SUMMARY REPORT OF THE JOINT HEALTH AND TREASURY TASK TEAM CHARGED WITH EXAMINING TREATMENT OPTIONS TO SUPPLEMENT COMPREHENSIVE CARE FOR HIV/AIDS IN THE PUBLIC HEALTH SECTOR

01 AUGUST 2003

ACRONYMS

AIDS	-	Acquired Immuno Deficiency Syndrome
ART	-	Anti-Retroviral Treatment
ARV	-	Anti-Retro Viral
CHC	-	Community Health Center
DOH	-	Department of Health
DOTS	-	Directly observed treatment short-course
HAART	-	Highly Active Antiretroviral Therapy
HIV	-	Human Immuno Deficiency Virus
MCC	-	Medical Control Council
NHLS	-	National Health Laboratory Services
NICD	-	National Institute for Communicable Diseases
OI	-	Opportunistic Infections
PEP	-	Post Exposure Prophylaxis
PIU	-	Programme Implementation Unit
PHC	-	Primary Health Care
PMTCT	-	Preventing Mother to Child Transmission of HIV
SA	-	South Africa
SANAC	-	South African National AIDS Council
STI	-	Sexually Transmitted Infection
TB	-	Tuberculosis
VCT	-	Voluntary Counseling and Testing
WHO	-	World Health Organization

Introduction

Government is committed to developing a comprehensive response to the HIV/AIDS epidemic, based on the premise that HIV causes AIDS, and that there is currently no known cure for AIDS. International best practice indicates the need for a comprehensive national programme, embracing preventive strategies, good quality medical treatment and strong social support. Government in particular sees the fight against AIDS as being anchored in a multi-pronged developmental intervention, in which the fight against poverty and under-development are central.

In July 2002, Government established a joint Health / Treasury task team to investigate issues relating to the financing of an enhanced response to HIV/AIDS, based on the national strategy as further elaborated in the April 17 2002, October 9 2002 and March 19 2003 Cabinet statements. A particular focus of the task team was on the second component of the national strategy, treatment, care and support for those infected and affected by HIV/AIDS. The team was tasked to assess in detail the resource requirements that would attend any decision on the introduction of antiretroviral therapy as an additional component in our treatment response. The terms of reference setting up the joint task team were mainly focused on the financing aspect. However in the course of the discussions of the draft report it became clear that it was vital to contextualise the work of the task team in a continuum of the different elements that constitute our comprehensive response.

In particular it is important to ensure that the discussion on the possible introduction of the ARV component in the public health system does not remove the focus on the other elements of the response which no doubt are more critical.

This specifically refers to the area of prevention as well as to interventions in the period after detection of a positive HIV test to the stage of a low CD^4 count (below 200). During this period, health and the quality of life can be significantly improved in those who are HIV positive by a series of interventions aimed at supporting the immune system. Key interventions would include lifestyle choices, good nutrition, the use of appropriate immune supplements and early detection and treatment of infections.

This report is a summary of the findings of the task team. Detailed findings are provided in the Full Report and Technical Appendices.

The facts and figures used in the report (on HIV prevalence, people in different stages of progression, number of children orphaned and so on) derive from statistical work done both

by government agencies and within the academic and private sectors. Assumptions are also made about the rigour of the methods used in HIV tests, taking into account that these have improved with time. Given that the infrastructure with regard to the latter requires much improvement in our country, the Report has factored such improvements into all its calculations on resource implications, including for the non-ARV option. Overall, while the data serve as broad indicators of trends, they should be taken as estimates.

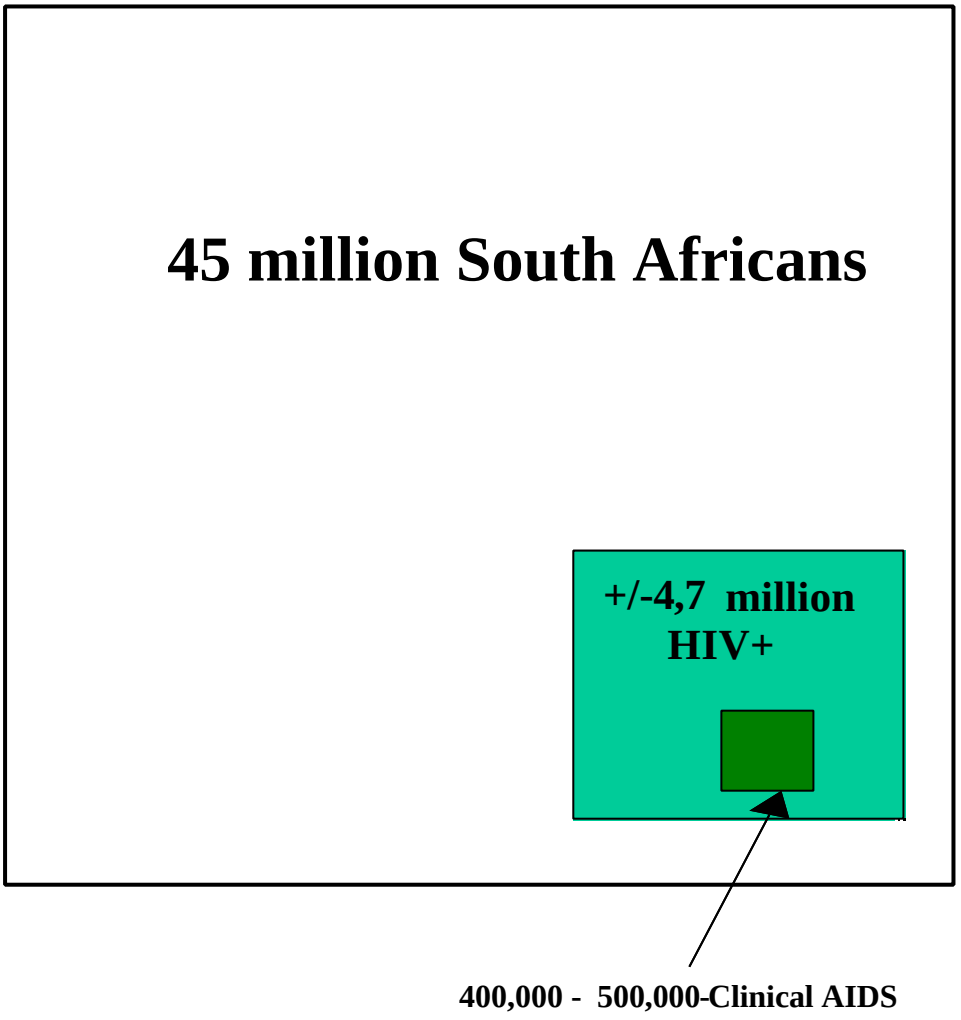
Government's Response to HIV/AIDS

On 17 April 2002, Cabinet reiterated its commitment to the *HIV/AIDS and STI Strategic Plan for South Africa, 2000-2005*, and called for all South Africans to take responsibility for their lives in respect of HIV/AIDS. Cabinet noted progress in the implementation of the *Strategic Plan*, and decided on a number of measures to strengthen and reinforce these efforts, including:

- Strengthening partnerships, especially via strengthening of SANAC
- Continued research on the use of nevirapine in preventing mother-to-child transmission, while the Department of Health implemented the temporary ruling of the Constitutional Court; and development of a universal roll-out plan in preparation for the post-December 2002 period
- Providing a protocol for a comprehensive package of care for survivors of sexual assault, including post-exposure prophylaxis with antiretroviral drugs
- Ensuring that no South African should be turned away without appropriate treatment and management of any infection or illness, irrespective of HIV status
- Noting that antiretroviral treatment can help to improve the conditions and health of people living with AIDS if administered at certain stages in the progression of HIV/AIDS and in accordance with international standards, Government committed to continue its efforts to remove systemic constraints on access to these drugs
- Alongside poverty alleviation and nutritional interventions, to encourage investigation into alternative treatments, particularly supplements and medication for boosting the immune system

Premise of Government's overall approach

Graphical Representation – HIV/AIDS and the Total Population



Over the years, as the world gathers more experience in the management of the HIV and AIDS pandemic, the appreciation of the importance of social conditions and particularly poverty, both in undermining the immune system in general and in increasing susceptibility to HIV infection as well as progression to AIDS, has grown.

Given this global experience, and taking into account the fact that there is no cure for AIDS, it is critical to emphasise that the approach of the South African government in dealing with the pandemic is premised on the following objectives:

- Ensuring that the overwhelming majority of South Africans who are not infected with HIV remain uninfected: The message of prevention and changing of lifestyles is therefore a critically important starting point in managing the pandemic. Added to this, in the broader social context, are the social programmes of government and the rest of society to continually improve the efforts to reduce poverty through job-creation, social services including grants and nutrition, education and moral renewal.

- Ensuring that South Africans who are infected with HIV but have not developed AIDS (currently estimated at about 4 million) progress as slowly as possible to the stage of the Syndrome: This requires enhanced efforts in the prophylaxis and treatment of opportunistic infections and in improved nutrition and lifestyles. Built into the options in this Report, on both ARV and non-ARV interventions, are calculations on such enhanced interventions. Awareness of one's condition and a change in lifestyles are also critical.

- Management of patients infected with HIV who have moved on to develop AIDS (currently estimated at between 400 000 and 500 000): Where all the interventions outlined above have run their course and individuals present with dangerously low CD4 counts, the question then arises whether, additional to all the other interventions, ARV's should be provided, in order to improve functionality and defer death. The Report presents the costs and benefits of different options in this regard.

As such, it should be emphasised that, ART is one among a very large number of interventions to manage the AIDS pandemic. It can only be introduced at a particular stage of the progression of the condition, and must always be combined with a comprehensive package of other interventions, including nutrition and treatment of opportunistic infections. The costs and complexity of this regimen and the benefits deriving from its introduction need to be weighed taking this fundamental premise into account.

The Task Team Report confines itself in the main to the issue of syndromic immune deficiency as a consequence of HIV infection. It therefore does not examine in any comprehensive way the causes and programmatic solutions to other manifestations of immune deficiency, mostly attached to poverty and related diseases such as kwashiorkor as

well as other illnesses some of which may be sexually transmitted. The report also does not deal with the macroeconomic impact and management of other diseases. The assumption of the Task Team is that these conditions are being dealt with within the realm of government's general health programmes and, more broadly, the social policies of the state.

Components of a Comprehensive Health Sector Response to HIV/AIDS

Prevention

Prevention remains and must always remain the cornerstone of all efforts to deal with the HIV/AIDS epidemic. Minimising the number of South Africans who become infected with HIV is the most effective mechanism for minimising the negative impact of HIV – especially since there is no cure for AIDS. The core elements of a comprehensive health sector prevention programme are already largely in place:

- Promoting abstinence, faithfulness and delaying the age of first sexual activity
- Promoting safe sex
- Free condom distribution
- Effective management of sexually transmitted infections
- Prevention of Mother to Child Transmission of HIV (PMTCT)
- Blood safety
- Post-exposure prophylaxis for occupational exposure and for survivors of sexual assault
- Expanded access to Voluntary Counselling and Testing (VCT)

Maintaining Health After HIV Infection

Encouraging early diagnosis of HIV infection via VCT services is clearly critical. Once an individual is diagnosed as HIV positive, the following services should be offered routinely:

- Healthy lifestyle advice
- Healthy diet and nutrition
- Prophylaxis for common opportunistic infections

Work is ongoing on the development of intersectoral guidelines and policy for nutritional support for people living with HIV, in collaboration with other agencies active in poverty alleviation and nutrition support.

There is considerable promise that healthy diet as well as complementary treatments to strengthen the immune system can help maintain health in people with HIV; research into the safety and effectiveness of these interventions is being coordinated by the Medical Research Council. This work offers the additional advantage that any general strengthening of the immune system would also help the body ward off a whole range of other infections not related to HIV. The central element in all these interventions is the recognition that the period during which HIV-infected persons can remain free of disease symptoms can be significantly prolonged through the use of simple and affordable interventions, and that this should be a central focus for those who are already HIV positive.

Effective prophylaxis significantly reduces the risk of acquiring a number of opportunistic infections, and thus has an important role in delaying progression to Stage 3 disease. Standard guidelines for the prophylaxis of common opportunistic infections are in widespread use in the public sector. Current advice does not foresee any need to add further prophylactic interventions to this list; the key need here is to expand the number of people who know their HIV status, and thence to expand the number of HIV positive people who are receiving prophylaxis.

Treatment as the Disease Progresses

Well-established and widely disseminated guidelines are in place in the public health system for the treatment of a wide range of opportunistic infections, complications and malignancies associated with HIV and AIDS. The Tuberculosis control programme treats a very large number of HIV-infected individuals, and has specific guidelines for treatment of HIV positive adults and children. Community and home based care and step-down care have been developed and strengthened at a growing number of sites across the country, to provide an effective platform for the delivery of basic treatment and care to people with AIDS. Guidelines for the nutritional support of patients in the advanced stages of HIV/AIDS are also being developed by the Department of Health.

In recognition of the gravity of the HIV/AIDS epidemic, and of the urgent need to expand the scale, scope and quality of the public health system's response to HIV/AIDS, Government approved the "Enhanced Response to HIV/AIDS and Tuberculosis in the Public Health Sector" in 2001.

Some members of the Technical Team were responsible for the development in 2001 of the "Enhanced Response to HIV/AIDS and Tuberculosis in the Public Health Sector", and the follow-up exercise in 2002, "Revising the Enhanced Response to HIV/AIDS and Tuberculosis in the Public Health Sector". Since 2001, very substantial increases in funding for the health sector response to HIV/AIDS have been channelled into the public health system, largely via provincial budgets. In total, earmarked funding for HIV/AIDS in 2003/04 is some R 1.5 billion greater than in 2001/02, and current commitments mean it will have risen by a further R 1.5. billion by 2005/06. The table below summarises the earmarked funding allocated to conditional grants and to the provincial equitable share under the original "Enhanced Response" and its revision during 2002, relative to an estimated baseline expenditure of R 4.4 billion in 2001/02.

Millions of Rands	2001/02	2002/03	2003/04	2004/05	2005/06
Baseline HIV/AIDS Spend	4,191	4,191	4,191	4,191	4,191
2001 ER Equitable Share		400	627	988	1,032
2002 ER Equitable Share			500	1,000	1,500
Conditional Grant	34	210	334	482	535
National Dept of Health	220	330	330	330	330
Funds Available	4,445	5,131	5,982	6,990	7,588

The table shows clearly the extent of additional funding directed HIV/AIDS in the public health sector since 2001. It is accepted that the baseline is an estimate only, and that it is effectively impossible to measure directly actual expenditure on HIV/AIDS via general health services. As noted, prior to 2002, "baseline" spending on HIV/AIDS has, to a considerable degree displaced other health service activity. The "baseline" estimate thus reflects a degree of "crowding out" of other health care services by HIV/AIDS, rather than deliberate targeting of resources. This should not, however, downplay the significance of the large real increases in earmarked resources for HIV/AIDS made available since 2002. Including the estimated "baseline" expenditure of R 4.4 billion, then the analysis of the task team indicates that, by 2004/05, the funds available to the health sector to deal with HIV/AIDS prevention, treatment, care and support will broadly be commensurate with the amounts required to fully provide at scale all health sector interventions included in the current policy package.

The task team considers that considerable further work is required to enhance the *quality* of service provision in the areas of both prevention and treatment. Central to this effort will be

improved effectiveness and targeting of prevention messages, the training and re-training of health professionals in the appropriate use of standard treatment guidelines, and the introduction of more effective processes for quality improvement and monitoring. The establishment of Regional Training Centres in each province (commencing during 2003, with funds available via the HIV/AIDS conditional grant) will be pivotal to meeting this challenge. Regional Training Centres' main function will be to develop curricula on HIV, AIDS and TB care, and to align the skills of health workers more closely with the requirements of national treatment guidelines.

Thus, policy and funding commitments made in the last two years leave South Africa well placed to offer a comprehensive package of prevention and care in the health sector. Pending the finalisation of nutrition support guidelines for people living with HIV, the treatment option not currently provided in Government's treatment package is antiretroviral therapy (ARV / ART).

Antiretroviral Therapy

Antiretroviral therapy has been demonstrated to significantly extend life, reduce mortality, and improve health status in people in Stage 3 and 4 of HIV disease. Current evidence shows that most people infected with HIV will reach a stage by which time the immune system will have deteriorated to such an extent that nutrition, complementary treatments and treatments with antibiotics will not be sufficient to deal with major opportunistic infections. This is defined as the point at which the individual develops an "AIDS – defining illness" and is more likely to occur when the CD4 count drops to below 200 cells/µl. At this stage in the progression of the disease the role of antiretroviral drugs becomes important.

The availability of an increasing number of ARV's and the rapid evolution of new information has introduced substantial challenges into treatment regimens.

A significant amount of clinical and scientific evidence on ARV use has been generated in developed countries. In order to enable developing countries to apply these technologies and treatment regimens the WHO published guidelines for scaling up antiretroviral therapy in

resource constrained setting with detailed recommendations for the use of ART in developing countries in 2002.

Three classes of antiretroviral agents are currently available for treatment of HIV infection. There are now 17 approved ARVs with which to design regimens of three agents for effective management of HIV disease at the stage when these are indicated.

The technical team convened a panel of clinical experts, which used the WHO guidelines as a foundation to produce a simple, high quality two regimen guideline and eligibility criteria suitable for use in the South African public sector.

In essence the Team concluded that tight selection criteria should be used for anyone entering this programme amongst amongst these are:

- A positive test for HIV infection based both on a screening as well as a confirmatory test based on WHO recommendations (Currently South Africa uses WHO Strategy III for the individual patient diagnosis of HIV infection. Strategy III calls for the use of three Elisa's based on differing test principles. This strategy has been validated using the Western Blot as a 'gold standard')
- CD4 count below 200 and a high viral load
- Clinical condition

It is the consideration of these three (3) factors taken together that would constitute the trigger for commencement of ART.

Over and above these, a detailed physical examination and clinical assessment would identify such confounding factors as other pre-existing disease, any drug therapy being used and therefore what known drug interventions should be anticipated and avoided in the particular circumstance.

Based on this careful assessment, a treatment decision will be made based on the two regimen guideline recommended.

Once on treatment a monitoring and follow-up schedule is recommended. This has been based on the experience in SA and elsewhere as well as serious consideration of the US (NIH) guidelines. Two differences from the NIH guidelines relate to

(i) 3 monthly review by an appropriately trained doctor as opposed to 6 monthly reviews recommended by the task team. In both instances, there are intervening monthly reviews by nurses.

(ii) Viral loads and CD4 counts done quarterly in NIH guidelines. The task team recommends these tests to be done at 3 months after commencement of treatment and thereafter 6 monthly.

These guidelines and criteria form the basis for the subsequent costing exercise. The team identified several guiding principles which would be critical for the successful implementation of ART, which informed the development and analysis of activities described in the report:

1. Commitment of significant resources both in the short term, medium and long time because treatment with ARV's is lifelong therapy
2. Provision of ARV'S must not divert resources from other essential public health programmes, nor from HIV prevention activities
3. Significant investment in human resource development at all levels including management and supervision
4. Facilities improvement as well expansion of laboratory infrastructure
5. Well developed pharmacovigilance plan
6. A well-resourced adherence plan targeting patients, their families, and communities as well as health-care providers
7. A national quality assurance system for the procurement, supply and distribution of high quality drugs.
8. Commitment to continue basic science research into drugs and clinical outcomes
9. A well designed monitoring and evaluation framework for the programme.

The panel considered in detail issues of resistance and toxicity and side-effects, and chose a combination of drugs specifically selected for ease of administration, compliance and their limited side-effect profile. The South African consensus version of the WHO guidelines

were compared in detail with the current United States Department of Health and Human Services *Guidelines for the use of antiretroviral agents in HIV-infected adults and adolescents*, generally regarded as the "gold standard" for ARV use in a highly-resourced setting. The Team undertook a costing and cost-effectiveness analysis of the US guidelines relative to the South African guidelines, which indicated that there would be very significant additional costs attached to the US guidelines, but that they would provide relatively marginal additional benefits in terms of survival.

Positive developments which further support the WHO guidelines include rapid reductions in prices, new medications and global experience in their utilization, opportunities emerging in the global trade regime, experience in the South African private sector, and the growing body of knowledge among the local scientists and health practitioners who contributed to the work of the task team and who would play a critical role in the operationalisation of government's decision in this regard.

Implementation planning for the introduction of ART would place considerable emphasis on a range of measures to maximise adherence to treatment by patients, in order to control the possible development of drug-resistant viral strains. A 5-year plan to strengthen and build the pharmacovigilance system has been developed and costed. The goals of the plan are to

- improve patient care and patient safety
- improve public health safety
- contribute to the assessment of benefit, harm, effectiveness and risk of ARVs in particular, but also of other drugs currently used in the health sector.
- Facilitate MCC regulatory function and understanding of adverse drug reaction patterns and trends.
- The 5-year plan for pharmacovigilance monitoring is based on having a central body which co-ordinates pharmacovigilance activities, captures pharmacovigilance data from satellite units around the country on a database and promotes pharmacovigilance initiatives

Resistance, Toxicity and Side Effects

The emergence of resistance is a function of several factors: prior treatment, pre-treatment levels of viremia, presence of pre-existing mutations, potency of the medicinal regimen, medicine therapeutic levels which are influenced by adherence to treatment, adequate dosing, and bioavailability related problems, amongst others. These factors have to be confronted as part of a global strategy to contain antimicrobial resistance.

Further, antiretroviral therapy is not without its hazards. More than most pharmaceutical agents, antiretroviral agents do have serious side-effects, although they are by no means unique in this respect. These side-effects vary in severity and duration, and may differ significantly between individuals.

While most are self-limiting, and resolve within the first three months of treatment, there have been instances where heart disease, cancer, abnormal cholesterol concentrations and so on have manifested themselves. In some patients, the side effects may be severe enough to lead them to discontinue treatment. There have also been cases of death as a direct result of ARV usage

HAART has only been in use since 1996, and experience in its use is growing with time. There are many unanswered questions with regard both to HIV infection and progression to AIDS, as there are on the efficacy of ARV's. The best scientific knowledge available has demonstrated that, properly used and carefully managed, these agents do help restore patients with AIDS to an appreciable level of human functionality and they do defer death.

As such, a decision to provide ART is ultimately about weighing the risks and benefits in relation to patients already in a desperate state of illness, and even more critically, it should be on the basis of sufficient information which enables the patient to make an informed choice, and then the patient's consent should be obtained and recorded. This choice should be underpinned by scientific rigour and ethical conduct on the part of medical practitioners.

The first few days of antiretroviral therapy are usually an adjustment period where patients have to get used to the medication. During this period many have gastrointestinal side effects, which are often transitory. In some cases, especially the dispersible formulation of

didanosine, the nausea and bloatedness can persist and result in patients not taking the drug. The enteric formulation is free of this side effect, as it does not have the buffer. Some can cause skin rashes, especially the non-nucleoside reverse transcriptase inhibitors. These rashes can be non-specific requiring symptomatic therapy, while occasionally they may be more severe, requiring stopping of the drug and (very rarely) hospitalisation. Other common but self-limiting adverse effects include headache, malaise and generalised weakness. There are also medium and long-term side effects that can manifest quite subtly at first. Peripheral neuropathy is a mostly reversible mid to long-term adverse event, seen mostly with stavudine when combined with didanosine, although both may cause this when not used together. Bone marrow suppression can occur with zidovudine and stavudine (as well as co-trimoxazole). This is usually detected on full blood analysis. There might be a drop in the levels of haemoglobin, neutrophil count or platelets.

Costs of the SA/WHO Consensus Guidelines

The consensus guidelines developed by the technical team would allow ART to be provided at the following costs per patient per year:

Total Cost – Adult	Current Prices / Manufacturer's Quotes	Best Prices
Regimen 1 - First Year	12,232	8,139
Regimen 1 – Subsequent Years	11,705	7,611
Regimen 1 - 9 months Pregnant Women	10,630	4,104
Regimen 2 – Per Year	18,177	10,554

These costings incorporate all relevant inputs required for the provision of ART, namely drugs, laboratory monitoring, and service delivery costs (staff and health facility operating costs). As the table makes clear, there is still considerable room for improvement from the current prices paid in South Africa to catch up with international best prices – but price decreases in recent months give very strong grounds for believing that considerably better prices could be secured by a public sector ARV programme. Costing of a basic nutritional supplementation intervention for people sick with AIDS (whether or not they are in receipt of ART) was also undertaken, and is incorporated in the analysis below on the assumption that 50% of people with AIDS may have inadequate access to food.

Costs of Universal Access to Comprehensive Treatment Packages

Two epidemiological and costing models were used to estimate the total costs of moving to universal access to comprehensive treatment for AIDS, including different levels of coverage of ART. The two models produced highly consistent results, increasing confidence in the robustness of the results generated. The modelling exercise considered the costs of universal access to a full range of treatment interventions (including nutrition) as per the current package ("No ARV" option); it then considered the additional costs (and associated savings) of moving to different levels of ARV coverage by the year 2008. The team used the models to examine the costs of four possible treatment scenarios:

- **"No ARV"**: Providing comprehensive access to current standard treatment guidelines for all who need it, but with no antiretroviral therapy for people with AIDS
- **"20% ARV coverage"**: Working up via phased implementation to provide ART for 20% of all new AIDS cases in 2008, with full access to non-ARV care for all those who need it
- **"50% ARV coverage"**: Working up via phased implementation to provide ART for 50% of all new AIDS cases in 2008, with full access to non-ARV care for all those who need it
- **"100% ARV coverage"**: Working up via phased implementation to provide ART for 100% of all new AIDS cases in 2008, with full access to non-ARV care for all those who need it

The different ART scenarios lead to different numbers of people being on ART by 2008 – the 20% scenario would see 200,000 people on ART by that year, the 50% scenario would require 600,000 people to be on treatment, and the 100% scenario would see 1.2 million people on treatment by 2008.

It should also be stressed that the actual pace of expansion of an ART programme would depend critically on our ability to ensure that the prerequisites for success are progressively put in place.

The total service delivery cost of each treatment scenario is presented below:

Billions of Rands Per Year

Scenario	2003	2005	2008	2010
No ARV	5.4	6.3	6.7	6.7
20% Cover	5.5	6.6	7.8 – 8.1	8.2 – 9.0
50% Cover	5.5	7.0	9.6 – 10.5	10.8 – 12.9
100% Cover	5.6 – 5.7	7.9 – 8.3	13.4 – 15.7	16.9 – 21.4

Total AIDS treatment & care costs by scenario (target year 2008)

The introduction of antiretroviral therapy would have a significant impact on AIDS mortality, reducing considerably the number of deaths from AIDS during the next decade (see figure below). It is to be hoped that ever-more effective treatment interventions for AIDS will continue to be developed in coming years, and that, in the long-term a cure for AIDS and/or an effective vaccine for HIV can be developed; the introduction of ART would clearly increase the prospects of currently-infected people that they may survive long enough to benefit from such future technical developments.

Between 2003 and 2010, the 20% ARV coverage scenario would result in 293,000 deaths being deferred until after 2010 (deaths of individuals who, without ART, would have died prior to 2010). The 50% ARV scenario would result in 733,000 such deaths being deferred until after 2010; and the 100% ARV scenario would defer 1,721,000 deaths over the same period. These results would be achieved at an incremental cost of between R 23,674 per death deferred (20% scenario) and R 26,238 per death deferred (100% scenario).

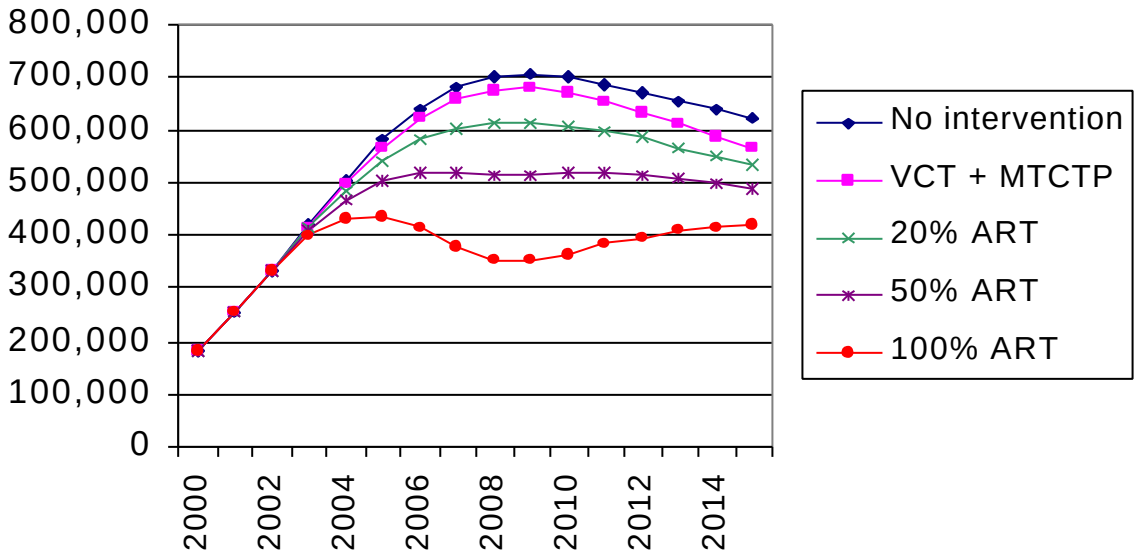


Figure 3: Impact of ART on AIDS Mortality

Antiretroviral therapy allows significant extension of life – conservatively estimated as 3.6 to 4.4 years of relatively illness-free life, when compared to non-ARV treatment. Under the 20% ARV coverage scenario, close to a million additional years of life would be saved relative to non-ARV care by 2010. 50% coverage would save an additional 2.3 million life years. 100% ARV coverage could save an additional 5 million years of life more than the non-ARV scenario over the period to 2010. It currently costs R 10,934 to gain one extra year of life, using non-ARV treatment. If ART were added to standard care, the cost of each additional year of life thus gained would be between R 7,435 and R 8,825 (the "incremental cost per life year gained" due to the addition of ART).

The addition of antiretroviral therapy to the public sector's treatment programme would also yield significant benefits in terms of deferring or reducing the number of children who would become orphans.

By allowing their parents to live longer, ART can defer the point at which a child is orphaned, allow children more time with their parents, and would allow better planning and organisation to support orphans at all levels of society. Without ART, it is estimated that 1.8 million children will become orphans between 2003 and 2010. 20% ARV coverage could reduce this total by 140,000 children; 50% coverage by 350,000; and 100% ARV coverage by as many as 860,000 children.

Other socio-economic benefits might plausibly be expected from expanding access to ART, but cannot currently be modelled. The team concluded, however, that there is currently no compelling evidence that ART would lead to any reduction in the number of new HIV infections occurring. The team therefore wishes to stress the need for continued enhancement of prevention programmes, even if a decision were taken to expand the treatment package to include ART.

Scenario	Total Annual Costs (Billions of Rands)	Outcomes (Cumulative benefits, 2003 to 2010)	Incremental Cost-Effectiveness
No ARV	2003 5.4 2005 6.3 2008 6.7 2010 6.7	No long-term mortality impact 4.2 million Years of Life Gained No effect on orphans	N/A R 10,934 per Year of Life Gained
20% ARV (by 2008)	2003 5.5 2005 6.6 2008 7.8 – 8.1 2010 8.2 – 9.0	293,269 deaths deferred 5.2 million Years of Life Gained 140,000 orphans deferred	R 23,674 per death deferred R 7,435 per Year of Life Gained
50% ARV (by 2008)	2003 5.5 2005 7.0 2008 9.6 – 10.5 2010 10.8 – 12.9	733,172 deaths deferred 6.6 million Years of Life Gained 350,000 orphans deferred	R 26,995 per death deferred R 8,061 per Year of Life Gained
100% ARV (by 2008)	2003 5.6 – 5.7 2005 7.9 – 8.3 2008 13.4 – 15.7 2010 16.9 – 21.4	1,721,329 deaths deferred 9.3 million Years of Life Gained 860,000 orphans deferred	R 26,238 per death deferred R 8,825 per Year of Life Gained

Presented in these terms, it is clear that moving from full coverage of non-ARV treatment to progressively higher levels of ARV coverage incurs net additional costs, but also yields progressively higher benefits in terms of reduced mortality, increased survival, and reductions in numbers of new orphans.

Under all scenarios, a comprehensive health sector prevention programme will be required, which will cost an additional R 550 to 570 million per year for the rest of the decade (in the absence of further fundamental technological developments in the area of prevention, such as discovery of an effective and affordable vaccine, etc.).

Public policy assumptions on roll-out

An analysis was made of critical public policy assumptions on the rollout. This analysis highlighted the following principles, which Government needs to adhere to in the enhancement of a comprehensive treatment strategy:

- Any programme (including any ARV programme) must ensure that it meets the needs of those in "desperate need" (i.e. the sickest and the poorest)
- Provision for the rural poor must not be delayed until after urban areas have been served, but must commence concurrently

- The State must have a clear, transparent and reasonable plan, which has the flexibility to address changing circumstances
- Phased implementation of programmes is acceptable, as long as the State is working towards the realisation of a programme to which everyone in need will ultimately have access
- Rationing on the basis of behaviour (e.g. poor adherence to treatment) is justifiable
- A coordinated national programme is required to ensure equitable resource allocation and roll-out across provinces

Strengthening the Pharmaceuticals Supply Chain

If a decision were made to implement an ART programme in the public sector, a number of actions would be required with respect to pharmaceuticals supply (it should be noted that most of these steps would be beneficial even without an ART programme):

- Establish a strong national price negotiations team and strategy to assertively negotiate reduced prices for ARVs and other essential drugs
- Strongly encourage the granting of voluntary licences by patent holders for local manufacture
- In the medium term, consider using the provisions of Article 31 of TRIPS to move forward with compulsory licensing
- Provincial drug supply management and delivery systems require strengthening

The resources required to strengthen both the pharmaceutical supply chain and the related regulatory functions of the Medicines Control Council have been estimated and are incorporated in the costs estimates for programme implementation presented below.

Implementation Requirements

Irrespective of whether or not ART is to be provided in the public sector, a number of measures are required to strengthen current services for those who are infected with HIV but who have not yet become sick with AIDS. These are:

- **Improved nutritional support for persons infected with HIV**: a substantial amount of resources will be directed towards strengthening HIV positive persons ability to prevent and combat disease through the newly developed *Nutritional Supplementation Programme for People with TB, HIV and AIDS (DOH, 2003*).

- The above will presuppose a stronger and more widely distributed and accessible **VCT infrastructure and capacity.** It will also necessitate a massive campaign for HIV testing and assessment of the clinical profile of those who may qualify for antiretroviral therapy. Within the Department of Health VCT programme steps are currently taking place in the context of the Revised VCT Strategy and progress is being made in this regards. These developments will be speeded up in the context of strengthening of care for people living with HIV and/or AIDS as proposed in this report.
- **Quality of care and training of service providers** – the central responsibility for strengthening quality care provision for people with AIDS will rest with planned provincial "Regional Training Centres", which will establish central expert teams in each province to provide training for health care providers, quality improvement activities, and accreditation of services and individuals. Development of these Regional Training Centres is already under way.
- **Improved availability and affordability of essential drugs** – continued efforts will be required by national and provincial pharmaceutical programmes to secure better prices for drugs required under existing treatment guidelines (including antiretrovirals currently used in prophylactic applications for PMTCT and PEP), and to ensure continuous improvement of drug availability and distribution systems

The team considered in detail the implementation actions and requirements for the introduction of ART in the public sector. The introduction of an ART programme is judged to be feasible, but would require careful planning and coordination. Recent experience of programme implementation (especially of PMTCT) indicates certain key lessons:

- Implementation takes time, and adequate set-up time must be allowed for
- While adequate resources must be provided, provinces and facilities must not be over-funded, as they have a finite absorption capacity in the early stages of any programme
- Strong national leadership and coordination is essential to avoid excessive disparities between provinces in the pace of implementation

The technical team has therefore recommended that a strong national programme implementation structure would be essential to any ARV programme, and that such a unit would require adequate resources (both financial and managerial) to successfully drive the early years of any implementation of ART. This structure would be required to oversee

logistical and operational activities across all nine provinces in the form of a *National Management Framework.* This structure would have a support and oversight role in all provinces, but would have a particular focus on driving and supporting implementation in provinces with weaker management and clinical capacity. It would be responsible for the following key tasks:

- Establishment of a national programme implementation structure (at national and provincial level), to oversee and support all implementation activities, to ensure equity in service development, and to monitor and review all aspects of the AIDS treatment programme
- Continued fast track registration of antiretrovirals and generic formulations by the MCC
- A fast-track process of negotiation with suppliers and activation of legally permitted (but thus far unused) mechanisms to achieve access to high-quality ARV drugs at the best po
- ssible prices
- Supporting VCT expansion based upon the revised strategy
- Collaboration with National Health Laboratory Service to ensure sufficient laboratory capacity and distribution systems to support patient monitoring
- A rapid and intensive training programme for health care professionals at those sites which would be commencing provision of ART
- Strengthening of the pharmacovigilance function of the MCC to support the introduction of ARVs
- Formalise engagement / interaction with the private sector
- Establishing strong referral systems within and outside the formal health sector
- Specific monitoring, evaluation and performance management systems to support implementation and assist with programme revision and development, and to ensure that ART is not displacing resources and effort from other health sector priorities

The national coordinating structure would be advised by a clinical expert panel, with direct links to the Essential Drug List structure and the Medical Research Council, as the research arm of Government. The national coordinating structure would require a dedicated national Programme Implementation Unit, which would take responsibility for the direct planning and execution of implementation plans, and for critical national functions. The introduction of antiretroviral treatment would be a significant undertaking, which would require a credible

Programme Implementation Unit with sufficient skills and personnel to meet the challenge. The team emphasises that accumulated experience shows clearly that failure to establish an adequate Implementation Unit would severely compromise the ability of any antiretroviral programme to achieve its objectives or to move to scale as per its mandated targets. Resources required for the national PIU and associated communication, monitoring, evaluation and research functions would be as follows (excluding training, which is detailed separately below):

	2003/04	2004/05	2005/06
Personnel	3,226,000	6,452,000	6,452,000
Non-Personnel	22,800,000	38,500,000	38,500,000

Monitoring, evaluation and research will be an essential component of any successful programme. Significant resources will be required to conduct a range of monitoring and evaluation activities, including:

- Monitoring of programme implementation success and problems
- Evaluating programme outcomes
- Evaluating programme costs and efficiency
- Surveillance of emergence and patterns of drug resistance (with NHLS / NICD)
- Rapid learning, sharing and dissemination of implementation lessons

Important areas for dedicated research funding via the national programme would include:

- MRC research programme on safety, effectiveness and costs of immune boosters, traditional and complementary interventions in maintaining health after HIV infection
- Effectiveness and costs of combined nutritional and pharmaceutical interventions
- Assessing any possible spillover effects (positive or negative) of ART on prevention messages, sexual behaviour and HIV incidence
- Continuous improvement of diagnostic technologies
- Investigation of alternative organisational models (e.g. expanding ART provision to primary care clinics etc.)

The preparatory training of health professionals to support an ARV programme would be funded centrally, and managed by the PIU. The scale and cost of training depends on the

precise coverage target and timetable selected. Analysis of the number of hospitals and CHCs (and staff from each) which would be required to achieve the trajectory for the 50% and 100% ARV coverage scenarios has been undertaken. Achieving the 100% coverage target by 2008 would require a faster implementation, with all hospitals and CHCs having joined the programme by the end of 2004. Assuming a need to provide detailed training 2 or 3 doctors, 2 pharmacists, and 12 nurses per facility, plus basic training for up to 50 community and health personnel (e.g. home-based care workers, VCT counsellors, TB DOTS supporters, PHC nurses, etc.) in adherence support for ART, the two scenarios suggest training requirements of the following order:

50% ARV coverage by 2008

	2003/04	2004/05	2005/06
Number of New Sites Joining Programme	80	120	156
Number of Staff to be Trained	5360	8040	10452
Cost of Training	R 8.1 million	R 12.1 million	R 15.8 million

100% ARV coverage by 2008

	2003/04	2004/05	2005/06
Number of New Sites Joining Programme	120	236	0
Number of Staff to be Trained	8040	15812	0
Cost of Training	R 12.1 million	R 23.8 million	0

It is the view of the Technical Team that implementation progress should be constantly reviewed if an ARV programme is introduced. The pace of implementation and expansion should explicitly be viewed as flexible. Setting fixed targets in terms of coverage rates of patients is likely to be highly problematic, as it will be virtually impossible to predict *a priori* the actual pace of expansion of the programme. Targets in terms of numbers of facilities offering the service would be less restrictive, but will still need to be explicitly flexible. If rapid progress proves to be achievable, there should be scope to bring forward expansion plans; if progress proves to be more difficult than originally envisaged, there should be scope for deceleration to allow problems to be resolved. Ultimately, making a firm and credible commitment to implementing the programme will be more valuable than setting arbitrary targets.

It is particularly important to stress that – whatever the long term coverage level that can be achieved – the early years of implementation of an ARV programme would require patience, and communication of the fact that, at least initially, numbers of patients on treatment will grow fairly slowly. In particular, once a decision to introduce ART were made, it is the team's view that six to nine months' preparatory activities are required before the first patients would start to receive medication on the ground. During this preparatory phase a few sites, may have to be identified where actual implementation of the programme may be initiated. This would enable practical lessons learnt to be factored into the general planning for the commencement of the programme on a wider scale. Failure to undertake adequate preparation would clearly be self-defeating, and these timescales must be clearly communicated to the public and to health workers from the very outset.

Provinces would require limited additional funding to establish programme management capability to liase and coordinate local implementation with the main national PIU:

	2003/04	2004/05	2005/06
Coordination per province	600,000	1,500,000	1,500,000
Total (x 9 provinces)	5,400,000	13,500,000	13,500,000

There will clearly be a need to ensure that provinces are adequately supported (both in terms of financial and managerial support) to allow an equitable and uniform roll-out of any ART programme. Provinces will therefore need additional managerial resources as outlined above, along with clear guidance and support from a strong national implementation unit. However, it is also important to consider briefly the importance of ensuring that the recurrent programme costs of providing the treatment package are secured by provinces as additional funds, in order to ensure that current resources are not strained even further. A number of factors will require consideration to ensure the success of an ART programme. A commitment of additional resources must be made *over the long term* – specifically to recognise that the long-term costs of ART are significant, and that they should not be allowed to erode the integrity of other health services over the years. It must also be recognised that the current formula for the division of revenue between provinces via the Equitable Share mechanism does not make provision for different rates of HIV prevalence or AIDS workload, and that additional funds allocated via this route cannot be securely ring-fenced for use in an

ART programme. The strengths of a nationally-driven and nationally funded programme in supporting equitable implementation are significant, as they may well be a better means of ensuring both that the ART programme succeeds, and that it does so without undermining other health priorities.

A decision to implement ART would require phased implementation over two to three years, and could not be undertaken overnight. Public hospitals (and, later in the implementation cycle, CHCs) would be selected in two or three implementation "waves"; selection for the first wave would include a number of well-equipped hospitals *and* a number of poorly-resourced and rural hospitals, which would be offered targeted support to rapidly enhance their capacity in key areas. Preparatory activities would involve infrastructure and systems strengthening, and targeted training of key staff.

A clear communication strategy is required in order to maximise the implementation of a strengthened care and support programme for South Africa. This communication needs to be effective and conducted at different levels: individual level; community and facility levels. Different strategies will be necessary to deal with the various levels. Similarly, different media and contents should be used for effective communications. Intensive and active communication would be required from the moment a decision to introduce ARV treatment were taken. Significant efforts will be required to continuously emphasise the benefits of early diagnosis, and to reinforce the message that everyone should know their HIV status – stressing that early diagnosis allows early provision of OI prophylaxis and (depending on the ultimate direction of policy) nutritional support, both of which can potentially defer the onset of illness.

One clear message at community level for example should be that not all HIV positive persons require ARVs. Given the experience in the USA and Europe, it will also be essential to stress that there remains no cure for AIDS. Key to the communication at individual level will be the need to continuously emphasise the necessity to adhere to therapy and the help that could be found in disclosing HIV status to a close family, community member or treatment supporter. In facilities, communication should target providers and users.

Resource Requirements

The long-term **service delivery costs** (i.e. operating costs) of the full package of health care and nutrition support under the three treatment scenarios are as follows:

Billions of Rands Per Year

Scenario	2003	2005	2008	2010
No ARV	5.4	6.3	6.7	6.7
50% Cover	5.5	7.0	9.6 – 10.5	10.8 – 12.9
100% Cover	5.6 – 5.7	7.9 – 8.3	13.4 – 15.7	16.9 – 21.4

It is vital to emphasise that the extra costs of introducing antiretroviral therapy would be additional to the current package of interventions. This is especially important over the long term, as ARV costs grow with increasing coverage levels; under-funding of such a programme in the long-term would displace other high-priority health interventions and destabilise the public health system.

It will be necessary to maintain targeted spending of R 550 to R 570 million per year for the foreseeable future to ensure that a **comprehensive and effective health sector prevention programme** is maintained, given currently available preventive interventions (n.b. this amount does not include prevention efforts in other sectors e.g. Education).

Under *all* scenarios (including non-ARV scenarios), a critical pre-requisite for successful implementation of improved treatment, care and support is the rapid establishment of Regional Training Centres:

Millions of Rands Per Year

	2003/04	2004/05	2005/06
Regional Training Centres	46.3	67	67

The **programme management, start-up and support costs** of establishing and implementing a successful ARV treatment programme (above and beyond the direct costs of providing the intervention at health facilities, captured above) are as follows:

Millions of Rands Per Year

	2003/04	2004/05	2005/06
National Programme Implementation Unit	26.0	45.0	45.0
Training Health Care Providers – 50% scenario	8.1	12.1	15.8
Training Health Care Providers – 100% scenario	12.1	23.8	0
Provincial Implementation Support	5.4	13.5	13.5
Strengthening Pharmaceutical Procurement	15.8	23.6	23.6
Stengthening Medicines Regulatory Activities	0.7	1	1
Strengthening Pharmacovigilance	1	1.5	1.5
Total Implementation – 50% Scenario	57.0	96.7	100.4
Total Implementation – 100% Scenario	61.0	108.4	84.6

Relative to the current treatment package, the **total additional funding requirements** to support movement towards universal access to ART by 2008 (including management costs) would be as follows:

Billions of Rands Additional Funding Required

	2003/04	2004/05	2005/06	2008/09	2010/11
50% ARV	0.1	0.4	0.8	2.9 – 3.8	4.1 – 6.2
100% ARV	0.2 – 0.3	0.7 – 1.8	1.7 – 2.1	6.7 – 8.9	10.2 – 14.7

Conclusion

South Africa has reached a particular stage in the HIV/AIDS epidemic. Information from various data sources clearly indicate the fact that the HIV epidemic is stabilising with a significant reduction of its pace in younger age groups. These data however also show the need to strengthen our current approach with regard to treatment, care and support in the face of increasing mortality due to HIV/AIDS, over and above both the other elements of the comprehensive strategy and government's integrated programmes to alleviate poverty.

The Task Team report shows how South Africa can strengthen its efforts in the areas of nutrition, management of opportunistic infections, and provision of antiretroviral therapy. It elaborates on the prerequisites for such a comprehensive programme to be put in place, and highlights the benefits that such an undertaking – if properly implemented – could yield from a health and societal perspective. Such proper implementation should encompass

dispassionate rigour with regard to the sustainability of the programme, including clarity from a public policy perspective on the fact that ART is one among the variety of interventions required to deal with AIDS, which interventions in turn are only part of the overall social programmes of government.

The possibility of considering sustainable antiretroviral therapy is a natural progression of the implementation of the comprehensive 5-year Strategic Plan. It has been occasioned, amongst other factors, by positive developments with regard to the many constraints that government had earlier identified. These positive developments include rapid reductions in prices, new medication and global experience in its utilization, opportunities emerging in the global trade regime, experience in the South African private sector, and the growing body of knowledge among local scientists and health practitioners who contributed to the work of the task team and who would play a critical role in the operationalisation of government's decision in this regard.

There is also now a better appreciation of the social dimensions of the pandemic of HIV and AIDS, both within South Africa and in the global arena. This allows policies on health care interventions to be appropriately located in a broader social and health context.

Many uncertainties remain, and our knowledge of HIV and AIDS continues to evolve rapidly; however, the contents of the Task Team Report emanate from the best available body of knowledge from a clinical, public health and health economics perspective. The same applies to reflections on the legal, constitutional and financial implications.

As stated earlier, given the costs, complexities and limitations of ART, a decision to provide such treatment is one about weighing the risks and benefits with regard to patients already in a desperate state of illness, and even more critically, it should be a matter of informed choice on the part of the patients. If and when ARV treatment is introduced, it will be necessary to provide all available information to patients on the benefits, the limitations and the possible adverse consequences of this treatment, and ensure not only informed consent on their part, but also a full appreciation of the responsibility that devolves upon the patients themselves.

Further, it should asserted that an even greater responsibility devolves upon health practitioners with regard to such matters as the rigour of HIV tests, counselling, management

of ARV prescription, and so on – in brief, ethical conduct in line with the requirements of the profession. Such responsibility, it is assumed, would include such sanctions for negligent or profit-driven management of ART as would apply to the management of other serious illnesses.

Success in the implementation of ART in the South African setting, as in other countries which have gone this route, depends not only on availability of funds, but also on adequate health infrastructure, affordable medicines and human resources with the requisite skills. The actual pace of expansion therefore would depend critically on our common ability to ensure that the conditions for success are progressively put in place.

Success also relies on strong partnership across society, including the communication of objective facts about the pandemic and its management. Creating false expectations or an atmosphere in which society lowers its guard on matters of awareness and lifestyle change, or engaging in mutually debilitating contestation around what can be achieved by when, can all have the effect of undermining not just the ART programme, but also the hard-won advances made thus far in the fight against HIV/AIDS.

Conversely, a cooperative relationship among all sectors, particularly in the implementation of this element of the comprehensive strategy, the spirit of *letsema* and *vuk'uzenzele*, a message of hope and responsibility as well as constructive engagement in the realm of practical work would ensure that South Africa advances even more decisively in this endeavour, which is literally a matter of life and death.