

Review

Provision of antiretroviral therapy in South Africa: the nuts and bolts

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Public sector antiretroviral provision had a slow start in South Africa despite a raging epidemic and a World AIDS conference that shed significant public light on the disparities of therapy access globally. This was largely due to political prevarication in the midst of AIDS denialism. There has been an unprecedented expansion in the HIV treatment programme since 2008. As a result, South Africa now has the largest number of patients on antiretroviral drugs in the world, and South African life expectancy has increased by more than a decade. However, this has led to a number of fiscal, logistic and operational challenges that the

country must face as the treatment programme continues to expand. Challenges include increasing detection within communities, linkage and retention in care, while strengthening operational support functions such as consistent drug supply, health staffing and infrastructure, diagnostic services, programme monitoring and sustainable financing. As a middle-income country, albeit with marked income inequality, and the heaviest HIV burden in the world, South Africa is a test case of whether a large-scale public health programme can boast of success in the face of numerous other health-system challenges.

Introduction

South Africa has the largest number of people living with HIV (PLHIV), estimated at 5.8 million, and by far the largest number of people on antiretroviral therapy (ART) in the world; almost 2.5 million have started ART in a country with a population of 51 million people [1,2]. Almost 1 in 10 people are living with HIV and the country comprises 25% of all people on ART in low- and middle-income countries [2]. It has taken South Africa 10 years to commence 2.5 million people on treatment and in 2012 a total of almost 376,000 patients started ART – almost 100,000 more than in the previous year [3]. Seven years ago, only 7% of South Africans in need – based on 2010 World Health Organization (WHO) guidelines – were on ART but by the end of 2010, this figure had jumped to 84% [4]. By March 2011, 1.46 million people were on antiretroviral drugs (ARVs). This number is expected to reach 3.1 million by 2015, representing very good coverage of individuals with CD4⁺ T-cell counts <350 cells/μl [5].

Besides the substantial logistical challenges that a programme of this scale presents, the size and expanding nature of the pool of those requiring treatment poses significant resource challenges. It is estimated that there are between 1.6 and 2 million additional PLHIV eligible for ART if the eligibility criteria for ART initiation are extended to CD4⁺ T-cell counts <500 cells/μl based on the 2013 WHO Treatment Guidelines [6,7]. The National Treasury has costed the expansion to a threshold of a CD4⁺ T-cell count of 500 cells/μl and while these figures have yet to be released publically, it has been estimated that this will cost an additional ZAR2 billion [7].

In addition to the potential increase in the number of PLHIV eligible for ART, between 300,000 and 500,000 people have become infected annually over the past decade, while the annual capacity of the South African Health System to start people on ART has expanded by only 20% [7].

South Africa is a middle-income country with a gross domestic product (GDP) similar to Brazil [8] but also

one of the highest Gini coefficients in the world [9]. The Gini coefficient, a measure of wealth disparity, indicates compelling reasons to provide free health services for common illnesses such as HIV to large strata of the population. The country currently spends about 4% of its GDP on public health services, of which 0.71% is devoted to HIV. This amounts to about ZAR7,000 (USD700) per patient per year [3]. With the largest ART treatment programme in the world, the South African Health Minister in 2013 requested as part of the total health budget, ZAR27.3 billion (USD2.7 billion) in which, among others, health infrastructure, HIV and TB, community health care and a national health insurance (NHI) plan were targeted [10]. The health budget in 2012/2013 was ZAR121 billion (USD12.1 billion) [10,11] and total health spend in 2011 was ZAR248.6 billion (USD24.8 billion) or 8.6% of GDP. The HIV programme has required an extra ZAR1.6 billion every year [7]. The South African bill for HIV was ZAR25 billion in 2013/2014 and the government provided ZAR19.9 billion (personal communication, Mark Blecher, Department of National Treasury, RSA). The conditional grant for HIV has increased by 44% a year or ZAR1.3 billion over the past 3 years [12]. A summary of HIV/AIDS expenditure from 2006/2007 to 2013/2014 and the proportion that is donor funding as presented by the National Treasury is shown in Figure 1.

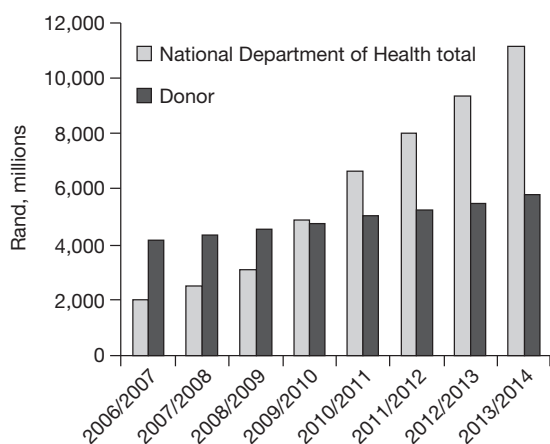
The South African Government (SAG) plans to implement an NHI scheme over the next few years, tied to a national community primary health

intervention. The aim is to improve overall health-care access including harnessing the resources of the private sector for public sector health care; this has, however, received criticism because of projected cost and the ambitious nature of the project [13]. A medium-term budget in 2013 made provision for early NHI work and included two conditional grants dedicated to supporting the NHI. One of these grants will go to contracting 600 private doctors to work part-time in government clinics. The South African HIV treatment programme is largely funded by the national fiscus, making it one of the few African programmes not wholly reliant on donor support [12,14]. Despite expanded treatment, challenges remain, not least that prevention efforts have remained ineffective despite a relatively large amount of investment in public messaging and condom distribution [4,15,16]. Continued new infections mean that people requiring treatment will continue to enter the ART programme for decades to come [5,7]. Ultimately, the South African health system will need to prepare for the provision of chronic ART, irrespective of CD4⁺ T-cell count for the 5 million citizens infected with HIV [7].

Looking back, looking forward

The complex political history in the past 15 years surrounding the SAG's response to HIV has been well documented [17–22]. A decade of prevarication and delay under President Thabo Mbeki and his health minister, Dr Manto Tshabalala-Msimang led to a large number of unnecessary deaths and perinatal HIV transmissions [19]. During the period of HIV denialism from 1998 until 2008 a campaign coordinated by a strong civil society HIV activist movement courageously spearheaded by the Treatment Action Campaign (TAC), brought local and international pressure to bear on the government unseen since the fall of apartheid [17,18]. The catastrophic scale of the generalized HIV epidemic in South Africa had a profound effect on individuals and communities. HIV caused South Africa's already severe tuberculosis (TB) epidemic to escalate alarmingly and created multiple social problems, including a large orphan population of almost 2 million [21,22]. The influx of funding via the Global Fund for HIV, TB and Malaria (GFATM) and the President's Emergency Fund for AIDS Relief (PEPFAR) from 2002 until 2011 allowed for increased coverage of prevention of mother-to-child-transmission (PMTCT) and expanded ART programmes [23,24]. Much of this was led by large non-governmental organizations that mushroomed with the influx of donor funds directed at this time, away from governmental structures. Attainment of 'universal access', although achieved in areas of the country, suffered from substantial geographical discrepancies,

Figure 1. Trends in two major funding flows for HIV/AIDS in South Africa



Personal communication from Mark Blecher, Department of National Treasury, RSA.

due in many cases to local or provincial alignment with national denialism [18,25].

A general commitment to a scientific and public health approach to HIV in the past decade has replaced the previous confused messaging from politicians and health officials [26]. The Department of Health, since 2009, has thrown political energy and financial resources at HIV treatment programmes [14,23]. Mother-to-child HIV transmission (MTCT) has decreased markedly from 8% in 2008 to 3.5% at 6 weeks in 2011, and is well on the way to the UNAIDS proposed target for 'MTCT eradication' [10]. No doubt, an effective and universal PMTCT programme will result in important reductions in lifetime ART and cost to society [27–29]. Treatment programmes have access to medication choices and monitoring that is in line with international guidelines, with the most recent improvements including fixed-dose combination ART, including for pregnant and lactating women and access to salvage regimens as reflected in the most recent government HIV treatment guidelines [30].

For the first time in over 20 years, life expectancy in the general populations has increased, by over a decade, associated with increasing access to ART [31,32]. Other societal benefits are also being realized, including early indications of reduced transmission [33]. The South African programme may be thought of as having gone from 'pole cat to poster child', having once been fiercely criticized during the period of denialism of 2000–2008 [34], with South African politicians receiving a standing ovation at the Vienna International AIDS conference in July 2010 [35].

Challenges remain

The success of a national ART programme is contingent on early identification of infection in PLHIV, rapid and appropriate starting of ART, high levels of viral suppression, management of toxicities as well as the retention in care of a high proportion of patients [36]. The ongoing effective provision of ART to millions of PLHIV in South Africa has placed additional service demands including increased HIV testing, CD4⁺ T-cell count testing, ART drug supply, health staffing, infrastructure, laboratory and programme monitoring on an already stretched public health infrastructure [37].

Here, we discuss a number of the challenges the country faces going forward, in the provision of an ever-expanding effective ART programme.

HIV testing, linkage to care and retention

The new global push to initiate ART at higher CD4⁺ T-cell count levels requires strategies to expand the pool of first-time testers, encourage repeat testing and ensure linkage to the health services – all of which present significant health system challenges. HIV testing is

a voluntary activity in South Africa that usually requires at least verbal consent. Despite a powerful rights-based constitution in which universal access to health is central, the first decade of HIV in South Africa was steeped in stigmatization and discrimination, making HIV testing a thorny issue [38,39]. Most infamous and illustrative of the intensity of stigmatization was the stoning and killing of Gugu Dlamini, a young single mother and AIDS activist after she publicly disclosed her HIV status in KwaZulu-Natal in 1998 [40]. Testing levels remained low until recently, as measured in serial surveys [41,42]. In 2010, the South African Health Ministry launched a nationwide campaign to test 15 million individuals over a 12-month period. Despite a faltering start, it was reported that almost 11 million individuals out of a population of 50 million tested over this period [10], and millions more in the subsequent 2 years [43]. The much acclaimed South African 2012–2016 National Strategic Plan recommends annual testing for all and whilst indications are that a large number of South Africans have tested, repeat testing is less frequent [44,45]. In 2006, South Africa adopted a rapid HIV point-of-care (POC) testing algorithm performed by qualified nurses, resulting in removal of some of the barriers to testing [46]. More recently, HIV rapid testing can be performed by trained lay counsellors further facilitating testing in a number of environments. The adoption of a higher CD4⁺ T-cell count threshold of <350 cells/μl in 2012 for initiation of ART has increased the proportion of asymptomatic PLHIV who are eligible for ART. However, predominantly health-facility-based HIV testing is a barrier to reaching these individuals and alternative pathways to care are required [47,48]. New strategies for HIV testing are being piloted; including home-based testing, self-testing, stand-alone HIV testing sites and mobile clinic testing [47–49] with universal testing in TB and antenatal clinics (ANC). In 2011, the policy of provider-initiated 'opt out' testing was recommended and this has now been widely adopted in the country [50]. As documented in other parts of the world, the South African 'treatment cascade', whereby individuals who test positive are linked to care, attain viral suppression and remain in care, is also associated with significant 'leakage' or loss of PLHIV at each stage in the process [51]. Innovative methods such as community-based follow up and cell phone messaging have been explored to enhance linkage to care [52–54]. As the treatment pool expands, more innovation in retaining and tracking individuals in care are required. ART eligibility was increased to CD4⁺ T-cell counts of 350 cells/μl from 200 cells/μl in 2010 exclusively for TB-coinfected patients and women attending ANC. This was expanded to all PLHIV in late 2011. In 2013, ART was recommended regardless of CD4⁺ T-cell count in TB-coinfected and pregnant women. These two conditions represent the most common pathway to HIV

diagnosis and treatment in the country. Both categories of patients attend health services for reasons other than HIV, making routine HIV testing feasible, whilst testing asymptomatic individuals in communities remains a challenge [54–56]. Mean CD4⁺ T-cell counts at treatment commencement remain relatively low (median CD4⁺ T-cell count at treatment initiation was 220 cells/μl in 2012 in Western Cape) [57,58], although there are some early indications this CD4⁺ T-cell count may be increasing [58]. With its twin objective – to determine ART eligibility and monitor treatment – CD4⁺ T-cell count testing has followed the same decentralization trend as HIV testing, with the use of novel POC CD4⁺ T-cell count tests. These tests may increase ART initiation rates and decrease pre-ART losses [59], although they must be weighed up against increased costs and complexity of implementation.

Despite these gains, the challenge of ‘late presenters’ continues to occur throughout sub-Saharan Africa, including South Africa, with the resultant ongoing burden of opportunistic infections including TB [60].

Retention and tracking of patients on ART within programmes remains a problem. Many patients move between sites as far as adjacent provinces with no way to track referral, due to a lack of a common patient identifier and electronic tracking systems. This results in probable over-estimation of loss to follow-up, which is estimated to be over 20% after 3 years [61–65]. The most recent National Strategic Plan recommended that development and implementation of a unique health sector identifier is a priority and there are indications that this may be acceptable to both patients and services [48]. This already exists in social services such as pension pay out points. This will allow transfer of electronic laboratory data between facilities, including clinical details, drug prescriptions and other information.

The initial phase of ART rollout in South Africa from 2002 began from specialist clinics where the expertise for HIV care was situated. A period of continuing education among primary health-care physicians from 2004 onwards enabled a move towards decentralization of ART to primary care facilities. This varied by province, initially challenged by a lack of political will fuelled by denialism, which manifested to varying degrees across the country. A vastly expanded number of primary facilities have now been accredited to deliver ART in accordance with the national plan to provide access to ART within every health district [10,26]. Even so, primary health facilities have increasingly become congested, burdened by an ever increasing pool of stable patients returning for ART, stretching scarce human resources, leading in some cases to decreased quality of care, especially adherence counselling, and longer waiting times, with resultant impact on retention in care [62–65]. Different provinces have responded in

different ways, with some provinces – like Western Cape and KwaZulu-Natal – adopting novel models of community care including lay adherence support and drug delivery in adherence clubs and community adherence groups outside of health facilities. These counsellor-managed and nurse-supported groups allow efficient and local delivery or pre-packaged ART (this is ART packaged into 1–4 monthly packages at a central dispensing unit for specific patients) to chronic, stable ART patients resulting in reduced burden on health services and improved retention without impact on treatment success [66–69].

Drug supply

In late 2013 almost 2.5 million people were receiving ART in South Africa. Over 90% of these individuals receive free ART services within the state sector through primary health clinics. The South African public sector adult treatment guidelines, largely driven by cost, have since their inception offered a first-line non-nucleoside reverse transcript inhibitor-based regimen with a protease-based second line. Many more drug options are licensed and available in the private sector. The most recent public sector guidelines do make provision for a third line under expert referral [30]. Paediatric treatment options have always been even more limited. South African ART programmes have relied on both originator and generic drug manufacturers [70]. The South African national drug policy of 1996 articulated a commitment to use of generic essential medicines, incentivized local manufacture of medicines, and strengthening of drug procurement, storage and safeguarding, distribution and dispensing systems [71].

South Africa has a drug regulatory agency, a vibrant generic manufacturing industry, and the country now accounts for 30% of the world’s generic ARV use while exporting some of these drugs to other countries. Economies of scale have allowed the government to negotiate competitive prices for a range of first-, second- and subsequent line ARVs, including generic fixed-dose combinations, such as tenofovir, emtricitabine and efavirenz [72,73]. The single tablet, once-a-day, fixed-dose combination, in particular, has been an important regimen simplification and has been used by government campaigns to encourage better adherence to programmes.

A recent audit of South African health-care facilities found major deficiencies in pharmacy services in health-care facilities, with large shortages of pharmacists and pharmacy assistants [37]. In addition, 77% of clinics audited did not have the complete list of ‘tracer’ essential medicines. Tracer medicines are specific drugs that are used to assess the integrity of the supply chain, based on their availability in the facility medicine room or pharmacy, and including some ARVs [37].

There have been widespread reports of ARV stock-outs since 2009, including in South Africa's largest provinces by population. The stock-outs have continued and have a variety of causes, ranging from poor forecasting, ordering problems, manufacturing capability and simply delivery logistics. At the end of 2012, there was a complete breakdown of service delivery at a medicines depot, which serves over 300 medical facilities in the Eastern Cape province of South Africa. The acute crisis was precipitated by a workers' strike at the depot, but occurred on a background of long-standing problems with service delivery. There was a strong civil society response to the crisis, and Médecins Sans Frontières (MSF) intervened to provide the depot with logistic support. Civil society organizations identified facilities with critical medicine stock shortages and mounted a campaign to encourage patients to return to health-care facilities to collect medication. The intervention was successful in restoring the depot to functionality and the response to the crisis demonstrated the critical role civil society can play in resolving service delivery crises [74]. The Southern African HIV Clinicians Society, an organization of health-care workers, together with TAC, Rural Doctors Association of South Africa (Rudasa) and MSF has created an online mechanism for health-care workers to report shortages and stock-outs to the National Department of Health [75]. ARV stock-outs have a number of serious negative consequences. They result in treatment interruptions, which may lead to treatment failure and acquired resistance, requiring therapy switch to more costly and less tolerable second-line treatment [76]. They may also undermine public confidence in the treatment programme. In case of low stock supplies, patients are often asked to return more frequently, which is costly to the patient, can affect adherence and brings additional burden to the health staff [77]. Various strategies have been adopted to attempt to minimize ARV stock-outs with varying success. A number of electronic drug accountability systems have been devised and are being used by provincial ART programmes [78–80]. Dispensing medication for 3–4 months at a time to stable, adherent patients results in less lost work time for patients and reduces the burden on overstretched dispensing systems [69]. Public–private partnerships for delivery of chronic medicines have been in the field in some parts of the country for a long time, albeit on a relatively small scale and are now being scaled up for ART distribution. To ensure uninterrupted drug supplies to community structures such as adherence clubs these centrally pre-packaged medications from central dispensing units are delivered to community-based venues or even directly to homes [69].

Tendering has been taken over by a recently established central procurement unit under the auspices of

the Essential Drugs Program. The ARV tender for high usage items is split in order to reduce the chances of interruptions in supply due to manufacturer failures. However, communication of accurate forecasts to manufacturers and timeous placement of orders are still inconsistent and will need to be bolstered as the treatment programme grows.

Treatment initiation thresholds

During the first decade of care, South African ART guidelines lagged behind those stipulated by the WHO for ART initiation, but in 2011 were brought in line with 2010 WHO recommendations for the first time [81]. The CD4⁺ T-cell threshold was initially raised from <200 cells/ μ l to <350 cells/ μ l in pregnant women and TB-coinfected patients shortly after the 2010 WHO announcement, and then for all patients in early 2012 [82]. There are many limitations and challenges to monitoring of access to ART in South Africa [5]. Nevertheless, estimates are that by the middle of 2011 the number of patients receiving ART in South Africa had increased to 1.79 million. The 79% ART coverage reached based on the eligibility criteria of CD4⁺ T-cells <200 cells/ μ l fell to 52% when assessed according to ART eligibility criteria of CD4⁺ T-cells <350 cells/ μ l adopted in 2012. The number of adults starting ART in 2010/2011 was 1.56 \times the number of adults who became ART eligible in 2010/2011, with women having a higher ratio of 1.96 than men [5].

The 2013 WHO Treatment guidelines call for initiation of ART in adults and adolescents at a CD4⁺ T-cell count threshold of <500 cells/ μ l and immediate treatment initiation for all children, pregnant women and TB-coinfected patients. If adopting these guidelines, South Africa has today an estimated additional 1.6–2 million ART eligible PLHIV [7,83]. Whilst there is enthusiasm in the health ministry to again be on par with WHO guidelines, there has been a call from implementers and opinion leaders in the field for caution [7,84,85]. Some of the controversy stems from a tension between the need to consolidate gains and ensure ongoing quality of services as the programme expands within the current CD4⁺ T-cell count threshold, and the aspirational ideals that treatment may offer for prevention if scaled up [85,86]. The WHO 2013 guidelines state that 'not all the observational studies have consistently shown the beneficial impact of initiating ART earlier on mortality and the incidence of non-AIDS events associated with chronic inflammation and ongoing viral replication'. They also caution that 'the long-term safety profile and the implication of earlier initiation on resistance and toxicity will also need to be closely monitored' [6]. Two large randomized clinical trials, START and TEMPRANO, will answer some of these questions for the field [87,88]. One of the considerations

for earlier treatment initiation includes the benefit of treatment as prevention. Two large studies are currently underway in South Africa (POPART, HPTN 071 and ANRS 12249) that will attempt to quantify the prevention benefits of earlier treatment [89].

Even the most recent moves to universal access at a 350 cells/ μ l CD4⁺ T-cell count threshold required massive up-scaling of drug procurement, distribution and dispensing capacity within the public health system. It is apparent now that the growing pool of chronic ART users will need their ongoing regular drug supplied in ways that the public sector has not heretofore utilized, for example, chronic dispensing units, home delivery and other non-health facility based mechanisms.

Health service staffing and infrastructure

South Africa's recent National Development Plan optimistically described that by 2030 'each community will have a clinic with nurses who love caring for people' [90]. Needless to say, there are significant challenges to achieving this goal: poorly located, inadequate and under-maintained infrastructure, failure of the public health system to meet demand and sustain quality, and uneven and often poor-quality public services have been identified as impediments to South Africa's development goals [39,91]. A recent audit conducted by the National Department of Health of all 4,200 public health facilities in South Africa, including around approximately 400 hospitals and 3,800 primary care facilities, found an average compliance score for infrastructure of 65%, with management of primary care buildings being the weakest area [37]. Of all clinics, 1.7% had no water, 1.1% no electricity and 14% no waste removal mechanisms and many more reported interruptions of these supplies. Significant investments in health infrastructure are required given current backlogs. The audit also noted poor human resource allocation, queue times, cleanliness and staff attitude [37]. The national government's plans to tackle these challenges include decentralization of health services, primary health care re-engineering with extensive use of lay community health-care workers as well as the NHI.

Decentralizing ART

Benefits of decentralization of patient care include improved retention rates among adults and children compared with centralized hospital services and enabling better coverage of services [92–96].

In 2008 there were only 362 functional ART clinics in the country. However by 2013, the health minister reported that there were 3,000 facilities initiating ART throughout the country [10,97]. This represents almost all health facilities in the country, and while access in rural areas remains uneven, the vast majority of the

population has access to health facilities with the ability to provide ART. This decentralization of ART, also recommended by the WHO, has been key to the rapid scale-up of ART seen in the past 2 years. Integration of TB and HIV services, and nurse-initiated ART also remain unevenly implemented in the country although both are strongly recommended in the guidelines. Integrated ART and ANC services reduce losses from care for TB-coinfected patients and during and immediately after pregnancy [98,99]. In addition, SAG's recent move to the WHO recommended PMTCT strategy option B of standard ART for all pregnant HIV-positive women will require scale-up of ART distribution within antenatal care services [100].

Health-care staffing

In South Africa there are 17.4 medical practitioners per 100,000 people and these are largely concentrated in urban areas [101]. These are relatively high levels of staffing compared with other African countries but staff are mal-distributed and not always effectively deployed. The public health approach adopted by South Africa and endorsed by WHO is designed to enable other health cadres to deliver care [102]. This has included a combination of nurses and community workers [94]. A randomized controlled study in South Africa, reported in the *Lancet* in 2010, concluded that primary health-care nurses were non-inferior to doctors in monitoring of first-line ART in a public health ART programme in South Africa [101] and nurse case management is a cost effective strategy [103].

In keeping with a nurse-led, doctor-supported ART programme, the number of nurses certified to initiate ARV treatment increased from 250 in February 2010 to 10,000 in April 2012 [10]. Task shifting of other important programmatic activities such as HIV testing and adherence counselling to community care workers has helped HIV testing and ART scale-up [94]. A new government initiative to change the way primary health care is delivered will see the adherence counsellor, home-based carer and TB treatment supporter rolled into one as a community health worker – known locally as a community care worker – employed and managed by non-governmental organizations for public sector facilities [104]. This new strategy is yet to be extensively rolled out nationally although the ART programme has relied heavily on non-governmental organizations and lay health worker support since its inception.

TB coinfection

An estimated 8.6 million people worldwide developed TB in 2012, of which 13% were HIV-positive: 75% of coinfecting patients lived in Africa. In South Africa TB incidence continues to rise, and in 2012 was reported at 1,003/100,000 (65% of whom were HIV-coinfected).

Nearly 120,000 of these patients died [105]. It is increasingly apparent that additional strategies are required in combination with Directly Observed Therapy, Short-course (DOTS), to impact and control endemic TB, and in the setting of high HIV burden on a background of HIV TB infection, both reactivation and high reinfection rates are important drivers [106]. The challenge to the HIV programme is the added morbidity and mortality of undiagnosed and untreated TB as well as the logistical challenge of managing both programmes in parallel. The solution has been to ensure both programmes can manage both diseases, so called integration [107]. Multidrug-resistant TB remains a public health threat, and whilst rates are still relatively low, it poses a significant challenge in numbers where TB notifications are high [108], in some areas requiring decentralized care.

Laboratory monitoring services

South Africa has a centralized state-funded laboratory service known as the National Health Laboratory Service (NHLS). The NHLS provides public health laboratory services to over 80% of the population through a national network of laboratories. The ART programme has placed large stress on the NHLS, as millions of specimens ranging from dried blood spots (DBS) for infant diagnosis, to viral loads and CD4⁺ T-cell count tests have required processing and reporting. In addition, laboratory monitoring costs are significant, resulting in the NHLS often carrying the burden for large laboratory monitoring costs, particularly from provinces with heavy treatment burdens. In 2012/2013 five million CD4⁺ T-cell count and 1.5 million viral load tests were performed. There were 62 functioning CD4⁺ T-cell count laboratories and 16 HIV viral load laboratories according to the NHLS annual report in 2012 [109]. Viral load monitoring of ART enabling earlier detection of adherence problems and treatment failure continues to be performed in centralized laboratories due to its technical complexity and expense [110]. Consequently, national guidelines make provision for a single annual viral load assessment per patient on ART [111]. Alternative ways such as the use of DBS, pooling samples, POC viral load tests and the increase in testing volumes to drive prices down will be essential in the scale-up of routine viral load monitoring [112,113]. Finding the balance between centralized and POC testing is a national priority in order to ensure cost-effective monitoring of ART performance [114].

Early infant diagnosis by PCR has moved over to DBS technology [115]. In 2011 there were 9 early infant diagnosis laboratories nationwide and 1,412 health-care workers were trained in 903 facilities to improve specimen and DBS collection [104]. HIV drug resistance testing is provided as a diagnostic service in only two NHLS laboratories in Cape Town and Johannesburg.

Numbers of facilities capable of this assay will need to grow as resistance becomes more prevalent as scale-up continues and the programme matures. Currently transmitted drug resistance in South Africa is estimated at <5% [116,117]. In addition, WHO treatment guidelines now recommend HIV drug resistance testing when assessing first-line ARV failures [6].

Programme monitoring

The monitoring of access to ART has been challenging for several reasons: ART services were introduced against the background of weak health information systems, limited infrastructure and diverse service providers with differing reporting requirements. The interpretation of public sector statistics was further complicated by changes in reporting practices in late 2009, with most provinces switching from reporting numbers of patients cumulatively started on ART to numbers currently on ART. Statistics from disease management programmes and programmes run by non-governmental organizations have not been routinely collected and reported. The estimation of ART coverage has also been hampered by uncertainty regarding the treatment need, the denominator in the coverage calculation. Mathematical models have been used to estimate numbers of HIV-positive individuals with CD4⁺ T-cell counts below different thresholds, but there is substantial uncertainty surrounding the rates of CD4⁺ T-cell decline that are assumed in these models, and there is also increasing recognition that these rates of CD4⁺ T-cell decline may differ between populations [5]. Data on enrolment and patients in care have nevertheless been reported nationally and triangulated with drug and laboratory utilization data [5]. Outcome data have been available from selected sites, either individually [62,63] or as part of collaborative analyses [65,118], substantiating the perceived clinical benefits of treatment, while at the same time demonstrating how scale-up resulted in inevitable difficulties to retain or confirm that patients were in care. Outcomes from routine government reporting were initially only available from monitoring systems in the Western Cape and Free State Provinces, based on a mix of paper-based systems and electronic capture [119,120]. The adaptation of the routine paper-based cohort monitoring later evolved into a flexible three-tier system comprising paper-based, electronic register and full electronic medical record systems. This approach was nationally adopted in 2010, and is being progressively implemented with a view to robust national estimates of uptake, retention and selected outcomes, although success nationally in this regard is yet to be demonstrated. South Africa has a well-functioning vital registration system covering the majority of deaths in the country, and it is hoped that together with the former, a crude assessment of programme impact will be

possible [121]. The National Strategic Plan for 2012–2016 proposed several measures to strengthen the monitoring and evaluation of South African ART programme, including the introduction of a single patient identifier in the health sector. A single patient identifier would help to understand factors determining retention in and access to care [122].

Donors and sustainability

The Health Minister, Dr Aaron Matsoeledi stated in his 2013 budget speech that South Africa started the early decades of the HIV epidemic ‘on the wrong footing’ [10]. This masks the tragic expense in terms of lives lost and unnecessary maternal transmissions [19]. International funding in the forms of GFATM and PEPFAR was instrumental in turning this around with PEPFAR alone providing a significant part of the dedicated programmatic financing of the AIDS programme since 2004 [24]. In 2010 the GFATM approved USD302 million (ZAR2.06 billion) for South Africa, over a period of 5 years, for the prevention, treatment and care of HIV and TB. Importantly, the majority of South Africa’s HIV response has been funded from the national tax base and not by donors, meaning that sustainability has always been relatively secure. However, donor funds have allowed for flexibility and the support of non-governmental organizations that have played a key role in the response. Since 2004, PEPFAR has invested more than USD3.7 billion (ZAR27 billion) in South Africa to tackle the HIV and TB epidemics, including over USD520 million between October 2012 and September 2013 [123]. A 5-year Partnership Framework Agreement was signed between the SAG and the US Government in 2010, providing a path for the transition of the PEPFAR programme from emergency assistance to sustainable activities [23]. The focus is to increase the SAG’s leadership and coordination of PEPFAR operations and to shift PEPFAR’s programmatic focus from direct service delivery to capacity development to sustain health outcomes in keeping with PEPFAR’s new strategy [124,125]. Encouragingly, the 2009/2010 SAG budget represented a 36% increase in HIV spending over the previous fiscal year and significant year on year increases have occurred through 2013 [126]. An additional ZAR2.3 billion would be needed to entirely replace donor funding.

Conclusion

There has been a significant shift in political will and support of the South African ART programme in the past 5 years with remarkable effect: millions of lives have been saved and infections averted in an era of new leadership [127]. However, the dual burden of TB and HIV disease continues unabated. HIV still represents

leading causes of disability adjusted life-years in Southern Africa [128,129]. South Africa continues to see HIV-related TB incidence increases and has not yet felt the impact of HIV prevention. The future depends on continued strengthening of health-care systems and the prevention of non-communicable diseases both related to HIV and to lifestyle. The health services infrastructure and human resources are already constrained – the innovative systems improvement and decentralized approaches that have started to be introduced as part of scaling-up services will be required to be developed as the programme continues to grow and the service expands to earlier individual treatment and even ‘a test and treat’ approach, with no specific eligibility criteria by CD4+ T-cell count. The challenge will be to maintain the current momentum, build on lessons learnt and integrate HIV and ART services whilst improving general primary care [7,130]. Ultimately, South Africa will need to provide chronic ART for 5–6 million citizens with HIV, for decades.

Disclosure statement

The authors declare no competing interests.

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