Mozambique: A prospective cohort study after a decade of antiretroviral drugs roll out. PLoS One. 2017;12(6):e0178134. https://doi.org/10.1371/journal.pone.0178134
56. Patel P, Borkowf CB, Brooks JT, Lasry A, Lansky A, Mermin J. Estimating per-act HIV transmission risk: A systematic review. AIDS. 2014;28(10):1509–1519. https://doi.org/10.1097/QAD.0000000000000298
57. Hansasuta P, Rowland-Jones SL. HIV-1 transmission and acute HIV-1 infection. Br Med Bull. 2001;58(1):109–127. https://doi.org/10.1093/bmb/58.1.109
58. Misra KHJ, Daskalakis D, Udeagu C. editor. Impact of PrEP on drug resistance and acute HIV infection, New York City, 2015–2017. Conference on Retroviruses and Opportunistic Infections; 2019 Mar 04–07. Seattle, WA; 2019.
59. Ananworanich J, Phanuphak N, De Souza M, et al. Incidence and characterization of acute HIV-1 infection in a high-risk Thai population. J Acquir Immune Defic Syndr. 2008;49(2):151–155.
60. Nash M, Huddart S, Badar S, Baliga S, Saravu K, Pai M. Performance of the Xpert HIV-1 viral load assay: A systematic review and meta-analysis. J Clin Microbiol. 2018;56(4):e01673-17. https://doi.org/10.1128/JCM.01673-17
61. Jani IV, Meggi B, Vubil A, et al. Evaluation of the whole-blood Alere Q NAT point-of-care RNA assay for HIV-1 viral load monitoring in a primary health care setting in Mozambique. J Clin Microbiol. 2016;54(8):2104. https://doi.org/10.1128/JCM.00362-16
62. Pilcher CD, Christopoulos KA, Golden M. Public health rationale for rapid nucleic acid or p24 antigen tests for HIV. J Infect Dis. 2010;201(Suppl 1):S7–S15. https://doi.org/10.1086/650393
63. Pastor L, Casellas A, Carrillo J, et al. IP-10 Levels as an accurate screening tool to detect acute HIV infection in resource-limited settings. Sci Rep. 2017;7(1):8104. https://doi.org/10.1038/s41598-017-08218-0
64. Powers KA, Miller WC, Pilcher CD, et al. Improved detection of acute HIV-1 infection in sub-Saharan Africa: Development of a risk score algorithm. AIDS. 2007;21(16):2237–2242. https://doi.org/10.1097/QAD.0b013e3282f08b4d
65. National Institute of Health (INS), United States Centers for Disease Control (CDC), University of California San Francisco (UCSF), Pathfinder International Population Services International (PSI), Mozambican Association for the Defence of Sexual Minorities (LAMBDA), International Training and Education Center for Health (I-TECH). Final Report: Integrated, biological and behavioral survey among men who have sex with men, Mozambique. San Francisco, CA: UCSF; 2011. Contract No.:U2GPS001468.
66. Mozambique Ministry of Health (MISAU), National Institute of Health (INS), United States Centers for Disease Control (CDC), et al. Final Report: Integrated biological and behavioral survey among people who inject drugs in Mozambique. Maputo: UCSF; 2014.
67. National Institute of Health (INS), United States Centers for Disease Control (CDC), University of California San Francisco (UCSF), Pathfinder International Population Services International (PSI), International Training and Education Center for Health (I-TECH). Final Report: Integrated biological and behavioral survey among female sex workers, Mozambique. San Francisco, CA: UCSF; 2011–2012. Contract No.:U2GPS001468.
68. United Nations Office on Drugs and Crime, The Joint United Nations Programme on HIV/AIDS (UNAIDS), The World Bank Group. HIV and prisons in sub-Saharan Africa. Geneva: UNAIDS; 2007.
69. Mozambique Ministry of Health (MISAU), National Institute of Health (INS), United States Centers for Disease Control (CDC), et al. Final Report: Integrated survey biological and behavioral analysis among Long Haul truck drivers. Maputo: MISAU; 2012. Contract No.:U2GPS001468.
70. Mozambique Ministry of Health (MISAU), National Institute of Health (INS), Ministry of Labour (MITRAB), United States Centers for Disease Control (CDC), University of California San Francisco (UCSF), International Training and Education Center for Health (I-TECH). Final Report: Integrated biological and behavioral survey among Mozambican workers in the mines of the Republic of South Africa. Maputo: UCSF; 2012. Contract No.:U2GPS001468.
71. International Organization for Migration (IOM). Briefing note on HIV and labour migration in Mozambique. Pretoria: IOM; 2007.
72. De Oliveira T, Kharsany AB, Graf T, et al. Transmission networks and risk of HIV infection in KwaZulu-Natal, South Africa: A community-wide phylogenetic study. Lancet HIV. 2017;4(1):e41–e50. https://doi.org/10.1016/S2352-3018(16)30186-2

73. The Joint United Nations Programme on HIV/AIDS (UNAIDS). Country overview – Mozambique Geneva [homepage on the Internet] [cited 2020 Jan 4]. Available from: https://www.unaids.org/en/regionscountries/countries/mozambique
74. Republic of Mozambique National Council for the Fight against HIV/AIDS. National strategic plan for the response to HIV and AIDS 2015–2019. Maputo: CNCS; 2015.
75. The Joint United Nations Programme on HIV/AIDS (UNAIDS). UNAIDS Data 2019 – Eastern and Southern Africa. Geneva: UNAIDS; 2019. Report No.:JC2959E.
76. Abdul-Quader AS, Gouws-Williams E, Tlou S, Wright-De Agüero L, Needle R. Key populations in sub-Saharan Africa: Population size estimates and high risk behaviors. AIDS Behav. 2015;19 (Suppl 1):S1–S2. https://doi.org/10.1007/s10461-014-0963-0
77. Demissie M, Johnston LG, Muleta M, et al. Prevalence of HIV and other infections and injection behaviours among people who inject drugs in Addis Ababa, Ethiopia. Afr J AIDS Res. 2018;17(3):259–264. https://doi.org/10.2989/16085906.2018.1511604
78. Telisinghe L, Charalambous S, Topp SM, et al. HIV and tuberculosis in prisons in sub-Saharan Africa. Lancet (London, England). 2016;388(10050):1215–1227. https://doi.org/10.1016/S0140-6736(16)30578-5
79. The Joint United Nations Programme on HIV/AIDS (UNAIDS). UNAIDS key population atlas Geneva [homepage on the Internet] [cited 2021 Mar 31]. Available from: https://kpatlas.unaids.org/dashboard
80. Nalá R, Cummings B, Horth R, et al. Men who have sex with men in Mozambique: Identifying a hidden population at high-risk for HIV. AIDS Behav. 2015;19(2):393–404. https://doi.org/10.1007/s10461-014-0895-8
81. Augusto Âdo R, Young PW, Horth RZ, et al. High burden of HIV infection and risk behaviors among female sex workers in three main urban areas of Mozambique. AIDS Behav. 2016;20(4):799–810. https://doi.org/10.1007/s10461-015-1140-9
82. Semá Baltazar C, Horth R, Boothe M, et al. High prevalence of HIV, HBsAg and anti-HCV positivity among people who injected drugs: Results of the first bio-behavioral survey using respondent-driven sampling in two urban areas in Mozambique. BMC Infect Dis. 2019;19(1):1022. https://doi.org/10.1186/s12879-019-4655-2
83. Baral S, Trapence G, Motimedi F, et al. HIV prevalence, risks for HIV infection, and human rights among men who have sex with men (MSM) in Malawi, Namibia, and Botswana. PLoS One. 2009;4(3):e4997. https://doi.org/10.1371/journal.pone.0004997
84. Heijnen M, Mumtaz GR, Abu-Raddad LJ. Status of HIV and hepatitis C virus infections among prisoners in the Middle East and North Africa: Review and synthesis. J Int AIDS Soc. 2016;19(1):20873. https://doi.org/10.7448/IAS.19.1.20873
85. United Nations, Department of Economic and Social Affairs, Population Division. New York, World population prospects 2019 [homepage on the Internet] [cited 2020 Aug 16]. Available from: https://population.un.org/wpp/

World AIDS Day 2020: Reflections on global and South African progress and continuing challenges

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2021 SPECIAL ANNIVERSARY COLLECTION

Southern African Journal of HIV Medicine
ISSN: (Online) 2078-6751, (Print) 1608-9693

World AIDS Day 2020: Reflections on global and South African progress and continuing challenges

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Dates:
Received: 18 Dec. 2020
Accepted: 29 Jan. 2021
Published: 10 Mar. 2021

How to cite this article:
Pillay Y, Johnson L. World AIDS Day 2020: Reflections on global and South African progress and continuing challenges. S Afr J HIV Med. 2021;22(1), a1205. https://doi.org/10.4102/sajhivmed.v22i1.1205

Background: Reflecting on progress and challenges in meeting global human immunodeficiency virus (HIV) targets is often done ahead of World AIDS Day. This article reflects on progress and the continuing challenges in meeting targets in South Africa (SA).

Objective: To review policy and implementation related progress and continuing challenges towards eliminating HIV as a public health threat by 2030.

Method: Policy analysis and review of modeling data from Thembisa 4.3.

Results: South Africa has made significant progress in the adoption of policies with two exceptions. While there are gaps in reaching the 90-90-90 implementation targets, progress has been made in the past decade.

Conclusion: While progress has been made in the past decade towards the global targets, much work remains to ensure that HIV transmission is curtailed and those that require treatment are initiated on treatment and are virally suppressed.

Keywords: HIV; prevention; treatment; viral suppression; PrEP.

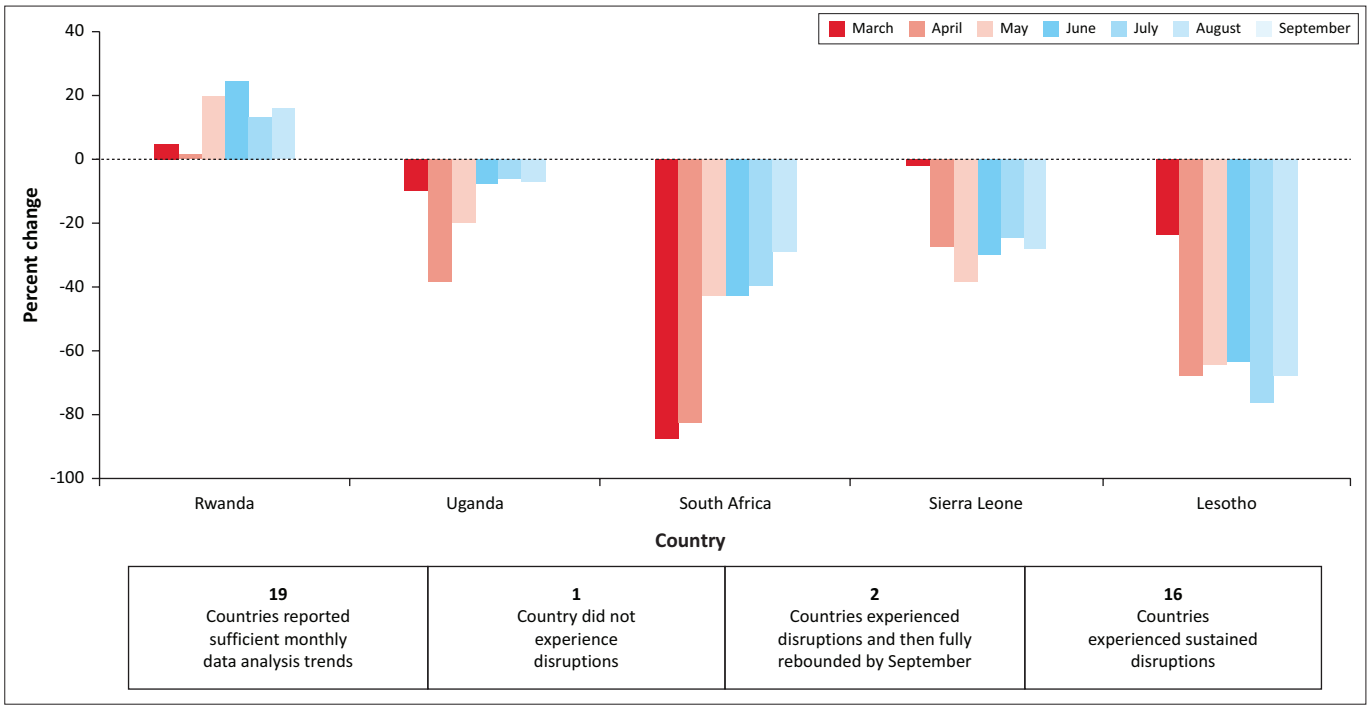
Introduction

South Africa (SA) recently commemorated World AIDS Day 2020. At the start of 2021, we reflect on areas 'done well' and those 'yet to show progress'. Three recent documents provide independent data with which SA can achieve this and rededicate healthcare workers to eliminating human immunodeficiency virus (HIV) as a public health threat by 2030. These articles are, the World AIDS Day Report 2020: 'Prevailing against pandemics by putting people at the centre', published by the Joint United Nations Programme on HIV/AIDS (UNAIDS),[1] the 2020 Global HIV Policy Report: Policy barriers to HIV progress[2] and current South African estimates as described in the 'Thembisa 4.3 model', a report published by the University of Cape Town.[3]

The annual UNAIDS World AIDS Day Report[1] focuses on progress in meeting targets and on areas of ongoing concern. Of the estimated 38 million people living with HIV (PLWH) globally, 12 million are not on treatment. In addition, in 2019, 1.7 million people were newly infected and 690 000 died of acquired immunodeficiency syndrome (AIDS)-related causes. Although the target was to have at least 30 million people worldwide on treatment by December 2020, actual numbers were 4 million off this goal! In September 2020, UNAIDS reported a shortfall in achieving its 90-90-90 global targets. By the end of 2019, these were only 81-67-59! Furthermore, the target of having ≥ 73% of all PLWH on antiretrovirals (ARVs) and exhibiting viral suppression by the end of 2020, is said to be 'unlikely'.[4] Even before the Coronavirus Disease 2019 (COVID-19) pandemic, the World Health Organization (WHO) had indicated that the global HIV response 'was stalling'![5]

Coronavirus Disease 2019 has negatively impacted the international HIV response. UNAIDS reports major disruptions in HIV-testing and access to antiretroviral therapy (ART).[1] Access to HIV prevention services for men who have sex with men (MSM) was interrupted in Cambodia, Honduras, Jamaica, SA and Togo. In addition, the number initiating ART continued to decline through to September 2020, in the Dominican Republic, Kyrgyzstan, Lesotho, Sierra Leone and SA. Figure 1 indicates a rebound in testing in Uganda and SA between March/April and August/September 2020, but persistently poor testing rates in Sierra Leone and Lesotho.

The UNAIDS report[1] also noted several positive initiatives prior to and in response to the COVID-19 pandemic. These include adopting new dispensing policies for stable HIV patients



Source: UNAIDS. Prevailing against pandemics by putting people at the centre [homepage on the Internet]. Geneva; 2020. Available from: https://www.unaids.org/sites/default/files/media_asset/prevailing-against-pandemics_en.pdf

FIGURE 1: Change in the number of human immunodeficiency virus tests and results returned per month compared with baseline of selected countries in 2020.

such as multi-month dispensing in Burundi, the Dominican Republic, Ethiopia, Mozambique, Papua New Guinea and SA. This reduced the need for clinic visits to collect ARV treatment. In Botswana, Kenya, Rwanda and SA, voluntary medical male circumcision (VMMC) has restarted since the imposition of strict lockdowns. Despite these initiatives, there is widespread concern about the disruption of essential services by COVID-19.

South Africa's policy related-progress and response to the HIV epidemic

Implementation of interventions to prevent HIV and get people onto treatment as soon as they are diagnosed starts with good policies. South Africa has long been feted as having exemplary policies. The 2020 Global HIV Policy Report[2] shows that amongst countries in eastern and southern Africa – countries with the largest burden of HIV – SA has the highest overall policy-adoption score. The report suggests that SA has yet to make progress in the following three areas. The use of national laws to take advantage of the flexibilities in the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) to procure medicines at more affordable prices, the decriminalisation of sex work and the personal possession and/or use of drugs. South Africa has used its large volumes and tender-pricing system to drive down national and global prices but has not utilised provisions of TRIPs such as compulsory licensing and parallel importation. Although the former Deputy President Mr. C. Ramaphosa publicly launched an HIV programme for sex workers and declared that 'sex work *is* work', this has not stopped police harassing sex workers.[6] With respect to the legalisation of drug-use, to date only the private use of marijuana is legal but not its sale. However, drug use by the more than 75 000 injecting-drug users continues to be criminalised in SA, a situation that fuels both HIV and hepatitis transmission.[7] South Africa must move more rapidly to a clearer policy on the decriminalisation of sex work and of injecting-drug use. In addition, the SA government must give greater consideration to the flexibilities of TRIPS where medicine prices are not being reduced to affordable levels.

Changes in the HIV epidemic over the past decade: Estimates from the Thembisa model

In this report, we have used estimates from the Thembisa 4.3 model, an integrated HIV/demographic mathematical model developed for SA. This assesses the impact of different HIV programmes at a national and provincial level. Estimates from the Thembisa 4.3 model were released in November 2020 ahead of World AIDS Day 2020.

Prevalence of HIV

The estimate is that there are 7.64 million people in the country living with HIV (PLWH: 4.84 million females ≥ 15 years, 2.49 million males ≥ 15 years and 310 000 children < 15 years). The total number of PLWH has increased from 5.9 million in 2010, an increase of 1.7 million between 2010 and 2019.

Incidence of HIV

With respect to new HIV infections, there were 201 000 new HIV infections in 2018–2019: 121 000 in women, 67 000 in men and 11 600 infections from mother-to-child-transmission (MTCT). The majority of the latter (69%) occurred during the breastfeeding period. The total number of new infections in 2009–2010 was 412 000 – which implies a 51% decline in new infections over the 2010–2019 period. However, it is more meaningful to assess changes in HIV incidence rates in 15–49-year-olds. Changes in population growth and the population age distribution affect the absolute numbers of new infections. Using this metric, HIV incidence rates in SA declined by 55% over the 2010–2019 period, with the decline being greatest in KwaZulu-Natal (KZN) (61%) and least in the province of the Western Cape (34%). This decline in HIV incidence in KZN was confirmed in population-based surveillance studies.[8] In terms of the drivers of these declines in KZN, high coverage of VMMC and greater access to ARVs have been suggested as contributory and recommended to be scaled up in other provinces.[9]

The highest Thembisa-model HIV incidence-rates are in MSM (2.60%) and female sex workers (FSWs) (5.50%). However, there have been significant declines in these cohorts. The incidence in MSM has declined from 5.69% and in FSWs from 10.96% in 2010. Although these are encouraging estimates, they largely reflect the impact of general HIV prevention and treatment programmes.[10] Interventions such as pre-exposure prophylaxis (PrEP), which has been provided to FSWs and MSM, still have low uptake and retention rates. The model estimates a 2019 PrEP coverage rate of 3% and 1% in FSWs and MSM, respectively. These groups require special attention with respect to prevention and significantly increased access to treatment.

Over the past decade, there has been concern about HIV-infection in adolescent girls and young women (AGYW) aged 15–24 years. The Thembisa model estimates that the incidence rate in this cohort has declined from 2.98% in 2008 to 1.30% in 2018. These reductions are largely because of increased HIV testing, ARV coverage and high levels of condom use. Whilst still unacceptably high, this decline is important. Human immunodeficiency virus-incidence rates in adolescent boys and young men (ABYM) are lower in both 2008 and 2018 periods: 1.03% and 0.33%, respectively.[10] Gender inequalities and transmission of HIV from older men to AGYW are posited as the main drivers of the incidence-differences between AGYW and ABYM.[11,12]

New infections at birth have declined from 18 300 in 2010 to 3600 in 2019: a decline of 80%. This is a consequence of the greater proportion of infected mothers on ART during pregnancy and at delivery, 32% in 2010 and 97% in 2019. However, the decline in new infections related to breastfeeding has been less dramatic: 22 000 (2010) to 8000 (2019) – a 63% decline. Breastfeeding mothers need greater support from healthcare professionals and their families/communities.

Pre-exposure prophylaxis in pregnant and breastfeeding mothers can reduce vertical transmission by 40%.[13] Pre-exposure prophylaxis is safe in breastfeeding – with minimal infant-drug exposure.[14] The use of PrEP as part of a comprehensive package of interventions in countries with a high HIV prevalence is endorsed by the WHO in both antenatal and postnatal care.[15]

Prevention of HIV

Prevention starts with knowing one's status. A combination of interventions accounts for prevention successes of the past decade. But greater effort is needed.

Test and treat

The Thembisa 'ever-tested-for-HIV' model estimates the percent of adults tested increased from 47.3% in 2010 to 76.3% in 2019. A total of 81% of SA women compared with 72% of men had ever-tested by 2019.

Condom use

Despite the provision of free male and female condoms by the SA government, their use at last sexual encounter increased marginally from 23% (2010) to 29% (2019) amongst women aged 25–49 years. Only 27% of 15- to 24-year-old females used a condom at their last sexual encounter. (Note that the Thembisa estimates are lower than self-reported rates as they are adjusted for social desirability-bias in self-reported data). As the most effective barrier method for the prevention of sexually transmitted infections (STIs) and unplanned pregnancies, more attention needs to be paid to convince South Africans of their value.

Circumcision

South Africa, supported by PEPFAR and the Global Fund, launched a large VMMC roll-out around 2008. The proportion of men aged 15–49 years who are circumcised has increased from 36.4% in 2010 to 57.5% in 2019.

Pre-exposure prophylaxis

The national SA-PrEP programme was introduced in 2016 and provided oral PrEP to sex workers. The programme was expanded in 2017 to include college and university students at onsite health clinics. Since 2018, PrEP has been provided in public health clinics.

Deaths associated with HIV

The 2018–2019 estimate of HIV- and AIDS-related deaths in SA is 74 000 PLWH: 31 000 deaths in women, 39 000 in males and 3900 in children. The higher number of male deaths follows men presenting late to facilities, fewer men knowing their status, fewer men on treatment. Deaths

TABLE 1: Progress towards the 90-90-90 targets in 2019.

Variable	Knowledge of HIV status (first 90% target)			Receiving ART if diagnosed (second 90% target)			Virally suppressed at < 1000 (third 90% target)		
	Adult male (%)	Adult female (%)	Children (%)	Adult male (%)	Adult female (%)	Children (%)	Adult male (%)	Adult female (%)	Children (%)
Eastern Cape	88.3	92.4	77.8	62.0	66.3	67.7	89.7	90.1	66.5
Free State	87.4	91.7	73.9	69.9	74.3	67.7	93.8	94.1	77.5
Gauteng	86.1	91.5	75.3	61.7	68.9	65.7	87.9	88.4	62.7
KwaZulu-Natal	92.0	94.9	79.1	74.8	76.7	68.2	94.5	94.7	78.7
Limpopo	89.5	93.3	71.6	63.5	70.1	58.0	88.1	88.7	62.9
Mpumalanga	88.9	92.9	72.5	68.4	72.3	64.7	91.7	92.0	71.1
Northern Cape	88.9	93.3	74.7	62.6	70.7	78.3	90.8	91.2	69.2
North West	86.7	91.8	81.8	54.1	63.7	70.3	91.0	91.4	70.2
Western Cape	88.5	93.1	77.2	62.9	68.4	72.6	93.6	94.0	77.1
National	90.6	94.2	78.9	66.6	73.6	69.8	91.8	92.3	72.2

Source: Johnson LF, Dorrington RE. Thembisa version 4.3: A model for evaluating the impact of HIV/AIDS in South Africa [homepage on the Internet]. 2020. Available from: https://www.thembisa.org/
HIV, human immunodeficiency virus; ART, antiretroviral therapy.

have declined from 2009 to 2010 when it was estimated that there were 183 000 deaths – a 60% decline. As PLWH live longer, they are likely to need care for comorbidities such as diabetes, hypertension and cardiovascular diseases.[16]

Antiretroviral coverage

Thembisa 4.3 estimates that ARV coverage increased from n = 530 877 (9.4%) in 2008 to n = 4 723 950 (62.7%) in 2018. Whilst this is a large increase in ARV coverage, males ≥ 15 years lag behind, increasing from 8.0% in 2008 to 57.2% by 2018. Women's ART coverage was 9.9% in 2008 and 66.2% in 2018. Performing worst of all are children < 15 years of age: from 11.3% in 2008 to 53.2% in 2018.

Increasing access and improving adherence to ARVs for growing numbers of South Africans means accessing the latest, safest and best-tolerated ARVs at lowest cost. The newest (November 2019) of fixed-dose combinations in the SA public health sector is TLD: tenofovir (TDF), lamivudine (3TC) and dolutegravir (DTG). Whilst there are concerns about the long-term consequences of weight gain – greater in women than men, the combination is well tolerated and presents the virus with a high-barrier to resistance. Paediatric-DTG in a dispersible tablet is an important advance for infants and children living with HIV who are ≥ 4 weeks of age and weigh at least 3 kilograms (kg). Despite being endorsed by the WHO, paediatric-DTG has not as yet been registered for use in SA.[17]

Meeting the UNAIDS 90-90-90 targets

How did SA do in the light of the UNAIDS' 90-90-90 targets? The Thembisa estimates for adult women, males and children are presented separately to illustrate the variation across these groups (Table 1). Adult women in SA had reached 94-74-92 in 2019; adult males, 91-67-92 and children fared worst, 79-70-72. Table 1 indicates a great deal of provincial variation. KwaZulu-Natal is the best performing province: 95% of adult KZN-women know their HIV status, 77% are on ART and 95% of these are estimated to be virally suppressed. The worst performing provinces with respect to women living with HIV are Gauteng (92-69-88) and North West (92-64-91). The latter does 'better' with children at 82-70-70, compared with the worst performing province, Limpopo at 72-58-63.

Conclusion

At the beginning of each December since 1988, the global AIDS community and partners reflect on progress made in turning the tide on the HIV epidemic and consider the challenges as well as the work that remains to eliminate HIV as a public health threat. The year 2020 was especially challenging given the impact of the COVID-19 pandemic on individuals, families, and the local and global community. Health and social services were disrupted in many parts of the world making it difficult for people to access services. There is now a need for recovery and a reset to ensure that the gains made in the HIV programme, in SA and globally, are not lost and that we can accelerate towards the new targets that UNAIDS[18] has proposed – of achieving the expanded 95-95-95 targets by 2025, as well as removing punitive laws, decreasing stigma and discrimination, and decreasing gender inequality and violence.

Acknowledgements

Competing interests

The authors declare that they have no financial or personal relationships that may have inappropriately influenced them in writing this article.

Authors' contributions

Y.P. conceptualised and wrote the first draft; L.J. provided the South African estimates and revised the draft.

Ethical consideration

This article followed all ethical standards for research without direct contact with human or animal subjects.

Funding information

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Data availability

All data are secondary data, which are publicly available and referenced.

Disclaimer

The views and opinions expressed in this article are those of the authors and do not necessarily reflect the official policy or position of any affiliated agency of the authors.

References

1. UNAIDS. Prevailing against pandemics by putting people at the centre [homepage on the Internet]. Geneva; 2020 [cited n.d.]. Available from: https://www.unaids.org/sites/default/files/media_asset/prevailing-against-pandemics_en.pdf
2. HIV Policy Lab. 2020 global HIV policy report: Policy barriers to HIV progress [homepage on the Internet]. 2020 [cited n.d.]. Available from: https://www.hivpolicylab.org/documents/reports/2020GlobalReport/2020%20HIV%20Policy%20Lab%20Executive%20Summary%20
3. Johnson LF, Dorrington RE. Thembisa version 4.3: A model for evaluating the impact of HIV/AIDS in South Africa [homepage on the Internet]. 2020 [cited n.d.]. Available from: https://www.thembisa.org/
4. UNAIDS. 90–90–90: Good progress, but the world is off-track for hitting the 2020 targets [homepage on the Internet]. 2020 [cited n.d.]. Available from: https://www.unaids.org/en/resources/presscentre/featurestories/2020/september/20200921_90-90-90
5. World Health Organization. World AIDS Day 2020: Global solidarity and resilient HIV services [homepage on the Internet]. 2020 [cited n.d.]. Available from: https://www.who.int/news-room/events/detail/2020/12/01/default-calendar/world-aids-day-2020?utm_source=Global+Health+NOW+Main+List&utm_campaign=f33aef1be0-EMAIL_CAMPAIGN_2020_11_30_02_11&utm_medium=email&utm_term=0_8d0d062dbd-f33aef1be0-2890801
6. Human Rights Watch. Why sex work should be decriminalized [homepage on the Internet]. 2019 [cited n.d.]. Available from: https://www.hrw.org/news/2019/08/07/why-sex-work-should-be-decriminalized
7. Scheibe A, Shelly S, Versfeld, A. Prohibitionist drug policy in South Africa – Reasons and effects. Int Dev Policy. 2020; Pt 3(12). https://doi.org/10.4000/poldev.4007
8. Vandormael A, Cuadros DC, Kim H-Y. The state of the HIV epidemic in rural KwaZulu-Natal, South Africa: A novel application of disease metrics to assess trajectories and highlight areas for intervention. Int J Epidemiol. 2020;49(2):666–675. https://doi.org/10.1093/ije/dyz269
9. Vandormael A, Akullian A, Siedner M, et al. Declines in HIV incidence among men and women in a South African population-based cohort. Nature. 2019;10(1):5482. https://doi.org/10.1038/s41467-019-13473-y
10. Johnson L, Meyer-Rath G, Dorrington R et al. The effect of HIV programmes in South Africa on national HIV incidence trends, 2000–2017. Poster presentation at the 23rd International AIDS Conference. San Francisco, CA: International AIDS Society; 2020 July 6–10.
11. Birdthistle I, Tanton C, Tomita A, et al. Recent levels and trends in HIV incidence rates among adolescent girls and young women in ten high-prevalence African countries: A systematic review and meta-analysis. Lancet Glob Health. 2019;7(11):e1521–e1540. https://doi.org/10.1016/S2214-109X(19)30410-3
12. De Oliverira T, Kharsany ABM, Graf T, et al. Transmission networks and risk of HIV infection in KwaZulu-Natal, South Africa: A community-wide phylogenetic study. Lancet HIV. 2017;4(1):e41–e50. https://doi.org/10.1016/S2352-3018(16)30186-2
13. Davey DLJ, Bekker L-G, Gomba Y, et al. Modelling the potential impact of providing preexposure prophylaxis in pregnant and breastfeeding women in South Africa. AIDS. 2019;33(8):1391–1395. https://doi.org/10.1097/QAD.0000000000002221
14. Mugwanya KK, Hendrix CW, Mugo NR, et al. Pre-exposure prophylaxis use by breastfeeding HIV-uninfected women: A prospective short-term study of antiretroviral excretion in breast milk and infant absorption. PLoS Med. 2016;13(9):e1002132. https://doi.org/10.1371/journal.pmed.1002132
15. World Health Organization. Preventing HIV during pregnancy and breastfeeding in the context of PrEP: Technical brief [homepage on the Internet]. 2017 [cited n.d.]. Available from: https://www.who.int/hiv/pub/toolkits/prep-preventing-hiv-during-pregnancy/en/
16. Mathebula RL, Maimela E, Ntuli NS. The prevalence of selected non-communicable disease risk factors among HIV patients on anti-retroviral therapy in Bushbuckridge sub-district, Mpumalanga province. BMC Public Health. 2020;20(1):247. https://doi.org/10.1186/s12889-019-8134-x
17. WHO. WHO welcomes FDA approval of new formulation of dolutegravir for young children living with HIV [homepage on the Internet]. 2020 [cited n.d.]. Available from: https://www.who.int/news/item/18-06-2020-who-welcomes-fda-approval-of-new-formulation-of-dolutegravir-for-young-children-living-with-hiv
18. UNAIDS. 2025 AIDS targets: Putting people living with HIV and communities at risk at the centre [homepage on the Internet]. Geneva; 2020 [cited n.d.]. Available from: https://aidstargets2025.unaids.org/

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ISSN: 1608-9693