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

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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

The concomitant epidemics of HIV and tuberculosis present a major public health problem in South Africa. Despite constituting just 0·7% of the world's population, South Africa accounted for 17% (about 5·5 million people) of the global burden of HIV infection in 2007.^{1,2} Furthermore, as a result of the convergence of a major pre-HIV-era tuberculosis epidemic, rising numbers of tuberculosis cases associated with the maturing HIV epidemic, and growing resistance to antituberculosis drugs, South Africa now has one of the most serious tuberculosis epidemics in the world (table 1).

The social, economic, and environmental conditions created by apartheid⁶—such as overcrowded squatter settlements, migrant labour, and deliberately underdeveloped health services for black people—provided a favourable environment for efficient transmission of HIV and tuberculosis.⁷ Hundreds of thousands of black people working in South Africa's cities were forced to live in overcrowded, poorly ventilated, single-sex hostels. These hostels were often served by sex workers (euphemistically referred to as “town wives”). The oscillatory migration lifestyle of these workers—ie, living temporarily in the cities and on the mines, with regular visits to wives and families in rural homelands—was key to the spread of tuberculosis⁸ and sexually transmitted infections⁹ in the first half of the 20th century.

Because these historical conditions continue to define the nature of the HIV and tuberculosis epidemics in South Africa, both diseases are crucial public health challenges in the post-apartheid era. Moreover, their control is fundamental to economic growth and development in the country's young democracy.¹⁰

Unfortunately, South Africa's response to the epidemics during the past decade has been marked by denialism, ineptitude, obtuseness, and deliberate efforts to under-

Key messages

- Worldwide, South Africa has the highest number of people living with HIV/AIDS, representing a quarter of the disease burden in sub-Saharan Africa and a sixth of the global disease burden.
- South Africa has one of the worst tuberculosis epidemics in the world, with high disease burden, incidence rates, and HIV co-infection rates, and growing epidemics of multidrug-resistant and extensively drug-resistant tuberculosis.
- Although South Africa has well formulated and broadly accepted Strategic Plans for HIV/AIDS and tuberculosis, insufficient political will and inadequate capacity to deliver on many of the urgently needed health-care interventions are major deficiencies in the country's response to the epidemics.
- The HIV/AIDS epidemic will continue to shape the South African health service. The successful scale-up of anti-retroviral therapy provision, leading to the creation of the world's largest HIV/AIDS treatment programme, is key to stimulating innovation to strengthen the overall health service.
- 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 effectively control the HIV and tuberculosis epidemics.

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| National data | |
|-----------------------------------------------------------------------------------------|-----------------------|
| HIV | |
| People living with HIV (n) | 5 400 000 |
| HIV prevalence in women attending antenatal clinics (% [95% CI]) | 29.1% (28.3–29.9) |
| HIV prevention | |
| People receiving voluntary counselling and HIV testing (n)* | 1 610 775 |
| Male condoms distributed (n) | 376 000 000 |
| Female condoms distributed (n) | 3 600 000 |
| Pregnant women who received nevirapine (n) | 186 646 |
| Pregnant women eligible for nevirapine who received it (n/N [%]) | 186 646/302 000 (62%) |
| HIV treatment | |
| Patients starting ART (n) | 273 400 |
| Patients eligible for ART who received it (n/N [%]) | 351 489/922 314 (38%) |
| Deaths from AIDS (n) | 345 640 |
| Tuberculosis | |
| People living with tuberculosis (n) | 482 000 |
| Tuberculosis case notification rate (per 100 000 population) | 628 |
| Tuberculosis treatment | |
| Notified tuberculosis cases (n) | 341 165 |
| Tuberculosis cases cured (n/N [%])† | 69 545/119 906 (58%) |
| Patients completing tuberculosis treatment but without sputa to confirm cure (n/N [%])† | 15 587/119 906 (13%) |
| Tuberculosis deaths (n) | 105 000 |
| HIV/tuberculosis co-infection rate (n/N [%]) | 337 400/482 000 (70%) |

Data from references 1, 3–5. ART=antiretroviral therapy. *Data from the 2006/07 financial year. †Data from 2005.

Table 1: Selected indicators of the HIV/AIDS and tuberculosis epidemics in South Africa, 2006

mine scientific evidence as the basis for action (panel 1 and figure 1).^{12,13} The change in administration in 2008, and the subsequent elections in 2009, however, have created new hope that the country will rise to the challenges of HIV and tuberculosis. Obtaining the best evidence available and taking decisive action are key to controlling both diseases. This report provides a historical perspective and overview of South Africa's evolving HIV and tuberculosis epidemics and how the government has responded to them, and concludes with a prioritised set of strategic steps for HIV and tuberculosis control.

The evolving HIV epidemic in South Africa

The HIV epidemic in South Africa has been characterised by high prevalence rates in young women (figure 2). In 1992, HIV prevalence rose most rapidly in teenage girls while remaining low in teenage boys. Peak HIV prevalence in men occurred at an age 5–7 years older than it did in women.⁹ The age-differential partnering pattern, in which older men partner with younger women, was first reported in a community-based HIV survey in 1992 and has been one of the key drivers of high rates of HIV transmission in South Africa.¹⁴ In 2006, a national community-based survey found that the age-specific HIV prevalence in young women (25–29 years) was more than 30%.¹⁵

Since the first cases of AIDS in 1982, the HIV epidemic in South Africa has evolved through the following four phases.

Concentrated epidemic phase (1982–87)

The first cases of AIDS in South Africa were identified in men who have sex with men. The widespread belief that AIDS was a homosexual 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 homosexual and bisexual community to proactively address these challenges was the precursor to human rights responses to the epidemic through the use of the legal system by the AIDS Law Project and subsequently through social mobilisation by the Treatment Action Campaign (panel 1).

Between 1983 and 1985, about 100 patients with haemophilia acquired HIV through contaminated blood and blood products.¹² The government immediately set up a fund to compensate the families of these patients. Although few families accessed the financial compensation available, it led to moral judgments by society that distinguished “innocent victims” who deserved compensation from those who were infected because of “immoral behaviours” and therefore not deserving of compensation. This type of thinking later shaped prevention of mother-to-child transmission policies, in which newborn babies, but not their mothers, were viewed as innocent victims.

The virus in haemophiliacs and men who have sex with men 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 any infected individuals.¹⁶ In 1986, a survey in 29 312 mine workers identified three HIV-infected men, all of whom were migrant workers from countries to the north of South Africa.¹⁷ The forced repatriation of these workers and the subsequent government policy to bar entry of HIV-infected migrant workers set the tone of the apartheid-era antihuman rights response to the epidemic.¹⁸

Initiation of the generalised epidemic (1988–94)

Whereas HIV subtype B, the dominant subtype in western Europe and the USA, continued to spread among men who have sex with men, 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 the prevalence of HIV infection, with a doubling time of a little over 1 year.¹⁹ HIV prevalence increased in pregnant women from 0.8% in 1990 to 7.6% in 1994.²⁰ Since 1990, heterosexual transmission has been the dominant mode of HIV transmission between adults in South Africa, with a concomitant epidemic in infants born to HIV-infected mothers. The spread of HIV has shown substantial geographical variation across the country (figure 3); the highest rates of HIV infection among women attending antenatal clinics have been reported in the provinces of KwaZulu-

Natal and Mpumalanga. The apartheid government labelled AIDS a “black disease” to reinforce racial prejudices about black sexual behaviour, and used fear as the main tactic in their media. An important aspect of the government’s response to HIV during this period was profiling based on race and sexual orientation, which led to the exclusion of men who have sex with men and black people from donating blood.

Rapid spread of HIV (1995–2000)

National seroprevalence surveys in pregnant women showed that HIV prevalence rose from 7·6% in 1994 to 20·5% in 2000, with wide variations in prevalence between provinces (figure 3) and local communities. HIV prevalence in young pregnant women (aged 20–24 years) in a rural KwaZulu-Natal community rose from 21·1% in 1995, to 39·3% in 1998, and 50·8% in 2001.²⁰ Phylogenetic mapping of HIV showed that a diversity of clade C viruses were circulating in South Africa since 1990;²² several mini-epidemics associated with each virus eventually coalesced, creating a generalised, well established HIV epidemic throughout the country. The migrant labour system created suitable social and behavioural conditions for the introduction of multiple viruses from several neighbouring countries to spread rapidly in South Africa.^{23,24} Multiple partnerships, (especially concurrent multiple partnerships) became the norm (town wife and rural wife) for a large segment of the population. Migrant couples, in which at least one partner is a migrant worker, were more likely than were non-migrant couples to have one or both partners infected with HIV (35% vs 19%; $p=0\cdot026$).²⁵

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).¹ However, the HIV incidence rate in 2006 in this group was estimated to be in excess of 5% per year.¹ Continuing high HIV incidence rates combined with the rising mortality rates resulted in progressively smaller increases in HIV prevalence during this period. By 2006, mortality exceeded the number of new HIV infections, despite the development of a large antiretroviral therapy (ART) programme. Life expectancy in South Africa had declined by almost 20 years, and infant and maternal mortality were at their highest rates ever.²⁶ Today, most adult South Africans are dying in the economically active period of their lives. Mean life expectancy is 48·4 years for men and 51·6 years for women.²⁷ These reversals in trends of key markers for monitoring the Millennium Development Goals provide some indication of the enormity of the developmental challenges that South Africa will be facing in the near future if the current epidemic trajectories are not halted or reversed.

The tuberculosis crisis in South Africa

Tuberculosis was introduced into South Africa in the 17th century by the arrival of European immigrants mainly from Britain and the Netherlands, many of whom

Panel 1: History of the South African response to HIV/AIDS and tuberculosis

Under apartheid, fragmentation of health services on a racial basis undermined tuberculosis control and led to poor coordination of the tuberculosis control programme. Voluntary organisations such as the South African National Tuberculosis Association and the Friends of the Sick Association provided supportive, preventive, and curative services to tuberculosis 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 HIV/AIDS ignored the epidemic in men who have sex with men and promoted racial stereotypes, fear, and stigma. The need to prioritise 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) and a range of anti-apartheid organisations, including the National Medical and Dental Association, South African Health Workers Congress, and the AIDS Consortium. In 1993, the National AIDS Convention of South Africa (NACOSA) was created, a coordinating body including representatives of the apartheid government and representatives of anti-apartheid HIV/AIDS activists.

Since the first democratic election in 1994, South Africa’s tuberculosis control policies have been brought in line with WHO policies. The NACOSA AIDS 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 projects (figure 1). However, while the country established a new politically stable non-racial society, HIV/AIDS and tuberculosis were not given high profile political support, including by President Mandela. The Mandela government’s response to HIV/AIDS was undermined by the 1996 controversy surrounding Sarafina II (an anti-AIDS play), Cabinet support for the toxic industrial solvent dimethylformamide (Virodene) as a cure for AIDS in 1997, and the government’s refusal in 1998 to fund the provision of 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, led by Zackie Achmat, was formed in 1998.

Between 1995 and 2005, the government made progress on tuberculosis control through the implementation of the DOTS (directly observed treatment, short course) strategy and a standardised recording system, and by strengthening central coordination of the tuberculosis control programme and disease control management at all levels. Despite this progress, the number of tuberculosis cases continued to rise, fuelled by the AIDS epidemic.

Following the second democratic elections in 1999, the support of President Mbeki and his Minister of Health, Manto Tshabala-Msimang, for unorthodox AIDS denialist theories put the government at odds with the public. There were public disputes on the cause of AIDS, the reliability of HIV testing, the safety and efficacy of antiretroviral drugs, and the statistics on morbidity and mortality due to HIV. On March 26, 2000, President Mbeki convened an international AIDS advisory panel, comprising 16 HIV/AIDS dissidents (who believe that HIV does not cause AIDS) and 16 HIV/AIDS scientists, with the mandate of informing him and the government on the most appropriate response to HIV/AIDS. This action served to rally world opinion through the Durban Declaration and the XIII International AIDS Conference, held in 2000 in South Africa. Community organisations, trade unions, activist groups, scientists, and health-care workers came together as a social movement with a call to put an end to the injustice of global inequity in access to HIV/AIDS treatment.

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HIV/AIDS activists repeatedly challenged health-service providers, government, and pharmaceutical companies to do more to bring HIV/AIDS treatment to poor people through petitions, marches, community mobilisation, and by highlighting the success of the pilot Médecins Sans Frontières treatment clinic in Khayelitsha, Cape Town. The HIV/AIDS lobby groups legally challenged 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. Community mobilisation and legal challenges were repeatedly used to coax the ministry of health to make better progress on the provision of nevirapine and HIV/AIDS treatment.

In 2003, the Mbeki government decided to provide antiretroviral therapy (ART) for free in public health services. Although this decision should have been made 3 years earlier, which could have saved an estimated 330 000 lives, this policy shift was widely applauded. In 2004, the government declared tuberculosis a national emergency and adopted a crisis plan with the goal of raising political commitment and securing additional financial resources for tuberculosis control.

For most of Mbeki's second term, he avoided HIV/AIDS but Tshabala-Msimang lurched from one controversy to another in her attempts to undermine the HIV/AIDS treatment programme and promote untested and unlicensed traditional remedies and vitamin supplements as alternatives to medical treatment of HIV/AIDS. Her insensitivity was manifest at the XVI International AIDS Conference in Toronto, Canada, where the South African Government's stand at the exhibition hall displayed, at her insistence, food such as garlic, beetroot, and lemons for HIV/AIDS treatment instead of ART. Following this incident, the government delegated overall responsibility for the HIV/AIDS response to the Deputy President, Mlambo-Ngcuka, who worked closely with the Deputy Minister of Health, Madlala-Routledge, to revive the previously defunct South African National AIDS Council in 2006.

In 2007, Madlala-Routledge's outspokenness led to her dismissal by Mbeki. By then, the 5-year Strategic Plan for South Africa for HIV/AIDS had been developed and adopted by SANAC through an inclusive process involving scientists and activists known to be critics of Mbeki. In parallel, the Tuberculosis Strategic Plan for South Africa was adopted in 2007 with the goal of providing patients with tuberculosis 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 in the Motlanthe government, the Minister of Health Barbara Hogan set about charting a new course for the country's response to HIV/AIDS. The new government, led by President Jacob Zuma, with Minister of Health Aaron Motsoaledi looks well set to build on the positive tone and spirit that pervaded the April, 2009, national general elections.

had been infected with *Mycobacterium tuberculosis* during the epidemic that had swept through Europe.⁸ The development of South Africa's mining industries in the late 19th century led to the infection of large numbers of previously unexposed black South Africans as a result of poor working conditions, silica dust exposure, overcrowded hostels, and poor nutrition. Oscillatory migration of city workers facilitated the spread of tuberculosis from cities to rural areas.

Unlike HIV/AIDS, tuberculosis is a notifiable disease in South Africa. Tuberculosis incidence rose steadily during the 20th century, peaking first in the 1960s with over 350 cases per 100 000 population per year. A decline during the 1970s²⁸ (possibly an artifact resulting from the

exclusion of data from the black homelands) was followed by a resurgence in the late 1990s. During the apartheid years, the poorly funded and fragmented public sector health services were ill equipped and uncommitted to tackling the tuberculosis epidemic in the indigent and most vulnerable populations. Standard treatment for many patients during the 1970s and 1980s consisted of 12 months or 18 months of inpatient treatment with para-aminosalicylic acid, isoniazid, and streptomycin. Even when ambulatory care became available in the late 1980s, diagnosis and treatment delivery remained health-facility-oriented, making them inaccessible to many of those most in need.

The tuberculosis control programme was strengthened by the introduction of the rifampicin-based directly observed therapy, short course (DOTS) strategy. However, any potential gains in tuberculosis control were countered by the maturing HIV epidemic, which fuelled a sharp rise in tuberculosis notification rates from the late 1990s. Tuberculosis case notification rates have risen by nearly four times, from 163 per 100 000 population in 1986 to 628 per 100 000 population in 2006 (figure 1).¹¹ Furthermore, WHO estimated South Africa's overall annual tuberculosis incidence rate to be 940 per 100 000 population in 2006.²⁴ The difference between the WHO estimate and the actual case notification rate is a reflection of lack of access to tuberculosis diagnostic services and the limitations of current diagnostic methods. In 2006, South Africa reported 341 165 tuberculosis cases, the fourth largest number of cases in the world, after the far more populous countries of India, China, and Indonesia.³

In communities where HIV prevalence exceeds 30% in pregnant women, annual tuberculosis notification rates as high as 1468 per 100 000 population were reported in 2004,²⁹ and continued to increase thereafter. Many cases of tuberculosis are associated with HIV; over 50% of new tuberculosis cases are in patients with HIV co-infection. Even in communities where HIV prevalence has reached a plateau, tuberculosis rates continue to rise because of increasing levels of immunodeficiency.²⁹ Before the emergence of the HIV epidemic, the Western Cape province had the highest rates of tuberculosis. Currently, the number of tuberculosis cases and notification rates are highest in KwaZulu-Natal province (1066 per 100 000 population in 2006), reflecting a combination of the highest HIV prevalence (39.1% in pregnant women in 2006) and the worst tuberculosis programme performance indicators.^{11,21} Historically, tuberculosis notification rates increased with advancing age, with men having a higher tuberculosis burden than women. Today, rates peak in women in their twenties and men in their thirties,²⁹ which reflects the age distribution of HIV infection.

Tuberculosis drug resistance—a result of poor performance of control programmes and low cure rates over many years—has emerged as a very serious

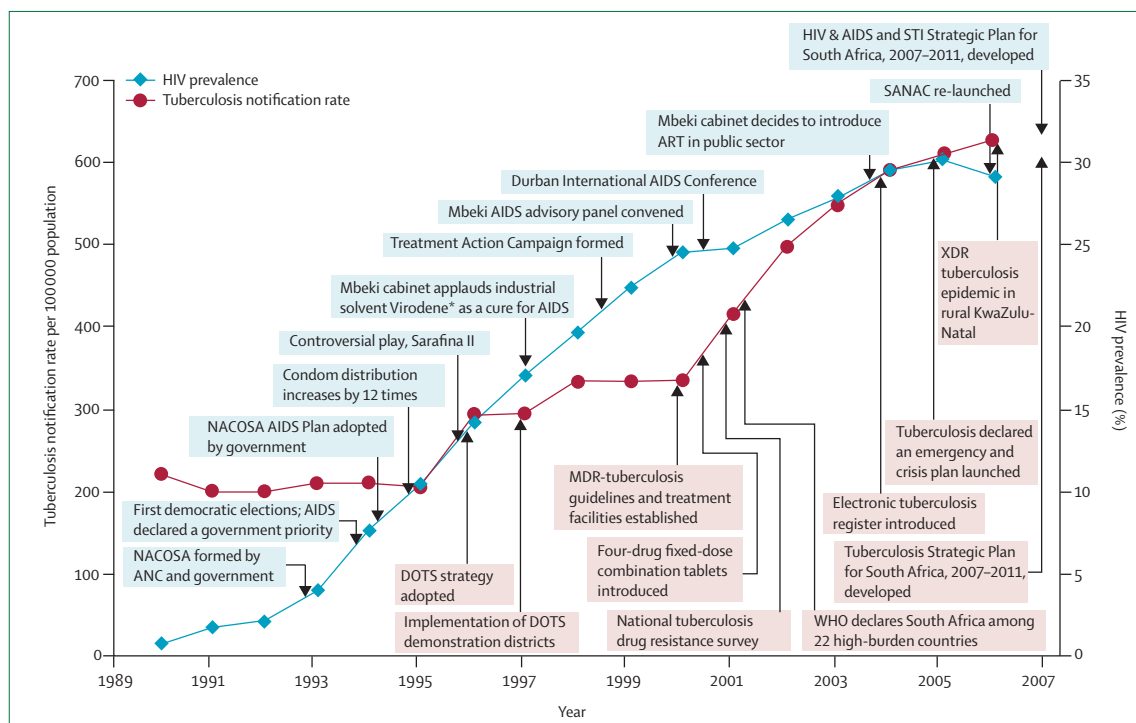


Figure 1: Historical overview of major events in the HIV and tuberculosis epidemics in South Africa, 1989–2007

Data from references 1 and 11. ANC=African National Congress. ART=antiretroviral therapy. DOTS=directly observed treatment, short course. MDR=multidrug-resistant. NACOSA=National AIDS Convention of South Africa. SANAC=South African National AIDS Council. XDR=extensively drug-resistant. *Dimethylformamide.

problem. In 2005, the national cure rate was 57.7% of new smear-positive tuberculosis cases,¹¹ far below the WHO target of 85%. In 2002, WHO estimated that over 14 000 cases of multidrug-resistant (MDR) tuberculosis occur every year in South Africa; the country ranks among the top ten countries in the world with the most cases of drug-resistant tuberculosis.³⁰ However, up-to-date incidence and prevalence estimates of drug-resistant tuberculosis are lacking. WHO estimated that 8238 (2%) of 453 929 new tuberculosis cases and 5796 (7%) of 86 642 tuberculosis re-treatment cases had MDR tuberculosis in 2006.³⁰ Numbers of cases have probably risen substantially in the ensuing years.

The problem of tuberculosis drug resistance in South Africa was highlighted by a 2006 outbreak in a rural hospital in KwaZulu-Natal province in which 72 (39%) of 185 culture-confirmed patients had MDR tuberculosis, 53 of whom had extensively drug-resistant (XDR) tuberculosis.³¹ In this outbreak, XDR tuberculosis was rapidly and almost uniformly fatal and all who were tested for HIV co-infection were found positive. Findings from further molecular epidemiological studies of patients with more than one tuberculosis episode suggest that exogenous nosocomial re-infection was frequently the source of this drug-resistant disease.³² The causal strain for the outbreak has been identified as F15/LAM4/KZN, which has been responsible for cases of MDR tuberculosis since 1994 and cases of XDR tuberculosis since 2001.³³

Initially thought to be a localised outbreak, this cluster has now taken on epidemic characteristics. The number of XDR-tuberculosis cases continued to increase and by September, 2007, 266 cases of XDR tuberculosis had been diagnosed in a rural KwaZulu-Natal district with a mortality of 84%.³⁴ XDR-tuberculosis cases have been identified in patients attending approximately 60 different health facilities in KwaZulu-Natal province and in all nine provinces of South Africa. The appearance and growth of resistance to antituberculosis drugs threatens the success of tuberculosis DOTS programmes and ART distribution programmes.

The yearly tuberculosis mortality rate increased by 2.8 times from 1990 to 2006, from 78 per 100 000 population to 218 per 100 000 population. Tuberculosis is the most common notified natural cause of death in South Africa.²¹ The combination of increasing tuberculosis cases, HIV/tuberculosis co-infection, drug-resistant tuberculosis cases, and tuberculosis mortality constitutes a crisis that demands urgent and sustained intervention.

Achievements and innovations in the responses to HIV and tuberculosis

Despite the history of antagonism between the government and the intended beneficiaries of its HIV/AIDS control programme, both during and after apartheid (panel 1), there have been notable achievements in the past 10 years. Five key achievements are shown in panel 2.

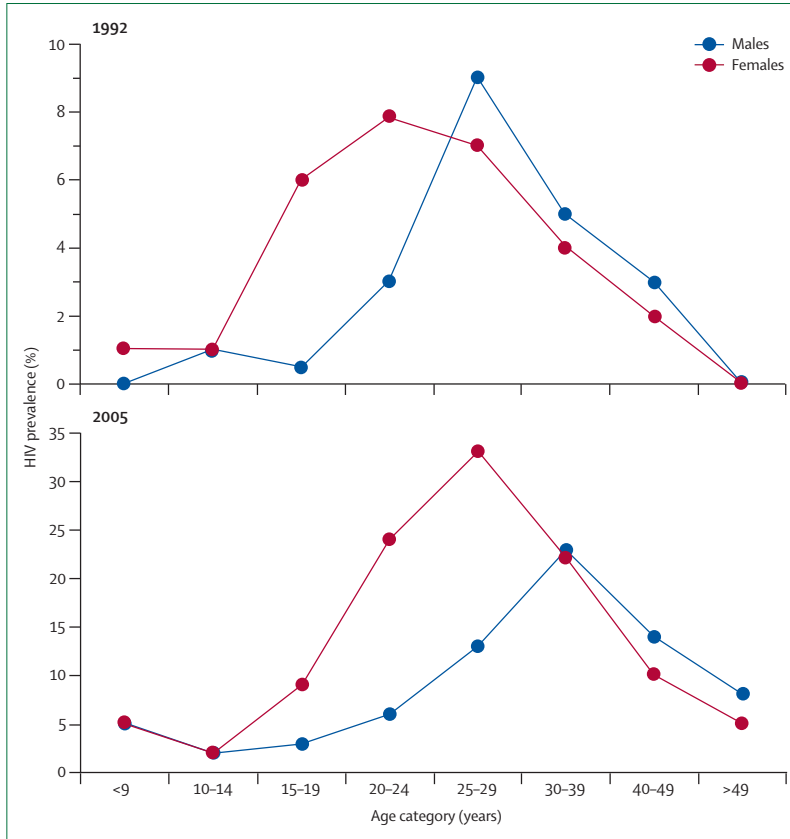


Figure 2: Age and sex disparities in HIV infection in South Africa, 1992 and 2005
Data from references 14 and 15.

The HIV & AIDS and STI Strategic Plan for South Africa, 2007–2011³⁵ and the Tuberculosis Strategic Plan for South Africa, 2007–2011¹¹ have been broadly welcomed. The publication of these comprehensive documents highlights that South Africa is not deficient in policy, but rather lacks either the will or the capacity to deliver. Despite these clear deficiencies, the sheer magnitude of the HIV and tuberculosis epidemics has stimulated the development of innovative means of delivering health care, the lessons of which might be harnessed to strengthen the overall health system.

Following a belated decision by the South African Government to provide ART (panel 1), its distribution has steadily gathered momentum and South Africa now has the largest ART programme in the world. Paradoxically, longstanding tuberculosis services have lagged behind and could benefit from the incorporation of key lessons made from the scale-up of ART. Although tuberculosis and HIV treatment outcomes are not directly comparable—eg, tuberculosis treatment is given for a defined period of 6–9 months whereas HIV treatment is lifelong—there is substantial disparity between diseases in the capacity to deliver treatment effectively. In 2005 in Western Cape province, which has a good provincial tuberculosis programme, the sputum-smear conversion rate at 2 months in new smear-positive tuberculosis cases was just 66·9%, the treatment default rate at 6 months 11·1%, and the tuberculosis cure rate 71·9% (falling well short of the WHO recommended goal of 85%).²¹ By contrast, data for the ART programme in the Western Cape from the same period showed that in over

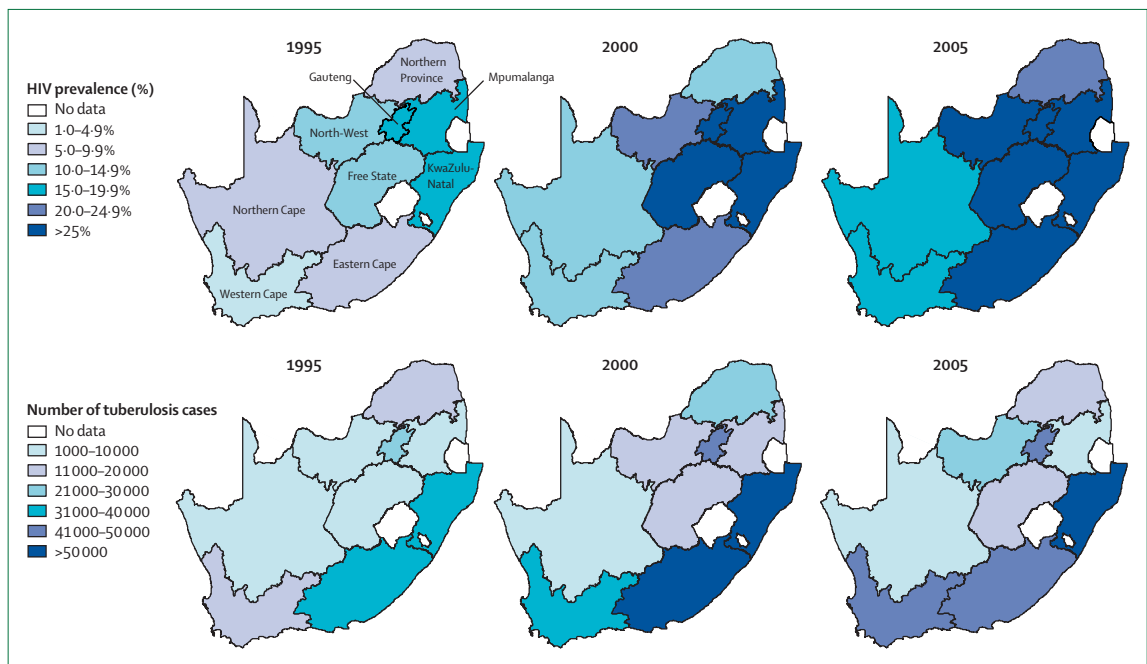


Figure 3: Geographical distribution of HIV and tuberculosis infections in South Africa in 1995, 2000, and 2005
Data from references 1 and 21.

16 000 patients treated, 90·6% achieved a viral load suppression of less than 400 copies per mL at 6 months, the loss to follow-up rate was just 4·2%, and 89·5% of patients were alive and remained on treatment at 6 months.³⁶ Furthermore, even after 4 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.^{37,38}

Many factors could cause this disparity between the success of ART and tuberculosis programmes, but a key factor underlying the high rates of patient retention and treatment compliance in ART services might be the widespread use of treatment literacy training for patients, often delivered by lay or peer counsellors.³⁹ These education programmes provide patients with detailed information about HIV infection (such as how anti-retroviral drugs 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. By marked contrast with this patient-centred approach, tuberculosis services typically fail to provide adequate treatment literacy and disempower patients because of the need for daily observation and recording of treatment compliance, which is often done at health-care facilities.

Both the HIV and tuberculosis epidemics have served as drivers of innovation in service delivery, monitoring, and assessment. The tuberculosis control programme has established a national electronic register that allows standardised recording and reporting of all notified tuberculosis cases and assessment of the national tuberculosis programme. HIV treatment programmes have taken this approach one step further by collecting patient data for clinical status, drug switching, drug-related adverse events, treatment adherence, CD4-cell count, viral load measurement, and treatment outcomes. Although these data are not nationally standardised, they provide a wealth of data for the status of the ART roll-out programme. Indeed, the level of detail in the data collected in HIV treatment programmes has enabled a performance management approach, in which ART roll-out programme indicators are used to provide feedback to health-service managers.

Task shifting (ie, a process of delegation whereby tasks that are usually undertaken by a particular category of health-care workers are moved, where appropriate, to other categories of health-care workers) has been an effective strategy in tuberculosis services through the use of community health-care workers, defaulter tracers, and treatment supporters, thereby improving case detection and follow-up to ensure continuity of care from investigation to diagnosis and cure. In addition to task shifting, HIV treatment programmes, facing a burden beyond the capacity of currently available health-care

Panel 2: South Africa's achievements in the response to HIV/AIDS and tuberculosis

Increase in male condom distribution and introduction of the female condom

The distribution of condoms has been a key part of the government's HIV prevention strategy; the number of male condoms distributed by the government rose from 8 million in 1994 to an estimated 376 million in 2006.⁴ The female condom was introduced in 1996 to increase HIV prevention options for women; in 2006, 3·6 million female condoms were distributed.⁴

Expansion of tuberculosis control efforts

The DOTS programme was adopted as the standard of care for tuberculosis in 1995 (although its implementation has been inconsistent). Surveillance for antituberculosis drug resistance has been enhanced, and programme performance and patient outcomes are more closely monitored through the tuberculosis register. There is improved national coordination and alignment of national policies with global best practice. The declaration of tuberculosis as a national emergency has focused greater political commitment and emphasis on the tuberculosis crisis.

Research contributions in HIV/AIDS and tuberculosis

Researchers in South Africa have made several major scientific contributions to HIV and tuberculosis prevention, pathogenesis, treatment, and control. There are at least 15 large HIV and/or tuberculosis 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 UK Wellcome Trust.

Scale-up of the free HIV/AIDS treatment programme

Since the government decision in November, 2003, to provide free AIDS treatment, an estimated 488 739 people were enrolled in the public sector roll-out programme within 4 years. South Africa now has the world's largest HIV/AIDS treatment programme, although only reaching about 38% of those who should be on ART.³ The US President's Emergency Plan for AIDS Relief and the Global Fund to Fight AIDS, Tuberculosis and Malaria are important financial supporters of this programme.

Development of the Strategic Plans for South Africa

The HIV & AIDS and STI Strategic Plan for South Africa, 2007–2011 has four priorities: (1) prevention; (2) treatment, care, and support; (3) legal and human rights; and (4) research, monitoring, and evaluation. The two overarching objectives are to reduce the HIV incidence rate by 50% and to initiate ART in 80% of people who need it.³⁵ The Tuberculosis Strategic Plan for South Africa, 2007–2011, sets out to (1) strengthen the implementation of the DOTS strategy; (2) address HIV and tuberculosis, MDR tuberculosis, and XDR tuberculosis; (3) contribute to health systems strengthening; (4) work collaboratively with all care providers; (5) empower people with tuberculosis and their communities; (6) coordinate and implement tuberculosis research; and (7) strengthen infection control.¹¹

ART=antiretroviral therapy. DOTS=directly observed treatment, short course. MDR=multidrug-resistant. XDR=extensively drug-resistant.

personnel, have created new regiments of health-care workers. These teams include lay counsellors, lay HIV/AIDS educators, and patients with good ART adherence who provide adherence counselling in HIV clinics and through community outreach. This concept has been extended further to home-based daily care to provide treatment for patients with XDR tuberculosis.³¹

To achieve the massive scaling up of HIV care in South Africa, millions of people had to access HIV testing, and this was achieved by several innovative means. Testing was done through dedicated voluntary counselling and

testing centres and community-based mobile clinics. Provider-initiated testing at health-care facilities focused on antenatal clinic attendees and patients with tuberculosis. Additionally, testing was facilitated through public and private sector partnerships and non-governmental organisations. A major innovation that made this possible was the development of simple, reliable, and cheap rapid HIV tests. To enhance the reliability of HIV testing, algorithms have been developed in which two different rapid tests are used to achieve diagnostic accuracy similar to that available through laboratory testing.

A rapid test is not available for the diagnosis of tuberculosis; however, the growing burden of drug-resistant tuberculosis has led to the assessment and adoption of a rapid diagnostic test for rifampicin and isoniazid resistance—the molecular line-probe assay.⁴⁰ Additionally, algorithms have been developed for the diagnosis of smear-negative tuberculosis. The need to manage HIV and tuberculosis in the same patient is stimulating the integration of HIV and tuberculosis services, with best practice examples at the Church of Scotland Hospital in Tugela Ferry,⁴¹ the CAPRISA eThekweni TB-HIV clinic in Durban,⁴² and the Médecins Sans Frontières clinic in Khayelitsha.⁴³

Public health action for HIV and tuberculosis control

South Africa is currently underperforming in its efforts to control HIV. An international HIV/AIDS scorecard of country-level HIV/AIDS programmes showed that South Africa was doing worse or no better than some of its neighbouring countries (table 2).⁴⁴ South Africa needs to improve in almost all the ten elements used in this international rating. With regard to financing, this index is rated as the mean of three indicators: the total expenditure on the response per person living with HIV; the total expenditure on HIV prevention per person living in the country; and domestic expenditure on HIV per person in the country as a proportion of gross national income. South Africa's rating in financing for the HIV/AIDS epidemic is on par with that for Zimbabwe and Mozambique, but worse than that achieved by Malawi, Namibia, and Botswana (table 2).⁴⁴ South Africa has the resources, and the capability, to rise to these challenges, but has not been able to devote resources equivalent to the scale of the problem to be able to deliver on the four priorities listed in the Strategic Plan for South Africa for HIV/AIDS (panel 2).³⁵ Similarly, the country has not been able to stimulate effective implementation of the Tuberculosis Strategic Plan for South Africa¹¹ (panel 2).

The first step to achieving the ambitious targets set out in these plans is for the country's political leadership to publicly acknowledge the extent of past successes and failures and to show unwavering commitment to the control of the epidemics. New high-level political

commitment needs to be passionate and persistent. Building on the foundations of the past efforts of organisations such as the Treatment Action Campaign, political commitment needs to infiltrate the general populace and to create the groundswell of a social movement. This commitment in turn needs to be translated into financial resources not only for health services but also for volunteer programmes, community mobilisation, local anti-AIDS and antituberculosis initiatives, partnerships, and advocacy programmes.

The UNAIDS HIV prevention strategy⁴⁵ advocates the important step of “know your epidemic”—ie, know who is at risk, who is being infected, and which communities are most affected. Adequate resources cannot be devoted to every person in an epidemic; detailed knowledge of the HIV/AIDS and tuberculosis epidemics will assist in making strategically important decisions on the deployment of resources. These data can be provided by serological and behavioural surveillance of sentinel groups and communities and by investigations that establish the most effective HIV prevention and treatment approaches in different settings. Active surveillance for drug-susceptible and drug-resistant tuberculosis is a crucial component of tuberculosis control activities and will help to guide rational deployment of resources. Much of these data are already available for HIV, but not for tuberculosis. However, South African scientists have had few, if any, opportunities to provide and interpret the available data for policy makers and planners for either epidemic. The past antagonism between scientists and the political leadership in South Africa needs to be reversed; a new partnership based on mutual respect between policy makers, planners, and researchers will help to develop the information base that can be used to guide action and monitor performance.

The extent to which the South African health-care service is dysfunctional is generally underestimated. The country's national department of health should provide clear leadership in addressing failing health-care systems. Although dedicated resources for HIV/AIDS from the department of health have expanded substantially from R676 million (US\$80 million) to R3·6 billion (\$0·4 billion) at a mean yearly increase of 24·8% over a 7-year period,⁴ an increase in funding is needed to rebuild the physical infrastructure, which has been damaged by years of neglect and underfunding.

Other necessary actions are to establish functioning management systems in every health service and to focus on addressing deficits in human resources. Human resource capacity can be enhanced by 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 strengthening the management capacity at all levels to ensure integration of HIV and tuberculosis into primary

| HIV element* | South Africa | Neighbouring countries | | | | | Other developing countries | |
|----------------------------------------------------|--------------|------------------------|--------|------------|---------|----------|----------------------------|--------|
| | | 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 |
| Tuberculosis indicators† | | | | | | | | |
| Population (million) | 48.6 | 1.9 | 13.9 | 21.4 | 2.1 | 13.3 | 191.8 | 1169.0 |
| Tuberculosis incidence (per 100 000 per year) | 948 | 731 | 346 | 431 | 747 | 782 | 48 | 168 |
| Tuberculosis mortality (per 100 000 per year) | 230 | 194 | 102 | 127 | 102 | 265 | 4 | 29 |
| HIV prevalence in incident tuberculosis cases (%) | 73% | 68% | 68% | 47% | 67% | 69% | 14% | 5% |
| Treatment success for new smear-positive cases (%) | 74% | 72% | 78% | 83% | 76% | 60% | 72% | 86% |

*The scores A–F, where A is a good score and F is a bad score (A=81–100%, B=61–80%, C=41–69%, D=21–40%, E=0–20%, F=no data reported) are ratings given by AIDS Accountability International and indicate how a country is performing based on the commitments they have made in response to the epidemic. Refer to reference 44 for a detailed explanation of each element and how the scores were derived. †Tuberculosis data from reference 45.

Table 2: Scorecard rating of the government's response to AIDS and key tuberculosis indicators for 2007 for South Africa compared with five neighbouring countries, Brazil, and India

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 these systems, it will not be possible to provide patient-centred and patient-friendly services that remove barriers to diagnosis and treatment access.

Rates of HIV and tuberculosis are high in health-care workers. Strategies should be implemented to ensure that health-care workers remain healthy, productive, and motivated, and are not lost because of illness, death, or migration into other sectors because of stigma and fear of being exposed to potentially untreatable tuberculosis. Skilled staff can be retained within the primary health-care services by providing market-related salaries, continuous training, and well equipped and safe health-care facilities in which to work. 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.⁴⁶

Priority action steps to achieve tuberculosis control

The cornerstone of tuberculosis control remains the detection and cure of new infectious tuberculosis cases under a DOTS programme. Integration of HIV and tuberculosis services and rapid and appropriate management of drug-resistant tuberculosis are other crucial components of tuberculosis control. The following four steps outlined below prioritise these interventions to make the best use of limited resources.

Step 1: improve the tuberculosis cure rate

A high cure rate is essential to interrupt the transmission of tuberculosis. South Africa's treatment success (cure or treatment completion) rate for new smear-positive tuberculosis cases needs to increase from 58% (table 1) to the WHO minimum target of 85%.⁴⁷ Mathematical models^{48,49} suggest that improving cure rates to 85% will reduce tuberculosis incidence and mortality. Every 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—eg, once-off cash incentives for patients who successfully complete tuberculosis treatment.

Step 2: improve the tuberculosis case detection rate

A high detection rate of new infectious tuberculosis cases under a DOTS programme is essential to reduce the duration that tuberculosis cases remain infectious and undiagnosed in a community. Modelling studies have shown that the effect of improved cure rates on tuberculosis control is substantially enhanced when combined with improved case detection.^{50,51} South Africa's case detection rate needs to increase from 62% to the WHO target of 70%.⁴⁷ Case detection can be improved by (1) ensuring that the presence or absence of tuberculosis is established in every symptomatic patient presenting to health services, (2) provider-initiated and intensified tuberculosis case finding in all HIV-infected individuals attending health services, (3) active screening of household contacts of infectious tuberculosis cases, and (4) identification of communities

with high tuberculosis prevalence to target programmes that promote increased identification of individuals with respiratory symptoms for tuberculosis investigation. Laboratory services will need to be strengthened to cope with the increased workload resulting from intensified case finding.

Step 3: integration of HIV and tuberculosis services

HIV and tuberculosis services should be integrated so that 90% of HIV-positive patients are screened for active tuberculosis and 90% of patients with tuberculosis are offered an HIV test. Tuberculosis care should include provider-initiated HIV testing, co-trimoxazole chemoprophylaxis, and ART, if needed. An estimated 10 000 deaths could be prevented every year by the initiation of ART in HIV/tuberculosis co-infected patients with CD4-cell counts below 500 cells per μL .⁴² Conversely, HIV care should include a strong emphasis on prevention of HIV-associated tuberculosis by use of ART in combination with the WHO 3I's strategy of intensified tuberculosis case finding, isoniazid preventive therapy, and tuberculosis infection control.⁵² A meta-analysis of randomised controlled trials showed that isoniazid preventive therapy in individuals with HIV might reduce tuberculosis by 33% overall and by 64% in individuals with documented tuberculosis infection.⁵³ Mathematical modelling suggests that widescale distribution of isoniazid preventive therapy alone would be fairly ineffective at improving tuberculosis control, but highly synergistic when combined with improved detection and cure, thereby having a long-term effect at the population level.⁵¹

Step 4: identification and treatment of drug-resistant tuberculosis

The first priority is to prevent the emergence of drug-resistant tuberculosis by ensuring high cure rates of drug-susceptible disease; however, since drug-resistant tuberculosis in South Africa is already widespread, culture and drug-susceptibility testing should be undertaken in at least 85% of re-treatment cases and, when indicated, in new tuberculosis cases. A mathematical model suggests that the implementation of culture and drug susceptibility testing in 37% of new tuberculosis cases and 85% of re-treatment cases could save around 50 000 lives, avert 7721 (14%) MDR-tuberculosis cases, and prevent 7069 (46%) MDR-tuberculosis deaths.⁵⁴ However, the model also estimated that there would be no effect on incidence of XDR tuberculosis.

To achieve the maximum effect on tuberculosis control, these four steps need to be combined.⁵¹ If the targets for tuberculosis detection and cure, tuberculosis and HIV service integration, and detection of drug resistance are met, South Africa will be on course to meet Millennium Development Goal 6 for reducing tuberculosis incidence and mortality.

Priority action steps to achieve HIV prevention

The priority steps for HIV prevention are founded on the urgent need to address risk factors and underlying vulnerability for infection, 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 a common understanding of the main drivers and risk factors in the HIV epidemic at a local and country level. South Africa has a vast amount of data for HIV prevalence and incidence, ranging from sentinel surveillance, population-based surveys, longitudinal cohort studies, and projections based on mathematical models. These data, however, remain irregular and disparate, therefore preventing national consensus on priorities for HIV control. The first step is the synthesis of all 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 major challenge is identifying the main reasons for the substantial age-differential partnering patterns (figure 2). The current post-denialism era provides the opportunity for policy makers and scientists to come together to generate evidence-based strategies for effective prevention of HIV.

Step 2: scale-up of behavioural, prevention of mother-to-child transmission, and HIV testing interventions

The scale-up of effective prevention interventions, even in the absence of any new prevention technologies, could have a substantial effect on the HIV epidemic.⁵⁵ Despite good progress being made in promotion of condoms, blood donation screening, provision of post-exposure prophylaxis 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. Prevention of mother-to-child transmission—a simple, cost-effective strategy with substantial life-saving benefit—needs to be scaled up from the current coverage rate of 60% to 95% of HIV-infected pregnant women receiving antiretroviral prophylaxis.³⁸ To reduce sexual transmission, behaviour change programmes need to place greater emphasis on avoidance of concurrent multiple partners, avoidance of large age difference partnering patterns, and knowledge of HIV status in addition to promotion of condoms. Individual interventions usually have modest effects, whereas combination interventions can have a synergistic outcome, especially if they achieve high coverage of the target population. The choice of which prevention methods should make up the combined intervention and the target populations for that intervention will need to be informed by a detailed understanding of the HIV epidemic.

Step 3: implement circumcision for HIV prevention

South Africa is at the forefront of clinical trials testing new prevention technologies, but the research findings are rarely translated 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,⁵⁶ and in 2008, 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 prevented by a programme of circumcision covering sub-Saharan Africa over the next two decades.⁵⁷

Step 4: legislative interventions on sex work, gender violence, and migrant labour

Although steps 2 and 3 for HIV prevention are essential components of the response to HIV and guided by detailed knowledge of the epidemic, a more fundamental approach is needed to address the underlying contextual issues of poverty, gender, and power disparities. Three structural interventions could help to achieve sustained reductions in HIV transmission: (1) legalisation and regulation of sex work; (2) concerted law enforcement on rape and violence against women in terms of current legislation; and (3) tax incentives to companies who join public-private housing partnerships 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.

Priority action steps for HIV treatment

Step 1: scale-up HIV testing

HIV testing needs to be expanded because it is an essential entry point to ART programmes. In South Africa, an estimated 7% of the population are tested for HIV every year—this proportion needs to increase to 25% per year.³⁵ To achieve this target, provider-initiated HIV testing should be the standard of care at all health-care facilities so that all those who come into contact with the health service are given the opportunity to find out their HIV status and access to treatment and prevention interventions. Furthermore, HIV testing needs to be accompanied by CD4-cell count measurement to identify HIV-infected individuals who are eligible for ART. The capacity to undertake about 9 million rapid HIV tests and 2 million laboratory CD4-cell counts every year is required for this programme to be successful.

Step 2: initiate ART in all patients with a CD4-cell count below 350 cells per μL

A mathematical model⁵⁸ suggests that changing the CD4-cell count threshold for the initiation of ART from 200 cells per μL to 350 cells per μL might reduce mortality from

HIV by 28% per year by 2010. Moreover, the model estimates that HIV incidence would decrease by up to 10% over a 10-year period. The recommendation to start ART in patients with CD4-cell counts below 200 cells per μL was widely supported when it was first made in 2003,¹² because of concerns about health-service capacity and the inexperience of health-care providers with HIV/AIDS treatment at the time. However, the potential for reducing mortality and HIV transmission, together with an increase in service capacity as a result of down-referral of stable patients on ART (ie, patients are referred from the specialist AIDS clinic to a general primary care clinic) and an increase in accredited ART distribution sites, has therefore led to a recommendation by the South African HIV Clinicians Society that ART is started in all patients with a CD4-cell count below 350 cells per μL .⁵⁹

Consideration should also be given to the potential benefits of even earlier initiation of ART that have been shown by observational data from large-scale ART programmes in the developed world.⁶⁰ Additionally, models based on South African data have suggested that a substantial prevention benefit would be derived from universal HIV testing with immediate initiation of ART irrespective of CD4-cell count.⁶¹

Step 3: maintain viral suppression in patients on ART

High levels of viral suppression are needed in patients on ART to reduce the incidence of opportunistic infections, hospital admissions, risk of ART resistance, and the need for alternative ART regimens. The South African ART programme has, until now, been able to achieve greater than 90% viral suppression.³⁶ This success is attributable to the quality of HIV/AIDS treatment services emanating from the accreditation process, the programme's patient-centred approach, treatment literacy, and intensive counselling. With the growing burden on HIV treatment services to provide ART, integrated tuberculosis services, co-trimoxazole prophylaxis, and isoniazid prophylaxis, and an increasing number of patients in pre-ART care, sustained efforts and vigilance will be needed to continue to achieve this rate of viral suppression in existing patients on long-term treatment and in new patients starting ART.

Step 4: integrate HIV prevention and treatment services

The historical separation of treatment and prevention services and the focus of prevention on uninfected individuals are counterproductive in a setting where more than 30% of the sexually active population is infected with HIV. Since the HIV-infected subpopulation is the source of new HIV infections, HIV treatment programmes have an important part to play in HIV prevention.⁶² For example, HIV treatment programmes need to include the full array of sexual and reproductive health services, including access to contraception, treatment of sexually transmitted infections, abortion, and prevention of mother-to-child transmission services. Additionally, HIV treatment should be an integral component of

HIV prevention programmes because availability of treatment is a potent promoter for the uptake of HIV testing, and treatment-induced low viral loads in infected individuals could reduce virus transmission. Findings from a modelling study show that the integration of prevention into treatment programmes could prevent as many as 29 million HIV infections worldwide by 2020.⁶³

Conclusion

South Africa has the world's worst HIV and tuberculosis epidemics. The current epidemic trajectory suggests that both epidemics will continue to worsen, leading to substantial increases in morbidity and mortality. The concomitant epidemics have exacerbated each other and have been further compounded by an increase in MDR tuberculosis and the emergence of XDR tuberculosis.

South Africa cannot afford to miss the window of opportunity created by the 2009 elections. Decisive action is needed to instil 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 tuberculosis control, HIV prevention, and HIV treatment as part of the aspirational 5-year Strategic Plans for South Africa^{11,35} will depend on the government's ability to build partnerships and to stimulate the development of 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. South Africa still awaits the opportunity to enjoy its newfound political freedoms without the overhanging threat of the HIV and tuberculosis epidemics.

Contributors

SDL and GJC were responsible for writing the tuberculosis-related sections and QAK was responsible for the HIV sections. SSAK took overall responsibility for editing and writing of the entire report.

Conflicts of interest

We declare that we have no conflicts of interest.

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