

Chapter XIV

Research Priorities

OVERVIEW

Research is a critical element of the plan for Comprehensive Treatment and Care for HIV and AIDS. The objective of the research agenda is to conduct studies whose answers will define the most effective provision of HIV and AIDS care and treatment, and guide programme implementation. Further new solutions for HIV and AIDS are needed as there is still no cure for AIDS, and it still proves impossible to eradicate totally the HIV virus from an infected individual, despite the progress in the past five years in the development of new antiretroviral drugs.

With regard to effective delivery of the antiretroviral drugs some of the critical questions to be asked would include: What is the most effective delivery of ARVs to persons who have progressed to a stage at which these drugs become necessary; What are the best approaches to prevent new infections with HIV; What are the best interventions, nutritional or otherwise, to extend the period in which HIV-infected people can be maintained without antiretroviral drugs - arresting progression to AIDS? The challenge is to protect the immune system from the depredations inflicted upon it by HIV infected CD4+ cells during the 5–14 years between initial seroconversion and AIDS. In Africa this decline seems to be more rapid than in developed countries.

When eventually the patient's immune system has been extensively destroyed and their CD4+ count drifts below 200 per ml, the research challenge becomes one of optimising delivery of currently available interventions such as antiretrovirals, nutritional interventions, antimicrobial prophylaxis and treatment of opportunistic infections, as well as the place of traditional and complementary medicines. Such research would include development of enhanced diagnostic and monitoring technology; new and improved drug regimens; better use of health systems to deliver these drugs; and behavioural research to improve compliance with medication regimens. This is the main thrust of the research

agenda: to conduct studies whose answers will define the most effective provision of HIV and AIDS care and treatment, and guide programme implementation.

The operational plan also seeks to engender research into one of the most important research question in AIDS: how to protect the immune system from continuing destruction caused by HIV-infected cells and other possible factors such as micronutrient deficiency, malnutrition, concomitant infection with other viruses and bacteria, and psychological stress.

Finally research in this programme on ‘immune reconstitution’ should be supported, including the effectiveness of putative immune modulators from traditional and complementary medicines – interventions that might permit AIDS patients to live out a normal and healthy lifespan despite continuing infection with HIV.

BACKGROUND AND RATIONALE

The scope of the treatment effort being undertaken creates an opportunity to understand the impact of ARVs in a largely treatment-naïve population. The information currently available on the use of ARVs derives from studies not representative of the South African situation, where local factors, including poverty, endemic clades of HIV, local host genetics, and the impact of co-infections with other pathogens such as tuberculosis remain to be evaluated. At the most basic level, formal research will be essential to understand the effectiveness, safety, and appropriateness of ARV use, and to refine the HIV and AIDS care and treatment programme moving forward. ARV use in South Africa is limited, indicating the need to monitor closely treatment effects when these drugs are made available in the public sector. The considerable research infrastructure available at multiple sites in South Africa, together with the strong research leadership from South African investigators, provide a sound platform upon which to rapidly develop a research programme that runs concomitantly with the implementation of antiretroviral therapy.

Rational development of a successful research agenda requires the ability to accurately track care delivery, during programme implementation. The health system’s performance in delivering care is the essential component of any health programme, including this one.

The implementation of the ARV plan will inform the research used to guide this programme.

The establishment of a high-quality, accurate database that includes all persons initiating ARV treatment is central to this research effort (see Chapter XI, *Patient Information Systems*). Targeted sample collection and storage will be essential for addressing some basic research questions. Funding will be needed to support both human resources and infrastructure, including storage facilities. Mechanisms will be established for investigators to submit research proposals for consideration to a representative review panel with a transparent review process that will prioritise competing research projects and access to data. Linkages to established research programmes (such as the MRC, South African AIDS Vaccine Initiative, academic research programmes, Comprehensive International Programme on Research on AIDS, and International AIDS Clinical Trials Group) will provide synergy and prevent duplication of effort. The research programme will be flexible, such that it can respond to newly arising issues and provide guidance for future efforts.

The substance of the research agenda is based on extensive use of quantitative and qualitative methods. While quantitative research is essential to assess the success of specific aspects of the programme, added strength derives from associated qualitative studies. Qualitative and behavioural research provides greater insight into clinical decisions. Qualitative research also gives voice to individuals, families, communities, and illuminating circumstances. Qualitative information from HIV-infected individuals is particularly critical to the success of the programme, as the introduction of HIV and AIDS care and treatment constitutes an entirely new future for the HIV-infected population. Care and treatment will also alter the relationships among the infected and their families, communities, and care providers.

APPROACH

Clinical Research

Most data that guide the use of ARVs have been generated in the setting of developed countries, and have focused on different strains of virus than those responsible for the

South African epidemic. Although there is no question that ARVs can be life extending, the optimal use of these drugs has not been determined in the South African setting. Operational research to define best practices in similar settings has been limited. The performance of VCT sites to diagnose HIV infection and laboratory facilities to monitor resistance and the response to treatment are critical to the success of the programme. Development and use of new diagnostic tests for CD4, viral load, and resistance monitoring, and new parameters on the timing, frequency and location of laboratory monitoring, need to be evaluated.

A significant concern of the ARV programme is the development of resistance and the transmission of resistant strains of the virus. There is a clear, immediate need to research and develop an early warning system that indicates the onset of resistance, both at the service point level and at a national level.

The impact of antiretroviral medications on adolescent growth and development in naïve populations is a unique area of inquiry. Little has been published on the interplay of these medications on post-pubescent physiology, including issues around contraception.

Epidemiological Research

Epidemiological research will constitute an important aspect of the research agenda. This area of research will augment information that is currently collected in routine reporting systems and research projects which constitute HIV and AIDS surveillance systems. These include studies such as the Department of Health annual prevalence surveys, Behavioural Surveillance, Youth Risk Surveillance surveys and HIV incidence studies. Epidemiological studies include studies that add information on the progression of the HIV and AIDS epidemic. Data collected in this ARV programme will provide important epidemiological data on morbidity and mortality related to AIDS. Epidemiological studies will be able to provide more detailed information on HIV and AIDS associated morbidity, mortality and disability in the context of the overall burden of disease in South Africa.

Health Systems Research

Health systems research will include a broad range of issues including questions related to activities aimed at improving the health system's capacity to handle the increased service

requirements established by the implementation plan. Research projects may define how best to facilitate the integration of ARV programmes with general health services and with other HIV-related programmes, to avoid the creation of vertical, specialised operating silos among programmes. Specific projects will for instance evaluate whether the initial implementation, as well as integration with existing programmes at the service points, will de-stigmatise and de-mystify HIV care. Special attention will be given to identifying impact of ARV roll out on treatment behaviours, and concerns and strategies related to available HIV therapy in the workplace. Studies will also assess how the HIV and AIDS care and treatment plan affects other health programmes.

HIV Prevention Research

Prevention of HIV infection is the foundation for management of HIV and AIDS. Prevention can be augmented through a successful treatment plan. The classical method of preventing viral infection is vaccination. However as yet no HIV vaccine exists, and current progress suggests that it will be at least 5–10 years before an effective vaccine is available. The well known maxim that ‘the only vaccine for HIV is prevention’ still rings true; and behavioural science research to investigate how to enable people to protect themselves from HIV infection (through modification of sexual behaviour, use of condoms, microbicides, diaphragms etc.) is a key priority in HIV and AIDS research.

Behavioural Research in Prevention, Treatment and Care

HIV and AIDS is as much a psychosocial phenomenon as it is a biomedical phenomenon. Thus, the behavioural science research agenda is critical to providing insights leading to the discovery of improved treatment regimens for HIV-infected individuals. For the behavioural science research agenda a high priority is (a) designing, implementing and evaluating HIV sexual risk-reduction programmes to prevent the acquisition of HIV; (b) elucidating factors associated with adherence to antiretroviral medication and designing adherence programmes; (c) making antiretroviral medication more easily accessible; (d) reducing stigma associated with being at risk and living with HIV and AIDS. Priority behavioural research objectives for each of the following sections have been identified and are listed in the annexes (Annex XiV.1).

AIDS in South Africa is a disease that is transmitted primarily by social interactions between sexual partners. These risky sexual behaviours can be changed. Effective primary prevention programmes to prevent the further spread of HIV can assist people in making and sustaining behavioural changes that reduce the probability of transmission of HIV. A critical component of the behavioural science research agenda is to discover how to change behaviours and conditions that lead to HIV transmission including preventing their initiation and maintaining protective behaviours once they are adopted. Currently, behavioural interventions are the only effective way of slowing the spread of HIV. Cumulatively, meta-analyses evaluating the efficacy of HIV prevention studies, provide strong empirical evidence that interventions designed for individuals are efficacious in reducing high risk sexual behaviours.

Subsequent to identifying risk factors, HIV prevention research efforts must address issues related to the initiation and maintenance of HIV and AIDS risk-reduction efforts. This process requires moving beyond HIV and AIDS prevention programme efforts that only focus on providing information, education and communication (IEC). Moving beyond the IEC agenda requires the development of evidence-based HIV prevention programmes. Moreover, interventions designed to enhance adherence to antiretroviral therapy must be a research priority.

Rapid advancement of meaningful and effective HIV related social and behavioural science research requires further development of methodological tools, including those for evaluating HIV prevention interventions. As methodology represents the essential building blocks of intervention research it needs to be given special attention. Research methods are required to increase recruitment, retention and compliance to protocols for adherence and HIV prevention research. Adherence and HIV prevention intervention efficacy should be evaluated by using rigorous research methods, including randomised controlled behavioural trials. Evaluations of behavioural intervention studies should use self-reports of behavioural outcomes, as well as, HIV sero-incidence data and other biological markers as outcome measures. In addition to assessing intervention efficacy, researchers should assess the cost-effectiveness of prevention programmes. Finally, more research is needed to address the pressing ethical issues in the conduct of adherence and HIV prevention research.

Social Research

The impact of HIV and AIDS is experienced not only by individuals, but also by families, communities, and societies. The effects of the epidemic at all of these levels must be understood and monitored so that strategies can be developed to prevent household, social, and economic disintegration. The predominant mode of HIV transmission in South Africa is heterosexual transmission. Thus, designing interventions involving both partners of the couple to enhance their communication skills and facilitate partner norms supportive of safer sex is critical. There has been increasing recognition of the importance of the family in preventing and adapting to HIV prevention efforts. Families may include consanguine relationships, extended families, and kin sharing similar values and norms. Fostering family norms supportive of safer sex and adherence, providing HIV and AIDS education within the context of the family, and enhancing communication skills between parent and their children to dialogue about HIV prevention can be effective strategies. Effective interventions at the community level involve the community (neighbourhoods, social network members, organizations, institutions) as a partner and can enhance community norms supportive of safer sex and adherence. Societal level interventions involve modifying economic, legal, policy, and regulatory practices such that they may facilitate safer sex and therapeutic efforts.

Women experience HIV and AIDS differently than men do in a number of important respects, some of which are physiological and some of which are social. Women progress to AIDS at lower viral load levels and higher CD4 counts than do men. Women are more vulnerable to HIV as a result of cultural attitudes, social and economic position. This may be partly explained because context of heterosexual relationships and social arrangements are often characterized by gender inequality in which women have less power than men further exacerbates their risk of HIV. It is important to understand the socially constructed aspects of male and female relationships including economic dependence, political decision making, access to health services, and education that may influence access to antiretrovirals and practice of safer sex efforts. HIV infected pregnant women have received a great deal of attention, however, this has mostly focused on their role in preventing transmission to their offspring. Greater attention must be given to the women themselves.

There has been a growing recognition that many individuals at risk of HIV and who become infected with HIV are also afflicted by a number of co-morbid conditions including other infectious diseases (hepatitis, sexually transmitted diseases, tuberculosis), substance abuse, mental illness, malaria (and other disease prevalent in South Africa) and poverty. Research needs to test the efficacy and effectiveness of interventions that simultaneously address multiple diagnoses and risk and improve HIV treatment adherence. In addition to assessing the efficacy of the interventions, research is needed to understand and improve the organization, management, access, delivery, cost-effectiveness, and cost-utility of health care, family planning, social services, drug treatment services, alcoholism treatment that reduce HIV risk behaviours and transmission.

Support research for the development, evaluation, diffusion and adoption of strategies to increase early identification, to improve treatment adherence, and to prevent or minimize the negative physical, psychological, cognitive and social consequences of HIV including stigmatisation of persons with or at risk for HIV infection. Support research strategies for promoting effective health care utilization among all persons with HIV infection and for promoting modifications in the health care delivery system to develop more effective, culturally sensitive methods to better serve treatment needs of infected populations.

Specific Research Projects

Within the framework of these three areas, there are a number of research questions that are of highest priority (note that this list assumes that a national treatment cohort with a uniform database will be established; thus, this is not listed as a specific objective). These include:

HIV/TB Co-infection

The burden of co-infection with TB presents a specific challenge in terms of treatment of HIV infection. Guidelines for initiation of therapy and for initial treatment regimens have been derived from settings lacking a high burden of TB infection. However, in South Africa, it is estimated that over 55% of persons with HIV infection may also have clinical tuberculosis¹. The optimal timing of treatment of TB and HIV in co-infected persons and the optimal regimens for effective treatment remain to be determined. Thus operational

research to answer the following critical questions must be part of the initial ARV implementation plan:

- *What is the best treatment strategy for HIV-infected TB patients?*
- *What are the ARV regimen options that are most effective in the setting of concomitant clinical TB?*
- *Does malaria have an effect on ARV therapies?*

Opportunistic Infection

Research on opportunistic infections, and the mechanisms of infection and treatment should be an important component of the research agenda. A number of important research questions will arise, including:

- *What is the incidence/prevalence of various opportunistic infections in South Africa*
- *Do clinical course/severity and response to treatment differ from study populations in other geographic areas*
- *What is the role of co-infection with sexually transmitted infections (such as HSV2) on -infections with HIV*

Drug Resistance

One of the major threats to future treatment options for HIV infection is the development of antiretroviral drug resistance. Use of sequential monotherapy and dual therapies, and inadequate adherence to triple combination therapies has resulted in widespread emergence of multi-drug resistance in developed countries. Surveillance studies have indicated transmission of drug resistant viruses that compromise options for treatment of newly diagnosed infections. Success of the ARV treatment programme in South Africa will depend on the potency of the regimens used and proper adherence to these regimens. Moreover, the impact of widespread nevirapine use in PMTCT programmes on development of resistant mutations needs to be determined. Thus operational research to answer the following critical questions must be part of the initial ARV rollout plan:

- *What is the impact of nevirapine PMTCT programmes on subsequent treatment of women and their children?*
- *What is the evolution of drug resistance in the treated population as the programme is rolled out?*
- *What is the prevalence of drug resistance in the untreated population (i.e., how much drug resistant virus is being transmitted)?*

What Are the Optimal Efficacy and Toxicity Monitoring Approaches in the South African Context?

Most studies of ARVs have been performed in settings in which resources for monitoring efficacy and toxicity have not been limited. This has led to frequent monitoring, but the optimal frequency of monitoring has not been determined in a prospective controlled fashion, nor has the cost effectiveness of different monitoring schedules been determined. In addition, as the cost of ARVs drops, it is expected that a major economic burden will be the cost of diagnostic tests. Many new approaches to more economical monitoring, both through new monitoring techniques and through adjustment of monitoring schedule, are being developed. However, the impact of these new approaches on the quality of care delivered has not been determined. Thus a major important focus of initial research efforts should be to determine the optimal means of monitoring treatment. Operational research issues related to this effort include:

- *What is the optimal use and frequency of CD4 testing?*
- *What is the optimal use and frequency of viral load testing?*

What Are the Behavioural/Social Issues That Affect Success of Treatment Efforts?

The ultimate success of ARV treatment programmes is highly dependent on strict adherence to treatment regimens. Although there are clear data indicating that high levels of adherence to ARVs can be achieved in resource limited settings, the relative efficacy of different approaches to maximize adherence has not been determined. Moreover, the impact of new programmes for HIV and AIDS treatment on other aspects of the health

care delivery system has not been defined. Operational research issues related to behavioural/social issues include:

- *What are the optimum strategies to maximize and monitor drug adherence?*
- *What is the effect of the availability of ARVs on uptake of VCT?*
- *What is the effect of the ARV programme on sexual behaviour?*
- *What is the effect of the ARV programme on stigmatisation?*

What Are the Optimal ARV Regimens and Treatment Strategies?

Studies that have determined optimal regimens for treatment of HIV infection have largely been conducted in resource rich settings, where access to frequent laboratory monitoring is readily available. In these settings there nevertheless remain a number of inadequately addressed questions. The optimal use of ARV regimens in settings where resources are more limited, and where nutritional challenges and co-infections are more prevalent, remain to be determined. These factors pose a new set of research questions, which include:

- *What effect do different CD4 counts have on treatment outcomes as it relates to initiation of therapy?*
- *What to start: Should the initial regimen be non-nucleoside reverse transcriptase inhibitor (NNRTI) based or protease inhibitor (PI) based?*
- *When to change: Should clinical, CD4 or VL indications be used to determine when to change therapy?*
- *What to do in pregnancy? What are the optimal first and second line regimens in pregnancy?*
- *What to do in paediatric infection? What are the optimal first and second line regimens in paediatric infection?*

What is the Role of Nutrition in Health Maintenance in HIV Infected Persons?

HIV infection drives a hypermetabolic state with resultant weight loss and reduction in muscle mass and subcutaneous fat. With advanced HIV disease, micronutrient deficiencies may supervene, exacerbating the immune deficiency state, and increasing susceptibility to opportunistic infections. There is therefore a need to determine the following:

- *What are the optimal approaches to the delivery of essential nutritional elements to PLWHAs?*
- *To what extent do nutrition programmes prolong the period of time prior to the need for ARV treatment?*
- *Does nutritional supplementation affect the frequency of occurrence of opportunistic infections?*
- *Does nutritional supplementation augment adaptive and innate immune responses?*

What is the role of traditional and complementary medicines in treatment of AIDS?

Claims have been made, in South Africa and other African countries, that various African traditional medicines are able to restore immune function, with many impressive case reports that attest to improved clinical state, rising CD4+ count, and reduced viral load in people living with AIDS who take these medications. Other ‘immunopotentiators’ that have been investigated in the USA include interleukines, structured treatment interruption, Chinese herbs, lentinin (shitaki mushrooms), and other cytokines in general. Traditional healer therapies might have some immuno-restorative qualities.

Research would focus on:

- safety and toxicity of such traditional medicines
- clinical efficacy in controlled clinical trials – some of which are already underway
- drug-drug interactions with ARVs

Does Advanced HIV Infection and AIDS Impair Absorption of Drugs?

This has not been extensively studied but there are indications that anti-TB medications may be malabsorbed in patients with advanced HIV disease and AIDS. The public health implications of low drug serum levels include the possibility of MDR-TB associated with HIV infection. Similarly, ARVs may also be malabsorbed, predisposing to sub-therapeutic doses, and drug resistance. The research questions posed by this observation include:

- *Determination of the bio-availability of antiretroviral drugs and anti-TB medications among HIV-infected TB patients compared with non-HIV infected TB cases.*
- *Is malabsorption related to the degree of immune deficiency in HIV-infected persons?*
- *What is the effect of intestinal parasites on drug absorption.*

Determinants of and interventions against progression of HIV to AIDS

HIV infection typically leads to severe immune deficiency associated with the loss of CD4 T-lymphocyte populations. Although progression rates in South Africa are not known, studies in other settings indicate that HIV infected individuals will progress to clinical AIDS and death within 7-10 years. In 20% of persons this occurs within 5 years and sustained asymptomatic states without a significant decline in CD4 T cell occur in about 2% of investigated populations. There are no such data in areas of the world hardest hit by this epidemic. The factors that influence these very different disease rates are unclear, but may relate to host genetic factors, different genetic features of the infecting virus strain, and the host immune response. These observations indicate that specific aspects of the human immune system may hold important determinants for disease progression. The key research questions for predominantly treatment-naïve populations include:

- *Determination of the benefits of population-level screen for genetic determinants of progression to assist in applying appropriate interventions at the appropriate times.*
- *Determination of the utility of immune-stimulants and modulators to assist in preservation of a stable host immune system and hence slow the progression to AIDS and delay the time until ARVs are needed.*

- *Determination of the effects of ARV treatment on immune reconstitution*
- *What are the mechanisms by which the small proportion of HIV infected cells are able to induce apoptosis of other uninfected CD4+ cells – a key research question that emerged from the discussions of the International Presidential AIDS Panel in South Africa in the year 2000 - the so called ‘bystander effect’*

Improving HIV care and treatment through adjunctive immune modulation

The use of HAART has been advocated as the most important intervention for HIV and AIDS. However there remain practical and virological limitations of the current regimens. Strategies that simultaneously investigate the potential for a combined virological approach and immune modulation aimed at improving control of viremia need to be explored. The pertinent questions include:

- *Determination of the effect of immune modulation as an adjunct to HAART on survival, improved and sustained protective immune systems as evidenced by slower progression to AIDS and the decline of the incidence of opportunistic infections.*
- *Will adjunctive immune modulation impact on immune recovery or are there critical states of immune destruction which are irreversible?*
- *What proportion of the infected population will be most responsive to immune modulators and are there surrogate predictors?*
- *Can immune modulation potentially replace HAART or reduce dependence on HAART?*

Cancer

Kaposi sarcoma and Non-Hodgkin’s Lymphoma are the main cancers in AIDS with cervical cancer in women with human papilloma virus being the third. This is especially common in South Africa where cervical cancer is the leading cancer in women.

- *Basic incidence/prevalence data, and information on progression is needed*
- *Studies on diagnosis and treatment are needed.*

SPECIAL CONSIDERATIONS

In addition to the highest priority research issues that will be addressed immediately, additional research issues of high merit will be considered for future study. It is expected that funds for these projects will be obtained from sources outside of the current programme. These issues include:

1. What is the role of traditional and complementary medications in the context of HIV care and ARV treatment?
2. What are the gender-specific differences in natural history of HIV disease and response to treatment? (For the former, a natural history cohort of HIV infected, untreated should be established.)
3. What are the metabolic complications of ARV treatment in the South African population?
4. Does micronutrient supplementation improve clinical disease outcomes for PLWHA?
5. What is the cost-effectiveness of ARV treatment in South Africa?
6. What are the optimal models of care for urban and rural health care facilities?
7. To what extent can one identify markers of good outcome of treatment in the early stages of intervention; likewise can one define markers of bad outcome that can allow for early intervention to improve outcome?
8. What is the overall effect of the HIV and AIDS care and treatment programme on access to health care?
9. What is the impact of the HIV and AIDS care and treatment programme on attitudes of health care providers, and on retention of health care workers?
10. Various research questions are identified in other chapters of the Operational Plan, such as the pharmacovigilance, traditional medicines and nutrition chapters.

ADMINISTRATIVE STRUCTURE

The research programme will be coordinated through the Health Information, Evaluation and Research Cluster at the national Department of Health.

Research Oversight

Although it is critical to the success of the programme that oversight of the research agenda remains the preserve of the Department of Health, appropriate mechanisms will be found to ensure an efficient mechanism for managing research. It is equally critical that the operational plan be subjected to ongoing critical evaluation by independent investigators. This will ensure a careful and dispassionate assessment of the HIV and AIDS care and treatment programme.

Review of Applications

A rigorous and transparent peer review process will be used to ensure that all proposals are relevant to the interests of patients and of government; are of the highest scientific quality; are conducted by scientists competent to the task; and have been authorized by the appropriate institutional review boards. Peer review could be facilitated through existing peer review mechanisms such as those of the Medical Research Council (MRC).

Allocation of Support

Recommendations for funding will be made by the Research Advisory Committee and approved by the Department of Health. Funds to support research questions deemed to be highest priority will be provided through government and other supporters.

Dissemination of Research Findings

Appropriate mechanisms will be established to disseminate the results of this research, facilitated by regular reports from funded investigators. Emphasis will be placed on using research findings to improve and strengthen the programme.

Sources of Funding

It is expected that networks similar to the clinical trial consortia will be established for the research programmes described above, and that twinning with external organizations will have immense capacity to leverage direct funding and strengthen research capacity. New funding strategies will also be developed.

Partnerships

The Health Information, Evaluation and Research Cluster at the national Department of Health will create and maintain links with local, regional and international organizations, institutions and collaborating partners. These linkages will facilitate exchange of ideas, especially among health systems with experience in operational research on ARV implementation.

In the field of diagnostics, especially in high TB- and HIV-burden countries, the Bill and Melinda Gates Foundation initiative, the Foundation for Innovative New Diagnostics (FINN), is expected to expand its current efforts into the development of new diagnostics to improve TB diagnosis among HIV-infected persons. It has to be emphasised that there is a need for new affordable diagnostics for HIV and other opportunistic infections that can potentially be adapted for use at programme level in resource-limited settings.

PROGRAMME ASSESSMENT

Formal review of the research agenda as well as of the management structure will be performed on a yearly basis by an independent panel comprised of scientists with expertise in HIV and AIDS. This panel will report to the Minister of Health.

The HIV and AIDS care and treatment plan also represents a unique opportunity to collect data that will inform not only South Africa's programme, but nascent programmes to expand HIV and AIDS care and treatment throughout sub-Saharan Africa and other affected regions of the world.