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HIV infection and tuberculosis in South Africa: an urgent need to escalate the public health response

Salim S. Abdool Karim, MBChB, PhD^{1,2,*}, Gavin J. Churchyard, MBChB, PhD^{3,4}, Quarraisha Abdool Karim, PhD^{1,2}, and Stephen D. Lawn, MD⁵

¹Centre for the AIDS Programme of Research in South Africa (CAPRISA), University of KwaZulu-Natal, Durban, South Africa

²Department of Epidemiology, Columbia University, New York, USA

³Aurum Institute for Health Research, Johannesburg, South Africa

⁴Department of Infectious Diseases & Tropical Medicine, London School of Hygiene & Tropical Medicine, London, UK

⁵Desmond Tutu HIV Centre, Institute for Infectious Diseases and Molecular Medicine, University of Cape Town, Cape Town, South Africa

Abstract

One of the greatest challenges facing post-apartheid South Africa is the control of the concomitant HIV and tuberculosis epidemics. HIV continues to spread relentlessly, and tuberculosis has been declared a national emergency. In 2007, South Africa, with 0.7% of the world's population, had 17% of the global burden of HIV infection, and one of the world's worst tuberculosis epidemics, compounded by rising drug resistance and HIV co-infection. Until recently, the South African Government's response to these diseases has been marked by denial, lack of political will, and poor implementation of policies and programmes. Nonetheless, there have been notable achievements in disease management, including substantial improvements in access to condoms, expansion of tuberculosis control efforts, and scale-up of free antiretroviral therapy (ART). Care for acutely ill AIDS patients and long-term provision of ART are two issues that dominate medical practice and the health-care system. Decisive action is needed to implement evidence-based priorities for the control of the HIV and tuberculosis epidemics. By use of the framework of the Strategic Plans for South Africa for tuberculosis and HIV/AIDS, we provide prioritised four-step approaches for tuberculosis control, HIV prevention, and HIV treatment. Strong leadership, political will, social mobilisation, adequate human and financial resources, and sustainable development of health-care services are needed for successful implementation of these approaches.

INTRODUCTION

South Africa ranks among the worst afflicted countries in the world for both HIV infection and tuberculosis (TB) (Table 1). Despite having just 0.7% of the world's population, South Africa was nevertheless home to about 17% (approximately 5.5 million people) of the global burden of HIV infection in 2007 (1,2). Further, the convergence of a major pre-HIV era TB epidemic,

Corresponding author: Salim S Abdool Karim, Director: CAPRISA - Centre for the AIDS Programme of Research in South Africa, 2nd Floor Doris Duke Medical Research Institute, Nelson R Mandela School of Medicine, University of KwaZulu-Natal, Private Bag X7, Congella 4013, South Africa, T: +27 31 260 4550, F: +27 31 260 4549, karims1@ukzn.ac.za.

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escalating numbers of TB cases resulting from a maturing HIV epidemic and growing TB drug resistance has resulted in South Africa bearing the brunt of the most serious TB crisis in the world (Figure 1).

Historically, apartheid created deeply-entrenched structural conditions where hundreds of thousands of workers were forced to live in over-crowded, poorly ventilated single-sex city hostels served by commercial sex workers (euphemistically referred to as ‘town-wives’). The ‘oscillatory migration’ lifestyle where workers living temporarily in the cities and on the mines periodically visited their wives and families in rural ‘homelands’, was key to the spread of both TB (3) and sexually transmitted infections (4) in the last century. The social, economic and environmental conditions created by apartheid in the form of overcrowded squatter settlements, migrant labour and deliberately under-developed health services for Blacks created the milieu for HIV and TB to flourish (5).

While these historical conditions continue to define the nature of the HIV and TB epidemics in South Africa, both are critical public health challenges in the post-apartheid era. Moreover, their control is fundamental to economic growth and development in the country’s young democracy (6). Unfortunately South Africa’s response to both the HIV and TB epidemics during the past decade (Panel 1) has been marked by denialism, ineptitude, obtuseness and deliberate efforts to undermine scientific evidence as the basis for action (7,8). However, the tide turned in 2008 and a change in administration has created new hope that the country will rise to the challenges posed by HIV and TB.

The road ahead is complex but one that must be traversed with the best evidence available and a willingness to take brave and decisive action to reverse the lost ground and to make critical gains to control both HIV and TB. This paper provides a historical perspective and an overview of the evolving HIV and TB epidemics in South Africa, the government responses, and concludes with a prioritised set of strategic steps as a way forward.

THE HIV AND TB EPIDEMICS IN SOUTH AFRICA

The Evolving HIV Epidemic in South Africa

From the outset, the signal characteristic of the HIV epidemic in South Africa was the high prevalence rates of HIV in young women (Figure 2). In 1992, the HIV prevalence rose most rapidly in teenage girls while it remained low in teenage boys. Peak HIV prevalence in men occurred at an age 5–7 years older than peak prevalence in women. This age-differential partnering pattern was first evident in a community based HIV survey in 1992 (9). By 2006, a national community based survey found that the age-specific HIV prevalence in young women had worsened substantially exceeding 30% (10).

Since the first cases of AIDS in 1982, the HIV epidemic in South Africa has evolved through four phases; an initial concentrated epidemic phase in the period up to 1987, the initiation of the generalised HIV epidemic phase during the period 1988 to 1994, the rapid spread of HIV phase from 1995 to 2000 and the post-2000 AIDS mortality phase where deaths due to AIDS became evident and increased rapidly.

Concentrated Epidemic Phase (1982–1987)—The first cases of AIDS were identified in men who have sex with men (MSM). Moral judgements and homophobia pervaded and the widespread belief that AIDS was a ‘gay disease’ created a sense of complacency in the general population about HIV risk and an excuse for the apartheid government not to act expeditiously. The mobilisation of the gay community to pro-actively address these challenges laid the early seeds for civil society’s human rights responses to the epidemic initially through the use of the

legal system by the AIDS Law Project and subsequently through social mobilisation by the Treatment Action Campaign.

Between 1983 and 1985, about 100 haemophiliacs acquired HIV through contaminated blood and blood products (7). The government immediately set up a fund to compensate the families of these patients and although few families accessed the financial compensation available it created a moral judgement distinguishing ‘innocent victims’ deserving of compensation from those infected from amoral behaviours and therefore not deserving of compensation. This type of thinking later shaped prevention of mother to child transmission (PMTCT) policies.

The virus in both MSM and haemophiliacs was subtype B. HIV infection in the general population was rare during this period, seroprevalence surveys in rural communities, pregnant women and hospital patients did not identify a single infected individual (11). A 1986 survey in 29,312 mine workers identified a small number of HIV positive men; all were migrant workers from countries to the north of South Africa(12). The forced repatriation of these workers and the subsequent government policy to bar HIV infected migrant workers set the tone of apartheid-era anti-human rights response to the epidemic (13).

Initiation of the Generalised Epidemic (1988–1994)—While HIV subtype B, the dominant subtype in Western Europe and the United States, continued to spread among MSM, HIV subtype C, the dominant subtype in Africa and Asia, started spreading in the general population in South Africa in about 1988. Between 1990 and 1994 there was an exponential increase in HIV infection with a doubling time of a little over one year (14). HIV prevalence increased in pregnant women from 0.8% in 1990 to 7.6% in pregnant women in 1994 (15). Since 1990, heterosexual transmission has been the dominant mode of transmission between adults in South Africa, with a concomitant epidemic in infants born to HIV infected mothers. HIV spread has shown marked geographical variation in distribution across South Africa (Figure 3) with the east coast provinces of KwaZulu-Natal and Mpumalanga experiencing the highest rates of HIV infection among women attending antenatal clinics. The apartheid government response painted AIDS as a ‘black disease’ and used fear as the main tactic in their media. An important aspect of the response was profiling which led to the exclusion of gays and blacks from donating blood.

Rapid Spread of HIV Phase (1995–2000)—National seroprevalence surveys in pregnant women have shown that HIV prevalence increased dramatically from 7.6% in 1994 to 20.5% in 2000, with wide variations between provinces (Figure 3) and local communities. HIV prevalence in young pregnant women (20–24 years) in a rural KwaZulu-Natal community increased from 21.1% in 1995, 39.3% in 1998 and 50.8% in 2001 (15). Phylogenetic mapping of HIV demonstrated the diversity of clade C viruses circulating in South Africa (16) with a number of mini-epidemics associated with each virus eventually coalescing to reveal a generalised well-established HIV epidemic in the country. The migrant labour system created the social and behavioural conditions for the introduction of multiple viruses from several neighbouring countries to spread rapidly in South Africa(17,18); multiple partnerships, especially concurrent multiple partnerships, became the norm (town wife and rural wife) for a large segment of the population. Migrant couples, where at least one partner is a migrant worker, were more likely than non-migrant couples to have one or both partners infected (35% versus 19%; $p = 0.026$) (19).

AIDS Mortality Phase (post-2000)—The national HIV seroprevalence in pregnant women increased from 24.8% in 2001 to a peak of 30.2% in 2005 and thereafter decreased to 29.1% in 2006 (Table 1). However, the HIV incidence rate in 2006 in this group was estimated to be in excess of 5% per annum (1). In the midst of continuing high HIV incidence rates, the rising mortality rates resulted in progressively smaller rises in HIV prevalence during this period. By

2006, mortality exceeded the number of new HIV infections despite the fact that South Africa had developed one of the largest ART programmes in the world. Life expectancy had declined by almost 20 years, and infant and maternal mortality rates (20) were at the highest rates ever. Today, most adult South Africans are dying in the economically active period of their lives. Average life expectancy is 48.4 years for men and 51.6 years for women (21). These reversals in trends of key markers for monitoring the millennium development goals (MDGs) provide some indication of the enormity of the development challenges that South Africa will be facing in the very near future if the current epidemic trajectories are not halted or reversed.

The TB Crisis in South Africa

Historically, TB was introduced into South Africa by the arrival of European immigrants mainly from Britain and Holland in the 17th century, many of whom were infected with *Mycobacterium tuberculosis* during the epidemic that had swept through Europe (3). The subsequent development of South Africa's mining industries beginning in the late 19th century created the conditions for rapid exposure and development of TB in large numbers of previously unexposed black South Africans through poor working conditions, silica dust exposure, over-crowded hostels and poor nutrition. 'Oscillatory migration', where migrant workers regularly returned to their rural home base facilitated the dissemination of TB to their families in rural areas.

Unlike AIDS, TB is a notifiable condition in South Africa. TB incidence rates increased steadily during the 20th century, peaking first in the 1960s at over 350/100,000 population, with an apparent decline during the 1970s (22) (possibly an artefact resulting from the exclusion of data from the black homelands) and a resurgence in the late 1990s. Of note is that the poorly funded and fragmented public sector health services during the apartheid years were ill-equipped and not committed to tackling the TB epidemic amongst the indigent and most vulnerable populations. Standard treatment for many patients during the 1970s and 1980s comprised 12 or 18 months of in-patient treatment with para-amino-salicylic acid (PAS), isoniazid and streptomycin. Even when this was changed to ambulatory care in the late 1980s, diagnosis and treatment delivery remained health facility-centred, rendering it inaccessible to many of those most in need.

The TB control programme was strengthened through introduction of rifampicin-based directly observed therapy – short course (DOTS) programme. However, the maturing HIV epidemic subsequently countered potential gains in TB control and fuelled a sharp increase in TB notification rates from the late 1990s. TB case notification rates have increased almost 4-fold from 163/100,000 in 1986 to 628/100,000 in 2006 (23) (Figure 1). Furthermore, the WHO estimated South Africa's overall annual TB incidence rate to be 940/100,000 in 2006 (24), reflecting the limitations in proportion of cases actually diagnosed. In that year South Africa reported an overall caseload of 341,165 TB cases, ranking just fourth in the world after the far more populous countries of India, China and Indonesia (24).

In communities where HIV prevalence exceeds 30% in pregnant women, annual TB rates as high as 1,500/100,000 were reported in 2004 (25) and continued to increase thereafter. Much of this TB is HIV-associated, with over 50% of new TB cases being in HIV-co-infected patients. Even in communities where HIV prevalence has reached a plateau, TB rates still continue to rise, due to the maturing HIV epidemic and increasing levels of immunodeficiency (25). Prior to the emergence of the HIV epidemic, the Western Cape Province had the highest TB rates. Currently, the total TB caseload (Figure 3) and the notification rates are the highest in KwaZulu-Natal (1,066/100,000 in 2006), reflecting a combination of the highest HIV prevalence (39.1% in pregnant women in 2006) and the worst TB programme performance indicators (23,26). Historically, TB notification rates increased with advancing age with men

having a higher TB burden compared to women. Today, rates peak among women in their twenties and men in their thirties (25), reflecting the age distribution of HIV infection.

TB drug resistance has emerged as an extremely serious problem, which is symptomatic of poor programme performance and TB cure rates over many years. The national cure rate was 57.7% of new smear-positive cases in 2005 (23), far below the WHO target of 85%. With over 14,000 cases of multi-drug resistant TB (MDR-TB) estimated in 2002 to occur annually, South Africa ranks among the top ten countries in the world for drug resistant TB (27). However, up to date incidence and prevalence estimates of drug resistant TB are lacking. In the last survey in 2002 of 4243 TB patients, 1.8% of new TB cases and 6.7% of TB re-treatment cases had MDR-TB (27). Rates have likely increased substantially in the ensuing years.

The crisis of TB and drug resistance in South Africa was highlighted all too vividly by a 2006 outbreak in a rural hospital in KwaZulu-Natal province where 39% (72/185) of culture-confirmed patients had MDR-TB, 53 of them with extensively drug resistant TB (XDR-TB) (28).. In this outbreak, XDR TB was rapidly and almost uniformly fatal and all who were tested were HIV co-infected. Further molecular epidemiological studies of patients with more than one TB episode suggest that exogenous nosocomial reinfection was frequently the source of this drug resistant disease (29). In this province, the causal strain for this outbreak has been identified as F15/LAM4/KZN and has been responsible for cases of MDR-TB since 1994 and XDR-TB from 2001 (30)..

Initially felt to be a localized outbreak, this cluster now has taken on epidemic characteristics. XDR-TB cases have continued to increase and by September 2007, 266 cases of XDR-TB had been diagnosed in a rural KwaZulu-Natal district with a mortality of 84% (31). XDR-TB cases have been identified in patients attending approximately 60 different health facilities in KwaZulu Natal Province and in all 9 provinces of South Africa. The appearance and growth of TB drug resistance threatens the gains made by TB DOTS programs and the historic antiretroviral treatment roll-out.

The annual TB mortality rate has increased 2.8-fold from 78/100,000 in 1990 to 218/100,000 in 2006 (Table 1). TB is the most common notified natural cause of death in South Africa (26). The confluence of increasing TB cases, HIV-TB co-infection, drug resistant TB cases, and TB mortality constitutes a crisis that demands urgent and sustained intervention.

ACHIEVEMENTS AND INNOVATIONS IN THE RESPONSES TO HIV AND TB

Despite the history of antagonism between the government and the intended beneficiaries of its AIDS control programme both during and after apartheid (panel 1), there have been significant accomplishments in the last 10 years. Five key accomplishments are highlighted in panel 2. National Strategic Plans for HIV (32) and for TB (23) have been developed through an inclusive process of consultation and have been broadly welcomed. Publication of these comprehensive documents highlights the fact that South Africa is not currently deficient in policy but rather lacks either the will or the capacity to deliver. Despite these clear deficiencies, the sheer magnitude of the TB and HIV epidemics has nevertheless stimulated the development of innovative means of delivering health care, the lessons of which might be harnessed to strengthen the overall health system.

Although belated, the scale-up of ART to the largest programme in the world is widely recognised as a major achievement in South Africa. Paradoxically, however, long-standing TB services have lagged behind and may benefit from incorporating key lessons from ART scale-up. Although TB and HIV treatment outcomes are not directly comparable, with TB treatment being for a defined period of 6–9 months whereas HIV treatment being lifelong, it is noteworthy that there is substantial disparity between the capacity to deliver treatment effectively. For

example, the Western Cape, which has a good provincial TB programme, the sputum smear conversion rate at 2 months among new smear-positive TB cases was just 66.9% in 2005, the treatment default rate at 6 months was 11.1% and the TB cure rate (71.9%) fell well short of the WHO recommended goal of 85% (26). In contrast, data for the ART programme in the Western Cape from the same period showed that among over 16,000 patients treated, 90.6% achieved viral load suppression <400 copies/mL at 6 months, the loss to follow-up rate was just 4.2% and 89.5% patients were alive and retained on treatment at 6 months (33). Furthermore, even after four years of follow-up, immunological and virological outcomes were excellent and sentinel ART services within the province have among the lowest rates of mortality and loss to follow-up in sub-Saharan Africa (34,35).

Many factors may underlie this apparent disparity, but a key factor underlying the high rates of patient retention and treatment compliance in the ART services may be the widespread use of treatment literacy training for patients, often delivered by lay or peer counsellors(36). These education programmes provide patients with detailed information on HIV infection, how antiretrovirals work, the importance of adherence and how to incorporate pill taking within daily routines and address the many social implications of their disease. In this way patients are empowered to take responsibility for their health and treatment and have ready access to advice and care when needed. In marked contrast to this patient-centred approach, TB services typically fail to provide adequate treatment literacy and disempower patients by requiring daily observation and recording of treatment compliance, which is often facility-based.

Both the TB and HIV epidemics have served as key drivers of innovation in service delivery, monitoring and evaluation. The TB control programme has established of a national electronic register that facilitates standardized recording and reporting and evaluation of the national TB programme. HIV treatment programmes have taken this one step further to collect longitudinal data on the clinical status, drug switching, drug-related adverse events, treatment adherence, CD4 cell count and viral load measurements and treatment outcomes. While these data are not nationally standardised yet, they provide a wealth of data on the status of the ART rollout programme. Indeed the level of detail in the data collected in HIV treatment programmes has enabled a performance management approach, where ART roll-out programme indicators are used to provide feedback to health service managers.

Task shifting has been effective in TB services through the use of community health care workers, defaulter tracers and treatment supporters, thereby improving case detection and holding to ensure continuity of care from investigation to diagnosis and cure. Similarly, HIV treatment programmes, saddled with a burden beyond the capacity of currently available health care personnel have, in addition to task shifting, created new cadres of health care workers. These include lay counselors, lay AIDS educators and enrolling patients with good ART adherence to provide adherence counseling in HIV clinics and through community outreach. This concept has been even further extended to home-based daily care to provide treatment for patients with XDR-TB (28).

To achieve the massive scaling up of HIV care in South Africa, millions of people had to access HIV testing and this was achieved through a number of innovative means. Testing was done through dedicated voluntary counseling and testing centres and community-based mobile clinics. Facility-based provider initiated testing especially focused on antenatal clinic attendees and TB patients. In addition, testing was facilitated through public sector partnerships with the private sector and non-governmental organisations. A major innovation that made this possible was the development of simple, reliable and cheap rapid HIV tests. To further enhance the reliability of HIV testing, algorithms have been developed where two different rapid tests are used to achieve diagnostic accuracy comparable to those available through laboratory testing.

While a similar rapid test is not available to diagnose TB, the growing burden of drug resistant TB has led to the evaluation and adoption of a rapid diagnostic for rifampicin and isoniazid resistance - the molecular line-probe assay (37). In addition, algorithms have been developed for diagnosing smear-negative TB. The need to manage TB and HIV in the same patient is stimulating the integration of TB and HIV services, with best practice examples at the Church of Scotland Hospital in Tugela Ferry (38), the CAPRISA eThekweni TB-HIV clinic in Durban (39) and the Medicins Sans Frontieres clinic in Khayelitsha (40).

These and other innovations in the TB and HIV treatment programmes, spawned by the sheer force of the burden these two infections place on the health system, are slowly trickling through to the rest of the health care service.

PUBLIC HEALTH ACTION FOR HIV AND TB CONTROL

South Africa is currently seriously under-performing in its efforts to control HIV. An international AIDS scorecard of country level AIDS programmes showed that South Africa was doing worse or no better than neighbouring countries (Table 2)(41). South Africa needs to improve in almost all of the ten elements used in this international rating. With regard to financing, this index is rated as the mean of three indicators: 1) The total expenditure on the response per person living with HIV, 2) the total expenditure on HIV prevention per person living in the country; and 3) domestic expenditure on HIV per person in the country as a proportion of Gross National Income. South Africa's rating in financing for the AIDS epidemic is on par with those of Zimbabwe and Mozambique but worse than that achieved by Malawi, Namibia and Botswana (Table 2) (41). South Africa has the resources, and the capability to rise to these challenges but has not been able to devote resources commensurate with the scale of the problem to be able to deliver on the four priorities of i) prevention, ii) treatment, care and support, iii) legal and human rights and iv) research, monitoring and evaluation articulated in the South African AIDS National Strategic Plan for 2007–2011 (32).

Similarly, it has not been able to galvanise effective implementation of the South African TB Strategic Plan(23), which sets out to i) strengthen the implementation of the current DOTS strategy, and to, in addition, to ii) address TB and HIV, MDR and XDR-TB, iii) contribute to health systems strengthening, iv) work collaboratively with all care providers, v) empower people with TB as well as communities, vi) coordinate and implement TB research, and vii) strengthen infection control.

To achieve the ambitious targets that have been set in the AIDS Strategic Plan(32), to reduce the HIV incidence rate by 50% and initiate antiretroviral therapy in 80% of those who need it, as well as the goals of the TB strategic plan(23), an enabling environment built on political commitment, genuine partnerships and a sustained commitment to rebuild the failing health service, is a prerequisite:

Political will and commitment

A necessary first-step forward is for the country's political leadership to publicly acknowledge the extent of the past successes and failures and demonstrate unwavering commitment to the control of the twin AIDS and TB epidemics. New high-level political commitment needs to be passionate and persistent. Building on the foundations of the past efforts of organisations like the Treatment Action Campaign, it needs to gain momentum as a collective commitment shared by the general populace and to create the groundswell of a social movement. With strong political leadership, a social movement, which galvanises all sectors of society, has a real chance of taking root and creating the conditions for a common shared vision and a commitment to the essential partnerships needed to turn the tide of these epidemics. This commitment in turn needs to be translated to financial resources not only for health services but also for

volunteer programmes, community mobilisation, local anti-AIDS and anti-TB initiatives, partnerships and advocacy programmes.

Evidence based approach to control of HIV and TB

The UNAIDS HIV prevention strategy advocates the important step of ‘know your epidemic’ i.e. know who is at risk, who is being infected, which communities are most affected, etc. It is simply not possible to devote adequate resources to every person in an epidemic; detailed knowledge of the TB and AIDS epidemics will assist in making strategically important decisions on the deployment of resources to maximise impact. This requires serological and behavioural surveillance in sentinel groups and communities as well as knowledge of what prevention tools and treatment approaches are effective in different settings in combating HIV. Similarly, active surveillance for both drug susceptible and resistant TB is a critical need and will help more rational deployment of TB targeted resources. Much of these data are already available for HIV, but not for TB. South African scientists have had few, if any, opportunities to provide and interpret the available data for policy-makers and planners to benefit planning and resource allocation in the response to the AIDS and TB epidemics. Reversing the past antagonism between scientists and the political leadership in the country, a new partnership based on mutual respect is needed between policy makers, planners and researchers to help develop the information base to guide action and monitor performance.

Sustainable development of the health care service

The extent to which the South African health care service is dysfunctional, is generally underestimated. The national department of health should provide clear leadership in addressing the failing health care systems. While ring-fenced resources for AIDS from the National Department of Health have expanded considerably from R676 million to R3.6 billion at an average annual rate of 24.8 % over a seven-year period (42), an increase in dedicated funding is required for building the physical infrastructure to overcome years of neglect and under-funding.

The more pressing challenge is to establish properly functioning management systems in each health service and to focus on addressing deficits in human resources. Human resource capacity can be increased through in-service training, increased output from training institutions of health care workers competent to work in primary health care services, task shifting, increased flexibility in health services roles, and a greater reliance on community based health care workers. Greater resources should be allocated to strengthen the management capacity at all levels to ensure integration of TB and HIV into primary health care services. There is a need to ensure that basic systems of staff performance management, individual staff accountability and procurement of supplies are in place. Without this, it will not be possible to provide patient-centred and patient-friendly services that remove the barriers to diagnosis and treatment access. Health care workers bear a high burden of TB and HIV. Strategies must be implemented to ensure that health care workers remain healthy, motivated and productive and are not lost due to illness, death or migration into other sectors because of stigma and fear of being exposed to potentially untreatable TB. Skilled staff can be retained within the primary health care services by providing market related salaries, ongoing training and well equipped, safe, health care facilities to work in. The cross-cutting issues of leadership, funding, human resources, management capacity, infrastructure and training are dealt with in more detail in the final paper of this series on Health in South Africa.

Priority action steps to achieve TB control

What proven interventions should be prioritized and scaled up in order to gain control of TB in South Africa? The cornerstone of TB control remains the detection and cure of new infectious TB cases under a DOTS programme. Integration of TB and HIV services and rapid and

appropriate management of drug resistant TB are also priorities for TB control. The steps outlined below prioritize these interventions in order to make the best use of limited resources.

Step 1: Improve the TB cure rate to 85%—A high cure rate is essential to interrupt the ongoing transmission of TB. South Africa's treatment success (cure or treatment completion) rate for new smear positive TB cases needs to increase from 74% to the WHO minimum target of 85% (43). Mathematical models (44,45) suggest that improving cure rates to 85% will reduce TB incidence and mortality. Each health care facility needs to establish its current cure rate and develop a locally appropriate plan to achieve the target within a specified period. Central policies to support local action should be considered, for example, the use of once-off cash incentives conditional on successful completion of TB treatment.

Step 2: Improve the TB case detection rate to 70%—A high detection rate of new infectious TB cases under a DOTS programme is essential to reduce the duration that TB cases remain infectious and undiagnosed in a community. South Africa's case detection rate needs to increase from 62% to the WHO target of 70% (43). Modelling (46,47) the impact of improved cure rates on TB control show that this is substantially enhanced when it is combined with improved case detection. Case detection can be improved by: i) ensuring that the presence or absence of TB is established in every symptomatic patient presenting to health services, ii) provider initiated intensified TB case finding in all HIV-infected individuals attending health services, iii) active screening of household contacts of infectious TB cases and iv) identifying high TB prevalence communities and initiating community programmes to promote the presentation of enquiry to identify individuals with respiratory symptoms for TB investigation. Laboratory services will need to be strengthened to cope with the increased load resulting from intensified case finding.

Step 3: Integration of TB and HIV services so that 90% of TB patients are offered an HIV test and 90% of HIV positive patients are screened for active TB—HIV services should be an integral component of TB care and include provider-initiated HIV testing, cotrimoxazole chemoprophylaxis and ART, if required. It is estimated that 10,000 deaths may be averted each year if ART is initiated in TB-HIV co-infected patients with CD4 counts below 500 (39). TB services should be an integral component of HIV care and include a strong emphasis on prevention of HIV-associated TB using ART in combination with the WHO 3I's strategy of Intensified TB case finding, Isoniazid preventive therapy (IPT) and TB Infection control (48). A meta-analysis of randomized controlled trials show that IPT in HIV-infected individuals may reduce TB by 33% overall and by 64% in individuals with documented TB infection (49). Mathematical modelling suggests that wide scale roll out of IPT alone may be relatively ineffective at improving TB control, but is highly synergistic when combined with improved detection and cure and may thereby have a long-term population level impact (47).

Step 4: Identification and treatment of drug resistant TB so that 85% of re-treatment TB cases have culture and drug-susceptibility testing—While the first priority is to prevent the emergence of drug-resistant TB by ensuring high cure rates of drug susceptible TB in step 1 above, the reality of widespread drug resistant TB in South Africa requires the implementation of culture and drug-susceptibility testing in at least 85% of re-treatment cases and, when indicated, in new TB cases. A mathematical model (50) suggests that implementing culture and drug susceptibility testing on 37% of new TB cases and 85% of retreatment cases will save approximately 50,000 lives, avert 7,721 (14%) MDR-TB cases and prevent 46% of MDR-TB deaths. However, the model also estimated that there would be no impact on incidence of XDR-TB.

In order to achieve the maximum impact on TB control the four interventions above need to be combined (47). By meeting the targets for TB detection and cure, TB and HIV service

integration and drug resistance detection, will place South Africa on the correct trajectory towards meeting the MDG6 for reducing TB incidence and mortality.

Priority action steps to achieve HIV prevention

The priority steps for HIV prevention are predicated on the urgent need to impact on both risk factors and underlying vulnerability, especially in young women and unborn children.

Step 1: ‘Know your epidemic’—A key lesson from three decades of responding to the HIV epidemic is the importance of knowledge of and a common understanding of the key drivers and risk factors in the HIV epidemic at a local and country level. South Africa has an unenviable amount of data on HIV prevalence and incidence ranging from sentinel surveillance, population based surveys, longitudinal cohort studies and projections based on mathematical models. These data however remain piecemeal and disparate and national consensus on nature and priorities in the HIV epidemic in South Africa has been lacking. The first step is the synthesis of all of the available data to generate a clear and coherent picture of the spatial distribution, demographic features, risk factors and key drivers of the epidemic. A key challenge within South Africa’s generalized epidemic is identification of the main reasons for the substantial age differential in partnering patterns (Figure 2) where young women and older men have the highest HIV incidence rates. In the current post-denialism era, the opportunity is now available for policy makers and scientists to come together to generate a common detailed and nuanced understanding of the epidemic to guide evidence based prioritisation for effective prevention of HIV.

Step 2: Scale-up of known effective behavioural, pMTCT and HIV testing interventions—The scale up of known prevention interventions, even in the absence of any new prevention technologies, could have a substantial impact on the trajectory of the HIV epidemic (51). While there has been good progress on condom promotion, blood donation screening, post-exposure prophylaxis provision for health care workers and universal precaution implementation, South Africa ranked poorly (Table 2) for its overall prevention response in relation to the government’s own stipulated targets. PMTCT coverage, which is a simple cost effective strategy with substantial life saving benefit needs to be increased from the current 60% to 95%. To reduce sexual transmission much more is needed on behaviour change programmes to promote abstinence, avoidance of concurrent multiple partners, avoidance of large age differential partnering patterns, and knowledge of HIV status. It is now widely recognized that individual interventions usually have modest effects, while combination interventions may have a synergistic outcome, especially if there is saturation of the target population. The choice of prevention modalities to make the combined intervention and the target populations will need to be informed by a detailed understanding of the HIV epidemic.

Step 3: Expanding the prevention ‘toolbox’: implement circumcision for HIV prevention—South Africa is at the forefront of clinical trials testing new prevention technologies but is ineffectual in translating the research findings into practice. A case in point is medical male circumcision. In 2005, the South African study in Orange Farm showed that circumcision is effective in preventing HIV infection (52) and in 2008 the WHO released its recommendations for the implementation of circumcision for HIV prevention. South Africa needs to urgently develop a policy and implementation plan to make circumcision a routine part of HIV prevention. Mathematical models estimate that 6 million infections could be averted by the progressive rollout of circumcision across sub-Saharan Africa over the next two decades (53).

Step 4: Reaching beyond HIV risk to HIV vulnerability: legislative interventions on sex work, gender violence and migrant labour—While steps 2 and 3 above are

essential components of the response guided by detailed knowledge of the HIV epidemic, a more fundamental approach is needed to address underlying contextual issues of poverty, gender and power disparities. As part of this, three structural interventions could impact substantially on vulnerability to achieve sustained reductions in HIV transmission; i) legalization and regulation of sex work, ii) concerted law enforcement on rape and violence against women in terms of current legislation and iii) tax incentives to companies who join public-private housing partnership to reverse the conjugal instability and family separation created by the migrant labour system. Gender inequity and migrant labour are key drivers in the South African HIV epidemic. While these require long-term social engineering, the three proposed interventions are a useful starting point.

Priority action steps for HIV treatment

Following a belated decision by the South African government to provide ART, the ART rollout has steadily gathered momentum and is now the biggest treatment programme in the world. However, the unmet need for HIV treatment remains substantial and steps need to be taken to improve HIV control through prevention and treatment.

Step 1: Scale up HIV testing to 20% of the South African population each year

—The biggest obstacle to HIV treatment access is lack of knowledge of HIV status. HIV testing needs to be expanded as it is an essential entry point to ART programmes. South Africa is currently reaching an estimated 7% of the population per year - this needs to increase to 20% per year. To achieve this, provider initiated HIV testing should be the standard of care at all health care facilities such that all those who come into contact with the health service are afforded the opportunity to know their HIV status and to access treatment and prevention interventions. This needs to be accompanied by a CD4 count to identify those HIV infected individuals eligible for ART. This will require the capacity to do about 9 million rapid HIV tests 2 million laboratory CD4 counts annually.

Step 2: Initiate ART in all patients with a CD4 count below 350 cells/mm³—

Changing the current guideline of initiating ART in patients with CD4 below 200 cells/mm³ to below 350 cells/mm³ has substantial potential therapeutic and preventive benefits. Mathematical models (54) suggest that changing the CD4 cell count threshold from 200 cells/mm³ to 350 cells/mm³ may decrease mortality by 28% per year by 2010. Moreover, the model suggests that HIV incidence would also decrease by up to 10% over a ten year period (54). The current guideline to initiate ART in patients with CD4 counts below 200 cells/mm³ was widely supported when initially created, in light of concerns about health service capacity and the inexperience of health care providers with AIDS treatment at the time. However, increasing capacity through down-referral of stable ART patients and the continuing increase in accredited ART rollout sites, together with the potential to substantially reduce mortality further and impact HIV transmission has led to the timeous recommendation by the South African HIV Clinicians Society to initiate ART in all patients with a CD4 count below 350 cells/mm³ (55).

Consideration should also be given to the potential benefits of even earlier initiation of ART that have been highlighted by observational data from large scale ART programmes in the developed world (56). In addition, models (57) based on South African data have suggested a substantial prevention benefit would be derived from universal HIV testing with immediate initiation of ART regardless of CD4 count.

Step 3: Maintain viral suppression in 90% of patients on ART—The South African ART rollout programme has been able to achieve greater than 90% viral suppression in patients receiving treatment (33). This success is testimony to the quality of AIDS treatment services

emanating from the accreditation process, the patient-centred approach, treatment literacy and intensive counselling. With an incrementally growing service burden to provide ART, integrated TB services, cotrimoxazole prophylaxis, isoniazid prophylaxis and an increasing number of patients in pre-ART care, HIV treatment services will need to maintain their efforts and vigilance to continue the initial successes. HIV treatment programmes need to continue their successful efforts to achieve viral suppression in 90% of existing patients in long term treatment and new patients initiating ART. This will reduce the incidence of opportunistic infections, hospital admissions, risk of ART resistance and the need for alternate ART regimens.

Step 4: Integrate HIV prevention and treatment services—The historical separation of treatment and prevention services as well as the focus of prevention only on those not already infected is counterproductive in a setting where over 30% of the sexually active population is already infected with HIV. Since the HIV infected sub-population is the source of new HIV infections, HIV treatment programmes have an important role to play in HIV prevention (58). For example, HIV treatment programmes need to include the full array of sexual and reproductive health services including access to contraception, sexually transmitted infection treatment, abortion, and PMTCT services. In addition, HIV treatment should be an integral component of HIV prevention programmes as availability of treatment is a potent promoter for the uptake of HIV testing and treatment induced low viral loads in infected persons could reduce HIV transmissibility. Modelling integration of prevention into treatment programmes suggests that as many as 29 million infections could be averted worldwide by 2020 (59). In this context, HIV testing needs to be expanded. Provider initiated HIV testing should be the standard of care at all health care facilities such that all those who come into contact with the health service are afforded the opportunity to know their HIV status to provide early treatment access and prevention interventions.

CONCLUSION

South Africa is experiencing the world's worst HIV and TB epidemics. The current epidemic trajectory suggests worsening of both epidemics with substantial increases in morbidity and mortality and the devastating impact of the premature loss of lives and economic productivity. The intertwined epidemics of HIV and TB have exacerbated each other and have been further compounded by the growth of MDR-TB and the emergence of XDR-TB.

Clearly, substantial bold action is needed. Having missed past opportunities, South Africa cannot afford to miss the window of opportunity created by the 2009 elections. Decisive action is needed to inculcate and nurture the necessary political will and commitment and to adopt an evidence-based approach to formulating policies and programmes. Implementation of our proposed four steps for TB control, HIV prevention and HIV treatment as part of the aspirational 5 year TB(23) and HIV(32) Strategic Plans will depend on the government's ability to build partnerships and to invigorate the development of the health care services.

This is a complex task which will need a long-term perspective with the prospect of many difficult and, perhaps, unpopular decisions. Twenty five years into the HIV epidemic and the country still awaits the opportunity to enjoy the fruits of freedom from racial oppression and tyranny without the looming spectre of the terrible twin epidemics of TB and HIV.

key messages panel

- i. Worldwide, South Africa has the highest number of people living with HIV/AIDS, representing one quarter of the disease burden in sub-Saharan Africa and one sixth of the global disease burden.

- ii. South Africa has one of the worst TB epidemics in the world; with high disease burden, incidence rates, HIV co-infection rates and growing MDR- and XDR-TB epidemics.
- iii. While South Africa has well formulated and broadly accepted National Strategic Plans for both AIDS and TB, inadequate will and capacity to deliver on many of the urgently needed health care interventions is a major deficiency in the country's response to the dual epidemics.
- iv. The AIDS epidemic has already made a lasting impression on and will continue to irrevocably shape the South African health service for decades to come. The successful scale-up of antiretroviral therapy provision, leading to the creation of the world's largest AIDS treatment programme, is the engine driving innovation to strengthen the overall health service.
- v. With the era of governmental denial and complacency, with its substantial cost in premature loss of life, now in the past, the newly elected South African government has the opportunity to actively support and adequately resource the implementation of an evidence-based public health policy to turn the tide on the TB and HIV epidemics.

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Figure 1.
Historical overview of major events in the AIDS and TB epidemics in South Africa 1989 – 2007

Figure 2.

Figure 3.
Age and gender disparities in HIV infection in South Africa

Table 1

Selected indicators of the AIDS & TB epidemics in South Africa in 2006

INDICATOR	
<i>Number of people living with HIV in South Africa</i>	5,400,000
<i>HIV Prevalence in women attending antenatal clinics</i>	29.1% (28.3 – 29.9)
<i>HIV prevention</i>	
Number of people receiving voluntary counseling and HIV testing in the 2006/2007 financial year	1,610,775
Number of male condoms distributed	376 million
Number of female condoms distributed	3.6 million
Number of pregnant women who received nevirapine	186,646
Proportion of pregnant women eligible for nevirapine who received it	186 646/302 000 (62%)
<i>HIV treatment</i>	
Number of patients initiating antiretroviral therapy	273,400
Proportion of patients eligible for antiretroviral therapy who received it	351 489/922 314 (38%)
<i>Number of AIDS deaths</i>	345,640
<i>Number of people living with TB</i>	482,000
<i>TB case notification rate</i>	628/100,000
<i>TB treatment</i>	
Number of notified TB cases	341,165
Proportion of TB cases cured (2005)	69 545/119 906 (58%)
Number of cases completing TB treatment but without sputa to confirm cure (2005)	15 587/119 906 (13%)
<i>Number of TB deaths</i>	105,000
<i>TB/HIV Co infection rate</i>	337 400/482 000 (70%)

Sources:(1), (42), (60), (24)

Table 2

Scorecard rating of South Africa's response to AIDS against commitments made by government compared to ratings for five neighboring countries as well as Brazil and India. Key TB indicators (2007) are also provided for these countries. Source: (41), (43)

HIV element*	Neighbouring Countries						Other developing countries	
	South Africa	Botswana	Malawi	Mozambique	Namibia	Zimbabwe	Brazil	India
Coordination	A	A	A	A	A	B	A	A
Prevention	C	A	D	C	B	D	F	F
Civil society	C	C	D	C	B	C	B	C
Human Rights Mainstreaming	C	D	A	C	B	B	A	C
Data collection	D	E	C	D	D	D	E	C
Treatment	D	B	D	D	A	E	B	E
Financing	E	C	D	E	C	E	D	F
Most at risk	F	F	F	E	F	F	E	F
Refer to <i>AIDS Accountability International. The HIV/AIDS Country Scorecard. Available from : http://aidsaccountability.org/ for a detailed explanation of each element and how the scores were derived.</i> A (81–100%), B (61–80%), C (41 – 69%), D (21–40%), E (0–20%), F (no data reported)								
TB indicators								
Population (million)	48.6	1.9	13.9	21.4	2.1	13.3	191.8	1 169.0
TB incidence (per 100 000 per year)	948	731	346	431	747	782	48	168
TB mortality (HIV– and HIV+ (per 100 000 per year))	230	194	102	127	102	265	4	29
HIV prevalence in incident TB cases	73	68	68	47	67	69	14	5
Treatment success for new smear positive cases (%)	74	72	78	83	76	60	72	86

Panel 1: History of the South African Response to HIV/AIDS and TB

Under apartheid fragmentation of health services along racial lines undermined TB control and led to poor coordination of the TB control programme. However, voluntary organizations such as the South African National Tuberculosis Association (SANTA) and the Friends of the Sick Association (FOSA) served a vital role in providing supportive, preventive and curative services to TB patients and their families.

From 1982, when the first case of AIDS was described in South Africa to 1994, little was done by the apartheid government to contain the HIV epidemic. Public media campaigns against AIDS ignored the epidemic among men who have sex with men (MSM) and promoted racial stereotypes, fear and stigma. The need to prioritize HIV prevention in South Africa was first publicly acknowledged in 1990 by the 'Maputo Statement on HIV and AIDS in Southern Africa', issued jointly by the banned and exiled African National Congress (ANC) with a range of in-country anti-apartheid organisations, including the National Medical and Dental Association (NAMDA), South African Health Workers Congress (SAHWCO), and the AIDS consortium. A major step forward was the creation, in 1993, of the National AIDS Convention of South Africa (NACOSA), a co-ordinating body involving representatives of the apartheid government and representatives of anti-apartheid AIDS activists.

Following the first democratic election in 1994, South Africa's TB control policies have been brought in line with World Health Organization (WHO) policies. In addition, the NACOSA Strategic Plan, which provided the first credible response to the HIV epidemic, was adopted by the Mandela government and prioritised as one of the ANC's Reconstruction and Development Programme Lead Project (Figure 1). However, AIDS and TB were not accorded high profile political support during this period, including by President Mandela, as the country grappled with the enormous challenge of establishing a new politically stable non-racial society. The Mandela government's response to AIDS was subsequently undermined by the 1996 controversy surrounding Sarafina II, an anti-AIDS play, Cabinet support for the toxic industrial solvent Virodene as a cure for AIDS in 1997 and the government's refusal in 1998 to fund the provision of antiretroviral zidovudine for pregnant women to prevent mother-to-child transmission of HIV. Spurred by the need for community action for AIDS treatment, The Treatment Action Campaign (TAC), led by Zackie Achmat, was formed in 1998.

While controversy raged on AIDS policy, the government continued making steady progress on TB control by implementation of the DOTS strategy, establishing a standardised recording system and strengthening central coordination of the TB control programme and disease control management at all levels. Despite this, TB cases continued to increase, fuelled by the impact of AIDS.

Following the second democratic elections in 1999, the personal support of President Mbeki and his Minister of Health, Manto Tshabala-Msimang for unorthodox AIDS denialist theories placed the government at odds with the general public including doctors and AIDS activists. There were public contestations on the etiology of AIDS, the reliability of HIV testing, the safety and efficacy of antiretrovirals and the statistics on morbidity and mortality due to HIV. On 26 March 2000, President Mbeki convened an International AIDS advisory panel, comprising 16 AIDS dissidents (who believe that HIV does not cause AIDS) and 16 AIDS scientists, with the mandate of informing him and the government on the most appropriate response to HIV. This marked the lowest point in the government's response to the HIV epidemic and served to rally world opinion through the Durban Declaration and the XIIIth International AIDS Conference, held in 2000 in South Africa. This brought community organisations, trade unions, activist groups like the TAC, scientists and health care workers together as a social movement with a clarion call to put an end to the injustice of global inequity in access to AIDS treatment.

Using the momentum of the 2000 AIDS Conference, AIDS activists repeatedly challenged health service providers, government and pharmaceutical companies to do more to bring AIDS treatment to poor people through petitions, marches, community mobilisation, and by pointing to the success of the pilot Medicins Sans Frontieres treatment clinic in Khayelitsha, Cape Town. Importantly, the AIDS lobby groups extended their 'taking to the streets' approach to legally challenging the government for failing to uphold the health rights enshrined in the South African constitution. In 2001, the Constitutional Court ruled against the government instructing it to provide nevirapine to all HIV positive pregnant women in South Africa in a landmark judgement that placed the onus on government for the 'progressive realisation' of the right to health care. Community mobilisation combined with legal challenges were repeatedly used to coax Tshabala-Msimang's Ministry of Health to make better progress on the provision of nevirapine and further to provide AIDS treatment.

In a surprising turnaround, the Mbeki government decided in 2003 to provide antiretroviral therapy for free in public health services. Although this decision should have been made three years earlier, which could have saved an estimated 330,000 lives, this policy shift was widely applauded. In 2004, the government declared TB a national emergency and adopted a crisis plan with the goal of raising the political commitment and securing additional financial resources for TB control.

For most of Mbeki's second term, he avoided AIDS but his Minister of Health Tshabala-Msimang lurched from one controversy to another in her attempts to undermine the AIDS treatment roll-out and promote untested and unlicensed traditional remedies and vitamin supplements as alternatives to 'Western' treatment of AIDS. Her insensitivity was manifest at the International AIDS Conference in Toronto, Canada where the South African government's stand at the conference exhibition hall displayed, at her insistence, food such as garlic, beetroot and lemons for AIDS treatment instead of antiretroviral therapy. Following the Toronto incident, the government delegated overall responsibility for the AIDS response to the Deputy President, Mlambo-Ngcuka. The Deputy President working closely with Deputy Minister of Health, Madlala-Routledge, proceeded immediately to re-build bridges with civil society, reviving the previously moribund South African National AIDS Council (SANAC) in 2006.

The continually growing epidemic of TB, alongside the HIV epidemic, placed a huge strain on already overstretched and under-developed health services leading to sub-optimal TB cure and treatment completion rates. The situation

Panel 1: History of the South African Response to HIV/AIDS and TB

was compounded by continuing weak central coordination, lack of accountability of the provinces to the national TB control programme, inadequate management capacity at all levels resulting in sub optimal implementation of DOTS, minimal integration of TB/HIV activities, inadequate MDR TB management and severely limited to absent infection control policies, facilities and practices. The emergence of an almost uniformly fatal epidemic of XDR-TB in 2006 in HIV infected patients in a small rural village in Tugela Ferry, KwaZulu-Natal sounded a wake-up call for an even more concerted effort for TB control and importantly to improve TB-HIV linkages and implement measures in AIDS clinics and hospital wards to reduce the nosocomial spread of TB.

In 2007, Madlala-Routledge's outspokenness eventually led to her dismissal by Mbeki. By then, however, a new 5-year AIDS National Strategic Plan had been developed and adopted by SANAC through an inclusive process involving scientists and activists known to be critics of Mbeki. In parallel, the South African TB Strategic Plan was adopted in 2007 with the goal of providing TB patients easy access to effective, efficient and high quality diagnostic, treatment and care services.

A few months later, In 2008, Mbeki was forced to resign from the presidency and the new Minister of Health Barbara Hogan in the Motlanthe government set about charting a new course for the country's response to AIDS. In a newfound spirit of hope, the government ushered in by the 2009 elections is better prepared to implement the widely supported 5 year National Strategic Plans for both AIDS and TB will require major investments in building capacity, infrastructure and partnerships to rapidly scale an evidence approach for the AIDS and TB control.

Panel 2: SOUTH AFRICAN ACHIEVEMENTS IN AIDS AND TB	
<i>Increase in male condom distribution and introduction of the female condom</i>	The distribution of public sector condoms has been a key part of the government's HIV prevention strategy; the number of male condoms distributed by the government increased from 8 million in 1994 to an estimated 376 million in 2006 (42). Further, the female condom was introduced in 1996 to increase HIV prevention options for women; in 2006, 3.6 million female condoms were distributed.
<i>Expansion of TB control Efforts</i>	The DOTS programme was adopted as the standard of care for TB in 1995 (though its implementation has been patchy), surveillance for TB drug resistance has been enhanced and programme performance and patient outcomes are more closely monitored through the TB register. Further, there is improved national co-ordination as well as alignment of national policies with global best practice. The declaration of TB as a national emergency has focused greater political commitment and emphasis on the TB crisis in South Africa
<i>Research contributions in AIDS and TB</i>	Researchers in South Africa have made several major scientific contributions HIV and TB prevention, pathogenesis, treatment and control. There are at least fifteen well established large HIV and/or TB research centres in South Africa, most located in Universities. The largest funders of research in these areas are the US National Institutes for Health, US Agency for International Development and the Wellcome Trust.
<i>Scale up of the free AIDS Treatment Programme</i>	Since the government decision in November 2003 to provide free AIDS treatment, an estimated 488,739 people were enrolled in the public sector rollout programme within 4 years. South Africa now has the world's largest AIDS treatment programme even though it has only reached about 35% of those who should be on ART. Financial support from the US President's Emergency Program for AIDS Relief and the Global Fund for AIDS, Tuberculosis and Malaria are important contributors to the success of the ART rollout.
<i>Development of the National Strategic Plans (NSP) for HIV and TB</i>	The AIDS NSP for 2007–2011(32) has four priorities. These are i) prevention, ii) treatment, care and support, iii) legal and human rights and iv) research, monitoring and evaluation. The two over-arching objectives to reduce the HIV incidence rate by 50% and initiate antiretroviral therapy in 80% of those who need it. The TB NSP(23) sets out to i) strengthen the implementation of the DOTS strategy, ii) address TB and HIV, MDR and XDR-TB, iii) contribute to health systems strengthening, iv) work collaboratively with all care providers, v) empower people with TB as well as communities, vi) coordinate and implement TB research, and vii) strengthen infection control.