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PERSPECTIVE

The new epidemic of non-communicable disease in people living with the human immunodeficiency virus

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The global focus on human immunodeficiency virus (HIV) infection in recent years has been on improving access to antiretroviral therapy (ART). World Health Organization (WHO) statistics indicate that in countries such as South Africa, Bangladesh, India and Malaysia, the uptake of ART is increasing rapidly. In South Africa, the country with the highest number of people globally on ART, the South African strategic plan on HIV has adopted a broad 20-year vision that at least 80% of eligible patients will be initiated on ART within this period.[1] In 2007, the WHO estimated that 5.7 million people in South Africa were living with HIV. By the end of that year, only 27% of those eligible to receive ART had been commenced on antiretrovirals. Since then there has been significant scale-up in treatment, and by latest estimates, despite the introduction of a higher ART CD4 entry point of 350 cell/mm^3, some 55% of eligible people are now on ART.[2] This favourable situation in South Africa is not unique; it reflects the increasing coverage in ART in Latin America, the Caribbean and South-East Asia.[2]

The successful scale-up of ART has resulted in new challenges, including sustaining large numbers of people on treatment, ensuring high volume drug supplies and meeting the huge costs of treatment.[3] The initial dire course of HIV disease has been modified, and millions of people in low- and middle-income countries are now able to live longer. However, living longer with HIV infection exposes patients to a new set of health issues. Opportunistic infections decrease on ART, but the potential for diseases of ageing, lifestyle-related disease and other non-communicable diseases (NCDs) increases.

There is currently a global move to identify and target NCDs, which include cancers, chronic respiratory disease, heart disease, stroke and diabetes.[4] This new approach was discussed at the recent United Nations high-level meeting on NCDs.[5] It is evident that the majority of deaths related to these diseases occur in low- and middle-income countries. A recent positive step was the undertaking at the 65th World Health Assembly to target a 25% reduction in mortality due to NCDs by 2025 in all 194 member states.[6] Interventions to help reach these targets include lifestyle modification, dietary interventions, smoking cessation and tobacco control. Considerable effort to achieve this goal will be required, from health policy makers and global advisory bodies to delivery at clinic level through non-governmental stakeholders and national policy roll-outs.

WHAT IS THE EXTENT OF THE PROBLEM OF NCDs IN HIV?

Infectious diseases associated with HIV have been a major focus in the era of ART. However, people living with HIV are also at increased risk of developing NCDs. A number of emergent organ-specific NCDs found in people with HIV are shown in the Table. These diseases are not trivial, and they may affect multiple organ systems, with debilitating and potentially fatal outcomes. Unfortunately, the true impact of these diseases on long-term mortality and morbidity, particularly in low- and middle-income countries, is not known. Available data on NCDs on patients on ART are almost exclusively from established HIV cohort data in high-income countries. For example, data on the natural history of chronic respiratory diseases,[15] lung cancer[16] and chronic obstructive pulmonary disease (COPD)[17] are from cohort studies performed in France[16] and the USA.[15,17] These data may not be applicable in countries with a high incidence of tuberculosis (TB), where the true extent of TB-associated obstructive lung disease is not known. This, coupled with increasing rates of smoking in low-income countries, suggests that the risk of developing COPD may be higher in people with HIV infection.

The lack of robust epidemiological cohort data is not limited to respiratory disease. With regard to coronary heart disease, North American men with HIV have up to double the risk[18] of developing coronary artery disease compared to their HIV-negative counterparts.[19] In African men, in whom hypertension is a well-established and common problem, the incidence of coronary artery disease is increasing rapidly with Westernisation,[20] but the true impact of this emergent disease is unknown. The effect of large-scale roll-outs of protease inhibitor (PI) based ART regimens on endothelial function and dyslipidaemia may create an additional risk factor for developing coronary disease. The use of ART and the increased risk of development of diabetes mellitis has been documented in the Multicentre AIDS Cohort Study,[14] where a four-fold increase in incidence over HIV-seronegative subjects was described. The true future impact of this emergent disease in low- and middle-income countries is not known.

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TABLE Non-infectious disease manifestations of HIV

Organ system	Disease
Respiratory[7]	Allergic rhinitis Chronic obstructive pulmonary disease Pulmonary arterial hypertension Sarcoidosis Interstitial lung disease[8] Lung cancer
Cardiac[9]	Coronary artery disease Dyslipidaemia Dilated cardiomyopathy
Endocrine[10]	Insulin resistance[11] Metabolic syndrome Thyroid disease Hypogonadism Addison's disease
Gastrointestinal[12]	HIV cholangiopathy Pancreatitis
Neurological[13]	Antiretroviral toxic neuropathy HIV dementia Minor cognitive motor disorder
Musculoskeletal[14]	Joint malignancy Osteonecrosis Hypertrophic osteoarthropathy Myositis
Opthalmological	Uveitis Retinal microvasculopathy

HIV = human immunodeficiency virus.

WHAT STEPS SHOULD WE TAKE TO IDENTIFY AND MANAGE EMERGENT NCDs?

The success story over the last 30 years has been the mobilisation of the scientific community and public health policy makers in developing new treatments and improving access to care for people with HIV. Many developing countries now have established HIV treatment programmes and developing infrastructure. There is still much work to be done, including reducing HIV infection rates, improving access to treatment and dealing with viral resistance. This key focus should continue, and there is no time for complacency. HIV health advocacy, however, now needs to be realigned to identifying emergent NCDs and lifestyle-related diseases in patients established on ART.

First, there is a lack of data on the longer-term consequences of HIV infection and its treatment. To date the majority of cohort data is from the industrialised world, and while these cohorts continue to add value to future care, robust prospective longitudinal clinical cohorts need to be established in low-income countries, where the burden of NCDs resides and where other risk factors for chronic diseases exist. A recent example is the 'Lung HIV' cohort funded by the National Institutes of Health.[15] This multicentre initiative, with both US and African sites, will provide information on the additive effect of cigarette smoking and TB on lung function decline in HIV.[21] Funding bodies should consider supporting scientific surveillance cohorts to include HIV-related NCDs, where monitoring lifestyle-related diseases will have the greatest downstream effects, and which will help to answer many of these unanswered questions expediently. National policy makers should be encouraged to implement monitoring tools for identifying, managing and recording the next wave of emergent lifestyle-related diseases and NCDs in patients with HIV.

Second, integrated preventive strategies employed in the care of patients with HIV, including lifestyle interventions such as smoking cessation, modifying dietary behaviour and primary prevention for coronary artery disease, need to be developed and will pay dividends. Such programmes should not be permitted to be overwhelmed by the need for treatment of infectious diseases such as TB. The roll-out of ART offers a framework for both scientific data collection and implementation of education for NCDs. We believe that health systems policies for NCDs should be complementary to existing ART programmes, as patients with HIV may be at higher risk of morbidity. The expansion of chronic care programmes for HIV now offers an established base to leverage integrated care for NCDs in patients with HIV.[22] For minimal additional input, with the lessons of HIV programme planning, the experience of effective management tools and tried monitoring systems, these can be called upon to incorporate additional care for NCDs in HIV.

Research plays an essential role in identifying this new generation of HIV-related NCDs. To improve the interface between this research and delivery, a clear research plan must be established. The operational domain of the research within local health programme structures should be clearly identified. A plan for implementation of research findings through programme managers or development managers will ensure a broader uptake of significant findings. Where appropriate, a planned health systems approach involving managers and policy makers to operationalise findings should be included as part of research planning.[23]

CONCLUSION

Many significant gains have been made in recent years in the fight against HIV. New issues, including treating viral resistance, managing long-term compliance and combating HIV-related infectious disease will require added focus in the immediate future. Preventing unrecognised NCDs from becoming the main future agenda in HIV is a priority that needs to be addressed in the present. The current global discussion on integrated care for chronic disease is even more relevant in people living with HIV.

Chronic HIV care programmes need to move beyond drug delivery and direct disease management to include NCD interventions. Such strategies include lifestyle education, primary prevention for cardiac disease, obesity management and smoking cessation, amongst others. National HIV programme managers should build on their HIV experience, and implement systems and evaluation strategies, including HIV-related NCDs, in their existing and developing programme structures. Researchers and funding bodies should be encouraged to partner and implement quality research studies on emergent NCDs in those settings where disease occurs.

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